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Part 1: Executive summary 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆,☆☆

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Toward international consensus on science

The International Liaison Committee on Resuscitation (ILCOR) was formed in 1993 and currently includes representatives from the American Heart Association (AHA), the European Resuscitation Council, the Heart and Stroke Foundation of Canada, the Australian and New Zealand Committee on Resuscitation, the Resuscitation Council of Southern Africa, the InterAmerican Heart Foundation, and the Resuscitation Council of Asia. The ILCOR mission is to identify and review international science and information relevant to cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) and to offer consensus on treatment recommendations. ECC includes all responses necessary to treat sudden life-threatening events affecting the cardiovascular and respiratory systems, with a particular focus on sudden cardiac arrest. For this 2015 consensus publication, ILCOR also included first aid topics in its international review and consensus recommendations.

In 1999, the AHA hosted the first ILCOR conference to evaluate resuscitation science and develop common resuscitation guidelines. The conference recommendations were published in the *Guidelines 2000 for CPR and ECC*.[1] Since 2000, researchers from the ILCOR member councils have evaluated and reported their International Consensus on CPR and ECC Science With Treatment Recommendations (CoSTR) in 5-year cycles. The conclusions and recommendations of the 2010 CoSTR were published at the end of 2010.[2,3] Since that time, ILCOR meetings and webinars have continued to identify and evaluate resuscitation science. The most recent ILCOR 2015 International Consensus Conference on CPR and ECC Science With Treatment Recommendations was held in Dallas in February 2015, and this publication contains the consensus science statements and treatment recommendations developed with input

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from the ILCOR task forces, the invited participants, and public comment.

The Parts of this CoSTR publication include a summary of the ILCOR processes of evidence evaluation and management of potential or perceived conflicts of interest, and then reports of the consensus of the task forces on adult basic life support (BLS; including CPR quality and use of an automated external defibrillator [AED]); advanced life support (ALS; including post-cardiac arrest care); acute coronary syndromes (ACS); pediatric BLS and ALS; neonatal resuscitation; education, implementation, and teams (EIT); and first aid.

The 2015 CoSTR publication is not a comprehensive review of every aspect of resuscitation medicine; not all topics reviewed in 2010 were rereviewed in 2015. This Executive Summary highlights the evidence evaluation and treatment recommendations of this 2015 evidence evaluation process. Not all relevant references are cited here, because the detailed systematic reviews are included in the individual Parts of the 2015 CoSTR publication.

A list of all topics reviewed can be found in Appendix A.

Evidence evaluation process

The 2015 evidence evaluation process started in 2012 when ILCOR representatives formed 7 task forces: BLS, ALS, ACS, pediatric BLS and ALS, neonatal resuscitation, EIT, and, for the first time, first aid. Each task force performed detailed systematic reviews based on the recommendations of the Institute of Medicine of the National Academies,[4] and the criteria of a measurement tool to assess systematic reviews (AMSTAR).[5] The task forces used the methodologic approach for evidence evaluation and development of recommendations proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[6] Each task force identified and prioritized the questions to be addressed (using the PICO [population, intervention, comparator, outcome] format)[7] and identified and prioritized the outcomes to be reported. Then, with the assistance of information scientists, a detailed search for relevant articles was performed in each of 3 online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk of bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[8] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[9] and GRADE for observational studies that inform both therapy and prognosis questions.[10]

Using the online GRADE Guideline Development Tool, the evidence reviewers created evidence profile tables[11] to facilitate evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[12] based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and publication bias (and occasionally other considerations).[6]

These evidence profile tables were then used to create a written summary of evidence for each outcome (the Consensus on Science statements). These statements were drafted by the evidence reviewers and then discussed and debated by the task forces until consensus was reached. Whenever possible, consensus-based treatment recommendations were created. These recommendations (designated as strong or weak and either for or against a therapy or diagnostic test) were accompanied by an overall assessment of the evidence, and a statement from the task force about the values and preferences that underlie the recommendations. Further details of the methodology of the evidence evaluation process are found in "Part 2: Evidence Evaluation and Management of Conflicts of Interest."

This summary uses wording consistent with the wording recommended by GRADE and used throughout this publication. Weak recommendations use the word *suggest*, as in, "We suggest. . .." Strong recommendations are indicated by the use of the word *recommend*, as in, "We recommend. . .."

In the years 2012–2015, 250 evidence reviewers from 39 countries completed 169 systematic reviews addressing resuscitation or first aid questions. The ILCOR 2015 Consensus Conference was attended by 232 participants representing 39 countries; 64% of the attendees came from outside the United States. This participation ensured that this final publication represents a truly international consensus process.

Many of the systematic reviews included in this 2015 CoSTR publication were presented and discussed at monthly or semimonthly task force webinars as well as at the ILCOR 2015 Consensus Conference. Public comment was sought at 2 stages in the process. Initial feedback was sought about the specific wording of the PICO questions and the initial search strategies, and subsequent feedback was sought after creation of the initial draft consensus on science statements and treatment recommendations.[13] A total of 492 comments were received. At each of these points in the process, the public comments were made available to the evidence reviewers and task forces for their consideration.

With the support of science and technology specialists at the AHA, a Web-based information system was built to support the creation of scientific statements and recommendations. An online platform known as the Scientific Evaluation and Evidence Review System (SEERS) was developed to guide the task forces and their individual evidence reviewers. The SEERS system was also used to capture public comments and suggestions.

To provide the widest possible dissemination of the science reviews performed for the 2015 consensus, as noted above, the list of completed systematic reviews is included in Appendix A. In addition, in each Part of the 2015 CoSTR document, each summary of the consensus on science and the treatment recommendations contains a live link to the relevant systematic review on the SEERS site. This link is identified by 3 or 4 letters followed by 3 numbers. These systematic reviews will be updated as additional science is published.

This publication was ultimately approved by all ILCOR member organizations and by an international editorial board (listed on the title page of this supplement). The AHA Science Advisory and Coordinating Committee and the Editor-in-Chief of *Circulation* obtained peer reviews of each Part of this supplement before it was accepted for publication. The supplement is being published online simultaneously by *Circulation* and *Resuscitation*.

Management of potential conflicts of interest

A rigorous conflict of interest (COI) management policy was followed at all times and is described in more detail in "Part 2: Evidence Evaluation and Management of Conflicts of Interest" of this 2015 CoSTR. A full description of these policies and their implementation can be found in "Part 4: Conflict of Interest Management Before, During, and After the 2010 International Consensus Conference on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations" in the 2010 CoSTR.[14] As in 2010, anyone involved in any part of the 2015 process disclosed all commercial relationships and other potential conflicts; in total, the AHA processed more than 1000 COI declarations. These disclosures were taken into account in assignment of task force co-chairs and members, writing group co-chairs, and other leadership roles. In keeping with the

AHA COI policy, a majority of the members of each task force writing group had to be free of relevant conflicts. Relationships were also screened for conflicts in assigning evidence reviewers for each systematic review.

As in 2010, dual-screen projection was used for all sessions of the ILCOR 2015 Consensus Conference. One screen displayed the presenter's COI disclosures continuously throughout his or her presentation. Whenever participants or task force members spoke, their relationships were displayed on one screen, so all participants could see potential conflicts in real time, even while slides were projected on the second screen. During all other ILCOR meetings and during all conference calls and webinars, relevant conflicts were declared at the beginning of each meeting and preceded any comments made by participants with relevant conflicts.

Applying science to improve survival

From consensus on science to guidelines

This publication presents international consensus statements that summarize the science of resuscitation and first aid and, wherever possible, treatment recommendations. ILCOR member organizations will subsequently publish resuscitation guidelines that are consistent with the science in this consensus publication, but they will also take into account geographic, economic, and system differences in practice and the availability of medical devices and drugs and the ease or difficulty of training. All ILCOR member organizations are committed to minimizing international differences in resuscitation practice and to optimizing the effectiveness of resuscitation practice, instructional methods, teaching aids, and training networks.

The recommendations of the ILCOR 2015 Consensus Conference confirm the safety and effectiveness of various current approaches, acknowledge other approaches as ineffective, and introduce new treatments resulting from evidence-based evaluation. *New and revised treatment recommendations do not imply that clinical care that involves the use of previously published guidelines is either unsafe or ineffective.* Implications for education and retention were also considered when developing the final treatment recommendations.

Ischemic heart disease is the leading cause of death in the world,[15] and in the United States cardiovascular disease is responsible for 1 in 3 deaths, approximately 786 641 deaths every year.[16] Annually in the United States, there are approximately 326 200 out-of-hospital cardiac arrests (OHCAs) assessed by emergency medical services (EMS) providers, and there are an additional estimated 209 000 treated in-hospital cardiac arrests (IHCAs).[16] There are no significant differences between Europe, North America, Asia, and Australia in the incidence of OHCA. The incidence of patients with OHCA considered for resuscitation is lower in Asia (55 per year per 100 000 population) than in Europe (86), North America (103), and Australia (113).[17] The incidence of patients in OHCA with presumed cardiac cause in whom resuscitation was attempted is higher in North America (58 per 100 000 population) than in the other 3 continents (35 in Europe, 32 in Asia, and 44 in Australia).[17] However, most victims die out of hospital without receiving the interventions described in this publication.

The actions linking the adult victim of sudden cardiac arrest with survival are characterized as the adult Chain of Survival. The links in this Chain of Survival are early recognition of the emergency and activation of the EMS system, early CPR, early defibrillation, early ALS, and skilled post–cardiac arrest/postresuscitation care. The links in the infant and child Chain of Survival are prevention of conditions leading to cardiopulmonary arrest, early CPR, early activation of the EMS system, early ALS, and skilled post–cardiac arrest/postresuscitation care.

Newest developments in resuscitation: 2010–2015

There is good evidence that survival rates after OHCA are improving.[18–22] This is particularly true for those cases of witnessed arrest when the first monitored rhythm is shockable (i.e., associated with ventricular fibrillation [VF] or pulseless ventricular tachycardia [pVT]), but increases in survival from nonshockable rhythms are also well documented.[23] These improvements in survival have been associated with the increased emphasis on CPR quality as well as improved consistency in the quality of post-cardiac arrest/post resuscitation care.

Each task force identified important developments in resuscitation science since the publication of the 2010 CoSTR. These developments are noted in brief below. After the brief list of developments, summaries of the evidence reviews are organized by task force.

Adult basic life support

The following is a summary of the most important evidence-based recommendations for performance of adult BLS:

- The EMS dispatcher plays a critical role in identifying cardiac arrest, providing CPR instructions to the caller, and activating the emergency response.[24–28]
- The duration of submersion is a key prognostic factor when predicting outcome from drowning.[29–40]
- The fundamental performance metrics of high-quality CPR remain the same, with an emphasis on compressions of adequate rate and depth, allowing full chest recoil after each compression, minimizing pauses in compressions, and avoiding excessive ventilation. Some additional registry data suggest an optimal range for compression rate and depth.[41,42]
- Public access defibrillation programs providing early defibrillation have the potential to save many lives if the programs are carefully planned and coordinated.[43–55]

Advanced life support

The most important developments in ALS included the publication of additional studies of the effects of mechanical CPR devices, drug therapy, and insertion of advanced airway devices on survival from cardiac arrest. In addition, the task force evaluated several studies regarding post-cardiac arrest care and the use of targeted temperature management (TTM).

- The evidence in support of mechanical CPR devices was again reviewed. Three large trials of mechanical chest compression devices[56–58] enrolling 7582 patients showed outcomes are similar to those resulting from manual chest compressions. While these devices should not routinely replace manual chest compressions, they may have a role in circumstances where high-quality manual compressions are not feasible.
- The Executive Summary for the 2010 CoSTR[2,3] noted the insufficient evidence that drug administration improved survival from cardiac arrest. The 2015 systematic review identified large observational studies that challenged the routine use of advanced airways[59–65] and the use of epinephrine[66–68] as part of ALS. Because of the inherent risk of bias in observational studies, these data did not prompt a recommendation to change practice but do provide sufficient equipoise for large RCTs to test whether advanced airways and epinephrine are helpful during CPR.
- Post-cardiac arrest care is probably the area of resuscitation that has undergone the greatest evolution since 2010, with substantial potential to improve survival from cardiac arrest. Recent improvements include further delineation of the effects, timing, and components of TTM, and awareness of the need to control

oxygenation and ventilation and optimize cardiovascular function.
- The effect and timing of TTM continues to be defined by many studies published after 2010. One high-quality trial could not demonstrate an advantage to a temperature goal of either 33 °C or 36 °C for TTM,[69] and 5 trials could not identify any benefit from prehospital initiation of hypothermia with the use of cold intravenous fluids.[70–74] The excellent outcomes for all patients in these trials reinforced the opinion that post-cardiac arrest patients should be treated with a care plan that includes TTM, but there is uncertainty about the optimal target temperature, how it is achieved, and for how long temperature should be controlled.

Acute coronary syndromes

The following are the most important evidenced-based recommendations for diagnosis and treatment of ACS since the 2010 ILCOR review:

- Prehospital ST-segment elevation myocardial infarction (STEMI) activation of the catheterization laboratory reduces treatment delays and also improves patient mortality.
- Adenosine diphosphate receptor antagonists and unfractionated heparin (UFH) can be given either prehospital or in-hospital for suspected STEMI patients with a planned primary percutaneous coronary intervention (PCI) approach.
- Prehospital enoxaparin may be used as an alternative to prehospital UFH as an adjunct for primary PCI for STEMI. There is insufficient evidence to recommend prehospital bivalirudin as an alternative.
- The use of troponins at 0 and 2 h as a stand-alone measure for excluding the diagnosis of ACS is strongly discouraged.
- We recommend against using troponins alone to exclude the diagnosis of ACS. We suggest that negative high-sensitivity troponin I (hs-cTnI) measured at 0 and 2 hours may be used together with low-risk stratification or negative cardiac troponin I (cTnI) or cardiac troponin T (cTnT) measured at 0 and 3 to 6 hours with very-low risk stratification to identify those patients who have a less than 1% 30-day risk of a major adverse high-sensitivity cardiac troponin I (hs-cTnI) cardiac event (MACE).
- We suggest withholding oxygen in normoxic patients with ACS.
- Primary PCI is generally preferred to fibrinolysis for STEMI reperfusion, but that decision should be individualized based on time from symptom onset (early presenters), anticipated time (delay) to PCI, relative contraindications to fibrinolysis, and other patient factors.
- For adult patients presenting with STEMI in the emergency department (ED) of a non-PCI-capable hospital, either transport expeditiously for primary PCI (without fibrinolysis) or administer fibrinolysis and transport early for routine angiography in the first 3 to 6 h (or up to 24 h).
- For select adult patients with return of spontaneous circulation (ROSC) after OHCA of suspected cardiac origin with ST-elevation on electrocardiogram (ECG), we recommend emergency cardiac catheterization laboratory evaluation (in comparison with delayed or no catheterization). In select comatose adult patients with ROSC after OHCA of suspected cardiac origin but without ST-elevation on ECG, we suggest emergency cardiac catheterization evaluation.

Pediatric basic and advanced life support

The most important new developments in pediatric resuscitation since 2010 include the publication of the results of a study of TTM in children following ROSC after OHCA. Additional new developments include refinement of long-standing recommendations regarding fluid therapy and antiarrhythmics. These new developments are summarized here:

- When caring for children remaining unconscious after OHCA, outcomes are improved when fever is prevented, and a period of moderate therapeutic hypothermia or strict maintenance of normothermia is provided.[75]
- The use of restricted volumes of isotonic crystalloid may lead to improved outcomes from pediatric septic shock in specific settings. When caring for children with febrile illnesses (especially in the absence of signs of overt septic shock), a cautious approach to fluid therapy should be used, punctuated with frequent patient reassessment.[76]
- The use of lidocaine or amiodarone for treatment of shock-resistant pediatric VF/pVT improves short-term outcomes, but there remains a paucity of information about their effects on long-term outcomes.[77]

Neonatal resuscitation

The Neonatal Task Force identified new information about the association between admission temperature in newly born infants and morbidity and mortality, evaluated new evidence regarding the role of routine intubation of nonvigorous infants born through meconium-stained amniotic fluid, and new evaluated evidence regarding the use of the ECG to assess heart rate. The systematic reviews of these topics will result in new recommendations.

- The admission temperature of newly born nonasphyxiated infants is a strong predictor of mortality and morbidity at all gestations. For this reason, it should be recorded as a predictor of outcomes as well as a quality indicator.[78–82]
- There is insufficient published human evidence to suggest routine tracheal intubation for suctioning of meconium in nonvigorous infants born through meconium-stained amniotic fluid as opposed to no tracheal intubation for suctioning.[83]
- It is suggested in babies requiring resuscitation that the ECG can be used to provide a rapid and accurate estimation of heart rate.[84–86]

Education, Implementation, and Teams

The most noteworthy reviews or changes in recommendations for EIT since the last ILCOR review in 2010 pertain to training and the importance of systems of care focused on continuous quality improvement.

Training

It is now recognized that training should be more frequent and less time consuming (high frequency, low dose) to prevent skill degradation; however, the evidence for this is weak.

- High-fidelity manikins may be preferred to standard manikins at training centers/organizations that have the infrastructure, trained personnel, and resources to maintain the program.
- The importance of performance measurement and feedback in cardiac arrest response systems (in-hospital and out-of-hospital) is well recognized but remains supported by data of low quality. CPR feedback devices (providing directive feedback) are useful to learn psychomotor CPR skills.
- Retraining cycles of 1 to 2 years are not adequate to maintain competence in resuscitation skills. The optimal retraining intervals are yet to be defined, but more frequent training may be helpful for providers likely to encounter a cardiac arrest.

Systems

- You can't improve what you don't measure, so systems that facilitate performance measurement and quality improvement initiatives are to be used where possible.
- Data-driven, performance-focused debriefing can help improve performance of resuscitation teams.
- There is increasing evidence (albeit of low quality) that treatment of post-cardiac arrest patients in regionalized cardiac arrest centers is associated with increased survival.[87,88] OHCA victims should be considered for transport to a specialist cardiac arrest center as part of a wider regional system of care.
- Advances in the use of technology and social media for notification of the occurrence of suspected OHCA and sourcing of bystanders willing to provide CPR. The role of technology/social media in the bystander CPR response for OHCA is evolving rapidly.

First aid

The First Aid Task Force reviewed evidence on the medical topics of stroke assessment, treatment of hypoglycemia in patients with diabetes, and on the injury topics of first aid treatment of open chest wounds and severe bleeding and on identification of concussion.

- The single most important new treatment recommendation of the 2015 International Consensus on First Aid Science With Treatment Recommendations is the recommendation in favor of the use of stroke assessment systems by first aid providers to improve early identification of possible stroke and enable subsequent referral for definitive treatment. The FAST (Face, Arm, Speech, Time)[89,90] tool and the Cincinnati Prehospital Stroke Scale[91] are recommended, with the important caveat that recognition specificity can be improved by including blood glucose measurement.
- First aid providers are often faced with the signs and symptoms of hypoglycemia. Failure to treat this effectively can lead to serious consequences such as loss of consciousness and seizures. The 2015 CoSTR recommends the administration of glucose tablets for conscious individuals who can swallow. If glucose tablets are not immediately available, then recommendations for various substitute forms of dietary sugars have been made.[92–94]
- The recommendation for the management of open chest wounds by not using an occlusive dressing or device, or any dressing or device that may become occlusive, emphasizes the inherent serious life-threatening risk of creating a tension pneumothorax.[95]
- Recommendations for the management of severe bleeding include the use of direct pressure, hemostatic dressings,[96–99] and tourniquets.[100–106] However, formal training in the use of hemostatic dressings and tourniquets will be required to ensure their effective application and use.
- The 2015 First Aid Task Force recommends the development of a simple validated concussion scoring system for use by first aid providers in the accurate identification and management of concussion (minor traumatic brain injury), a condition commonly encountered by first aid providers in the prehospital environment.

Summary of the 2015 ILCOR consensus on science with treatment recommendations

The following sections contain summaries of the key systematic reviews of the 2015 CoSTR. These summaries are organized by task force. Note that there are few references cited in the summaries; we refer the reader to the detailed information prepared by each task force in other Parts of the 2015 CoSTR.

Adult basic life support

The ILCOR 2015 Consensus Conference addressed intervention, diagnostic, and prognostic questions related to the performance of BLS. The body of knowledge encompassed in this Part comprises 23 systematic reviews, with 32 treatment recommendations, derived from a GRADE evaluation of 27 randomized clinical trials and 181 observational studies of variable design and quality conducted over a 35-year period. These have been grouped into (1) early access and cardiac arrest prevention, (2) early high-quality CPR, and (3) early defibrillation.

Early access and cardiac arrest prevention

Early access for the victim of OHCA begins when a bystander contacts the EMS dispatcher, who then coordinates the emergency response to that cardiac arrest. The dispatcher's role in identifying possible cardiac arrest, dispatching responders, and providing instructions to facilitate bystander performance of chest compressions has been demonstrated in multiple countries with consistent improvement in cardiac arrest survival. Dispatchers should be educated to identify unconsciousness with abnormal breathing. This education should include recognition of, and significance of, agonal breaths across a range of clinical presentations and descriptions. If the victim is unconscious with abnormal or absent breathing, it is reasonable to assume that the patient is in cardiac arrest at the time of the call. On the basis of these assessments, dispatchers should provide instructions to callers for compression-only CPR for adults with suspected OHCA.

Two systematic reviews involved cardiac arrest prevention: one addressed deployment of search-and-rescue operations for drowning, and the other addressed education regarding opioid-associated life-threatening emergencies. In reviewing the evidence to support the rational and judicious deployment of search-and-rescue operations for drowning victims, evidence demonstrates that submersion duration can be used to predict outcome. In contrast, age, EMS response interval, water type (fresh/salt), water temperature, and witness status should not be used when making prognostic decisions. The systematic reviews in 2015 also demonstrated that rescuers should consider opioid overdose response education with or without naloxone distribution to persons at risk for opioid overdose in any setting.

Early high-quality cardiopulmonary resuscitation

Similar to the 2010 ILCOR BLS treatment recommendations, the importance of high-quality CPR was re-emphasized, with a goal of optimizing all measures of CPR quality, which include adequate compression rate and depth, allowing full chest recoil after each compression, minimizing interruptions in chest compressions, and avoiding excessive ventilation. The systematic reviews clearly showed that all rescuers should be providing chest compressions to all victims of cardiac arrest. Those with additional training, who are able and willing, should also give rescue breaths. Laypersons should initiate CPR for presumed cardiac arrest without concern of harm to patients not in cardiac arrest.

With respect to skills, laypersons and healthcare providers should compress the chest on the lower half of the sternum at a rate of at least 100 compressions per minute (not to exceed 120 compressions per minute) with a compression depth of approximately 2 inches (5 cm) while avoiding excessive chest compression depths of greater than 2.4 inches (6 cm) in an average-sized adult. All rescuers need to avoid leaning on the chest between compressions to allow full chest-wall recoil.

Rescuers must attempt to minimize the frequency and duration of interruptions in compressions to maximize the number of compressions actually delivered per minute. For adult patients receiving CPR with no advanced airway, the interruption of chest

compressions for delivery of 2 breaths should be less than 10 s, and the chest compression fraction (i.e., total CPR time devoted to compressions) should be as high as possible, and at least 60%. Results from systematic reviews propose the use of real-time audiovisual feedback and prompt devices during CPR in clinical practice as part of a comprehensive system of care for patients in cardiac arrest.

With respect to sequencing, a compression-ventilation ratio of 30:2 is recommended, commencing CPR with compressions rather than ventilations, and pausing chest compressions every 2 min to assess the cardiac rhythm.

Other highlights in 2015 included evidence from EMS systems that use bundles of care focusing on providing high-quality, minimally interrupted chest compressions while transporting the patient from the scene of cardiac arrest to the hospital system of care. Where similar EMS systems* have adopted bundles of care involving minimally interrupted cardiac resuscitation,† the bundle of care is a reasonable alternative to conventional CPR for witnessed shockable OHCA.

The task force noted a large ongoing trial of continuous chest compressions by EMS staff compared with conventional (30 compressions to 2 breaths) CPR (https://clinicaltrials.gov/ct2/show/NCT01372748). Until the results of this study are available, based on the available evidence, it is reasonable for EMS systems that have already introduced bundles of care including minimally interrupted chest compressions to continue to use them for adult patients with a witnessed cardiac arrest and an initial shockable rhythm.

Early defibrillation

Rapid defibrillation with CPR is the treatment of choice for VF/pVT in the out-of-hospital and in-hospital settings. The 2015 CoSTR highlights the evidence surrounding the clinical benefit of the use of automatic external defibrillators in the out-of-hospital setting by laypeople and healthcare providers alike.

At the system level, one of the major 2015 highlights is the affirmation of the global importance of the implementation of public access defibrillation programs for patients with OHCAs.

At the rescuer level for an unmonitored cardiac arrest, the 2015 CoSTR advises a short period of CPR followed by rhythm analysis and shock delivery, if indicated, as soon as the defibrillator is ready for use. With respect to the timing of rhythm check, rescuers must resume chest compressions after shock delivery for adults in cardiac arrest in any setting. CPR should be continued for 2 min before reassessing for signs of life.

Advanced life support

The topics reviewed by the ILCOR ALS Task Force are grouped as follows: (1) defibrillation strategies for VF or pVT; (2) airway, oxygenation, and ventilation; (3) circulatory support during CPR; (4) physiologic monitoring during CPR; (5) drugs during CPR; (6) cardiac arrest in special circumstances; and (7) post resuscitation care.

The systematic reviews showed that the quality of evidence for many ALS interventions is low or very low, and this led to predominantly weak recommendations. For some issues, despite a low quality of evidence, the values and preferences of the task force led to a strong recommendation for an intervention. This was especially true when there was consensus that not undertaking the intervention could lead to harm. Treatment recommendations were left unchanged unless there were compelling reasons for a change. The rationale for any change is addressed in the values, preferences, and insights that follow treatment recommendations. The most important developments and recommendations in ALS since the 2010 ILCOR review are described below.

Defibrillation strategies for VF or pulseless VT

There were no major developments since 2010. We suggest that if the first shock is not successful and the defibrillator is capable of delivering shocks of higher energy, it is reasonable to increase the energy for subsequent shocks.

Airway, oxygenation, and ventilation

We suggest using the highest possible inspired oxygen concentration during CPR. The evidence showed equipoise between the choice of an advanced airway or a bag-mask device for airway management during CPR, and the choice between a supraglottic airway or tracheal tube as the initial advanced airway during CPR. The role of waveform capnography during ALS is emphasized, including to confirm and to continuously monitor the position of a tracheal tube during CPR.

Circulatory support during CPR

We recommend against the routine use of the impedance threshold device in addition to conventional CPR but could not achieve consensus for or against the use of the impedance threshold device when used together with active compression-decompression CPR. We suggest against the routine use of automated mechanical chest compression devices but suggest that they are a reasonable alternative to use in situations where sustained high-quality manual chest compressions are impractical or compromise provider safety. We suggest that extracorporeal CPR is a reasonable rescue therapy for selected patients with cardiac arrest when initial conventional CPR is failing in settings where this can be implemented.

Physiologic monitoring during CPR

Using physiologic measurement in addition to clinical signs and ECG monitoring has the potential to help guide interventions during ALS. We have not made a recommendation for any particular physiologic measure to guide CPR, because the available evidence would make any estimate of effect speculative. We recommend against using end-tidal carbon dioxide ($ETCO_2$) threshold or cutoff values alone to predict mortality or to decide to stop a resuscitation attempt. We suggest that if cardiac ultrasound can be performed without interfering with the standard advanced cardiovascular life support protocol, it may be considered as an additional diagnostic tool to identify potentially reversible causes of cardiac arrest.

Drug therapy during CPR

We suggest that standard-dose (defined as 1 mg) epinephrine be administered to patients in cardiac arrest after considering the observed benefit in short-term outcomes (ROSC and admission to hospital) and our uncertainty about the benefit or harm on survival to discharge and neurologic outcome. We suggest the use of amiodarone in adult patients with refractory VF/pVT to improve rates of ROSC. These statements are not intended to change current practice until there are high-quality data on long-term outcomes.

Cardiac arrest in special circumstances

The systematic review found a very low quality of evidence for specific interventions for ALS in pregnant women. We suggest delivery of the fetus by perimortem cesarean delivery for women in cardiac arrest in the second half of pregnancy. As a result of the lack of comparative studies, the task force is unable to make any evidence-based treatment recommendation about the use of intravenous lipid emulsion to treat toxin-induced cardiac arrest. We recommend the use of naloxone by intravenous, intramuscular, subcutaneous, intraosseous, or intranasal routes in respiratory arrest associated with opioid toxicity, but make no recommendation on modifying standard ALS in opioid-induced cardiac arrest.

Post-cardiac arrest care

We recommend avoiding hypoxia and also suggest avoiding hyperoxia in adults with ROSC after cardiac arrest. We suggest

the use of 100% inspired oxygen until the arterial oxygen saturation or the partial pressure of arterial oxygen can be measured reliably in adults with ROSC after cardiac arrest. We suggest maintaining the $Paco_2$ within a normal physiologic range as part of a post-ROSC bundle of care. We suggest that hemodynamic goals (e.g., mean arterial pressure, systolic blood pressure) be considered during postresuscitation care and as part of any bundle of postresuscitation interventions.

We recommend selecting and maintaining a constant target temperature between 32 °C and 36 °C for those patients in whom temperature control is used. In adults who remain unresponsive after OHCA, we recommend TTM for those with an initial shockable rhythm and suggest TTM for those with an initial nonshockable rhythm. We suggest TTM for adults with IHCA with any initial rhythm who remain unresponsive after ROSC. If TTM is used, we suggest a duration of at least 24 h. We recommend against routine use of prehospital cooling with rapid infusion of large volumes of cold intravenous fluid immediately after ROSC.

We suggest prevention and treatment of fever in persistently comatose adults after completion of TTM between 32 °C and 36 °C.

We recommend the treatment of seizures in post-cardiac arrest patients but suggest that routine seizure prophylaxis is not used in these patients. We suggest no modification of standard glucose management protocols for adults with ROSC after cardiac arrest.

In comatose post-cardiac arrest patients treated with TTM, we suggest that clinical criteria alone are not used to estimate prognosis after ROSC. We suggest prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, to minimize results that inaccurately suggest a poor outcome. We recommend that the earliest time to prognosticate a poor neurologic outcome is 72 h after ROSC, and the interval should be extended longer if the residual effect of sedation and/or paralysis confounds the clinical examination. We suggest that multiple modalities of testing (clinical examination, neurophysiologic measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings.

We recommend that all patients who have restoration of circulation after CPR and who subsequently progress to death be evaluated as potential organ donors.

Acute coronary syndromes

The ACS Task Force reviewed the evidence related specifically to the diagnosis and treatment of ACS in the out-of-hospital setting and during the first hours of care in -hospital, typically in the ED. The topics reviewed by the ACS Task Force are grouped as follows: (1) diagnostic interventions in ACS, (2) therapeutic interventions in ACS, (3) reperfusion decisions in STEMI, and (4) hospital reperfusion decisions after ROSC. The most important developments and recommendations in ACS since the 2010 ILCOR review are described below.

Diagnostic interventions in ACS

Prehospital ECG acquisition may not only facilitate earlier diagnosis of STEMI and provide the opportunity for rapid prehospital and in-hospital reperfusion, but there is evidence of a substantial mortality benefit. We recommend prehospital 12-lead ECG acquisition with hospital notification for adult patients with suspected STEMI. Nonphysicians may perform ECG interpretation to recognize STEMI in a system where there is a strong initial education program, ongoing oversight, possible adjunctive computer interpretation, and a quality assurance program. The computer-assisted ECG interpretation can be used as an adjunct or in conjunction with the interpretation of a physician or other trained professional. In this way, recognition of STEMI by the computer interpretation can be verified by individual interpretation, and lack of recognition by the computer would not be used solely to rule out STEMI. When STEMI is recognized prehospital and primary PCI is the planned reperfusion strategy, prehospital STEMI activation of the catheterization laboratory reduces treatment delays and mortality.

There is renewed focus on the use of troponins to exclude the likelihood of ACS and enable safe discharge from the ED. The use of troponins at 0 and 2 h as a stand-alone measure for excluding the diagnosis of ACS is strongly discouraged. The diagnosis of MACE (defined as future ACS or major adverse cardiac events within the next month) may be excluded by combining negative (defined as less than 99th percentile) hs-cTnI measured at 0 and 2 h with low risk stratification or by combining cTnI or cTnT measured at 0 and 3 to 6 h with very-low-risk stratification.

Therapeutic interventions in ACS

Adenosine diphosphate receptor antagonists and UFH can be administered either in the prehospital or in-hospital setting for suspected STEMI patients with a planned primary PCI approach. They have been shown to be safe and effective when given prehospital, although the benefit of prehospital administration is insufficiently clear to recommend this as routine practice. Prehospital enoxaparin may be used as an alternative to prehospital UFH as an adjunct for primary PCI for STEMI. There is insufficient evidence to suggest prehospital administration of bivalirudin compared with prehospital administration of UFH in identified STEMI patients to recommend a change in existing practice.

We suggest withholding oxygen in normoxic patients with ACS. This is based on absence of a detectable difference in mortality and potential benefit in reduced infarct size when oxygen is withheld. Although much of the evidence for oxygen use in ACS comes from studies before the modern reperfusion era, there is 1 recently published RCT and 2 RCTs that have yet to be published that will provide further evidence on this topic.[107]

Reperfusion decisions in STEMI

STEMI systems-of-care decisions will depend on the regional resources, including the capability of the local prehospital system and availability of PCI centers. When fibrinolysis is the planned treatment strategy for patients with STEMI, prehospital fibrinolysis is preferable to in-hospital fibrinolysis, where the transport times are commonly greater than 30 min, because it is associated with decreased mortality without evidence of increased intracerebral or major hemorrhage. Prehospital fibrinolysis requires knowledgeable prehospital personnel using well-established protocols, comprehensive training programs, and quality assurance programs under medical oversight. In geographic regions where PCI facilities exist and are available, direct triage and transport for PCI is preferred to prehospital fibrinolysis because it is associated with less intracranial hemorrhage, although it has not been shown to provide a survival benefit.

When making individual decisions about primary PCI versus fibrinolysis, important features include time from symptom onset, anticipated time (delay) to PCI, and other patient factors such as comorbidities, infarct location, and infarct size. Fibrinolysis is most effective in terms of myocardial salvation and survival in patients with STEMI presenting within 2 to 3 h after the onset of symptoms. In patients with STEMI presenting less than 2 h after symptom onset, primary PCI is preferred only when it can be performed with a time delay of less than 60 min. In patients presenting 2 to 3 h after symptom onset, either fibrinolysis or primary PCI can be selected as reperfusion strategy, provided that the primary PCI delay will be within 60 to 120 min. In patients with STEMI presenting 3 to 6 h after symptom onset, primary PCI is the treatment of choice when it can be accomplished with a delay of no more than 120 min. In patients presenting more than 6 h after symptom onset, primary PCI may represent the best option for reperfusion even if this can

only be accomplished with a long delay to primary PCI (e.g., more than 120 min). If fibrinolysis is chosen, it should be followed by routine early (within 3–24 h) angiography and PCI if indicated.

Adult patients presenting with STEMI in the ED of a non-PCI-capable hospital should be transferred emergently to a PCI center for primary PCI if this can be accomplished within an appropriate timeframe as discussed above. This is associated with a reduced incidence of mortality, reinfarction, and stroke with no additional harm in terms of major hemorrhage in comparison with immediate in-hospital fibrinolysis and transfer only for rescue PCI. When these patients cannot be transported to PCI in a timely manner, fibrinolytic therapy followed by routine transfer for angiography within 3 to 6 and up to 24 h may represent an equally effective and safe alternative to immediate transfer to primary PCI. Routine transport of patients with STEMI undergoing fibrinolytic therapy in the ED of a non-PCI hospital for early routine angiography in the first 3 to 6 h (or up to 24 h) is associated with less reinfarction and may be preferred to fibrinolysis, and then transfer only for ischemia-guided angiography. The routine use of PCI immediately (within 2 h) after fibrinolysis is strongly discouraged because it is associated with increased incidence of major and intracranial bleeding without any expected additional benefit to primary PCI alone.

Hospital reperfusion decisions after ROSC

The majority of patients who have an OHCA have underlying ischemic heart disease. Acute coronary artery occlusion is known to be the precipitating factor in many of these patients. It may be manifested by ST-segment elevation or left bundle branch block on post-ROSC 12-lead ECG but may also be present in the absence of these findings.

Patients who experience ROSC after OHCA and remain comatose with ST-elevation on post-ROSC 12-lead ECG should be transferred immediately for cardiac catheterization laboratory evaluation. This has been associated with considerable benefit in terms of survival to hospital discharge and neurologically intact survival in select groups of patients in comparison with cardiac catheterization later in hospital stay or no catheterization. Emergency cardiac catheterization is suggested for select adult patients who have no ST-elevation on ECG but remain comatose following ROSC from OHCA of suspected cardiac origin.

Pediatric basic and advanced life support

The Pediatric Task Force evaluated 21 PICO questions by way of systematic reviews. They are grouped here into categories of pre-cardiac arrest care, BLS care during cardiac arrest, ALS care during cardiac arrest, and post-cardiac arrest care. The most important evidence-based treatment recommendations chosen by the task force co-chairs are listed here.

Pre-cardiac arrest care

Response systems and assessment. The Pediatric Task Force suggested the use of pediatric rapid response team/medical emergency team systems within hospitals that care for children. The use of early warning scores in pediatrics was assessed, but the evidence was so limited that no specific recommendation could be made.

Atropine for emergent tracheal intubation. The task force concluded that, in light of the limited literature available, no specific recommendation could be made for the use of atropine during emergency tracheal intubation.

Prearrest care of pediatric dilated cardiomyopathy or myocarditis. The task force concluded that, in light of the limited literature available, no specific recommendation could be made.

Prearrest care of shock. The use of restricted volumes of isotonic crystalloid may lead to improved outcomes from pediatric septic shock in specific settings. For children with febrile illnesses, particularly without signs of overt septic shock, a cautious approach to fluid therapy should be combined with frequent patient reassessment.[76]

BLS care during cardiac arrest

Sequence of chest compressions and ventilation: Compressions–airway–breathing versus airway-breathing-compressions. The task force concluded that, in light of the limited literature available, no specific recommendation could be made. The task force acknowledged the equipoise that exists to allow resuscitation councils to decide on using either compressions–airway–breathing (C–A–B) or airway–breathing–compressions (A–B–C) in their guidelines.

Chest compression depth. The task force suggested that rescuers compress the chests of *infants* in cardiac arrest by at least one third the anterior-posterior dimension or approximately 1.5 in. (4 cm), and compress the chest of *children* in cardiac arrest by at least one third the anterior-posterior dimension or approximately 2 in. (5 cm).

Compression-only CPR versus conventional CPR (i.e., compressions plus breaths). The pediatric task force recommends that rescuers provide rescue breaths and chest compressions for pediatric IHCA and OHCA, because most pediatric cardiac arrests are caused by asphyxia. If rescuers cannot provide rescue breaths, they should at least perform chest compressions.

Pediatric advanced life support during cardiac arrest

Energy doses for defibrillation. The task force suggested the routine use of an initial dose of 2 to 4 $J\,kg^{-1}$ of monophasic or biphasic defibrillation waveforms for infants or children in VF or pVT cardiac arrest. There was insufficient evidence from which to base a recommendation for second and subsequent defibrillation doses.

The use of invasive blood pressure monitoring or $ETCO_2$ *monitoring to guide CPR quality.* The task force suggested that, in light of the limited literature available, no specific recommendation could be made for the routine use of invasive blood pressure or $ETCO_2$ monitoring to guide CPR quality.

The use of vasopressors and antiarrhythmics in cardiac arrest. The task force suggested that, in light of the limited pediatric literature available, no specific recommendation could be made regarding the use of vasopressors during pediatric cardiac arrest. The task force considered that the short-term outcomes of ROSC and survival to hospital admission overrode any uncertainty of the absolute effect on long-term survival and neurologic outcome with the use of epinephrine. Consensus by the task force was that providers continue to use epinephrine for pediatric cardiac arrest per their current council-specific practice, albeit that the evidence in pediatrics is poor.

Although the use of lidocaine or amiodarone for treatment of shock-resistant pediatric VF/pVT improves short-term outcomes, there are few data on their effects on long-term outcomes.[77]

Extracorporeal membrane oxygenation for CPR. The task force suggested that extracorporeal membrane oxygenation with resuscitation may be considered for infants and children with cardiac diagnoses who have IHCA in settings that provide the expertise, resources, and systems to optimize the use of extracorporeal membrane oxygenation during and after resuscitation. The task force believes that there was insufficient evidence from which to suggest

for or against the routine use of extracorporeal membrane oxygenation with resuscitation in infants and children *without cardiac diagnoses* who have IHCA.

Intra-arrest prognostication. The task force suggested that for infants and children in IHCA, predictors of positive patient outcome such as age younger than 1 year and the presence of an initial shockable rhythm were helpful in aiding prognostication. For infants and children in OHCA, age older than 1 year and the presence of VF/pVT as the presenting rhythm were important predictors of positive outcome. Duration of cardiac arrest was not found to be helpful by itself. Importantly, the task force considers it obligatory to assimilate multiple factors to help guide prognostication and decision making during resuscitation, while not adhering to unproven expectations of outcomes.

Post-cardiac arrest care

Postresuscitation care begins when a patient develops sustained ROSC. For children remaining unconscious after OHCA, outcomes are improved when fever is prevented, and a period of moderate therapeutic hypothermia or strict maintenance of normothermia is provided.[75]

Post-ROSC Pao_2 and post-ROSC ventilation. The task force suggested that rescuers measure the patient's Pao_2 after ROSC and target a value appropriate to the specific patient's condition. In the absence of specific patient data, they suggested that rescuers target normoxemia after ROSC. The task force suggested that rescuers measure $Paco_2$ after ROSC and target a value appropriate to the specific patient's condition. The evidence was insufficient to make a recommendation for a specific $Paco_2$ target.

Post-ROSC fluid/inotropes. The task force made a strong recommendation that for infants and children after ROSC, parenteral fluids and/or inotropes or vasopressors should be used to maintain a systolic blood pressure of at least greater than fifth percentile for age.

Post-ROSC electroencephalogram as a prognosticator. The task force suggested that the use of electroencephalogram within the first 7 days after pediatric cardiac arrest may assist in prognostication. The evidence surrounding the use of electroencephalogram by itself as a prognostic tool after pediatric cardiac arrest was thought to be insufficient to make a recommendation.

Post-ROSC predictive factors. The task force agreed that multiple variables should be used to predict outcomes for infants and children after cardiac arrest, and that it was unclear what the impact of evolving post-ROSC care (therapeutic hypothermia or TTM, fever avoidance, prevention of hypotension/optimizing cardiovascular function) will have on tentative predictors of outcome.

Neonatal resuscitation

Since the last publication of CoSTR, several controversial neonatal resuscitation issues have been identified. The highlights of these topics are below.

Initial stabilization

ECG Assessment of heart rate. Neonatal resuscitation success has traditionally been determined by detecting an increase in heart rate through auscultation. The data suggest that the ECG provides a more accurate heart rate in the first 3 min of life, but there were no available data to determine whether this changes outcome.

Delayed cord clamping and milking of the umbilical cord. Delayed umbilical cord clamping can be associated with increased placental transfusion and cardiac output and more stable neonatal blood pressure. The existing RCTs had small sample sizes and enrolled very few extremely premature infants or infants who required resuscitation. Although delayed cord clamping is suggested for preterm infants not requiring immediate resuscitation after birth, there is insufficient evidence to recommend an approach to cord clamping for preterm infants who do require resuscitation immediately after birth,

There is some evidence that milking the umbilical cord (from the placenta toward the infant) may have beneficial effects similar to delayed cord clamping, so it may be a rapid alternative to delayed cord clamping. However, there is insufficient published human evidence of benefit, particularly in very premature (less than 29 weeks of gestation) infants. Cord milking may be considered on an individual basis or in a research setting, because it may improve initial mean blood pressure, hematologic indices, and intracranial hemorrhage. This technique should be studied in infants requiring resuscitation.

Temperature management

Maintaining temperature. The admission temperature of newly born nonasphyxiated infants is a strong predictor of mortality and morbidity at all gestations, and it should be recorded as a predictor of outcomes as well as a quality indicator. The temperature of newly born nonasphyxiated infants should be maintained between 36.5 °C and 37.5 °C after birth through admission and stabilization.

To maintain the temperature of preterm infants of less than 32 weeks of gestation under radiant warmers in the hospital delivery room, a combination of interventions (including an environmental temperature of 23 °C to 25 °C, warm blankets, plastic wrapping without drying, cap, and thermal mattress) are effective in reducing hypothermia (temperature less than 36.0 °C). However, the effect of any one intervention has not been established.

In a resource-limited setting, it can be difficult to maintain the infant's temperature, especially for the first 1 to 2 h after birth, and there is a dose-dependent increase in mortality for temperatures below 36.5 °C. Premature infants demonstrate a 12-fold increase in mortality compared with term babies. Once a well baby of more than 30 weeks of gestation has been dried, the infant's legs, torso, and arms may be put in a clean food-grade plastic bag and swaddled or can be nursed with skin-to-skin contact with the mother or with kangaroo mother care; these approaches are favored over swaddling or placement in an open cot, crib, or incubator.

Rate of rewarming the newborn. When the infant is unintentionally hypothermic (temperature less than 36 °C) at hospital admission, there is insufficient evidence to determine if rapid (0.5 °C h^{-1} or greater) or slow (less than 0.5 °C h^{-1}) rewarming is more effective and associated with better outcome.

Respiratory support in the delivery room

Several randomized clinical trials and animal studies have provided additional information about the potential effect of several ventilation strategies designed to establish functional residual capacity immediately after birth.

For spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room, the task force suggests that the initial use of *continuous positive airway pressure* (CPAP) rather than immediate intubation and positive-pressure ventilation may be sufficient to augment the infant's respiratory effort with a low risk of adverse outcome. It is important to note that infants included in the studies were likely to have been treated with antenatal steroids, so this approach should be

studied in infants who have not received antenatal steroids and in high-risk preterm infants with lower gestational age.

Administration of a *sustained positive-pressure inflation* to preterm infants who have not established spontaneous respiration at birth may reduce the need for intubation at 72 h, but the optimal method to administer sustained lung inflations and long-term effects of the inflations have not been established. For this reason, the task force suggests against the routine use of initial sustained inflation (greater than 5 s duration) for preterm infants without spontaneous respirations immediately after birth, but a sustained inflation may be considered in individual clinical circumstances or research settings.

There is benefit to using *positive end-expiratory pressure* (PEEP) to assist in establishment of a functional residual capacity during transition of the fluid-filled lung to an air-breathing organ. The task force reviewed evidence regarding the effect of the use of PEEP during intermittent mandatory ventilation and the value of specific devices to maintain the PEEP. The task force suggests the use of PEEP maintained with either a self-inflating bag, a flow-inflating bag, or a T-piece for premature newborns during delivery room resuscitation. No recommendation is possible for term infants because of insufficient data. There is also insufficient evidence to support the use of one device over another.

Intubation and tracheal suctioning in nonvigorous infants born through meconium-stained amniotic fluid versus no intubation for tracheal suctioning

Aspiration of meconium before delivery, during birth, or during resuscitation can cause severe meconium aspiration syndrome, but it is unclear if intervention at or after birth can affect the outcome. For more than 25 years, providers routinely performed tracheal intubation and direct tracheal suctioning for all meconium-stained newborns, until a randomized trial showed it was unnecessary in infants who were vigorous at birth.[108] The practice of direct tracheal suctioning of infants who had respiratory compromise at birth (i.e., they were depressed/nonvigorous at birth) has persisted, but the practice is controversial, with only a very low quality of evidence (i.e., historic controls) to suggest benefit. After the 2015 systematic review, the Neonatal Task Force concluded that there is insufficient published evidence to support routine tracheal intubation for suctioning of meconium in even nonvigorous infants born through meconium-stained amniotic fluid, because it likely delays ventilation.

Oxygen concentration for initiating resuscitation of premature newborns

High concentrations of inspired oxygen can be toxic to newborn lungs, so the oxygen concentration for term babies is generally started at 21% (room air). There has been ongoing controversy regarding the optimal inspired oxygen concentration for resuscitation of preterm babies. After the systematic review, the Neonatal Task Force recommends *against* initiating resuscitation of preterm newborns (less than 35 weeks' gestational age) with high-oxygen concentrations (65–100%) and instead recommends initiating resuscitation with a low-oxygen concentration (21–30%).

Circulatory support: Chest compressions

Although the evidence supporting the 2-thumb over the 2-finger technique of chest compressions is based on manikin rather than human data, the 2-thumb technique with fingers encircling the chest generated higher blood pressure and less fatigue than use of 2 fingers. As a result, the 2 thumb-encircling hands technique is the preferred technique for newborn chest compressions during 2-rescuer CPR. These chest compressions should still be delivered over the lower third of sternum, using a 3:1 compression-to-ventilation ratio. This ratio has been shown to deliver more breaths than the 15:2 ratio used for 2-rescuer pediatric CPR in animal models and in a manikin study. The task force considers the 3:1 ratio appropriate, because asphyxia is the predominant cause of cardiovascular collapse in the newborn and effective resuscitation requires significant focus on ventilation.

Oxygen delivery during CPR (neonatal)

Despite animal evidence showing no advantage to the use of 100% oxygen, by the time resuscitation of a newborn has reached the stage of chest compressions, the rescuers should already have attempted to achieve ROSC by using effective ventilation with low-concentration oxygen. Thus, once chest compressions are needed, it would seem prudent to try increasing the supplementary oxygen concentration. If used, the supplementary oxygen should be weaned as soon as the heart rate has recovered. It is important to note that there are no human data to inform this question.

Assisted-ventilation devices and CPR feedback devices

Tracheal intubation is a difficult skill to learn and perform, and it is difficult to maintain competence in the technique. After review of 3 randomized trials involving 469 patients, the task force suggests that the laryngeal mask may be used as an alternative to tracheal intubation during resuscitation of the late-preterm and term newborn (more than 34 weeks of gestation) if ventilation via the face mask or intubation is unsuccessful.

Although use of flow and volume monitors and capnography are feasible, because there is no evidence that they are effective in improving important outcomes, the task force suggests against the routine use of flow and volume monitoring or capnography for babies who receive positive-pressure ventilation at birth, until more evidence becomes available.

Use of CPR feedback devices during neonatal cardiac arrest

In asystolic/bradycardic neonates, the task force suggests against the routine use of any single feedback device such as $ETCO_2$ monitors or pulse oximeters for detection of ROSC until more evidence becomes available.

For the critical outcomes of improved perfusion, decreased time to ROSC, decreased hands-off time, increased survival rates, or "improved neurologic outcomes," no specific data were identified.

Induced hypothermia in resource-limited settings

The task force suggests that newly born infants at term or near term with evolving moderate-to-severe hypoxic-ischemic encephalopathy in low-income countries and/or other settings with *limited resources* may be treated with therapeutic hypothermia.

Cooling should be considered, initiated, and conducted only under clearly defined protocols with treatment in neonatal care facilities with the capabilities for multidisciplinary care and availability of adequate resources to offer intravenous therapy, respiratory support, pulse oximetry, antibiotics, anticonvulsants, and pathology testing. Treatment should be consistent with the protocols used in the randomized clinical trials in developed countries, i.e., cooling to commence within 6 h, strict temperature control at 33 °C to 34 °C for 72 h, and rewarming over at least 4 h.

Prognostication

Delivery room assessment at less than 25 weeks of gestation and prognostic score. There is insufficient evidence to support the prospective use of any delivery room prognostic score presently described over estimated gestational age assessment alone in preterm infants of less than 25 weeks of gestation. No score has been shown to improve the ability to estimate the likelihood of survival through either 30 days or in the first 18 to 22 months after birth.

In individual cases, when constructing a prognosis for survival at gestation below 25 weeks, it is reasonable to consider variables including perceived accuracy of gestational age assignment, the presence or absence of chorioamnionitis, and the level of care available at the delivery facility. It is also recognized that decisions about appropriateness of resuscitation of those below 25 weeks of gestation will be influenced by region-specific guidelines established by regional resuscitation councils.

Apgar score of 0 for 10 or more minutes. An Apgar score of 0 at 10 min is a strong predictor of mortality and morbidity in late-preterm and term infants. The task force suggests that, in babies with an Apgar score of 0 after 10 min of resuscitation, if the heart rate remains undetectable, it may be reasonable to stop resuscitation; however, the decision to continue or discontinue resuscitative efforts should be individualized. Variables to be considered may include whether the resuscitation was considered to be optimal; availability of advanced neonatal care, such as therapeutic hypothermia; specific circumstances before delivery (e.g., known timing of the insult); and wishes expressed by the family.

Among infants of 35 weeks of gestation or more with an Apgar score of 0 for 10 or more minutes, the likelihood of dying or having severe or moderate developmental disabilities at 18 to 24 months is very high. Studies that included 69 infants with an Apgar score of 0 at 10 min after birth who were successfully resuscitated and randomized to hypothermia or normothermia, and case series of 21 additional infants who were managed with therapeutic hypothermia, suggest improvement in outcome compared with previously reported cohorts. Among these 90 infants, 45 (50%) died, and 22 (24%) survived without major or moderate disability at 18 to 24 months. However, the number of infants with no heart rate at 10 min who died in the delivery room is unknown.

Predicting death or disability in resource-limited settings of newborns of more than 34 weeks of gestation based on apgar score and/or absence of breathing. Absence of spontaneous breathing or an Apgar score of 1 to 3 at 20 min of age, in babies of more than 34 weeks of gestation but with a detectable heart rate, are strong predictors of mortality or significant morbidity. In settings where *resources are limited*, we suggest that it may be reasonable to stop assisted ventilation in babies with no spontaneous breathing despite presence of heart rate or Apgar score of 1 to 3 at 20 or more minutes. Importantly, each of the studies reviewed was conducted in a setting where therapeutic hypothermia was likely to be available.

Resuscitation training

Frequency. The task force suggests that training should be recurrent and considered more frequently than once per year. This retraining may be composed of specific tasks and/or behavioral skills, depending on the needs of the trainees.

Neonatal resuscitation instructors. The task force suggests that training of resuscitation instructors incorporate timely, objective, structured, individually targeted verbal and/or written feedback. There was no evidence identified to show improvement in critical outcomes. There was some evidence to show that training instructors improved some important outcomes. While common sense dictates that instructors be properly prepared before engaging learners, it is clear that such instruction must be based on specific learning objectives targeting the specific skills that are necessary to facilitate learning.

Education, implementation, and teams

The ILCOR EIT Task Force organized its work into 3 major sections: (1) BLS training, (2) ALS training, and (3) implementation.

There remains considerable variability in cardiac arrest survival in and out of hospital and, therefore, substantial opportunity to save many more lives.[109–111] The Formula for Survival[112] postulates that optimal survival from cardiac arrest requires high-quality science, education of lay providers and healthcare professionals, and a well-functioning Chain of Survival[113] (implementation). Organizations providing care for cardiac arrest victims should train healthcare providers in teams, using evidence-informed educational practice and tailoring the training to the required skills of the practitioner and team. Additionally, organizations should implement systems-level processes such as data-driven continuous quality improvement to optimize survival from cardiac arrest. The most important developments and recommendations in EIT since the 2010 ILCOR review are described below.

Basic life support training

BLS is critically important to the care of cardiac arrest victims, but, unfortunately, only a minority of cardiac arrest victims actually receive bystander CPR. Recent training in CPR,[114] along with dispatcher-assisted CPR,[115] may help overcome barriers and save more lives. For healthcare professionals, the quality of CPR delivered is critical because poor compliance with recommended guidelines has been associated with lower survival.[116,117] Suboptimal CPR[118] harms patients and is preventable.[119] Quality improvement processes are needed to try to minimize its occurrence.

Video- or computer-based instruction may enable more rescuers to be trained in CPR. Despite heterogeneity in the delivery of video- and/or computer-based instruction, and in the evaluation methods among different studies, we suggest that video- and/or computer-based self-instruction with synchronous or asynchronous hands-on practice may be an effective alternative to instructor-led courses.

Although use of an AED does not require formal training, it may be helpful for the lay rescuer to have consolidated some of these skills through an instructional program. For lay providers learning AED skills, self-instruction combined with short, instructor-led training may be acceptable to replace longer traditional courses. For healthcare providers learning AED skills, self-directed training (as short as 40 min) may be useful in place of traditional training.

CPR skills are known to deteriorate within the weeks to months after resuscitation training, well before the current recertification timeline for resuscitation organizations. We suggest that individuals likely to encounter cardiac arrest consider more frequent retraining to optimize their skills so they are best prepared to deal with an arrest. Part of the decay in skills may be related to poor training in the initial course or retraining sessions. Instructors are often unable to identify poor-quality compressions, which limits the quality of corrective feedback that is provided. We suggest the use of feedback devices that provide directive feedback on compression rate, depth, release, and hand position during training. If feedback devices are not available, we suggest the use of tonal guidance (examples include music and metronome) during training to improve compression rate.

The ILCOR EIT Task Force recommends BLS training for individuals (family or caregivers) caring for high-risk populations, based on the willingness to be trained and the fact that there is low risk of harm and high potential of benefit. We placed lesser value on associated costs and the potential that skills may not be retained without ongoing CPR training. Because cardiac arrest is life threatening, the likelihood of benefit is high relative to possible harm.

Communities may train bystanders in compression-only CPR for adult OHCA as an alternative to training in conventional CPR. In making this recommendation, we took into account that willingness to perform bystander CPR in the community may be increased when compression-only CPR is offered as an alternative

technique.[120–123] Communities should consider existing bystander CPR rates and other factors such as local epidemiology of OHCA and cultural preferences when deciding on the optimal community CPR training strategy.

Advanced life support training

Published data suggest that without ongoing education, the skills learned in ALS courses are lost over a period of months.[114,124] Coupled with increasing pressures from administrators to justify the time and costs of training away from the clinical workplace, there needs to be thoughtful evidence-based decision making in educational practice.

Primarily on the basis of studies demonstrating improved skill performance at course conclusion, we suggest the use of high-fidelity manikins when training centers/organizations have the infrastructure, trained personnel, and resources to maintain the program. If high-fidelity manikins are not available, we suggest the use of low-fidelity manikins is acceptable for standard ALS training in an educational setting. In making these recommendations, we took into account the well-documented, self-reported participant preference for high-fidelity manikins (versus low-fidelity manikins) and the likely impact of this preference on willingness to train.[124] We considered the positive impact of skill acquisition at course completion, as well as the lack of evidence of sustained impact on the learner. We also considered the relative costs of high- versus low-fidelity manikins.

The ILCOR EIT Task Force suggested that team and leadership training be included as part of ALS training for healthcare providers. In making this recommendation, we placed emphasis on the potential benefit, lack of harm, and high level of acceptance of team and leadership training and lesser value on associated costs.

Compared with standard retraining intervals of 12 to 24 months, the ILCOR EIT Task Force suggested that more frequent manikin-based refresher training for students of ALS courses may better maintain competence. The optimal frequency and duration of this retraining has not yet been determined. We consider the rapid decay in skills after standard ALS training may compromise patient care. Refresher training, in the form of frequent, low-dose in situ training with the use of manikins, offers promise.[125] The potential cost savings of integrating these sessions into daily workflow rather than removing staff for standard refresher training may be important, as might a reduced total time of retraining. A recent study demonstrates improved learning from “frequent, low-dose” compared with “comprehensive, all-at-once” instruction and a learner preference for this format.[126]

Implementation

Barriers within an organization may delay implementation of guidelines into practice by years, and modifying caregiver behaviors may take several years more.[127–132] Publishing guidelines is not sufficient without including the tools to get them implemented.

The ILCOR EIT Task Force suggested that OHCA patients should be considered for transport to a specialist cardiac arrest center as part of a regionalized system of care. In making this recommendation, the task force recognized that the development of cardiac arrest centers be considered as a health improvement initiative, without supportive evidence from randomized trials, such as has been performed for other conditions (e.g., myocardial infarction, stroke, major trauma).

Technology, including social media, may serve to notify citizen CPR responders of cardiac arrests, thereby shortening the time to onset of bystander CPR and defibrillation, which can be achieved before EMS arrives. Despite limited evidence, the EIT Task Force suggested that individuals in close proximity to a suspected OHCA who are willing and able to perform CPR be notified of the event via technology or social media. In making this recommendation, we place value on the time-sensitive benefit of CPR and AED use in OHCA and the limitations of optimized EMS systems to improve response times. We also recognize that there are individuals willing and able to provide BLS in most communities and these novel technologies can help to engage these individuals.

Performance measurement and quality-improvement initiatives in organizations that treat cardiac arrest may be critical in preventing cardiac arrest and improving outcomes from cardiac arrest, and should be implemented. Greater value is placed on the potential for lives saved and the concept that you can only improve what you can measure, and lesser value is placed on the costs associated with performance measurement and quality-improvement interventions. Assessing clinical performance and using a system to continuously assess and improve quality can improve compliance with guidelines.

One potential quality-improvement activity might be team-based debriefing of CPR team performance. Data-driven, performance-focused debriefing of rescuers after IHCA in both adults and children may help to improve subsequent performance. Data-driven, performance-focused debriefing of rescuers after OHCA in both adults and children may also be helpful.

Prevention of cardiac arrest is an important step in our goal to save more lives. We suggest hospitals consider the introduction of an early warning scoring system or rapid response team/medical emergency team system to reduce the incidence of IHCA and in-hospital mortality. This recommendation places a high value on the prevention of IHCA and death relative to the cost of the system. Such a system should provide elements of care that include (1) staff education about the signs of patient deterioration; (2) appropriate and regular vital signs monitoring of patients; (3) clear guidance (e.g., via calling criteria or early warning scores) to assist staff in the early detection of patient deterioration; (4) a clear, uniform system of calling for assistance; and (5) a clinical response to calls for assistance. The best method for the delivery of these components is unclear.[124]

First aid

Important medical topics reviewed for 2015 include use of supplementary oxygen for purposes other than patients with chest pain, positioning for shock and recovery, use of bronchodilators for patients with asthma who have acute shortness of breath, use of a second dose of epinephrine for anaphylaxis, and the administration of aspirin for chest pain.

- No evidence was found to support a change in current practice for the use of supplementary oxygen by first aid providers.
- The position recommended for the patient in shock remains the supine position, although there is some evidence suggesting passive raising of the legs between 30° and 60° may have a transient (7 min or less) benefit.
- There is a change in recommendations for the position of a normally breathing, unresponsive person. Because a potential need has been shown for advanced airway management in the supine position versus a lateral recumbent position, we are now recommending that the lateral recumbent position be used as a “recovery” position.
- Assisting with the administration of inhaled bronchodilators is recommended for patients with asthma who have acute shortness of breath.
- Although questions remain regarding the ability of a first aid provider to recognize anaphylaxis, the use of a second dose of epinephrine via autoinjector is beneficial when a first dose fails to improve symptoms. Adverse effects were not reported in studies included, although this may reflect the administration of epinephrine with an autoinjector, thus limiting opportunity for an inadvertent overdose injection.

- The use of aspirin for chest pain has been previously reviewed; however, the task force agreed that this topic should be looked at again in light of the newly implemented GRADE methodology and the emergence of newer medications used for acute myocardial infarction. Thus, the original question asking if aspirin should be administered for patients with myocardial infarction was reviewed, followed by a review of the early (i.e., prehospital) use of aspirin for chest pain versus delayed (i.e., in-hospital) administration of aspirin.
- A new review topic is the use of Stroke Assessment Systems to aid with recognition of stroke, with findings that will have enormous implications for first aid and public health. This review found a significant decrease in time between symptom onset and arrival at hospital or ED with the use of these assessment "tools"—use of such tools may reduce the degree of damage from stroke when treatment is initiated early.
- A new review looks at use of oral dietary sugars for symptomatic hypoglycemia in diabetics. The studies for this review administered various forms of dietary sugars – such as specific candies, dried fruit strips, juice, or milk – in a dose-equivalent amount compared with glucose tablets to diabetics with symptomatic hypoglycemia who were conscious and able to swallow and follow commands. It was concluded that, as a group, dietary sugar products were not as effective as glucose tablets for relief of hypoglycemia, but all studied forms showed benefit and potential usefulness in cases where glucose tablets are not available.

First aid trauma emergencies

Important trauma topics reviewed for 2015 included the first aid management of hemorrhage, angulated fractures, open chest wounds, burns (cooling of burns and burns dressings), and dental avulsion. Two additional important trauma topics were cervical spinal motion restriction and the recognition of concussion by first aid providers.

The correct management of hemorrhage and the enhancement of hemostasis in the first aid setting are essential to maintaining the circulating blood volume in acute trauma. Three PICO reviews focused on critical interventions for severe bleeding:

- There was inadequate evidence to support the use of proximal pressure points or limb elevation to control bleeding. The use of localized cold therapy is suggested for closed bleeding in extremities to aid hemostasis, but there was no evidence to support this therapy for open bleeding.
- The use of hemostatic dressings in first aid is supported when standard first aid hemorrhage control (e.g., direct wound pressure) fails to control severe bleeding or cannot be applied.
- Similarly, the evidence supports the use of tourniquets in the civilian setting when standard first aid hemorrhage control (e.g., direct wound pressure) fails to control severe external limb bleeding.

The task force recognized that the use of hemostatic dressings and tourniquets will have cost and training implications. However, the task force thought that these costs would be moderate and justified considering the benefit of maintaining circulating blood volume in the management of trauma.

There was no evidence to support the straightening of an angulated fracture in the first aid situation, and the task force did not make a recommendation. The task force recognized the need to protect the victim from further injury by splinting the fracture in position to reduce pain or to enable safe extrication and transportation.

The application of an occlusive dressing or device by first aid providers to an open chest wound may lead to an unrecognized tension pneumothorax. The task force suggested that these wounds be left open with local control of bleeding, rather than risk occlusion.

There is a growing body of scientific evidence showing complications related to use of cervical collars. This evidence, combined with concern for potential secondary injury due to neck movement during attempts to apply a collar, has led to a suggestion (weak recommendation) against the use of cervical collars by first aid providers. The task force acknowledges that first aid providers may not be able to distinguish between high- and low-risk criteria for spinal injuries, and recognizes the possible need for alternative methods of cervical spine motion restriction or stabilization, but these were not formally reviewed. The task force thought that formal spinal motion restriction in high-risk individuals is best accomplished by trained emergency medical rescuers or healthcare professionals.

The recognition of concussion after head trauma is a common challenge for first aid. No simple concussion scoring system was found that would assist the first aid provider in making this important diagnosis; however, there are more advanced scoring systems for use by healthcare professionals.

The correct first aid management of burns is critical to their eventual outcome. Cooling burns is a widespread first aid practice, but it is supported by only a low quality of scientific evidence. No evidence was found as to the preferred method of cooling, the temperature of the coolant, or the duration of cooling. It was recommended that active cooling begin as soon as possible by using cool or nonfreezing water or cooling adjuncts such as gel pads.

A comparison of wet with dry dressings for thermal burns yielded no recommendation. There were no studies comparing plastic wrap, considered a dry dressing, with a wet dressing.

It is widely recommended that an avulsed tooth be replanted immediately in the conscious victim. However, first aid providers may not have the skills or the willingness to undertake this procedure. This review suggests a series of commercially available storage solutions and simple household mediums, when available, for the short-term storage of an avulsed tooth until reimplantation can be accomplished.

Education

Education in first aid continues to be a topic with few scientific studies. In the 2010 review of educational topics, no evidence was found to support or recommend any method of evaluating or monitoring a first aid trainee's educational progress or the specific frequency of retraining to retain skills and knowledge.[133] The task force decided to investigate the basic question, is there documented evidence of benefit in terms of patient outcomes as a result of first aid training?

Many questions remain and research is desperately needed, particularly in the realm of teaching techniques for first aid and methods to evaluate the retention of skills.

Future directions

The science of resuscitation is evolving rapidly. It would not be in the best interests of patients if we waited 5 or more years to inform healthcare professionals of therapeutic advances in this field. ILCOR members will continue to review new science and, when necessary, publish interim advisory statements to update treatment guidelines so that resuscitation practitioners may provide state-of-the-art patient care. Existing gaps in our knowledge will be closed only by continuing high-quality research into all facets of CPR. Readers are encouraged to review the information on the SEERS site to learn of new developments and recommendations for resuscitation and first aid (https://volunteer.heart.org/apps/pico/Pages/default.aspx SEERS).

Disclosures

2015 CoSTR Part 1: Executive summary: writing group disclosures.

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						None	American Heart Association†	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

Acknowledgments

We acknowledge the considerable contributions made by the late Professor Ian Jacobs, PhD, to this 2015 CoSTR. Professor Jacobs led ILCOR with passion and vision from 2011 to October 19, 2014.

Appendix A.

CoSTR evidence-based PICO worksheets: master Appendix.

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 3	BLS	BLS 343	Chest compression rate	Among adults and children who are in cardiac arrest in any setting (P), does any specific rate for external chest compressions (I), compared with a compression rate of about 100 min^{-1} (C), change survival with neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR quality (O)?	Julie Considine, Nicolas Mpotos, Swee Lim
		BLS 345	Rhythm check timing	Among adults and children who are in cardiac arrest in any setting (P), does checking the cardiac rhythm immediately after defibrillation (I), compared with immediate resumption of chest compressions with delayed check of the cardiac rhythm (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; recurrence of VF (O)?	Giuseppe Ristagno, Husein Lockhat
		BLS 346	Timing of CPR cycles	Among adults who are in cardiac arrest in any setting (P), does pausing chest compressions at another interval (I), compared with pausing chest compressions every 2 minutes to assess the cardiac rhythm (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; coronary perfusion pressure; cardiac output (O)?	Joshua Reynolds, Violetta Raffay
		BLS 347	Public-access defibrillation	Among adults and children who are in cardiac arrest outside of a hospital (P), does implementation of a public-access AED program (I), compared with traditional EMS response (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; bystander CPR rates; bystander use of AED; time to commence CPR (O)?	Andrew Travers, Ian Drennan
		BLS 348	Check for circulation during BLS	Among adults and children who are in cardiac arrest in any setting (P), does interruption of CPR to check circulation (I), compared with no interruption of CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; chest compression fraction (O)?	Martin Botha, Andrea Scapigliati
		BLS 352	Passive ventilation technique	Among adults and children who are in cardiac arrest in any setting (P), does addition of any passive ventilation technique (e.g., positioning the body, opening the airway, passive oxygen administration) to chest compression – only CPR (I), compared with just chest compression – only CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander initiated CPR; oxygenation (O)?	Emmanuelle Bourdon, Volker Wenzel
		BLS 353	Harm from CPR to victims not in cardiac arrest	Among adults and children who are not in cardiac arrest outside of a hospital (P), does provision of chest compressions from lay rescuers (I), compared with no use of chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; harm (e.g., rib fracture); complications; major bleeding; risk of complications (e.g., aspiration); survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to admission (O)?	Raul Gazmuri, Hermann Brugger
		BLS 357	Hand position during compressions	Among adults and children who are receiving chest compressions in any setting (P), does delivery of chest compressions on the lower half of the sternum (I), compared with any other location for chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; cardiac output; harm (eg, rib fracture); coronary perfusion pressure (O)?	Ian Drennan, Sung Phil Chung
		BLS 358	Minimizing pauses in chest compressions	Among adults and children who are in cardiac arrest in any setting (P), does minimization of pauses in chest compressions for cardiac rhythm analysis or ventilations (I), compared with prolonged pauses in chest compressions for rhythm analysis or ventilations (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; CPR quality; rhythm control (O)?	Rudolph Koster, Tetsuya Sakamoto

Appendix A (*Continued*)

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		BLS 359	Dispatcher instruction in CPR	Among adults and children who are in cardiac arrest outside of a hospital (P), does the ability of a dispatch system to provide CPR instructions (I), compared with a dispatch system where no CPR instructions are ever provided (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; delivery of bystander CPR; time to first shock; time to commence CPR; CPR parameters (O)?	Christian Vaillancourt, Michael Sayre
		BLS 360	EMS chest compression—only versus conventional CPR	Among adults who are in cardiac arrest outside of a hospital (P), does provision of chest compressions with delayed ventilation by EMS (I), compared with chest compressions with early ventilation by EMS (C), change survival with favorable neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; time to first compressions; CPR quality (O)?	David Stanton, Andrew Travers
		BLS 361	Feedback for CPR quality	Among adults and children who are in cardiac arrest in any setting (P), does real-time feedback and prompt device regarding the mechanics of CPR quality (e.g., rate and depth of compressions and/or ventilations) (I), compared with no feedback (C), change survival with favorable neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander CPR rates; time to first compressions; time to first shock; CPR quality (O)?	Julie Considine, Joyce Yeung
		BLS 362	Compression ventilation ratio	Among adults and children who are in cardiac arrest in any setting (P), does delivery of CPR with another specific compression-ventilation ratio (I), compared with CPR that uses a 30:2 compression-ventilation ratio (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; hands-off time (O)?	Bo Lofgren, Jason Buick
		BLS 363	CPR before defibrillation	Among adults and children who are in VF or pulseless VT (pVT) in any setting (P), does a prolonged period of chest compressions before defibrillation (I), compared with a short period of chest compressions before defibrillation (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; rhythm control (O)?	Mohamud Daya, Jan-Thorsten Graesner
		BLS 366	Chest compression depth	Among adults who are in cardiac arrest in any setting (P), does a different chest compression depth during CPR (I), compared with chest compression depth to 5 cm (2 in.) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR quality; coronary perfusion pressure; cardiac output; bystander CPR performance (O)?	Ahamed Idris, Koen Monsieurs
		BLS 367	Chest wall recoil	Among adults and children who are in cardiac arrest in any setting (P), does maximizing chest wall recoil (I), compared with ignoring chest wall recoil (C), change Survival with Favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days AND/OR 1 year, Survival only at discharge, 30 days, 60 days, 180 days AND/OR 1 year, ROSC, coronary perfusion pressure, cardiac output (O)?	Tyler Vadeboncoeur, Keith Couper
		BLS 372	Chest compression–only CPR versus conventional CPR	Among adults who are in cardiac arrest outside of a hospital (P), does provision of chest compressions (without ventilation) by untrained/trained laypersons (I), compared with chest compressions with ventilation (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander CPR performance; CPR quality (O)?	Andrew Travers, E. Brooke Lerner
		BLS 373	Analysis of rhythm during chest compression	Among adults and children who are in cardiac arrest in any setting (P), does analysis of cardiac rhythm during chest compressions (I), compared with standard care (analysis of cardiac rhythm during pauses in chest compressions) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; time to commence CPR; CPR quality (O)?	Alfredo Sierra, Kevin Nation
		BLS 661	Starting CPR	Among adults and children who are in cardiac arrest in any setting (P), does CPR beginning with compressions first (30:2) (I), compared with CPR beginning with ventilation first (2:30) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Carl McQueen, Julie Considine

Appendix A (*Continued*)

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		BLS 740	Dispatcher recognition of cardiac arrest	Among adults and children who are in cardiac arrest outside of a hospital (P), does the description of any specific symptoms to the dispatcher (I), compared with the absence of any specific description (C), change the likelihood of cardiac arrest recognition (O)?	Manya Charette, Mike Smyth
		BLS 811	Resuscitation care for suspected opioid-associated emergencies	Adults and children with suspected opioid-associated cardiac/respiratory arrest in the pre-hospital setting (P), does bystander naloxone administration (intramuscular or intranasal), in addition to standard CPR (I), compared with conventional CPR (I), compared with conventional CPR only (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Theresa Olasveengen, Aaron Orkin
		BLS 856	Drowning search and rescue	In adults and children who are submerged in water (P), does any particular factors in search and rescue operations (e.g., duration of submersion, salinity of water, water temperature, age of victim) (I), compared with no factors (C), change Survival with Favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days AND/OR 1 year, Survival only at discharge, 30 days, 60 days, 180 days AND/OR 1 year, ROSC (O)?	Joost Bierens, Linda Quan
		BLS 891	Opioid overdose response education	Adults and children at risk of suspected cardiac/respiratory arrest due to opioids in the prehospital setting (P), does opioid overdose response education with or without naloxone distribution (I), compared with no overdose response education or overdose prevention education only (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Aaron Orkin, Theresa Olasveengen
Part 4	ALS	ALS 428	Antiarrhythmic drugs for cardiac arrest	Among adults who are in cardiac arrest in any setting (P), does administration of antiarrhythmic drugs (e.g., amiodarone, lidocaine, other) (I), compared with not using antiarrhythmic drugs (no drug or placebo) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Katie Dainty, Thomas Pellis, Steve Lin
		ALS 431	Postresuscitation seizure prophylaxis	Among adults with ROSC after cardiac arrest in any setting (P), does seizure prophylaxis (I), compared with no prophylaxis (C), reduce the incidence of seizures, or improve survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Romergryko Geocadin, William Stacey
		ALS 433	Steroids for cardiac arrest	Among adults who are in cardiac arrest in any setting (P), does corticosteroid or mineralocorticoid administration during CPR (I), compared with not using steroids (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Sarah Todhunter, Tonia Nicholson
		ALS 435	Cardiac arrest associated with pulmonary embolism	Among adults who are in cardiac arrest due to PE or suspected PE in any setting (P), does any specific alteration in treatment algorithm (e.g., fibrinolytics, or any other) (I), compared with standard care (according to 2010 treatment algorithm) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Wolfgang Wetsch, Bernd Boettiger
		ALS 436	Cardiac arrest during pregnancy	Among pregnant women who are in cardiac arrest in any setting (P), do any specific interventions (I), compared with standard care (usual resuscitation practice) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Carolyn Zelop, Jill Mhyre
		ALS 441	Opioid toxicity	Among adults who are in cardiac arrest or respiratory arrest due to opioid toxicity in any setting (P), does any specific therapy (e.g., naloxone, bicarbonate, or other drugs) (I), compared with usual ALS (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Allan Mottram, Fred Severyn, Mohammed Alhelail
		ALS 448	Oxygen dose after ROSC in adults	Among adults who have ROSC after cardiac arrest in any setting (P), does an inspired oxygen concentration titrated to oxygenation (normal oxygen saturation or partial pressure of oxygen) (I), compared with the use of 100% inspired oxygen concentration (C), change survival to 30 days with good neurologic outcome, survival to hospital discharge with good neurologic outcome, improve survival, survival to 30 days, survival to hospital discharge (O)?	Jasmeet Soar, Michael Donnino

Appendix A (*Continued*)

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		ALS 449	Organ donation	In adults and children who are receiving an organ transplant in any setting (P), do organs retrieved from a donor who has had CPR (I), compared with organs retrieved from a donor who did not have CPR (C), have improved immediate graft function (30 days), 1-year graft function, or 5-year graft function (O)?	Stephen West, Clifton Callaway
		ALS 450	Prognostication in comatose patients treated with hypothermic TTM	Among adults with ROSC who are treated with hypothermia (P), does any clinical variable when abnormal (e.g., clinical exam, EEG, somatosensory evoked potentials [SSEPs], imaging, other) (I), compared with any clinical variable when normal (C), reliably predict death or poor neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; death only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Claudio Sandroni, Eyal Golan
		ALS 459	$ETCO_2$ to predict outcome of cardiac arrest	Among adults who are in cardiac arrest in any setting (P), does any $ETCO_2$ level value, when present (I), compared with any $ETCO_2$ level below that value (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Brian O'Neil, Edison Paiva
		ALS 469	Confirmation of correct tracheal tube placement	Among adults who are in cardiac arrest, needing/with an advanced airway, in any setting (P), does use of devices (e.g., 1. Waveform Capnography, 2. CO_2 Detection Device, 3. Esophageal detector device or 4. Tracheal ultrasound) (I), compared with not using devices (C), change placement of the ET tube between the vocal cords and the carina, success of intubation (O)?	Sarah Heikal, Markus Skifvars
		ALS 470	Defibrillation strategies for ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT)	Among adults who are in ventricular fibrillation or pulseless ventricular tachycardia in any setting (P), does any specific defibrillation strategy (e.g., 1. energy dose, or 2. shock waveform) (I), compared with standard management (or other defibrillation strategy) (C), change Survival with Favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days AND/OR 1 year, Survival only at discharge, 30 days, 60 days, 180 days AND/OR 1 year, ROSC, termination of arrhythmia (O)?	Giuseppe Ristagno, Charles Deakin
		ALS 479	Cardiac arrest during coronary catheterization	Among adults who have a cardiac arrest in the cardiac catheterization laboratory (P), does any special intervention or change in care (e.g., catheterization during CPR, cardiopulmonary bypass, balloon pump, different timing of shocks) (I), compared with standard resuscitation care (e.g., CPR, drugs, and shocks according to 2010 treatment algorithm) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Ian Drennan, Peter Kudenchuk
		ALS 493	Postresuscitation antiarrhythmic drugs	Among adults with ROSC after cardiac arrest in any setting (P), do prophylactic antiarrhythmic drugs given immediately after ROSC (I), compared with not giving antiarrhythmic drugs (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; development of cardiac arrest; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; recurrence of VF; incidence of arrhythmias (O)?	Thomas Pellis, Steve Lin
		ALS 570	Postresuscitation hemodynamic support	Among adults with ROSC after cardiac arrest in any setting (P), does titration of therapy to achieve a specific hemodynamic goal (e.g., MAP greater than 65 mmHg) (I), compared with no hemodynamic goal (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Michael Fries, Michael Parr
		ALS 571	Postresuscitation ventilation strategy	Among adults with ROSC after cardiac arrest in any setting (P), does ventilation to a specific $Paco_2$ goal (I), compared with no specific strategy or a different $Paco_2$ goal (C), change survival at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Asger Granfeldt, Bo Lofgren
		ALS 579	Impedance threshold device	Among adults who are in cardiac arrest in any setting (P), does use of an inspiratory ITD during CPR (I), compared with no ITD (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Peter Morley, Jasmeet Soar
		ALS 580	Glucose control after resuscitation	Among adults with ROSC after cardiac arrest in any setting (P), does a specific target range for blood glucose management (e.g., strict 4–6 mmol L^{-1}) (I), compared with any other target range (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Janice Zimmerman, Jonathon Sullivan

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		ALS 656	Monitoring physiological parameters during CPR	Among adults who are in cardiac arrest in any setting (P), does the use of physiological feedback regarding CPR quality (e.g., arterial lines, $ETCO_2$ monitoring, SpO_2 waveforms, or others) (I), compared with no feedback (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; change in physiologic values by modifications in CPR (O)?	Amit Chopra, Natalie Wong
		ALS 658	Ultrasound during CPR	Among adults who are in cardiac arrest in any setting (P), does use of ultrasound (including echocardiography or other organ assessments) during CPR (I), compared with conventional CPR and resuscitation without use of ultrasound (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Katherine Berg, Lars Wiuff Andersen
		ALS 659	Epinephrine versus vasopressin	Among adults who are in cardiac arrest in any setting (P), does use of epinephrine (I), compared with vasopressin (C), change survival to 30 days with good neurologic outcome, survival to 30 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC (O)?	Laurie Morrison, Clifton Callaway, Steve Lin
		ALS 713	Prognostication in absence of TTM	Among adults who are comatose after cardiac arrest and are not treated with TTM (P), does any clinical finding when normal (e.g., clinical exam, EEG, SSEPs, imaging, other) (I), compared with any clinical finding when abnormal (C), reliably predict death or poor neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; death only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Claudio Sandroni, Tobias Cronberg
		ALS 714	SGAs versus tracheal intubation	Among adults who are in cardiac arrest in any setting (P), does SGA insertion as first advanced airway (I), compared with insertion of a tracheal tube as first advanced airway (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR parameters; development of aspiration pneumonia (O)?	Jerry Nolan, Charles Deakin
		ALS 723	ECPR versus manual or mechanical CPR	Among adults who are in cardiac arrest in any setting (P), does the use of ECPR techniques (including extracorporeal membrane oxygenation or cardiopulmonary bypass) (I), compared with manual CPR or mechanical CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Mayuki Aibiki, Tzong-luen Wang
		ALS 778	SDE versus HDE	In adult patients in cardiac arrest in any setting (P), does HDE (at least 0.2 mg kg^{-1} or 5 mg bolus dose) (I), compared with SDE (1 mg bolus dose) (C), change survival to 180 days with good neurologic outcome, survival to 180 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC (O)?	Laurie Morrison, Clifton Callaway, Steve Lin
		ALS 782	Mechanical CPR devices	Among adults who are in cardiac arrest in any setting (P), do automated mechanical chest compression devices (I), compared with standard manual chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Steven Brooks, Laurie Morrison
		ALS 783	Basic versus advanced airway	Among adults who are in cardiac arrest in any setting (P), does insertion of an advanced airway (tracheal tube or SGA) (I), compared with basic airway (bag-mask device with or without oropharyngeal airway) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR parameters; development of aspiration pneumonia (O)?	Jerry Nolan, Jan-Thorsten Graesner
		ALS 784	Timing of administration of epinephrine	Among adults who are in cardiac arrest in any setting (P), does early epinephrine delivery by IV or IO route (e.g., less than 10 min after the beginning of resuscitation) (I), compared with delayed timing of epinephrine delivery (e.g., more than 10 min after the beginning of resuscitation) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Tonia Nicholson, Michael Donnino
		ALS 788	Epinephrine versus placebo	Among adults who are in cardiac arrest in any setting (P), does the use of epinephrine (I), compared with placebo or not using epinephrine (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Laurie Morrison, Clifton Callaway, Steve Lin

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		ALS 789	Epinephrine versus vasopressin in combination with epinephrine	Among adults who are in cardiac arrest in any setting (P), does use of both vasopressin and epinephrine (I), compared with using epinephrine alone (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Clifton Callaway, Laurie Morrison, Steve Lin
		ALS 790	Targeted temperature management	Among patients with ROSC after cardiac arrest in any setting (P), does inducing mild hypothermia (target temperature 32 °C–34 °C) (I), compared with normothermia (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Joshua Reynolds, Katherine Berg
		ALS 791	Duration of TTM	In patients with ROSC after cardiac arrest in any setting (P), does induction and maintenance of hypothermia for any duration other than 24 h (I), compared with induction and maintenance of hypothermia for a duration of 24 h (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Theodoros Xanthos, Lars Wiuff Andersen
		ALS 802	Timing of induced hypothermia	Among patients with return of pulses after cardiac arrest in any setting (P), does induction of hypothermia before some time point (e.g., 1 h after ROSC or before hospital arrival) (I), compared with induction of hypothermia after that time point (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Theodoros Xanthos, Michael Cocchi
		ALS 808	Ventilation rate during continuous chest compression	Among adults with cardiac arrest with a secure airway receiving chest compressions (in any setting, and with standard tidal volume) (P), does a ventilation rate of 10 breaths/min (I), compared with any other ventilation rate (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Koen Monsieurs, Jasmeet Soar, Gino Vissers
		ALS 834	Lipid therapy for cardiac arrest	In adult patients with cardiac arrest due to suspected drug toxicity (e.g., local anesthetics, tricyclic antidepressants, others) (P), does administration of IV lipid (I), compared with no IV lipid (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Eric Lavonas, Mohammed Alhelail
		ALS 868	Seizure treatment	Among adults with ROSC after cardiac arrest in any setting (P), does effective seizure treatment (I), compared with no seizure control (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Romergryko Geocadin, William Stacey
		ALS 879	Prevention of fever after cardiac arrest	Among adults with ROSC after cardiac arrest in any setting (P), does prevention of fever to maintain strict normothermia (I), compared with no fever control (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Katherine Berg, Lars Wiuff Andersen
		ALS 889	Oxygen dose during CPR	In adults with cardiac arrest in any setting (P), does administering a maximal oxygen concentration (e.g., 100% by face mask or closed circuit) (I), compared with no supplementary oxygen (e.g., 21%) or a reduced oxygen concentration (e.g., 40%–50%) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Anthony Lagina, Jasmeet Soar
Part 5	ACS	ACS 332	ED Fibrinolysis and transport only for rescue PCI versus transport for PCI	Among adult patients with STEMI in the ED (of a non–PCI-capable hospital) (P), does transfer to a PCI center (I), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (C), change short-term survival, stroke, major bleeding, reinfarction (O)?	Nikolaos Nikolaou, Abdulaziz Alali
		ACS 334	ED fibrinolysis and then routine early angiography versus only rescue PCI	Among adult patients with STEMI in the ED (of a non–PCI-capable hospital) who have received immediate in-hospital fibrinolysis (P), does routine transport for angiography at 3 to 6 h (or up to 24 h) (I), compared with only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (C), change death, intracranial hemorrhage, major bleeding, stroke, reinfarction (O)?	Michelle Welsford, Robert O'Connor
		ACS 335	Prehospital ADP-receptor antagonists in STEMI	Among adult patients with suspected STEMI outside of the hospital (P), does prehospital administration of an ADP-receptor antagonist (clopidogrel, prasugrel, or ticagrelor) in addition to usual therapy (I), compared with administration of an ADP-receptor antagonist in-hospital (C), change death, intracranial hemorrhage, revascularization, stroke, major bleeding, reinfarction (O)?	Karen Woolfrey, Daniel Pichel

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		ACS 336	Prehospital ECG	Among adult patients with suspected STEMI outside of a hospital (P), does prehospital 12-lead ECG with transmission or notification (I), compared with no ECG or no transmission/notification (C), change death, or time to treatment (first medical contact-to-balloon time, first medical contact-to-needle time, door-to-balloon time, door-to-needle time) (O)?	Michelle Welsford, Abdulaziz Alali
		ACS 337	Delayed PCI versus fibrinolysis stratified by time from symptoms	Among patients with STEMI stratified by time from symptom onset to presentation when fibrinolysis is readily available (P), does delayed PCI (I), compared with fibrinolysis (C), change mortality, reinfarction, major bleeding, intracranial hemorrhage (O)?	Anthony Scott, Hiroshi Nonogi
		ACS 338	Prehospital fibrinolysis versus ED fibrinolysis	Among adults who are suspected of having STEMI outside of a hospital (P), does prehospital fibrinolysis (I), compared with in-hospital fibrinolysis(C), change death, intracranial hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?	Chris Ghaemmaghami, Darren Walters
		ACS 340	PCI after ROSC with ST elevation	Among adult patients with ROSC after cardiac arrest with evidence of ST elevation on ECG (P), does emergency cardiac catheterization laboratory evaluation* (I), compared with cardiac catheterization later in the hospital stay or no catheterization (C), change hospital mortality and neurologically favorable survival (O)?	Darren Walters, Chris Ghaemmaghami
		ACS 341	Prehospital triage to PCI center versus prehospital fibrinolysis	Among adult patients with suspected STEMI outside of a hospital (P), does direct triage and transport to a PCI center (I), compared with prehospital fibrinolysis (C), change death, intracranial hemorrhage, major bleeding (O)?	Michelle Welsford, Michael Longeway
		ACS 559	Computer-assisted ECG STEMI interpretation	Among adult patients with suspected STEMI outside of a hospital (P), does the use of computer-assisted ECG interpretation (I), compared with physician ECG interpretation and/or clinical diagnosis of STEMI (C), change identification of STEMI on an ECG with acceptable rates of FNs to allow earlier identification and FPs, minimizing unnecessary intervention (O)?	Chi Keong Ching, Catherine Patocka
		ACS 562	Prehospital anticoagulants versus none in STEMI	Among adult patients with suspected STEMI outside of hospital transferred for primary PCI (P), does any anticoagulant administered prehospital (e.g., bivalirudin, dalteparin, enoxaparin, fondaparinux, UFH) (I), compared with no anticoagulant administered prehospital (C), change death, intracranial hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?	Farzin Beygui, Vincent Roule
		ACS 568	Prehospital anticoagulants vs UFH for STEMI	Among adult patients with suspected STEMI outside of a hospital transferred for primary PCI (P), does any anticoagulants prehospital (e.g., bivalirudin, dalteparin, enoxaparin, fondaparinux) (I), compared with UFH pre-hospital (C), change death, ICH, revascularization, major bleeding, stroke, reinfarction (O)?	Farzin Beygui, Vincent Roule
		ACS 737	Biomarkers to rule out ACS	In patients presenting to the ED with chest pain suspected to be of cardiac etiology (P), does a negative troponin test at presentation and 1, 2, 3, and 6 h (I), compared with a positive test (C), exclude the diagnosis of ACS (O)?	Robert O'Connor, Michelle Welsford
		ACS 779	ED fibrinolysis and routine early angiography versus transport for PCI	Among adult patients with STEMI in the ED of a non–PCI-capable hospital (P), does immediate in-hospital fibrinolysis and routine transfer for angiography at 3 to 6 h (or up to 24 h) (I), compared with transfer to a PCI center (C), change 30-day mortality, stroke, major bleeding, reinfarction (O)?	Nikolaos Nikolaou, Farzin Beygui
		ACS 873	Prehospital STEMI activation of the catheterization laboratory	Among adult patients with suspected STEMI outside of a hospital (P), does prehospital activation of catheterization laboratory (I), compared with no prehospital activation of the catheterization laboratory (C), change mortality, major bleeding, stroke, reinfarction (O)?	Karen Woolfrey, Daniel Pichel
		ACS 882	ED fibrinolysis and immediate PCI versus immediate PCI alone	Among adults who are having STEMI in the ED (P), does fibrinolytic administration combined with immediate PCI (I), compared with immediate PCI alone (C), change death, intracranial hemorrhage, reinfarction, urgent target vessel revascularization, major bleeding (O)?	Hiroshi Nonogi, Anthony Scott
		ACS 884	Non-physician STEMI ECG interpretation	Among adult patients with suspected STEMI outside of a hospital (P), do nonphysicians (e.g., nurses and paramedics) (I), compared with physicians (C), change identification of STEMI on an ECG with acceptable rates of FNs to allow earlier identification and FPs, minimizing unnecessary angiography (O)?	Chi Keong Ching, Catherine Patocka

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		ACS 885	PCI after ROSC without ST elevation	Among adult patients with ROSC after cardiac arrest without evidence of ST elevation on ECG (P), does emergency cardiac catheterization laboratory evaluation (I), compared with cardiac catheterization later in the hospital stay or no catheterization (C), change hospital mortality and neurologically favorable survival (O)?	Chris Ghaemmaghami, Darren Walters
		ACS 887	Supplementary oxygen in ACS	Among adult patients with suspected ACS and normal oxygen saturation in any setting (prehospital, emergency, or in-hospital) (P), does withholding oxygen (I), compared with routine supplementary oxygen (C), change death, infarct size, chest pain resolution, ECG resolution (O)?	Anthony Scott, Anthony Seto
Part 6	Peds	Peds 387	Post-ROSC TTM	Among infants and children who are experiencing ROSC after cardiac arrest in any setting (P), does the use of TTM (e.g., therapeutic hypothermia) (I), compared with the use of normothermia (C), change survival to hospital discharge, ICU LOS (O)?	Ian Maconochie, Mark Coulthard
		Peds 394	Chest compression depth	In infants and children receiving chest compressions (in or out of hospital) (P), does the use of any specific chest compression depth (I), compared with the depth specified in the current treatment algorithm (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, complication rate, or intermediate physiological endpoints (O)?	Gabrielle Nuthall, Fernanda Sá
		Peds 397	Pediatric METs and RRTs	For infants and children in the in-hospital setting (P), does the use of pediatric METs/RRTs (I), compared with not using METs/RRTs (C), change cardiac or pulmonary arrest frequency outside of the intensive care unit (ICU), overall hospital mortality (O)?	Kee Chong Ng, Dianne Atkins
		Peds 405	Energy doses for defibrillation	Among infants and children who are in VF or pVT in any setting (P), does a specific energy dose or regimen of energy doses for the initial or subsequent defibrillation attempt(s) (I), compared with 2 to 4 J kg^{-1} (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; ROSC; termination of arrhythmia (O)?	Robert Bingham, Stuart Dalziel
		Peds 407	ECPR for IHCA	In infants and children with IHCA (P), does the use of ECMO for resuscitation, also called ECPR (I), when compared with conventional resuscitative treatment (CPR without the use of ECMO) (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, or survival to intensive care discharge (O)?	Anne-Marie Guerguerian, Ericka Fink
		Peds 414	Chest compression–only CPR versus conventional CPR	Among infants and children who are in cardiac arrest in any setting (P), does compression-only CPR (I), compared with the use of conventional CPR (C), change neurologically intact survival at 1 year, survival to hospital discharge, improved ICU LOS, neurologically intact survival at 30 days (O)?	Jonathan Duff, Dominique Biarent
		Peds 424	Vasopressor use during cardiac arrest	Among infants and children in cardiac arrest (P), does the use of no vasopressor (epinephrine, vasopressin, combination of vasopressors) (I), compared with any use of vasopressors (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, ROSC (O)?	Vinay Nadkarni, David Kloeck
		Peds 544	Post-ROSC Pao_2	Among infants and children with ROSC after cardiac arrest (in- or out-of-hospital setting) (P), does the use of a targeted Pao_2 strategy (I), compared with a strategy of no targeted Pao_2 (C), change ICU LOS, survival to 180 days with good neurologic outcome, survival to hospital discharge, survival to ICU discharge, survival to 6 months (O)?	Allan de Caen, Amelia Reis
		Peds 545	Fluid resuscitation in septic shock	Among infants and children who are in septic shock in any setting (P), does the use of restricted volumes of resuscitation fluid (I1) when compared with nonrestricted volumes (C1), or the use of noncrystalloid fluids (I2) when compared with crystalloid fluids (C2), change survival to hospital discharge, need for mechanical ventilation or vasopressor support, complications, time to resolution of shock, hospital length of stay (LOS), ventilator-free days, total intravenous (IV) fluids administered (O)?	Richard Aickin, Peter Meaney
		Peds 709	Sequence of chest compressions and ventilations: C–A–B versus A–B–C	Among infants and children who are in cardiac arrest in any setting (P), does the use of a circulation-airway-breathing approach to initial management (I), compared with the use of an airway-breathing-circulation approach to initial management (C), change ROSC, survival to hospital discharge, survival to 180 days with good neurologic outcome, time to first compressions (O)?	Naoki Shimizu, Christoph Eich

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		Peds 813	Post-ROSC predictive factors	Among infants and children with return of circulation (P), does the presence of any specific factors (I), compared with the absence of those factors (C), change survival to 180 days with good neurologic outcome; survival to 60 days with good neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to 30 days with good neurologic outcome; survival to hospital discharge with good neurologic outcome (O)?	Thomaz Bittencourt Couto, Marc Berg
		Peds 814	Intra-arrest prognostic factors	Among infants and children during cardiac arrest (P), does the presence of any specific intra-arrest prognostic factors (I), compared with the absence of these factors (C), change survival to 180 days with good neurologic outcome; survival to 60 days with good neurologic outcome; survival to hospital discharge with good neurologic outcome; survival to 30 days with good neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Audrey Shibata, Steve Schexnayder
		Peds 815	Post-ROSC ventilation: $Paco_2$ goals	Among infants and children with ROSC after cardiac arrest in any setting (P), does ventilation to a specific $Paco_2$ target (I), compared with ventilation to no specific $Paco_2$ target (C), change survival with favorable neurologic outcome, survival to 180 days with good neurologic outcome, survival to 30 days with good neurologic outcome, the likelihood of a good quality of life after discharge from the hospital, survival to hospital discharge, survival to hospital discharge, survival to 30 days, survival to 60 days, survival to 6 months, survival to ICU discharge (O)?	Javier Urbano, Janice Tijssen
		Peds 818	PEWS	For infants and children in the in-hospital setting (P), does the use of a pediatric early warning score (I), compared with not using a pediatric early warning score (C), change overall hospital mortality, Cardiac arrest frequency outside of the ICU (O)?	Alexis Topjian, Antonio Rodriguez-Nunez
		Peds 819	Prearrest care of pediatric dilated cardiomyopathy or myocarditis	For infants and children with myocarditis or dilated cardiomyopathy and impending cardiac arrest (P), does a specific approach (I), compared with the usual management of shock or cardiac arrest (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; cardiac arrest frequency; ROSC (O)?	Graeme MacLaren, Ravi Thiagarajan
		Peds 820	Post-ROSC fluid/inotropes	In infants and children after ROSC (P), does the use of parenteral fluids and inotropes and/or vasopressors to maintain targeted measures of perfusion such as blood pressure (I), as compared with not using these interventions (C), change patient satisfaction; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; harm to patient (O)?	Melissa Parker, Takanari Ikeyama
		Peds 821	Atropine for emergency intubation	In infants and children requiring emergency tracheal intubation (P), does the use of atropine as a premedication (I), compared with not using atropine (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 90 days, 180 days, and/or 1 year after event; the incidence of cardiac arrest; survival to hospital discharge; the incidence of peri-intubation shock or arrhythmias (O)?	Gene Ong, Jos Bruinenberg
		Peds 822	Post-ROSC EEG	For infants and children who have had cardiac arrests in the in-hospital or out-of-hospital setting (P), does any use of neuroelectrophysiology information (EEG) (I), compared with none (C), predict survival at 1 year with good neurologic outcome, survival to 180 days with good neurologic outcome, survival to 60 days with good neurologic outcome, survival to 6 months, survival to 30 days with good neurologic outcome, survival to hospital discharge with good neurologic outcome, survival with favorable neurologic outcome, survival to hospital discharge (O)?	Stuart Friess, Corsino Rey
		Peds 825	Amiodarone versus lidocaine for shock-resistant VF or pVT	In children and infants with shock-refractory VF or pVT (P), does amiodarone (I), compared with lidocaine (C), change survival to hospital discharge, ROSC, recurrence of VF, termination of arrhythmia, risk of complications (e.g., need for tube change, airway injury, aspiration) (O)?	Dianne Atkins, Mary McBride, Brad Marino
		Peds 826	Invasive blood pressure monitoring during CPR	In children and infants undergoing CPR (P), does using invasive hemodynamic monitoring to titrate to a specific systolic/diastolic blood pressure (I), compared with not using invasive hemodynamic monitoring to titrate to a specific systolic/diastolic blood pressure (C), change survival to hospital discharge, 60 days after event, 180 days after event with favorable neurologic outcome, or the likelihood of ROSC or survival to hospital discharge (O)?	Tia Raymond, Jonathan Egan

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		Peds 827	$ETCO_2$ monitoring during CPR	In infants and children in cardiac arrest (P), does adjustment of chest compression technique to achieve a specific $ETCO_2$ threshold (I), compared with not using $ETCO_2$ to adjust chest compression technique (C), change survival to 180 days with good neurologic outcome, the likelihood of survival to discharge, ROSC (O)?	Remigio Veliz, Monica Kleinman
Part 7	NRP	NRP 589	Temperature maintenance in the delivery room—prognosis	In nonasphyxiated babies at birth (P), does maintenance of normothermia (core temperature 36.5 °C or greater and 37.5 °C or less) from delivery to admission (I), compared with hypothermia (less than 36 °C) or hyperthermia (greater than 37.5 °C) (C), change survival to hospital discharge, respiratory distress, survival to admission, hypoglycemia, intracranial hemorrhage, or infection rate (O)?	Jonathan Wyllie, Jeffrey Perlman
		NRP 590	CPAP and IPPV—intervention	In spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room (P), does the use of CPAP (I), compared with intubation and IPPV (C), improve outcome (O)?	Tetsuya Isayama, Ben Stenson
		NRP 599	Maintaining infant temperature during delivery room resuscitation—intervention	Among preterm neonates who are under radiant warmers in the hospital delivery room (P), does increased room temperature, thermal mattress, or another intervention (I), compared with plastic wraps alone (C), reduce hypothermia (less than 36 °C) on admission to neonatal intensive care unit (NICU) (O)?	Daniele Trevisanuto, Maria Fernanda de Almeida
		NRP 605	Thumb versus 2-finger techniques for chest compression—intervention	In neonates receiving cardiac compressions (P), does the use of a 2-thumb technique (I), compared with a 2-finger technique (C), result in return of spontaneous circulation (ROSC), improved neurologic outcomes, improved survival, improved perfusion and gas exchange during CPR, and decreased compressor fatigue (O)?	Myra Wyckoff, Lindsay Mildenhall
		NRP 618	Laryngeal mask airway—intervention	In newborn infants at near term (greater than 34 weeks) or term who have indications for intermittent positive pressure for resuscitation (P), does use of a laryngeal mask as a primary or secondary device (I), compared with mask ventilation or endotracheal intubation (C), improve response to resuscitation or change outcome (O), including indicators of neonatal brain injury, achieving stable vital signs, increasing Apgar scores, long-term outcomes, reducing the need for subsequent intubation, or neonatal morbidity and mortality?	Edgardo Szyld, Enrique Udaeta
		NRP 734	Limited-resource–induced hypothermia—intervention	In term infants with moderate/severe hypoxic-ischemic encephalopathy managed in resource-limited countries (P), does therapeutic hypothermia to core temperature of approximately 33.5 °C for 72 h delivered by passive hypothermia and/or ice packs (I), versus standard therapy (C), improve the rates of death, neurodevelopmental impairments at 18 months to 2 years (O)?	Jeffrey Perlman
		NRP 738	Oxygen delivery during CPR (neonatal)—intervention	In neonates receiving cardiac compressions (P), does 100% O_2 as the ventilation gas (I), compared with lower concentrations of oxygen (C), increase survival rates, improve neurologic outcomes, decrease time to ROSC, or decrease oxidative injury (O)?	Myra Wyckoff, Lindsay Mildenhall
		NRP 787	Delayed cord clamping in preterm infants requiring resuscitation (intervention)	In preterm infants, including those who received resuscitation (P), does delayed cord clamping (greater than 30 s) (I), compared with immediate cord clamping (C), improve survival, long-term developmental outcome, cardiovascular stability, occurrence of intraventricular hemorrhage (IVH), necrotizing enterocolitis, temperature on admission to a newborn area, and hyperbilirubinemia (O)?	Masanori Tamura, Susan Niermeyer
		NRP 793	Maintaining infant temperature during delivery room resuscitation—intervention	In newborn infants (greater than 30 weeks of gestation) in low-resource settings during and/or after resuscitation/stabilization (P), does drying and skin-to-skin contact or covering with plastic (I), compared with drying and no skin-to-skin or use of radiant warmer or incubator (C), change body temperature (O)?	Sithembiso Velaphi, Hege Ersdal, Nalini Singhal
		NRP 804	Babies born to mothers who are hypothermic or hyperthermic in labor—prognosis	In newborn babies (P), does maternal hypothermia or hyperthermia in labor (I), versus normal maternal temperature (C), result in adverse neonatal effects (O)? Outcomes include mortality, neonatal seizures, and adverse neurologic states.	Henry Lee, Marilyn Escobedo
		NRP 805	Delivery room assessment for less than 25 weeks and prognostic score	In extremely preterm infants (less than 25 weeks) (P), does delivery room assessment with a prognostic score (I), compared with gestational age assessment alone (C), change survival to 18 to 22 months (O)?	Steven Ringer, Steve Byrne

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		NRP 806	Newborn infants who receive PPV for resuscitation, and use of a device to assess respiratory function—diagnostic	In newborn infants who receive PPV for resuscitation (P), does use of a device to assess respiratory function with or without pressure monitoring (I), compared with no device (C), change survival to hospital discharge with good neurologic outcome, IVH, time to heart rate greater than 100/min, bronchopulmonary dysplasia, pneumothorax (O)?	Helen Liley, Vishal Kapadia
		NRP 809	Sustained inflations—intervention	In term and preterm newborn infants who do not establish spontaneous respiration at birth (P), does administration of 1 or more pressure-limited sustained lung inflations (I), compared with intermittent PPV with short inspiratory times (C), change Apgar score at 5 min, establishment of FRC, requirement for mechanical ventilation in first 72 h, time to heart rate greater than 100/min, rate of tracheal intubation, overall mortality (O)?	Jane McGowan, David Boyle
		NRP 849	Umbilical cord milking—intervention	In very preterm infants (28 weeks or less) (P), does umbilical cord milking (I), in comparison with immediate umbilical cord clamping (C), affect death, neurodevelopmental outcome at 2 to 3 years, cardiovascular stability, i.e., need for pressors, need for fluid bolus, initial mean blood pressure, IVH (any grade, severe grade), temperature on admission, hematologic indices (initial hemoglobin, need for transfusion), hyperbilirubinemia, need for phototherapy, or need for exchange transfusion (O)?	Marya Strand, Takahiro Sugiura
		NRP 858	Warming of hypothermic newborns—intervention	In newborns who are hypothermic (temperature less than 36.0 °C) on admission (P), does rapid rewarming (I), compared with slow rewarming (C), change mortality rate, short and long-term neurologic outcome, hemorrhage, episodes of apnea and hypoglycemia, or need for respiratory support (O)?	Cheo Yeo, Daniele Trevisanuto
		NRP 859	Resuscitation training frequency	For course participants including (a) trainees and (b) practitioners (P), does frequent training (I), compared with less frequent training (annual or biennial) (C), change all levels of education or practice, prevention of adverse outcomes, overall mortality, scenario performance, medical knowledge, psychomotor performance, provider confidence, course satisfaction (O)?	Chris Colby, Khalid Aziz
		NRP 860	Predicting death or disability of newborns of greater than 34 weeks based on Apgar and/or absence of breathing—prognosis	In newborn infants of greater than 34 weeks of gestation, receiving PPV at birth in settings where resources are limited (P), does presence of heart rate with no spontaneous breathing or Apgar scores of 1 to 3 at greater than 5 min predict mortality or morbidity or cerebral palsy (O)?	Sithembiso Velaphi, Nalini Singhal, Hege Ersdal
		NRP 862	Use of feedback CPR devices for neonatal Cardiac arrest—diagnostic	In asystolic/bradycardic neonates receiving cardiac compressions (P), does the use of feedback devices such as end-tidal carbon dioxide ($ETCO_2$) monitors, pulse oximeters, or automated compression feedback devices (I), compared with clinical assessments of compression efficacy (C), decrease hands-off time, decrease time to ROSC, improve perfusion, increase survival rates, or improve neurologic outcomes (O)?	Lindsay Mildenhall, Takahiro Sugiura
		NRP 864	Oxygen concentration for resuscitating premature newborns—intervention	Among preterm newborns (less than 37 weeks of gestation) who receive PPV in the delivery room (P), does the use of high O_2 (50–100%) as the ventilation gas (I), compared with low concentrations of O_2 (21–30%) (C), decrease mortality, decrease bronchopulmonary dysplasia, decrease retinopathy, decrease IVH (O)?	Gary Weiner, Douglas McMillan
		NRP 865	Intubation and tracheal suctioning in nonvigorous infants born though MSAF versus no intubation for tracheal suctioning—intervention	In nonvigorous infants at birth born through MSAF (P), does tracheal intubation for suctioning (I), compared with no tracheal intubation (C), reduce meconium syndrome or prevent death (O)?	Sithembiso Velaphi, Jeffrey Perlman
		NRP 867	Neonatal resuscitation instructors	In neonatal resuscitation instructors (P), does formal training on specific aspects of how to facilitate learning (I), compared with generic or nonspecific training (C), change clinical outcome, improve all levels of education or practice (O)?	Helen Liley, Louis Halamek
		NRP 870	T-piece resuscitator and self-inflating bag—intervention	In newborns (preterm and term) receiving ventilation (PPV) during resuscitation (P), does using a T-piece resuscitator with PEEP (I), compared with using a self-inflating bag without PEEP (C), achieve spontaneous breathing sooner and/or reduce the incidence of pneumothorax, bronchopulmonary dysplasia, and mortality (O)?	Yacov Rabi, Han Suk Kim

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		NRP 895	Chest compression ratio—intervention	In neonates receiving cardiac compressions (P), do other ratios (5:1, 9:3, 15:2, synchronous, etc) (I), compared with 3:1 compressions to ventilations (C), increase survival rates, improve neurologic outcomes, improve perfusion and gas exchange during CPR, decrease time to ROSC, decrease tissue injury, or decrease compressor fatigue (O)?	Qi Feng, Myra Wyckoff
		NRP 896	Apgar score of 0 for 10 min or longer—prognosis	In infants with a gestational age of 36 weeks or greater and an Apgar score of 0 for 10 min or longer, despite ongoing resuscitation (P), what is the rate of survival to NICU admission and death or neurocognitive impairment at 18 to 22 months (O)?	Ruth Guinsburg, Jane McGowan
		NRP 897	Outcomes for PEEP versus No PEEP in the delivery room—intervention	In preterm/term newborn infants who do not establish respiration at birth (P), does the use of PEEP as part of the initial ventilation strategy (I), compared with no PEEP (C), improve Apgar score at 5 min, intubation in the delivery room, chest compressions in the delivery room, heart rate greater than 100 min^{-1} by 2 min of life, time for heart rate to rise above 100 min^{-1}, air leaks, oxygen saturation/oxygenation, FIO_2 in the delivery room, mechanical ventilation in the first 72 h, bronchopulmonary dysplasia, survival to discharge (O)?	Yacov Rabi, Colm O'Donnell
		NRP 898	ECG/EKG (I) in comparison to oximetry or auscultation for the detection of heart rate	In babies requiring resuscitation (P), does electrocardiography (ECG/EKG) (I), compared with oximetry or auscultation (C), measure heart rate faster and more accurately (O)?	Marya Strand, Hege Ersdal
Part 8	EIT	EIT 623	High-fidelity manikins in training	Among participants undertaking ALS training in an education setting (P), does the use of high-fidelity manikins (I), compared with the use of low-fidelity manikins (C), change patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Adam Cheng, Andy Lockey
		EIT 624	Cardiac arrest centers	Adults and children in OHCA (P), does transport to a specialist cardiac arrest center (I), compared with no directed transport (C), change neurologically intact survival at 30 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, hospital admission, ROSC (O)?	Judith Finn, Dion Stub
		EIT 628	Timing for BLS retraining	Among students who are taking BLS courses (P), does any specific interval for update or retraining (I), compared with standard practice (i.e., 12 or 24 monthly) (C), change patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Taku Iwami, Theresa Olasveengen
		EIT 631	Team and leadership training	Among students who are taking ALS courses in an educational setting (P), does inclusion of specific leadership or team training (I), compared with no such specific training (C), change patient outcomes, bystander CPR performance, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Koen Monsieurs, Elaine Gilfoyle
		EIT 633	Timing for advanced resuscitation training	Among students who are taking ALS courses in an educational setting (P), does any specific interval for update or retraining (I), compared with standard practice (i.e., 12 or 24 monthly) (C), change/improve patient outcomes, skill performance in actual resuscitations, skill performance between course completion and 1 year; skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Matthew Ma, Chih-wei Yang, Farhan Bhanji
		EIT 634	Resource-limited settings	Among students who are taking BLS or ALS courses in a resource-limited educational setting (P), does any educational approach (I), compared with other approaches (C), change clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, cognitive knowledge (O)?	David Kloeck, Traci Wolbrink
		EIT 637	Precourse preparation for advanced life support courses	Among students who are taking ALS courses in an educational setting (P), does inclusion of specific precourse preparation (e.g., eLearning and pretesting) (I), compared with no such preparation (C), change survival rates, skill performance in actual resuscitations, cognitive knowledge, skill performance at course conclusion, skill performance at 1 year, skill performance at time between course conclusion and 1 year (O)?	Andy Lockey, Mary Mancini, John Billi
		EIT 638	Medical emergency teams for adults	Among adults who are at risk for cardiac or respiratory arrest in the hospital (P), does use of the Early Warning Score (EWS)/response teams/MET systems (I), compared with no such responses (C), change survival to hospital discharge, in-hospital incidence of cardiac/respiratory arrest, survival to hospital discharge with good neurologic outcome (O)?	Mary Mancini, Robert Frengley

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		EIT 640	Measuring performance of resuscitation systems	Among resuscitation systems caring for patients in cardiac arrest in any setting (P), does a performance measurement system (I), compared with no system (C), change survival to hospital discharge, skill performance in actual resuscitations, survival to admission, system-level variables (O)?	Blair Bigham, Robert Schultz
		EIT 641	Implementation of guidelines in communities	Within organizations that provide care for patients in cardiac arrest in any setting (P), does implementation of resuscitation guidelines (I), compared with no such use (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, bystander CPR performance, ROSC (O)?	Jon Rittenberger, Theresa Olasveengen, Patrick Ko
		EIT 645	Debriefing of resuscitation performance	Among rescuers who are caring for patients in cardiac arrest in any setting (P), does briefing or debriefing (I), compared with no briefing or debriefing (C), change survival, skill performance in actual resuscitations, improve quality of resuscitation (e.g., reduce hands-off time), cognitive knowledge (O)?	Robert Greif, Dana Edelson
		EIT 647	CPR instruction methods (self-instruction versus traditional)	Among students who are taking BLS courses in an educational setting (P), does video or computer self-instructions (I), compared with traditional instructor-led courses (C), change survival, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Ming-Ju Hsieh, Matthew Ma, Judy Young
		EIT 648	CPR feedback devices in training	Among students who are taking BLS or ALS courses in an educational setting (P), does CPR feedback device use (I), compared with no use of CPR feedback devices (C), change improve patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Joyce Yeung, Mary Ann McNeil
		EIT 649	Basic life support training for high-risk populations	For people at high risk of OHCA (P), does focused training of likely rescuers (e.g., family or caregivers) (I) compared with no such targeting (C), change survival with favorable neurologic outcome at discharge, ROSC, bystander CPR performance, number of people trained in CPR, willingness to provide CPR (O)?	Janet Bray, Marion Leary
		EIT 651	AED training methods	Among students who are taking AED courses in an educational setting (P), does any specific training intervention (I), compared with traditional lecture/practice sessions (C), change clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge, use of AEDs (O)?	Jan Breckwoldt, Henrik Fischer
		EIT 878	Social media technologies	For OHCA (P), does having a citizen CPR responder notified of the event via technology or social media (I), compared with no such notification (C), change survival to hospital discharge with good neurologic outcome, survival to hospital discharge, hospital admission, ROSC, bystander CPR rates, time to first compressions (O)?	Zuzana Triska, Steven Brooks
		EIT 881	Compression-Only CPR Training	Among communities that are caring for patients in cardiac arrest in any setting (P), does teaching compression-only CPR (I), compared with conventional CPR (C), change survival rates, bystander CPR rates, willingness to provide CPR (O)?	Jonathan Duff, Aaron Donoghue
Part 9	First aid	FA 500	Second dose of epinephrine for anaphylaxis	Among adults and children experiencing severe anaphylaxis requiring the use of epinephrine (P), does administration of a second dose of epinephrine (I), compared with administration of only 1 dose (C), change resolution of symptoms, adverse effects, complications (O)?	Athanasios Chalkias, Barbara Caracci, Emmy De Buck
		FA 503	Straightening of an angulated fracture	Among adults and children who receive first aid for an angulated long bone fracture (P), does realignment of the fracture prior to splinting (I), compared with splinting as found (C), change neurologic injury, vascular injury, splinting, pain, time to medical transportation (O)?	Ryan Fringer, Catherine Patocka
		FA 517	Recovery position	Among adults who are breathing and unresponsive outside of a hospital (P), does positioning in a lateral, side-lying, recovery position (I), compared with supine position (C), change overall mortality, need for airway management, the incidence of aspiration, the likelihood of cervical spinal injury, complications, incidence of cardiac arrest (O)?	Janel Swain, S Seitz
		FA 519	Oxygen administration for first aid	Among adults and children who exhibit symptoms or signs of shortness of breath, difficulty breathing, or hypoxemia outside of a hospital (P), does administration of supplementary oxygen (I), compared with no administration of oxygen (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; shortness of breath; time to resolution of symptoms; or therapeutic endpoints (e.g., oxygenation and ventilation) (O)?	Michael Nemeth, Chih-Hung Wang
		FA 520	Optimal position for shock	Among adults and children who receive first aid for shock (P), does positioning of the patient (I), compared with not positioning the patient (C), change overall mortality, complications, incidence of cardiac arrest, vital signs, hospital length of stay (O)?	Anthony Handley, Luis Lojero-Wheatley, Justin DeVoge

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		FA 525	First aid treatment for an open chest wound	Among adults and children who are being treated for an open chest wound outside of a hospital (P), does occlusive bandage application or occlusive device (I), compared with a nonocclusive dressing (C), change or improve survival, respiratory arrest, oxygen saturation, vital signs, the rate of cardiac and respiratory arrests, improve therapeutic endpoints (oxygenation and ventilation) (O)?	Wei-tien Chang, Kyee Han
		FA 530	Control of bleeding	Among adults and children with bleeding (P), does application of localized cold therapy, elevation of extremity, and/or application of pressure over proximal pressure points (I), compared with direct pressure alone (C), change overall mortality, hemostasis, major bleeding, complications, hospital length of stay (O)?	Richard Bradley, Jae-Hyug Woo
		FA 534	Bronchodilator use for asthma with difficulty breathing	Among adults and children in the prehospital setting who have asthma and are experiencing difficulty in breathing (P), does bronchodilator administration (I), compared with no bronchodilator administration (C), change time to resolution of symptoms, time to resumption of usual activity, complications, harm to patient, therapeutic endpoints (e.g., oxygenation and ventilation), need for advanced medical care (O)?	Andrew MacPherson, Nathan Charlton, Ian Blanchard
		FA 540	Eye chemical injury: irrigation	Among adults and children who have a chemical or other unknown substance enter the conjunctival sac (P), does irrigation with isotonic saline, balanced salt solution, or other commercial eye irrigation solutions (I), compared with irrigation with water (C), change tissue healing, functional recovery, pain, complications, time to resumption of usual activity, restoration to the preexposure condition, time to resolution of symptoms (O)?	Ralph Shenefelt, L. Kristian Arnold, Janel Swain
		FA 584	Exertional dehydration and oral rehydration	Among adults and children with exertion-related dehydration (P), does drinking oral carbohydrate-electrolyte (CE) liquids (I), compared with drinking water (C), change volume/hydration status, vital signs, development of hyperthermia, development of hyponatremia, need for advanced medical care, blood glucose, patient satisfaction (O)?	Rita Herrington, Amy Kule, Jestin Carlson
		FA 586	Aspirin for chest pain (early vs. late)	Among adults who are experiencing chest pain outside of a hospital (P), does early administration of aspirin (I), compared with later administration of aspirin (C), change cardiovascular mortality, complications, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay, chest pain resolution (O)?	Janel Swain, Thomas Evans
		FA 768	Use of a tourniquet	Among adults and children with severe external limb bleeding (P), does the application of a tourniquet (I), compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, blood loss, incidence of cardiac arrest (O)?	Jan Jensen, Michael Reilly
		FA 769	Hemostatic dressings	In patients with severe external bleeding (P), does the application of topical hemostatic dressings plus standard first aid (I), compared with standard first aid alone (C), change overall mortality, vital signs, hemostasis, complications, blood loss, major bleeding, incidence of cardiac arrest (O)?	Jan Jensen, Richard Bradley
		FA 770	Cooling of burns	Among adults and children with thermal injuries (P), does active cooling of burns (I), compared with passive cooling (C), change pain, complications, wound healing, need for advanced medical care, patient satisfaction, rates of fasciotomy, depth or breadth of burn (O)?	Natalie Hood, Nathan Charlton
		FA 771	Wet compared with dry burn dressings	Among adults and children with thermal injuries (P), does the use of a wet dressing (I), compared with dry dressing (C), change complications, pain, tissue healing, need for advanced medical care, patient satisfaction, rates of fasciotomy (O)?	Emmy De Buck, Ian Blanchard
		FA 772	Cervical spinal motion restriction	Among adults and children with suspected blunt traumatic cervical spinal injury (P), does cervical spinal motion restriction (I), compared with no cervical spinal motion restriction (C), change neurologic injury, complications, overall mortality, pain, patient comfort, movement of the spine, hospital length of stay (O)?	Tessa Dieltjens, Jeff Woodin
		FA 773	First aid training	Among adults and children receiving first aid (P), does care from a trained first aid provider (I), compared with care from an untrained person (C), change increase survival rates, recognition of acute injury or illness, prevent further illness or injury (i.e., harm), time to resolution of injury, the likelihood of harm (e.g., infection), time to resolution of symptoms (O)?	Jeffrey Pellegrino, Danita Koehler
		FA 794	Dental avulsion	Among adults and children with an avulsed permanent tooth (P), does storage of the tooth in any solution prior to replantation (I), compared with storage in whole milk or the patient's saliva (C), change success of reimplantation, tooth survival or viability, infection rate, pain, malfunction (eating, speech), color of the tooth (O)?	Nele Pauwels, Bryan Kitch
		FA 795	Hypoglycemia treatment	Among adults and children with symptomatic hypoglycemia (P), does administration of dietary forms of sugar (I), compared with standard dose (15–20 g) of glucose tablets (C), change time to resolution of symptoms, risk of complications (e.g., aspiration), blood glucose, hypoglycemia, hospital length of stay (O)?	Jestin Carlson, Susanne Schunder-Tatzber

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Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
		FA 799	Concussion	Among adults and children with suspected head injury without loss of consciousness (P), does use of a simple concussion scoring system (I), compared with standard first aid assessment without a scoring system (C), change time to recognition of the deteriorating patient, the likelihood of a poor neurologic outcome, survival to 30 days with good neurologic outcome, need for advanced medical care, time to medical transportation, or likelihood of differentiating between minor head contusion and more serious concussion (O)?	Richard Rusk, Christina Gruber
		FA 801	Stroke recognition	Among adults with suspected acute stroke (P), does the use of a rapid stroke scoring system or scale (I), compared with standard first aid assessment (C), change time to treatment (e.g., door to drug), recognition of acute injury or illness, discharge with favorable neurologic status, survival with favorable neurologic outcome, or increased public/layperson recognition of stroke signs (O)?	Pascal Cassan, Jeffrey Ferguson, Daniel Meyran
		FA 871	Aspirin for chest pain: administration	Among adults experiencing chest pain due to suspected MI (P), does administration of aspirin (I), compared with no administration of aspirin (C), change cardiovascular mortality, complications, adverse effects, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay (O)?	Thomas Evans, Janel Swain

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Part 2: Evidence evaluation and management of conflicts of interest 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆,☆☆

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> Facts are stubborn things; and whatever may be our wishes, our inclinations, or the dictates of our passions, they cannot alter the state of facts and evidence.—John Adams, second President of the United States

Introduction

The international resuscitation community, under the guidance of the International Liaison Committee on Resuscitation (ILCOR), has continued its process to identify and summarize the published resuscitation science in the documents known as the ILCOR Consensus on Science with Treatment Recommendations (CoSTR). The accompanying articles represent the culmination of many years work, where a total of 250 evidence reviewers from 39 countries completed 165 systematic reviews on resuscitation related questions.

Process before 2015

The processes previously used by ILCOR in the development of their CoSTR were specifically tailored to the complex needs of resuscitation science. At the time that the evidence evaluation was undertaken for the 2010 publication, there were still no other processes which could deal with the complexity of literature that we need to evaluate: from randomized controlled trials to case series, and from mathematical models to animal studies. The 2010 evidence evaluation process required completion of an electronic worksheet,[1] that included a table, summarizing the evidence addressing individual questions. It included 3 options for the direction of support (supportive, neutral and opposing), 5 Levels of Evidence, and a quality assessment of the individual studies (good, fair or poor).[2,3]

Improvements for the 2015 process

When developing the process to be adopted for the 2015 CoSTR, ILCOR made a commitment to use the best available methodological tools to conduct its evaluation of the published resuscitation literature. To this end, ILCOR agreed to perform systematic reviews based on the recommendations of the Institute of Medicine of the

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National Academies,[4] and to use the methodological approach proposed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group.[5]

In addition, ILCOR leveraged technologic innovations, with the support of science and technology specialists at the American Heart Association, to build a Web-based information system that would support the creation of scientific statements and recommendations that adhere to the GRADE methodology. An online platform known as the Scientific Evaluation and Evidence Review System (SEERS: www.ilcor.org/seers) was developed to guide the taskforces and their individual evidence reviewers, and enabled those responsible for tasks to better monitor progress in real time and receive assignments as indicated by the progression in work flow. One key feature of the SEERS system is the ability to open all components of the process to the public for comments and suggestions. SEERS functions as the repository of all the information and reviews processed since 2012 by the task forces, and Evidence Reviewers and discussions at the C2015 Conference. It remains the home for the 15 GRADE tutorials and 13 GRADE "ask the expert" seminars, as well as housing the training videos produced by AHA staff.

The GRADE process

Why introduce the GRADE process?

The methodological approach proposed by the GRADE Working Group has been developed over the past decade by key health professionals, researchers, and guideline developers in an attempt to provide a consistent and transparent process for use in guideline development.[6] It provides guidance for the rating of quality of evidence and the grading of strength of recommendations in health care. It is now widely used in the guideline development processes throughout the world including by organizations such as the Cochrane Collaboration, the World Health Organization, the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the American Thoracic Society.[7] The GRADE approach has been refined to the point that it is now able to incorporate the variety of studies that make up the body of resuscitation science.

What is different about the GRADE process?

The GRADE process outlines a systematic and explicit consideration of study design, study quality, consistency, and directness of evidence to be used in judgments about the quality of evidence for each outcome of each specific question. The GRADE process is, therefore, much more outcome-centric than our previous processes. GRADE considers evidence as a function of the totality of data that informs a prioritized outcome across studies, as opposed to information evaluated at the level of the individual study. The GRADE approach facilitates appropriate consideration of each outcome when grading overall quality of evidence and strength of recommendations, and it reduces the likelihood of mislabeling the overall quality of evidence when evidence for a critical outcome is lacking.[6]

The 2015 ILCOR evidence evaluation process

The 2015 ILCOR evidence evaluation followed a complex but systematic process. In general, the steps followed are consistent with those outlined by the Institute of Medicine.[4] During the development of this process, a transition was made to a more complete online process, using a combination of existing and newly developed tools. The steps in the evidence review process are outlined in Table 1.

Table 1
Summary outline of the evidence evaluation process for the ILCOR 2015 CoSTR.

- Task forces select, prioritize, and refine questions (using PICO format)
- Task forces allocate level of importance to individual outcomes.
- Task forces allocate PICO question to task force question owner and 2 evidence reviewers
- Task force works with information specialists to develop and fine-tune search strategies (for PubMed, Embase, and Cochrane)
- Public invited to comment on PICO question wording, as well as the proposed search strategies
- Revised search strategies used to search databases (PubMed, Embase, and Cochrane)
- The articles identified by the search are screened by the evidence reviewers using inclusion and exclusion criteria
- Evidence reviewers agree on final list of studies to include
- Evidence reviewers agree on assessment of bias for individual studies
- GRADE evidence profile table created
- Draft consensus on science statements and treatment recommendations created
- Public invited to comment on draft consensus on science and treatment recommendations
- Detailed iterative review of consensus on science and treatment recommendations to create final version
- Peer review of final CoSTR document

CoSTR indicates Consensus on Science with Treatment Recommendations; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; ILCOR, International Liaison Committee on Resuscitation; and PICO, Population, Intervention, Comparator, Outcome.

Task forces, task force question owners, evidence reviewers, evidence evaluation specialist/GRADE/methodology experts

Seven task forces evaluated the resuscitation literature: Acute Coronary Syndromes; Advanced Life Support; Basic Life Support; Education, Implementation, and Teams; First Aid; Neonatal Resuscitation; and Pediatric Life Support. Each task force appoints Task Force Question Owners and Evidence Reviewers to oversee the evidence evaluation process for each question. The task forces were supported by online resources[5,8] as well as telephone, face-to-face, and Web-based educational sessions provided by a GRADE methodologist and an evidence evaluation expert, with advice from a specifically formed ILCOR Methods Group.

Components of the 2015 ILCOR systematic reviews

The evidence evaluation follows a standard format. The key components of this format are described in detail below.

Agree on PICO-formatted question and prioritizing outcomes

Each task force identified the potential questions to be addressed on the basis of known knowledge gaps, priorities as part of previous recommendations, current issues raised by individual resuscitation councils, the known published literature, and areas of controversy. The task forces were then required to prioritize these questions for formal review, and to develop agreed-upon wording by using the PICO (population, intervention, comparator, outcome) format.[9]

As part of the PICO question development, the GRADE process required designation of up to 7 key outcomes for each PICO question. The task force then allocated a score for each outcome on a scale from 1 to 9.[10] Critical outcomes were scored 7 to 9, important outcomes were scored 4 to 6, and those of limited importance were scored 1 to 3. The types of outcomes used (and their possible relevant importance score) included neurologically intact survival (e.g., critical 9), discharge from hospital alive (eg, critical 8), and return of spontaneous circulation (e.g., important 6).

The explicit preference of this process was that if evidence was lacking for a key outcome, this was acknowledged rather than excluding that outcome.

Develop search strategy

Detailed strategies to search the published literature were developed in conjunction with information specialists. Initial draft search strategies were developed for each of 3 databases: PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). These strategies were developed to optimize the sensitivity and specificity of the search and then refined on the basis of feedback from the resuscitation community and public comment. The articles identified by the final search strategies were combined into a single database for more detailed analysis by the evidence reviewers.

Identify articles for inclusion and exclusion

Each evidence reviewer used the SEERS online process to screen the identified articles for further review. The initial screening, based on formal inclusion and exclusion criteria, was performed by using each article's title and abstract, and then a review of the full text of the article was performed if needed. Specific inclusion and exclusion criteria varied according to the individual PICO questions, but generic criteria included such items as a requirement for the study to be published in the peer-reviewed literature (not just in abstract form) and to specifically address the individual components of the PICO question. The evidence reviewers were also asked to check for studies that may have been missed in the initial search, by reviewing the references of the identified studies, and performing a forward search on key studies (e.g., by the use of "cited by" in PubMed).

Bias assessment of individual studies

The Cochrane Collaboration's tool was used for assessing the risk of bias for randomised controlled trials.[11] The GRADE tool was used to assess the risk of bias of observational studies (for both therapy and prognosis questions) (Table 2).[12,13]

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool was used for assessing risk of bias in studies of diagnostic accuracy.[14] If there were significant differences in the risks of bias for different outcomes, evidence reviewers were instructed to create a separate row in the table for each outcome. Individual studies can be allocated an overall "low" risk of bias if most or all key criteria listed above are met, and any violations are not crucial. Individual studies that have a crucial limitation in 1 criterion or some limitations in multiple criteria, sufficient to lower the confidence in the estimate of effect, are considered at "moderate" risk of bias. Individual studies that have a crucial limitation in 1 or more criteria, sufficient to substantially lower the confidence in the estimate of effect, are considered at "high" risk of bias.

The two (or more) individual evidence reviewers for each question created a reconciled (agreed) risk of bias assessment for each of the included studies, which was recorded by using an electronic template (Fig. 1).

GRADE evidence profile tables

The GRADE working group has developed validated evidence tables known as *evidence profile tables*. These tables incorporate information on the quality of evidence for each outcome-dedicated row and provide information on effect size and precision, and they can provide information about varying effects across a variety of baseline risks.[15] The evaluation of the evidence supporting each outcome incorporates the information from study design and the five core GRADE domains: risk of bias, imprecision, indirectness, inconsistency, and other considerations (e.g., publication bias).[5] An overall assessment is then made of the quality of evidence to support each outcome (high, moderate, low, or very low).

Table 2
Bias assessment tools.

Randomized controlled trials	
Selection bias	• Was the method used to generate the allocation sequence described in sufficient detail to allow an assessment of whether it should produce comparable groups? • Was the method used to conceal the allocation sequence described in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrollment?
Performance bias	• Were measures used to blind study participants and personnel from knowledge of which intervention a participant received? • Was the intended blinding effective?
Detection bias	• Were measures used to blind outcome assessors from knowledge of which intervention a participant received? • Was the intended blinding effective?
Attrition bias	• Were the outcome data complete for each main outcome, including attrition and exclusions from the analysis?
Reporting bias	• Did the study report appropriate outcomes (ie, to avoid selective outcome reporting)?
Other bias	• Was the study otherwise free of important sources of bias not already reported previously?
Observational studies	
Selection bias	• Were appropriate eligibility criteria developed and applied to both the cohort of interest and the comparison cohort? • Was confounding adequately controlled for?
Detection bias	• Was measurement of exposure and outcome appropriate and consistently applied to both the cohort of interest and the comparison cohort?
Attrition bias	• Was follow-up complete?

The completion of these evidence profile tables was facilitated by online access to the Guideline Development Tool (GDT).[16] See Fig. 2.

GRADE evidence profile tables: Study design. The methodological type of study is used by the GRADE process as the starting point for the estimate of overall risk of bias. The rating for each type of study varies according to type of question being asked.

For PICO questions related to therapeutic interventions, evidence supported by RCTs starts as high-quality evidence (⊕⊕⊕⊕). Evidence supported by observational studies starts as low-quality evidence (⊕⊕).[17] For PICO questions related to diagnostic accuracy, evidence supported by valid diagnostic accuracy studies (cross-sectional or cohort studies, in patients with diagnostic uncertainty and direct comparison with an appropriate reference standard) starts as high-quality evidence (⊕⊕⊕⊕).[18] The overwhelming majority of outcomes for the PICO questions were associated with very low quality of evidence (⊕).

GRADE evidence profile tables: Core domains.

Risk of bias. The overall risk of bias for each study relevant to each key outcome was allocated in the bias assessment in individual studies process. In the evidence profile table, a summary assessment is required across the included studies for each outcome. The 3 possible categories are as follows:

- No serious limitations: most information is from studies at low risk of bias.
- Serious limitations: most information is from studies at moderate risk of bias.
- Very serious limitations: most information is from studies at high risk of bias.

RCT bias assessment

Study	Year	Design	Total Patients	Population	Industry Funding	Allocation: Generation	Allocation: Concealment	Binding: Participants	Binding: Assessors	Outcome: Complete	Outcome: Selective	Other Bias
Jones	2002	RCT	152	OHCA	Partly	Low	Low	High	Low	Low	Low	Unclear
Stevens	2002	RCT	36	OHCA	No	High	High	High	Low	Low	Low	Unclear
Laurence	2005	RCT	74	OHCA	No	Low	Low	High	High	Low	Low	Unclear
Zhang	2005	RCT	188	OHCA	Yes	High	High	High	High	Low	High	High
Lopez	2012	RCT	34	OHCA	No	Low	Low	High	Low	Low	Low	Unclear
Simons	2013	RCT	202	OHCA	No	Low	Low	High	Low	Low	Low	Low

Non-RCT bias assessment

Study	Year	Design	Total Patients	Population	Industry Funding	Eligibility Criteria	Exposure/Outcome	Confounding	Follow up
Jinas	2013	Non-RCT	65	OHCA	No	High	High	High	Low
Ruessel	2014	Non-RCT	69	OHCA	No	Unclear	Low	Low	Low

Fig. 1. Example of bias assessment tables (RCTs and non-RCTs).

Evidence across studies may be ranked down for risk of bias by either one level, for serious limitations, or two levels, for very serious limitations.

Inconsistency. Inconsistency is a concept that considers the extent to which the findings of studies that look at the same outcomes agree with each other in a consistent way. Variability in the magnitude of effect may be because of differences in PICO or other differences in study design. Reviewers were asked to document limitations when (1) point estimates varied widely across studies, (2) confidence intervals (CIs) showed minimal or no overlap (ie, studies appear to have different effects), or (3) statistical tests of heterogeneity were suggestive of inconsistency.[19] Again reviewers were asked to assess the studies that report that outcome as having:

- No serious inconsistency.
- Serious inconsistency.
- Very serious inconsistency.

Evidence across studies may be ranked down for inconsistency (by either 1 [for serious limitations] or 2 levels [for very serious limitations]).

Indirectness of evidence. The GRADE process describes direct evidence as "research that directly compares the interventions in which we are interested, delivered to the populations in which we are interested, and measures the outcomes important to patients.".[20] Concerns about directness therefore arise when there are differences in the Population (e.g., patients in cardiac arrest versus not in cardiac arrest), Intervention (e.g., different techniques to induce therapeutic hypothermia), Comparison (e.g., conventional CPR using 2010 guidelines versus conventional CPR using 2000 guidelines), or outcomes (e.g., return of spontaneous circulation versus termination of ventricular fibrillation for 5 s), or where

Author(s): Peter Morley, Eddy Lang
Date:
Question: Drug X compared to Standard Care for Out-of-Hospital Cardiac Arrests
Setting: Prehospital Arrests in Victoria, Australia
Bibliography (systematic reviews): Ruessel, 2014 75; Jinas, 2013 342

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Drug X	Standard Care	Relative (95% CI)	Absolute (95% CI)		
Survival to hospital discharge (Ruessel, 2014 75; Jinas 2013 342)												
2	cohort studies	serious[1]	not serious	not serious	serious[2,3]	none	17/64 (26.6%)	23/70 (32.9%)	**RR 0.81** (0.48 to 1.37)	62 fewer per 1000 (from 122 more to 171 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Survival to hospital (Ruessel, 2014 75; Jinas 2013 342)												
2	cohort studies	serious[1]	not serious	not serious	serious[2,3]	none	30/64 (46.9%)	30/70 (42.9%)	**RR 1.09** (0.75 to 1.59)	39 fewer per 1000 (from 107 fewer to 253 more)	⊕◯◯◯ VERY LOW	IMPORTANT

MD – mean difference, RR – relative risk

1. Inadequate control for confounders
2. 95% CI unable to exclude significant harm
3. Total numbers <100 patients

Fig. 2. Example of GRADE evidence profile table completed by using the guideline development tool.

there are no head-to-head comparisons between interventions. Important differences in outcome measures include time frame (e.g., hospital discharge vs 6-month survival) or other surrogate outcomes (e.g., hospital admission vs neurologically intact survival). Usually data that rely on surrogate outcomes would result in an allocation of serious or very serious limitations.

Limitations in more than one type of directness may suggest a need to rate the studies as having very serious limitations.

In general, allocating limitations as serious or very serious should be considered only where there is a compelling reason to think that the biology in the population of interest is so different that the magnitude of effect will differ substantially (eg. cardiac arrest victim vs stroke victim). Evidence from animal studies, manikins or other models would generally be rated as having very serious limitations (but this would be dependent on the key outcomes listed).

Again reviewers are asked to assess the studies that report that outcome as

- No serious indirectness.
- Serious indirectness.
- Very serious indirectness.

Any of these concerns may result in a rating down of the quality of evidence for directness (by either one [serious limitations] or two levels [very serious limitations]).

Imprecision. The assessment of precision and imprecision is complex. The CI around a result enable us to assess the range in which the true effect lies. If the CIs were not sufficiently narrow (such as overlap with a clinical decision threshold, eg. a 1% absolute difference in survival to hospital discharge), the quality would be rated as having serious limitations (or as very serious limitations if the CI is very wide). Another way of describing this is where the recommendation would be altered if the upper boundary of the CI or the lower boundary of the CI represented the true effect. Factors that may further influence this decision include the importance of the outcome, the adverse effects, the burden to the patient, the resources required, and the difficulty of introducing a technique into practice.[21] If the total number of patients included in the evidence for each outcome being evaluated does not exceed the number of patients generated by a conventional sample size calculation for a single adequately powered trial, evidence reviewers were advised to consider rating down for imprecision. This "optimal information size" can be estimated using calculators and tables.[21] Even if the optimal information size is met, and the CI overlaps no effect (ie, CI includes relative risk [RR] of 1.0) evidence reviewers were instructed to rate down the quality of the evidence for imprecision if the CI fails to exclude important benefit or important harm (e.g., a 25% increase in mortality).[21]

Reviewers were asked to assess the studies that reported that outcome as

- No serious imprecision.
- Serious imprecision.
- Very serious imprecision.

If problems with precision were detected, the quality of evidence for precision was rated down (by either one [for serious limitations] or two levels [for very serious limitations]).

Publication bias. Unidentified studies may yield systematically different estimates of beneficial effects of an intervention. Studies with positive results are much more likely to be published (odds ratio, 3.9; 95% CI, 2.68–5.68).[22] Biased conclusions can result from early review (missing studies with delayed publication [even more likely with negative studies]), restricting the search to English language journals, or not including grey literature (e.g., clinical trial registers, abstracts, theses). Discrepancies between meta-analyses of small studies and subsequent large RCTs occur in approximately 20% of cases, in part due to publication bias.

Reviewers should allocate strongly suspected (bias) when the evidence consists of a number of small studies, especially if these are industry sponsored or if the investigators share another conflict of interest.[23] The risk of publication bias in observational studies is probably larger than in RCTs (particularly small studies, data collected automatically, or data collected for a previous study). The use of graphical or statistical testing for publication bias may be useful but has limitations, and is not routinely recommended. Additional information about unpublished trials can be found in databases such as www.clinicaltrials.gov. GRADE suggests that the rating for publication bias across studies should be allocated:

- undetected, or
- strongly suspected.

If publication bias is strongly suspected the quality of evidence is rated down by one level.

Rating up the quality of observational studies. The GRADE group recommends that methodologically rigorous observational studies may have their quality rated up where there is a large magnitude of effect, where there is a dose–response gradient, or when all plausible confounders or biases would reduce the demonstrated effect. Obviously consideration for rating down the quality of evidence (risk of bias, imprecision, inconsistency, indirectness, and publication bias) must precede considerations for rating up the quality.[24] Only a very small number of the systematic reviews identified evidence that met these criteria.

Magnitude of effect. A large magnitude effect would be considered justification to increase the rating by 1 level (eg, from low to moderate) if the RR was 2 to 5, or 0.2 to 0.5 with no plausible confounders. The reviewer would be more likely to rate up if the above size of effects occurred rapidly and out of keeping with prior gradient of change; in these situations, they would usually be supported by indirect or lower levels of evidence. If above criteria are all met, and the RR is very large (e.g., greater than 5–10) or very low (RR less than 0.2), rating up by 2 levels (from low to high) could be considered.

Dose–response effect. A dose–response gradient, such as increased effect with an increased dose, or decreased time to intervention, or increased intensity or duration of an educational intervention, increases the confidence in the findings of observational studies. In this setting, rating up the quality of evidence by 1 level could be considered.

Issues around confounding. If all plausible prognostic factors are accurately measured in observational studies, and if all the observed residual confounders and biases would diminish the observed effect, then the effect estimate would be strengthened. In this setting, rating up the quality of evidence by 1 level could be considered.

GRADE evidence profile tables: Estimate of effect. We asked evidence reviewers to complete the effect size column for each row in the evidence profile tables with an estimate for both relative and absolute effects. For example, binary outcomes required RR (or odds ratio), of the intervention compared to control, with 95% CIs and absolute effect of intervention - control as absolute percentage, with 95% CIs. It is the absolute differences that allow accurate assessment of precision.

There was significant discussion about the exact principles to be employed to determine whether a meta-analysis of data should be performed. There are statistical concerns about the simple combining of results from trials,[25] but there are also significant

concerns about performing a meta-analysis when it would not be appropriate.[26]

If several RCTs or observational studies were identified that published results for outcomes considered critical or important, and these studies were closely matched to the PICO question, the evidence reviewers were encouraged to complete an Assessing the Methodological Quality of Systematic Reviews (AMSTAR) checklist to ensure that the appropriate principles for performance of the meta-analysis were considered.[27] In scenarios where it was thought that the data should not be combined into a meta-analysis, the authors were instructed to list the outcomes for each study, or, if a simple mathematical combination of data was performed, this would be accompanied by a statement suggesting that the data were simply pooled (combined without being weighted).

Guideline development tool

The GRADE process takes a very comprehensive approach to the determination of the direction and strength of any recommendations. During the conduct of the systematic reviews, an updated online tool developed by the GRADE Working Group became available for use. An online Guideline Development Tool[16] developed by the GRADE Working Group was used to help assess the overall balance between benefits and risks or harms for each option, including consideration of dimensions such as patient values and preferences and resource considerations.[28] The ILCOR task forces were encouraged to use this tool to assist in their deliberations.

Creation of consensus on science statements

The completed evidence profile tables were then used to create a written summary of evidence for each outcome: the consensus on science statements. The structure of the new 2015 consensus on science statement was developed as a means of providing an explicit narrative to communicate the evidence synthesis and quality judgments found in the evidence profiles. These statements are supported by a categorization of the overall quality of the evidence (high, moderate, low, or very low) and include reasons for their downgrading or upgrading. The recommended standard consensus on science format was as follows:

> For the important outcome of *Z* (e.g., return of spontaneous circulation), we have identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 2 observational studies (#1, #2) enrolling 421 patients showing no benefit (RR, 0.81; 95% CI, 0.33–2.01).

Creation of agreed treatment recommendations

Consensus-based treatment recommendations were then created whenever possible. These recommendations were accompanied by an overall assessment of the evidence and a statement from the task force about the values and preferences that underlie the recommendations. These are supported by a categorization of the overall quality of the evidence (high, moderate, low, or very low) and strength of recommendation (strong or weak).

The recommended standard treatment recommendation format was as follows:

> We suggest/recommend for/against *X* in comparison with *Y* for out-of-hospital cardiac arrest (weak/strong recommendation, very low/low/moderate/high quality of evidence).

The GRADE process encourages organizations to commit to making a recommendation by using "we recommend" for strong recommendations and "we suggest" for weak recommendations in either a positive or negative direction (ie, "suggest/recommend," "for/against"). In the unusual circumstances in which task forces chose not to make recommendations, they were encouraged to specify whether this was because they had very low confidence in effect estimates (very limited data), because they felt that the balance between desirable and undesirable consequences was so close they could not make a recommendation (data exists, but no clear benefits), or because the two management options had very different undesirable consequences (and local values and preferences would decide which direction to take).

Values and preferences and task force insights

The task forces were encouraged to provide a values and preferences statement whenever a treatment recommendation was made. This is an overarching term that includes perspectives, beliefs, expectations, and goals for health and life as well as the processes used in considering the potential benefits, harms, costs, limitations, and inconvenience of the management options in relation to one another.[28] Task forces were encouraged to provide additional explanatory comments whenever possible to help readers gain more insight into the perspectives of the discussion.

Developing consensus

Each task force used regular audio conferencing and webinars, where the systematic reviews were electronically presented for discussion and feedback. Additional face-to-face meetings were held at least once each year to provide opportunities to learn about the process and to facilitate collaboration between the seven task forces. Consensus was obtained through detailed discussion and feedback provided by the ILCOR task force members, the GRADE and evidence evaluation experts, the ILCOR methods group, the public, and the individual international resuscitation councils.

Public consultation

To ensure as much broad input as possible during the evidence evaluation process, public comment was sought at two main points. Initial feedback was sought about the specific wording of the PICO questions and the initial search strategies. Subsequent feedback was sought after creation of the initial draft consensus on science statements and treatment recommendations.[29] A total of 492 comments were received. At each of these points in the process, the public comments were made available to the evidence reviewers and task forces for their consideration.

Challenging areas

Lower levels of evidence

In many resuscitation scenarios, there are no RCTs or even good observational studies, so there is a need to explore other population groups. The GRADE process is very explicit about the allocation of quality of evidence to support the individual outcomes. Extrapolation of data from other patient groups (e.g., adult versus pediatric, cardiac arrest versus shock), mathematical models, and animal studies means that this evidence, irrespective of methodological quality, would be downgraded for at least serious indirectness. This usually resulted in a very low quality of evidence, and many task forces found this initially challenging.

Diagnostic and prognostic questions

The GRADE process has been developed specifically to deal with questions that address alternative management strategies. It has been modified to enable consideration of questions that relate to diagnosis,[18] but it was not developed to address questions about risk or prognosis.

A few diagnostic questions were addressed in the 2015 process, and ideally the best diagnostic questions relate their outcomes

to when a particular diagnostic strategy is used or not used (i.e., actually an intervention question).

The first of a series of GRADE articles about studies addressing prognosis has been published only recently,[30] so, unfortunately, these details were not available to the evidence reviewers for this process. A couple of approaches to prognosis were used, including the use of existing observational study bias assessment tools or a modification of these.

Discordant recommendations

There were several situations when task forces were keen to use a strong recommendation when the quality of evidence did not support this. This is not unexpected given the few published RCTs and good observational studies available in the resuscitation literature. Task forces were made aware of the importance of clarifying their rationale when they wished to make such discordant recommendations. They were encouraged to use standardized wording (e.g., "Intervention may reduce mortality in a life-threatening situation, and adverse events not prohibitive" or "A very high value is placed on an uncertain but potentially life-preserving benefit").[31] In keeping with this approach, the number of discordant recommendations in ILCOR was limited in the 2015 process, as were the number of strong recommendations.

Management of conflicts of interest throughout the CoSTR process

To ensure the integrity of the evidence evaluation and consensus on science development process, ILCOR followed its rigorous conflict of interest (COI) management policies at all times. A full description of these policies and their implementation can be found in Part 4 of the 2010 CoSTR.[32,33] All persons involved in any part of the process disclosed all commercial relationships and other potential conflicts, and in total, the AHA processed more than 1000 COI declarations. These disclosures were taken into account in assignment of task force co-chairs and members, writing group co-chairs, and other leadership roles. Relationships were also screened for conflicts in assigning task force question owners and evidence reviewer roles for individual PICO questions. Individuals were reassigned when potential conflicts surfaced. Participants, co-chairs, and staff raised COI questions and issues throughout the process and referred them to the COI co-chairs if they could not be resolved within their group. The COI co-chairs kept a complete log of all COI-related issues and their resolutions. None of the issues required serious intervention, such as replacement of any leader roles. As a result of commercial relationships, however, several PICO questions were reassigned to evidence reviewers or question owners without potential conflicts. As in 2010, the phone number for the COI hotline was broadly disseminated throughout the 2015 Consensus Conference for anonymous reporting; no calls were received.

As in 2010, the dual-screen projection method was used for all sessions at the 2015 Consensus Conference. One screen displayed the presenter's COI disclosures continuously throughout his or her presentation. The same was true for all questions or comments from participants or task force members: whenever they spoke, their relationships were displayed on one screen, so that all participants could see potential conflicts in real time, while slides were projected on the second screen. Individuals also abstained from voting on any issue for which they had a conflict. Such abstentions, along with any other issues that arose, were recorded on a COI attestation completed by the COI monitor for each session. As in 2010, the COI system ran smoothly and did not impede the progress of the evidence discussions.

Summary

The process for evaluating the resuscitation science has evolved considerably over the past 2 decades. The current process, which incorporates the use of the GRADE methodology, culminated in the 2015 CoSTR publication, which in turn will inform the international resuscitation councils' guideline development processes. Over the next few years, the process will continue to evolve as ILCOR moves toward a more continuous evaluation of the resuscitation science.

Disclosures

2015 CoSTR Part 2: Evidence evaluation: writing group disclosures.

	Employment	Research grant	Other research support	Speakers' bureau/honoraria	Expert witness	Ownership interest	Consultant/advisory board	Other
Writing group member								
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Michael R. Sayre	University of Washington	None	None	None	None	None	None	None
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

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Part 3: Adult basic life support and automated external defibrillation 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆

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Introduction

This Part of the *2015 International Consensus on Cardiopulmonary Resuscitation* (CPR) and *Emergency Cardiovascular Care* (ECC) *Science With Treatment Recommendations* (CoSTR) presents the consensus on science and treatment recommendations for adult basic life support (BLS) and automated external defibrillation (AED). After the publication of the 2010 CoSTR, the Adult BLS Task Force developed review questions in PICO (population, intervention, comparator, outcome) format.[1] This resulted in the generation of 36 PICO questions for systematic reviews. The task force discussed the topics and then voted to prioritize the most important questions to be tackled in 2015. From the pool of 36 questions, 14 were rated low priority and were deferred from this round of evidence evaluation. Two new questions were submitted by task force members, and 1 was submitted via the public portal. Two of these (BLS 856, and BLS 891) were taken forward for evidence review. The third question (368: Foreign-Body Airway Obstruction) was deferred after a preliminary review of the evidence failed to identify compelling evidence that would alter the treatment recommendations made when the topic was last reviewed in 2005.[2]

Each task force performed a systematic review using detailed inclusion and exclusion criteria, based on the recommendations of the Institute of Medicine of the National Academies.[3] With the assistance of information specialists, a detailed search for relevant articles was performed in each of 3 online databases (PubMed, Embase, and the Cochrane Library).

Reviewers were unable to identify any relevant evidence for 3 questions (BLS 811, BLS 373, and BLS 348), and the evidence review was not completed in time for a further question (BLS 370). A revised PICO question was developed for the opioid question (BLS 891). The task force reviewed 23 PICO questions for the 2015 consensus on science and treatment recommendations, including BLS 811, BLS 373, and BLS 348. The PICO flow is summarized in Fig. 1

Using the methodological approach proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group,[4] the reviewers for each question created a reconciled risk-of-bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[5] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[6] and GRADE for observational studies that inform both therapy and prognosis questions.[7] GRADE evidence profile tables[8] were then created to facilitate an evaluation of the evidence in support of each of the

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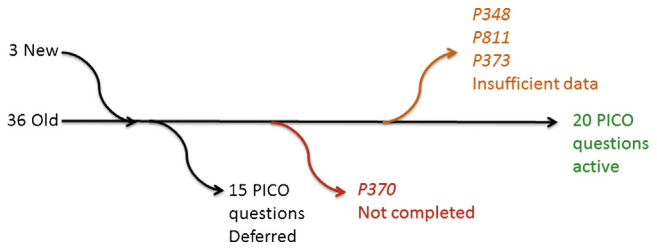

Fig. 1. Flow of PICO questions in the BLS task force.

critical and important outcomes. Critical outcomes were defined as neurologically favorable outcome (level 9), survival (level 8), and return of spontaneous circulation (ROSC; level 7). Given the heterogeneity of time points evaluated in the studies related to BLS/AED, time intervals were pooled across outcomes. For neurologic outcome and survival, we considered the outcomes at discharge, 30 days, 60 days, 180 days, and/or 1 year. Important outcomes included physiologic and process end points.

The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[9] based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias).[10] These evidence profile tables were then used to create a written summary of evidence for each outcome (the consensus on science statements). Whenever possible, consensus-based treatment recommendations were then created. These recommendations (designated as strong or weak) were accompanied by an overall assessment of the evidence and a statement from the task force about the values and preferences that underlie the recommendations. A strong recommendation typically contains the words "we recommend," while a weak recommendation contains the words "we suggest." Further details of the methodology that underpinned the evidence evaluation process are found in "Part 2: Evidence Evaluation and Management of Conflicts of Interest."

The body of knowledge encompassed in this CoSTR comprises 23 individual systematic reviews with 32 treatment recommendations, derived from a GRADE evaluation of 27 randomized clinical trials and 181 observational studies of variable design and quality conducted over a 35-year period. The treatment recommendations in this Part are limited to recommendations for adults. Where there is overlap with pediatric topics, readers are referred to "Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support."

The actions linking the victim of sudden cardiac arrest with survival are called the Chain of Survival and form the order of presentation of the systematic reviews in this publication, as follows:

Early Access and Cardiac Arrest Prevention

- Dispatcher recognition of cardiac arrest (BLS 740)
- Dispatcher instruction (BLS 359)
- Resuscitation care for suspected opioid-associated emergencies (BLS 811)
- Opioid overdose response education (BLS 891)
- Drowning (BLS 856)

Early, High-Quality CPR

- Starting CPR (BLS 661)
- Chest compression-only CPR vs conventional CPR (BLS 372)
- CPR before defibrillation (BLS 363)
- Hand position during compressions (BLS 357)
- Chest compression rate (BLS 343)
- Chest compression depth (BLS 366)
- Chest wall recoil (BLS 367)
- Minimizing pauses in chest compressions (BLS 358)
- Compression-ventilation ratio (BLS 362)
- Timing of CPR cycles (BLS 346)
- Check for circulation during BLS (BLS 348)
- Feedback for CPR quality (BLS 361)
- EMS chest compression-only versus conventional CPR (BLS 360)
- Passive ventilation technique (BLS 352)
- Harm from CPR to victims not in cardiac arrest (BLS 353)

Early defibrillation

- Public-access defibrillation (BLS 347)
- Rhythm check timing (BLS 345)
- Analysis of rhythm during chest compression (BLS 373)

Early access and cardiac arrest prevention

Early access: emergency medical dispatch

The first contact with emergency medical services (EMS) is usually via a 9-1-1 or 1-1-2 emergency call. The correct and timely identification of cardiac arrest is critical to ensuring (1) the appropriate dispatch of a high-priority response, (2) the provision of telephone CPR instructions, and (3) the activation of community first responders carrying AEDs. In an observational study in the Netherlands, cases of cardiac arrest that were missed at initial telephone triage had much worse outcomes, 5% survival versus 14%.[11] Optimizing EMS dispatch is likely to be one of the most cost-effective solutions to improving outcomes from cardiac arrest. Thus, optimizing the ability of dispatchers to identify cardiac arrest and deliver telephone CPR instructions is critical to improving outcomes.

Dispatcher recognition of cardiac arrest (BLS 740)

Among adults and children who are in cardiac arrest outside of a hospital (P), does the description of any specific symptoms to the dispatcher (I), compared with the absence of any specific description (C), change the likelihood of cardiac arrest recognition (O)?

Consensus on science

For the critical outcome of **cardiac arrest recognition**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 cluster RCT,[12] as well as very-low-quality evidence from 26 non-RCTs comprising 8 before–after observational studies,[13–20] 9 prospective single-arm observational studies,[13,21–28] 8 retrospective single-arm observational studies,[29–36] and 1 case–control study.[11] A total of 17 420 patients were included in these 27 studies.

"Cardiac arrest recognition" was reported heterogeneously across the included studies, precluding meta-analysis. Seven observational studies reported the sensitivity of dispatch protocols to recognize cardiac arrest,[17,18,21,29–32] with results that ranged from 38% to 96.9% and specificity that exceeded 99% in the 2 studies that reported this outcome.[29,30] Recognition rates of cardiac arrest ranged from 18% to 83% where reported.[22,25]

The majority of the study dispatch centers used scripted dispatch protocols with questions to identify patients who are unconscious and not breathing or not breathing normally. Four before–after studies[16–18,20] suggested that introducing scripted dispatch protocols or modifying existing protocols can help increase cardiac arrest recognition. One study reported an increase in cardiac arrest recognition[16] while 3 reported an increase in the rates of telephone-assisted CPR after the introduction of scripted

dispatch protocols.[17,18,20] One study also reported an increase in "high-acuity" calls after a modification to the seizure protocol.[19]

Recognition of unconsciousness with abnormal breathing is central to dispatcher recognition of cardiac arrest. Many terms may be used by callers to describe abnormal breathing: difficulty breathing, poorly breathing, gasping breathing, wheezing breathing, impaired breathing,[22] occasional breathing, barely/hardly breathing, heavy breathing, labored or noisy breathing, sighing, and strange breathing.[11] Agonal breaths were reported in approximately 30% of cases in 1 study,[13] which can make obtaining an accurate description of the patient's breathing pattern challenging for dispatchers. The presence of agonal breaths were mentioned as a factor negatively affecting cardiac arrest recognition in 10 studies,[13–15,18,22,23,25,33,35,37] with 1 study reporting that agonal breaths were present in 50% of nonidentified cardiac arrest calls.[18] Other terms reported in the studies that may help identify possible cardiac arrest cases include "dead," "is dead," "cold and stiff," "blue," "gray," or "pale."[27] The aforementioned descriptions, however, may be limited, owing to cultural influences and language translation limitations.

Three before–after studies suggested that offering dispatchers additional education that specifically addresses agonal breaths can increase the rates of telephone-assisted CPR[14,15] and decrease the number of missed cases.[37]

There is evidence from 3 studies that failure to recognize cardiac arrest may be associated with failure to follow scripted protocols by omitting specified questions about consciousness and breathing.[23,24,26]

Treatment recommendation

We recommend that dispatchers determine if a patient is unconscious with abnormal breathing. If the victim is unconscious with abnormal or absent breathing, it is reasonable to assume that the patient is in cardiac arrest at the time of the call (strong recommendation, very-low-quality evidence).

We recommend that dispatchers be educated to identify unconsciousness with abnormal breathing. This education should include recognition and significance of agonal breaths across a range of clinical presentations and descriptions (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we placed a higher value on the recognition of cardiac arrest by dispatchers, and we placed a lower value on the potential harms arising from inappropriate CPR and the potential need for increased resources. In this situation, we believe that the benefits associated with increased numbers of cardiac arrest patients receiving timely and appropriate interventions outweigh the undesirable effects (potential for patients not in cardiac arrest to inappropriately receive chest compressions, potential need for increased resources).

We recognize that the evidence in support of these recommendations comes from mainly observational studies of very low quality. Large, high-quality RCTs addressing this question are unlikely to be conducted. We believe that the available evidence shows consistent results favoring scripted dispatch protocols and that education including a description of the presenting signs of cardiac arrest and populations at risk (e.g., patients presenting with seizures) enables dispatchers to identify cardiac arrest. We recognize that dispatch protocols for a range of conditions (including but not limited to "seizures," "breathing problems," "chest pains," "falls," and "unknown problem") optimized to identify potential cardiac arrest without undue delay may further improve early recognition of cardiac arrest.

Knowledge gaps

High-quality data from RCTs are currently lacking. Further studies are required to determine the following:

- What are the identifying key words used by callers that are associated with cardiac arrest?
- Should there be "trigger" words or phrases from the bystander that are so likely to indicate cardiac arrest that the dispatcher can skip parts of the protocol and shorten the time to dispatch and to CPR instruction?
- What is the impact of adherence to or failure to follow dispatch protocols?
- What is the most appropriate educational content to ensure that dispatchers are able to recognize the significance of abnormal and agonal breaths?
- What is the most appropriate refresher training interval for dispatchers?
- Is there a difference in recognition rates between dispatchers with a clinical background and those without a clinical background?

Dispatcher instructions (BLS 359)

Among adults and children who are in cardiac arrest outside of a hospital (P), does the ability of a dispatch system to provide CPR instructions (I), compared with a dispatch system where no CPR instructions are ever provided (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; delivery of bystander CPR; time to first shock; time to commence CPR; CPR parameters (O)?

Introduction

Bystander CPR rates remain relatively low in most communities. Dispatcher-assisted telephone CPR instructions have been demonstrated to improve bystander CPR rates.

This review identified 1 meta-analysis,[38] 3 randomized trials,[39–41] and 11 observational studies.[15,17,18,20,27,34,42–46] The population evaluated in most studies were adults with a presumed cardiac cause of their cardiac arrest and excluded traumatic and/or asphyxial causes of cardiac arrest.[17,20,42,44,41] Two studies evaluated all out-of-hospital arrests,[15,34] although benefit was limited to the cardiac cause subgroup in 1 of these studies.[15] Two studies evaluated telephone-assisted CPR in children.[45,46]

Some studies evaluated the survival benefit of dispatch-assisted CPR instructions and compared systems where such instructions can be offered to systems where they were never or infrequently offered.[15,17,18,20,27,34,43–45] Other studies compared traditional CPR to chest compression-only CPR instructions delivered by telephone.[39–42]

Consensus on science

For the critical outcome of **survival with favorable neurologic outcome**, we have identified very-low-quality evidence from 2 RCTs,[39,40] 2 cohort studies,[45,46] and 1 before–after study.[15] The level of evidence was downgraded for risk of bias, indirectness, and imprecision. Four studies reported no benefit in neurologic outcomes.[39,45,46,40] The before–after study, which included dispatcher instructions to start compression-only CPR as part of a bundle of interventions used as part of a quality improvement initiative, noted improved neurologic outcomes at 12 months (odds ratio [OR], 1.81; 95% confidence interval [CI], 1.2–2.76).[15]

For the critical outcome of **survival**, we identified very-low-quality evidence from 3 RCTs.[39–41] The level of evidence was downgraded for risk of bias, indirectness, and imprecision. Meta-analysis of these trials found an absolute survival benefit of 2.4%

(95% CI, 0.1%–4.9%) in favor of telephone-assisted continuous chest compressions over telephone-assisted traditional CPR (number needed to treat [NNT], 41; 95% CI, 20–1250; relative risk [RR], 1.22; 95% CI, 1.01–1.46).[38]

We also identified 6 before–after studies.[15,17,18,20,42,43] One study was inconsistent with the others and found decreased survival, although it was not powered to evaluate survival outcomes.[18] One study showed a survival benefit at 1 year (population of 73 patients) from an educational program for dispatchers on continuous chest compressions and agonal breaths (adjusted OR, 1.81; 95% CI, 1.20–2.76).[15]

We also identified 5 cohort studies.[27,34,44–46] One study showed a survival benefit at 30 days when, after an educational program, telephone-assisted CPR was provided to a pediatric out-of-hospital cardiac arrest (OHCA) population versus not (adjusted OR, 1.46; 95% CI, 1.05–2.03).[45] A second cohort study in the pediatric (less than 18 years of age) population showed survival benefit at 30 days when telephone-assisted CPR was provided (adjusted OR for group not receiving CPR, 0.70; 95% CI, 0.56–0.88).[46]

For the critical outcome of **ROSC**, we identified very-low-quality evidence from 1 RCT[40] and 1 before–after study.[18] The studies were downgraded for indirectness and imprecision. Neither study showed a statistically significant benefit.

For the important outcome of **delivery of bystander CPR**, we identified very-low-quality evidence from 6 before–after studies: 1 study compared 2 medical priority dispatch system versions,[42] 3 studies compared telephone-assisted CPR versus not,[17,18,43] and 2 studies[15,20] compared various educational programs. In addition, we identified 1 cohort study.[45] The level of evidence was downgraded for indirectness and imprecision. All showed a strong association between telephone-assisted CPR and bystander CPR. The cohort study showed increased performed chest compressions (adjusted OR, 6.04; 95% CI, 4.72–7.72) and ventilation (adjusted OR, 3.10; 95% CI, 2.44–3.95) from telephone-assisted CPR, and an absolute increase in bystander CPR rate of 40.9% (95% CI, 36.1–45.5).[45]

For the important outcome of **time to commence CPR**, we have identified very-low-quality evidence from 4 before–after studies[15,17,20,43] and 1 cohort study.[44] The level of evidence was downgraded for risk of bias, inconsistency, indirectness, and imprecision. None of these reported a statistically significant benefit.

For the important outcome of **CPR parameter**, assessed with initial rhythm of ventricular fibrillation (VF)/pulseless ventricular tachycardia (PVT), we have identified very-low-quality evidence from 1 RCT[41] and 1 before–after study.[18] The studies were downgraded for risk of bias, indirectness, and imprecision. Neither study showed a statistically significant benefit.

Treatment recommendation

We recommend that dispatchers provide chest compression-only CPR instructions to callers for adults with suspected OHCA (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we placed a higher value on the initiation of bystander CPR and a lower value on the harms of performing CPR on patients who are not in cardiac arrest. We recognize that the evidence in support of these recommendations comes from randomized trials and observational data of variable quality. However, the available evidence consistently favors telephone CPR protocols that use a compression-only CPR instruction set, suggesting a dose effect—that is, quick telephone instructions in chest compressions result in more compressions and faster administration of CPR to the patient.

Knowledge gaps

- What is the optimal instruction sequence for coaching callers in telephone-assisted CPR?
- What is the impact of telephone CPR instructions on noncardiac etiology arrests in adult and pediatric patients?
- What is the impact of the dispatchers' background (non-healthcare professional versus paramedic or nurse)?
- What are the time-interval benchmarks for the completion of each step in the instruction process (transfer to ambulance dispatch, cardiac arrest recognition, dispatch of resources, initiation of instructions, etc.)?
- What is the benefit or role in the use of an AED locator or enhanced citizen response or "dual-dispatch" system?
- What is the impact of language barriers to performance?
- What are the best methods to optimize initial training methodology, retraining frequency interval, and quality improvement programs for optimal dispatcher performance and effectiveness?
- What is the optimal system approach to provide instructions to the highest number of cardiac arrest patients?
- How many chest compressions should be given, and for how long, before ventilation instructions are introduced?

Resuscitation care for suspected opioid-associated emergencies (BLS 811)

In adults and children with suspected opioid-associated cardio/respiratory arrest in the prehospital setting (P), does bystander naloxone administration (intramuscular or intranasal), in addition to conventional CPR (I), compared with conventional CPR only (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Opioid overdose is a leading cause of death in many communities and at-risk populations. With widespread implementation of community naloxone distribution programs, there is a need for evaluating the evidence of such initiatives to provide guidance for policy makers.

Consensus on science

We did not identify any published studies to determine if adding intranasal or intramuscular naloxone to conventional CPR is superior to conventional CPR alone for the management of adults and children with suspected opioid-associated cardiac or respiratory arrest in the prehospital setting. An additional search was performed to assess available evidence for overdose education and naloxone distribution programs (see BLS 891).

Treatment recommendation

No treatment recommendation can be made for adding naloxone to existing BLS practices for the BLS management of adults and children with suspected opioid-associated cardiac or respiratory arrest in the prehospital setting.

Values, preferences, and task force insights

All patients with suspected opioid-associated cardiac or respiratory arrest should receive standard BLS care, with or without the addition of naloxone. In making this recommendation, we place greater value on the potential for lives saved by recommending immediate BLS care and education, with or without naloxone, and lesser value on the costs associated with naloxone administration, distribution, or education.

Knowledge gaps

- Further research is needed to determine the optimal components of overdose response education for BLS and first aid providers, the role of naloxone, and how these educational programs should be implemented and evaluated.

Opioid overdose response education (BLS 891)

In adults and children at risk of suspected cardio/respiratory arrest due to opioids in the prehospital setting (P), does opioid overdose response education, with or without naloxone distribution (I), compared with no overdose response education or overdose prevention education only (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Opioid overdose events have increased dramatically and become a leading cause of premature, preventable mortality in many communities. With widespread implementation of various community programs, there is a need for evaluating the evidence of such initiatives to provide guidance for policy makers.

Consensus on science

For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for risk bias, inconsistency, indirectness, and imprecision) from 3 observational before–after studies.[47,48] Only 1 of 3 studies[49] attempted to correct for any confounding factors expected in interventional studies by using historic controls. This study did observe a dose-response gradient with 0.73 (95% CI, 0.57–0.91) and 0.54 (95% CI, 0.39–0.76) adjusted-rate ratios for lethal overdose in communities with low and high implementation, respectively.[49] The remaining 2 observational studies reported reductions in rate ratios for lethal overdose in communities, 0.62 (95% CI, 0.54–0.72)[50] and 0.70 (95% CI, 0.65–0.74).[47]

Treatment recommendation

We suggest offering opioid overdose response education, with or without naloxone distribution, to persons at risk for opioid overdose in any setting (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place greater value on the potential for lives saved by recommending overdose response education, with or without naloxone, and lesser value on the costs associated with naloxone administration, distribution, or education.

Knowledge gaps

- Further research is needed to determine the optimal components of opioid overdose response education, the role of naloxone, and how these educational programs should be implemented and evaluated.

Drowning search and rescue (BLS 856)

In adults and children who are submerged in water (P), does any particular factor in search-and-rescue operations (e.g., duration of submersion, salinity of water, water temperature, age of victim) (I), compared with no factors (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

This question was initiated in response to a request that ILCOR review the evidence for prognostic factors that predict outcome in relation to a drowning incident. Drowning is the third leading cause of unintentional injury death worldwide, accounting for nearly 400 000 deaths annually. Care of a submersion victim in high-income countries often involves a multiagency approach, with several different organizations being independently responsible for different phases of the victim's care, from the initial aquatic rescue, on-scene resuscitation, transfer to hospital, and hospital and rehabilitative care. Attempting to rescue a submerged victim has substantial resource implications and may place rescuers at risk themselves.

The systematic review included observational studies with control groups, which presented data enabling us to calculate RRs or reported ORs for the following prognostic factors: (1) age, (2) EMS response time, (3) salinity, (4) submersion duration, and (5) water temperature. The review excluded single case reports and case series less than 5 or without comparator groups. Full details of the search strategy and included articles are summarized in Scientific Evidence Evaluation and Review System (SEERS). It is worth highlighting that, in accordance with GRADE guidelines for prognostic studies, evidence from observational studies starts as high. In reviewing the summaries of evidence, one should note that the studies reviewed extended over a 30-year period. It is possible that outcomes may have changed over time, although this was not observed in the 2 studies that evaluated outcomes over time.[51,52] The populations evaluated varied between studies and included emergency service data, coroners' registries, emergency department, and intensive care admissions.

Consensus on science

Age. For the critical outcome of **favorable neurologic outcome**, we identified very-low-quality evidence from 11 observational studies (downgraded for risk of bias inconsistency, indirectness, and imprecision) comprising 4054 patients.[51,53–62] Of the 7 pediatric studies, 6 found that young age, variably defined as less than 3, 4, 5, or 6 years, was not associated with favorable neurologic outcome.[53–57,59] A single pediatric study including 166 children aged less than 15 years reported better outcomes in children aged less than 5 years (RR, 0.12; 95% CI, 0.03–0.44).[58]

Four studies considered drowning victims of all ages; 3 found no relationship between age and outcome.[60–62] One reported worse outcomes among children aged greater than 5 years (RR, 0.66; 95% CI, 0.51–0.85).[51]

For the critical outcome of **survival**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 6 observational studies, which included 1313 patients.[63–68] Three studies found that age was not associated with outcome.[64,66,68] Two showed better outcomes associated with younger ages (less than 58 years: RR, 0.27; 95% CI, 0.08–0.96[65]; less than 46 years: RR, 0.98; 95% CI, 0.99–0.99),[67] and 1 favored older age (3 years or older: RR, 1.51; 95% CI, 1.19–1.9).[63]

EMS response interval. No studies were identified that addressed the critical outcome of favorable neurologic outcome.

For the critical outcome of **survival**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 2 observational studies, including 746 patients in the Swedish EMS OHCA registry.[65,69] EMS response intervals of

less than 10 min were associated with better survival: RR of 0.29 (95% CI, 0.13–0.66)[69] and reported OR of 0.44 (95% CI, 0.06–0.83).[65]

Salinity. For the critical outcome of **favorable neurologic outcome**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 4 observational studies,[51,57,61,70] which included 1842 drowning victims, of which 370 occurred in salt water and 1427 in fresh water. Two showed salt water was associated with better outcomes (RR, 1.3; 95% CI, 1.12–1.5[61]; RR, 1.2; 95% CI, 1.1–1.4[57]), and 2 showed water type was not associated with outcome (RR, 1.1; 95% CI, 0.95–1.2[70]; RR, 1.14; 95% CI, 0.9–1.4[51]).

For the critical outcome of **survival**, we identified very-low-quality evidence (downgraded for risk of bias imprecision, inconsistency, indirectness, and imprecision) from 3 studies.[63,66,71] One reported better outcomes for salt water (RR, 1.34; 95% CI, 1.19–1.52),[71] 1 showed no difference (RR, 1.22; 95% CI, 0.95–1.56),[63] and 1 showed worse survival in cases with salt water drowning (RR, 0.18; 95% CI, 0.03–1.43).[66]

Submersion duration. For the purposes of this review, we considered studies in 3 groups. We defined those with short submersion intervals (less than 5–6 min), those with intermediate duration (less than 10 min), and those with prolonged submersion intervals (less than 20–25 min).

Short submersion intervals (less than 5–6 min). For the critical outcome of **favorable neurologic outcome**, we identified moderate-quality evidence from 12 observational studies (downgraded for bias and indirectness, upgraded for dose-response gradient), which included 2409 cases.[51–53,55–59,62,72–74] All studies noted worse outcomes among patients with submersion durations exceeding 5 min (RRs ranged between 0.05[51] and 0.61[58]). The 713/826 patients (86.3%) who had outcome information available and were submerged for short durations had good outcomes compared to 128/1150 (11%) with longer submersion durations.

For the critical outcome of **survival**, we identified low-quality evidence (downgraded for risk of bias, indirectness, and imprecision; upgraded for dose-response gradient) from 5 observational studies comprising 317 cases.[63,64,71,75,76] All studies noted worse outcomes among patients with prolonged compared to short submersion durations (RRs ranged between 0.27[75] and 0.83[76]). The 159/170 patients (93.5%) submerged for short durations had good outcomes compared to 45/84 (53%) with longer submersion durations.

Intermediate submersion intervals (less than 10 min). For the critical outcome of **favorable neurologic outcome**, we identified moderate-quality evidence (downgraded for bias, indirectness, and imprecision; upgraded for dose-response gradient) from 9 observational studies that included 2453 cases.[51,52,55,57,58,72,73,77,78] All studies noted worse outcomes among patients with prolonged submersion durations compared with intermediate submersion durations (RRs ranged between 0.02[51] and 0.45[58,73]). The 787/1019 patients (77.2%) submerged for intermediate durations had good outcomes compared to the 36/962 (3.7%) with longer submersion durations.

For the critical outcome of **survival**, we identified low-quality evidence (downgraded for bias, indirectness, and imprecision; upgraded for dose-response gradient) from 2 observational studies[71,79] comprising 121 cases. The first study[71] reported 56/73 (77%) of those submerged for less than 10 min survived compared with none of the 7 patients who were submerged for more prolonged periods survived (RR not estimable; absolute difference, 76.7%; 39.7–94.9%). The second study[79] also noted better survival among those submerged for less than 10 min (46/50 [96%] survived) compared with those submerged for more than 10 min (2/5 [40%] survived).[79]

Prolonged submersion intervals (less than 15–25 min). For the critical outcome of **favorable neurologic outcome**, we identified low-quality evidence (downgraded for risk of bias and imprecision, upgraded for dose-response gradient) from 3 observational studies that included 739 cases.[52,55,57] In 1 study ($n = 398$),[57] submersion less than 20 min was associated with improved survival (289/370 [78%] good outcome versus 1/27 [4%] good outcome; RR, 0.05; 95% CI, 0.01–0.31). The second study[55] reported better outcomes if submersion duration was less than 25 min (68/101, or 67%) versus submersion duration longer than 25 min (0/4, 0%). The third study, which included hypothermic children in cardiac arrest, observed 12/66 (18%) survivors who were submerged for less than 25 min compared with 0/39 who were submerged for more than 25 min.[52]

For the critical outcome of **survival**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from a single study[75] comprising 49 patients. Cases with a submersion interval of less than 15 min had an overall survival rate of 82% (33/39) compared with none of the 2 victims whose submersion duration exceeded 15 min (RR not estimable; absolute difference, 84.6% [17.3%–92.8%]).

Water temperature. For the critical outcome of **favorable neurologic outcome**, we identified very-low-quality evidence (downgraded for risk bias, inconsistency, indirectness, and imprecision) from 2 studies[51,52] of 1254 cases. The largest study ($n = 1094$) included all unintentional drownings in open waters (lakes, ponds, rivers, ocean) in a single large region, collected from medical examiners, EMS systems, and all regional hospitals.[51] Water temperatures were measured within a month of the drowning incident. Univariate analysis according to temperatures less than or greater than 6 °C or less than or greater than 16 °C found no difference in neurologic survival: RR, 1.11 (95% CI, 0.9–1.37); RR, 1.02 (95% CI, 0.81–1.27); absolute difference, −0.5% (−7.5% to 6.1%), respectively. Multivariate analysis also showed that water temperature was not associated with outcome. The second study included 160 hypothermic children who required resuscitation after submersion. Water temperatures were estimated based on the season. Submersion in the winter (water temperature estimated as 0–8 °C) was associated with better outcomes than submersion in spring or summer (water temperature 6–28 °C) (univariate OR, 4.55; 95% CI, 1.37–15.09).

For the critical outcome of **survival**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from a single study[65] that included 250 patients. This study included only drowning victims who had an OHCA and received EMS care, and it included those with intentional (suicide and homicide) drowning. This study showed no relationship between water temperature less than or greater than 15 °C and outcome (RR, 0.94; 95% CI, 0.34–2.62; absolute difference, 0.36%, −6.4% to 6.5%).

Witnessed status. The definition of witnessed versus unwitnessed was inconsistently defined in the studies reviewed. It was often unclear if witnessed related to the submersion or time of cardiac arrest.

For the critical outcome of **favorable neurologic outcome**, we found very-low-quality evidence (downgraded for indirectness and imprecision) from 1 observational study[60] involving 1737 patients. Univariate analysis reported by the study authors indicates an unadjusted OR for good outcomes in the group where submersion was witnessed (OR, 16.33; 95% CI, 5.58–47.77). In multivariate analysis, witnessed status was related to favorable outcome (adjusted OR, 11.8; 95% CI, 2.84–49.08); however, the analysis did not include submersion duration, which several studies have reported is an independent predictor.

For the critical outcome of **survival**, we found low-quality evidence (downgraded for risk of bias, indirectness, and imprecision)

from 4 studies[60,66,67,69] involving a total of 2857 victims. Two studies[65,67] were from the same EMS system, and both used multivariate analysis. The smaller study (255 victims) showed that witnessed status was not significantly associated with improved survival (RR, 0.55; 95% CI, 0.17–1.75; absolute difference, 3%; −3.1% to 11.2%).[65] However, in the larger subsequent study from that same EMS system, witnessed status predicted better outcome (reported univariate analysis $P = 0.05$; adjusted OR, 2.5; 95% CI, 1.38–4.52).[67] A further study[66] showed no association of witnessed status with improved survival (RR, 0.82; 95% CI, 0.26–2.59). A large observational study from Japan[60] reported an unadjusted OR of 7.38 (95% CI, 3.81–14.3) and an adjusted OR of 6.5 (95% CI, 2.81–15.02), although the unusual population of much older victims, most drowning in bathtubs, with very low favorable outcomes limited the generalizability of these findings.

Treatment recommendations

We recommend that submersion duration be used as a prognostic indicator when making decisions surrounding search and rescue resource management/operations (strong recommendation, moderate-quality evidence for prognostic significance).

We suggest against the use of age, EMS response time, water type (fresh or salt), water temperature, and witness status when making prognostic decisions (weak recommendation, very-low-quality evidence for prognostic significance).

We acknowledge that this review excluded exceptional and rare case reports that identify good outcomes after prolonged submersion in icy cold water.

Values, preferences, and task force insights

In making these recommendations, the task force placed priority on producing simple guidance that may assist those responsible for managing search and rescue operations. The public comments highlighted the difficult moral dilemmas facing the rescuer in these often emotionally charged and fast-moving environments. While it is hoped that the information will also be of interest to those managing the initial resuscitation and intensive care treatment of drowning victims, the factors evaluated were limited to those available at the scene of the drowning incident and excluded factors available after the victim was rescued (e.g., patient regurgitation, cardiopulmonary arrest duration, EMS response time, CPR duration, hospitalization[80,81]).

The recommendations presented place a relatively high value on the associations demonstrated in the exploratory prognostication modeling but acknowledge that these have not been prospectively validated as clinical decision rules. Submersion durations of less than 10 min are associated with a very high chance of favorable outcome, and submersion durations more than 25 min are associated with a low chance of favorable outcomes. Given the known difficulties with accurate timing, we suggest the time of the emergency service call as the start point for estimating submersion duration.

This question raised significant debate during the plenary conference session, task force discussion, and public comment. The main areas of controversy related to (1) how ILCOR intended the information presented would be used, and (2) the prognostic value of water temperature. We clarified in the introduction to this section that the review is intended to provide evidence from the published literature to support those responsible for search-and-rescue operations about chances of survival.

In recommending submersion duration as a factor, we acknowledge that definitions of submersion were either absent or varied between studies, and, in many studies, the precise submersion duration was not known. The 2015 Utstein consensus on drowning defines submersion duration as the duration of time that liquid covering the nose and mouth prevents air from entering the lungs.[82] We suggest that the studies are interpreted as assuming the point from which continuous submersion started (i.e., not when the person is struggling and intermittently submerging then drawing breath). Because the underwater interval is seldom documented with a timepiece, estimates can be imprecise. The Utstein consensus recommended cross-referencing submersion point with the emergency call and ambulance arrival times when possible.

The scope of this systematic review was limited to large case series and cohort studies with control groups. The review, therefore, excluded rare and exceptional case reports of survival after prolonged submersion in ice-cold water. One such example is the series of case reports presented by Tipton and Golden, which identified 26 survivors after submersion, 8 reports documented favorable outcomes in victims submerged for longer than 25 min in mostly ice-cold water.[83] A further case series noted 80% of victims surviving after cardiac arrest after immersion in ice-cold water (2 °C) for up to 2.5 h.[84] This review included more than 1000 drowning victims and produced conflicting results on the role of water temperature. Both studies noted difficulty in estimating water temperature, which is likely to be reflected in real-life rescue situations. Thus, a combination of uncertainty in the published evidence and practical difficulties of measurement led us to suggest against the routine use of water temperature as a prognostic factor.

The task force is very grateful for insightful comments submitted during the public commenting process.

High-quality CPR

Early high-quality CPR saves lives. This section reviews the evidence surrounding how to start CPR, as well as optimal chest compression characteristics, compression-only CPR, pulse checks, and ventilation. Although the systematic reviews considered adult and pediatric data, treatment recommendations in this Part are limited to adult patients. The reader is referred to "Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support" for related pediatric recommendations.

In making these recommendations, we note that several components of chest compressions can alter their effectiveness: hand position, position of the rescuer, position of the victim, and depth and rate of compression and release. The relative importance of each of these components remains to be determined; thus, optimal chest compressions are defined by compressions of the correct position, depth, and rate, ensuring full release and minimizing interruptions.

Collectively, we continue to place strong emphasis on the importance of delivering high-quality CPR.

Starting CPR (BLS 661)

Among adults and children who are in cardiac arrest in any setting (P), does CPR beginning with compressions first (30:2) (I), compared with CPR beginning with ventilation first (2:30) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Delivering high-quality chest compressions as early as possible is vital to high-quality CPR and optimizes the chance of ROSC and survival after cardiac arrest. Thus, a major change after publication of the *2010 International Consensus on CPR and ECC Science With Treatment Recommendations* was the recommendation that, for adult victims of cardiac arrest, CPR should begin with giving chest compressions rather than opening the airway and delivering rescue breaths. This treatment recommendation is based on a

review of science from the perspective of developing a treatment recommendation for adults.

Consensus on science

There were no human studies identified in this evidence review, but 4 manikin studies were identified; 1 randomized study[85] focused on adult resuscitation, 1 randomized study focused on pediatric resuscitation,[86] and 2 observational studies focused on adult resuscitation.[87,88] Compared with the previous review in 2010, this review also identified 3 new studies that were included for analysis.[85,86,88] Overall, the reviewers had serious concerns for trial methodology of included studies. The nature of comparing 2 different resuscitation protocols meant that all studies suffered from performance and detection bias because healthcare professionals were not blinded to the intervention (C-A-B versus A-B-C).

For the important outcome of **time to commencement of chest compressions**, we identified very-low-quality evidence from 1 randomized manikin study[86] representing 155 two-person teams and very-low-quality evidence from 2 observational manikin studies[87,88] representing 40 individual rescuers[88] and 33 six-person teams.[87] All studies were downgraded due to risk of bias. All studies found that C-A-B decreased the time to commencement of chest compression. The randomized trial found a statistically significant 24.13-second difference ($P < 0.05$) in favor of C-A-B.[86] The observational studies found statistically significant decreases of 20.6 s ($P < 0.001$)[88] and 26 s ($P < 0.001$),[87] respectively.

For the important outcome of **time to commencement of rescue breaths**, we identified very-low-quality evidence from 2 randomized manikin studies[85,86] representing 210 two-person teams. Both studies were downgraded due to risk of bias. Lubrano[86] found a statistically significant 3.53-s difference ($P < 0.05$) in favor of C-A-B during a respiratory arrest scenario; however, in a cardiac arrest scenario, A-B-C decreased the time to commencement of rescue breaths by 5.74 s ($P < 0.05$).[85] Marsch found that C-A-B decreased time to commencement of rescue breaths by 5 s ($P = 0.003$). The clinical significance of these differences is unknown.[85]

For the important outcome of **time to completion of first CPR cycle** (30 chest compressions and 2 rescue breaths), we identified low-quality evidence from 1 randomized manikin study[85] representing 55 two-person teams. Marsch[85] found that C-A-B decreased time to completion of first CPR cycle by 15 s ($P < 0.001$). The clinical significance of this difference is unknown.

Treatment recommendation

We suggest commencing CPR with compressions rather than ventilations (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation in the absence of human data, we placed a high value on time to specific elements of CPR (chest compressions, rescue breathing, completion of first CPR cycle). In making this recommendation in the absence of human data, given that most cardiac arrests in adults are cardiac in cause, we placed a high value on reducing time to specific elements of CPR (chest compressions and completion of first CPR cycle).

We refer the reader to the systematic review Peds 709 (see "Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support") for recommendations in children.

Chest compression-only CPR versus conventional CPR (BLS 372)

Among adults who are in cardiac arrest outside of a hospital (P), does provision of chest compressions (without ventilation) by untrained/trained laypersons (I), compared with chest compressions with ventilation (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander CPR performance; CPR quality (O)?

Introduction

Bystander CPR is a key life-saving factor in the Chain of Survival. This foundational principle was evaluated in the ILCOR 2000 Consensus on Science and was accepted in the 2005, 2010, and 2015 consensuses without reevaluation. The review in 2000 found that CPR before EMS arrival can (1) prevent VF/pVT from deteriorating to asystole, (2) increase the chance of defibrillation, (3) contribute to preservation of heart and brain function, and (4) improve survival.[89] A large systematic review from 79 studies involving 142 740 patients confirmed that bystander CPR improves survival from 3.9% to 16.1%.[90]

Although the practice of bystander CPR is accepted, a key question is whether bystanders should perform chest compression-only CPR or conventional CPR. Advocates of chest compression-only CPR note that it is easier to teach, remember, and perform compared with chest compressions with assisted ventilation. Others are concerned that chest compressions without assisted ventilation are less effective because of inadequate oxygenation and worse respiratory acidosis. These concerns are especially pertinent in the setting of asphyxial cardiac arrests (and perhaps others with a non-cardiac cause) and in the setting of prolonged CPR.[91]

It is not feasible to conduct RCTs of bystander-initiated, compression-only CPR versus bystander conventional CPR. Therefore, the clinical evidence for this question is derived from 2 sources: observational studies, and RCTs of dispatcher-assisted CPR. The benefits of telephone-assisted CPR are summarized in our EMS dispatch question (see BLS 359).

Further, much of the research on this topic has been done on patients whose arrests are presumed to be of cardiac origin, which would be difficult, if not impossible, to coach bystanders to determine in a brief training session. In addition, the research was often conducted in settings with short EMS response intervals. It is likely that a time threshold exists beyond which the absence of ventilation may be harmful.[92,93] Thus, the generalizability of the findings from the studies to all settings is cautioned. These factors taken together mean that the data available for considering this question are indirect.

When observational studies are conducted for bystander CPR, a key factor in evaluating the data is determining how the investigator determined the type of bystander CPR that was performed. In some cases, providers stayed on the scene and interviewed the bystanders about the care they provided. However, in studies of registry data, EMS providers visually evaluated bystanders' actions as they took over care during this high-stress, high-risk, and time-intensive event. This issue led to many studies being downgraded for validity because determination of the type of bystander CPR may have been biased.

Consensus on science

For the critical outcome of **survival with favorable neurologic outcome at 12 months**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from a single observational study of 1327 adult cardiac arrest victims of a presumed cardiac cause. The study reported no overall difference between compression-only and conventional CPR (OR, 0.98; 95% CI, 0.54–1.77).[92]

For the critical outcome of **survival with favorable neurologic outcome at 30 days**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 4 observational studies that enrolled 40 646 patients.[91,93–95] These studies reported no overall difference in outcomes.

For the critical outcome of **survival with favorable neurologic outcome at discharge**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 1 randomized trial[40] and 3 observational studies.[96–98] The randomized trial enrolled 1268 patients and reported no difference in outcomes (OR, 1.25; 95% CI, 0.94–1.66). The observational studies enrolled 2195 patients and also found no overall differences between compression-only and conventional CPR.

For the critical outcome of **survival at 30 days**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 randomized trial[41] and 2 observational studies.[99,100] The randomized trial enrolled 1276 patients and found no difference in outcomes (OR, 1.24; 95% CI, 0.85–1.81).[41] The observational studies enrolled 11 444 patients, and found no overall difference between compression-only and conventional CPR.[99,100]

For the critical outcome of **survival at 14 days**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[101] enrolling 829 patients, which found no difference between compression-only and conventional CPR (OR, 0.76; 95% CI, 0.46–1.24).

For the critical outcome of **survival to discharge**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 1 randomized trial[102] and 2 observational studies.[103,104] The randomized trial enrolled 520 patients and found no difference in outcomes (OR, 1.4; 95% CI, 0.88–2.22).[102] The observational studied enrolled 2486 patients and reported no difference between compression-only and conventional CPR.

Treatment recommendations

We recommend that chest compressions should be performed for all patients in cardiac arrest (strong recommendation, very-low-quality evidence).

We suggest that those who are trained and willing to give rescue breaths do so for all adult patients in cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, the task force strongly endorsed the 2010 ILCOR Consensus on Science that all rescuers should perform chest compressions for all patients in cardiac arrest.[105,106] We also highlight the 2015 dispatcher CPR recommendation that "dispatchers should provide chest compression-only CPR instructions to callers for adults with suspected OHCA."

The task force draws attention to the potential gains from the simplicity of teaching compression-only CPR.

The task force further acknowledges the potential additional benefits of conventional CPR when delivered by trained laypersons, particularly in settings where EMS response intervals are long and for asphyxial causes of cardiac arrest.

We refer the reader to Ped 414 systematic review (see "Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support") for recommendations in children.

CPR before defibrillation (BLS 363)

Among adults and children who are in VF or pulseless VT (pVT) in any setting (P), does a prolonged period of chest compressions before defibrillation (I), compared with a short period of chest compressions before defibrillation (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; rhythm control (O)?

Introduction

The optimal initial approach to a patient found in VF outside of the hospital has been unclear. Observational studies have supported a short period of CPR followed by early analysis of cardiac rhythm and administration of a shock, if indicated. Other studies support a longer period of CPR before administration of a shock.

Our literature review retained 13 articles. These included 5 RCTs,[107–111] 4 observational cohort studies,[112–115] 3 meta-analyses,[116–118] and 1 subgroup analysis of data reported in the RCT by Rea et al.[119] For the purposes of this evidence review, the GRADE table is limited to pooled data from the 5 RCTs. All of the studies were conducted in the out-of-hospital setting.

The intervention assessed was a short period of chest compressions before attempted defibrillation with a longer period of chest compressions, defined as between 90 and 180 s, before attempted defibrillation. In all of the RCTs reviewed, chest compressions were performed before initial analysis while the defibrillator equipment was being applied. The exact duration of this period was documented precisely in only 1 RCT[110] and was noted to be between 30 and 60 s.

Consensus on science

For the critical outcome of **survival to 1 year with favorable neurologic outcome** (Cerebral Performance Category [CPC] of 2 or less), we identified low-quality evidence (downgraded for bias and imprecision) from a single randomized trial that showed no benefit from a short period of CPR before shock delivery (OR, 1.18; 95% CI, 0.522–2.667).[111]

For the critical outcome of **survival to hospital discharge with favorable neurologic outcome** (defined as CPC score of 2 or less, modified Rankin Scale score of 3 or less), we identified low-quality evidence (downgraded for inconsistency and imprecision) from 4 RCTs that showed no benefit from a short period of CPR before shock delivery (OR, 0.95; 95% CI, 0.786–1.15).[107,109–111]

For the critical outcome of **survival to 1 year**, we identified low-quality evidence (downgraded for bias and imprecision) from 2 RCTs that showed no benefit from a short period of CPR before shock delivery (OR, 1.15; 95% CI, 0.625–2.115).[108,111]

For the critical outcome of **survival to hospital discharge**, we identified low-quality evidence (downgraded for bias and imprecision) from 4 RCTs that showed no benefit from a short period of CPR before shock delivery (OR, 1.095; 95% CI, 0.695–1.725).[107–109,111]

With respect to **ROSC**, we identified low-quality evidence (downgraded for bias and imprecision) from 4 RCTs that showed no benefit from a short period of CPR before shock delivery (OR, 1.193; 95% CI, 0.871–1.634).[107–109,111]

Subgroup analyses. Two subgroup analyses were also considered in this review. One subgroup analysis looked at enrollments based on EMS response interval, comparing those with intervals of less than 4–5 min versus those with intervals of 4–5 min or more. Within this subgroup, 1 study[111] found a favorable relationship with CPR for 180 s before defibrillation when the response interval was 5 min or more, but this relationship was not confirmed in 3 other RCTs.[107,108,110]

The second subgroup analysis[119] examined outcomes from early versus late analysis based on baseline EMS agency VF/pVT survival rates. Among EMS agencies with low baseline survival to hospital discharge (defined as less than 20% for an initial rhythm of VF/pVT), higher neurologically favorable survival was associated with early analysis and shock delivery, as opposed to CPR and delayed analysis and shock delivery. Yet for EMS agencies with higher baseline survival to hospital discharge (greater than 20%), 3 min of CPR followed by analysis and defibrillation resulted in higher neurologically favorable survival. Although no study has suggested harmful effects from up to 180 s of CPR before defibrillation, an exploratory

analysis from 1 RCT[110] suggested a decline in survival to hospital discharge from a prolonged period of CPR (180 s) with delayed shock delivery in patients with an initial rhythm of VF/pVT that had received bystander CPR, compared with a shorter period of CPR (30–60 s) followed by shock delivery.

Evidence summary. In summary, the evidence suggests that among unmonitored patients with cardiac arrest outside of the hospital and an initial rhythm of VF/pVT, there is no benefit to a period of CPR of 90–180 s before defibrillation when compared with immediate defibrillation with CPR being performed while the defibrillator equipment is being applied.

Treatment recommendation

During an unmonitored cardiac arrest, we suggest a short period of CPR until the defibrillator is ready for analysis and, if indicated, defibrillation.

Values, preferences, and task force insights

In making these recommendations, we placed a higher value on the delivery of early defibrillation and a lower value on the as-yet-unproven benefits of performing CPR for a longer period of time. We recognize that the evidence in support of these recommendations comes from randomized trials of variable quality conducted in several countries with a variety of EMS system configurations. The available evidence suggests a minimal effect size overall, while recognizing that it remains possible that, in systems with higher baseline survival rates, a longer period of CPR may be superior.

The task force notes that these recommendations apply to unmonitored victims in cardiac arrest. In witnessed, monitored VF/pVT arrest where a patient is attached to a defibrillator, shock delivery should not be delayed.

Knowledge gap

- What system level characteristics might influence adopted strategy?
- What effect does the quality of bystander CPR have?
- Can electrocardiographic waveform characteristics be used to determine optimal strategy?
- If CPR first strategy is adopted, what is the optimal duration of CPR (90 s, 120 s, or 180 s)?

Hand position during compressions (BLS 357)

Among adults and children who are receiving chest compressions in any setting (P), does delivery of chest compressions on the lower half of the sternum (I), compared with any other location for chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; cardiac output; harm (e.g., rib fracture); coronary perfusion pressure (O)?

Introduction

Hand position is just one of several components of chest compressions that can alter effectiveness. In making this recommendation, we considered the evidence in an attempt to define the optimal compression method. We balanced this against the current recommendation for using the lower half of the sternum[105] and the resource implications of changing current recommendations.

The task force also noted previous recommendations that the lower half of the sternum could be identified by instructing a rescuer, "Place the heel of your hand in the center of the chest with the other hand on top."[120,121] This instruction should be accompanied by a demonstration of placing the hands on the lower half of the sternum.[121]

This review focused on studies reporting clinical or physiologic outcomes related to hand position during chest compression. The scope differed from the 2010 CoSTR review, which also included computed tomographic, echocardiographic, and manikin studies reporting on the anatomic structures that would be compressed with different hand positions and the efficiency of different instructional techniques for locating hand position.

Consensus on science

There were no studies reporting the critical outcomes of favorable neurologic outcome, survival, or ROSC.

For the important outcome of **physiologic end points**, we identified 3 very-low-quality studies (downgraded for risk of bias, indirectness, and imprecision).[122–124] One crossover study in 17 adults with prolonged resuscitation from nontraumatic cardiac arrest observed improved peak arterial pressure during compression, systole (114 ± 51 mmHg versus 95 ± 42 mmHg) and end-tidal carbon dioxide ($ETCO_2$; 11.0 ± 6.7 mmHg versus 9.6 ± 6.9 mmHg) when compressions were performed in the lower third of the sternum compared with the center of the chest, whereas arterial pressure during compression recoil peak right atrial pressure and coronary perfusion pressure did not differ.[122] A second crossover study in 30 adults observed no difference between $ETCO_2$ values and hand placement.[123] A further crossover study in 10 children observed higher peak systolic pressure and higher mean arterial blood pressure when compressions were performed on the lower third of the sternum compared with the middle of the sternum.[124]

Treatment recommendation

We suggest performing chest compressions on the lower half of the sternum on adults in cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a high value on consistency with current treatment recommendations in the absence of compelling data suggesting the need to change the recommended approach.

Knowledge gaps

- The use of physiologic feedback to optimize hand position in individual patients

Chest compression rate (BLS 343)

Among adults and children who are in cardiac arrest in any setting (P), does any specific rate for external chest compressions (I), compared with a compression rate of about 100/min (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR quality (O)?

Introduction

Chest compression rate can be defined as the actual rate used during each continuous period of chest compressions over 1 min, excluding any pauses. It differs from the number of chest compressions actually delivered in 1 min, which takes into account any interruptions in chest compressions.

In the 2010 CoSTR, we recommended a manual chest compression rate of at least 100/min in adults. We noted the absence of a specific upper limit for compression rate.[105] This review notes the publication of important new observational studies in

humans that suggest the need to limit the upper rate of chest compressions.[125,126]

Consensus on science

No studies addressed the critical outcome of favorable neurologic outcome.

For the critical outcome of **survival to hospital discharge**, we identified very-low-quality evidence from 2 observational studies[125,126] representing 13 469 adult patients. Both studies were downgraded due to risk of bias.[125] They compared chest compression rates of greater than 140/min, 120–139/min, less than 80/min, and 80–99/min with the control rate of 100–119/min. When compared with the control chest compression rate of 100–119/min, there was a

- 4% decrease in survival to hospital discharge with compression rates of greater than 140/min,
- 2% decrease in survival to hospital discharge with compression rates of 120–139/min,
- 1% decrease in survival to hospital discharge with compression rates of less than 80/min,
- 2% decrease in survival to hospital discharge with compression rates of 80–99/min.

The study found a significant relationship between chest compression rate categories and survival without adjustment and when adjusted for covariates, including CPR quality measures such as compression depth and fraction (global test, $P = 0.02$). The study showed chest compression depth declined with increasing chest compression rate. The relationship of reduced compression depth at different compression rates was as follows: for a compression rate of 100–119/min, 35% of compressions had a depth less than 3.8 cm; for a compression rate of 120–139/min, 50% of compressions had a depth less than 3.8 cm; and for a compression rate of 140/min or greater, 70% of the compressions had a depth less than 3.8 cm.

In the second study,[126] there was a 4.1% decrease in survival to hospital discharge with chest compression rates of greater than 140/min and a 1.9% increase in survival to hospital discharge with rates of less than 80/min when compared with the control rate of 80–140/min. The adjusted ORs for survival to hospital discharge were 0.61 ($P = 0.18$) for rates of greater than 140/min and 1.32 ($P = 0.42$) for rates of less than 80/min and, therefore, showed no significant difference in survival to hospital discharge.

For the critical outcome of **ROSC**, we identified very-low-quality evidence from 3 observational studies[125–127] representing 13 566 adult patients. All studies were downgraded due to risk of bias. All studies had different interventions and different control chest compression rates: 100–119/min,[125] 80–140/min,[126] and 80–119/min.[127]

High compression rates. There was a significant decrease in ROSC with chest compression rates of greater than 140/min (OR, 0.72; $P = 0.006$). However, significance was lost when the model was adjusted for covariates (gender, witnessed arrest, bystander CPR, first known EMS rhythm, location).[125] There was a 5% decrease in ROSC with rates of greater than 140/min,[126] and 9% increase in ROSC with rates of greater than 120/min[127] when compared with their respective control chest compression rates.

Low compression rates. With chest compression rates of less than 80/min, there was a 3% increase in ROSC in 1 study[126] and 25% decrease in ROSC in other.[127] The adjusted ORs for ROSC were 1.01 ($P = 0.95$) for rates of greater than 140/min[126] and 1.18 ($P = 0.79$) for rates of less than 80/min.[126] Comparison of mean chest compression rates of 95.5–138.7/min with 40.3–72.0/min showed a +33% increase in ROSC ($P = 0.00925$).[127] Comparison of mean chest compression rates of 87.1–94.8/min with 40.3–72.0/min showed a +33% increase in ROSC ($P = 0.00371$).[127]

For the important outcome of **systolic blood pressure**, we identified very-low-quality evidence from 1 observational study[128] where a mechanical CPR device (Thumper, Michigan Instruments, MI) was used to deliver incremental increases in chest compression rate (from 80 to 140/min) among 18 adult patients. Within subject comparisons showed increasing the compression rate reduced systolic blood pressure (to 74% of baseline at a rate of 140/min, $P < 0.05$) but had no effect on diastolic pressure.

For the important outcome of **$ETCO_2$ levels**, very-low-quality evidence from 2 observational studies[128,129] included 41 adult patients. Both studies were downgraded due to risk of bias. One study showed no difference for compression rates in the range of 60–140/min,[128] while the second showed a small (2 mmHg) increase at higher compression rates.[129]

For the important outcome of **number of chest compressions per minute**, very-low-quality evidence from 1 observational study[126] representing 3098 adult patients was identified. This study was downgraded due to risk of bias. This study compared chest compression rates of greater than 140/min and less than 80/min with the control rate of 80–140/min. The number of chest compressions delivered per minute increased with higher chest compression rates.

Treatment recommendations

We recommend a manual chest compression rate of 100–120/min (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a high value on compatibility with the previous guidelines recommendation of a lower compression threshold of at least 100/min to minimize additional training and equipment costs (e.g., reprogramming feedback devices, educational programs). We consider the new evidence that has emerged since 2010 CoSTR as sufficient to suggest that the upper threshold should be limited to no more than 120/min.

Knowledge gaps

- Does optimizing chest compression rate based on a patient's physiologic response improve outcome?

Chest compression depth (BLS 366)

Among adults who are in cardiac arrest in any setting (P), does a different chest compression depth during CPR (I), compared with chest compression depth to 5 cm (2 in.) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR quality; coronary perfusion pressure; cardiac output; bystander CPR performance (O)?

Introduction

In 2010, we recommended that it is reasonable to compress the sternum at least 5 cm (2 in.) for all adult cardiac arrest victims. We stated that there was insufficient evidence to recommend a specific upper limit for chest compression depth. Important new data have emerged since 2010, which has prompted the revision of our treatment recommendation.

The reader is reminded of our 2010 recommendation that CPR should be performed on a firm surface when possible. Air-filled mattresses should be routinely deflated during CPR. There was insufficient evidence for or against the use of backboards during

CPR. If a backboard is used, rescuers should minimize delay in initiation of chest compressions, minimize interruption in chest compressions, and take care to avoid dislodging catheters and tubes during backboard placement.

Consensus on science

For the critical outcome of **survival with good neurologic outcome** (CPC 1-2), we found low-quality evidence (downgraded for imprecision, upgraded for a dose-response gradient), from 1 observational study[130] suggesting that a compression depth in adults of more than 5 cm (2 inches) is better than all other compression depths during manual CPR. Adjusted OR for each 5 mm increase in mean chest compression depth was 1.33 (1.03–1.71) for favorable functional outcome. Upon review by the evidence evaluation experts during the final iterative ILCOR process (see Part 2), 1 citation was excluded from the final consensus on science.[133]

For the critical outcome of **survival to hospital discharge**, we found very-low-quality evidence (downgraded for imprecision), from 3 observational studies[132,134,135] suggesting that survival may improve with increasing compression depth. The adjusted ORs for survival to hospital discharge per 5 mm increase in mean chest compression depth were 1.09 (95% CI, 0.94 to 1.27),[134] 1.04 (95% CI, 1.00 to 1.08),[135] and 1.30 (95% CI, 1.03 to 1.65).[132] In the largest study (9136 patients) a covariate-adjusted spline analysis showed a maximum survival at a mean depth of 4.0 to 5.5 cm (1.6 to 2.2 inches), with a peak at 4.6 cm (1.8 inches).[135]

For the critical outcome of **ROSC**, we found low-quality evidence (downgraded for imprecision, upgraded for a dose-response gradient) from 4 observational studies[134,135,137,140] suggesting that a compression depth of more than 5 cm (2 inches) in adults is better than all other compression depths during manual CPR. The largest study reported that ROSC increased with each 5 mm increment (adjusted OR 1.06 [95% CI: 1.04 to 1.08, $P < 0.001$]) and that the adjusted OR for ROSC for patients receiving chest compressions with a depth of 3.8 to 5.1 cm (1.5 to 2 inches) compared with more than 5.1 cm (more than 2 inches) was 0.86 (95% CI, 0.75–0.97).[135] Upon review by the evidence evaluation experts during the final iterative ILCOR process (see Part 2), 4 citations were excluded from the final consensus on science.[133,136,138,139]

For the important outcome of **injury**, we found very-low-quality evidence (downgraded for serious risk of bias, imprecision, and very serious indirectness) from 1 observational study suggesting that a compression depth of more than 6 cm (2.4 in.) is associated with an increased rate of injury in adults when compared with compression depths of 5–6 cm (2–2.4 in.) during manual CPR. This study included 170 of 353 patients (183 excluded for incomplete data), and injuries were reported in 63% with compression depth more than 6 cm (more than 2.4 in.) and 31% with compression depth less than 6 cm. Further, injuries were reported in 28%, 27%, and 49% with compression depths less than 5 cm (less than 2 in.), 5–6 cm (2–2.4 in.), and more than 6 cm (more than 2.4 in.), respectively.[139]

Treatment recommendations

We recommend a chest compression depth of approximately 5 cm (2 in.) (strong recommendation, low-quality evidence) while avoiding excessive chest compression depths (greater than 6 cm [greater than 2.4 in.] in an average adult) (weak recommendation, low-quality evidence) during manual CPR.

Values, preferences, and task force insights

In making this recommendation, we place a high value on the consistency with our previous recommendations given the resource implications (e.g., training, reprogramming CPR devices) of making a change, and consistency in data showing harm from compressions that are too shallow. In addition, we note new data from the US and Canadian Resuscitation Outcomes Consortium group reporting a "sweet spot" for compression depth between 4.03 and 5.53 cm (between 1.59 and 2.2 in.; peak, 4.56 cm [1.8 in.]) and harm from excessive compression depths.[133] We used the term *approximately 5 cm* (approximately 2 in.) to reflect these findings plus the known variation in patient shapes and sizes around the world.

We refer the reader to Ped 394 systematic review (see "Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support") for recommendations in children.

Knowledge gaps

- We need additional studies on the relationship of compression depth and injuries, and how these factors may vary in relation to differences in body/chest size and differences in chest wall compliance and between adults and children. We also need additional studies on the relationship and interaction between chest compression rate and depth.

Chest wall recoil (BLS 367)

Among adults and children who are in cardiac arrest in any setting (P), does maximizing chest wall recoil (I), compared with ignoring chest wall recoil (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; coronary perfusion pressure; cardiac output (O)?

Introduction

Critical to hemodynamically effective CPR is blood returning to the chest between compressions. Venous return is in part influenced by the pressure gradient between extrathoracic and intrathoracic veins. Leaning on the chest wall between compressions, precluding full chest wall recoil, could raise intrathoracic pressure and reduce right heart filling, coronary perfusion pressure, and myocardial blood flow.[140,141] Observational studies indicate that leaning is common during CPR in adults and children.[141,142] This question sought to examine the effect of chest wall leaning during standard manual CPR on outcome.

Consensus on science

For the critical outcomes of ROSC, survival at hospital discharge, and survival with favorable neurologic/functional outcome, we found no evidence to address the question.

For the important outcome of **coronary perfusion pressure**, we found 3 observational studies: 2 in animal models[140,143] and 1 in anesthetized children not in cardiac arrest,[144] which provided very-low-quality evidence, downgraded for serious risk of bias and very serious indirectness. All 3 studies reported a reduced coronary perfusion pressure with incomplete chest recoil. In anesthetized children undergoing mechanical ventilation during cardiac catheterization, Glatz et al. analyzed the effect of leaning by applying a force on the chest corresponding to 10% and 20% of body weight; this resulted in a proportional reduction in coronary perfusion pressure.[144] Yannopoulos et al. and Zuercher et al. reported in swine models of VF that leaning on the chest precluding full chest recoil reduced the coronary perfusion pressure in a dose-dependent manner.[140,143]

For the important outcome of **cardiac output/cardiac index**, we found 2 observational studies (1 in an animal model and 1 in anesthetized children not in cardiac arrest) also representing very-low-quality evidence downgraded for serious risk of bias and very serious indirectness.[140,144] The study in animals reported a proportional reduction in cardiac index when 10% and 20% of the forces applied during compression remained between compressions.[140]

In contrast, Glatz et al. found that leaning forces had no effect on cardiac output.[144]

Treatment recommendation

We suggest that rescuers performing manual CPR avoid leaning on the chest between compressions to allow full chest wall recoil (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, the task force placed high value on consistency with previous recommendations and in ensuring that a clear recommendation is provided for CPR training and practice. We acknowledge that some studies have reported a leaning threshold below which there are possibly no adverse hemodynamic effects, but the task force anticipates that this would be difficult to measure and teach.

Knowledge gaps

- Impact of full chest recoil in humans and the impact of this recommendation on rescuer performance when factoring in depth, rate, and duty cycle.
- Identification of best options to monitor full chest recoil.

Minimizing pauses in chest compressions (BLS 358)

Among adults and children who are in cardiac arrest in any setting (P), does minimization of pauses in chest compressions for cardiac rhythm analysis or ventilations (I), compared with prolonged pauses in chest compressions for rhythm analysis or ventilations (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; CPR quality; rhythm control (O)?

Introduction

For adults in cardiac arrest without an advanced airway, such as an endotracheal tube, chest compressions are often briefly paused to allow for ventilation. Some CPR guidelines suggest that the duration of pauses for ventilation should not exceed 5 s. However, forceful insufflations to comply with the guideline carry a risk of gastric insufflation, and may not be feasible for mouth-to-mouth ventilation.

Preshock intervals include the time required for assessment of the rhythm, charging, and actually delivering a shock. *Postshock intervals* reflect the time from shock delivery to resumption of chest compression. Achieving short preshock and postshock pauses requires awareness of the importance of minimizing the pause, attention during training, and an excellent interplay among the rescuers working together during a resuscitation attempt. In this systematic review, we examine the possible consequences of interruptions of chest compressions on various critical and important outcomes.

Consensus on science

For the critical outcome of **favorable neurologic outcome**, we found 1 low-quality observational study (downgraded for imprecision)[145] enrolling 199 patients. This study compared survival against a reference ventilation range of 5–6 s and found no difference with longer ranges of time for 2 breaths delivered by lay rescuers, ranging over 10–12 s (adjusted OR, 1.30; 95% CI, 0.29–5.97) and 13 s or greater (adjusted OR, 2.38; 95% CI, 0.46–12.1). We found no studies addressing pauses for rhythm analysis and shock.

For the critical outcome of **survival to hospital discharge**, there were no studies examining duration required to deliver 2 breaths. For perishock pauses, we identified moderate-quality evidence (downgraded for indirectness) from 1 RCT that compared 2 AED algorithms.[146] The study enrolled 845 patients but found no benefit (OR, 0.81; 95% CI, 0.33–2.01) of reducing preshock and postshock pauses. We found moderate-quality evidence from 3 observational studies (upgraded for dose–response gradient)[147–149] including 3327 patients showing a strong relationship with shorter preshock and postshock pauses (less so for postshock pauses) or higher chest compression fraction.

For the critical outcome of **ROSC**, we found no studies addressing the duration required to deliver 2 breaths. For perishock pause, we found 1 very-low-quality observational study[150] (downgraded for risk of bias and imprecision) including 35 patients, indicating benefit from limiting preshock and postshock pauses and 1 very-low-quality study (downgraded for risk of bias)[151] including 2103 patients, suggesting benefit from achieving chest compression fractions (i.e., total CPR time devoted to compressions) greater than 40%.

For the important outcome of **shock success**, we found 1 very-low-quality observational study (downgraded for imprecision)[136] including 60 patients, indicating benefit of shorter preshock pauses: OR of 1.86 (95% CI, 1.10–3.15) for every 5 s.

Treatment recommendations

We suggest that in adult patients receiving CPR with no advanced airway, the interruption of chest compressions for delivery of 2 breaths should be less than 10 s (weak recommendation, low-quality evidence).

We recommend that total preshock and postshock pauses in chest compressions be as short as possible. For manual defibrillation, we suggest that preshock pauses be as short as possible and no more than 10 s (strong recommendation, low-quality evidence).

We suggest during conventional CPR that chest compression fraction (i.e., total CPR time devoted to compressions) should be as high as possible and at least 60% (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place a high priority on minimizing interruptions for chest compressions. We seek to achieve this overall objective by balancing it with the practicalities of delivering 2 effective breaths between cycles of chest compressions to the patient without an advanced airway.

Knowledge gaps

- Analysis of causes and consequences of pauses for other reasons or without obvious reason.
- Measures to avoid (unnecessary) pauses for rhythm analysis, such as rhythm analysis during chest compressions.

Compression–ventilation ratio (BLS 362)

Among adults and children who are in cardiac arrest in any setting (P), does delivery of CPR with another specific compression–ventilation ratio (I), compared with CPR that uses a 30:2 compression–ventilation ratio (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; hands-off time (O)?

Introduction

For adults in cardiac arrest without an advanced airway, such as an endotracheal tube, chest compressions are often briefly paused to allow for ventilation. In 2005, many guidelines for adults in cardiac arrest were changed from a compression–ventilation

ratio of 15:2 to a ratio of 30:2. This structured review identified 4 observational cohort before–after studies, all conducted in the out-of-hospital setting, that evaluated a bundle of care interventions implemented after the 2005 guidelines and used a 30:2 compression–ventilation ratio, compared with care before the 2005 guidelines that used a 15:2 compression–ventilation ratio.[152–155] No studies were identified that compared a 30:2 compression–ventilation ratio to a compression–ventilation ratio other than 15:2. One observational cohort study,[156] although meeting our inclusion criteria, was excluded due to concerns regarding the study design, analytical technique, and challenges with data reporting and abstraction.

Consensus on science

For the critical outcome of **survival with favorable neurologic outcome at discharge**, we found very-low-quality evidence from 2 observational studies[152,153] that were downgraded for risk of bias and indirectness. Of the 1711 patients included, those who were treated under the 2005 guidelines with a compression–ventilation ratio of 30:2 had slightly higher survival than those patients treated under the 2000 guidelines with a compression–ventilation ratio of 15:2 (8.9% versus 6.5%; RR 1.37 [0.98–1.91]).

For the critical outcome of **survival to hospital discharge**, we identified very-low-quality evidence from 4 observational studies.[152–155] The level of evidence was downgraded for risk of bias and indirectness. Of the 4183 patients included, those who were treated under the 2005 guidelines with a compression–ventilation ratio of 30:2 had slightly higher survival than those patients treated under the 2000 guidelines with a compression-ventilation ratio of 15:2 (11.0% versus 7.0%; RR 1.75 [1.32–2.04]).

For the critical outcome of **survival to 30 days**, we identified very-low-quality evidence from 1 observational study[155] that was downgraded for risk of bias and indirectness. Patients treated under the 2005 guidelines had slightly higher survival than those patients treated under the 2000 guidelines (16.0% versus 8.3%; RR 1.92 [1.28–2.87]).

For the critical outcome of any **ROSC**, we identified very-low-quality evidence from 2 observational studies.[152,153] The studies were downgraded for risk of bias and indirectness. Patients treated under the 2005 guidelines had a ROSC more often than those patients treated under the 2000 guidelines (38.7% versus 30.0%; RR 1.30 [1.14–1.49]).

For the critical outcome of **ROSC at hospital admission**, we identified very-low-quality evidence from 2 observational studies.[153,155] The studies were downgraded for risk of bias and indirectness. Of the 1708 patients included, those treated under the 2005 guidelines had ROSC at hospital admission more often than those patients treated under the 2000 guidelines (34.5% versus 17.1%; RR 2.02 [1.69-2.41]).

For the important outcome of **hands-off time**, we identified very-low-quality evidence from 2 observational studies[153,154] that were downgraded for risk of bias and indirectness. Patients who were treated with the use of the 2005 guidelines had less hands-off time than those patients treated under the 2000 guidelines.

Treatment recommendation

We suggest a compression–ventilation ratio of 30:2 compared with any other compression–ventilation ratio in patients in cardiac arrest (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we placed a high priority on consistency with our 2005 and 2010 treatment recommendations and the findings identified in this review, which suggest that the bundle of care (which included changing to a compression to ventilation ratio of 30:2 from 15:2) resulted in more lives being saved. We note that there would likely be substantial resource implications (e.g., reprogramming, retraining) associated with a change in recommendation, and an absence of any data addressing our critical outcomes to suggest our current recommendation should be changed.

Timing of CPR cycles (BLS 346)

Among adults who are in cardiac arrest in any setting (P), does pausing chest compressions at another interval (I), compared with pausing chest compressions every 2 min to assess the cardiac rhythm (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; coronary perfusion pressure; cardiac output (O)?

Introduction

The 2005 and 2010 CoSTR publications recommended that pausing chest compressions to undertake a rhythm check should occur every 2 min. This recommendation is supported by indirect evidence that rescuer fatigue occurs by about 2 min, and a rhythm check is a natural time point, when possible, to change the compressor.

Feedback from the public comment period for this publication supported maintaining consistency with previous recommendations.

Consensus on science

There are currently no studies that directly address the question of optimal CPR intervals and their effect on the identified critical outcomes of survival with favorable neurologic or functional outcome at discharge or survival only at discharge or the important outcomes of ROSC, coronary perfusion pressure, cardiac output.

Treatment recommendation

We suggest pausing chest compressions every 2 min to assess the cardiac rhythm (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we placed a high priority on consistency with previous recommendations and the absence of contradictory evidence to prompt a change. We placed value on simplifying resuscitation logistics by coordinating rhythm and pulse checks with standard recommendations for rotating the provider performing chest compressions every 2 min.

Knowledge gaps

- Does the optimal interval for rhythm checks differ for patients with different initial cardiac rhythms?
- Does the duration between collapse and EMS arrival affect the optimal interval to interrupt compressions to check rhythm?
- Do different intervals interfere with the overriding goal of minimizing interruptions in chest compressions?
- What is the relationship between rescuer fatigue, chest compression quality, and the optimal interval to check rhythm?
- What effect does the timing of rhythm checks have on the timing of drug administration?

Check for circulation during BLS (BLS 348)

Among adults and children who are in cardiac arrest in any setting (P), does interruption of CPR to check circulation (I), compared with no interruption of CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days,

and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; chest compression fraction (O)?

Introduction

In the 2015 PICO development process, additional questions were developed to address knowledge gaps identified in 2010. As a result of significant similarities in other BLS PICO questions, very rigid study inclusion criteria were applied. Only comparative human studies assessing the PICO listed outcomes were considered.

Consensus on science

Of the 654 articles found during the search, and a follow-up search performed early in 2015 identifying a potential additional 112 studies, none were found to relate to the specific question.

Treatment recommendation

Outside of the ALS environment where invasive monitoring is available, there is insufficient data around the value of a pulse check while performing CPR. We therefore do not make a treatment recommendation regarding the value of a pulse check.

Values, preferences, and task force insights

Emphasis should remain on minimizing interruptions in chest compressions and avoiding pausing for a pulse check without strong suspicion of ROSC (e.g., clinically or by hemodynamic monitoring).

Knowledge gaps

- Human data around value/accuracy of circulation assessment.

Feedback for CPR quality (BLS 361)

Among adults and children who are in cardiac arrest in any setting (P), does real-time feedback and prompt device regarding the mechanics of CPR quality (e.g., rate and depth of compressions and/or ventilations) (I), compared with no feedback (C), change survival with favorable neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander CPR rates; time to first compressions; time to first shock; CPR quality (O)?

Introduction

The use of CPR feedback or prompt devices during CPR in clinical practice or CPR training is intended to improve CPR quality as a means to improving ROSC and survival. The forms of CPR feedback or prompt devices include audio and visual components such as voice prompts, metronomes, visual dials, numerical displays, waveforms, verbal prompts, and visual alarms. Visual displays enable the rescuer to see compression-to-compression quality parameters, including compression depth and rate, in real time. All audio prompts may guide CPR rate (e.g., metronome) and may offer verbal prompts to rescuers (e.g., "push harder," "good compressions").

The use of CPR feedback or prompt devices should be considered as part of a broader system of care that should include comprehensive CPR quality improvement initiatives, rather than an isolated intervention. The reader is referred to the relevant sections of the Education, Implementation, and Teams Task Force recommendations, EIT 640: Measuring Quality of Systems, EIT 645: Debriefing of Resuscitation Performance, and EIT 648: CPR Feedback Devices During Training (see "Part 8: Education, Implementation, and Teams").

Consensus on science

This review identified 12 studies, of which 2 studies were randomized studies[131,135] and 10 studies were observational of before–after design.[129,138,141,157–163] The included studies were 9 studies in 3716 adults[129,131,135,138,157,159–162] and 3 studies of 34 pediatric patients.[141,158,163] Four studies included patients with in-hospital cardiac arrest,[141,157,158,163] 7 studies with OHCA[131,135,138,159–162] and 1 study[129] had a mixture of patients from in and out-of-hospital settings.

Feedback devices examined included accelerometer-based devices[131,135,138,141,157,159,161–163] and audiotape of prompts.[129,158,160] Compared with the previous evidence review performed in 2010, this review identified 8 new studies that were included for analysis.[131,135,138,141,159,161–163] The nature of using feedback or prompt devices meant that all studies suffered from performance and detection bias because healthcare professionals were not blinded to intervention (feedback or no feedback).

For the critical outcome of **favorable neurologic outcome**, we identified moderate-quality evidence from 1 cluster-randomized study[131] representing 1586 patients, and very-low-quality evidence from 2 observational studies in adults[159,162] representing 670 patients. All studies were downgraded due to risk of bias. The randomized trial found no difference in the number of patients who achieved favorable neurologic outcome (control 10.1% versus 10.3%, $P = 0.855$). No studies showed a statistically significant difference in favorable neurologic outcome with the use of CPR feedback. Effect of CPR feedback on survival with favorable neurologic outcome ranged from −0.8% to 5.8%.

For the critical outcome of **survival to hospital discharge**, we identified moderate-quality evidence from 1 cluster-randomized study[131] representing 1586 patients, and very-low-quality evidence from 4 observational studies in adults,[138,157,159,162] and 1 observational study in children[163] representing 1192 patients. All studies were downgraded due to risk of bias. The randomized trial found no difference in the number of patients who achieved survival to hospital discharge (control 44.7% versus 44.3%, $P = 0.962$). No studies showed a statistically significant difference in survival to hospital discharge with the use of CPR feedback. The effect of CPR feedback on survival to hospital discharge ranged from −0.9 to 5.2.

For the critical outcome of **ROSC**, we identified moderate-quality evidence from 2 randomized studies[131,135] representing 1886 patients, and very-low-quality evidence from 7 observational studies in adults[135,138,157,159–162] and 1 observational study in children[163] representing 3447 patients. All studies were downgraded due to risk of bias. The randomized trial found no difference in the number of patients who achieved ROSC (control 44.7% versus 44.3%, $P = 0.962$). Only 1 study[162] showed a statistically significant difference in ROSC with the use of feedback; however, in this study, feedback was activated at the discretion of the physician, and no details were provided regarding the decision-making process to activate or not activate feedback. Effect of CPR feedback on ROSC ranged from −4.4% to 17.5%: 1 study demonstrated a 50% increase in ROSC with CPR feedback; however, this small study had only 4 patients in each group.[163]

For the important outcome of **chest compression rate**, we identified moderate-quality evidence from 2 randomized studies[131,135] representing 1474 patients, and very-low-quality evidence from 4 observational studies: 3 in adults[138,157,159] representing 777 patients, and 1 in children[163] representing 8 patients. All studies were downgraded due to risk of bias. The cluster RCT[131] found a significant difference of −4.7/min (95% CI, −6.4 to −3.0/min) when feedback was used, and the prospective randomized trial[137] showed no difference in compression rates with and without feedback. In both randomized trials, compression rates were all close to international recommendations of 100/min. One observational study[157] showed no difference in chest compression rates with and without feedback, and, again, all compression rates were close to

international recommendations of 100/min. The other 2 observational studies[138,159] showed lower compression rates in the group with CPR feedback: 128 to 106/min (difference, −23; 95% CI, −26 to −19)[159] and 121–109/min (difference, −12; 95% CI, −16 to −9).[138] The pediatric study[163] found a median difference of −10/min with feedback, and, again, the chest compression rate in the control group exceeded 120/min. The use of CPR feedback devices may be effective in limiting compression rates that are too fast.

For the important outcome of **chest compression depth**, we identified moderate-quality evidence from 2 randomized studies[131,135] representing 1296 patients, and very-low-quality evidence from 4 observational studies: 3 in adults[138,157,159] representing 777 patients and 1 in children[163] representing 8 patients. All studies were downgraded due to risk of bias. The cluster RCT[131] found a significant +1.6 mm (95% CI, 0.5–2.7) (cluster adjusted) difference in chest compression depth with feedback. However, this is of questionable clinical significance, and the average compression depths in both arms were less than international recommendations of 5 cm (2 in.) in adults (3.96 cm [1.55 in.] and 3.87 cm [1.52 in.]). The prospective randomized trial[135] found no significant difference in compression depth with and without feedback, and all compression depths were close to, but slightly less than, international recommendations of 5 cm (2 in.) in adults. One observational study[157] showed no difference in chest compression depth with and without feedback, and all compression rates were close to, but less than, international recommendations of 5 cm (2 in.) in adult patients (4.4 and 4.3 cm or 1.7 in.). Two observational studies[138,159] showed significantly deeper chest compressions in the groups with CPR feedback: Bobrow et al[159] found a 1.06 cm (0.42 in.) increase with feedback (5.46 versus 4.52 cm, or 2.15 versus 1.78 in.) (mean difference, 0.97 cm; 95% CI, 0.71–1.19 cm), while the findings by Kramer–Johansen[138] were more modest (increase from 3.4 to 3.88 cm, or [from 1.3 to 1.5 inches]) (mean difference, 0.4 cm; 95% CI, 0.2–0.6). The pediatric study[163] found no median difference in compression depth. The use of CPR feedback devices did not seem to make an appreciable difference in chest compression depth.

For the important outcome of **chest compression fraction**, we identified moderate-quality evidence from 1 randomized study[131] and very-low-quality evidence from 3 observational studies in adults[138,157,159] and 1 in children.[163] All studies were downgraded due to risk of bias. The randomized study found a cluster adjusted difference of +1.9% (65.9% versus 64.0%; $P = 0.016$) when CPR prompt devices were used. Although statistically significant, such a small difference has questionable clinical significance. The adult studies found no significant difference between groups, and the sample size of the pediatric study was too small to enable inferential statistical analysis. The use of CPR feedback devices did not seem to make an appreciable difference in chest compression fraction.

For the important outcome of **ventilation rate**, we identified very-low-quality evidence from 3 observational studies in adults[138,157,159] representing 532 patients. All studies were downgraded due to risk of bias. None of the studies showed a significant difference in ventilation rate with and without CPR feedback.

For the important outcome of **$ETCO_2$**, we identified very-low-quality evidence from 2 observational studies in adults[129,159] representing 131 patients. All studies were downgraded due to risk of bias. Kern[129] found that the $ETCO_2$ was significantly higher when CPR feedback was used (+6.3 mmHg with compression rate feedback of 120/min and +4.3 mmHg with compression rate feedback of 80/min). Bobrow[159] found an absolute difference of −2.2 mm Hg with CPR feedback. The clinical significance of these differences is questionable.

For the important outcome of **leaning force** during chest compressions, we identified very-low-quality evidence from 1 observational study in children[141] representing 20 patients. This study was downgraded due to risk of bias. Leaning force was decreased by 0.9 kg with the use of feedback.

Treatment recommendation

We suggest the use of real-time audiovisual feedback and prompt devices during CPR in clinical practice as part of a comprehensive system for care for cardiac arrest (weak recommendation, very-low-quality evidence).

We suggest against the use of real-time audiovisual feedback and prompt devices in isolation (i.e., not part of a comprehensive system of care) (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on development of systems of care with continuous quality improvement than on cost. Resource-poor environments may choose not to adopt this technology in favor of allocating resources to other system developments. Devices that provide real-time CPR feedback also document CPR metrics that may be used to debrief and inform strategies aimed at improving CPR quality. Currently available audiovisual feedback devices provide information on key CPR parameters such as compressions and ventilation; however, the optimal targets and the relationships among different targets have not been fully defined.

Knowledge gaps

- In adults and children sustaining in-hospital or out-of-hospital cardiac arrest, what effect does a chest compression rate of 100–120/min, compared with rates of less than 100/min or greater than 120/min, have on CPR quality improvement initiatives compared with no such initiatives on survival and other clinical and cost-effectiveness outcomes?

EMS chest compression-only versus conventional CPR (BLS 360)

Among adults who are in cardiac arrest outside of a hospital (P), does provision of chest compressions with delayed ventilation by EMS (I), compared with chest compressions with early ventilation by EMS (C), change survival with favorable neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; time to first compressions; CPR quality (O)?

Introduction

The treatment of a patient with OHCA is extremely complex from several perspectives. Operationally, there is very significant heterogeneity in EMS systems design (e.g., emergency medical responder versus emergency medical technician versus paramedic versus physician based) and resource availability (e.g., number of rescuers, equipment, evidence-based protocols, quality improvement programs). Clinically, there is extreme patient and arrest location variability, with patients located in urban, rural, and remote patient settings and in unpredictable and diverse environments with variable rates of bystander CPR and AED use. Logistically, the initial EMS care of an OHCA victim involves several concurrent goals with complex interactions of scene safety, patient assessment, patient care, communication, extrication, and transport.

This systematic review found no studies that directly addressed the question of EMS compression-only CPR compared with conventional CPR. Four North American observational studies were identified, which adopted a bundled intervention for adult patients, with a presumed cardiac cause of their cardiac arrest.[164–167] EMS response intervals in these settings were generally within 5–6 min.

The bundled interventions were broadly similar and comprised 200 initial chest compressions, a single shock rather than stacked shocks, and immediate resumption of a further 200 chest compressions before rhythm/pulse check. Epinephrine was given early and endotracheal intubation delayed. Basic airway adjuncts were used with either passive oxygen insufflation or bag-mask ventilation (ventilation rate 8/min). The findings from the review provide evidence about the effects of the bundled intervention rather than delayed ventilation in isolation.

Consensus on science

For the critical outcome of **survival to hospital discharge** with favorable neurologic outcome in all OHCAs, we have identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational trial[166] that enrolled 1019 patients showing no benefit (unadjusted OR, 1.07; 95% CI, 1.41–8.79).

For the critical outcome of **survival with favorable neurologic outcome** in the subset of witnessed arrest/shockable rhythm OHCA, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 3 observational studies[164–166] that enrolled 1325 patients showing benefit: OR, 3.6 (95% CI, 1.77–7.35)[164]; OR, 5.24 (95% CI, 2.16–12.75)[165]; and adjusted OR, 2.5 (95% CI, 1.3–4.6).[166]

For the critical outcome of **survival to hospital discharge** in the subgroup of all OHCAs, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 3 observational studies[167,168] showing benefit: OR, 3.26 (95% CI, 2.46–4.34)[167]; OR, 2.50 (95% CI, 1.75–3.58; cohort)[168]; and OR, 3.05 (95% CI, 1.07–8.66; before–after).[168]

For the critical outcome of **survival to hospital discharge** in the subgroup of witnessed arrest/shockable rhythm cardiac arrest, we identified very-low-quality evidence (downgraded for indirectness and imprecision) in 3 observational studies[164,165,168] that showed benefit: OR, 3.67 (95% CI, 1.98–7.12)[164]; OR, 5.58 (95% CI, 2.36–13.20)[165]; OR, 2.94 (95% CI, 1.82–4.74); and OR, 4.3 (95% CI, 0.98–19.35).[168]

For the critical outcome of **ROSC** in all out of hospital cardiac arrest patients, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) in 1 observational study[166] showing no benefit (OR, 0.85; 95% CI, 0.64–1.11) to EMS provision of chest compressions with delayed ventilation.

Treatment recommendation

We suggest that where EMS systems[2] have adopted bundles of care involving minimally interrupted cardiac resuscitation,[3] the bundle of care is a reasonable alternative to conventional CPR for witnessed shockable out of hospital cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

This recommendation places a relatively high value on (1) the importance of provision of high-quality chest compressions and (2) simplifying resuscitation logistics in the out-of-hospital setting in a defined EMS system with demonstrated clinical benefit, and a relatively low value on the uncertain effectiveness, acceptability, feasibility, and resource use in different EMS systems compared with those in this CoSTR.

We acknowledge the pending results of the important and very large clinical trial NCT01372748 with a primary aim to compare survival at hospital discharge after continuous chest compressions versus conventional CPR with interrupted chest compressions in patients with OHCA.

Knowledge gaps

The following knowledge gaps currently exist:

- The need for higher-quality evidence (e.g., RCT).
- The effect of delayed ventilation versus 30:2 high-quality CPR.
- The duration of maximum delay in positive-pressure ventilation.

Passive ventilation technique (BLS 352)

Among adults and children who are in cardiac arrest in any setting (P), does addition of any passive ventilation technique (e.g., positioning the body, opening the airway, passive oxygen administration) to chest compression-only CPR (I), compared with just chest compression-only CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander initiated CPR; oxygenation (O)?

Introduction

During chest compression-only CPR in the out of hospital setting, some described EMS systems have chosen to provide passive ventilation in the form of an airway maneuver and/or device combined with an oxygen-delivery mask. No studies were found describing this in the lay rescuer setting.

Three studies were identified. Two compared intermittent positive-pressure ventilation via an endotracheal tube with continuous insufflation of oxygen through a modified endotracheal tube.[169,170] The third study compared placement of an oropharyngeal airway and administration of oxygen by nonrebreather mask or by bag-mask ventilation during a bundle of care involving 200 continuous chest compressions and delayed intubation.[166]

Consensus on science

For the critical outcome of **favorable neurologic outcome**, we identified very-low-quality evidence (downgraded due to serious risk of bias and indirectness) from 1 retrospective study, which involved 1019 patients that showed no difference between passive (nonrebreather mask) and active (bag-mask) ventilation[166] (adjusted OR, 1.2; 95% CI, 0.8–1.9).

For the critical outcome of **survival**, we found very-low-quality evidence from a single retrospective study (downgraded for serious indirectness and risk of bias).[166] This study reported no significant difference in survival (RR, 1.1; 95% CI, 0.72–1.54).

For the critical outcome of **ROSC**, we found very-low-quality evidence (downgraded for serious indirectness and risk of bias) from 2 RCTs[169,170] and 1 observational study.[166] None of the studies showed any significant difference: OR, 0.88 (95% CI, 0.6–1.3)[170]; OR, 0.8 (95% CI, 0.7–1.0)[166]; and RR, 1.27 (95% CI, 0.6–2.61).[169]

Treatment recommendation

We suggest against the routine use of passive ventilation techniques during conventional CPR (weak recommendation, very-low-quality evidence).

We suggest that where EMS systems have adopted bundles of care involving continuous chest compressions, the use of passive ventilation techniques may be considered as part of that bundle for patients in OHCA (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place priority on consistency with our previous recommendations in the absence of

[2] Priority-based dispatch systems, multitiered response, EMS in urban and rural communities.

[3] Up to 3 cycles of passive oxygen insufflation, airway adjunct insertion, and 200 continuous chest compressions with interposed shocks.

compelling evidence for improvement in any of our critical outcomes. We acknowledge that where EMS systems have adopted a bundle of care that includes passive ventilation, it is reasonable to continue in the absence of compelling evidence to the contrary.

Knowledge gaps

- Which elements of the bundled care (compressions, ventilations, delayed defibrillation) are most important?
- What is the optimal method for ensuring a patent airway?
- Is there a critical volume of air movement required to maintain effectiveness?
- How effective is passive insufflation in children?

Harm from CPR to victims not in cardiac arrest (BLS 353)

Among adults and children who are not in cardiac arrest outside of a hospital (P), does provision of chest compressions from lay rescuers (I), compared with no use of chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; harm (e.g., rib fracture); complications; major bleeding; risk of complications (e.g., aspiration); survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to admission (O)?

Introduction

Many lay rescuers are concerned that delivering chest compressions to a person who is not in cardiac arrest could lead to serious complications and, thus, are reluctant to initiate CPR even when a person is actually in cardiac arrest. Studies reporting harm from CPR to persons not in cardiac arrest were reviewed.

Consensus on science

For the important outcome of "**harm**," we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 4 observational studies enrolling 762 patients who were not in cardiac arrest and received CPR by lay rescuers outside the hospital.[171–174] Three of the studies[171–173] reviewed the medical records to identify harm, and 1 included follow-up telephone interviews.[171] Pooled data from these 3 studies, encompassing 345 patients, found an incidence of bone fracture (ribs and clavicle) of 1.7% (95% CI, 0.4–3.1%), pain in the area of chest compression of 8.7% (95% CI, 5.7–11.7%), and no clinically relevant visceral injury. The fourth study[174] relied on fire department observations at the scene, and there were no reported injuries in 417 patients.

Treatment recommendation

We recommend that laypersons initiate CPR for presumed cardiac arrest without concerns of harm to patients not in cardiac arrest (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the survival benefit of CPR initiated by laypersons for patients in cardiac arrest against the low risk of injury in patients not in cardiac arrest.

Knowledge gaps

- More studies are needed with robust methodology to identify harm and provide follow-up after hospital discharge. Many of the conditions prompting initiation of CPR for those not in cardiac arrest are associated with reduced responsiveness and have poor prognosis. Whether chest compressions and rescue breaths could accentuate these conditions independent of physical injury, though unlikely, is not known at the present time.
- The incidence of chest wall bone fractures was substantially lower than the incidence reported after CPR in patients who were in cardiac arrest. This is likely the result of shorter duration of CPR (approximately 6 min) initiated by laypersons but stopped by professional rescuers, and younger patient age in the studies reviewed. However, the possibility of underreporting due to nonsystematic diagnostic studies cannot be excluded, and further research is warranted.
- Could the accuracy of dispatcher-assisted protocol be enhanced to reduce the frequency of CPR performed on patients not in cardiac arrest without compromising the initiation of CPR on patients in cardiac arrest?

Early defibrillation

This section reviews (1) the evidence surrounding the clinical benefit of AEDs in the out-of-hospital setting by laypeople and healthcare providers, and (2) the complex choreography of care needed to ensure high-quality CPR and effective defibrillation. Collectively, we continue to place strong emphasis on the importance of rapid defibrillation as the treatment of choice for VF/pVT in the out-of-hospital and hospitalized settings.

Public-access defibrillation (BLS 347)

Among adults and children who are in cardiac arrest outside of a hospital (P), does implementation of a public-access AED program (I), compared with traditional EMS response (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; bystander CPR rates; bystander use of AED; time to commence CPR (O)?

Introduction

Population (e.g., rates of witnessed arrest) and EMS program (e.g., response intervals) characteristics affect survival and can vary considerably. The concept of early defibrillation is well established in improving outcome from cardiac arrest. This review identified 15 relevant studies (1 RCT and 14 observational studies) spanning the years 2002–2013, with the associated variations in recommended practice of bystander CPR during these periods. The authors recognize that some studies may involve repeat analysis and reporting of the same cardiac arrest population, which limits the ability to provide a summative effect measure in the reported analyses.

Consensus on science

For the critical outcome of **survival to 1 year with favorable neurologic outcome**, we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational trial[175] enrolling 1394 patients showing improved outcomes with public-access defibrillation (unadjusted OR, 3.53; 95% CI, 1.41–8.79).

For the critical outcome of **survival 30 days with favorable neurologic outcome**, we identified very-low-quality evidence (downgraded for inconsistency and indirectness) from 3 observational studies[176–178] enrolling 182 119 patients demonstrating improved survival (range, 31.6–55%) with public-access defibrillation compared with no program (range, 3–37%).

For the critical outcome of **survival to discharge with favorable neurologic outcome**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 1 randomized trial[179] and 3 observational studies.[175,180,181] The randomized trial enrolled 235 patients and found no difference in favorable neurologic outcomes (CPC, 1–2; RR, 1.73; 95% CI, 0.95–3.19). The observational studies included 4581 patients demonstrating improved survival (range, 4.1–50%) with public-access defibrillation compared with no program (1.4–14.8%), and 1 observational pilot study (20 patients)[182] showing reduced

survival (0% versus 30.7) with public-access defibrillation compared with no program.

For **survival to 30 days**, we identified very-low-quality evidence (downgraded for indirectness) from 3 observational studies[176,178,183] enrolling 14 135 patients demonstrating improved survival (range, 37.2–65.5%) with public-access defibrillation compared with no program (23.3–48.5%). If combined in a formal meta-analysis, a summary effect measure of OR 1.63 (95% CI, 1.41–1.88) would be generated. However, we recognize the limitations of significant heterogeneity in the study populations and the fact that some patient data were reported in more than 1 publication.

For **survival to discharge**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized trial[179] and 9 observational studies.[175,180,181,184–189] The randomized trial enrolled 235 participants and observed improved survival (adjusted RR, 2.0; 95% CI, 1.07–3.77). The observational studies enrolled 46 070 patients demonstrating improved survival (range, 4.4–51%) with public-access defibrillation compared with no program (1.4–25.0%) and 1 observation pilot study (20 patients)[182] showing reduced survival (0% versus 30.7%) when public-access defibrillation programs were present.

Treatment recommendation

We recommend the implementation of public-access defibrillation programs for patients with OHCAs (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we considered the societal impact of delayed defibrillation and balanced this against the costs of setting up a comprehensive public-access defibrillation program. We place a higher value on a single randomized trial supported by multiple large-scale, international observational studies. Together, these indicate that the magnitude of change on outcome may vary based on the setting or community within which programs are introduced. Public sites with large population densities may benefit the most from public-access defibrillation programs.

Knowledge gaps

The following knowledge gaps currently exist:

- Community or program characteristics of effective public AED programs.
- Cost-benefit, cost-effectiveness, cost-utility of public AED programs.
- Optimal public AED deployment strategies.
- Effectiveness of public AED with chest compression-only CPR versus 30:2 high-quality CPR.
- Effectiveness of public AED programs with optimal postarrest care.
- Effectiveness of public AED programs with volunteer-enhanced EMS response models and/or digital/social media tools/applications for public AED deployment.

Rhythm check timing (BLS 345)

Among adults and children who are in cardiac arrest in any setting (P), does checking the cardiac rhythm immediately after defibrillation (I), compared with immediate resumption of chest compressions with delayed check of the cardiac rhythm (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; recurrence of VF (O)?

Introduction

The 2010 CoSTR stated that interruptions in chest compressions during CPR must be minimized. Legitimate reasons for the interruption of CPR were highlighted as the needs to ventilate, to assess the rhythm or ROSC, and to defibrillate. This question sought to identify the optimal timing of rhythm checks in relation to attempted defibrillation. Public comments on this question during the consultation process highlighted concerns about drug administration without first confirming whether ROSC had been achieved after shock delivery. This latter concern fell outside the remit of this question but has been highlighted as an area requiring future research.

This review identified 5 observational studies relevant to this question. In each case, the studies evaluated omitting a rhythm check immediately after CPR as part of a bundle of interventions (e.g., elimination of 3 stacked shocks and postshock rhythm and pulse checks). Thus, the evidence presented in this review must be considered as indirect evidence with respect to this narrow question.

Consensus on science

For the critical outcome of **survival with favorable neurologic outcome at discharge**, we identified very-low-quality evidence (downgraded for serious risk of bias, indirectness, and imprecision) from 3 observational studies enrolling 763 OHCAs showing a harmful effect for interrupting chest compressions to check rhythm immediately after shock delivery (RR, 0.62; 95% CI, 0.51–0.75).[165,168,190]

For the critical outcome of **survival hospital discharge**, we identified low-quality evidence from 1 RCT enrolling 845 OHCAs showing no benefit for interrupting chest compressions to check rhythm immediately after shock delivery (RR, 0.80; 95% CI, 0.55–1.15)[146] and very-low-quality evidence (downgraded for serious risk of bias and indirectness) from 3 observational studies enrolling 3094 OHCAs showing a harm effect for checking rhythm immediately after defibrillation (RR, 0.55; 95% CI, 0.45–0.67).[165,168,190] In addition, for the same outcome, we identified very-low-quality evidence from 1 observational study of 528 victims of OHCA showing potential harm for interrupting chest compressions to check rhythm immediately after shock delivery (RR, 0.42; 95% CI, 0.29–0.61).[168]

For the critical outcome of **survival to hospital admission**, we identified low-quality evidence from 1 RCT enrolling 845 victims of OHCA showing no benefit for interrupting chest compressions to check rhythm immediately after shock delivery (RR, 0.99; 95% CI, 0.85–1.15).[146]

For the critical outcome of **ROSC**, we identified very-low-quality evidence (downgraded for serious risk of bias and indirectness) from 2 observational studies enrolling 2969 victims of OHCA showing a harm effect for interrupting chest compressions to check rhythm immediately after shock delivery (RR, 0.69; 95% CI, 0.61–0.78).[168,190]For the important outcome of **recurrence of VF**, we identified low-quality evidence from 1 RCT, enrolling 136 OHCAs showing no benefit for interrupting chest compressions to check rhythm immediately after shock delivery (RR, 1.00; 95% CI, 0.81–1.23).[191.]

Treatment recommendation

We suggest immediate resumption of chest compressions after shock delivery for adults in cardiac arrest in any setting (weak recommendation, very-low-quality evidence).

If there is alternative physiologic evidence of ROSC (e.g., arterial waveform or rapid rise in $ETCO_2$), chest compressions can be paused briefly for rhythm analysis.

Values, preferences, and task force insights

In making this recommendation, we place a higher value on avoiding interruptions in chest compressions for an intervention showing no benefit for critical and important outcomes. Also, this recommendation assumes that shocks are generally effective and that a perfusing rhythm is generally not present immediately after elimination of VF.

Knowledge gaps

- Utility of other monitoring methods (e.g., arterial waveform, $ETCO_2$).
- The timing of rhythm checks during advanced life support interventions, including drug administration.

Analysis of rhythm during chest compression (BLS 373)

Among adults and children who are in cardiac arrest in any setting (P), does analysis of cardiac rhythm during chest compressions (I), compared with standard care (analysis of cardiac rhythm during pauses in chest compressions) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; time to commence CPR; CPR quality (O)?

Introduction

Motion artifacts effectively preclude the possibility of reliably assessing the heart rhythm during chest compressions. This has 2 undesirable consequences: first, it forces the rescuer to stop chest compressions to assess the rhythm to determine if a shock (or another shock) is required. Second, during chest compressions, possible recurrence of VF cannot be recognized, eliminating the possible beneficial effect of immediate defibrillation in case of refibrillation. Some modern defibrillators contain filtering modalities that allow visual or automated rhythm analysis during chest compressions. This review sought to examine the use of such technology to determine if it leads to better clinically meaningful outcomes in human cardiac arrest.

Consensus on science

There are currently no human studies that address the identified critical outcomes criteria of favorable neurologic outcome, survival, or ROSC or the important outcomes criteria of CPR quality, time to commencing CPR, or time to first shock.

Treatment recommendations

We suggest against the introduction of artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR unless as part of a research program.

We suggest that where EMS systems have already integrated artifact-filtering algorithms into clinical practice, it is reasonable to continue with their use.

Values, preferences, and task force insights

In making this recommendation, we placed priority on avoiding the costs of introducing a new technology where the effectiveness or harm on patient outcomes remains to be determined. Where such technologies have already been implemented, we place priority on avoiding the likely costs and inconvenience of their withdrawal from practice. We encourage such systems to report on their experiences to build the evidence base regarding the use of these technologies in clinical practice.

Knowledge gaps

- Among adults and children in cardiac arrest, the analysis of cardiac rhythm during chest compressions offers the potential to reduce pauses in chest compressions. The clinical value of this requires evaluation.

2005 and 2010 topics not reviewed in 2015

The following topics were included in 2010 but not in this publication (deferred standardized reviews):

- Etiology of cardiac arrest
- Incidence of cardiac arrest
- Recognition of cardiac arrest
- Facedown victim
- Finding the right hand placement
- Lay rescuer compression-only versus no CPR
- Rescuer fatigue in chest compression-only CPR
- Alternative compression techniques
- Interposed abdominal compressions (IAC) CPR
- Harm to rescuers from CPR
- Opening the airway
- Foreign-body airway obstruction
- Barrier devices
- Oropharyngeal adjuncts
- Tidal volumes and ventilation rates

The reader is referred to the 2010 CoSTR publication for the reviews.[105,192]

The following topics were included in 2005 but not in this publication:

- Devices for airway positioning
- Duty cycle
- CPR in prone position
- Leg-foot chest compressions
- Mouth-to-nose ventilation
- Mouth-to-tracheal stoma ventilation
- Recovery position
- Airway opening
- CPR for drowning victim in water
- Removing drowning victim from water
- Improving EMS response interval

The reader is referred to the 2005 publication for the reviews.[196,197]

Summary

This review comprises the most extensive literature search and evidence evaluation to date on the most important international BLS interventions, diagnostics, and prognostic factors for cardiac arrest victims. It reemphasizes that the critical lifesaving steps of BLS are (1) prevention, (2) immediate recognition and activation of the emergency response system, (3) early high-quality CPR, and (4) rapid defibrillation for shockable rhythms.

Highlights in prevention indicate the rational and judicious deployment of search-and-rescue operations in drowning victims and the importance of education on opioid-associated emergencies. Other 2015 highlights in recognition and activation include the critical role of dispatcher recognition and dispatch-assisted chest compressions, which has been demonstrated in multiple international jurisdictions with consistent improvements in cardiac arrest survival.

Similar to the 2010 ILCOR BLS treatment recommendations, the importance of high quality was reemphasized across all measures of CPR quality: rate, depth, recoil, and minimal chest compression pauses, with a universal understanding that we all should be providing chest compressions to all victims of cardiac arrest. This review continued to focus on the interface of BLS sequencing and ensuring high-quality CPR with other important BLS interventions, such as ventilation and defibrillation. In addition, this consensus statement highlights the importance of EMS systems, which employ bundles of care focusing on providing high-quality chest compressions while extricating the patient from the scene to the next level of care. Highlights in defibrillation indicate the global importance of increasing the number of sites with public-access defibrillation programs.

Whereas the 2010 ILCOR Consensus on Science provided important direction for the "what" in resuscitation (i.e., what to do), the 2015 consensus has begun with the GRADE methodology to provide direction for the quality of resuscitation. We hope that resuscitation councils and other stakeholders will be able to translate this body of knowledge of international consensus statements to build their own effective resuscitation guidelines.

Disclosures

2015 CoSTR Part 3: Adult Basic Life Support and Automated External Defibrillation: Writing Group Disclosures.

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Rudolph W. Koster	Academic Medical Center	Physio Control†; Zoll Medical†; Cardiac Science†; Defibtech† Philips†	None	None	None	None	None	None
Swee Han Lim	Singapore General Hospital	None	None	None	None	None	None	None
Kevin J. Nation	Waikato Hospital	New Zealand Resuscitation Council*	None	None	None	K J Nation 7 R C McKeany*	None	None
Theresa M. Olasveengen	Ulleval University Hospital	Oslo Cardiopolmonary Resuscitation Research Network*	None	None	None	None	None	None
Tetsuya Sakamoto	Teikyo University School of Medicine	None	None	None	None	None	None	None
Michael R. Sayre	University of Washington	None	Physio-Control Inc†	None	None	None	None	None
Alfredo Sierra	Inter-American Heart Foundation	None	None	None	None	None	None	None
Michael A. Smyth	University of Warwick	None	None	None	None	None	None	None
David Stanton	Resuscitation Council of Southern Africa	None	None	None	None	None	None	None
Christian Vaillancourt	University of Ottawa, Ottawa Hospital Research Institute	Heart and Stroke Foundation of Canada*	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

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Appendix A.

CoSTR Part 3: PICO Appendix

Part	Task Force	PICO ID	Short Title	PICO Question	Evidence Reviewers
Part 3	BLS	BLS 343	Chest compression rate	Among adults and children who are in cardiac arrest in any setting (P), does any specific rate for external chest compressions (I), compared with a compression rate of about 100/min (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC;	Julie Considine, Nicolas Mpotos, Swee Lim
Part 3	BLS	BLS 345	Rhythm check timing	Among adults and children who are in cardiac arrest in any setting (P), does checking the cardiac rhythm immediately after defibrillation (I), compared with immediate resumption of chest compressions with delayed check of the cardiac rhythm (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; recurrence of VF (O)?	Giuseppe Ristagno, Husein Lockhat
Part 3	BLS	BLS 346	Timing of CPR cycles	Among adults who are in cardiac arrest in any setting (P), does pausing chest compressions at another interval (I), compared with pausing chest compressions every 2 minutes to assess the cardiac rhythm (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; coronary perfusion pressure; cardiac output (O)?	Joshua Reynolds, Violetta Raffay
Part 3	BLS	BLS 347	Public-Access Defibrillation	Among adults and children who are in cardiac arrest outside of a hospital (P), does implementation of a public-access AED program (I), compared with traditional EMS response (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; bystander CPR rates; bystander use of AED; time to commence CPR (O)?	Andrew Travers, Ian Drennan
Part 3	BLS	BLS 348	Check for circulation during BLS	Among adults and children who are in cardiac arrest in any setting (P), does interruption of CPR to check circulation (I), compared with no interruption of CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; chest compression fraction (O)?	Martin Botha, Andrea Scapigliati
Part 3	BLS	BLS 352	Passive ventilation technique	Among adults and children who are in cardiac arrest in any setting (P), does addition of any passive ventilation technique (e.g., positioning the body, opening the airway, passive oxygen administration) to chest compression–only CPR (I), compared with just chest compression–only CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander initiated CPR; oxygenation (O)?	Emmanuelle Bourdon, Volker Wenzel
Part 3	BLS	BLS 353	Harm From CPR to Victims Not in Cardiac Arrest	Among adults and children who are not in cardiac arrest outside of a hospital (P), does provision of chest compressions from lay rescuers (I), compared with no use of chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; harm (e.g., rib fracture); complications; major bleeding; risk of complications (e.g., aspiration); survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to admission (O)?	Raul Gazmuri, Hermann Brugger
Part 3	BLS	BLS 357	Hand position during compressions	Among adults and children who are receiving chest compressions in any setting (P), does delivery of chest compressions on the lower half of the sternum (I), compared with any other location for chest compressions (C), survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; cardiac output; harm (eg, rib fracture); coronary perfusion pressure (O)?	Ian Drennan, Sung Phil Chung
Part 3	BLS	BLS 358	Minimizing pauses in chest compressions	Among adults and children who are in cardiac arrest in any setting (P), does minimization of pauses in chest compressions for cardiac rhythm analysis or ventilations (I), compared with prolonged pauses in chest compressions for rhythm analysis or ventilations (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; CPR quality; rhythm control (O)?	Rudolph Koster, Tetsuya Sakamoto

Appendix A (*Continued*)

Part	Task Force	PICO ID	Short Title	PICO Question	Evidence Reviewers
Part 3	BLS	BLS 359	Dispatcher instruction in CPR	Among adults and children who are in cardiac arrest outside of a hospital (P), does the ability of a dispatch system to provide CPR instructions (I), compared with a dispatch system where no CPR instructions are ever provided (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; delivery of bystander CPR; time to first shock; time to commence CPR; CPR parameters (O)?	Christian Vaillancourt, Michael Sayre
Part 3	BLS	BLS 360	EMS Chest Compression–Only Versus Conventional CPR	Among adults who are in cardiac arrest outside of a hospital (P), does provision of chest compressions with delayed ventilation by EMS (I), compared with chest compressions with early ventilation by EMS (C), change survival with favorable neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; time to first compressions; CPR quality (O)?	David Stanton, Andrew Travers
Part 3	BLS	BLS 361	Feedback for CPR quality	Among adults and children who are in cardiac arrest in any setting (P), does real-time feedback and prompt device regarding the mechanics of CPR quality (e.g., rate and depth of compressions and/or ventilations) (I), compared with no feedback (C), change survival with favorable neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander CPR rates; time to first compressions; time to first shock; CPR quality (O)?	Julie Considine, Joyce Yeung
Part 3	BLS	BLS 362	Compression ventilation ratio	Among adults and children who are in cardiac arrest in any setting (P), does delivery of CPR with another specific compression-ventilation ratio (I), compared with CPR that uses a 30:2 compression-ventilation ratio (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; hands-off time (O)?	Bo Lofgren, Jason Buick
Part 3	BLS	BLS 363	CPR Before Defibrillation	Among adults and children who are in VF or pulseless VT (pVT) in any setting (P), does a prolonged period of chest compressions before defibrillation (I), compared with a short period of chest compressions before defibrillation (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; rhythm control (O)?	Mohamud Daya, Jan-Thorsten Graesner
Part 3	BLS	BLS 366	Chest compression depth	Among adults who are in cardiac arrest in any setting (P), does a different chest compression depth during CPR (I), compared with chest compression depth to 5 cm (2 inches) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR quality; coronary perfusion pressure; cardiac output; bystander CPR performance (O)?	Ahamed Idris, Koen Monsieurs
Part 3	BLS	BLS 367	Chest wall recoil	Among adults and children who are in cardiac arrest in any setting (P), does maximizing chest wall recoil (I), compared with ignoring chest wall recoil (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; coronary perfusion pressure; cardiac output (O)?	Tyler Vadeboncoeur, Keith Couper
Part 3	BLS	BLS 372	Chest Compression–Only CPR Versus Conventional CPR	Among adults who are in cardiac arrest outside of a hospital (P), does provision of chest compressions (without ventilation) by untrained/trained laypersons (I), compared with chest compressions with ventilation (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; bystander CPR performance; CPR quality (O)?	Andrew Travers, E. Brooke Lerner
Part 3	BLS	BLS 373	Analysis of rhythm during chest compression	Among adults and children who are in cardiac arrest in any setting (P), does analysis of cardiac rhythm during chest compressions (I), compared with standard care (analysis of cardiac rhythm during pauses in chest compressions) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; time to first shock; time to commence CPR; CPR quality (O)?	Alfredo Sierra, Kevin Nation
Part 3	BLS	BLS 661	Starting CPR	Among adults and children who are in cardiac arrest in any setting (P), does CPR beginning with compressions first (30:2) (I), compared with CPR beginning with ventilation first (2:30) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Carl McQueen, Julie Considine
Part 3	BLS	BLS 740	Dispatcher recognition of cardiac arrest	Among adults and children who are in cardiac arrest outside of a hospital (P), does the description of any specific symptoms to the dispatcher (I), compared with the absence of any specific description (C), change the likelihood of cardiac arrest recognition (O)?	Manya Charette, Mike Smyth

Appendix A (*Continued*)

Part	Task Force	PICO ID	Short Title	PICO Question	Evidence Reviewers
Part 3	BLS	BLS 811	Resuscitation care for suspected opioid-associated emergencies	Adults and children with suspected opioid-associated cardiorespiratory arrest in the pre-hospital setting (P), does bystander naloxone administration (intramuscular or intranasal), in addition to conventional CPR (I), compared with conventional CPR only (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Theresa Olasveengen, Aaron Orkin
Part 3	BLS	BLS 856	Drowning Search and Rescue	In adults and children who are submerged in water (P), does any particular factors in search and rescue operations (e.g., duration of submersion, salinity of water, water temperature, age of victim) (I), compared with no factors (C), change Survival with Favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days AND/OR 1 year, Survival only at discharge, 30 days, 60 days, 180 days AND/OR 1 year; ROSC (O)?	Joost Bierens, Linda Quan
Part 3	BLS	BLS 891	Opioid overdose response education	Adults and children at risk of suspected cardio/respiratory arrest due to opioids in the prehospital setting (P), does opioid overdose response education with or without naloxone distribution (I), compared with no overdose response education or overdose prevention education only (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Aaron Orkin, Theresa Olasveengen

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Part 4: Advanced life support 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆,☆☆

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Resuscitation

Introduction

The International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support (ALS) Task Force performed detailed systematic reviews based on the recommendations of the Institute of Medicine of the National Academies[1] and using the methodological approach proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[2] Questions to be addressed (using the PICO [population, intervention, comparator, outcome] format)[3] were prioritized by ALS Task Force members (by voting). Prioritization criteria included awareness of significant new data and new controversies or questions about practice. Questions about topics no longer relevant to contemporary practice or where little new research has occurred were given lower priority. The ALS Task Force prioritized 42 PICO questions for review. With the assistance of information specialists, a detailed search for relevant articles was performed in each of 3 online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk of bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[4] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[5] and GRADE for observational studies that inform both therapy and prognosis questions.[6]

GRADE evidence profile tables[7] were then created to facilitate an evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[8] based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias).[9]

These evidence profile tables were then used to create a written summary of evidence for each outcome (the consensus on science statements). Whenever possible, consensus-based treatment recommendations were then created. These recommendations (designated as strong or weak) were accompanied by an overall assessment of the evidence and a statement from the task force about the values, preferences, and task force insights that

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underlie the recommendations. Further details of the methodology that underpinned the evidence evaluation process are found in "Part 2: Evidence Evaluation and Management of Conflicts of Interest."

The task force preselected and ranked outcome measures that were used as consistently as possible for all PICO questions. Longer-term, patient-centered outcomes were considered more important than process variables and shorter-term outcomes. For most questions, we used the following hierarchy starting with the most important: long-term survival with neurologically favorable survival, long-term survival, short-term survival, and process variable. In general, *long-term* was defined as from hospital discharge to 180 days or longer, and *short-term* was defined as shorter than to hospital discharge. For certain questions (e.g., related to defibrillation or confirmation of tracheal tube position), process variables such as termination of fibrillation and correct tube placement were important. A few questions (e.g., organ donation) required unique outcomes.

The International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations (CoSTR) statements in this Part are organized in the approximate sequence of interventions for a patient: defibrillation, airway, oxygenation and ventilation, circulatory support, monitoring during cardiopulmonary resuscitation (CPR), drugs during CPR, and special circumstances. We also include statements for postresuscitation care, prognostication of neurologic outcome, and organ donation.

Defibrillation Strategies for Ventricular Fibrillation (VF) or Pulseless Ventricular Tachycardia (pVT)

- Biphasic waveform (ALS 470)
- Pulsed biphasic waveform (ALS 470)
- First-shock energy (ALS 470)
- Single shock versus stacked shocks (ALS 470)
- Fixed versus escalating defibrillation energy levels (ALS 470)
- Recurrent VF (ALS 470)

Airway, Oxygenation, and Ventilation

- Oxygen dose during CPR (ALS 889)
- Basic versus advanced airway (ALS 783)
- Supraglottic airways (SGAs) versus tracheal intubation (ALS 714)
- Confirmation of correct tracheal tube placement (ALS 469)
- Ventilation rate during continuous chest compressions (ALS 808)

Circulatory Support During CPR

- Impedance threshold device (ITD) (ALS 579)
- Mechanical CPR devices (ALS 782)
- Extracorporeal CPR (ECPR) versus manual or mechanical CPR (ALS 723)

Physiological Monitoring During CPR

- End-tidal carbon dioxide ($ETCO_2$) to predict outcome of cardiac arrest (ALS 459)
- Monitoring physiological parameters during CPR (ALS 656)
- Ultrasound during CPR (ALS 658)

Drugs During CPR

- Epinephrine versus placebo (ALS 788)
- Epinephrine versus vasopressin (ALS 659)
- Epinephrine versus vasopressin in combination with epinephrine (ALS 789)
- Standard-dose epinephrine (SDE) versus high-dose epinephrine (HDE) (ALS 778)
- Timing of administration of epinephrine (ALS 784)
- Steroids for cardiac arrest (ALS 433)
- Antiarrhythmic drugs for cardiac arrest (ALS 428)

Cardiac Arrest in Special Circumstances

- Cardiac arrest during pregnancy (ALS 436)
- Lipid therapy for cardiac arrest (ALS 834)
- Opioid toxicity (ALS 441)
- Cardiac arrest associated with pulmonary embolism (PE) (ALS 435)
- Cardiac arrest during coronary catheterization (ALS 479)

Postresuscitation Care

- Oxygen dose after return of spontaneous circulation (ROSC) in adults (ALS 448)
- Postresuscitation ventilation strategy (ALS 571)
- Postresuscitation hemodynamic support (ALS 570)
- Postresuscitation antiarrhythmic drugs (ALS 493)
- Targeted temperature management (ALS 790)
- Timing of induced hypothermia (ALS 802)
- Prevention of fever after cardiac arrest (ALS 879)
- Postresuscitation seizure prophylaxis (ALS 431)
- Seizure treatment (ALS 868)
- Glucose control after resuscitation (ALS 580)
- Prognostication in comatose patients treated with hypothermic targeted temperature management (TTM) (ALS 450)
- Prognostication in the absence of TTM (ALS 713)
- Organ donation (ALS 449)

The 2010 CoSTR statements[10,11] that have not been addressed in 2015 are listed under the relevant section.

Summary of ALS treatment recommendations

The systematic reviews showed that the quality of evidence for many ALS interventions is low or very low, and this led to predominantly weak recommendations. For some issues, despite a low quality of evidence, the values and preferences of the task force led to a strong recommendation. This was especially so when there was consensus that not doing so could lead to harm. In addition, treatment recommendations were left unchanged unless there were compelling reasons not to do so. The rationale for any change is addressed in the values, preferences, and insights that follow treatment recommendations. The most important developments and recommendations in ALS since the 2010 ILCOR review are as follows:

Defibrillation strategies for VF or pVT:

- There were no major developments since 2010. We suggest if the first shock is not successful and the defibrillator is capable of delivering shocks of higher energy, it is reasonable to increase the energy for subsequent shocks.

Airway, oxygenation, and ventilation:

- We suggest using the highest possible inspired oxygen concentration during CPR.
- There was equipoise between the choice of an advanced airway or a bag-mask device for airway management during CPR, and

the choice between a SGA or tracheal tube as the initial advanced airway during CPR.
- The role of waveform capnography during ALS was emphasized, including its use to confirm and to continuously monitor the position of a tracheal tube during CPR.

Circulatory support during CPR:
- We recommend against the routine use of the ITD in addition to conventional CPR but could not achieve consensus for or against the use of the ITD when used together with active compression-decompression (ACD) CPR.
- We suggest against the routine use of automated mechanical chest compression devices but suggest they are a reasonable alternative to use in situations where sustained high-quality manual chest compressions are impractical or compromise provider safety.
- We suggest ECPR is a reasonable rescue therapy for select patients with cardiac arrest when initial conventional CPR is failing in settings where this can be implemented.

Physiological monitoring during CPR:
- Physiological measurement in addition to clinical signs and electrocardiographic monitoring has the potential to help guide interventions during ALS.
- We have not made a recommendation for any particular physiological measure to guide CPR, because the available evidence would make any estimate of effect speculative.
- We recommend against using $ETCO_2$ cutoff values alone as a mortality predictor or for the decision to stop a resuscitation attempt.
- We suggest that if cardiac ultrasound can be performed without interfering with standard advanced cardiovascular life support (ACLS) protocol, it may be considered as an additional diagnostic tool to identify potentially reversible causes.

Drugs during CPR:
- We suggest SDE (defined as 1 mg) be administered to patients in cardiac arrest after considering the observed benefit in short-term outcomes (ROSC and admission to hospital) and our uncertainty about the benefit or harm on survival to discharge and neurologic outcome. Our statement is not intended to change current practice until there are high-quality data on long-term outcomes.
- We suggest the use of amiodarone in adult patients with refractory VF/pVT to improve rates of ROSC. Our statement is not intended to change current practice until there are high-quality data on long-term outcomes.

Cardiac arrest in special circumstances:
- The systematic review found very-low-quality evidence for specific interventions for ALS in the pregnant woman. We suggest delivery of the fetus by perimortem cesarean delivery for women in cardiac arrest in the second half of pregnancy.
- The lack of comparative studies led to the task force being unable to make any evidence-based treatment recommendation about the use of intravenous (IV) lipid emulsion to treat toxin-induced cardiac arrest.
- We recommend the use of naloxone by IV, intramuscular, subcutaneous, intraosseous (IO), or intranasal routes in respiratory arrest associated with opioid toxicity but make no recommendation regarding the modification of standard ALS in opioid-induced cardiac arrest.

Postresuscitation care:
- We recommend avoiding hypoxia in adults with ROSC after cardiac arrest.
- We suggest avoiding hyperoxia in adults with ROSC after cardiac arrest.
- We suggest the use of 100% inspired oxygen until the arterial oxygen saturation or the partial pressure of arterial oxygen can be measured reliably in adults with ROSC after cardiac arrest.
- We suggest maintaining $PaCO_2$ within a normal physiological range as part of a post-ROSC bundle of care.
- We suggest hemodynamic goals (e.g., mean arterial pressure [MAP], systolic blood pressure [SBP]) be considered during postresuscitation care and as part of any bundle of postresuscitation interventions.
- We recommend selecting and maintaining a constant target temperature between 32 °C and 36 °C for those patients in whom temperature control is used.
- We recommend TTM as opposed to no TTM for adults with out-of-hospital cardiac arrest (OHCA) with an initial shockable rhythm who remain unresponsive after ROSC.
- We suggest TTM as opposed to no TTM for adults with OHCA with an initial nonshockable rhythm who remain unresponsive after ROSC.
- We suggest TTM as opposed to no TTM for adults with in-hospital cardiac arrest (IHCA) with any initial rhythm who remain unresponsive after ROSC.
- We suggest that if TTM is used, duration should be at least 24 h.
- We recommend against routine use of prehospital cooling with rapid infusion of large volumes of cold IV fluid immediately after ROSC.
- We suggest prevention and treatment of fever in persistently comatose adults after completion of TTM between 32 °C and 36 °C.
- We suggest against routine seizure prophylaxis in post-cardiac arrest patients.
- We recommend the treatment of seizures in post-cardiac arrest patients.
- We suggest no modification of standard glucose management protocols for adults with ROSC after cardiac arrest.
- Comatose patients treated with TTM:
  - We suggest against the use of clinical criteria alone before 72 h after ROSC to estimate prognosis.
  - We suggest prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of incorrectly predicting poor outcome is minimized.
  - We recommend that the earliest time to prognosticate a poor neurologic outcome is 72 h after ROSC, and should be extended longer if the residual effect of sedation and/or paralysis confounds the clinical examination.
  - We suggest that multiple modalities of testing (clinical exam, neurophysiological measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings.
- We recommend that all patients who have restoration of circulation after CPR and who subsequently progress to death be evaluated for organ donation.

Defibrillation strategies for VF or pVT

The task force restricted its review to new studies since the 2010 CoSTR[12,13] and topics not reviewed in 2010. There are no major differences between the recommendations made in 2015 and those made in 2010. The PICO questions have been grouped into (1) waveforms, (2) first-shock energy, (3) single shock versus 3 shocks, (4) fixed versus escalating energy levels, and (5) refibrillation. In reviewing these, shock success is usually defined as termination of VF 5 s after the shock.

Consensus on science and treatment recommendations for the use of automated external defibrillators can be found in "Part 3: Adult Basic Life Support, and Automated External Defibrillation" and for infants or children requiring defibrillation in "Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support."

Biphasic waveform (ALS 470)

Among adults who are in VF or pVT in any setting (P), does any specific defibrillation strategy, such as biphasic waveform (I), compared with standard management (or other defibrillation strategy), such as monophasic waveform (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; termination of arrhythmia (O)?

Introduction

All newly manufactured defibrillators currently deliver shocks using biphasic waveforms. Although it has not been shown conclusively in randomized clinical studies that biphasic defibrillators save more lives than monophasic defibrillators, biphasic defibrillators achieve higher first-shock success rates at lower energy levels and appear to cause less postshock myocardial dysfunction.[12,13]

Consensus on science

No new randomized trials of biphasic waveforms since 2010 were identified.

Treatment recommendation

We recommend that a biphasic waveform (biphasic truncated exponential [BTE] or rectilinear-biphasic [RLB]) is used for both atrial and ventricular arrhythmias in preference to a monophasic waveform (strong recommendation, very-low-quality evidence). In the absence of biphasic defibrillators, monophasic defibrillators are acceptable.

Values, preferences, and task force insights

In making this strong recommendation, we place a high value on the reported higher first-shock success rate for termination of fibrillation with a biphasic waveform, the potential for less postshock myocardial dysfunction, and the existing 2010 CoSTR.[12,13] The task force acknowledges that many emergency medical services (EMS) systems and hospitals around the world continue to use older monophasic devices.

Pulsed biphasic waveform (ALS 470)

Among adults who are in VF or pVT in any setting (P), does any specific defibrillation strategy, such as pulsed biphasic waveform (I), compared with standard management (or other defibrillation strategy) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; termination of arrhythmia (O)?

Introduction

The pulsed biphasic waveform that is used in clinical practice had not previously been reviewed in 2010. The single published study[14] of this waveform used a non-impedance compensated waveform (i.e., the current delivered is not adjusted for the impedance of the chest), whereas the waveform in clinical use is an impedance-compensated waveform (i.e., the current delivered is adjusted for the impedance of the chest).

Consensus on science

For the critical outcome of **survival to hospital discharge**, very-low-quality evidence (downgraded for very serious risk of bias and serious indirectness) from 1 cohort study (i.e., no control group)[14] with a total of 104 patients that used a 130 J–130 J–180 J pulsed biphasic waveform protocol documented a survival rate of 9.8%. This compares with a weighted average BTE survival rate of 33.1% at 150–200 J.[14]

For the important outcome of **termination of fibrillation**, the same very-low-quality evidence (downgraded for very serious risk of bias and serious indirectness) from 1 cohort study[14] with a total of 104 patients documented first-shock termination rates at 130 J of 90.4% with a pulsed biphasic waveform, comparable with BTE waveforms (weighted average 91.8%) at 150–200 J.[14]

Treatment recommendation

We recommend following the manufacturer's instructions for first and subsequent shock energy levels for the pulsed biphasic waveform (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this strong recommendation, we have placed a high value on following the manufacturer's guidance in the absence of high-quality data to suggest otherwise. The available very-low-quality data showing the efficacy of a non-impedance compensated pulsed biphasic waveform do not enable direct comparison with other biphasic waveforms. In addition, no clinical studies attest to the efficacy of this waveform in its current impedance-compensated form.

First-shock energy (ALS 470)

Among adults who are in VF or pVT in any setting (P), does any specific defibrillation strategy, such as specific first-shock energy level (I), compared with standard management (or other defibrillation strategy), such as a different first-shock energy level (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; termination of arrhythmia (O)?

Introduction

In 2010, it was concluded that it was reasonable to start at a selected energy level of 150–200 J for a BTE waveform, and no lower than 120 J for an RLB waveform for defibrillation of VF/pVT cardiac arrest, acknowledging that the evidence was limited.[12,13]

Consensus on science

For the important outcome of **termination of VF/pVT**, low-quality evidence (downgraded for imprecision and risk of bias, respectively) from a post hoc report from an RCT and a cohort study showed a first-shock success rate of 73 of 86 (85%) and 79 of 90 (87.8%), respectively, when using a 120 J initial shock with an RLB waveform.[15,16]

Treatment recommendations

We recommend an initial biphasic shock energy of 150 J or greater for BTE waveforms, and 120 J or greater for RLB waveforms (strong recommendation, very-low-quality evidence). If a monophasic defibrillator is used, we recommend an initial monophasic shock energy of 360 J (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these strong recommendations, the working group was keen to acknowledge manufacturer's instructions and recognize that evidence for the optimal first-shock energy level was lacking. We also considered that although monophasic defibrillators are no longer manufactured, they are still used in many countries.

Single shock versus stacked shocks (ALS 470)

Among adults who are in VF or pVT in any setting (P), does any specific defibrillation strategy, such as a single shock (I),

compared with standard management (or other defibrillation strategy), such as 3 stacked shocks (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; termination of arrhythmia (O)?

Introduction

In 2010, it was recommended that when defibrillation was required, a single shock should be provided with immediate resumption of chest compressions after the shock.[12,13] This recommendation was made for 2 reasons: (1) in an attempt to minimize perishock interruptions to chest compressions, and (2) because it was thought that with the greater efficacy of biphasic shocks, if a biphasic shock failed to defibrillate, a further period of chest compressions could be beneficial. It was acknowledged that there was no clinical evidence to support improved outcomes from this strategy.

Consensus on science

For the critical outcome of **survival to 1 year**, we have identified low-quality evidence (downgraded for serious risk of bias and serious indirectness) from 1 RCT enrolling 845 OHCA patients showing no difference in single versus 3 stacked shocks (odds ratio [OR], 1.64; 95% confidence interval [CI], 0.53–5.06).[17]

For the critical outcome of **survival to hospital discharge**, we have identified low-quality evidence (downgraded for serious risk of bias and serious indirectness) from 1 RCT enrolling 845 OHCA patients showing no difference in single versus 3 stacked shocks (OR, 1.29; 95% CI, 0.85–1.96).[17]

For the critical outcome of **survival to hospital admission**, we have identified very-low-quality evidence (downgraded for serious risk of bias and serious indirectness) from 1 RCT enrolling 845 OHCA patients showing no difference in single versus 3 stacked shocks (OR, 1.02; 95% CI, 0.78–1.34).[17]

For the critical outcome of **ROSC**, we have identified low-quality evidence (downgraded for serious risk of bias and serious indirectness) from 1 RCT enrolling 845 OHCA patients showing no difference in single versus 3 stacked shocks (OR, 0.94; 95% CI, 0.72–1.23).[17]

For the important outcome of **recurrence of VF** (refibrillation), we have identified low-quality evidence (downgraded for serious risk of bias, serious indirectness, and serious imprecision) from 1 RCT enrolling 136 OHCA patients showing no difference in single versus 3 stacked shocks (OR, 1.00; 95% CI, 0.47–2.13).[18]

Treatment recommendation

We recommend a single-shock strategy when defibrillation is required (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this strong recommendation, the task force has placed a greater value on not changing current practice and minimizing interruptions in chest compressions whilst acknowledging that studies since 2010 have not shown that any specific shock strategy is of benefit for any survival end point. There is no conclusive evidence that a single-shock strategy is of benefit for ROSC or recurrence of VF compared with 3 stacked shocks, but in view of the evidence suggesting that outcome is improved by minimizing interruptions to chest compressions, we continue to recommend single shocks. The task force is aware that there are some circumstances (e.g., witnessed, monitored VF cardiac arrest with defibrillator immediately available) when 3 rapid stacked shocks could be considered.

Fixed versus escalating defibrillation energy levels (ALS 470)

Among adults who are in VF or pVT in any setting (P), does any specific defibrillation strategy, such as fixed shock energy level (I), compared with standard management (or other defibrillation strategy), such as escalating shock energy level (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; termination of arrhythmia (O)?

Introduction

In 2010, we recommended that for second and subsequent biphasic shocks, the same initial energy level was acceptable, but that it was reasonable to increase the energy level when possible (i.e., with manual defibrillators).[12,13]

Consensus on science

For the critical outcome of **survival with favorable neurologic outcome at hospital discharge**, we identified very-low-quality evidence (downgraded for serious risk of bias, serious imprecision, and serious indirectness) from 1 RCT enrolling 221 OHCA patients showing no benefit of one strategy over the other (OR, 0.78; 95% CI, 0.34–1.78).[19]

For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for serious risk of bias, serious imprecision, and serious indirectness) from 1 RCT enrolling 221 OHCA patients showing no benefit of one strategy over the other (OR, 1.06; 95% CI, 0.52–2.16).[19]

For the critical outcome of **ROSC**, we have identified very-low-quality evidence (downgraded for serious risk of bias, serious imprecision, and serious indirectness) from 1 RCT enrolling 221 OHCA patients showing no benefit of one strategy over the other (OR, 1.095; 95% CI, 0.65–1.86).[19]

Treatment recommendation

We suggest if the first shock is not successful and the defibrillator is capable of delivering shocks of higher energy, it is reasonable to increase the energy for subsequent shocks (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we have considered that an escalating shock energy may prevent the risk of refibrillation (see ALS 470). We also consider this to be in line with current practices where rescuers will escalate shock energy if initial defibrillation attempts fail and the defibrillator is capable of delivering a higher shock energy.

Recurrent VF (refibrillation) (ALS 470)

Among adults who are in VF or pVT in any setting (P), does any specific defibrillation strategy (I), compared with standard management (or other defibrillation strategy) (C), improve termination of refibrillation (O)?

Introduction

Refibrillation is common and occurs in the majority of patients after initial first-shock termination of VF.[20] Refibrillation was not specifically addressed in 2010 guidelines. Distinct from refractory VF, defined as fibrillation that persists after 1 or more shocks, recurrence of fibrillation is usually defined as recurrence of VF during a documented cardiac arrest, occurring after initial termination of VF while the patient remains under the care of the same providers (usually out-of-hospital).

Consensus on science

For the important outcome of **termination of refibrillation**, low-quality evidence (downgraded for serious risk of bias) from 2 observational studies[16,21] with a total of 191 cases of initial fibrillation showed termination rates of subsequent refibrillation were unchanged when using fixed 120 or 150 J shocks, respectively, and another observational study[20] (downgraded for confounding factors) with a total of 467 cases of initial fibrillation showed termination rates of refibrillation declined when using repeated 200 J shocks, unless an increased energy level (360 J) was selected.

Treatment recommendation

We suggest an escalating defibrillation energy protocol to prevent refibrillation (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this weak recommendation, we considered the lack of studies showing myocardial injury from biphasic waveforms, making it reasonable to consider increasing defibrillation energy levels when delivering shocks for refibrillation if the energy dose delivered by the defibrillator can be increased. It is unclear from current studies whether repeated episodes of VF are more resistant to defibrillation and require a higher energy level or whether a fixed energy level is adequate.

Defibrillation knowledge gaps

- Considering that defibrillation is one of the few interventions that improves outcome from cardiac arrest, high-quality studies of optimal defibrillation strategies are sparse.
- The dose–response curves for defibrillation of shockable rhythms is unknown and the initial shock energy, subsequent shock energies, and maximum shock energies for each waveform are unknown. In particular, the strategy of delivering shock energy at maximum defibrillation output to improve current defibrillation efficacy rates remains unanswered.
- Studies of optimal defibrillation energies for refibrillation are contradictory, and it remains unclear whether refibrillation is a different form of fibrillation that requires the same or higher energy levels for successful termination of fibrillation.
- The selected energy is a poor comparator for assessing different waveforms, as impedance compensation and subtleties in waveform shape result in a different transmyocardial current between devices for any given selected energy. The optimal energy levels may ultimately vary between different manufacturers and associated waveforms.
- We would encourage manufacturers to undertake high-quality clinical trials to support their defibrillation strategy recommendations. Caution is also urged in attributing the outcomes observed to any one portion of the elements of bundled care.
- The task force did not address the topic of hands-on defibrillation strategies, its efficacy, and safety, although we realize it is a topic of interest for future studies.

2010 CoSTR defibrillation topics not reviewed in 2015

- CPR before defibrillation
- Self-adhesive defibrillation pads compared with paddles
- Placement of paddles/pads
- Size of paddles/pads
- Composition of conductive material
- Biphasic compared with monophasic defibrillation waveform
- Multiphasic compared with biphasic defibrillation waveform
- Waveforms, energy levels, and myocardial damage
- Shock using manual versus semiautomatic mode
- Cardioversion strategy in atrial fibrillation
- Pacing (e.g., transcutaneous, transvenous, needle, and fist)
- Implantable cardioverter-defibrillator or pacemaker
- Predicting success of defibrillation and outcome (VF waveform analysis)
- Defibrillation in the immediate vicinity of supplementary oxygen
- Algorithm for transition from shockable to nonshockable rhythm

Airway, oxygenation, and ventilation

The use of supplementary oxygen (when it is available) during CPR is accepted practice, but in other circumstances (e.g., acute myocardial infarction), there is increasing evidence that administration of high-concentration oxygen may be harmful.

The optimal strategy for managing the airway has yet to be determined, but several observational studies have challenged the premise that tracheal intubation improves outcomes. Options for airway management can be categorized broadly into bag-mask ventilation with simple airway adjuncts, SGAs, and tracheal intubation. In this section, we present the evidence for the use of oxygen and airway devices during CPR, for how to confirm correct tracheal tube placement, and for ventilation rate once an advanced airway device (either a tracheal tube or SGA) has been inserted.

Oxygen dose during CPR (ALS 889)

In adults with cardiac arrest in any setting (P), does administering a maximal oxygen concentration (e.g., 100% by face mask or closed circuit) (I), compared with no supplementary oxygen (e.g., 21%) or a reduced oxygen concentration (e.g., 40–50%) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

It has generally been considered appropriate to administer 100% oxygen, whenever available, during cardiac arrest; however, in some other medical emergencies, the use of 100% is now being challenged.

Consensus on science

There are no adult human studies that directly compare maximal inspired oxygen with any other inspired oxygen concentration.

For the critical outcome of **survival to hospital discharge with favorable neurologic outcome** (Cerebral Performance Category [CPC] 1 or 2), we identified very-low-quality evidence (downgraded for very serious risk of bias, very serious indirectness, and serious imprecision) from 1 observational study[22] enrolling 145 OHCA patients who had a PaO_2 measured during CPR that showed no difference between an intermediate PaO_2 and low PaO_2 (11/83 [13.3%] versus 1/32 [3.1%]; relative risk [RR], 4.2; 95% CI, 0.57–31.52; $P = 0.16$), or between a high PaO_2 and low PaO_2 (7/30 [23.3%] versus 1/32 [3.1%]; RR, 7.45; 95% CI, 0.98–57.15; $P = 0.053$).

For the important outcome of **ROSC**, we identified very-low-quality evidence (downgraded for very serious risk of bias, very serious indirectness, and serious imprecision) from 1 observational study[22] enrolling 145 OHCA patients who had a PaO_2 measured during CPR that showed improved ROSC in those with a higher PaO_2: intermediate PaO_2 versus low PaO_2 (47/83 [56.6%] versus 7/32 [21.9%]; RR, 2.59; 95% CI, 1.31–5.12; $P = 0.006$); high PaO_2 versus low PaO_2 (25/30 [83.3%] versus 7/32 [21.9%]; RR, 3.81; 95% CI, 1.94–7.48; $P = 0.0001$); high PaO_2 versus intermediate PaO_2 (25/30 [83.3%] versus 47/83 [56.6%]; RR, 1.47; 95% CI, 1.15–1.88; $P = 0.002$).

In the single identified study,[22] all patients had tracheal intubation and received 100% inspired oxygen during CPR. The worse

outcomes associated with a low PaO_2 during CPR could be an indication of illness severity.

Treatment recommendation

We suggest the use of the highest possible inspired oxygen concentration during CPR (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we have considered the limited available evidence and the need to correct tissue hypoxia during CPR, and see no reason to change the current treatment recommendation.

Knowledge gaps

- The optimal arterial or tissue oxygen targets during CPR are unknown.
- A method of reliably monitoring oxygen targets during CPR has not been established.
- The feasibility of controlling inspired oxygen concentration during CPR remains unclear.
- Prospective clinical trials may be warranted to explore different inspired oxygen concentrations during CPR.
- The role and feasibility of alternatives to oxygen/air mixtures during CPR are unknown.

Basic versus advanced airway (ALS 783)

Among adults who are in cardiac arrest in any setting (P), does insertion of an advanced airway (tracheal tube or SGA) (I), compared with basic airway (bag-mask device with or without oropharyngeal airway) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR parameters; development of aspiration pneumonia (O)?

Introduction

The optimal approach to managing the airway during cardiac arrest has been unclear, and several recent observational studies have challenged the assumption that advanced airways are necessarily superior to basic airway techniques.

Consensus on science

All advanced airways (I) versus bag-mask device (C). For the critical outcome of **1-year survival**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, indirectness, and imprecision, and serious inconsistency) from 1 observational study of 1278 OHCAs showing a similar unadjusted rate of survival with insertion of an advanced airway (tracheal tube, esophageal obturator airway [EOA] or laryngeal mask airway [LMA]) compared with a bag-mask device (3.7% versus 5.6%; OR, 0.65; 95% CI, 0.4–1.1).[23]

For the critical outcome of **favorable neurologic survival at 1 month**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness and serious inconsistency) from 1 observational study of 648 549 OHCAs showing a lower unadjusted rate of survival with insertion of an advanced airway (tracheal tube, LMA, laryngeal tube, or Combitube) compared with management with a bag-mask device (1.1% versus 2.9%; OR, 0.38; 95% CI, 0.36–0.39).[24] When adjusted for all known variables, the OR was 0.32 (95% CI, 0.30–0.33).

For the critical outcome of **favorable neurologic survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 1 observational study of 10 691 OHCAs showing a lower unadjusted rate of survival with insertion of an advanced airway (tracheal tube, LMA, laryngeal tube, or Combitube) compared with management with a bag-mask device (5.3% versus 18.6%; OR, 0.25; 95% CI, 0.2–0.3).[25] In an analysis of 3398 propensity-matched patients from the same study, the OR for favorable neurologic survival at hospital discharge (bag-mask device versus advanced airway) adjusted for all variables was 4.19 (95% CI, 3.09–5.70).

For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 2 observational studies: 1 of 10 691 OHCAs showed a lower unadjusted rate of survival with insertion of an advanced airway (tracheal tube or LMA) compared with a bag-mask device (7.7% versus 21.9%; OR, 0.30; 95% CI, 0.3–0.3)[25]; 1 of 5278 OHCAs showed a similar unadjusted rate of survival with insertion of an advanced airway (tracheal tube or LMA) compared with a bag-mask device (6.6% versus 7.0%; OR, 0.94; 95% CI, 0.7–1.3).[26]

Tracheal intubation (I) versus bag-mask device (C). For the critical outcome of **favorable neurologic survival at 1 month**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 1 observational study of 409 809 OHCAs showing a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (1.0% versus 2.9%; OR, 0.35; 95% CI, 0.31–0.38).[24] In an analysis of 357 228 propensity-matched patients from the same study, the OR for favorable neurologic survival at 1 month (tracheal intubation versus bag-mask device) adjusted for all variables was 0.42 (95% CI, 0.34–0.53).

For the critical outcome of **survival at 1 month**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 2 observational studies. One of 409 809 OHCAs showed a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (4.2% versus 5.3%; OR, 0.77; 95% CI, 0.74–0.81).[24] In an analysis of 357 228 propensity-matched patients from the same study, the OR for survival at 1 month (tracheal intubation versus bag-mask device) adjusted for all variables was 0.88 (95% CI, 0.79–0.98). Another study of 10 783 OHCAs also showed a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (3.6% versus 6.4%; OR, 0.54; 95% CI, 0.5–0.7).[27]

For the critical outcome of **favorable neurologic survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 1 observational study of 7520 OHCAs showing a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (5.4% versus 18.6%; OR, 0.25; 95% CI 0.2–0.3).[25]

For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, indirectness, and imprecision, and serious inconsistency) from 6 observational studies. One observational study of 7520 OHCAs showed a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (8.3% versus 21.9%; OR, 0.25; 95% CI, 0.2–0.3).[25] One study of 4887 OHCAs showed a similar unadjusted rate of survival with insertion of a tracheal tube compared with a bag-mask device (8.0% versus 7.0%; OR, 1.16; 95% CI, 0.7–1.9).[26] Among 496 propensity-matched OHCAs in the same study, the OR for survival to discharge (tracheal intubation versus bag-mask device) was 1.44 (95% CI, 0.66–3.15).[26] One observational study of 1158 OHCAs showed a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (3.7% versus 10.8%; OR, 0.32; 95% CI, 0.2–0.6).[28] One observational study of 8651 OHCAs showed a lower unadjusted rate of survival

with tracheal intubation compared with a bag-mask device (3.7% versus 9.1%; OR, 0.41; 95% CI, 0.3–0.5).[29] One observational study of 1142 OHCAs showed a lower unadjusted rate of survival with tracheal intubation compared with a bag-mask device (6.3% versus 28.6%; OR, 0.17; 95% CI, 0.1–0.2).[30]

Supraglottic airways (I) versus bag-mask device (C). For the critical outcome of **favorable neurologic survival at 1 month**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 1 observational study of 607 387 OHCAs showing a lower unadjusted rate of survival with insertion of an SGA (LMA, laryngeal tube, or Combitube) compared with a bag-mask device (1.1% versus 2.9%; OR, 0.38; 95% CI, 0.37–0.40).[24] In an analysis of 357 228 propensity-matched patients from the same study, the OR for favorable neurologic survival at 1 month (SGA versus bag-mask device) adjusted for all variables was 0.36 (95% CI, 0.33–0.40).

For the critical outcome of **favorable neurologic survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency) from 1 observational study of 5039 OHCAs showing a lower unadjusted rate of survival with an SGA compared with a bag-mask device (5.2% versus 18.6%; OR, 0.24; 95% CI, 0.2–0.3).[25]

For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, indirectness, and imprecision, and serious inconsistency) from 2 observational studies. One observational study of 5039 OHCAs showed a lower unadjusted rate of survival with an SGA compared with a bag-mask device (6.7% versus 21.9%; OR, 0.26; 95% CI, 0.2–0.3).[25] Another study of 262 OHCAs also showed a lower unadjusted rate of survival with an SGA compared with a bag-mask device (0.0% versus 10.7%).[28]

Laryngeal mask airway (I) versus bag-mask device (C). For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, indirectness, and imprecision, and serious inconsistency) from 1 observational study of 5028 OHCAs showing a similar unadjusted rate of survival with insertion of an LMA compared with a bag-mask device (5.6% versus 7.0%; OR, 0.80; 95% CI, 0.5–1.2).[26] Among 772 propensity-matched OHCAs in the same study, the OR for survival to discharge (LMA versus bag-mask device) was 0.45 (95% CI, 0.25–0.82).[26]

Treatment recommendation

We suggest using either an advanced airway or a bag-mask device for airway management during CPR (weak recommendation, very-low-quality evidence) for cardiac arrest in any setting.

Values, preferences, and task force insights

In the absence of sufficient data obtained from studies of IHCA, it is necessary to extrapolate from data derived from OHCA.

The type of airway used may depend on the skills and training of the healthcare provider. Tracheal intubation may result in unrecognized esophageal intubation and increased hands-off time in comparison with insertion of an SGA or a bag-mask device. Both a bag-mask device and an advanced airway are frequently used in the same patient as part of a stepwise approach to airway management, but this has not been formally assessed.

Knowledge gaps

- There are no RCTs of initial airway management during cardiac arrest.
- The type and duration of training required for each device is unknown.
- During cardiac arrest, is a stepwise approach to airway management commonly used? It is not clear how this can be studied rigorously.

SGAs versus tracheal intubation (ALS 714)

Among adults who are in cardiac arrest in any setting (P), does SGA insertion as first advanced airway (I), compared with insertion of a tracheal tube as first advanced airway (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR parameters; development of aspiration pneumonia (O)?

Introduction

SGAs are generally considered easier to insert than tracheal tubes are, and their use in cardiac arrest has been increasing.

Consensus on science

SGAs (combitube, LMA, laryngeal tube) versus tracheal intubation. For the critical outcome of **favorable neurologic survival**, we have identified very-low-quality evidence (downgraded for very serious concerns about risk of bias, inconsistency, and indirectness) from 1 observational study of 5377 OHCAs showing no difference between tracheal intubation and insertion of a SGA (adjusted OR, 0.71; 95% CI, 0.39–1.30),[31] from 1 observational study of 281 522 OHCAs showing higher rates of favorable neurologic outcome between insertion of an SGA and tracheal intubation (OR, 1.11; 95% CI, 1.0–1.2),[24] and from 2 studies showing higher rates of favorable neurologic outcome between tracheal intubation and insertion of an SGA (8701 OHCAs: adjusted OR, 1.44; 95% CI, 1.10–1.88)[25] and (10 455 OHCAs: adjusted OR, 1.40; 95% CI, 1.04–1.89).[32]

SGAs (EOA and LMA) versus tracheal intubation. For the critical outcome of **neurologically favorable 1-month survival**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, inconsistency, indirectness, and imprecision) from 1 observational study of 138 248 OHCAs that showed higher rates of neurologically favorable 1-month survival with tracheal intubation compared with insertion of an EOA or LMA (OR, 0.89; 95% CI, 0.8–1.0).[33]

For the critical outcome of **1-month survival**, we have identified very-low-quality evidence (downgraded for very serious concerns about risk of bias, inconsistency, indirectness, and imprecision) from 1 observational study that showed no difference in 1-month survival between tracheal intubation and insertion of an EOA of an LMA (OR, 0.75; 95% CI, 0.3–1.9)[23] and very-low-quality evidence (downgraded for very serious risk of bias, inconsistency, indirectness, and imprecision) from another observation study that showed higher 1-month survival with tracheal intubation compared with insertion of an EOA of an LMA (OR, 1.03; 95% CI, 0.9–1.1).[33]

LMA (I) versus tracheal intubation (C). For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, inconsistency, indirectness, and imprecision) from 1 observational study of 641 OHCAs that showed lower rates of survival to hospital discharge with insertion of an LMA compared with tracheal tube (OR, 0.69; 95% CI, 0.4–1.3).[26]

Esophageal gastric tube airway (I) versus tracheal intubation (C). For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias and imprecision) from 1 RCT enrolling 175 OHCAs showing no difference between esophageal gastric tube airway and tracheal intubation (OR, 1.19; 95% CI, 0.5–3.0).[34]

Combitube (I) versus tracheal intubation (C). For the critical outcome of **survival to hospital discharge**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, inconsistency, indirectness, and imprecision) from 1 RCT enrolling 173 OHCAs that showed no difference between Combitube and tracheal intubation (OR, 2.38; 95% CI, 0.5–12.1)[35] and very-low-quality evidence from 1 observational study of 5822 OHCAs that showed no difference between tracheal intubation by paramedics, and Combitube insertion by emergency medical technicians (adjusted OR, 1.02; 95% CI, 0.79–1.30).[36]

Treatment recommendation

We suggest using either an SGA or tracheal tube as the initial advanced airway during CPR (weak recommendation, very-low-quality evidence) for cardiac arrest in any setting.

Values, preferences, and task force insights

In the absence of sufficient data obtained from studies of IHCA, it is necessary to extrapolate from data derived from OHCA.

The type of airway used may depend on the skills and training of the healthcare provider. Tracheal intubation requires considerably more training and practice. Tracheal intubation may result in unrecognized esophageal intubation and increased hands-off time in comparison with insertion of an SGA. Both an SGA and tracheal tube are frequently used in the same patients as part of a stepwise approach to airway management, but this has not been formally assessed.

Knowledge gaps

- There are no RCTs of initial airway management during cardiac arrest.
- The type and duration of training required for each device is unknown.
- During the management of cardiac arrest, is a stepwise approach to airway management commonly used? It is not clear how this can be studied rigorously.

Confirmation of correct tracheal tube placement (ALS 469)

Among adults who are in cardiac arrest, needing/with an advanced airway during CPR in any setting (P), does use of devices (e.g., waveform capnography, CO_2 detection device, esophageal detector device, or tracheal ultrasound) (I), compared with not using devices (C), change placement of the tracheal tube in the trachea and above the carina, or success of intubation (O)?

Introduction

Unrecognized esophageal intubation is a serious complication of attempted tracheal intubation during CPR. There are several potential methods for confirming correct placement of a tracheal tube: capnography and detection of CO_2, use of an esophageal detection device, and tracheal ultrasound.

Consensus on science

Waveform capnography. For the important outcome of **detection of correct placement of a tracheal tube during CPR**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[37] showing that the use of waveform capnography compared with no waveform capnography in 153 critically ill patients (51 with cardiac arrest) decreased the occurrence of unrecognized esophageal intubation on hospital arrival from 23% to 0% (OR, 29; 95% CI, 4–122).

For the important outcome of **detection of correct placement of a tracheal tube during CPR**, we identified low-quality evidence (downgraded for serious risk of bias and imprecision) from 3 observational studies[38–40] with 401 patients and 1 randomized study[41] including 48 patients that showed that the specificity for waveform capnography to detect correct tracheal placement was 100% (95% CI, 87–100%). The sensitivity was 100% in 1 study[38,39] when waveform capnography was used in the prehospital setting immediately after intubation, and esophageal intubation was less common than the average (1.5%). The sensitivity was between 65% and 68% in the other 3 studies[39–41] when the device was used in OHCA patients after intubation in the emergency department (ED). The difference may be related to prolonged resuscitation with compromised or nonexistent pulmonary blood flow. Based on the pooled sensitivity/specificity from these studies and assumed esophageal intubation prevalence of 4.5%, the false-positive rate (FPR) of waveform capnography was 0% (95% CI, 0–0.6%).

Colorimetric CO_2 detection devices. For the important outcome of **detection of correct placement of a tracheal tube during CPR**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 7 observational studies[38,42–47] including 1119 patients that evaluated the diagnostic accuracy of colorimetric CO_2 devices. The specificity was 97% (95% CI, 84–99%), the sensitivity was 87% (95% CI, 85–89%), and the FPR was 0.3% (95% CI, 0–1%).

Esophageal detection devices. For the important outcome of **detection of correct placement of a tracheal tube during CPR**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, inconsistency, and a strong suspicion of publication bias) from 4 observational studies[40,43,48,49] including 228 patients, low-quality evidence (downgraded for risk of bias and indirectness) from 1 randomized study[41] including 48 patients, and very-low-quality evidence (downgraded for risk of bias, indirectness, inconsistency, and a strong suspicion of publication bias) from 1 observational study[50] including 168 patients that evaluated esophageal detection devices. The pooled specificity was 92% (95% CI, 84–96%), the pooled sensitivity was 88% (95% CI, 84–192%), and the FPR was 0.2% (95% CI, 0–0.6%). Low-quality evidence (downgraded for risk of bias and suspected publication bias) from 1 observational study[41] showed no statistically significant difference between the performance of a bulb (sensitivity 71%, specificity 100%)- and a syringe (sensitivity 73%, specificity 100%)-type esophageal detection devices in the detection of tracheal placement of a tracheal tube.

Ultrasound for tracheal tube detection. For the important outcome of **detection of correct placement of a tracheal tube during CPR**, we identified low-quality evidence (downgraded for suspicion of publication bias and indirectness) from 3 observational studies[51–53] including 254 patients in cardiac arrest that evaluated the use of ultrasound to detect tracheal tube placement. The pooled specificity was 90% (95% CI, 68–98%), the sensitivity was 100% (95% CI, 98–100%), and the FPR was 0.8% (95% CI, 0.2–2.6%).

Treatment recommendations

We recommend using waveform capnography to confirm and continuously monitor the position of a tracheal tube during CPR in addition to clinical assessment (strong recommendation, low-quality evidence).

We recommend that if waveform capnography is not available, a nonwaveform CO_2 detector, esophageal detector device, or ultrasound in addition to clinical assessment is an alternative (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these strong recommendations, and despite the low-quality evidence, we place a high value on avoiding unrecognized

esophageal intubation. The mean incidence of unrecognized esophageal intubation in cardiac arrest was 4.3% (range, 0–14%) in the 11 studies we assessed. Unrecognized esophageal placement of an advanced airway is associated with a very high mortality. We, therefore, place value on recommending devices with a low FPR (i.e., the device indicates tracheal placement but the tube is in the esophagus).

In addition, waveform capnography is given a strong recommendation, because it may have other potential uses during CPR (e.g., monitoring ventilation rate, assessing quality of CPR).

Knowledge gaps

- The evidence is limited on the value of CO_2 devices after prolonged cardiac arrest.
- There are very few studies comparing the practical implications (cost, timeliness) of these devices.
- The use of ultrasound requires further studies.

Ventilation rate during continuous chest compression (ALS 808)

Among adults with cardiac arrest with a secure airway receiving chest compressions (in any setting, and with standard tidal volume) (P), does a ventilation rate of 10 breaths/min (I), compared with any other ventilation rate (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Hyperventilation during CPR has been shown to be harmful, but once an advanced airway has been placed, the optimal ventilation rate remains uncertain.

Consensus on science

We did not identify any evidence to address the critical outcomes of survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival at discharge, 30 days, 60 days, 180 days, and/or 1 year.

We identified very-low-quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency and imprecision) from 10 animal studies[54–63] and 1 human observational study[64] that does not enable us to estimate with confidence the effect of a ventilation rate of 10/min compared with any other rate for the important outcome of ROSC.

Treatment recommendation

We suggest a ventilation rate of 10 breaths/min in adults with cardiac arrest with a secure airway receiving continuous chest compressions (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we have valued the need to suggest a ventilation rate that is already in use. We note that the Australian and New Zealand Committee on Resuscitation (ANZCOR) currently recommends a ventilation rate of 6–10 breaths/min and would see no reason for this to change. We did not assess effect of tidal volume and any other ventilation variables during CPR and have therefore not addressed these in the treatment recommendation.

Knowledge gaps

- Ventilation rates lower than 10/min need to be assessed during ALS.
- We do not know the ideal tidal volume and any other ventilation variables during CPR.

2010 CoSTR topics not reviewed in 2015

- Oropharyngeal and nasopharyngeal adjuncts
- Monitoring ventilator parameters during CPR
- Thoracic impedance to confirm airway placement
- Cricoid pressure
- Automatic ventilators versus manual ventilation during CPR

Circulatory support during CPR

The ALS Task Force reviewed the evidence for 3 technologies for which there have been significant developments since 2010: (1) the ITD, (2) automated mechanical chest compression devices, and (3) ECPR. All are already in use in some settings, have strong proponents for their use, and have cost implications for their implementation such that there was considerable debate in reaching a consensus on science and treatment recommendation. In addition, some studies of these technologies had support and involvement of device manufacturers. Some of this debate is presented in the narrative that follows each treatment recommendation.

Impedance threshold device (ALS 579)

Among adults who are in cardiac arrest in any setting (P), does use of an inspiratory ITD during CPR (I), compared with no ITD (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

The ITD is designed to reduce the intrathoracic pressure during the decompression phase of chest compression. There is some evidence the ITD increases blood flow during CPR. The ITD has been studied during conventional CPR and during ACD CPR.

Consensus on science

ITD plus conventional CPR (I) versus conventional CPR (C). For the critical outcome of **neurologically favorable survival at hospital discharge** (assessed with modified Rankin Scale [mRS] score of 3 or less), there was 1 RCT[65] of high quality in 8718 OHCAs that was unable to demonstrate a clinically significant benefit from the addition of the ITD to conventional CPR (RR, 0.97; 95% CI, 0.82–1.15).

For the critical outcome of **survival to hospital discharge**, there was 1 RCT[65] of high quality in 8718 OHCAs that was unable to demonstrate a clinically significant benefit from the addition of the ITD to conventional CPR (RR, 1; 95% CI, 0.87–1.15).

ITD plus ACD CPR (I) versus ACD CPR (C). For the critical outcome of **neurologically favorable survival**, there were no studies identified that compared the use of ITD with ACD CPR with ACD CPR in cardiac arrests.

For the critical outcome of **survival to hospital discharge**, there were 2 RCTs[66,67] of very low quality (downgraded for serious imprecision and very serious indirectness because of pre-2000 resuscitation practices) that that were unable to demonstrate a clinically significant benefit from the addition of the ITD to ACD CPR in a total of 421 OHCAs (RR, 0.91; 95% CI, 0.07–12.7[66] and RR, 1.25; 95% CI, 0.5–3.1).[67]

ITD plus ACD CPR (I) versus conventional CPR (C). For the critical outcome of **neurologically favorable survival** (CPC ≤2) at 12 months, there was 1 publication reporting results from a randomized study[68] of very low quality (downgraded for very serious risk of bias and serious imprecision) in 2738 OHCAs that was unable to demonstrate a clinically significant benefit from the addition of the

ITD to ACD CPR (when compared with conventional CPR: RR, 1.34; 95% CI, 0.97–1.85).

For the critical outcome of **neurologically favorable survival at hospital discharge**, there was 1 RCT[68] that incorporated the presumed cardiac etiology subset published in 2011[69] of very low quality (downgraded for very serious risk of bias, serious inconsistency, and serious imprecision) in 2738 OHCAs that was unable to demonstrate a clinically significant benefit (using CPC ≤2) from the addition of the ITD to ACD CPR (when compared with conventional CPR: RR, 1.28; 95% CI, 0.98–1.69). Similar data (neurologically intact survival at hospital discharge) were also reported that used mRS of 3 or less, and were unable to demonstrate a clinically significant benefit (lower CI was 3 more/1000 in Frascone [number needed to treat, NNT, of 333] and 6 more/1000 [NNT of 167] in Aufderheide).[68,69]

For the critical outcome of **survival to 12 months**, there were 2 publications reporting results from a single randomized study,[68] which incorporated the presumed cardiac etiology subset published in 2011,[69] of very low quality (downgraded for very serious risk of bias and serious imprecision) in 2738 OHCAs that was unable to demonstrate a clinically significant benefit from the addition of the ITD to ACD CPR (when compared with conventional CPR): Frascone: RR, 1.39 (95% CI, 1.04–1.85; lower CI was 2 more/1000; NNT, 500); Aufderheide: RR, 1.49 (95% CI, 1.05–2.12; lower CI was 4 more/1000; NNT, 250).

For the critical outcome of **survival to hospital discharge**, there were 3 publications reporting results from 2 randomized studies[69,70] (which incorporated the presumed cardiac etiology subset published in Aufderheide[69]) of very low quality (downgraded for very serious risk of bias, serious indirectness, and serious imprecision) in a total of 2948 OHCAs that were unable to demonstrate a clinically significant benefit from the addition of the ITD to ACD CPR (when compared with conventional CPR): Frascone: RR, 1.17 (95% CI, 0.94–1.45); Aufderheide: RR, 1.26 (95% CI, 0.96–1.66); Wolcke: RR, 1.41 (95% CI, 0.75–2.66).

Treatment recommendation

We recommend against the routine use of the ITD in addition to conventional CPR (strong recommendation, high-quality evidence).

A consensus recommendation could not be reached for the use of the ITD when used together with ACD CPR.

Values, preferences, and task force insights

In making a recommendation against the routine use of the ITD alone, we place a higher value on not allocating resources to an ineffective intervention over any yet-to-be-proven benefit for critical or important outcomes.

Because of the concern about allocating resources to an intervention with equivocal benefit for critical or important outcomes, a consensus recommendation could not be reached for ITD combined with ACD CPR. The task force thought that the decision on use of the ITD plus ACD combination should be left to individual Council guidelines.

Public comments posted online were reviewed and considered by the task force, specifically regarding the use of the ITD and ACD CPR combination and the task force's interpretation of the data from 2 publications from the same study[68,69] using the GRADE process, and how the data from these studies had been analyzed and interpreted. The task force received feedback from the investigator(s) of this study in the public commenting period and in an open session. In addition, it considered an editorial on the analysis of this study[71] and discussed the publications[68,69] and their clinical significance in its closed sessions. The NNTs were discussed and the use of the CI closest to unity as a measure of study precision. It was also noted that the critical and important endpoints for this and the other ALS PICO questions were agreed *a priori* and posted for public commenting before searches took place, hence the difference in our hierarchy of outcomes compared with the actual primary and secondary outcomes reported in the study that made up the 2 publications. The task force appreciated the challenges of studying a combined intervention and conducting a large cardiac arrest study. There was also discussion of the involvement of the manufacturer in the design and reporting of the study and that sponsorship of drug and device studies by manufacturers can lead to more favorable results and conclusions.[72] There was considerable debate on this topic in both closed and open task force sessions such that a consensus could not be achieved by the task force on a treatment recommendation for the use of the ITD when used together with ACD CPR.

Knowledge gaps

- Optimal compression and ventilation rates for ITD CPR and ACD plus ITD CPR may or may not be different from those for conventional CPR.
- The independent effects of ITD and ACD CPR are uncertain.
- Effectiveness studies should examine other geographical settings and populations.

Mechanical CPR devices (ALS 782)

Among adults who are in cardiac arrest in any setting (P), do automated mechanical chest compression devices (I), compared with standard manual chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Providing high-quality manual CPR is tiring, and there is evidence that CPR quality deteriorates with time. Mechanical CPR devices may enable the delivery of high-quality CPR for a sustained period, but at the time of writing the 2010 CoSTR, their impact on outcome was unclear.

Consensus on science

For the critical outcome of **survival to 1 year**, we identified moderate-quality evidence (downgraded for serious risk of bias) from 1 cluster RCT[73] using the Lund University Cardiac Arrest System (LUCAS) device showing no benefit or harm when compared with manual chest compressions (5.4% versus 6.2%; RR, 0.87; 95% CI, 0.68–1.11).

For the critical outcomes of **survival at 180 days with good neurologic outcome** and **survival at 30 days with favorable neurologic outcome**, we identified moderate-quality evidence (downgraded for serious risk of bias) from one RCT[74] using a LUCAS device and enrolling 2589 OHCA patients that did not show benefit or harm when compared with manual chest compressions at 180 days (8.5% versus 7.6%; RR, 1.11; 95% CI, 0.86–1.45) or 30 days (7.3% versus 8.1%; RR, 1.11; 95% CI, 0.84–1.45).

For the critical outcome of **survival to 180 days**, we identified moderate-quality evidence (downgraded for serious risk of bias) from 1 RCT[74] using a LUCAS device enrolling 2589 OHCA patients showing no benefit or harm when compared with manual chest compressions where quality of chest compressions in the manual arm was not measured (8.5% versus 8.1%; RR, 1.06; 95% CI, 0.81–1.41).

For the critical outcome of **survival to hospital discharge with favorable neurologic outcome** (defined as CPC 1–2 or mRS 0–3), we have identified moderate-quality evidence (downgraded for serious risk of bias) from 3 RCTs enrolling 7582 OHCA patients

showing variable results.[74–76] One study[75] (n = 767) showed harm with the use of a load-distributing band mechanical chest compression device compared with manual chest compressions (7.5% of patients in the control group versus 3.1% in the intervention group; P = 0.006; RR, 0.41; 95% CI, 0.21–0.79). Two other RCTs[74,76] (n = 6820), one using a load-distributing band and the other using a LUCAS, did not show benefit or harm when compared with manual chest compressions: load-distributing band study: 4.14% survival in the intervention group versus 5.25% for manual compressions (RR, 0.79; 95% CI, 0.60–1.03); LUCAS: 8.31% intervention versus 7.76% manual compressions (RR, 1.07; 95% CI, 0.83–1.39).

For the critical outcome of **survival to hospital discharge**, we identified moderate-quality evidence (downgraded for serious risk of bias) from 5 RCTs[74–78] enrolling 7734 OHCA patients and 150 IHCA patients showing heterogeneous results. One study of patients with IHCAs[77] (n = 150) showed benefit with use of a piston device compared with manual chest compressions (32.9% versus 14.7%; P = 0.02; RR, 2.21; 95% CI, 1.17–4.17). Two other RCTs[74,78] of LUCAS did not show benefit or harm (9.0% versus 9.15%; RR, 0.98; 95% CI, 0.77–1.25 and 8.0% versus 9.72%; RR, 0.82; 95% CI, 0.29–2.33, respectively, for LUCAS versus manual compressions). One large RCT[76] (n = 4231) using a load-distributing band device showed equivalence when compared with high-quality manual chest compressions (9.34% versus 10.93%; RR, 0.85; 95% CI, 0.71–1.02).

For the critical outcome of **survival to 30 days**, we identified moderate-quality evidence (downgraded for serious risk of bias) from 2 RCTs[73,74] (n = 7060) using the LUCAS device showing no benefit or harm when compared with manual chest compressions and where quality of compressions in the manual arm was not measured (6.3% versus 6.85%; RR, 0.92; 95% CI, 0.73–1.16 and 8.82% versus 8.07%; RR, 1.02; 95% CI, 0.97–1.31, respectively).

For the important outcome of **ROSC**, we identified low-quality evidence (downgraded for serious risk of bias and serious inconsistency) from 7 RCTs enrolling 11 638 cardiac arrest patients (IHCA and OHCA).[73,74,76–80] Two studies[77,79] (n = 167) showed benefit with mechanical chest compression devices compared with manual compressions: 14.29% versus 0% (RR, not applicable) and 55.26% versus 37.84% (RR, 1.46; 95% CI, 1.02–2.08), respectively. One study[76] (n = 4231) showed harm with mechanical devices; however, there was no adjustment for interim analyses: 28.59% versus 32.32% (RR, 0.88; 95% CI, 0.81–0.97). Four studies[8,73,74,78] (n = 7240) did not show benefit or harm when compared with manual chest compressions: 47.06% versus 17.75% (RR, 2.67; 95% CI, 0.85–8.37), 31.60% versus 31.39% (RR, 1.01; 95% CI, 0.92–1.10), 35.38% versus 34.60% (RR, 1.02; 95% CI, 0.92–1.14), and 40.54% versus 31.94% (RR, 1.27; 95% CI, 0.82–1.96), respectively.

Treatment recommendations

We suggest against the routine use of automated mechanical chest compression devices to replace manual chest compressions (weak recommendation, moderate-quality evidence).

We suggest that automated mechanical chest compression devices are a reasonable alternative to high-quality manual chest compressions in situations where sustained high-quality manual chest compressions are impractical or compromise provider safety (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

The task force placed value on ensuring high-quality chest compressions with adequate depth, rate, and minimal interruptions, regardless of whether they are delivered by machine or human. The task force also considered that application of a mechanical chest compression device without a focus on minimizing interruptions in compressions and delay to defibrillation could cause harm.

In making a recommendation for mechanical compression devices for use in some settings, we place value on the results from a large, high-quality RCT[76] showing equivalence between very-high-quality manual chest compressions and mechanical chest compressions delivered with a load-distributing band in a setting with rigorous training and CPR quality monitoring. Also, the task force acknowledges the existence of situations where sustained high-quality manual chest compressions may not be practical. Examples include CPR in a moving ambulance where provider safety is at risk, the need for prolonged CPR where provider fatigue may impair high-quality manual compressions (e.g., hypothermic arrest), and CPR during certain procedures (e.g., coronary angiography or preparation for ECPR).

Our task force agreed that there was an adequate amount of data generated from RCTs for the systematic review to exclude observational studies. We agreed that despite the availability of several observational studies comparing manual and mechanical chest compressions, the inherent risk of bias related to patient selection, group allocation, and uncontrolled confounders supports a decision to exclude them from the process of developing this CoSTR statement.

We conducted a universal literature search for RCTs studying any type of automated mechanical chest compression device. Prior to initiating the review, we planned to parse the data by device type if an effect specific to device was observed in the analysis. Although we did not undertake a formal analysis by device, there were no obvious device-specific effects observed.

The task force did consider some data that are not included in the evidence profile tables or CoSTR statement. Specifically, the PARAMEDIC (prehospital randomized assessment of a mechanical compression device in cardiac arrest) study[73] showed an association between mechanical chest compressions and worse survival with good neurologic outcome (CPC 1–2) at 3 months (adjusted OR, 0.72; 95% CI, 0.52–0.99). This was not included in our consensus on science, because survival with good neurologic outcome at 90 days was not an *a priori* outcome identified by the group.

After assessing the evidence, there was much debate over the ultimate wording of our recommendation. Some members thought a weak recommendation supporting mechanical chest compression devices as a reasonable alternative to manual chest compressions was most appropriate, whereas others thought a recommendation against the routine use of mechanical chest compression devices was more appropriate. There was general agreement that the bulk of evidence reviewed suggests no significant difference or equivalence between mechanical and manual chest compressions related to critical and important clinical outcomes. The task force weighed this with the data from a few studies suggesting a negative association between mechanical chest compression and outcomes as well as the potential resource implications associated with implementation of mechanical devices in any setting. With these factors in mind, the task force concluded that available clinical evidence did not support a recommendation for broad and universal implementation of mechanical chest compression devices across all clinical settings in favor of high-quality manual chest compressions.

Public comments provided online were reviewed by the task force. Comments suggested that we consider special circumstances where mechanical chest compressions may be more practical than the continued provision of high-quality chest compression and circumstances where provider safety might be improved with the use of mechanical versus manual chest compressions. Delivery of manual compressions in a moving ambulance by an unrestrained provider was seen as a particularly unsafe situation. Mechanical devices may allow providers to remain seated and restrained in this situation while chest compressions continue. Accordingly, we have included a treatment recommendation to address these situations

not directly addressed in the literature reviewed but deemed to represent reasonable situations for the use of this technology.

Knowledge gaps

- Are mechanical chest compression devices superior to manual chest compressions in special situations such as the moving ambulance, prolonged CPR, or during procedures such as coronary angiography?
- Are there certain subgroups of patients who may benefit differentially from mechanical or manual chest compressions (e.g., shockable versus non-shockable initial rhythm)?
- Is one type of mechanical chest compression device superior to another with respect to important clinical outcomes?

ECPR versus manual or mechanical CPR (ALS 723)

Among adults who are in cardiac arrest in any setting (P), does the use of ECPR techniques (including extracorporeal membrane oxygenation or cardiopulmonary bypass) (I), compared with manual CPR or mechanical CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Extracorporeal techniques require vascular access and a circuit with a pump and oxygenator and can provide a circulation of oxygenated blood to restore tissue perfusion. This has the potential to buy time for restoration of an adequate spontaneous circulation and treatment of reversible underlying conditions. This is commonly called extracorporeal life support (ECLS), and more specifically ECPR when done during cardiac arrest. These techniques are increasingly being used for OHCA. We considered ECLS for IHCA and OHCA separately.

Consensus on Science

ECPR for IHCA. For the critical outcome of **favorable functional survival at 180 days or 1 year after IHCA**, we identified very-low-quality evidence (downgraded for risk of bias from selection of cases for ECPR, crossover in treatments, and imprecision) from 2 non-RCTs,[81,82] comparing 144 patients treated with ECPR to 434 patients treated with conventional CPR. At 180 days, favorable outcome increased with ECPR (RR, 3.78; 95% CI, 2.26–6.31), even in propensity-matched samples.[82] At 1 year, favorable outcome was not different with ECPR (RR, 1.72; 95% CI, 0.74–4.01).

For the critical outcome of **survival to 30, 180 days, or 1 year after IHCA**, we identified very-low-quality evidence (downgraded for risk of bias from selection of cases for ECPR, crossover in treatments, and imprecision) from 2 non-RCTs,[81,82] comparing 144 patients treated with ECPR to 434 patients treated with conventional CPR. These studies found improved survival at 30 days (RR, 2.25; 95% CI, 1.28–3.96) and 180 days (RR, 2.81; 95% CI, 1.79–4.39 and RR, 2.50; 95% CI, 1.31–4.80), but not 1 year (RR, 1.92; 95% CI, 0.88–4.15). A propensity-matched sample found improved survival at 180 days[82] (RR, 3.20; 95% CI, 1.25–8.18).

For the important outcome of **favorable functional survival at hospital discharge after IHCA**, we identified very-low-quality evidence (downgraded for risk of bias from selection of cases for ECPR, crossover in treatments, and imprecision) from 2 non-RCTs,[81,82] comparing 144 patients treated with ECPR to 434 patients treated with conventional CPR. These studies found improved favorable outcome with ECPR (RR, 2.23; 95% CI, 1.11–4.52 and adjusted RR, 3.63; 95% CI, 2.18–6.02), even in propensity-matched samples (RR, 4.67; 95% CI, 1.41–15.41).[82]

For the important outcome of **survival to hospital discharge after IHCA**, we identified very-low-quality evidence (downgraded for risk of bias from selection of cases for ECPR, crossover in treatments, and imprecision) from 2 non-RCTs,[8,81] comparing 144 patients treated with ECPR to 434 patients treated with conventional CPR. These studies found improved survival to hospital discharge in the entire cohort (RR, 2.33; 95% CI, 1.23–4.38 and RR, 2.81; 95% CI, 1.85–4.26). One of these studies found improved survival to hospital discharge in propensity-matched samples (RR, 3.17; 95% CI, 1.36–7.37).[82]

ECPR for OHCA. For the critical outcome of **favorable functional survival at 30, 90, or 180 days after OHCA**, we identified very-low-quality evidence from 2 non-RCTs (downgraded for risk of bias for selection of cases for ECPR and imprecision), comparing 311 patients treated with ECPR to 312 patients treated with conventional CPR.[83,84] One study reported increased favorable outcome with ECPR at 30 days (RR, 7.92; 95% CI, 2.46–25.48) and 180 days (RR, 4.34; 95% CI, 1.71–11.00).[84] The other study reported increased favorable outcome at 90 days (RR, 5.48; 95% CI, 1.52–19.84), but this association was not present in the propensity-matched sample (RR, 3.50; 95% CI, 0.81–15.16).[83]

For the critical outcome of **survival to 30, 90, or 180 days after OHCA**, we identified very-low-quality evidence (downgraded for risk of bias from selection of cases for ECPR and imprecision) from 2 non-RCTs, comparing 311 patients treated with ECPR to 312 patients treated with conventional CPR.[83,84] One study reported increased survival with ECPR at 30 days (RR, 3.94; 95% CI, 2.24–6.92) and 180 days (RR, 5.42; 95% CI, 2.65–11.09),[84] and the other study reported increased survival with ECPR at 90 days (RR, 6.17; 95% CI, 2.37–16.07), even in a propensity-matched sample (RR, 4.50; 95% CI, 1.08–18.69).[83]

For the important outcome of **favorable functional survival at hospital discharge after OHCA**, we identified no comparative studies.

For the important outcome of **survival to hospital discharge after OHCA**, we identified very-low-quality evidence (downgraded for risk of bias from selection of cases for ECPR and imprecision) from 1 non-RCT comparing 53 patients treated with ECPR to 109 patients treated with conventional CPR.[83] Survival to hospital discharge was higher in patients treated with ECPR (RR, 4.99; 95% CI, 2.21–11.30), though not in propensity matched samples (RR, 3.00; 95% CI, 0.92–9.74).

Treatment recommendation

We suggest ECPR is a reasonable rescue therapy for selected patients with cardiac arrest when initial conventional CPR is failing in settings where this can be implemented (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this weak recommendation, we note that the published series used selected patients for ECPR and that guidelines for clinical practice should apply to similar populations. Published comparative studies are limited by the bias created when experienced clinicians select the best candidates to receive ECPR, perhaps using unmeasured variables. We acknowledge that ECPR is a complex intervention that requires considerable resource and training that is not universally available, but put value on an intervention that may be successful in individuals where usual CPR techniques have failed. In addition, ECPR can buy time for another treatment such as coronary angiography and percutaneous coronary intervention (PCI).

Knowledge gaps

- Controlled clinical trials are needed to assess the effect of ECPR versus traditional CPR on clinical outcomes in patients with cardiac arrest.
- What is the optimal flow rate for ECPR in the treatment for cardiac arrest?
- Which subgroups of patients can benefit most from a strategy of ECPR?
- What type of patients should be considered for ECPR?
- What role, if any, should prehospital ECPR play in resuscitating patients from OHCA?
- What is the optimal target temperature for patients on ECPR after cardiac arrest?
- What are reliable prognostic factors for patients treated with ECPR after cardiac arrest?

2010 CoSTR topics not reviewed in 2015

- Interposed abdominal compression CPR
- ACD CPR
- Open-chest CPR

Physiological monitoring during CPR

The ability to monitor real-time physiological variables and obtain ultrasound images during CPR, in addition to clinical signs and electrocardiographic monitoring, has the potential to enable rescuers to tailor ALS interventions. Strategies for physiological monitoring include the use of $ETCO_2$, arterial pressure, central venous pressure (enabling monitoring of coronary perfusion pressure and aortic diastolic pressure), and cerebral oximetry (regional cerebral oxygenation).

$ETCO_2$ to predict outcome of cardiac arrest (ALS 459)

Among adults who are in cardiac arrest in any setting (P), does any $ETCO_2$ level value, when present (I), compared with any $ETCO_2$ level below that value (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

$ETCO_2$ is the partial pressure of CO_2 at the end of an exhaled breath. It reflects cardiac output (CO) and pulmonary blood flow, as CO_2 is transported by the venous system to the right side of the heart and then pumped to the lungs by the right ventricle. During CPR, $ETCO_2$ values are low, reflecting the low CO generated by chest compression. Although $ETCO_2$ values higher than 10 mm Hg have been correlated to ROSC,[85–89] there is uncertainty if any $ETCO_2$ value measured during CPR can reliably predict survival or survival with good neurologic outcome.

Consensus on science

We did not identify any evidence to address the critical outcome of **neurologically intact survival**.

For the critical outcome of **survival at discharge**, we have identified low-quality evidence (downgraded for serious risk of bias and serious imprecision) from 1 observational study enrolling 127 patients[90] showing a correlation with initial $ETCO_2$ 10 mm Hg (1.33 kPa) or greater when compared with less than 10 mm Hg (OR, 11.4; 95% CI, 1.4–90.2).

For the critical outcome of **survival at discharge**, we have identified low-quality evidence (downgraded for serious risk of bias and serious imprecision) from 1 observational study enrolling 127 patients[90] showing a correlation with 20 min of $ETCO_2$ 20 mm Hg (2.67 kPa) or greater when compared with less than 20 mm Hg (OR, 20.0; 95% CI, 2.0–203.3).

For the important outcome of **ROSC**, we have identified moderate-quality evidence (downgraded for serious risk of bias) from 3 observational studies enrolling 302 patients[90–92] showing a correlation with initial $ETCO_2$ 10 mm Hg or greater when compared with less than 10 mm Hg (OR, 10.7; 95% CI, 5.6–20.3).

For the important outcome of **ROSC**, we have identified very-low-quality evidence (downgraded for very serious risk of bias, serious inconsistency, and serious imprecision) from 3 observational studies enrolling 367 patients[90,93,94] showing correlation with 20 min $ETCO_2$ 10 mm Hg or greater when compared with less than 10 mm Hg (OR, 181.6; 95% CI, 40.1–822.6).

Treatment recommendations

We recommend against using $ETCO_2$ cutoff values alone as a mortality predictor or for the decision to stop a resuscitation attempt (strong recommendation, low-quality evidence).

We suggest that an $ETCO_2$ 10 mm Hg or greater measured after tracheal intubation or after 20 min of resuscitation, may be a predictor of ROSC (weak recommendation, low-quality evidence).

We suggest that an $ETCO_2$ 10 mm Hg or greater measured after tracheal intubation, or an $ETCO_2$ 20 mm Hg or greater measured after 20 min of resuscitation may be a predictor of survival to discharge (weak recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making the strong recommendations against using a specific $ETCO_2$ cutoff value alone as a mortality predictor or for the decision to stop a resuscitation attempt, we have put a higher value on not relying on a single variable ($ETCO_2$) and cutoff value when their usefulness in actual clinical practice, and variability according to the underlying cause of cardiac arrest, has not been established and there are considerable knowledge gaps.

The task force was concerned that the etiology (e.g., asphyxia, PE) of cardiac arrest could affect $ETCO_2$ values, and that there was a risk of self-fulfilling prophecy if specific threshold values were followed. There was concern about the accuracy of $ETCO_2$ values measured during CPR. During open discussions there were requests that the ILCOR recommendation be far more prescriptive to prevent futile and prolonged resuscitation attempts.

Knowledge gaps

- The effects on $ETCO_2$ of timing, etiology of arrest, ventilation rate, and chest compression quality are not fully understood.
- The role of $ETCO_2$ with a bag-mask device or SGA requires further study.
- Are $ETCO_2$ values measured during CPR accurate?
- The $ETCO_2$ cutoff values to reliably predict short- and long-term outcomes is not known.

Monitoring physiological parameters during CPR (ALS 656)

Among adults who are in cardiac arrest in any setting (P), does the use of physiological feedback regarding CPR quality (e.g., arterial lines, $ETCO_2$ monitoring, Spo_2 waveforms, or others) (I), compared with no feedback (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; change in physiologic values by modifications in CPR (O)?

Introduction

Several physiological variables such as $ETCO_2$, coronary perfusion pressure, aortic diastolic pressure, and cerebral oximetry measurements have been used to assess and guide the quality of CPR.

Consensus on science

We found no studies that addressed the critical and important outcomes.

For the outcome of **change in physiologic values by modifications in CPR**, we identified 13 observational studies that provided very-low-quality evidence (downgraded for serious risk of bias, serious inconsistency, serious indirectness, and serious imprecision) comparing different CPR techniques (standard, lower sternal, active compression–decompression, intra-abdominal compression, mechanical thumper, ITD, band chest compression, load-distributing band, vest CPR) with the use of physiologic monitoring (arterial line, $ETCO_2$, oxygen saturation as measured by pulse oximetry (Spo_2), coronary perfusion pressure, cerebral oximetry, near-infrared spectroscopy) in 469 subjects.[66,80,95–105] Differences were detected between different CPR techniques, although this was not consistent across different modalities. Given the heterogeneity of CPR techniques used across studies, data could not be pooled. There were no studies that were found that used physiologic feedback to evaluate CPR quality.

Treatment recommendation

We make no treatment recommendation for any particular physiological measure to guide CPR, because the available evidence would make any estimate of effect speculative.

Values, preferences, and task force insights

In making no recommendation, we have placed high value on the lack of evidence and the need for further studies in this area.

Knowledge gaps

- Studies of the effect of using physiologic feedback to evaluate CPR quality and modifications in CPR technique are required.
- Studies that measure the effect of physiological monitoring to guide resuscitation on ROSC and survival with good neurologic outcome are required.

Ultrasound during CPR (ALS 658)

Among adults who are in cardiac arrest in any setting (P), does use of ultrasound (including echocardiography or other organ assessments) during CPR (I), compared with conventional CPR and resuscitation without use of ultrasound (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Ultrasound has been increasingly used as a diagnostic and prognostic tool for critically ill patients, particularly in intensive care units (ICUs).[106] Specific protocols for evaluation during CPR enable assessment of myocardial contractility and may help identify potentially treatable causes, such as hypovolemia, pneumothorax, pulmonary thromboembolism, or restrictive pericardial effusion, without interfering in patient care.[107]

Consensus on science

For the critical outcome of **survival**, we identified 1 observational study.[108] The evidence was downgraded for very high risk of bias (significant confounding, selection bias) and imprecision (small sample size). Therefore, we concluded that the data do not provide enough evidence to address the PICO question.

For the important outcome of **ROSC**, we identified very-low-quality evidence (downgraded for imprecision [small sample size] and very high risk of bias [no information about randomization allocation, lack of blinding, lack of blinding in outcome assessors]) from 1 RCT investigating the use of cardiac ultrasound during ACLS, compared with no use of cardiac ultrasound during ACLS in adult patients with pulseless electrical activity arrest.[109] This study enrolled 100 patients in a convenience sample and reported ROSC for at least 10 s in 34% of patients in the ultrasound group versus 28% in the group with no ultrasound ($P = 0.52$).

Treatment recommendations

We suggest that if cardiac ultrasound can be performed without interfering with standard ACLS protocol, it may be considered as an additional diagnostic tool to identify potentially reversible causes (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation we have placed a higher value on the potential harm from interruptions in chest compressions. There is currently inadequate evidence to evaluate whether there is any benefit of cardiac ultrasound during ACLS. Although this was not specifically part of the question, the task force discussed the importance of the need for an individual trained in ultrasound during resuscitation to minimize interruption in chest compression. The task force agreed there will be circumstances where ultrasound identification of a potentially reversible cause of cardiac arrest or 'pseudo' pulseless electrical activity may be useful.

Knowledge gaps

It remains unclear if the addition of ultrasound during ACLS improves outcomes:

- All data are from OHCA. All data are from non-VF patients, primarily assessing pulseless electrical activity.
- A systematic review of the diagnostic utility of ultrasound should be done. There are some articles investigating whether ultrasound findings predict probability of survival.
- Pretest probability (suspicion of an ultrasound-detectable etiology) is important for choosing to do ultrasound, because ultrasound will interfere to some extent with CPR.
- It is unknown if the findings of ultrasound during CPR are correctly interpreted, because images are compared with findings from patients with pulse (e.g., right ventricular dilation occurs in all cardiac arrest, separate from PE).
- It remains unclear if the addition of ultrasound during CPR improves outcomes. The vast majority of literature on ultrasound during cardiac arrest has focused on the prognostic value of cardiac ultrasound findings. Randomized trials investigating whether use of ultrasound during CPR has an effect on patient outcomes are needed.

Drugs during CPR

In 2010, ILCOR reduced routine drug administration in adult cardiac arrest to vasopressor and antiarrhythmic drugs. The science was insufficient to comment on critical outcomes such as survival to discharge and survival to discharge with good neurologic outcome with either vasopressors or antiarrhythmic drugs. There was also insufficient evidence to comment on the best time to give drugs to optimize outcome. The task force made a decision to include only RCTs in this systematic review and meta-analysis. Where the number of RCTs was few, we looked for

recent published systematic reviews or where there were no recent reviews, expanded the search to include observational studies.

Epinephrine versus placebo (ALS 788)

Among adults who are in cardiac arrest in any setting (P), does the use of epinephrine (I), compared with placebo or not using epinephrine (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Since 2010, there have been 2 randomized drug trials in cardiac arrest: one compared drugs with no drugs[110] and another compared epinephrine with placebo.[111] The Olasveengen trial compared a bundle of drugs given intravenously to a control group of patients randomized to no intravenous access and, therefore, no drugs. A post hoc subgroup analysis of the trial comparing those patients who did or did not receive epinephrine[112] revealed an advantage with epinephrine for admission to hospital but suggested an association with harm for the outcomes of survival to discharge and functional survival as measured by CPC. The Olasveengen original trial[110] was excluded from our review; however, the post hoc subgroup analysis was included in the systematic review of observational and randomized trials, which we have used to comment on the body of work defined by adjusted and unadjusted observational studies.[113]

Consensus on science

For all 4 long-term and short-term outcomes, we found 1 underpowered RCT that provided low-quality evidence (downgraded for selection and ascertainment bias) comparing SDE with placebo[111] in 534 subjects.

For the critical outcome of **survival to discharge**, there was uncertain benefit or harm of SDE over placebo (RR, 2.12; 95% CI, 0.75–6.02; $P = 0.16$; absolute risk reduction [ARR], 2.14%; 95% CI, −0.91% to 5.38%, or 21 more patients/1000 survived with epinephrine [95% CI, 9 fewer patients/1000 to 54 more patients/1000 survived with epinephrine]).

For the critical outcome of **survival to discharge with good neurologic outcome** (defined as CPC of 1–2), there was uncertain benefit or harm of SDE over placebo (RR, 1.73; 95% CI, 0.59–5.11; $P = 0.32$; ARR, 1.4%; 95% CI, −1.5% to 4.5%, which translates to 14 more patients/1000 survived with a CPC score of 1 or 2 with epinephrine [95% CI, 15 fewer patients/1000 to 45 more patients/1000 survived with a CPC score of 1 or 2 when given epinephrine]).

For the important outcome of **survival to admission**, patients who received SDE had higher rates of survival to admission (RR, 1.95; 95% CI, 1.34–2.84; $P = 0.0004$; ARR, 12%; 95% CI, 5.7–18.9%, which translates to 124 more patients/1000 survived to admission with epinephrine [95% CI, 57–189 more patients/1000 survived to admission]).

For the important outcome of **ROSC in the prehospital setting**, 151 more patients/1000 achieved ROSC with epinephrine (95% CI, 90–212 more patients/1000 achieved ROSC with epinephrine) when compared with those who received placebo (RR, 2.80; 95% CI, 1.78–4.41; $P < 0.00001$; ARR, 15%; 95% CI, 9–21%).

While observational studies were excluded from the primary evidence evaluation, the task force did make some comparison of the randomized trial data with prior conclusions drawn from large observational data sets. Using the analysis published by Patanwala[113] in 2014 when the Jacobs trial[111] is compared with adjusted observational trials[114,115] for the critical outcome of **survival to discharge and functional survival with a CPC of 1 or 2**, in settings with very low survival rates after cardiac arrest, 4.7% OHCA[114] and 14% IHCA,[115] in the OHCA setting, the use of epinephrine was associated with worse outcomes for survival to discharge (5.4% with epinephrine versus 4.7% without epinephrine; unadjusted OR, 1.15; 95% CI, 1.07–1.53; adjusted OR, 0.46; 95% CI, 0.42–0.51) and for functional survival (1.4% with epinephrine versus 2.2% without epinephrine; unadjusted OR, 0.61; 95% CI, 0.53–0.71%; adjusted OR, 0.31; 95% CI, 0.26–0.36).[114] In the in-hospital setting, the use of epinephrine was not significantly associated with either survival to discharge (OR, 1.16; 95% CI, 0.52–2.58) or functional survival (CPC, 1–2; OR, 0.43; 95% CI, 0.08–2.29).

Treatment recommendation

We suggest SDE be administered to patients in cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

We make this statement after considering the observed benefit in short-term outcomes (ROSC and admission to hospital) and our uncertainty about the benefit or harm on survival to discharge and neurologic outcome given the limitations of the observational studies. Our statement is not intended to change current practice until there are high-quality data on long-term outcomes. We have considered 1 mg to be the standard dose of epinephrine.

Knowledge gaps

- Dose response and placebo-controlled efficacy trials are needed to evaluate the use of epinephrine in cardiac arrest. We are aware of an ongoing randomized study of epinephrine (adrenaline) versus placebo for OHCA in the United Kingdom (PARAMEDIC 2: The Adrenaline Trial, ISRCTN73485024).

Epinephrine versus vasopressin (ALS 659)

Among adults who are in cardiac arrest in any setting (P), does use of epinephrine (I), compared with vasopressin (C), change survival to 30 days with good neurologic outcome, survival to 30 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC (O)?

Consensus on science

A single RCT[116] ($n = 336$) of low quality (downgraded for high risk of bias) compared multiple doses of SDE with multiple doses of standard-dose vasopressin in the ED after OHCA. Much of the methodology is unclear, and there was 37% postrandomization exclusion. The primary outcome measure was a CPC score of 1 or 2; however, neither the sample size estimate nor power calculation were included in the article.

For the critical outcome of **survival to discharge with favorable neurologic outcome** (CPC 1 or 2), there was no advantage with vasopressin (RR, 0.68; 95% CI, 0.25–1.82; $P = 0.44$ or ARR, −1.6; 95% CI, −6 to 2.4, which translates to 16 fewer patients/1000 surviving with CPC 1 or 2 with vasopressin [95% CI, 60 fewer patients/1000 to 24 more patients/1000 survive with CPC 1 or 2]).

For the critical outcome of **survival to discharge**, RR was 0.68 (95% CI, 0.25–1.82; $P = 0.44$ or ARR, 1.8%; 95% CI, −3.1 to 6.7, which translates to 18 more patients/1000 surviving to discharge with vasopressin [95% CI, 31 fewer patients/1000 surviving to discharge with vasopressin to 67 more patients/1000 surviving to discharge]).

For the important outcome of **ROSC**, there was no observed advantage with vasopressin (RR, 0.93; 95% CI, 0.66–1.31; $P = 0.67$).

Treatment recommendations

We suggest vasopressin should not be used instead of epinephrine in cardiac arrest (weak recommendation, low-quality evidence).

We suggest that those settings already using vasopressin instead of epinephrine can continue to do so (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

The recommendation considers the fact that vasopressin is already used in some settings, and the available data do not indicate any reason to stop using vasopressin if current treatment protocols already include vasopressin instead of epinephrine. Conversely, there is also no evidence to indicate that settings that use epinephrine should switch to using vasopressin.

Knowledge gaps

- Until high-quality, adequately powered trials are completed comparing epinephrine with placebo, trials involving vasopressin are not required unless as a third arm against epinephrine and placebo.

Epinephrine versus vasopressin in combination with epinephrine (ALS 789)

Among adults who are in cardiac arrest in any setting (P), does use of both vasopressin and epinephrine (I), compared with using epinephrine alone (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Consensus on science

For the critical outcome of **survival to hospital discharge with CPC of 1 or 2**, we found very-low-quality evidence (downgraded for very serious bias and serious imprecision) from 3 RCTs[117–119] ($n = 2402$) comparing SDE with vasopressin and epinephrine combination therapy that showed no superiority with vasopressin and epinephrine combination (RR, 1.32; 95% CI, 0.88–1.98 and ARR, 0.5%; 95% CI, −0.2% to 1.3%, which translates to 5 more patients/1000 [95% CI, 2 fewer patients/1000 to 13 more/1000] surviving to hospital discharge with a CPC of 1 or 2 with vasopressin in combination with epinephrine).

For the critical outcome of **survival to hospital discharge**, we found very-low-quality evidence (downgraded for very serious bias and serious imprecision) from 5 RCTs[117–121] ($n = 2438$) comparing SDE to vasopressin and epinephrine combination therapy that did not show superiority with vasopressin and epinephrine combination therapy in survival to discharge (RR, 1.12; 95% CI, 0.84–1.49; $P = 0.45$ and ARR, −0.17%; 95% CI, −1.3 to 1, which translates to 2 fewer patients/1000 [95% CI, 13 fewer patients/1000 to 10 more/1000] surviving to hospital discharge with vasopressin in combination with epinephrine).

For the important outcome of **survival to admission**, we found moderate-quality evidence (downgraded for serious bias) from 5 RCTs[117–121] ($n = 2438$) showing no significant differences in survival to hospital admission with vasopressin and epinephrine combination therapy (RR, 0.88; 95% CI, 0.73–1.06; $P = 0.17$).

For the important outcome of **ROSC**, we found moderate-quality evidence (downgraded for serious bias) from 6 RCTs[117–122] showing no ROSC advantage with vasopressin and epinephrine combination therapy (RR, 0.96; 95% CI, 0.89–1.04; $P = 0.31$).

Treatment recommendation

We suggest against adding vasopressin to SDE during cardiac arrest (weak recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we preferred to avoid the additional expense and implementation issues required to add a drug (vasopressin) that has no evidence of additional benefit for patients.

Knowledge gaps

- Until high-quality, adequately powered trials are completed comparing epinephrine with placebo, trials involving vasopressin in combination with epinephrine are not required unless as a third arm against epinephrine and placebo.

SDE versus HDE (ALS 778)

In adult patients in cardiac arrest in any setting (P), does HDE (at least 0.2 mg/kg or 5 mg bolus dose) (I), compared with SDE (1 mg bolus dose) (C), change survival to 180 days with good neurologic outcome, survival to 180 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC (O)?

Consensus on science

For the critical outcome of **survival to hospital discharge with CPC 1 or 2**, we found very-low-quality evidence (downgraded for very serious indirectness and serious imprecision) from 2 RCTs comparing SDE with HDE[123,124] ($n = 1920$) and cumulative RR that did not show any CPC 1 or 2 survival to discharge advantage with HDE (RR, 1.2; 95% CI, 0.74–1.96; ARR, −0.4%, 95% CI, −1.2 to 0.5, which translates to 3 fewer patients/1000 surviving to discharge with a CPC score of 1 or 2 [95% CI, 12 fewer to 5 more patients/1000 surviving to discharge with a CPC score of 1–2]).

For the critical outcome of **survival to hospital discharge**, we found very-low-quality evidence (downgraded for very serious indirectness and serious imprecision) from 5 RCTs comparing SDE with HDE[123–127] ($n = 2859$) that did not show any survival to discharge advantage with HDE (RR, 0.97; 95% CI, 0.71–1.32; ARR, −0.1%; 95% CI, −0.1 to 0.7, which translated to 1 fewer patient/1000 surviving to discharge with HDE [95% CI, 10 fewer patients/1000 to 7 more patients/1000]).

For the important outcome of **survival to hospital admission**, we found low-quality evidence (downgraded for very serious indirectness) from 4 RCTs comparing SDE with HDE[123–125,128] ($n = 2882$) showing a survival to hospital admission advantage with HDE (RR, 1.15; 95% CI, 1.0–1.32).

For the important outcome of **ROSC**, we found low-quality evidence (downgraded for very serious indirectness) from 6 RCTS comparing SDE with HDE[123–128] ($n = 3130$) showing a ROSC advantage with HDE (RR, 1.17; 95% CI, 1.03–1.34).

Treatment recommendation

We suggest against the routine use of HDE in cardiac arrest (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this statement, we acknowledge that HDE improves short-term outcomes but note that the low-quality evidence failed to show an improvement in the critical outcomes of survival and neurologic outcome. The absolute magnitude of effects of HDE versus SDE on ROSC (RR, 1.17; 95% CI, 1.03–1.34) and admission to hospital (RR, 1.15; 95% CI, 1.0–1.32) are modest. These HDE studies were published in the 1990s, and since then care and outcomes for cardiac arrest have changed dramatically, making it hard to interpret the relevance of these results for current care.

Knowledge gaps

- Until high-quality, well-powered trials are completed comparing epinephrine with placebo, trials addressing dose response of epinephrine are not required except as a third arm embedded in an epinephrine-versus-placebo trial.

Timing of administration of epinephrine (ALS 784)

Among adults who are in cardiac arrest in any setting (P), does early epinephrine delivery by IV or IO route (e.g., less than 10 min after the beginning of resuscitation) (I), compared with delayed timing of epinephrine delivery (e.g., more than 10 min after the beginning of resuscitation) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Consensus on science

In-hospital cardiac arrest. For IHCA, for the critical outcome of **survival to hospital discharge**, there was 1 observational study[129] of low quality (downgraded for serious risk of bias and upgraded for dose–response effect) in 25 095 IHCA patients with a non-shockable rhythm that showed an improved outcome with early administration of adrenaline: compared with reference interval of 1–3 min, adjusted OR for survival to discharge was 0.91 (95% CI, 0.82–1.00) when epinephrine was given after 4–6 min, 0.74 (95% CI, 0.63–0.88) when given after 7–9 min, and 0.63 (95% CI, 0.52–0.76) when given at more than 9 min after onset of arrest.

For IHCA, for the critical outcome of **neurologically favorable survival at hospital discharge** (assessed with CPC 1 or 2), there was 1 observational study[129] of low quality (downgraded for serious risk of bias and upgraded for dose–response effect) in 25 095 patients with IHCA with a non-shockable rhythm that showed an improved outcome from early administration of adrenaline: compared with reference interval of 1–3 min, adjusted OR was 0.93 (95% CI, 0.82–1.06) with epinephrine given after 4–7 min, 0.77 (95% CI, 0.62–0.95) when given after 7–9 min, and 0.68 (95% CI, 0.53–0.86) when given at more than 9 min after onset of arrest.

For IHCA, for the important outcome of **ROSC**, there was 1 observational study[129] of low quality (downgraded for serious risk of bias and upgraded for dose–response effect) in 25 095 patients with IHCA with a non-shockable rhythm that showed an improved outcome from early administration of adrenaline: adjusted OR compared with reference interval of 1–3 min of 0.90 (95% CI, 0.85–0.94) when given after 4–7 min, 0.81 (95% CI, 0.74–0.89) when given after 7–9 min, and 0.70 (95% CI, 0.61–0.75) when given after 9 min.

No studies were identified that looked specifically at the effect of timing on administration of epinephrine after IHCA with an initial shockable rhythm.

Out-of-hospital cardiac arrest. For the critical outcome of **neurologically favorable survival at hospital discharge** (assessed with CPC 1 or 2), there was very-low-quality evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 4 observational studies[130–133] involving more than 262 556 OHCAs, showing variable benefit from early administration of epinephrine. One study of 1556 OHCAs who had achieved ROSC[130] demonstrated an association between the administration of epinephrine and worse CPC, but shorter times of administration were associated with less negative effects: adjusted OR of 0.54 (95% CI, 0.32–0.91) for good CPC with epinephrine at less than 9 min versus no prehospital epinephrine, and adjusted OR of 0.17 (95% CI, 0.09–0.34) for epinephrine at more than 22 min.

Another study enrolling 209 577 OHCAs[131] did not show any significant difference in **1-month CPC 1 or 2** with epinephrine given in less than 9 min compared with no epinephrine (OR, 0.71; 95% CI, 0.54–0.92 and OR, 0.95; 95% CI, 0.62–1.37).

Another study enrolling 3161 subjects[132] showed an association with improved 1-month neurologic outcome in VF/pVT OHCA with early epinephrine (at 10 min or less from EMS call to administration) compared with no epinephrine (OR, 6.34; 95% CI, 1.49–27.02). A fourth study enrolling more than 49 000 cases[133] demonstrated a non-significant association with improved neurologic survival with early epinephrine (less than 10 min from EMS-initiated CPR): OR of 1.39 (95% CI, 1.08–1.78) versus OR of 2.01 (95% CI, 0.96–4.22).

For the critical outcome of **survival to hospital discharge after OHCA**, there was very-low-quality evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision), from 4 observational studies[127,131,133,134] enrolling more than 420 000 OHCAs that showed variable effect from early administration of adrenaline. Goto[131] showed no significant difference in 1-month survival for shockable rhythms, but improved 1-month survival for shockable rhythms with epinephrine at less than 9 min (OR, 0.95; 95% CI, 0.77–1.16 and OR, 1.78; 95% CI, 1.5–2.1). Another study[133] showed an association with improved survival with early epinephrine (less than 10 min from EMS CPR): for arrests of cardiac origin: OR, 1.73 (95% CI, 1.46–2.04); for non-cardiac origin: OR, 1.89 (95% CI, 1.37–2.61). A third study[134] did not show any overall survival benefit for early epinephrine compared with late (epinephrine at more or less than 10 min): OR, 0.91 (95% CI, 0.35–2.37).

For the important outcome of **ROSC**, there was very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 4 observational studies[127,131,134,135] of more than 210 000 OHCAs showing an association with improved outcome and early administration of adrenaline. One study[135] showed increased ROSC for patients receiving the first vasopressor dose early (less than 10 versus more than 10 min after EMS call): OR, 1.91 (95% CI, 1.01–3.63).

Another study[131] showed an association with improved ROSC for epinephrine given at less than 9 min after arrest versus none (for non-shockable rhythms: OR, 8.83; 95% CI, 8.01–9.73; for shockable rhythms: OR, 1.45; 95% CI, 1.20–1.75). A third study[134] showed an association with improved ROSC for early epinephrine versus late (more or less than 10 min after EMS call): OR, 1.78 (95% CI, 1.15–2.74).

The design flaws for most of the observational OHCA studies included the use of a "no epinephrine" control group as the comparator, thus not allowing for actual estimates of the effect of timing, and the lack of known timing of epinephrine administration upon arrival in the ED. The relationship of timing of defibrillation to timing of epinephrine is unknown for studies including shockable rhythms. These design issues make the question of timing of epinephrine difficult to interpret in the OHCA setting despite attempts to control for other confounders.

Treatment recommendation

For cardiac arrest with an initial non-shockable rhythm, we suggest that if epinephrine is to be administered, it is given as soon as feasible after the onset of the arrest (weak recommendation, low-quality evidence).

For cardiac arrest with an initial shockable rhythm, we found insufficient evidence to make a treatment suggestion regarding the timing of administration of epinephrine, particularly in relation to defibrillation, and the optimal timing may vary for different groups of patients and different circumstances.

Values, preferences, and task force insights

In making the recommendation for non-shockable rhythms, we place a higher value on being able to modify a current (standard) treatment at minimal cost.

For shockable rhythms, we place a higher value on early defibrillation than on administration of epinephrine but did not think there is sufficient evidence to make a treatment recommendation. Although we acknowledge that the pathophysiology of IHCA and OHCA is likely to be different, we were confident that the same recommendations could apply to both settings.

Knowledge gaps

- Until high-quality, well-powered trials are completed comparing epinephrine with placebo, trials addressing the timing of epinephrine doses are not required except as a third arm embedded in an epinephrine-versus-placebo trial.

Steroids for cardiac arrest (ALS 433)

Among adults who are in cardiac arrest in any setting (P), does corticosteroid or mineralocorticoid administration during CPR (I), compared with not using steroids (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

We identified studies that assessed the use of methylprednisolone, hydrocortisone, or dexamethasone during CPR. Studies usually bundled the steroid with other vasoactive drugs. All studies examined either IHCA or OHCA. Because the pathophysiology and epidemiology of IHCA and OHCA are so different, we considered these situations separately.

Consensus on science

In-hospital cardiac arrest. For the critical outcome of **survival to discharge with favorable neurologic outcome**, there was low-quality evidence (downgraded for indirectness and for imprecision) from 1 RCT[136] in 268 patients with IHCA that showed improved outcome with methylprednisolone, vasopressin, and epinephrine during cardiac arrest, and hydrocortisone in those with post-ROSC shock compared with only epinephrine and placebo (18/130 [13.9%] versus 7/138 [5.1%]; RR, 2.94; 95% CI, 1.16–6.50, which translates to 98 more/1000 surviving with good neurologic outcome [95% CI, from 8 to 279 more/1000 surviving with good neurologic outcome]).

For the critical outcome of **survival to discharge**, there was low-quality evidence (downgraded for indirectness and for imprecision) from 1 RCT[137] of 100 patients with IHCA that showed improved outcome with the combination of methylprednisolone, vasopressin, and epinephrine during cardiac arrest and hydrocortisone after ROSC for those with shock, compared with the use of only epinephrine and placebo (9/48 [19%] versus 2/52 [4%]; RR, 4.87; 95% CI, 1.17–13.79, which translates to 149 more/1000 surviving to discharge [95% CI, 7–492 more/1000 surviving to discharge]).

For the important outcome of **ROSC**, there was low-quality evidence (downgraded for indirectness and imprecision) from 2 RCTs[136,137] involving 368 patients with IHCA showing improved outcome with the use of methylprednisolone and vasopressin in addition to epinephrine, compared with the use of placebo and epinephrine alone (combined RR, 1.34; 95% CI, 1.21–1.43, which translates to 130–267 more achieving ROSC with the combination of methylprednisolone, vasopressin, and epinephrine during cardiac arrest, compared with the use of only epinephrine and placebo [95% CI, 130–267 more achieving ROSC]).

Out-of-hospital cardiac arrest. For the critical outcome of **survival to discharge**, there was very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT and 1 observational study[138,139] showing no association with benefit with the use of steroids. Paris had no long-term survivors and Tsai showed survival to discharge in 8% (3/36) receiving hydrocortisone compared with 10% (6/61) receiving placebo ($P = 0.805$).

For the important outcome of **ROSC**, we found very-low-quality evidence from 1 RCT[138] and 1 observational study[139] with a combined total of 183 patients. The RCT[138] showed no improvement in ROSC (and ICU admission) with dexamethasone given during cardiac arrest compared with placebo (5.4% [2/37] versus 8.7% [4/46]), but the observational study[139] showed an association with improved ROSC with hydrocortisone compared with no hydrocortisone (58% versus 38%; $P = 0.049$).

Treatment recommendation

For IHCA, the task force was unable to reach a consensus recommendation for or against the use of steroids in cardiac arrest.

We suggest against the routine use of steroids during CPR for OHCA (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation for IHCA, it was noted that there were no studies assessing the effect of the addition of steroids alone to standard treatment for IHCA. Also, although the triple-agent drug regimen appears to suggest an association with improved outcome, the population studied had very rapid ALS, a high incidence of asystolic cardiac arrest, and low baseline survival compared with other IHCA studies, so some of the observed effects might be peculiar to the population studied.

In making this recommendation for OHCA, we considered the cost and distraction from the addition of treatments for which there is very low confidence in any effect. The different recommendation for OHCA and IHCA was influenced by the physiological differences between these conditions, such as the incidence of sepsis, adrenal insufficiency from critical illness, and cardiovascular etiologies.

Knowledge gaps

- It is unclear which aspect of bundled treatments such as epinephrine, vasopressin, and steroids are related to any observed treatment effect. The alternative possibility is that bundled treatments require synergistic action, because other studies with each agent (vasopressin and steroids) have failed to find the same effect.
- Confidence in the treatment effects from bundled treatments will increase if confirmed in further studies.

Antiarrhythmic drugs for cardiac arrest (ALS 428)

Among adults who are in cardiac arrest in any setting (P), does administration of antiarrhythmic drugs (e.g., amiodarone, lidocaine, other) (I), compared with not using antiarrhythmic drugs (no drug or placebo) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Antiarrhythmic drugs can be used during cardiac arrest for refractory ventricular dysrhythmias. *Refractory VF/pVT* is defined differently in many trials but generally refers to failure to terminate VF/pVT with 3 stacked shocks, or with the first shock. In an ongoing clinical trial from which results are not yet available, refractory VF refers to "persistent or recurrent VF/pVT after 1 or more shocks."[140]

Consensus on science

Comparative data on the use of antiarrhythmic drugs were identified for amiodarone, lidocaine, magnesium, and nifekalant. The data reviewed for magnesium only addressed the use of this drug for undifferentiated VF/pVT and not the treatment of *torsades de pointes* or known hypomagnesemic patients. Nifekalant is only available in certain regions.

Amiodarone (I) versus no amiodarone (C). For the critical outcome of **survival with favorable neurologic/functional outcome at discharge**, there was moderate-quality evidence (downgraded due to serious risk of indirectness) from 1 RCT involving 504 OHCA patients, which detected no difference with administration of amiodarone (300 mg after 1 mg of adrenaline) compared with no drug (7.3% versus 6.6%; *P* = not significant [NS]; RR, 1.11; 95% CI, 0.59–2.10).[141]

For the critical outcome of **survival at discharge**, there was moderate-quality evidence (downgraded due to serious risk of indirectness) from 1 RCT involving 504 OHCA patients that detected no difference with the administration of amiodarone (300 mg after 1 mg of adrenaline) compared with no drug (13.4% versus 13.2%; *P* = NS; RR, 1.02; 95% CI, 0.65–1.59).[141]

For the important outcome of **ROSC**, there was moderate-quality evidence (downgraded due to serious risk of indirectness) from 1 RCT involving 504 OHCA patients that showed higher ROSC with administration of amiodarone (300 mg after 1 mg of adrenaline) compared with no drug (64% versus 41%; *P* = 0.03; RR, 1.55; 95% CI, 1.31–1.85).[141]

Lidocaine (I) versus no lidocaine (C). For the critical outcome of **survival at discharge**, there was very-low-quality evidence (downgraded for very serious risk of bias and serious indirectness) from 2 retrospective observational studies that did not detect a difference with treatment. In 290 OHCA patients, rates of survival with administration of lidocaine (50 mg, repeatable up to 200 mg) or with no drug did not differ (14% versus 8%; *P* = NS).[142] In 116 OHCA patients, survival with administration of lidocaine (100 mg) compared with no drug did not differ (11% versus 2%; *P* = NS).[143]

For the important outcome of **ROSC**, there was very-low-quality evidence (downgraded for very serious risk of bias and serious indirectness) from 2 retrospective observational single-center studies, which showed conflicting results. In 290 OHCA patients, rates of ROSC were not different after administration of lidocaine (50 mg, repeatable up to 200 mg) compared with no drug (45% versus 23%; *P*<0.001).[142] In 116 OHCA patients who had OHCA with VF refractory to 3 shocks, a similar rate of ROSC was documented with administration of lidocaine (100 mg) compared with no drug (55% versus 54%; *P* = NS).[143]

Magnesium (I) versus no magnesium (C). For the critical outcome of **survival with favorable neurologic/functional outcome at discharge**, there was low-quality evidence (downgraded for serious risk of imprecision and indirectness) from 1 single-center RCT of 156 IHCA patients with all initial rhythms (50% in VF/pVT), which showed similar survival with favorable neurologic outcome with administration of magnesium (2 g [8 mmol] bolus followed by infusion of 8 g [32 mmol] in 24 h) compared with no drugs (favorable return to independent living 14.5% versus 7.5%; *P* = NS; RR, 1.93; 95% CI, 0.75–4.96; median Glasgow Coma Scale [GCS] score at hospital discharge 15 [interquartile range, 15–15] versus 15 [interquartile range, 15–15]; *P* = NS).[144]

For the critical outcome of **survival at discharge**, there was low-quality evidence (downgraded for serious risk of imprecision and indirectness) from 4 RCTs, which showed no differences in outcome with treatment. One single-center RCT of 156 IHCA patients with all initial rhythms (50% in VF/pVT) showed similar survival with administration of magnesium (2 g [8 mmol] bolus followed by infusion of 8 g [32 mmol] in 24 h) compared with no drugs (21% versus 21%; *P* = NS; adjusted OR, 1.22; 95% CI, 0.53–2.81).[144] One single-center trial of 67 OHCA patients with all rhythms and ongoing CPR at ED arrival detected no difference with administration of magnesium (5 g [20 mmol] bolus) compared with no drugs (1 versus 0 patients; *P* = 0.46).[145]

A multicenter study of 109 OHCA patients with VF did not detect a difference in survival with administration of magnesium (2 g [8 mmol] bolus) compared with no drugs (3.6% versus 3.7%; *P* = 1.0; unadjusted RR of increased survival, 0.98; 95% CI, 0.53–2.81).[146] A single-center trial of 105 OHCA patients with VF did not detect a difference in survival with administration of magnesium (2 g [8 mmol] bolus, repeatable once) compared with no drugs (4% versus 2%; *P* = 0.99).[147]

For the important outcome of **ROSC**, there was low-quality evidence (downgraded for serious risk of imprecision and indirectness) from 3 RCTs that did not detect a difference with treatment. One single-center trial of 67 OHCA patients with all rhythms and ongoing CPR at ED arrival detected no difference with administration of magnesium (5 g [20 mmol] bolus) compared with no drugs (23% versus 22%; *P* = 0.97).[145] A multicenter study of 109 OHCA patients with VF did not detect difference in ROSC rates with administration of magnesium (2 g [8 mmol] bolus) compared with no drugs (25% versus 19%; *P* = 0.39).[146] A single-center trial of 105 OHCA patients with VF did not detect a difference in ROSC rates with administration of magnesium (2 g [8 mmol] bolus, repeatable once) compared with no drugs (17% versus 13%; *P* = 0.56).[147]

Nifekalant (I) versus no nifekalant (C). For the critical outcome of **survival at discharge**, there was very-low-quality evidence (downgraded for very serious risk of bias, very serious indirectness, and imprecision) from 1 retrospective single-center observational study of 63 patients with cardiac arrest upon or during hospitalization, which found improved survival with administration of nifekalant (loading dose 0.27 mg/kg followed by infusion of 0.26 mg/kg/h) compared with no drug in historic controls (OR for cardiac death, 0.26; 95% CI, 0.07–0.95; *P* = 0.041).[148]

Treatment recommendations

We suggest the use of amiodarone in adult patients with refractory VF/pVT to improve rates of ROSC (weak recommendation, moderate-quality evidence).

We suggest the use of lidocaine or nifekalant as an alternative to amiodarone in adult patients with refractory VF/pVT (weak recommendation, very-low-quality evidence).

We recommend against the routine use of magnesium in adult patients (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we considered the reported beneficial effects of amiodarone on the important outcome of survival to hospital admission. We acknowledged that there was the uncertainty about any beneficial or harmful effects of these drugs on the critical outcomes of survival or favorable neurologic survival. Although the evidence supporting their use is weaker, in making a recommendation for lidocaine and nifekalant as alternatives to amiodarone, the task force recognized that amiodarone is not available or currently used in some countries. The small quantity of new data made the task force place value on not changing current clinical practice.

Knowledge gaps

- There is a need for sufficiently powered RCTs to detect a difference in survival to hospital discharge or favorable neurologic outcomes.

- A potential source of bias reducing confidence in prior trials of amiodarone is use of the polysorbate solvent for the drug. This solvent is known to reduce blood pressure, and its use as placebo may have created a bias for worse outcomes in placebo groups. Future studies should account for this effect or use other solvents.
- There is an ongoing trial comparing amiodarone to lidocaine and to placebo designed and powered to evaluate for functional survival.[140]
- No data address how to select a second-line agent when VF/pVT is refractory to the first drug.

2010 CoSTR topics not reviewed in 2015

- IV fluids during cardiac arrest
- Drugs for atrial fibrillation
- Drugs for narrow complex tachycardia
- Drugs for monomorphic wide complex tachycardia
- Drugs for undifferentiated stable wide complex tachycardia
- Drugs for polymorphic wide complex tachycardia
- Drugs for *torsades de pointes*
- Drugs for bradycardia
- Atropine for cardiac arrest
- Calcium for cardiac arrest
- Fibrinolytics for cardiac arrest
- Buffering agents for cardiac arrest

Cardiac arrest in special circumstances

There are numerous special circumstances where additional interventions and/or modifications to ALS may be required. The ILCOR ALS Task Force prioritized 5 topics for review: (1) cardiac arrest during pregnancy, (2) lipid therapy for cardiac arrest associated with overdose, (3) opioid toxicity, (4) cardiac arrest caused by PE, and (5) cardiac arrest during coronary catheterization.

Cardiac arrest during pregnancy (ALS 436)

Among pregnant women who are in cardiac arrest in any setting (P), do any specific interventions (I), compared with standard care (usual resuscitation practice) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

The aim of this PICO review was to assess whether commonly applied additions to the standard practice of resuscitation led to improved outcomes in pregnant women. Specific emphasis was placed on uterine displacement for the purpose of decreasing aortocaval compression, and perimortem cesarean delivery as interventions to improve outcome in the mother and newborn.

Consensus on science

There were no comparative studies of uterine displacement for women in cardiac arrest before delivery. No studies compared different maneuvers (e.g., manual displacement versus left pelvic tilt) to achieve optimal uterine displacement for women in cardiac arrest before delivery.

Physiologic reviews and studies of uterine displacement maneuvers in non-arrest pregnant women support that uterine displacement might be physiologically beneficial for women in cardiac arrest.[149] Any benefit would have to be weighed against the potential interference or delay with usual resuscitation care.

For the critical outcomes of survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year, and survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year, and the important outcomes of ROSC, we found 3 observational studies of 154 subjects collectively[150–152] that provided very-low-quality evidence (downgraded for very serious risk of bias and imprecision, and serious inconsistency) comparing cardiac arrest resuscitation with or without perimortem cesarean delivery. The procedures to ascertain cases and controls in these studies were significantly different so that the pooled comparison of any of the assigned outcomes is considered inappropriate.

Treatment recommendations

We suggest delivery of the fetus by perimortem cesarean delivery for women in cardiac arrest in the second half of pregnancy (weak recommendation, very-low-quality evidence).

There is insufficient evidence to define a specific time interval by which delivery should begin. High-quality usual resuscitation care and therapeutic interventions that target the most likely cause(s) of cardiac arrest remain important in this population.

There is insufficient evidence to make a recommendation regarding the use of left lateral tilt and/or uterine displacement during CPR in the pregnant patient.

Values, preferences, and task force insights

In making this statement, we place value on maternal and neonatal survival, on the absence of data on left lateral tilt and uterine displacement in women with cardiac arrest, and on our uncertainty about the absolute effect of either uterine displacement or perimortem delivery during CPR on any of the assigned outcomes. The task force thought not making a recommendation for or against the use of left lateral tilt or uterine tilt is unlikely to change current practice or guidelines.

Knowledge gaps

- Research in the area of maternal resuscitation is lacking because cardiac arrest in pregnancy is rare. Most evidence is extrapolated from non-pregnant people, manikin or simulation studies, and case reports.
- The heterogeneous nature of the etiologies of maternal cardiac arrest, variations in gestational age and body mass index of the cases, variations in the location (e.g., out-of-hospital, ED, obstetric unit), and context of arrest and personnel available to immediately respond, and absence of information about the quality of usual resuscitation care all further hamper interpretation of the limited available data.
- Systematic data collection in pregnant women who have experienced cardiac arrest will require a national or international registry and/or coordinated prospective population-level surveillance to compile a sufficiently large and robust data set to evaluate the effect of either uterine displacement or perimortem delivery on maternal ROSC, maternal survival, functionally intact maternal survival, neonatal survival, and functionally intact neonatal survival.
- A particular emphasis on cardiovascular etiologies of arrest is warranted given increasing numbers of women with congenital heart conditions having children, the increasing prevalence of cardiomyopathy among pregnant and postpartum women, and the preponderance of cardiovascular disease evident in maternal mortality surveillance reports.[153]

Lipid therapy for cardiac arrest (ALS 834)

In adult patients with cardiac arrest due to suspected drug toxicity (e.g., local anesthetics, tricyclic antidepressants, others) (P), does administration of IV lipid (I), compared with no IV lipid (C), change survival with favorable neurologic/functional outcome at

discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Lipid therapy for cardiac arrest associated with drug toxicity, and in particular local anesthetic toxicity, is becoming increasingly common. Based on laboratory and preclinical data showing that IV administration of lipid solutions can absorb lipid-soluble drugs, studies examined whether this therapy would be useful for cardiac arrest related to drug overdose. We set out to identify studies comparing outcomes with IV lipids to no IV lipids.

Consensus on science

We identified no human comparative studies in cardiac arrest and periarrest states relevant to the PICO question. Many case reports and case series described resuscitation that included administration of lipid.

Treatment recommendation

We are unable to make any evidence-based treatment recommendation about the use of IV lipid emulsion to treat toxin-induced cardiac arrest.

Values, preferences, and task force insights

Although there are many case reports and case series of patients who were resuscitated after administration of IV lipid, the absence of any comparative data made it impossible to determine anything besides temporal association of the therapy with outcome. Despite the paucity of data, we do not wish to discourage the use of an antidote with some theoretical basis in a dire clinical situation.

Knowledge gaps

- Comparisons are needed of patients with similar clinical characteristics who were treated and who were not treated with IV lipids after suspected drug toxicity.

Opioid toxicity (ALS 441)

Among adults who are in cardiac arrest or respiratory arrest due to opioid toxicity in any setting (P), does any specific therapy (e.g., naloxone, bicarbonate, or other drugs) (I), compared with usual ALS (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

Opioid toxicity is associated with respiratory depression that can lead to cardiorespiratory arrest. This is becoming an increasingly common cause of death in many countries.[154] The specific role of education and availability of naloxone for those with a high risk of opioid overdose is addressed in "Part 3: Adult Basic Life Support and Automated External Defibrillation." Here we address whether any specific modifications to ALS are required when cardiac arrest is precipitated by opioid toxicity.

Cardiac arrest and respiratory arrest were considered separately. We sought evidence that compared results with any changes in usual resuscitation sequences or interventions in the setting of opioid overdose. Administration of the opioid antagonist naloxone was the only intervention for which literature was identified.

Consensus on science

For the important outcome of **survival with favorable neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year, survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year, ROSC, after opioid-induced cardiac arrest**, we found no study with comparative data beyond standard ALS care.

For the important outcome of **survival with favorable neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year, survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year, ROSC, after opioid-induced respiratory arrest**, we found no comparative studies. There were 12 studies of which 5 compared intramuscular and intranasal routes of naloxone administration (2 RCT,[156,157] 3 non-RCT,[158–160] and 7 assessed the safety of naloxone use or were observational studies of naloxone use).[161–169] These studies report that naloxone is safe and effective in treatment of opioid-induced respiratory depression, that complications are rare and dose related, and that mortality is rare when patients refuse transfer after initial naloxone administration.

Treatment recommendation

We recommend the use of naloxone by IV, intramuscular, subcutaneous, IO, or intranasal routes in respiratory arrest associated with opioid toxicity (strong recommendation, very-low-quality evidence). The dose of naloxone required will depend on the route.

We can make no recommendation regarding the modification of standard ALS in opioid-induced cardiac arrest.

Values, preferences, and task force insights

In making these recommendations, we place a high value on the potential of the opioid antagonist naloxone to reverse opioid-induced respiratory depression.

Knowledge gaps

- There are no data on the use of any additional ALS therapies in opioid-induced cardiac arrest. In respiratory arrest, there is only evidence for the use of naloxone—no other adjuncts or changes in sequence of interventions. Studies of naloxone use in respiratory arrest were observational, looked at safety, or compared routes of administration.

Cardiac arrest associated with PE (ALS 435)

Among adults who are in cardiac arrest due to PE or suspected PE in any setting (P), does any specific alteration in treatment algorithm (e.g., fibrinolytics, or any other) (I), compared with standard care (according to 2010 treatment algorithm) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

The possible treatments for massive PE include fibrinolytic therapy, surgical embolectomy, and percutaneous mechanical thrombectomy. Most retrospective studies do not make subgroup analysis of patients with suspected or confirmed PE. These treatments were assessed separately as therapies during cardiac arrest as a consequence of PE. The reported outcomes and follow-up of patients is very heterogeneous between studies.

Consensus on science

Fibrinolysis. For the critical outcome of **survival with favorable neurologic status at 30, 90, or 180 days**, there was very-low-quality evidence (downgraded for serious imprecision) from 1 RCT comparing fibrinolytics versus placebo during cardiac arrest.[170] In this double-blinded RCT, 37 of the 1050 patients randomized to receive either fibrinolytic treatment (tenecteplase) or placebo during CPR had confirmed PE as primary cause of cardiac arrest. However, this study was not powered to reach significance in this

small subgroup. Patients in whom PE was suspected were furthermore subject to use of open-label fibrinolysis and were not included in the trial at all. The 30-day survival in this subgroup was not statistically different ($P = 0.31$; RR, 7.19; 95% CI, 0.37–139.9) between tenecteplase (2/15, 13.3%) and placebo (0/22, 0%).

For the important outcome of **survival to hospital discharge**, very-low-quality evidence (downgraded for very serious risk of bias and imprecision) from 2 retrospective observational studies showed there was no difference in discharge rates: 9.5% fibrinolysis versus 4.8% control[171] and 19.4% fibrinolysis versus 6.7% control (RR, 2.9; 95% CI, 0.75–13.8).[172]

For the important outcome of **ROSC**, very-low-quality evidence from 2 studies (downgraded for very serious risk of bias) showed benefit for the use of fibrinolytic drugs compared with controls in patients with PE: ROSC was reported to be significantly higher in a retrospective analysis (81.0% fibrinolysis versus 42.9% control; $P = 0.03$).[171] In a separate study, ROSC (66.7% in fibrinolysis group versus 43.3% in control group; RR, 1.5; 95% CI, 0.8–8.6) was not different, but 24-hour survival (52.8% fibrinolysis versus 23.3% control; RR, 2.3; 95% CI, 1.1–4.7) showed favorable results for the use of fibrinolytic drugs.[172]

Surgical embolectomy. We found very-low-quality evidence (downgraded for very serious risk of publication bias) from 2 case series[173,174] with no control groups and a total of 21 patients requiring CPR with a 30-day survival rate of 12.5% and 71.4%, respectively.

Percutaneous mechanical thrombectomy. For the important outcome of **ROSC**, very-low-quality evidence (downgraded for very serious risk of bias and very serious imprecision) from 1 case series of 7 patients with cardiac arrest with no control group,[175] ROSC was achieved in 6 of 7 patients (85.7%) treated with percutaneous mechanical thrombectomy.

Treatment recommendations

We suggest administering fibrinolytic drugs for cardiac arrest when PE is the suspected cause of cardiac arrest (weak recommendation, very-low-quality evidence).

We suggest the use of fibrinolytic drugs or surgical embolectomy or percutaneous mechanical thrombectomy for cardiac arrest when PE is the known cause of cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we acknowledge the use of thrombolytic drugs, surgical embolectomy or percutaneous mechanical thrombectomy, or a combination for known PE in non-cardiac arrest patients. We acknowledge the potential risk of bleeding after fibrinolysis and place value in the choice of intervention taking into account location, availability of interventions, and contraindications to fibrinolysis.

Knowledge gaps

- There is a paucity of data on the topic of pulmonary embolus and its diagnosis and management during cardiac arrest. Further high-quality studies are required.

Cardiac arrest during coronary catheterization (ALS 479)

Among adults who have a cardiac arrest in the cardiac catheterization laboratory (P), does any special intervention or change in care (e.g., catheterization during CPR, cardiopulmonary bypass, balloon pump, different timing of shocks) (I), compared with standard resuscitation care (e.g., CPR, drugs, and shocks according to 2010 treatment algorithm) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?

Introduction

We examined the literature for any studies comparing novel treatments during cardiac arrest that occurs during cardiac catheterization in addition to standard ALS approaches (e.g., defibrillation) to cardiac arrest. The search was intended to find studies about any changes in sequence of interventions or about routine use of advanced circulatory support techniques.

Consensus on science

There were no comparative studies evaluating the survival benefit of mechanical CPR; however, individual noncomparative case series reported variable survival rates.

For the critical outcomes of **survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 90 days, 180 days, and 1 year**, and the outcomes of **survival at 30 days, 60 days, 90 days, and 180 days, and 1 year**, no studies were identified.

For the critical outcomes of **survival to discharge and survival to 6 months**, and the important outcome of **ROSC**, very-low-quality evidence (downgraded for very serious imprecision and risk of bias) from 1 observational study[176] compared ECLS with intra-aortic balloon pump and medical therapy for cardiogenic shock during PCI for ST-segment elevation myocardial infarction. There were 21 subjects with cardiac arrest during PCI, and all survivors were in the ECLS group.

Treatment recommendation

We suggest the use of ECLS as a rescue treatment when initial therapy is failing for cardiac arrest that occurs during coronary catheterization (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this weak recommendation, the task force puts a higher value on usual ALS measures such as defibrillation.

We have not made a specific recommendation here regarding the use of automated mechanical chest compressions, because we found no studies that addressed this question. We have suggested previously that automated mechanical chest compression devices are a reasonable alternative to high-quality manual chest compressions in situations where sustained high-quality manual chest compressions are impractical or compromise provider safety. This earlier weak recommendation could, therefore, apply to cardiac arrest during coronary catheterization. ECLS encompasses ECPR. We have already suggested ECPR is a reasonable rescue therapy for selected patients with cardiac arrest when initial conventional CPR is failing in settings where this can be implemented.

Knowledge gaps

- There is a lack of data about specific interventions to treat cardiac arrest during coronary catheterization.

2010 CoSTR topics not reviewed in 2015

- Anaphylaxis and cardiac arrest
- Asthma and cardiac arrest
- Post-op cardiothoracic surgery cardiac arrest
- Cardiac tamponade
- Noncardiac etiology cardiac arrest
- Benzodiazepine toxicity
- β-blocker toxicity

- Calcium channel blocker toxicity
- Carbon monoxide toxicity
- Cocaine toxicity
- Cyanide toxicity
- Tricyclic antidepressant toxicity
- Digoxin toxicity
- Electrolyte disturbances
- Avalanche victims

Postresuscitation care

Since 2010, there has been a considerable quantity of data published with the domain of postresuscitation care. The ILCOR ALS Task Force prioritized 9 topics for review: (1) oxygen dose after ROSC, (2) post-ROSC ventilation strategy, (3) hemodynamic support, (4) antiarrhythmic drugs, (5) TTM, (6) post-cardiac arrest seizures, (7) glucose control, (8) prognostication, and (9) organ donation.

Oxygen dose after ROSC in adults (ALS 448)

Among adults who have ROSC after cardiac arrest in any setting (P), does an inspired oxygen concentration titrated to oxygenation (normal oxygen saturation or partial pressure of oxygen) (I), compared with the use of 100% inspired oxygen concentration (C), change survival to 30 days with good neurologic outcome, survival to hospital discharge with good neurologic outcome, improve survival, survival to 30 days, survival to hospital discharge (O)?

Introduction

Previous preclinical work suggests that hyperoxia may be injurious in the post-cardiac arrest period. However, whether these findings apply to humans remains unclear. This PICO question evaluated whether titration of oxygen in post-cardiac arrest patients alters outcome.

Consensus on science

30% versus 100% inspired oxygen for 60 min after ROSC. For the critical outcome of **survival to hospital discharge with favorable neurologic outcome** (CPC 1 or 2), 1 RCT enrolling 32 OHCA (of which 4 excluded) patients (very-low-quality evidence, downgraded for serious risk of bias, indirectness, and imprecision)[177] showed no difference between 30% inspired oxygen for 60 min after ROSC versus 100% inspired oxygen for 60 min after ROSC (8/14 versus 6/14; unadjusted RR for survival, 1.33; 95% CI, 0.63–2.84).

For the critical outcome of **survival to hospital discharge**, 1 RCT (very-low-quality evidence, downgraded for small numbers, lack of blinding, indirectness, misallocation of patients)[177] showed no difference between 30% inspired oxygen for 60 min after ROSC and 100% inspired oxygen for 60 min after ROSC (10/14 versus 10/14; unadjusted RR for survival, 1.0; 95% CI, 0.63–1.60).

Hyperoxia versus normoxia. For the critical outcome of **survival to 12 months with favorable neurologic outcome** (CPC 1 or 2), 1 study[178] of very-low-quality evidence (downgraded for very serious risk of bias and indirectness) showed no harmful effect associated with hyperoxia during the first 24 h of ICU care.

For the critical outcome of **survival to hospital discharge with favorable neurologic outcome** (CPC 1 or 2), 5 low-quality (downgraded as very serious bias and serious inconsistency, indirectness, confounding) observational studies showed conflicting results.[179–183] Two studies showed hyperoxia was worse than normoxia.[179,181]

Three studies reported favorable neurologic outcome as CPC 1 or 2. Very-low-quality evidence (downgraded because of very serious bias and serious inconsistency, indirectness, confounding) from a single-center study of 170 ICU patients treated with therapeutic hypothermia showed that the maximum PaO_2 in the first 24 h after arrest was associated with a worse outcome (poor neurologic status at hospital discharge; adjusted OR, 1.485; 95% CI, 1.032–2.136).[181] Very-low-quality evidence (downgraded because of very serious bias and serious inconsistency, indirectness, confounding) from a single-center study of 193 ICU patients showed that the first PaO_2 after ROSC was not associated with outcome (hyperoxia adjusted OR for poor neurologic outcome, 1.05; 95% CI, 0.45–2.42).[182] Very-low-quality evidence (downgraded because of very serious bias and serious inconsistency, indirectness, confounding) from a single-center study of 184 ICU patients showed that oxygen exposure over first 24 h of ventilation was not associated with outcome with unadjusted and adjusted outcomes (effect size cannot be estimated from data).[183]

Two studies used surrogate measures of favorable neurologic outcome. Very-low-quality evidence (downgraded because of very serious bias and serious inconsistency, indirectness, confounding) from an observational study[179] showed worse independent functional survival at hospital discharge (hyperoxia versus normoxia, 124/1156 versus 245/1171 [29% versus 38%]; unadjusted OR, 0.45; 95% CI, 0.36–0.58). Very-low-quality evidence (downgraded because of very serious bias and serious inconsistency, indirectness, confounding) from an observational study[180] showed no difference in discharge to home (hyperoxia versus normoxia [27 versus 34%]; effect size cannot be estimated from data).

For the critical outcome of **survival to discharge (or survival to 30 days)**, very-low-quality evidence (downgraded because of very serious bias and serious inconsistency, indirectness, confounding) from 7 observational studies showed conflicting results.[179–181,183–186] Four studies showed hyperoxia worse than normoxia.[179,181,183,184]

One study showed a worse outcome with hyperoxia versus normoxia based on the first ICU PaO_2 (in-hospital mortality 63% versus 45%; adjusted OR hyperoxia exposure, 1.8; 95% CI, 1.5–2.2).[179] Another study showed a 100 mm Hg increase in PaO_2 was associated with a 24% increase in mortality risk (OR, 1.24; 95% CI, 1.18–1.31).[184] One study showed no association between hyperoxia versus normoxia (based on the worse PaO_2 in first 24 h on ICU; adjusted OR for hospital mortality, 1.2; 95% CI, 1.0–1.5).[180] A single-center study of 170 ICU patients treated with therapeutic hypothermia documented that the maximum PaO_2 in the first 24 h after arrest was associated with a worse outcome.[181] Survivors had lower maximum PaO_2 (198 mm Hg; interquartile range, 152.5–282) versus nonsurvivors (254 mm Hg; interquartile range, 172–363); adjusted OR—higher PaO_2 increased in-hospital mortality (OR, 1.439; 95% CI, 1.028–2.015). In a data linkage study of worse PaO_2 (highest/lowest) in first 24 on ICU, hyperoxia was not associated with outcome (hospital mortality 47% versus 41%; adjusted OR hyperoxia versus normoxia, 1.2; 95% CI, 0.51–2.82).[185] Another study of 122 ICU patients showed no difference between patients with hyperoxia (PaO_2 greater than 300 mm Hg in first 24 h after arrest) and normoxia (22/49 versus 25/70; unadjusted OR, 0.68; 95% CI, 0.32–1.44) for 30-day survival or survival to discharge (20/49 versus 24/70; unadjusted OR, 0.76; 95% CI, 0.36–1.61).[186] In another study of 184 ICU patients, the 36% with severe hyperoxia had a mortality of 54%, and the presence of severe hyperoxia was associated with decreased survival in both unadjusted and adjusted analysis (adjusted OR for survival, 0.83 per hour exposure; 95% CI, 0.69–0.99).[183]

For the important outcome of **survival to ICU discharge**, very-low-quality evidence (downgraded because of very serious bias, serious indirectness, confounding) from 2 observational studies showed no harm from hyperoxia.[185,186] In a data linkage

study of worse PaO_2 (highest/lowest) in first 24 on ICU, hyperoxia was not associated with outcome (ICU mortality 35% versus 32% for hyperoxia versus normoxia; unadjusted OR, 1.16; 95% CI, 0.56–2.40).[185] One observational study enrolling 122 ICU admissions patients showed no difference in survival to 30 days between patients with hyperoxia (PaO_2 greater than 300 mm Hg in first 24 h after arrest) and normoxia (ICU discharge 53% versus 46%; adjusted OR, 0.75; 95% CI, 0.36–1.55).[186]

Hypoxia versus normoxia. For the critical outcome of **survival to discharge (or survival to 30 days)**, very-low-quality evidence (downgraded because of very serious bias and serious indirectness, confounding) from 2 of 3 observational studies showed worse outcomes with hypoxia.[179,180,185] One study showed a worse outcome with hypoxia versus normoxia based on the first ICU PaO_2 (57% versus 45%; adjusted OR hypoxia exposure, 1.3; 95% CI, 1.1–1.5).[179] Another study documented that hypoxia versus normoxia (based on the worse PaO_2 in first 24 h on ICU) was associated with higher hospital mortality of 60% versus 47% (OR, 1.2; 95% CI, 1.1–1.4) but no difference in discharge to home (hypoxia/poor oxygen exchange versus normoxia 26% versus 24%).[180] In a data linkage study of worse PaO_2 (highest/lowest) in first 24 h on ICU, there was no difference in outcome between hypoxia and normoxia (for in-hospital mortality, 51% versus 41%; adjusted OR hypoxia versus normoxia, 0.93; 95% CI, 0.47–1.87).[185]

For the important outcome of **survival to ICU discharge**, very-low-quality evidence (downgraded because of very serious bias, serious indirectness, and confounding) from 1 observational study showed hypoxia was associated with a worse outcome.[185] Worse PaO_2 (highest/lowest) in first 24 h in ICU was associated with a worse unadjusted outcome (ICU mortality 49% versus 32% for hypoxia versus normoxia; unadjusted OR, 2.15; 95% CI, 1.23–3.77; RR, 0.74; 95% CI, 0.56–0.96).

Treatment recommendations

We recommend avoiding hypoxia in adults with ROSC after cardiac arrest in any setting (strong recommendation, very-low-quality evidence).

We suggest avoiding hyperoxia in adults with ROSC after cardiac arrest in any setting (weak recommendation, very-low-quality evidence).

We suggest the use of 100% inspired oxygen until the arterial oxygen saturation or the partial pressure of arterial oxygen can be measured reliably in adults with ROSC after cardiac arrest in any setting (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we think, despite the very-low-quality evidence, there is likely to be far greater actual harm from hypoxia and, therefore, make a strong recommendation that hypoxia should be avoided. The evidence for harm associated with hyperoxia is of very low quality and inconsistent, hence the weak recommendation.

Knowledge gaps

- There is a lack of clinical trials evaluating titration of oxygen after ROSC.
- Observational data vary considerably on definitions of hyperoxia and the optimal timing and mechanisms for measurement (arterial oxygenation versus oxygen saturation).
- Future studies are necessary to define the optimal approach to titration of oxygen in post-cardiac arrest patients taking into account measurement as well as timing/duration.

Postresuscitation ventilation strategy (ALS 571)

Among adults with ROSC after cardiac arrest in any setting (P), does ventilation to a specific $PaCO_2$ goal (I), compared with no specific strategy or a different $PaCO_2$ goal (C), change survival at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

Post-cardiac arrest patients often have pulmonary injury and/or aspiration, and also have the added concern of ischemia-reperfusion injury to the brain. Thus, the post-cardiac arrest ventilator management may need to consider both brain and lung injury when determining specific strategies for mechanical ventilation. This PICO question addressed whether mechanical ventilation after cardiac arrest to achieve any specific $PaCO_2$ goal was superior to any other $PaCO_2$ goal.

Consensus on science

No studies have specifically randomized patients to ventilation to a specific $PaCO_2$ goal.

Hypocapnia. For the critical outcome of **neurologically favorable survival**, 2 very-low-quality cohort studies[182,187] with a total of 8376 patients (downgraded for very serious concerns about risk of bias and imprecision) showed hypocapnia (less than 3.0 kPa and less than 4.7 kPa, respectively) was associated with a worse outcome. For the critical outcome of **death (or failure to be discharged home)**, 1 very-low-quality cohort study[188] of 6881 patients (downgraded for very serious concerns about risk of bias and imprecision) showed hypocapnia (less than 4.7 kPa) was associated with a worse outcome.

Hypercapnia. For the critical outcome of **neurologically favorable survival**, 3 observational cohort studies showed inconsistent associations between hypercapnia and outcome (very-low-quality evidence, downgraded for very serious concerns about risk of bias, imprecision, and inconsistency). One study[182] with a total of 123 patients showed worse outcome in patients ventilated to hypercapnia ($PaCO_2$ greater than 6.7 kPa). One study[187] with a total of 850 patients showed no difference in outcome for patients ventilated to hypercapnia ($PaCO_2$ greater than 6.0 kPa). One study[178] with a total of 409 patients showed better outcome for patients ventilated to hypercapnia ($PaCO_2$ 5.1–10.1 kPa).

For the critical outcome of **death (or failure to be discharged home)**, 2 cohort studies showed uncertain associations with outcome (downgraded for very serious concerns about risk of bias and imprecision). One study[188] with a total of 16 542 patients, showed no difference in outcome for patients ventilated to hypercapnia ($PaCO_2$ greater than 6.0 kPa). One study[187] with a total of 850 patients showed a higher mean $PaCO_2$ in survivors.

Treatment recommendation

We suggest maintaining $PaCO_2$ within a normal physiological range as part of a post-ROSC bundle of care (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, the task force did not find good evidence to suggest or recommend either hypercarbia or hypocarbia. In the absence of evidence to that end, combined with a potential suggestion of harm, we suggest maintaining normocarbia. Many physiological considerations may influence selection of $PaCO_2$ goals for individual patients.

Knowledge gaps

- There are no randomized prospective controlled trials evaluating different $PaCO_2$ goals in post-cardiac arrest patients.
- Evaluation of optimal $PaCO_2$ goals may need to be determined in populations both with and without lung injury.

Postresuscitation hemodynamic support (ALS 570)

Among adults with ROSC after cardiac arrest in any setting (P), does titration of therapy to achieve a specific hemodynamic goal (e.g., MAP greater than 65 mm Hg) (I), compared with no hemodynamic goal (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

In the post-cardiac arrest period, patients often have persistent tissue hypoperfusion/hemodynamic instability. The optimal approach to resuscitation of patients after cardiac arrest remains unknown.

Consensus on science

There are no RCTs addressing hemodynamic goals after resuscitation.

Titration of therapy to achieve a specific hemodynamic goal (e.g., MAP of more than 65 mm Hg) compared with no hemodynamic goal. For the critical outcome of **survival with favorable neurologic/functional outcome**, very-low-quality evidence (downgraded for risk of bias and publication bias) from 1 multicenter retrospective nonintervention study including 8736 subjects showed post-cardiac arrest SBP less than 90 mm Hg was associated with higher mortality (65% versus 37%) and diminished discharge functional status in survivors (49% versus 38%).[189]

For the critical outcome of **survival**, very-low-quality evidence (downgraded for risks of bias and publication bias) from 2 retrospective single-center studies including 2282 patients showed reduced survival for patients with post-ROSC SBP less than 90 mm Hg[190] and less than 100 mm Hg.[191]

Bundle of therapies with a specific blood pressure target compared with no bundle. For the critical outcome of **survival with favorable neurologic/functional outcome**, we found very-low-quality evidence (downgraded for risks of bias and publication bias) from 7 studies that included 813 subjects. One pre-/poststudy of early goal-directed therapy of 36 patients with a MAP target greater than 80 mm Hg showed no difference in mortality or neurologic outcome at hospital discharge.[192] One prospective observational study of 118 patients using historic controls showed that aiming for MAP greater than 65 mm Hg increased survival to hospital discharge with a favorable neurologic outcome at 1 year in 34 of 61 (56%) versus 15 of 58 (26%) in the control period (OR, 3.61; CI, 1.66–7.84; $P = 0.001$).[193] One cohort study of 148 patients showed no difference in neurologic outcome at hospital discharge when a MAP less than 75 mm Hg was a threshold for intervention.[194] One retrospective study of 136 patients identified groups with MAP greater than 100 mm Hg or less than 100 mm Hg after ROSC. Good neurologic recovery was independently and directly related to MAP measured during 2 h after ROSC ($r^2 = 0.26$).[195] One before-and-after observational study of a care bundle, including 55 subjects aiming for a MAP greater than 65 mm Hg within 6 h, showed no change of in-hospital mortality (55.2% [bundle] versus 69.2% [prebundle]) or CPC 1 or 2 (31% versus 12%).[196] In 1 prospective single-center observational study of 151 patients receiving a bundle of therapies where 44 (29%) experienced good neurologic outcome, a time-weighted average MAP threshold greater than 70 mm Hg had the strongest association with good neurologic outcome (OR, 4.11; 95% CI, 1.34–12.66; $P = 0.014$).[197] One retrospective study of bundle therapy targeting a MAP greater than 80 mm Hg in 168 patients showed survivors had higher MAPs at 1 h (96 versus 84 mm Hg), 6 h (96 versus 90 mm Hg; $P = 0.014$), and 24 h (86 versus 78 mm Hg) when compared with nonsurvivors. Increased requirement for vasoactive drugs was associated with mortality at all time points. Among those requiring vasoactive drugs, survivors had higher MAPs than nonsurvivors at 1 h (97 versus 82 mm Hg) and 6 h (94 versus 87 mm Hg).[198]

For the critical outcome of **survival**, we found very-low-quality evidence (downgraded for risks of bias and publication bias) from 2 studies including 91 patients that assessed the impact of postresuscitation goal-directed/bundles of care (including blood pressure targets) on survival. One pre-/poststudy of early goal-directed therapy of 36 patients including a MAP target greater than 80 mm Hg showed no difference in mortality at hospital discharge.[192] One pre-/postobservational study of a care bundle including 55 patients aiming for a MAP greater than 65 mm Hg within 6 h resulted in an in-hospital mortality of 55.2% (bundle) versus 69.2% (prebundle) ($P = 0.29$; RR, 0.80; 95% CI, 0.53–1.21).[196]

Treatment recommendations

We suggest hemodynamic goals (e.g., MAP, SBP) be considered during postresuscitation care and as part of any bundle of postresuscitation interventions (weak recommendation, low-quality evidence).

There is insufficient evidence to recommend specific hemodynamic goals; such goals should be considered on an individual patient basis and are likely to be influenced by post-cardiac arrest status and pre-existing comorbidities (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place a higher value on the recognition that while hemodynamic goals are likely important to optimize outcome, specific targets remain unknown and likely vary depending on individual physiology and comorbid status.

Knowledge gaps

- There are no prospective, randomized trials on specific hemodynamic targets or goals with respect to outcome.
- Comorbidities and the complexities of individual-based physiology should ideally be taken into account in future investigations into hemodynamic targets/goals.
- Future studies of measurement of actual blood flow and tissue perfusion, particularly cerebral perfusion, and the role of noninvasive technology are desirable.

Postresuscitation antiarrhythmic drugs (ALS 493)

Among adults with ROSC after cardiac arrest in any setting (P), do prophylactic antiarrhythmic drugs given immediately after ROSC (I), compared with not giving antiarrhythmic drugs (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; development of cardiac arrest; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; recurrence of VF; incidence of arrhythmias (O)?

Introduction

After ROSC from cardiac arrest, the decision to initiate or continue therapy with antiarrhythmic medications remains uncertain.

Literature was found for both β-blocking medications and lidocaine. We identified no studies of magnesium, amiodarone, procainamide, bretylium, or nifekalant.

Consensus on science

β-Blockers (I) versus no β-blockers (C). For the critical outcome of **survival at 6 months**, we have identified very-low-quality evidence (downgraded for serious risk of bias, indirectness, and imprecision) from 1 observational study of 98 patients resuscitated from OHCA showing a higher rate of survival with administration of β-blockers (metoprolol or bisoprolol) for 72 h after ROSC compared with no drug (55.7% versus 21.1%; $P < 0.001$; RR, 2.65; 95% CI, 1.08–6.46) and after adjusting for the Utstein variables (specific OR data not available; $P = 0.002$).[199]

Lidocaine (I) versus no lidocaine (C). For the important outcome of **recurrence of VF**, we identified very-low-quality evidence (downgraded for serious risk of bias and indirectness) from 1 observational study of 1721 patients resuscitated from OHCA showing a lower adjusted (adjusted by the Utstein variables and matched by propensity scores) rate of recurrence of VF following lidocaine bolus and/or continuous infusion immediately after ROSC compared with no drug (OR, 0.34; 95% CI, 0.26–0.44).[200]

For the critical outcome of **survival to hospital discharge**, we identified very-low-quality evidence (downgraded for serious risk of bias and indirectness) from 1 observational study of 1721 patients resuscitated from OHCA showing a higher rate of survival to hospital discharge after adjusting for the Utstein variables (OR, 1.49; 95% CI, 1.15–1.95) but no difference after propensity-matching analysis (OR, not reported).[200]

Treatment recommendation

We make no recommendation about the routine prophylactic use of antiarrhythmic drugs post after ROSC (GRADE used for evidence evaluation and synthesis only, very low confidence in effect estimate).

Values, preferences, and task force insights

The available data were too limited to have any confidence in any effect, and, therefore, no recommendation is made. We also place value on avoiding known side effects of medications when the treatment effect was unproven or unknown. The studies evaluated were all observational, and no causal relation could be determined. Moreover, they were performed before changes in current practice (i.e., currently amiodarone is used during cardiac arrest more than lidocaine).

Knowledge gaps

- There are no randomized trials for any antiarrhythmic drug in the post-cardiac arrest period.
- Patients resuscitated from VF/pVT who have received an antiarrhythmic medication during the cardiac arrest period are a specific population of interest.

Targeted temperature management (induced hypothermia)

Post-cardiac arrest ischemia-reperfusion injury to the brain may be attenuated by induced hypothermia. Several PICO questions are addressed in this section: TTM for (a) OHCA with shockable rhythm, (b) OHCA with nonshockable rhythms, and (c) IHCA with any rhythm; the optimal target temperature; the duration of TTM; and the timing of TTM.

Targeted temperature management (ALS 790)

Among patients with ROSC after cardiac arrest in any setting (P), does inducing mild hypothermia (target temperature 32–34 °C) (I), compared with normothermia (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

This PICO review was divided into 2 questions. The first question evaluated whether induced hypothermia should be initiated for postarrest patients. Evidence was evaluated separately for OHCA with shockable rhythms, OHCA with nonshockable rhythms, and IHCA (all rhythms). The second question evaluated the optimal target temperature for postarrest patients.

Consensus on science

OHCA arrest with a shockable rhythm. For the critical outcome of **survival with favorable neurologic outcome**, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[201] and 1 quasi-randomized trial[202] enrolling 275 and 77 patients, showing a benefit in patients with OHCA with VF or pVT as an initial rhythm. In these studies, cooling to 32–34 °C compared with no temperature management was associated with good neurologic outcome at 6 months (RR, 1.4; 95% CI, 1.08–1.81) and survival to hospital discharge (OR, 2.65; 95% CI, 1.02–6.88). For the critical outcome of **survival**, 1 study[201] showed benefit in patients treated with induced hypothermia (RR for 180-day mortality, 0.74; 95% CI, 0.58–0.95), while another study found no significant difference (51% versus 68% hospital mortality; RR, 0.76; 95% CI, 0.52–1.10).[202]

OHCA with nonshockable rhythms. We found no RCTs comparing mild induced hypothermia (32–34 °C) to no temperature management in patients with OHCA with pulseless electrical activity or asystole (i.e., nonshockable) as the initial rhythm.

For the critical outcome of **survival with favorable neurologic outcome**, we found 3 cohort studies including a total of 1034 patients, providing overall very-low-quality evidence (downgraded for risk of bias and imprecision) for no difference in poor neurologic outcome in patients with nonshockable OHCA (adjusted pooled OR, 0.90; 95% CI, 0.45–1.82).[203–205]

One additional retrospective study that used a large registry, including 1830 patients, provided very-low-quality evidence (downgraded for risk of bias and imprecision) for an increase in poor neurologic outcome in patients with nonshockable OHCA (adjusted OR, 1.44; 95% CI, 1.039–2.006).[206] These data were not pooled with the above studies due to the lack of temperature data and limited patient information available.

For the critical outcome of **survival**, we found very-low-quality evidence (downgraded for risk of bias and imprecision) of a benefit in mortality at 6 months (OR, 0.56; 95% CI, 0.34–0.93) from one of these studies.[204]

IHCA. We found no RCTs comparing mild induced hypothermia (32–34 °C) to no temperature management in patients with IHCA. For the critical outcome of **survival to hospital discharge**, we found very-low-quality evidence (downgraded for risk of bias and imprecision) in 1 retrospective cohort study including 8316 patients that showed no benefit in patients with IHCA of any initial rhythm who were treated with TTM versus no active temperature management (OR, 0.9; 95% CI, 0.65–1.23).[207]

For the critical outcome of **neurologically favorable survival**, we found very-low-quality evidence (downgraded for risk of

bias and imprecision) from the same observational study showing no benefit (OR, 0.93; 95% CI, 0.65–1.32). Although we found numerous before-and-after studies on the implementation of temperature management, these data are extremely difficult to interpret in light of other changes in post-cardiac arrest care that accompanied implementation, making it impossible to isolate the effect of temperature on outcomes after cardiac arrest. For this reason, we excluded all before-and-after studies. Other observational studies with concurrent controls also represent low-quality evidence due to residual confounding and other factors. We, therefore, did not include these in the consensus on science, except for specific patient populations lacking higher quality (i.e., RCT) evidence.

Target temperature. For the critical outcomes of **survival and survival with favorable neurologic outcome**, we found moderate-quality evidence (downgraded for imprecision) from 1 RCT including 939 patients. This study compared cooling to 33 °C compared with tight temperature control at 36 °C in adult patients with OHCA of any initial rhythm except unwitnessed asystole, and found no benefit (HR for mortality at end of trial, 1.06; 95% CI, 0.89–1.28; RR for death or poor neurologic outcome at 6 months, 1.02; 95% CI, 0.88–1.16).[208]

For the critical outcome of **survival with favorable neurologic outcome**, we found low-quality evidence (downgraded for risk of bias and imprecision) in 1 additional small pilot RCT enrolling 36 patients comparing 32 °C with 34 °C in patients with OHCA VF/pVT or asystole. This study found no benefit (neurologically intact survival 44.4% versus 11.1%; $P = 0.12$), although with only 36 patients it was underpowered.

Treatment recommendations

We recommend selecting and maintaining a constant target temperature between 32 °C and 36 °C for those patients in whom temperature control is used (strong recommendation, moderate-quality evidence). Whether certain subpopulations of cardiac arrest patients may benefit from lower (32–34 °C) or higher (36 °C) temperatures remains unknown, and further research may help elucidate this.

We recommend TTM as opposed to no TTM for adults with OHCA with an initial shockable rhythm who remain unresponsive after ROSC (strong recommendation, low-quality evidence).

We suggest TTM as opposed to no TTM for adults with OHCA with an initial nonshockable rhythm who remain unresponsive after ROSC (weak recommendation, very-low-quality evidence).

We suggest TTM as opposed to no TTM for adults with IHCA with any initial rhythm who remain unresponsive after ROSC (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place a higher value on the potential for increased survival with good neurologic outcome as compared with the possible risks (which appear to be minimal) and the cost of TTM. We emphasize that the mortality after cardiac arrest is high and the treatment options are limited. Although the evidence for TTM compared with no temperature management is of low quality, it is the only post-ROSC intervention that has been found to improve survival with good neurologic outcome. We have, therefore, made our recommendation strong in spite of the low-quality evidence.

Knowledge gaps

- There is no high-quality evidence to support or refute the use of TTM in adults with OHCA and nonshockable initial rhythm, or adults with IHCA and any initial rhythm.
- There is no evidence to support or refute specific temperature targets tailored to individual patients based on post-cardiac arrest injury severity.
- Studies including more detailed neurocognitive evaluations to determine outcome in a more granular fashion are also needed.

Duration of TTM (ALS 791)

In patients with ROSC after cardiac arrest in any setting (P), does induction and maintenance of hypothermia for any duration other than 24 h (I), compared with induction and maintenance of hypothermia for a duration of 24 h (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

The hypothermia trials published in 2002 used 12 h and 24 h of cooling,[201,202] which was adopted in subsequent guidelines.[209] The optimal duration for TTM remains unknown.

Consensus on science

We found no human trials comparing different durations of TTM after cardiac arrest.

For the critical outcome of **favorable neurologic outcome**, very-low-quality evidence (downgraded for risk of bias and imprecision) from 2 observational trials found no difference in duration of hypothermia[210] and no difference in mortality or poor neurologic outcome with 24 h compared with 72 h of hypothermia.[211] Previous trials treated patients with 12–28 h of TTM.[201,202,208] One trial provided strict normothermia (less than 37.5 °C) after hypothermia until 72 h after ROSC.[208]

Treatment recommendations

We suggest that if TTM is used, duration should be at least 24 h, as done in the 2 largest previous RCTs[201,208] (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a high value on not changing current clinical practice, which most commonly is a TTM duration of 24 h. We further note that the 2 largest trials related to TTM both used at least 24 h, one of which found an outcome benefit when compared with not using TTM.

Knowledge gaps

- There is no direct evidence to support or refute any specific duration of TTM.
- Controlled, randomized, human trials to evaluate duration of TTM are needed.

Timing of induced hypothermia (ALS 802)

Among patients with return of pulses after cardiac arrest in any setting (P), does induction of hypothermia before some time point (e.g., 1 h after ROSC or before hospital arrival) (I), compared with induction of hypothermia after that time point (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

Prior recommendations suggest that cooling should be initiated as soon as possible after ROSC, but this recommendation was based only on preclinical data and rational conjecture.[209] This question

addressed whether early cooling was superior to delayed cooling. Early cooling was defined as prehospital cooling before hospital arrival. Because multiple trials were available, only RCTs were included.

Consensus on science

Five RCTs[212–216] used cold IV fluids after ROSC to induce hypothermia, 1 trial used cold IV fluid during resuscitation,[217] and 1 trial used intra-arrest intranasal cooling.[218] The volume of cold fluid ranged from 20 to 30 mL/kg and up to 2 L, though some patients did not receive the full amount before hospital arrival. One small feasibility trial was not included.[219] All 7 trials suffered from the unavoidable lack of blinding of the clinical team, and 3 also failed to blind the outcomes assessors.

For the critical outcome of **favorable neurologic outcome**, 5 trials with a total of 1867 subjects with OHCA[213–216,218] provided overall moderate-quality evidence (downgraded for risk of bias), showing that neurologic outcomes did not differ after initiation of induced hypothermia in the prehospital environment compared with later initiation (RR, 1.00; 95% CI, 0.95–1.06).

For the critical outcome of **mortality**, 7 trials with a total of 2237 subjects provided moderate-quality evidence (downgraded for risk of bias), showing no overall difference in mortality for patients treated with prehospital cooling (RR, 0.98; 95% CI, 0.92–1.04) compared with those who did not receive prehospital cooling. No individual trial found an effect on either poor neurologic outcome or mortality.

For the outcome of **rearrest**, 4 RCTs provided low-quality evidence (downgraded for risk of bias and inconsistency) for an increased risk among subjects who received prehospital induced hypothermia (RR, 1.22; 95% CI, 1.01–1.46).[212,213,215,216] This result was driven by data from the largest trial.[216]

For the outcome of **pulmonary edema**, 3 trials reported no pulmonary edema in any group. Two small pilot trials[212,217] found no difference between groups, and 1 trial showed an increase in pulmonary edema in patients who received prehospital cooling (RR, 1.34; 95% CI, 1.15–1.57).[216] These trials provided overall low-quality evidence (downgraded for risk of bias and inconsistency).

Treatment recommendations

We recommend against routine use of prehospital cooling with rapid infusion of large volumes of cold IV fluid immediately after ROSC (strong recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place high value on not recommending an intervention with no proven benefit despite a large number of patients studied. We further note that the meta-analysis driven by the results from the largest study found also noted an increased risk of rearrest with prehospital induction of mild hypothermia using rapid infusion of cold IV fluid.[216] This recommendation is specific to the prehospital setting after ROSC, and we acknowledge that cold IV fluid might still be used in patients who have been further evaluated or in other settings.

Knowledge gaps

- Early cooling strategies, other than rapid infusion of large volumes of cold IV fluid, and cooling during CPR in the prehospital setting have not been studied adequately.
- Whether certain patient populations (e.g., patients for whom transport time to a hospital is longer than average) might benefit from early cooling strategies remains unknown.

Prevention of fever after cardiac arrest (ALS 879)

Among adults with ROSC after cardiac arrest in any setting (P), does prevention of fever to maintain strict normothermia (I), compared with no fever control (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

Fever is associated with poor outcome in many critical illnesses with neurologic injury. Increased temperature may aggravate ischemia-reperfusion injury and neuronal damage through increased metabolic activity. We examined whether fever prevention improves outcomes in patients not receiving TTM and in patients after the use of TTM.

No interventional or observational studies were identified addressing whether fever prevention (or treatment) after cardiac arrest improves outcome. We, therefore, included studies that examined the association between fever and outcomes.

Consensus on science

Fever after ROSC without TTM. For the critical outcomes of survival with **good neurologic/functional outcome and/or survival only**, we found very-low-quality evidence from 5 observational studies (downgraded for risk of bias and indirectness) that fever after ROSC is associated with poor outcome when TTM is not used.[221–225]

Fever after TTM. For the critical outcomes of **survival with good neurologic/functional outcome and/or survival only**, we found very-low-quality evidence from 6 observational studies ($n = 856$) (downgraded for risk of bias and indirectness) that fever after TTM is not associated with outcome.[225–230] For the same critical outcomes, we also found very-low-quality evidence from 2 observational studies ($n = 411$) (downgraded for risk of bias, inconsistency, and indirectness) that fever after TTM is associated with poor outcome.[231,232]

Treatment recommendation

We suggest prevention and treatment of fever in persistently comatose adults after completion of TTM between 32 °C and 36 °C (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we recognize that TTM always should be used in comatose patients after cardiac arrest, and that fever will not occur during this time. Thus, fever management is primarily a concern after TTM has been completed. Despite substantial limitations of the included studies, expert opinion within the task force combined with the fact that fever prevention is common practice for other neurologic injuries in the ICU and the relative low risk of harm associated with fever prevention prompted us to recommend in favor of fever prevention.

Knowledge gaps

- In the absence of RCTs, whether the prevention or treatment of fever after cardiac arrest is beneficial remains unclear.
- It is unclear how long fever prevention is necessary, and what technique (e.g., external, internal, pharmacologic) is best.
- Data to date cannot distinguish whether fever causes increased neurologic injury or severe neurologic injury causes temperature dysregulation.

Postresuscitation seizure prophylaxis (ALS 431)

Among adults with ROSC after cardiac arrest in any setting (P), does seizure prophylaxis (I), compared with no prophylaxis (C), reduce the incidence of seizures, or improve survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

Seizures, and particularly status epilepticus (SE), are associated with poor outcomes in comatose post-cardiac arrest patients. While seizure and SE can be the result of severe brain injury caused by cardiac arrest, these disorders also have the potential to exacerbate brain injury caused by cardiac arrest. We examined whether seizure prophylaxis or effective seizure management improve outcomes of post-cardiac arrest patients.

Consensus on science

For the critical outcome of **survival with favorable neurologic/functional outcome**, moderate-quality evidence (downgraded for indirectness) from 2 prospective double-blinded randomized clinical trials involving a total of 312 subjects[233,234] and 1 nonrandomized prospective clinical trial that used historic controls with 107 subjects[235] detected no benefit of seizure prophylaxis.

In 1 block randomized trial,[234] OHCA patients with ROSC received either placebo, diazepam, magnesium sulfate, or diazepam plus magnesium sulfate. The percentage of patients independent at 3 months was 25.3% (19/75) in the placebo group, 34.7% (26/75) in the magnesium group, 17.3% (13/75) in the diazepam group, and 17.3% (13/75) in the diazepam plus magnesium group (for magnesium: RR, 1.22; 95% CI, 0.81–1.83). After adjusting for baseline imbalances, outcomes did not differ between groups. In a trial of thiopental versus placebo within 1 h of ROSC,[233] 1-year survival with good cerebral function was 15% (20/131) in the placebo group and 18% (24/131) in the thiopental group (RR, 1.20; 95% CI, 0.70–2.06). After multivariate adjustment, groups did not differ (OR, 1.18; 95% CI, 0.76–1.84). A nonrandomized clinical trial[235] showed no benefit of barbiturate therapy in comatose post-cardiac arrest patients using a combination of thiopental and phenobarbital when compared with historic controls. In this study, survival to hospital discharge with favorable neurologic outcome was 38% (20/53) in the barbiturate group and 26% (14/54) in the historic control group (ARR, 11.8%; 95% CI, −5.8 to 28.5; or 118 more patients/1000; 95% CI, 58 fewer to 285 more patients/1000). One case series showed that 9 of 10 patients with anesthesia-associated cardiac arrest survived with good neurologic outcome when single-dose phenytoin was administered early after ROSC.[236]

For the important outcome of **seizure prevention**, we identified low-quality evidence downgraded for indirectness from 2 prospective double-blinded RCTs[233,234] showing no benefit of seizure prophylaxis. In 1 trial of thiopental treatment,[233] 21% (28/131) of control subjects and 13% (17/131) of thiopental-treated subjects had seizures (ARR, −8.4%; 95% CI, −17.5 to 0.8; 84 fewer patients/1000; 95% CI, 175 fewer to 8 more patients/1000). The incidence of seizures in a second trial[234] was 11.9% in all treatment groups (double placebo, magnesium plus placebo, diazepam plus placebo, and diazepam plus magnesium).

Treatment recommendation

We suggest against routine seizure prophylaxis in post-cardiac arrest patients (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, the task force acknowledged the lack of confidence in a treatment effect on the critical outcome of survival with good neurologic function treatment. The task force also considered that seizure prophylaxis in other forms of acute brain injuries is not associated with improved outcomes, and that most drugs have significant side effects.

Knowledge gaps

- Standardized definitions for diagnosing seizures in comatose post-cardiac arrest patients have not been used.
- The utility of continuous electroencephalogram (EEG) versus intermittent EEG monitoring versus no EEG in the diagnosis and treatment of seizures in comatose post-cardiac arrest patients remains controversial due to resource utilization and lack of evidence for improved outcomes.
- There are no RCTs designed to evaluate the impact of seizure prophylaxis after ROSC on incidence of seizures and neurologic outcome.
- There are inadequate data regarding the timing, duration, dosing, and choice of antiepileptic drugs for seizure prophylaxis in comatose post-cardiac arrest patients.

Seizure treatment (ALS 868)

Among adults with ROSC after cardiac arrest in any setting (P), does effective seizure treatment (I), compared with no seizure control (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Consensus on science

There are no RCTs addressing this question.

For the critical outcome of **survival with favorable neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year**, very-low-quality evidence (downgraded for lack of concurrent comparative data) from 3 case series[237–239] showed only 1/47 post-cardiac arrest patient treated for seizures or SE survived with good neurologic function. The antiepileptic drugs used were widely variable (phenytoin, levetiracetam, sodium valproate, clonazepam, propofol, and midazolam); included general anesthetics; and the drug, dose, and timing of therapy were not consistently reported. In these reports, no post-cardiac arrest patients with seizures were left untreated, providing no insight into the impact of antiepileptic drug therapy on survival or neurologic outcome. In 1 study, effective seizure control was achieved in 4/5 patients treated for seizures, and 0/5 survived with good neurologic function.[239] In 1 study, effective seizure control was achieved in 0/24 patients with SE, and 1/24 patients survived with good neurologic function.[237]

Treatment recommendation

We recommend the treatment of seizures in post-cardiac arrest patients (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we acknowledge very low confidence in the estimated treatment effect. However, ongoing seizures have the potential to worsen brain injury, and treatment of recurrent seizures and SE is the standard of care in other patient populations.

Knowledge gaps

- Standardized definitions for diagnosing seizures in comatose post-cardiac arrest patients have not been used.
- The utility of continuous EEG versus intermittent EEG monitoring versus no EEG in the diagnosis and treatment of seizures in comatose post-cardiac arrest patients remains controversial due to resource utilization and lack of evidence for improved outcomes.
- There are no RCTs designed to evaluate the impact of seizure prophylaxis after ROSC on incidence of seizures and neurologic outcome.
- There are inadequate data regarding the timing, duration, dosing, and choice of antiepileptic drugs for seizure prophylaxis in comatose post-cardiac arrest patients.
- The threshold for treating epileptiform activity other than convulsive seizures (e.g., generalized epileptiform discharges) is poorly defined.

Glucose control after resuscitation (ALS 580)

Among adults with ROSC after cardiac arrest in any setting (P), does a specific target range for blood glucose management (e.g., strict 4–6 mmol/L) (I), compared with any other target range (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

Glycemic control with insulin is now common for critically ill patients, and hyperglycemia after cardiac arrest is associated with worse neurologic outcomes. We examined whether specific glucose values other than those selected for other critically ill patients should be targeted in patients after resuscitation from cardiac arrest.

Consensus on science

For the critical outcome of **survival to hospital discharge**, there was moderate-quality evidence (downgraded for risk of bias due to lack of blinding) from 1 RCT of 90 subjects showing reduced 30-day mortality (RR, 0.94; 95% CI, 0.53–1.68) when subjects were assigned to strict (4–6 mmol/L) versus moderate (6–8 mmol/L) glucose control.[240] One before-and-after observational study of 119 subjects provided very-low-quality evidence (downgraded for multiple potential confounding variables) of reduced in-hospital mortality (RR, 0.46; 95% CI, 0.28–0.76) after implementation of a bundle of care that included defined glucose management (5–8 mmol/L).[193] The effect of glucose management cannot be separated from the effects of other parts of the bundle.

Treatment recommendation

We suggest no modification of standard glucose management protocols for adults with ROSC after cardiac arrest (weak recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we considered the lack of evidence that the approach to glucose management chosen for other critical care populations should be modified for the post-cardiac arrest patients. Moreover, we noted that strict glycemic control is labor intensive, and in other populations, implementation of strict glycemic control is associated with increased episodes of hypoglycemia, which might be detrimental. Avoiding hypoglycemia was considered more important than the unproven benefits of treating moderate hyperglycemia.

Knowledge gaps

- It remains unknown whether maintaining serum glucose within a specific range or minimizing variability in post-cardiac arrest patients will improve survival and/or neurologic outcome.

Neurologic prognostication

In contemporary practice, many comatose post-cardiac arrest patients will not survive or will survive with an unfavorable neurologic outcome. In some regions, family and treating teams may limit or withdraw life-sustaining treatment when unfavorable neurologic outcomes are expected. Therefore, reliable strategies for timely prognostication are a critical component of any cardiac arrest system of care.

The decision to limit treatment of comatose post-cardiac arrest patients should never rely on a single prognostication element. The consensus of the task force was that a multimodal approach should be used in all cases, with all supplementary tests considered in the context of the clinical examination. The most reliable combination and timing for each assessment remain to be determined and require further research.

Reported reliability (FPR and 95% CIs) of any predictor of poor outcome in post-cardiac arrest patients is specific to the time points after cardiac arrest or rewarming when they are measured. In addition, although several elements are associated with poor outcome when measured before 72 h after ROSC, it is the consensus of the task force that decisions to limit treatments must consider that neurologic prognosis is uncertain before at least 72 h after ROSC. We acknowledge that other non-neurological factors may contribute to decisions to limit treatment.

Separate PICO questions addressed prognostication of comatose post-cardiac arrest patients treated with hypothermic TTM and patients not treated with hypothermic TTM. This approach was chosen because hypothermic TTM can alter the natural history of coma and may also delay recovery of CNS function. Moreover, patients may be exposed to larger doses and durations of pharmacologic sedation and neuromuscular blockade to prevent or treat shivering during TTM, and the metabolism of these agents may be delayed during hypothermic TTM. Prognostic elements that are reliable in comatose post-cardiac arrest patients not treated with hypothermic TTM may be less reliable at the same time point in patients treated with TTM.

This review identified clinical signs, neurophysiological measurements, blood or cerebrospinal fluid markers, or imaging studies that had high specificity for poor neurologic outcome, defined as death, vegetative state, or severe cerebral disability (CPC 3–5). This approach was justified by the need to identify signs or measurements that might be used to justify limiting life-sustaining treatment. To quantify the specificity of the finding, we examined the FPR of each sign for predicting unfavorable neurologic outcome, with a goal of 0% FPR. The 95% CI of the FPR was calculated, and we tended to recommend a finding as useful if the FPR was less than 5%, and suggest that a finding might be useful if the FPR was less than 10%. In most cases, clinical signs and findings were considered individually, because few studies considered combinations of clinical findings.

Prognostication in comatose patients treated with hypothermic TTM (ALS 450)

Among adults with ROSC who are treated with hypothermia (P), does any clinical variable when abnormal (e.g., clinical exam, EEG, somatosensory evoked potentials [SSEPs], imaging, other) (I), compared with any clinical variable when normal (C), reliably predict death or poor neurologic outcome at discharge, 30 days, 60 days,

180 days, and/or 1 year; death only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Consensus on science

Clinical examination. No study on clinical examination reported blinding of the treating team to the results of the index test.

For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified very-low-quality evidence (downgraded for very serious risk of bias and imprecision) from 4 studies on corneal reflex, pupillary reflex, motor response, GCS, or myoclonus (295 patients).[238,241–243]

For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified very-low-quality evidence (downgraded for very serious risk of bias and very serious imprecision) from 5 studies on corneal reflex, pupillary reflex, motor response, brainstem reflexes, or myoclonus (388 patients).[244–248]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified low- or very-low-quality evidence (downgraded for very serious risk of bias and serious or very serious imprecision) from 4 studies on corneal reflex, pupillary reflex, motor response, brainstem reflexes, or myoclonus (642 patients).[249–252]

Corneal reflex. In patients who are comatose after resuscitation from cardiac arrest and are treated with TTM, bilaterally absent corneal reflexes at 72–120 h from ROSC predicted poor outcome, with 2 (0–7)% FPR and 25 (18–32)% sensitivity[241,248,251,253] (301 subjects; very-low-quality evidence).

Pupillary reflex. Bilaterally absent pupillary light reflexes (PLR) on hospital admission predicted poor outcome, with 32 (19–48)% FPR and 86 (71–95)% sensitivity[242,254] (86 patients; very-low-quality evidence). Bilaterally absent PLR at 72–108 h from ROSC predicted poor outcome, with 1 (0–3)% FPR and 19 (14–25)% sensitivity[241,248,249,251,254] (5 studies, 383 subjects; low-quality evidence downgraded for very serious bias).

Motor response to pain. On hospital admission, bilaterally absent or extensor motor responses, corresponding to a motor score 1 or 2 (M1–2) of the GCS, predicted a poor outcome, with 53 (36–68)% FPR and 92 (75–99)% sensitivity[242] (66 patients; very-low-quality evidence). At 36–108 h from ROSC, an M1–2 predicted a poor outcome, with 70 (65–74)% sensitivity and 10 (7–15)% FPR[245,247–251] (635 subjects; very-low-quality evidence).

One study[248] indicated that both absent corneal reflexes and motor response to pain at 72 h predicted poor outcome (CPC 4–5) more accurately in patients who did not receive any sedative drugs 12 h or less before neurologic assessment than in those who did.

Combination of clinical signs. Bilateral absence of 1 or more brainstem reflexes (pupillary, corneal, or oculocephalic) at 36–72 h from arrest predicted a poor outcome, with 8 (4–14)% FPR and 56 (48–63)% sensitivity (3 studies; 304 patients; very-low-quality evidence).[246,247,255] In 1 study (103 subjects; very-low-quality evidence), the combined absence of corneal reflex, PLR, and M1–2 at 72 h from ROSC predicted poor outcome, with 0 (0–8)% FPR and 15 (7–26)% sensitivity.[245] In that study, the index test was used as a criterion for withdrawal of life-sustaining treatment. A GCS of 4 or less at 96 h from ROSC predicted poor outcome, with 5 (1–15)% FPR and 46 (28–66)% sensitivity[243] (72 subjects; very-low-quality evidence).

Myoclonus and status myoclonus. Presence of myoclonus within 72 h from ROSC predicted a poor outcome, with 5 (3–8)% FPR and 39 (35–44)% sensitivity (6 studies,[238,246,247,249,250,252] 845 subjects; very-low-quality evidence). In 1 study[245] (103 subjects; very-low-quality evidence), presence of myoclonus within 7 days after ROSC predicted poor outcome, with 11 (3–26)% FPR and 54 (41–66)% sensitivity.

In 3 studies[241,248,256] (215 patients; low-quality evidence) presence of status myoclonus (defined as a continuous prolonged and generalized myoclonus) within 72–120 h from ROSC predicted poor outcome, with 0 (0–4)% FPR and 16 (11–22)% sensitivity. However, reports of good neurologic recovery despite an early-onset, prolonged, and generalized myoclonus have been published.[252,257–259] In some of these cases,[252,257] myoclonus persisted after awakening and evolved into a chronic action myoclonus (Lance-Adams syndrome).

Electrophysiology. For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified very-low-quality evidence (downgraded for very serious bias and very serious imprecision) from 8 studies on short-latency SSEPs, EEG, or Bispectral Index (BIS; 571 subjects).[238,241,254,256,260–262]

For the critical outcome of **survival with unfavorable neurologic status or death at 30 days**, we identified 1 study on SSEPs (77 subjects; very-low-quality evidence, downgraded for serious bias and very serious imprecision).[263] For the critical outcome of **survival with unfavorable neurologic status or death at 60 days**, we identified 1 study on brainstem auditory evoked potentials (26 subjects; very-low-quality evidence downgraded for serious bias and very serious imprecision).[264]

For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified 5 studies on SSEPs or EEG (362 subjects; low- or very-low-quality evidence, downgraded for serious or very serious bias and/or very serious imprecision).[245–248,265]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 10 studies on SSEPs, EEG, or BIS (566 subjects; moderate-, low-, or very-low-quality evidence downgraded for serious or very serious bias and/or very serious imprecision).[249–251,266–272]

For the critical outcome of **survival with unfavorable neurologic status or death at 1 year**, we identified 1 study on EEG (106 subjects; very-low-quality evidence).[252]

Short Latency SSEPs. In most prognostication studies, absence of the N20 wave after rewarming has been used—alone or in combination—as a criterion for deciding on withdrawal of life-sustaining treatment, with a consequent risk of self-fulfilling prophecy.

In patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM, a bilaterally absent N20 SSEP wave during TTM predicted poor outcome, with 2 (0–4)% FPR and 28 (22–34)% sensitivity[249,263,266,271] (424 subjects; moderate-quality evidence, downgraded for serious bias). A bilaterally absent N20 SSEP wave after rewarming predicted poor outcome, with 1 (0–3)% FPR (9 studies,[245–251,254,261,265] 629 subjects; very-low-quality evidence downgraded for very serious bias and serious inconsistency) and 45 (41–50)% sensitivity.

SSEP recording is prone to electrical interference. In 1 study,[249] 3 subjects with a bilaterally absent N20 during TTM rapidly recovered consciousness after rewarming and ultimately had a good outcome. In a post hoc assessment, 2 experienced neurophysiologists reviewed blindly the original tracings and concluded that the SSEP recordings were undeterminable because of excessive noise.

EEG. Definitions of *burst suppression* were inconsistent among studies. Definitions of *epileptiform activity*, *electrographic seizures*, and *SE* were inconsistent among studies.

Absence of background reactivity. Absence of background reactivity on the EEG recorded during TTM predicted poor outcome, with 2 (1–7)% FPR and 63 (54–72)% sensitivity (3 studies,[238,246,247] 249 subjects; very-low-quality evidence downgraded for very serious bias and serious imprecision). Absence of background reactivity on the EEG recorded after rewarming predicted poor outcome, with

0 (0–3)% FPR and 62 (53–70)% sensitivity (3 studies,[238,247,250] 223 subjects; very-low-quality evidence downgraded for very serious bias and serious imprecision). One group of investigators provided 3 of the 4 prognostication studies on absent EEG reactivity after cardiac arrest.

Burst suppression. Presence of burst suppression on initial EEG immediately after induction of TTM predicted poor outcome, with 0 (0–5)% FPR and 31 (19–44)% sensitivity (2 studies,[267,268] 119 subjects; very-low-quality evidence downgraded for very serious bias and serious inconsistency). Presence of burst suppression on EEG during TTM predicted poor outcome, with 6 (1–15)% FPR and 70 (56–82)% sensitivity (2 studies,[247,266] 107 patients; very-low-quality evidence downgraded for very serious bias, serious inconsistency, and very serious imprecision). In 1 study[268] (95 subjects; very-low-quality evidence) presence of burst suppression on EEG after rewarming predicted poor outcome, with 0 (0–5)% FPR and 18 (8–34)% sensitivity.

Epileptiform activity. Presence of epileptiform discharges on EEG during TTM[262] (38 subjects) or after rewarming[250] (108 patients) predicted poor outcome, with 8 (0–39)% and 12 (3–31)% FPR, respectively. Quality of evidence was very low in both studies, downgraded for very serious bias and very serious imprecision. Presence of electrographic seizures with nonreactive EEG background during TTM[247] (61 patients), electrographic seizures during TTM[262] (38 subjects), or electrographic seizures both during TTM and after rewarming[238] (54 subjects) predicted poor outcome, with 0% FPR (95% CIs, 0–10, 0–22, and 0–9, respectively; very-low-quality evidence downgraded for very serious bias and serious or very serious imprecision).

Presence of SE during TTM[273] (51 subjects) or after rewarming[272] (30 subjects) predicted poor outcome, with 0% FPR (95% CIs, 0–22 and 0–13, respectively). However, in another study,[252] the presence of an SE within 72 h from ROSC was associated with good outcome in 2 cases (FPR 6 [1–21]%). In both those patients, SE was first recorded at 40 h or greater from ROSC (shortly after rewarming), and the EEG was reactive (very-low-quality evidence, downgraded for serious or very serious bias and very serious imprecision).

In 1 study[268] (95 subjects), presence of electrographic SE on a burst suppression pattern was associated with an invariably poor outcome (CPC 4–5; FPR 0 [0–5]%), while an electrographic SE on a continuous background was still compatible with recovery of consciousness (FPR 4 [0–12]%; very-low-quality evidence downgraded for very serious bias and very serious imprecision).

Flat or low-amplitude EEG. In 1 study[266] (46 subjects), a flat or low-amplitude (less than 20 mcV) EEG during TTM at 24 h from cardiac arrest predicted poor outcome, with 0 (0–11)% FPR and 40 (19–64)% sensitivity. In another study[268] (95 subjects), however, a flat (less than 10 mcV) EEG recorded during TTM at a median of 8 h from cardiac arrest or immediately after rewarming was followed by recovery of consciousness (FPR 46 [32–59]% and 5 [1–15]%, respectively; very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).

Bispectral index. In 1 study[270] (45 subjects), a lowest BIS value of 0 during TTM, corresponding to a flat or low-amplitude EEG, predicted a poor outcome, with 0 (0–6)% FPR and 50 (31–69)% sensitivity. However, in another study[269] (75 subjects), a lowest BIS value of 0 during TTM predicted poor outcome, with 10 (3–23)% FPR. The quality of evidence was very low (downgraded for very serious bias and very serious imprecision).

EEG grades. In 1 study[238] (54 subjects; very-low-quality evidence), a grade 3 EEG, corresponding to 1 pattern among unreactive, burst suppression, focal or generalized seizures, generalized periodic epileptiform discharges, SE, low amplitude (10 mcV or less), or alpha-theta coma, predicted poor outcome, with 6 (1–20)% FPR during TH and 0 (0–9)% FPR after rewarming.

Other neurophysiological tests. In 1 study[264] (26 subjects; very-low-quality evidence), absence of brainstem auditory evoked potentials wave V during induction of TTM predicted poor outcome, with 0 (0–31)% FPR and 56 (31–78)% sensitivity. In 1 pilot study[265] (17 subjects; very-low-quality evidence), the bilateral absence of pain-related middle-latency cortical evoked potentials predicted poor outcome, with 0 (0–53)% FPR and 85 (55–98)% sensitivity.

Blood and cerebrospinal fluid markers. Blood marker thresholds vary because of heterogeneous measurement techniques,[274–276] the presence of extraneuronal sources of biomarkers (hemolysis, non-central nervous system sources, and neuroendocrine tumors for neuron-specific enolase [NSE],[277] muscle and adipose tissue breakdown for S100B),[278] and the incomplete knowledge of the kinetics of their blood concentrations in the first few days after ROSC.

For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified 4 studies on NSE (354 subjects; low- or very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).[241,279–281] For the critical outcome of survival with unfavorable neurologic status or death at 60 days, we identified 1 study on NSE (73 subjects; very-low-quality evidence).[282]

For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified 3 studies on NSE (248 patients, very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).[246–248]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 8 studies on NSE or S100B (810 patients; moderate-, low-, or very-low-quality evidence, downgraded for serious or very serious bias and/or serious or very serious imprecision).[249,251,269,272,283–286]

NSE. In comatose resuscitated patients who are treated with TTM, the threshold for prediction of poor outcome with 0% FPR varied between 49.6 mcg/L and 151.4 mcg/L at 24 h from ROSC[272,284,285,287] (309 subjects; very-low-quality evidence, downgraded for serious or very serious bias and very serious imprecision), between 25 mcg/L and 151.5 mcg/L at 48 h[251,272,279,281,282,284–287] (10 studies, 919 subjects; moderate- to very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision), and between 57.2 mcg/L and 78.9 mcg/L at 72 h[280–282] (193 subjects; low- or very-low-quality evidence).

Limited evidence[282,284,288] suggests that not only the NSE absolute concentrations but also their trends over time may have predictive value. Limited evidence[284,288] suggests that the discriminative value of NSE levels at 48–72 h is higher than at 24 h.

S100B. For S100B, the documented thresholds for a 0% FPR were 0.18 and 0.21 mcg/L at 24 h after ROSC[283,285] (2 studies, total 66 subjects; very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision) and 0.3 mcg/L at 48 h (1 study, 75 subjects; very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).

Imaging. All studies on prognostication after cardiac arrest using imaging have a small sample size with a consequent low precision and are prone to selection bias, because the imaging studies were performed at discretion of treating physician, which may have caused a selection bias and overestimated their performance. Imaging studies depend partly on subjective human decision in identifying the region of interest to be studied and in the interpretation of results.

For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified 3 studies on computed tomography (CT; 273 subjects; low- or very-low-quality evidence downgraded for serious or very serious bias and serious or very serious imprecision).[241,279,289]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 6 studies on CT or magnetic resonance imaging (MRI; 246 subjects; very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).[251,287,290–293]

CT scan. The main CT finding of global anoxic-ischemic cerebral insult after cardiac arrest is cerebral edema,[294] which appears as a reduction in the depth of cerebral sulci (sulcal effacement) and an attenuation of the gray matter/white matter (GM/WM) interface, due to a decreased density of the GM. This attenuation has been quantitatively measured as the ratio (GWR) between the GM and the WM densities.

In 4 studies[254,279,289,290] (total 276 subjects; low- or very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision), a reduced GWR at the level of the basal ganglia on brain CT performed within 2 h from ROSC predicted an almost invariably poor outcome (FPR from 0% to 8%). Measurement techniques and thresholds for GWR varied among studies.

In 1 study[241] (102 subjects; low-quality evidence downgraded for serious bias and serious imprecision), a global cerebral edema on brain CT at a median of 1 day after cardiac arrest predicted poor outcome, with 0 (0–5)% FPR.

MRI. The main MRI finding of anoxic-ischemic cerebral injury is a hyperintensity in diffusion weighted imaging (DWI) sequences due to cytotoxic edema. Presence of DWI abnormalities in cortex or basal ganglia (1 study, 21 subjects; very-low-quality evidence) or both (2 studies, 30 subjects; very-low-quality evidence) between 2 and 6 days from ROSC was associated with poor outcome (FPR, 0–9%). Precision of prediction, however, was very low, due to the small size of these studies.

Postischemic DWI abnormalities can be quantified using apparent diffusion coefficient (ADC). ADC values between 700 and 800×10^{-6} mm^2/s are considered normal. In 1 study[293] (22 subjects; very-low-quality evidence downgraded for very serious bias and very serious imprecision), presence of more than 10% of brain volume with ADC less than 650×10^{-6} mm^2/s predicted poor outcome, with 0 (0–28)% specificity. In another study,[295] a low ADC at the level of putamen, thalamus, or occipital cortex also predicted poor outcome, with 0% FPR (95% CIs, 0–24%). The ADC thresholds varied according to the brain area studied.

Treatment recommendations

We suggest against the use of clinical criteria alone before 72 h after ROSC to estimate prognosis (weak recommendation, low-quality evidence).

We suggest that multiple modalities of testing (clinical exam, neurophysiological measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings (weak recommendation, low-quality evidence).

Clinical examination. We recommend using bilaterally absent PLRs or the combined absence of both pupillary and corneal reflexes at least 72 h after ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM (strong recommendation, low-quality evidence).

We suggest against using an absent (M1) or extensor motor response to pain (M2) alone to predict poor outcome, given its high FPR. However, due to its high sensitivity, this sign may be used to identify the population with poor neurologic status needing prognostication or to predict poor outcome in combination with other more robust predictors (weak recommendation, very low-quality evidence).

We suggest against the use of myoclonus during the first 72 h from ROSC as a predictor for prognosticating a poor neurologic outcome (weak recommendation, low-quality evidence).

We suggest that the presence of a status myoclonus during the first 72 h from ROSC be considered at 72 h after ROSC (in combination with other factors) as a predictor for prognosticating a poor neurologic outcome (weak recommendation, low-quality evidence).

We suggest prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false-positive results is minimized. We recommend that the earliest time to prognosticate a poor neurologic outcome is 72 h after ROSC, and should be extended longer if the residual effect of sedation and/or paralysis confounds the clinical examination (weak recommendation, low-quality evidence).

Electrophysiology. We recommend using bilateral absence of N20 SSEP wave measured at least 72 h after ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM (strong recommendation, low-quality evidence).

SSEP recording requires appropriate skills and experience, and utmost care should be taken to avoid electrical interference from muscle artifacts or from the ICU environment, as well as confounding drugs. This test is only ordered in the appropriate clinical context.

We suggest using persistent absence of EEG reactivity to external stimuli at 72 h or longer after ROSC (weak recommendation, low-quality evidence), presence of persistent burst suppression after rewarming, or intractable and persistent SE (weak recommendation, very-low-quality evidence) to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM.

We recommend against using BIS to predict poor outcome during TTM in patients who are comatose after resuscitation from cardiac arrest and are treated with TTM (strong recommendation, very-low-quality evidence).

Blood markers. We suggest using utmost care and preferably sampling at multiple serial time points (24–72 h) when assessing NSE, to avoid false-positive results due to hemolysis (weak recommendation, very-low-quality evidence).

We suggest using serial high-serum values of NSE at 48–72 h from ROSC in combination with other predictors for predicting poor neurologic outcome in patients who are comatose after cardiac arrest and who are treated with TTM (weak recommendation, very-low-quality evidence). However, no threshold-enabling prediction with 0 FPR can be recommended, and NSE levels are insufficiently specific to be used alone for estimating prognosis.

Imaging. We suggest using brain imaging studies for prognostication only in centers where specific experience is available (weak recommendation, very-low-quality evidence).

We suggest using the presence of a marked reduction of the GM/WM ratio on brain CT within 2 h after ROSC or the presence of extensive diffusion restriction on brain MRI at 2–6 days after ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are treated with TTM (weak recommendation, very-low-quality evidence). Early imaging markers of poor prognosis should not prevent support for a sufficient period to observe other clinical features, although some extreme CT scan findings are consistent with herniation and brain death.

Knowledge gaps

Clinical examination.

- Prospective studies are needed to investigate the pharmacokinetics of sedative drugs and neuromuscular blocking drugs in

post-cardiac arrest patients, especially those treated with controlled temperature.
- Studies are needed to investigate the reproducibility of clinical signs used to predict outcome in comatose postarrest patients.
- There is no universally accepted definition of *status myoclonus*. A recently proposed definition[296] suggests using the term *status myoclonus* to indicate a continuous and generalized myoclonus persisting for 30 min in comatose survivors of cardiac arrest.

Electrophysiology.

- In most prognostication studies, results of SSEPs were not blinded and were used as a criterion for limitation or suspension of life-sustaining treatment. Blinded studies on SSEPs are needed to assess the relevance of self-fulfilling prophecies for SSEPs.
- Definitions of EEG-based predictors are inconsistent among prognostication studies. Future studies should comply with recently recommended definitions.[297]
- The stimulation modalities for eliciting EEG reactivity have not been standardized.

Blood markers.

- There is a need for standardization of the measuring techniques for NSE and S100 in cardiac arrest patients.
- Little information is available on the kinetics of the blood concentrations of biomarkers in the first few days after cardiac arrest.

Imaging.

- Prospective studies in unselected patient populations are needed for evaluating the prognostic accuracy of imaging studies in comatose patients resuscitated from cardiac arrest.

Prognostication in absence of TTM (ALS 713)

Among adults who are comatose after cardiac arrest and are not treated with TTM (P), does any clinical finding when normal (e.g., clinical exam, EEG, SSEPs, imaging, other) (I), compared with any clinical finding when abnormal (C), reliably predict death or poor neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; death only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Consensus on science

No study on clinical examination reported blinding of the treating team to the results of the index test. Blinding of the treating team is very difficult to achieve for predictors based on clinical examination, which implies a risk of self-fulfilling prophecy.

For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified 2 studies on pupillary reflex and motor response or oculocephalic reflex (151 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[298,299]

For the critical outcome of **survival with unfavorable neurologic status or death at 30 days**, we identified 1 study on GCS (97 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[300]

For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified 2 studies on corneal reflex, pupillary reflex, motor response, oculovestibular reflex, GCS, or myoclonus (97 patients; very-low-quality evidence downgraded for serious or very serious bias and serious or very serious imprecision).[301,302]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 4 studies on brainstem reflexes, motor response, or myoclonus (650 patients; very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).[303–306]

For the critical outcome of **survival with unfavorable neurologic status or death at 1 year**, we identified 3 studies on brainstem reflexes, motor response, GCS, or myoclonus (172 patients; very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).[307–309]

Clinical examination.

Pupillary reflex. In 1 study[299] (98 patients; very-low-quality evidence), an absent PLR on hospital admission predicted poor outcome, with 8 (1–25)% FPR and 56 (43–67)% sensitivity. At 24 h[298,302,306] (3 studies, 496 patients), 48 h[298,303,306] (3 studies, 403 patients), and 72 h[298,306] (2 studies, 382 patients) from ROSC, the FPRs of PLR for prediction of poor outcome were 9 (4–18)%, 4 (0–12)%, and 0 (0–8)%, respectively. Sensitivity ranged from 18 (15–23)% to 21 (17–25)%; (very-low-quality evidence, downgraded for serious or very serious bias and very serious imprecision).

Corneal reflex. In patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM, an absent corneal reflex at 24 and 48 h after ROSC predicted poor outcome, with 17 (9–27)% and 7 (2–20)% FPR. Sensitivities were 37 (32–42)% and 30 (25–35)%, respectively[302,303,306] (3 studies, 497 subjects; very-low-quality evidence downgraded for very serious bias, serious inconsistency, and very serious imprecision).

Oculovestibular reflex. In 2 studies[302,303] (65 patients; very-low-quality evidence downgraded for very serious bias, serious inconsistency, and very serious imprecision), the bilateral absence of oculovestibular reflex at 24 h from ROSC predicted poor outcome, with 0 (0–18)% FPR and 38 (25–53)% sensitivity. In 1 study[303] (19 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision), the bilateral absence of oculovestibular reflex at 48 h from ROSC predicted poor outcome, with 0 (0–35)% FPR and 25 (5–57)% sensitivity.

Combination of ocular reflexes. In 1 study[306] (386 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision), the combined absence of both pupillary and corneal reflexes at 24, 48, and 72 h from ROSC predicted a poor outcome, with 5 (1–17)%, 3 (0–17)%, and 0 (0–15)% FPR, respectively, and 13–14% sensitivity. In 1 study[307] (60 patients; very-low-quality evidence downgraded for serious bias and very serious imprecision), the absence of more than 1 among pupillary, corneal, and oculocephalic reflex at 6–12, 24, and 48 h from ROSC predicted poor outcome, with 0 (0–22)% FPR.

Motor response to pain. At 24 h from ROSC, an absent or extensor motor response, corresponding to a motor score 1 or 2 (M1–2) of the GCS, predicted a poor outcome, with 27 (12–48)% FPR and 76 (71–80)% sensitivity[302,306] (2 studies, 462 patients; very-low-quality evidence downgraded for serious bias, serious inconsistency, and serious imprecision). At 72 h from ROSC, an M1–2 predicted a poor outcome, with 15 (5–31)% FPR and 39 (33–44)% sensitivity[301,306] (2 studies, 322 patients; very-low-quality evidence downgraded for serious bias, serious inconsistency, and very serious imprecision).

An absent extensor or abnormal flexion to pain (M1–3) predicted a poor outcome at 12, 24, and 48 h from ROSC with 57 (37–76)%, 35 (21–52)%, and 10 (3–24)% FPR, respectively[298,303,307] (3 studies, 120 patients; very-low-quality evidence downgraded for very serious bias, serious inconsistency, and very serious imprecision). At 72 h, the FPR of this sign was 6 (0–29)%[298] (1 study, 27 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).

GCS. A GCS of 4 or less on admission, at 24 h, and at 48 h from ROSC predicted poor outcome, with 40 (19–64)%, 25 (5–57)%, and 0 (0–22)% FPR, respectively[307,308] (2 studies, 119 patients;

very-low-quality evidence downgraded for serious bias and very serious imprecision). Sensitivity ranged from 54 (37–71)% to 74 (58–86)%. A GCS of 5 or less at 72 h from ROSC predicted poor outcome, with 75 (63–86)% sensitivity and 7 (1–24)% FPR.

Myoclonus and status myoclonus. Presence of myoclonus on admission[305] (1 study, 107 patients; very-low-quality evidence) or at 24 h from ROSC[302] (1 study, 75 patients; very-low-quality evidence) predicts a poor outcome, with 0 (0–14)% and 0 (0–5)% FPR, respectively. A status myoclonus within 24 h, at 36–48 h, and 72 h from ROSC predicted a poor outcome, with 0 (0–7)%, 0 (0–5)%, and 0 (0–14)% FPR, respectively[304,306] (2 studies, 464 patients; very-low-quality evidence downgraded for very serious bias and serious imprecision). Sensitivity ranged from 2% to 29%.

Electrophysiology. For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified 2 studies on short-latency SSEPs (63 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision)[310,311] and 3 studies on EEG (46 patients; very-low-quality evidence, downgraded for very serious bias and very serious imprecision).[312–314]

For the critical outcome of **survival with unfavorable neurologic status or death at 30 days**, we identified 2 studies on SSEPs (80 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[315,316]

For the critical outcome of **survival with unfavorable neurologic status or death at 60 days**, we identified 2 studies on EEG (54 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[317,318]

For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified 2 studies on SSEPs or EEG (102 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[302,319]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 6 studies on SSEPs or EEG (733 patients; very-low-quality evidence downgraded for serious or very serious bias and serious or very serious imprecision).[271,303,320–323]

For the critical outcome of **survival with unfavorable neurologic status or death at 1 year**, we identified 6 studies on SSEPs or EEG (829 patients; low- or very-low-quality evidence downgraded for serious or very serious bias and very serious imprecision).[306,307,324–327]

Short latency SSEPs. Bilateral absence of the N20 wave of short-latency SSEPs predicted death or vegetative state, with 0 (0–12)% FPR as early as 8 h from cardiac arrest. An FPR of 0% was also confirmed at 24, 48, and 72 h after ROSC (95% CIs from 0–3 to 0–9) with consistent sensitivity (43–46%). Among all patients in whom N20 SSEP wave was absent in the first 7 days from cardiac arrest, there was only 1 case of false-positive result.[302] Quality of evidence was very low in all but 1 study, downgraded for serious or very serious bias and serious or very serious imprecision.

Studies assessing the predictive value of a delayed or absent N70 SSEP from 24 h to 72 h after ROSC reported a false-positive prediction from 1 (0–7)% to 58 (28–85)%[302,306,320,321,324] (5 studies, 657 subjects; very-low-quality evidence downgraded for serious or very serious bias and serious or very serious imprecision).

Blinding of SSEP results, along with criteria for withdrawal of life-sustaining treatment, was not reported in most prognostication studies in resuscitated patients who were not treated with TTM.

Electroencephalography. In 1 study[303] (26 patients; very-low-quality evidence downgraded for serious bias and very serious imprecision), an EEG grade 3–5 at 24 and 48 h predicted poor outcome (CPC 3–5), with 0% FPR (95% CIs, 0–22 and 0–24, respectively). An EEG grade 4–5 at 72 h or less from ROSC predicted poor outcome, with 0 (0–11)% FPR and 44 (34–54)% sensitivity[307,313,315] (3 studies, 125 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision). EEG grading systems were not consistent among studies.

Presence of burst suppression within 48 h from ROSC was compatible with recovery of consciousness (FPR 5 [0–26]%[302]; 1 study, 72 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision), while a burst suppression at 72 h from ROSC predicted poor outcome, with 0 (0–11)% FPR[306] (1 study, 277 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).

A low-voltage EEG (20–21 mcV or less) predicted a poor outcome, with 0 (0–15)% FPR within 48 h from ROSC[302] (1 study, 72 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision) and with 0 (0–11)% FPR at 72 h from ROSC[306] (1 study, 283 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision). Sensitivity was 15 (7–28)% and 31 (25–37)%, respectively.

Presence of alpha coma within 72 h or from 1 to 7 days after ROSC was not consistently associated with poor outcome (positive predictive value, 96 [80–100]% and 88 [74–96]%)[303,312,314,318,325,326] (6 studies, 68 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).

Blood markers. In patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM, high concentrations of biomarkers predict a poor outcome. Advantages of biomarkers over other predictors such as EEG and clinical examination include quantitative results and likely independence from the effects of sedatives. However, the thresholds associated with 0% FPR vary between studies, and S100B thresholds are less well documented than NSE thresholds.

The main reasons for the observed variability in biomarkers' thresholds include the use of heterogeneous measurement techniques,[274–276] the presence of extraneuronal sources of biomarkers (hemolysis and neuroendocrine tumors for NSE,[277] muscle and adipose tissue breakdown for S100B,[278] and the incomplete knowledge of the kinetics of their blood concentrations in the first few days after ROSC.

For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified 2 studies on S100B (99 patients; low- or very-low-quality evidence downgraded for very serious bias and/or very serious imprecision)[328,329] and 1 study on NSE (73 patients; very-low-quality evidence downgraded for serious bias and very serious imprecision).[280]

For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified 1 study on NSE (32 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision)[248] and 1 study on S100B (27 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[319]

For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 3 studies on NSE or S100B (618 patients; moderate-, low-, or very-low-quality evidence downgraded for serious bias and/or serious or very serious imprecision).[285,323,330]

For the critical outcome of **survival with unfavorable neurologic status or death at 1 year**, we identified 2 studies on NSE or S100B (86 patients; very-low-quality evidence downgraded for very serious bias and very serious imprecision).[331,332]

Neuron-specific enolase. In resuscitated patients with poor neurologic outcome, the blood levels of NSE are higher than those in patients with good neurologic outcome. However, the threshold for prediction of poor outcome with 0% FPR varied between 13.3 and 47.6 mcg/L at 24 h from ROSC[285,306,319] (3 studies, 332

patients; very-low-quality evidence), between 8.8 and 65 mcg/L at 48 h[285,319,330,331] (4 studies, 277 patients; moderate- to very-low-quality evidence), and between 15 and 90.9 mcg/L at 72 h[280,319,331] (3 studies, 301 patients; low- or very-low-quality evidence).

S100B. For S100B, the documented thresholds for 0% FPR ranged between 0.19 and 5.2 mcg/L at 24 h after ROSC[285,319] (2 studies, total 60 patients; very-low-quality evidence) and between 0.12 and 0.8 mcg/L at 48 h[285,319,329,331] (4 studies, 158 patients; very-low-quality evidence). In 1 study (27 patients; very-low-quality evidence), the threshold for prediction of poor outcome with 0% FPR at 72 h was 0.5 mcg/L.

Imaging. All prognostication studies on imaging have a small sample size, and in all of them, imaging was performed at the discretion of the treating physician, which may have caused a selection bias and overestimated the performance of index tests. Another limitation is that these methods depend partly on subjective human decision in identifying the region of interest to be studied and in the interpretation of results.

For the critical outcome of **survival with unfavorable neurologic status or death at discharge**, we identified 3 studies on CT (113 patients; very-low-quality evidence)[294,333,334] and 2 studies on MRI (40 patients; very-low-quality evidence).[316,335] For the critical outcome of **survival with unfavorable neurologic status or death at 90 days**, we identified 2 studies on MRI (61 patients; low- or very-low-quality evidence).[301,336] For the critical outcome of **survival with unfavorable neurologic status or death at 180 days**, we identified 3 studies on MRI (34 patients; very-low-quality evidence).[292,293,337]

CT scan. The main CT finding of global anoxic-ischemic cerebral insult after cardiac arrest is cerebral edema,[294] which appears as a reduction in the depth of cerebral sulci (sulcal effacement) and an attenuation of the GM/WM interface, due to a decreased density of the GM. This attenuation has been quantitatively measured as the GWR between the GM and the WM densities.

In 2 studies[333,334] (total 60 patients; very-low-quality evidence), a GWR between the caudate nucleus and the posterior limb of internal capsule (CN/PIC) below 1.22 within 24 h or below 1.18 within 48 h from ROSC predicted poor outcome, with 0 (0–28)% and 17 (0–64)% FPR, respectively. At 72 h from ROSC, the presence of diffuse brain swelling on CT predicts a poor outcome, with 0 (0–45)% FPR and 52 (37–67)% sensitivity[294] (1 study, 53 patients; very-low-quality evidence).

MRI. The main MRI finding of anoxic-ischemic cerebral injury is a hyperintensity in DWI sequences due to cytotoxic edema. In a small study subpopulation[292] (12 patients; very-low-quality evidence), presence of diffuse DWI abnormalities in cortex or brainstem at a median of 80 h from ROSC predicted poor outcome, with 0 (0–35)% FPR. In another small study[337] (12 patients; very-low-quality evidence), presence of extensive (cortex, basal ganglia, and cerebellum) DWI changes predicted poor outcome, with 0 (0–45)% FPR.

Postischemic DWI abnormalities can be quantified by using ADC. ADC values between 700 and 800×10^{-6} mm^2/s are considered normal.[335] In 1 study[338] (80 patients; very-low-quality evidence), a whole-brain ADC less than 665×10^{-6} mm^2/s predicted poor outcome, with 0 (0–21)% FPR and 40 (28–53)% sensitivity. In a small subset of another study[293] (10 patients; very-low-quality evidence), presence of more than 10% of brain volume with ADC less than 650×10^{-6} mm^2/s predicted poor outcome, with 88 (47–100)% sensitivity and 0 (0–78)% FPR. In another study, an ADC below various thresholds at the level of putamen, thalamus, or occipital cortex at less than 120 h from ROSC also predicted poor outcome, with 0 (0–31)% FPR. Finally, in 2 studies[301,335] (total 24 patients; very-low-quality evidence), the presence of extensive cortical global DWI or fluid-attenuated inversion recovery changes within 7 days from arrest predicted poor outcome, with 0 (0–78)% FPR.

Treatment recommendations

Clinical examination. We recommend using the absence of PLR (or the combined absence of both pupillary and corneal reflexes) at 72 h or greater from ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM (strong recommendation, very-low-quality evidence).

We suggest against using an absent or extensor motor response to pain ($M \leq 2$) alone to predict poor outcome, given its high FPR (weak recommendation, very-low-quality evidence). However, due to its high sensitivity, this sign may be used to identify the population with poor neurologic status needing prognostication or to predict poor outcome in combination with other more-robust predictors.

We suggest using the presence of myoclonus or status myoclonus within 72 h from ROSC in combination with other predictors to predict poor outcome in comatose survivors of cardiac arrest (weak recommendation, very-low-quality evidence).

We suggest prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false-positive results is minimized (weak recommendation, very-low-quality evidence).

Electrophysiology. We recommend using bilateral absence of the N20 SSEP wave within 72 h from ROSC to predict poor outcome in patients who are comatose after cardiac arrest and who are not treated with TTM (strong recommendation, very-low-quality evidence). SSEP recording requires appropriate skills and experience, and utmost care should be taken to avoid electrical interference from muscle artifacts or from the ICU environment.

We suggest using the presence of burst suppression on EEG at 72 h from ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are not treated with TTM (strong recommendation, very-low-quality evidence).

We suggest against using EEG grades for prognostication due to the inconsistencies in their definitions (weak recommendation, very-low-quality evidence).

We suggest against using low-voltage EEG for prognostication, given the potential interferences of technical factors on EEG amplitude (weak recommendation, very-low-quality evidence).

Blood markers. We suggest using high serum values of NSE at 24–72 h from ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are treated with therapeutic hypothermia (weak recommendation, very-low-quality evidence). However, no threshold-enabling prediction with 0 FPR can be recommended. We suggest using utmost care and preferably sampling at multiple time points when assessing NSE, to avoid false-positive results due to hemolysis.

Imaging. We suggest using the presence of a marked reduction of the GM/WM ratio on brain CT within 48 h after ROSC or the presence of extensive reduction in diffusion on brain MRI at 2–6 days after ROSC only in combination with other more-established predictors for prognosticating a poor neurologic outcome in patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM (weak recommendation, very-low-quality evidence).

We suggest using brain-imaging studies for prognostication only in centers where specific experience is available (weak recommendation, very-low-quality evidence).

Knowledge gaps
Clinical examination.

- Prospective studies are needed to investigate the pharmacokinetics of sedative drugs and neuromuscular blocking drugs in post–cardiac arrest patients, independently from treatment with TTM.
- Clinical studies are needed to evaluate the reproducibility of clinical signs used to predict outcome in comatose postarrest patients.
- There is no universally accepted definition of *status myoclonus*. A recently proposed definition suggests using the term *status myoclonus* to indicate a continuous and generalized myoclonus persisting for 30 min or more in comatose survivors of cardiac arrest.

Electrophysiology.

- Blinded studies on SSEPs are needed to assess the relevance of self-fulfilling prophecy for this predictor.
- The definitions of *low-voltage EEG* and *burst suppression*, and the EEG grades are inconsistent among prognostication studies. Future studies should comply with recently recommended definitions.

Blood markers.

- There is a need for standardization of the measuring techniques for NSE and S100 in cardiac arrest patients.
- Little information is available on the kinetics of the blood concentrations of biomarkers in the first few days after cardiac arrest.

Imaging.

- Prospective studies in unselected patient populations and including evaluation of inter-rater agreement are needed to determine the prognostic accuracy of imaging studies in comatose patients resuscitated from cardiac arrest.

2010 CoSTR topics not reviewed in 2015

- Postresuscitation hemofiltration
- IV fluids following cardiac arrest
- Neuroprotective drugs
- Postresuscitation treatment protocol

Organ donation (ALS 449)

In adults and children who are receiving an organ transplant in any setting (P), do organs retrieved from a donor who has had CPR (I), compared with organs retrieved from a donor who did not have CPR (C), have improved immediate graft function (30 days), 1-year graft function, or 5-year graft function (O)?

Introduction

Resuscitation from cardiac arrest is not always successful, and many patients who are initially resuscitated from cardiac arrest will subsequently die in the hospital. Whether these nonsurviving patients can become organ donors has been debated because of the potential injury to organs during the initial cardiac arrest.

The committee reviewed experience about donation from this population that has accumulated in recent years. Two situations were separately considered. In the first, an individual who dies after being resuscitated by successful CPR may become an organ donor after brain death or having withdrawal of life-sustaining treatment. In the second situation, an individual may die because of unsuccessful CPR in a center with a rapid response system that allows procurement of organs after unsuccessful CPR. For kidney transplants, the primary outcomes were graft function, because recipients can survive with renal replacement therapy even with graft failure. For other organs, recipient death was considered equivalent to graft failure. Only studies that allowed comparison of organs procured in these situations with other organs from non-CPR donors were selected for review.

Consensus on science

Donors with prior CPR. Two nonrandomized studies provided low-quality evidence that the mean yield of organs procured from donors who had been resuscitated by CPR before donation was 3.9[339] or 2.9.[340]

For the important outcome of **immediate graft survival**, low-quality evidence from nonrandomized studies did not detect any worse outcome when donors have had CPR and resuscitation for adult hearts (3239 organs[340–347]), pediatric hearts (557 organs, 4 studies), adult lungs (1031 organs[340,345,348]), pediatric lungs (105 organs[340]), adult kidneys (5000 organs[340,349]), pediatric kidneys (1122 organs[340,350]), adult livers (2911 organs[340,341]), pediatric livers (689 organs[340,350]), adult intestines (25 organs[340,351]), and pediatric intestines (79 organs[340]).

For the important outcome of **graft survival for 1 year**, low-quality evidence from nonrandomized studies did not detect any worse outcome when donors have had CPR and resuscitation for adult hearts (3230 organs[340–342,344–347]), pediatric hearts (1605 organs[340,350,352,353]), adult lungs (1031 organs[340,345,348]), pediatric lungs (105 organs[340]), adult kidneys (5000 organs[340,341]), pediatric kidneys (1122 organs[340]), adult livers (2911 organs[340,341]), pediatric livers (689 organs[340]), adult intestines (25 organs[340,351]), and pediatric intestines (79 organs[340]).

For the important outcome of **graft survival for 5 years**, low-quality evidence from nonrandomized studies did not detect any worse outcome when donors have had CPR and resuscitation for adult hearts (3230 organs[340–342,344–347]), pediatric hearts (1537 organs[340,353,354]), adult lungs (1031 organs[340,345,348]), pediatric lungs (105 organs[340]), adult kidneys (5000 organs[340,341]), pediatric kidneys (1122 organs[340]), adult livers (2911 organs[340,341]), pediatric livers (689 organs[340]), adult intestines (25 organs[340]), and pediatric intestines (79 organs[340]).

Donors with ongoing CPR (uncontrolled non-heart-beating donors or uncontrolled donation after circulatory death). Two nonrandomized studies provided low-quality evidence that the mean number of organs procured from donors with ongoing CPR was 1.5[355] and 3.2.[356]

For the important outcome of **immediate graft survival**, low-quality evidence from nonrandomized studies did not detect any worse outcome when organs were recovered from non–heart-beating donors with ongoing CPR compared with other types of donors for adult kidneys (203 organs[357–360]) or adult livers (64 organs[355,358,361,362]).

For the important outcome of **graft survival for 1 year**, low-quality evidence from nonrandomized studies did not detect any worse outcome when organs were recovered from non–heart-beating donors with ongoing CPR compared with other types of donors for adult kidneys (199 organs[357,358,360]) or adult livers (60 organs[355,358,361]).

For the important outcome of **graft survival for 5 years**, low-quality evidence from nonrandomized studies did not detect any worse outcome when organs were recovered from non–heart-beating donors with ongoing CPR compared with other types of

donors for adult kidneys (177 organs[357,360]) or adult livers (34 organs[355]).

Treatment recommendation

We recommend that all patients who have restoration of circulation after CPR and who subsequently progress to death be evaluated for organ donation (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we consider the absence of any evidence of worse graft function from donors with antecedent CPR, the desirability of providing more organs to waiting recipients, and the absence of any risk to the donor. As in all organ donations, the function of the donated organ determines whether procurement and transplantation proceed. Therefore, there is also precaution to ensure the safety of the recipient.

Treatment recommendation

We suggest that patients who fail to have restoration of circulation after CPR and who would otherwise have termination of CPR efforts be considered candidates for kidney or liver donation in settings where programs exist (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we consider the evidence that kidney grafts obtained from donors in whom CPR failed can function at rates comparable to kidneys obtained from other donors, and that recipients can safely tolerate delayed graft function that is common with kidneys obtained in this manner. We also consider the immediate lifesaving potential of liver grafts, which offsets the potentially greater rate of long-term graft failure in livers obtained from donors with ongoing CPR.

Knowledge gaps

- The optimal methods for organ procurement after failed CPR are unknown.
- Barriers to consenting to this organ donation and the acceptability of these practices in different settings are unknown.

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Disclosures. 2015 CoSTR Part 4: advanced life support: writing group

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Bernd W. Böttiger	University of Cologne	None	European Resuscitation Council (ERC)[b]	None	None	None	None	None
Steven C. Brooks	Queen's University	Heart and Stroke Foundation of Canada[b]; CIHR[b]; NIH[b]	None	None	None	None	None	None
Charles D. Deakin	Southampton University Hospital NHS Trust	Resuscitation Council UK[b]; National Institute for Health Research[b]	Resuscitation[a]	None	Several Coroner's cases relating to oesophageal intubation and capnography[b]	None	None	South Eastern Ontario Academic Medical Association[b]
Saul Drajer	Inter-American Heart Foundation	None	None	None	None	Prometheus Medical[b]	Smiths Medical[a]	None
Walter Kloeck	Resuscitation Council of Southern Africa	None	None	None	None	None	None	None
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Jerry P. Nolan	Royal United Hospital, Bath	The Cardiac Arrest Individual Registry and Outcomes (CAIRO) Programme. 2013–2015[b]; NIHR Programme Development Grant (RP-DG-0612-10004) Improving Outcomes from Out of Hospital Cardiac Arrest NIHR Health Technology Assessment Programme Grant (HTA – 12/127/126) for a randomized placebo controlled trial of adrenaline for out of hospital cardiac arrest[a]; NIHR Health Technology Assessment Programme Grant (HTA – 12/167/102) for a randomized trial of the effectiveness of a supra-glottic airway device versus tracheal intubation in the initial airway management of out of hospital cardiac arrest (AIRWAYS-2)[a]	None	None	None	None	None	None
Kazuo Okada	Resuscitation Council of Asia	None	None	None	None	None	None	None
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						None	American Heart Association[b]	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

[a] Modest.

[b] Significant.

Appendix A. CoSTR Part 4: PICO Appendix

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 4	ALS	ALS 428	Antiarrhythmic drugs for cardiac arrest	Among adults who are in cardiac arrest in any setting (P), does administration of antiarrhythmic drugs (e.g., amiodarone, lidocaine, other) (I), compared with not using antiarrhythmic drugs (no drug or placebo) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Katie Dainty, Thomas Pellis, Steve Lin
Part 4	ALS	ALS 431	Postresuscitation seizure prophylaxis	Among adults with ROSC after cardiac arrest in any setting (P), does seizure prophylaxis (I), compared with no prophylaxis (C), reduce the incidence of seizures, or improve survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Romergryko Geocadin, William Stacey
Part 4	ALS	ALS 433	Steroids for cardiac arrest	Among adults who are in cardiac arrest in any setting (P), does corticosteroid or mineralocorticoid administration during CPR (I), compared with not using steroids (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Sarah Todhunter, Tonia Nicholson
Part 4	ALS	ALS 435	Cardiac arrest associated with pulmonary embolism	Among adults who are in cardiac arrest due to PE or suspected PE in any setting (P), does any specific alteration in treatment algorithm (e.g., fibrinolytics, or any other) (I), compared with standard care (according to 2010 treatment algorithm) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Wolfgang Wetsch, Bernd Böttiger
Part 4	ALS	ALS 436	Cardiac arrest during pregnancy	Among pregnant women who are in cardiac arrest in any setting (P), do any specific interventions (I), compared with standard care (usual resuscitation practice) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Carolyn Zelop, Jill Mhyre
Part 4	ALS	ALS 441	Opioid toxicity	Among adults who are in cardiac arrest or respiratory arrest due to opioid toxicity in any setting (P), does any specific therapy (e.g., naloxone, bicarbonate, or other drugs) (I), compared with usual ALS (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Allan Mottram, Fred Severyn, Mohammed Alhelail
Part 4	ALS	ALS 448	Oxygen dose after ROSC in adults	Among adults who have ROSC after cardiac arrest in any setting (P), does an inspired oxygen concentration titrated to oxygenation (normal oxygen saturation or partial pressure of oxygen) (I), compared with the use of 100% inspired oxygen concentration (C), change survival to 30 days with good neurologic outcome, survival to hospital discharge with good neurologic outcome, improve survival, survival to 30 days, survival to hospital discharge (O)?	Jasmeet Soar, Michael Donnino
Part 4	ALS	ALS 449	Organ donation	In adults and children who are receiving an organ transplant in any setting (P), do organs retrieved from a donor who has had CPR (I), compared with organs retrieved from a donor who did not have CPR (C), have improved immediate graft function (30 days), 1-year graft function, or 5-year graft function (O)?	Stephen West, Clifton Callaway
Part 4	ALS	ALS 450	Prognostication in comatose patients treated with hypothermic TTM	Among adults with ROSC who are treated with hypothermia (P), does any clinical variable when abnormal (e.g., clinical exam, EEG, somatosensory evoked potentials [SSEPs], imaging, other) (I), compared with any clinical variable when normal (C), reliably predict death or poor neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; death only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Claudio Sandroni, Eyal Golan
Part 4	ALS	ALS 459	$ETCO_2$ to predict outcome of cardiac arrest	Among adults who are in cardiac arrest in any setting (P), does any $ETCO_2$ level value, when present (I), compared with any $ETCO_2$ level below that value (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Brian O'Neil, Edison Paiva
Part 4	ALS	ALS 469	Confirmation of correct tracheal tube placement	Among adults who are in cardiac arrest, needing/with an advanced airway, in any setting (P), does use of devices (e.g., 1. waveform capnography, 2. CO_2 detection device, 3. esophageal detector device, or 4. tracheal ultrasound) (I), compared with not using devices (C), change placement of the ET tube between the vocal cords and the carina, success of intubation (O)?	Sarah Heikal, Markus Skrifvars
Part 4	ALS	ALS 470	Defibrillation strategies for Ventricular Fibrillation (VF) or Pulseless Ventricular Tachycardia (pVT)	Among adults who are in ventricular fibrillation or pulseless ventricular tachycardia in any setting (P), does any specific defibrillation strategy (e.g., 1. energy dose, or 2. shock waveform) (I), compared with standard management (or other defibrillation strategy) (C), change Survival with Favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days and/or 1 year, Survival only at discharge, 30 days, 60 days, 180 days and/or 1 year, ROSC, termination of arrhythmia (O)?	Giuseppe Ristagno, Charles Deakin

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 4	ALS	ALS 479	Cardiac arrest during coronary catheterization	Among adults who have a cardiac arrest in the cardiac catheterization laboratory (P), does any special intervention or change in care (e.g., catheterization during CPR, cardiopulmonary bypass, balloon pump, different timing of shocks) (I), compared with standard resuscitation care (e.g., CPR, drugs, and shocks according to 2010 treatment algorithm) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Ian Drennan, Peter Kudenchuk
Part 4	ALS	ALS 493	Postresuscitation antiarrhythmic drugs	Among adults with ROSC after cardiac arrest in any setting (P), do prophylactic antiarrhythmic drugs given immediately after ROSC (I), compared with not giving antiarrhythmic drugs (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; development of cardiac arrest; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; recurrence of VF; incidence of arrhythmias (O)?	Thomas Pellis, Steve Lin
Part 4	ALS	ALS 570	Postresuscitation Hemodynamic Support	Among adults with ROSC after cardiac arrest in any setting (P), does titration of therapy to achieve a specific hemodynamic goal (e.g., MAP greater than 65 mm Hg) (I), compared with no hemodynamic goal (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Michael Fries, Michael Parr
Part 4	ALS	ALS 571	Postresuscitation ventilation strategy	Among adults with ROSC after cardiac arrest in any setting (P), does ventilation to a specific $PaCO_2$ goal (I), compared with no specific strategy or a different $PaCO_2$ goal (C), change survival at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Asger Granfeldt, Bo Lofgren
Part 4	ALS	ALS 579	Impedance threshold device	Among adults who are in cardiac arrest in any setting (P), does use of an inspiratory ITD during CPR (I), compared with no ITD (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Peter Morley, Jasmeet Soar
Part 4	ALS	ALS 580	Glucose control after resuscitation	Among adults with ROSC after cardiac arrest in any setting (P), does a specific target range for blood glucose management (e.g., strict 4–6 mmol/L) (I), compared with any other target range (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Janice Zimmerman, Jonathon Sullivan
Part 4	ALS	ALS 656	Monitoring physiological parameters during CPR	Among adults who are in cardiac arrest in any setting (P), does the use of physiological feedback regarding CPR quality (e.g., arterial lines, $ETCO_2$ monitoring, SpO_2 waveforms, or others) (I), compared with no feedback (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; change in physiologic values by modifications in CPR (O)?	Amit Chopra, Natalie Wong
Part 4	ALS	ALS 658	Ultrasound during CPR	Among adults who are in cardiac arrest in any setting (P), does use of ultrasound (including echocardiography or other organ assessments) during CPR (I), compared with conventional CPR and resuscitation without use of ultrasound (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Katherine Berg, Lars Wiuff Andersen
Part 4	ALS	ALS 659	Epinephrine versus vasopressin	Among adults who are in cardiac arrest in any setting (P), does use of epinephrine (I), compared with vasopressin (C), change survival to 30 days with good neurologic outcome, survival to 30 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC (O)?	Laurie Morrison, Clifton Callaway, Steve Lin
Part 4	ALS	ALS 713	Prognostication in absence of TTM	Among adults who are comatose after cardiac arrest and are not treated with TTM (P), does any clinical finding when normal (e.g., clinical exam, EEG, SSEPs, imaging, other) (I), compared with any clinical finding when abnormal (C), reliably predict death or poor neurologic outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; death only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Claudio Sandroni, Tobias Cronberg
Part 4	ALS	ALS 714	SGAs versus tracheal intubation	Among adults who are in cardiac arrest in any setting (P), does SGA insertion as first advanced airway (I), compared with insertion of a tracheal tube as first advanced airway (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR parameters; development of aspiration pneumonia (O)?	Jerry Nolan, Charles Deakin
Part 4	ALS	ALS 723	ECPR versus manual or mechanical CPR	Among adults who are in cardiac arrest in any setting (P), does the use of ECPR techniques (including extracorporeal membrane oxygenation or cardiopulmonary bypass) (I), compared with manual CPR or mechanical CPR (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Mayuki Aibiki, Tzong-Luen Wang

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 4	ALS	ALS 778	SDE versus HDE	In adult patients in cardiac arrest in any setting (P), does HDE (at least 0.2 mg/kg or 5 mg bolus dose) (I), compared with SDE (1 mg bolus dose) (C), change survival to 180 days with good neurologic outcome, survival to 180 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC (O)?	Laurie Morrison, Clifton Callaway, Steve Lin
Part 4	ALS	ALS 782	Mechanical CPR devices	Among adults who are in cardiac arrest in any setting (P), do automated mechanical chest compression devices (I), compared with standard manual chest compressions (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Steven Brooks, Laurie Morrison
Part 4	ALS	ALS 783	Basic versus advanced airway	Among adults who are in cardiac arrest in any setting (P), does insertion of an advanced airway (tracheal tube or SGA) (I), compared with basic airway (bag-mask device with or without oropharyngeal airway) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; CPR parameters; development of aspiration pneumonia (O)?	Jerry Nolan, Jan-Thorsten Graesner
Part 4	ALS	ALS 784	Timing of administration of epinephrine	Among adults who are in cardiac arrest in any setting (P), does early epinephrine delivery by IV or IO route (e.g., less than 10 min after the beginning of resuscitation) (I), compared with delayed timing of epinephrine delivery (e.g., more than 10 min after the beginning of resuscitation) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Tonia Nicholson, Michael Donnino
Part 4	ALS	ALS 788	Epinephrine versus placebo	Among adults who are in cardiac arrest in any setting (P), does the use of epinephrine (I), compared with placebo or not using epinephrine (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Laurie Morrison, Clifton Callaway, Steve Lin
Part 4	ALS	ALS 789	Epinephrine versus vasopressin in combination with epinephrine	Among adults who are in cardiac arrest in any setting (P), does use of both vasopressin and epinephrine (I), compared with using epinephrine alone (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Clifton Callaway, Laurie Morrison, Steve Lin
Part 4	ALS	ALS 790	Targeted temperature management	Among patients with ROSC after cardiac arrest in any setting (P), does inducing mild hypothermia (target temperature 32–34 °C) (I), compared with normothermia (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Joshua Reynolds, Katherine Berg
Part 4	ALS	ALS 791	Duration of TTM	In patients with ROSC after cardiac arrest in any setting (P), does induction and maintenance of hypothermia for any duration other than 24 h (I), compared with induction and maintenance of hypothermia for a duration of 24 h (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Theodoros Xanthos, Lars Wiuff Andersen
Part 4	ALS	ALS 802	Timing of induced hypothermia	Among patients with return of pulses after cardiac arrest in any setting (P), does induction of hypothermia before some time point (e.g., 1 h after ROSC or before hospital arrival) (I), compared with induction of hypothermia after that time point (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Theodoros Xanthos, Michael Cocchi
Part 4	ALS	ALS 808	Ventilation rate during continuous chest compression	Among adults with cardiac arrest with a secure airway receiving chest compressions (in any setting, and with standard tidal volume) (P), does a ventilation rate of 10 breaths/min (I), compared with any other ventilation rate (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Koen Monsieurs, Jasmeet Soar, Gino Vissers
Part 4	ALS	ALS 834	Lipid therapy for cardiac arrest	In adult patients with cardiac arrest due to suspected drug toxicity (e.g., local anesthetics, tricyclic antidepressants, others) (P), does administration of IV lipid (I), compared with no IV lipid (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Eric Lavonas, Mohammed Alhelail
Part 4	ALS	ALS 868	Seizure treatment	Among adults with ROSC after cardiac arrest in any setting (P), does effective seizure treatment (I), compared with no seizure control (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Romergryko Geocadin, William Stacey
Part 4	ALS	ALS 879	Prevention of fever after cardiac arrest	Among adults with ROSC after cardiac arrest in any setting (P), does prevention of fever to maintain strict normothermia (I), compared with no fever control (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Katherine Berg, Lars Wiuff Andersen

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 4	ALS	ALS 889	Oxygen dose during CPR	In adults with cardiac arrest in any setting (P), does administering a maximal oxygen concentration (e.g., 100% by face mask or closed circuit) (I), compared with no supplementary oxygen (e.g., 21%) or a reduced oxygen concentration (e.g., 40–50%) (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC (O)?	Anthony Lagina, Jasmeet Soar

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Part 5: Acute coronary syndromes 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆

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Introduction

Since 2000, the International Liaison Committee on Resuscitation (ILCOR) has published the International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (CoSTR) every five years based on review of cardiopulmonary resuscitation (CPR) science. Seven task forces with representatives from the seven member resuscitation organizations create the CoSTR that enables regional resuscitation organizations to create their individual guidelines. The different guidelines are based on the scientific evidence and incorporate or adjust for regional considerations.

Why acute coronary syndromes?

Coronary heart disease remains among the leading causes of mortality globally. There is considerable research focus worldwide on improving outcomes in patients with acute coronary syndromes (ACS). Undoubtedly, this has led to improved health and dramatically improved morbidity and mortality in much of the world. Indeed, timely and appropriate care of ACS can reduce and prevent cardiac arrest. Some of the recommended interventions for ACS, however, are considered resource intensive and/or require significant infrastructure, such as well-trained emergency medical services personnel to administer fibrinolysis, and cardiac catheterization laboratories that require capital and experienced staff. These regional disparities present challenges to regional and national health authorities as guidelines evolve and become more complex.

The American College of Cardiology with the American Heart Association, European Society of Cardiology, and other organizations have developed guidelines for treatment and management of patients with ST-segment elevation myocardial infarction (STEMI) and non-STEMI ACS. These guidelines primarily focus on the hospital setting, and, for many years, the prehospital and emergency department (ED) management of patients was based on extrapolation of in-hospital evidence. There is now increasing interest and evidence on the prehospital decisions and management of ACS. The time-sensitive nature of ACS forces us to scrutinize not only the time goals to deliver the interventions but also the proper sequencing of them. For these reasons, the ACS Task Force emphasized the evidence review for 2015 on the management of ACS before the patient is admitted.

There has been renewed interest of late in focusing less on the individual aspects of STEMI care and more on the systems

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of care. This is in recognition that the system may be more than the sum of its parts. In STEMI care, this system integrates awareness and prevention, prehospital care, in-hospital care, specialty centers, and rehabilitation and secondary prevention. The ACS Task Force concentrated on the questions that will inform regional systems-of-care decisions. If a patient with ACS or STEMI presents to prehospital care, a local hospital, or a specialty center, there needs to be a common but nuanced approach to diagnosis and treatment. However, the specifics of that treatment may depend on local resources. The questions covered were intentionally focused to answer questions based on different community resources.

Evidence evaluation and GRADE process

Each task force performed a detailed systematic review based on the recommendations of the Institute of Medicine of the National Academies[1] and using the methodological approach proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[2] After identification and prioritization of the questions to be addressed (using the PICO (population, intervention, comparator, outcome) format),[3] with the assistance of information specialists, a detailed search for relevant articles was performed in each of three online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk of bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[4] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[5] and GRADE for observational studies that inform both therapy and prognosis questions.[6]

GRADE evidence profile Tables [7] were then created to facilitate an evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[8] based on the study methodologies and the five core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias).[9]

These evidence profile tables were then used to create a written summary of evidence for each outcome (the consensus on science statements). Whenever possible, consensus-based treatment recommendations were then created. These recommendations (designated as strong or weak) were accompanied by an overall assessment of the evidence and a statement from the task force about the values and preferences that underlie the recommendations.

Further details of the methodology that underpinned the evidence evaluation process are found in "Part 2: Evidence evaluation and management of conflicts of interest."

The ILCOR ACS task force process

The 2015 ILCOR ACS Task Force included expert cardiology, emergency, and prehospital physicians from Singapore, Japan, Australia, New Zealand, Greece, Belgium, France, the United States, Canada, and Panama. These 12 experts, along with an additional 5 expert evaluators (paramedics and residents/fellows), reviewed 18 topics related to the acute initial management of ACS and STEMI. The task force reviewed the evidence specifically related to diagnosis and treatment of STEMI (and ACS) in the out-of-hospital setting and the first hours of care in the in-hospital setting, typically in the ED. The evidence evaluation took place over three years leading up to the ILCOR 2015 International Consensus on CPR and ECC Science with Treatment Recommendations (C2015) meeting, with ongoing refinement of recommendations being made as new evidence was published. The purpose of the review was to generate current, evidence-based consensus on science and treatment recommendations for healthcare providers who serve as the initial point of contact for patients with signs and symptoms suggestive of ACS.

The ACS Task Force spent considerable time preparing for the introduction of the GRADE process through group in-person, online, and self-directed educational sessions. The ACS Task Force had five in-person meetings (Vienna, Austria, October 2012; Melbourne, Australia, April 2013; Banff, Canada, April 2014; Chicago, United States, November 2014; Dallas, United States, January/February 2015) plus nine webinars (June 2014 to January 2015). Use of the Scientific Evidence Evaluation and Review System (SEERS) website facilitated offline evidence review and online repository of progress and findings. This enabled periodic review and approval by task force members (TFMs), task force co-chairs, evidence evaluation experts, and senior editors.

The major steps from selection of review topics to the final CoSTR were:

- Topics prioritized for review.
- 20 topics assigned to lead TFM. Two deferred after scant new research found.
- PICO questions formed for each topic.
- Importance of potential outcomes graded according to GRADE methodology.
- Comprehensive search strategies run, search results uploaded online (SEERS).
- ACS TFMs, along with five additional external evidence reviewers paired to perform the following blinded duplicate processes:
  - Study inclusion/exclusion (non-RCTs excluded when there was evidence from several RCTs).
  - Data extraction.
  - Bias assessments.
- GRADE evidence profile tables formed.
- Formal meta-analysis performed if appropriate.
- Consensus on science reported according to evidence profile tables.
- Quality of evidence determined across all outcomes.
- Strength of recommendations determined.
- Values, preferences, and resource implications, reported.
- Additional commentary.
- Potential gaps in the literature related to the systematic reviews identified.
- Systematic reviews posted for public comments.
- Comments accessed and distributed to the TFMs electronically.
- Comments considered in the context of the draft recommendations; if necessary, amendments made by the TF co-chairs.
- Systematic reviews presented at the C2015 conference—invited topic matter experts provide critical commentary. Feedback from public commentary and invited experts was reviewed and incorporated where needed.
- Key new evidence reviewed and incorporated.
- The CoSTR editorial board signs off on final CoSTR.

An iterative process was used in which TFMs presented their interim evidence evaluation and gained input from the task force, evidence evaluation experts, public, and invited topic matter experts. They presented the key articles and findings to the task force at face-to-face meetings or webinars to enable discussion, refinement, and expert input. Additionally, evidence evaluation experts acted as methodological support advisors for GRADE and other aspects of systematic review development. These were discussed during face-to-face and webinar meetings and were collated for consideration into this final document.

Regional resuscitation organizations will need to determine where the interventions are applicable in their systems and thus how to implement the evidence into practice.

ACS task force abstract

The ACS Task Force ultimately completed 18 systematic reviews (14 based on meta-analyses) on more than 110 relevant studies spanning 40 years. The treatment recommendations were grouped by major topics as outlined below:

Diagnostic interventions in ACS:

- Prehospital electrocardiography (ECG) (ACS 336).
- Computer-assisted ECG STEMI interpretation (ACS 559).
- Nonphysician ECG STEMI interpretation (ACS 884).
- Prehospital STEMI activation of the catheterization laboratory (ACS 873).
- Biomarkers to rule out ACS (ACS 737).

Therapeutic interventions in ACS:

- Prehospital adenosine diphosphate (ADP)-receptor antagonists in STEMI (ACS 335).
- Prehospital anticoagulants versus none in STEMI (ACS 562).
- Prehospital anticoagulants versus unfractionated heparin (UFH) in STEMI (ACS 568).
- Supplementary oxygen in ACS (ACS 887).

Reperfusion decisions in STEMI:

- Prehospital fibrinolysis versus ED fibrinolysis (ACS 338).
- Prehospital triage to percutaneous coronary intervention (PCI) center versus prehospital fibrinolysis (ACS 341).
- ED fibrinolysis and immediate PCI versus immediate PCI alone (ACS 882).
- Delayed PCI versus fibrinolysis stratified by time from symptoms (ACS 337).
- Transport for PCI versus ED fibrinolysis and transport only for rescue PCI (ACS 332).
- ED fibrinolysis and routine early angiography versus transport for PCI (ACS 779).
- ED fibrinolysis and then routine early angiography versus only rescue PCI (ACS 334).

Hospital reperfusion decisions after return of spontaneous circulation (ROSC):

- PCI after ROSC with ST elevation (ACS 340).
- PCI after ROSC without ST elevation (ACS 885).

Some topics were not prioritized for review in the 2015 ILCOR process. Those topics not reviewed from 2005 and 2010 and/or not yet reviewed are:

- History and physical examination in the diagnosis of ACS.
- Chest pain observation units and protocols.
- Institutional requirements for performing interventions in ACS.
- Use of new biomarkers or other imaging tests for the diagnosis of ACS (rule-in).
- Use and timing of nitrates, β-blockers, ACE inhibitors, morphine, statins, glycoprotein IIb-IIIa antagonists, antiarrhythmics, analgesics, and anxiolytics in the prehospital, ED, and in-hospital settings.
- Use of antiplatelet and anticoagulant medications in-hospital.
- Administration of aspirin (early aspirin use was reviewed by the First Aid Task Force for 2015; see FA 871 and FA 586 in "Part 9: First aid").
- Optimal metrics of system performance/comparison regarding prompt revascularization in STEMI.

Summary of new treatment recommendations

The following is a summary of the most important new reviews or changes in recommendations for diagnosis and treatment of ACS since the last ILCOR review in 2010:

Diagnostic interventions in ACS:

- The role of prehospital ECG was reemphasized. Newer evidence suggests that prehospital ECG may not only facilitate earlier diagnosis of STEMI and provide the opportunity for rapid prehospital and in-hospital reperfusion, but there is evidence of a substantial mortality benefit. This is relevant to patients that will undergo primary percutaneous coronary intervention (PPCI) or fibrinolysis.
- Computer-assisted ECG STEMI interpretation is still suggested as an adjunct to recognize STEMI, given the high specificity of the computer algorithms evaluated. The strength of recommendation is reduced to a weak recommendation, because there was very low confidence in the effect size provided by the existing literature.
- Nonphysician ECG STEMI interpretation is suggested if adequate diagnostic performance can be maintained through carefully monitored programs.
- For prehospital STEMI activation of the catheterization laboratory, newer evidence suggests that it can not only reduce treatment delays but also improve patient mortality.
- The use of troponins at 0 and 2 h as a stand-alone measure for excluding the diagnosis of ACS is strongly discouraged. Excluding the diagnosis of ACS (defined as less than 1% 30-day major adverse cardiac event [MACE]) can be accomplished by negative* high-sensitivity cardiac troponin (hs-cTnI) measured at 0 and 2 h with low-risk stratification or by combining negative* cardiac troponin I (cTnI) or cardiac troponin T (cTnT) measured at 0 and 3 to 6 h with very low risk stratification.

Therapeutic interventions in ACS:

- ADP-receptor antagonists can be given either prehospital or in-hospital for suspected STEMI patients with a planned primary PCI approach.
- UFH can be administered in either the prehospital or in-hospital setting in suspected STEMI patients with a planned primary PCI approach.
- Prehospital enoxaparin may be used as an alternative to prehospital UFH as an adjunct for primary PCI for STEMI. We have insufficient confidence in the treatment effect for prehospital administration of bivalirudin compared with prehospital administration of UFH in prehospital-identified STEMI patients to recommend a change in existing practice.
- We suggest withholding oxygen in comparison with routine oxygen supplementation in normoxic patients with ACS.

Reperfusion decisions in STEMI:

- When fibrinolysis is the planned treatment strategy, we recommend using prehospital fibrinolysis in comparison with in-hospital fibrinolysis for STEMI where transport times are greater than 30 min and prehospital personnel are well trained.

- Where PCI facilities exist and are available in a geographic region we suggest that direct triage and transport for PCI is preferred to prehospital fibrinolysis for STEMI.
- We recommend against the routine use of fibrinolytic administration combined with immediate PCI, compared with immediate PCI alone in patients with STEMI.
- We provide recommendations on PCI versus fibrinolysis based on time from symptom onset and potential delay to PCI.
- After fibrinolysis of STEMI patients in the ED (when primary PCI is not available on-site), we suggest transport for early routine angiography in the first 3–6 h (or up to 24 h) rather than only transport for ischemia-guided angiography.
- For adult patients presenting with STEMI in the ED of a non-PCI-capable hospital, we recommend emergency transfer without fibrinolysis to a PCI center as opposed to immediate in-hospital fibrinolysis and transfer only for rescue PCI.
- For patients presenting with STEMI in the ED of a non-PCI hospital, we suggest fibrinolytic therapy with routine transfer for angiography within 3 to 6 and up to 24 h as an alternative to immediate transfer to PPCI.

Hospital reperfusion decisions after ROSC:

- We recommend emergency cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select adult patients with ROSC after out-of-hospital cardiac arrest (OHCA) of suspected cardiac origin with ST elevation on ECG.
- We suggest emergency cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select adult patients who are comatose with ROSC after OHCA of suspected cardiac origin without ST elevation on ECG.

Diagnostic interventions in ACS

Acute coronary syndromes refers to a spectrum of clinical disorders that include acute myocardial infarction (AMI) with and without ST elevation and unstable angina pectoris. The term myocardial infarction, as defined by the World Health Organization, is used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia (no evidence of a cause other than ischemia). Criteria for diagnosis of AMI include[10]:

- Detection of increase and/or decrease of cardiac biomarkers (preferably troponin) with at least 1 value above the 99th percentile of the upper reference limit.
- Evidence of myocardial ischemia with at least one of the following: symptoms, ECG changes, or supportive imaging.

Symptoms of ischemia include various combinations of chest, upper extremity, jaw, or epigastric discomfort with exertion or at rest. The discomfort usually lasts 20 min or less (may have any duration, but if it is greater than 20 min, then it is more likely an infarction); often is diffuse, not localized, not positional, and not affected by movement of the region; and may be accompanied by dyspnea, diaphoresis, nausea, or syncope. ECG changes indicative of new ischemia include new ST-T changes, new left bundle branch block, or development of pathological Q waves in the ECG. Imaging may show evidence of new loss of viable myocardium or new regional wall motion abnormality.

This diagnostic interventions section (Section 6) will focus on the value of the prehospital ECG in recognizing or "ruling in" STEMI, and on the use of diagnostic tests including biomarkers to identify low-risk chest pain and thus "rule out" ACS.

The ECG

In the ED and out-of-hospital settings, the ECG is essential for the initial triage and initiation of management of patients with possible ACS. It is well recognized that signs and symptoms alone may not be sufficiently sensitive to diagnose AMI or ischemia in the prehospital or ED setting. Prehospital ECG acquisition and interpretation is critical in early recognition of STEMI and other high-risk ACS patients. The ACS task force focused its attention on the use of the prehospital ECG for recognition of STEMI patients. Accurate recognition and advance notification of the hospital has the potential of minimizing in-hospital treatment delays, thus improving patient outcomes.

In many studies of prehospital ECG STEMI recognition, physician interpretation is considered to be the gold standard. This approach, however, is limited by the fact that physicians are not always available on scene, which increases the possibility of false ECG readings. The prehospital ECG can be interpreted in four ways: on-scene interpretation by a physician, nonphysician, or computer, or transmission off-site to a physician or other experienced healthcare provider.

This section will review the evidence for the use of the prehospital ECG in STEMI recognition, its value when used to notify the hospital and/or activate the catheterization laboratory, and the evidence for use of adjunctive computer interpretation and/or interpretation by nonphysicians in the prehospital setting.

This science review has focused on the ability of prehospital ECG recording with advance notification to affect not only patient treatment delays but also patient outcomes. We have also addressed accuracy of ECG interpretation by nonphysicians with or without the aid of computer interpretation. In the latter two analyses, it was impossible to provide pooled estimates for diagnostic performance because of considerable heterogeneity among the included studies. Rather, ranges for observed sensitivity and specificity across studies are provided. Based on these values, we have calculated false-positive (FP) and false-negative (FN) results over an arbitrarily chosen spectrum of disease prevalence from 5% to 20%. Large variations within the existing evidence preclude extrapolation from these data to other situations and recommendations with general applicability to all systems of care that might be considering implementation of the reviewed diagnostic strategies. Each system should make every effort to achieve optimal diagnostic performance for prehospital ECG interpretation and STEMI recognition regardless of the diagnostic strategy they are using. The sensitivity and specificity of the diagnostic performance should be considered in conjunction with local prevalence of STEMI among transferred patients to determine the expected FP and FN rates for a particular system. This is highly important for effective balancing between patient risk for undue treatment delays in those with FN ECG readings and inappropriate resource allocation from false system alarms in case of FP ECG interpretations.

Prehospital ECG (ACS 336)

Among adult patients with suspected STEMI outside of a hospital (P), does prehospital 12-lead ECG with transmission or notification (I), compared with no ECG or no transmission/notification (C), change death, or time to treatment (first medical contact-to-balloon time, first medical contact-to-needle time, door-to-balloon time, door-to-needle time) (O)?

Consensus on science

For the critical outcome of 30-day mortality in STEMI patients who receive PCI, we have identified low-quality evidence (downgraded for bias, upgraded for treatment effect) from 9 observational studies[11–19] enrolling 20,402 patients showing benefit of prehospital 12-lead ECG and hospital notification compared with no ECG

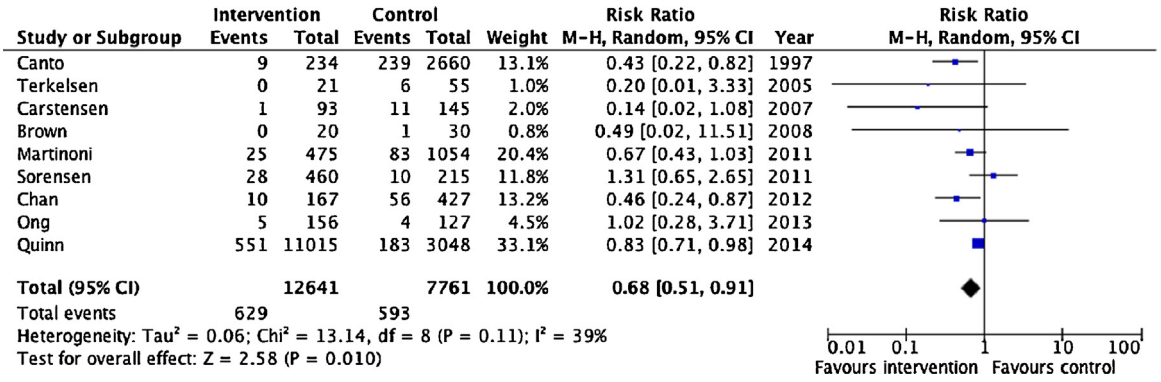

Fig. 1. Thirty-day mortality in STEMI patients undergoing PPCI with and without prehospital ECG and hospital notification (random effects model). Intervention = prehospital ECG; control = without prehospital ECG.

or no notification (relative risk (RR), 0.68; 95% confidence interval (CI), 0.51–0.91) (Fig. 1). This is a 32% relative reduction in mortality.

For the critical outcome of 30-day mortality in STEMI patients who receive fibrinolysis, we have identified low-quality evidence (downgraded for bias, upgraded for treatment effect) from two observational studies[11,19] enrolling 59,631 patients showing benefit of prehospital ECG and hospital notification compared with no 12-lead ECG or no notification (RR, 0.76; 95% CI, 0.71–0.82) (Fig. 2). This is a 24% relative reduction in mortality.

For the important outcomes of first medical contact-to-reperfusion, door-to-balloon, and door-to-needle time in STEMI patients, we have identified very-low-quality evidence (downgraded for serious risk of bias) in 7 observational studies,[12,15–17,20–22] 14 observational studies,[11–14,16–18,20–26] and 3 observational studies,[11,26,27] respectively, of consistent reduction in times to reperfusion with prehospital 12-lead ECG and hospital notification. The time to treatment results could not be pooled because of heterogeneity in estimate of effect size.

Treatment recommendation

We recommend prehospital 12-lead ECG acquisition with hospital notification for adult patients with suspected STEMI (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we are placing a higher value on the consistent mortality-benefit and consistent reduction-in-reperfusion times in a large number of patients (greater than 80,000) over the risk of bias inherent in observational studies.

Knowledge gaps

- This question did not specifically address the method for ECG interpretation. We did not find direct comparison of different systems of ECG STEMI recognition (with and without adjunctive computer algorithm).

Computer-assisted ECG STEMI interpretation (ACS 559)

Among adult patients with suspected STEMI outside of a hospital (P), does the use of computer-assisted ECG interpretation (I), compared with physician ECG interpretation and/or clinical diagnosis of STEMI (C), change identification of STEMI on an ECG with acceptable rates of FNs to allow earlier identification and FPs, minimizing unnecessary intervention (O)?

Consensus on science

For the important outcomes of FP and FN, we have identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 2 cohort studies[28,29] enrolling 1112 patients/ECGs of FP for STEMI recognition ranging from 0% to 8.7% (assuming STEMI prevalence of 5% (highest expected FP results)) and FN ranging from 4.4% to 8.4% (assuming STEMI prevalence of 20% (highest expected FN results)). Note that sensitivity ranged from 0.58 to 0.78, and specificity ranged from 0.91 to 1.

For the important outcome of FP/all positive results, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 6 observational studies[14,30–33] enrolling 1949 ECGs of FP/all positive results for STEMI recognition ranging from 0% to 42.9%.

Treatment recommendations

We suggest computer-assisted ECG interpretation can be used as an adjunct* to recognize STEMI, given the high specificity of the computer algorithms evaluated (weak recommendation, very-low-quality evidence).

We suggest computer-assisted ECG interpretation not be used alone to rule out STEMI, because of the poor sensitivity and thus the considerable risk for FN results of the computer algorithms evaluated (weak recommendation, very-low-quality evidence).

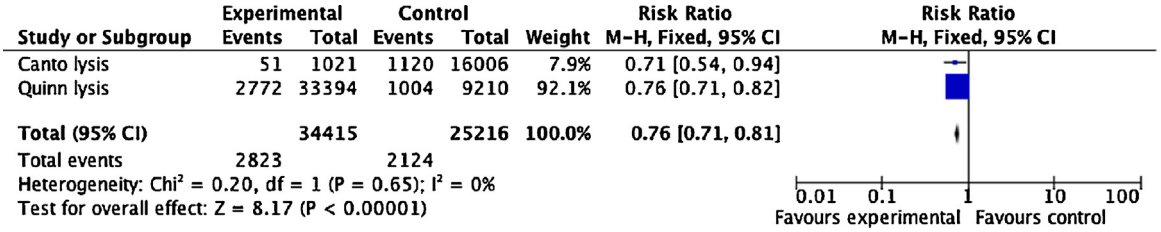

Fig. 2. Thirty-day mortality in STEMI patients undergoing fibrinolysis with and without prehospital ECG and hospital notification (fixed effects model). Experimental = prehospital ECG; control = without prehospital ECG.

Values, preferences, and task force insights

In making this recommendation, we put a higher value on minimizing treatment delays of patients with STEMI over possible wasted resources resulting from FP system activation.

Recognition of STEMI on ECG may achieve highest accuracy if computer-assisted interpretation is implemented as an adjunct to on-site healthcare provider interpretation in the context of strong initial education programs, quality assurance programs, and ongoing oversight.

As was pointed out in the public comments, it is difficult to perform head-to-head comparisons or combine data from these studies, because they have used different proprietary computer interpretation algorithms and different gold standards. It is likely that different algorithms perform differently. Computer interpretation algorithms can be updated periodically, which may change their effectiveness, making previous studies less relevant unless the algorithm and version are the same as is used in your setting. Last, some of the algorithms can now be adjusted to favor either lower FP results or lower FN results, depending on the needs or how it is used. Therefore, in choosing to use such a computer algorithm as an adjunct, careful consideration of the individual algorithm's reported performance and evaluation of this in your own settings are key.

The use of computer ECG interpretation did not yield equally effective performances across the various systems of care where it has been used with observed sensitivities ranging from 0.58 to 0.78 and specificity ranging from 0.91 to 1. This may be due to the algorithm performance (different performance with different types of STEMI), but it may also be related to the quality of obtained ECG and the level of training and individual expertise in acquiring the ECG. It is possible that the performance characteristics of a computer algorithm are different in controlled, in-hospital settings in stable patients compared with prehospital settings. Therefore, each system of care has to evaluate performance of any specific algorithm in the particular context where the algorithm is used. Diagnostic performance should always be considered in conjunction with local STEMI prevalence, because very high or low prevalence rates may lead to unacceptable FP and/or FN rates despite sensitivity and specificity rates that may seem satisfactory as stand-alone values. This approach may give important clues as to whether this method fits best in comparison with other existing options of ECG interpretation such as transmission of ECG for interpretation by an experienced provider.

Knowledge gaps

- Different computer algorithms have not been compared. The optimal ECG computer algorithm for implementation with adjunctive nonexpert interpretation has not been determined.

Nonphysician STEMI ECG Interpretation (ACS 884)

Among adult patients with suspected STEMI outside of a hospital (P), do nonphysicians (e.g., nurses and paramedics) (I), compared with physicians (C), change identification of STEMI on an ECG with acceptable rates of FNs to allow earlier identification and FPs, minimizing unnecessary angiography (O)?

Consensus on science

For the important outcomes of FP and FN results, we have identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and publication bias) from 3 studies[34–36] including 1360 ECGs of FP results of STEMI recognition ranging from 0.3% to 30.5% (under the assumption of a disease prevalence of 5% (highest expected FP results)), and FN results did not exceed 4% (under the assumption of 20% prevalence (highest expected FN results)). Sensitivity ranged from 80% to 99.6%, and specificity ranged from 68% to 96.8%.

For the important outcome of FP/all positive tests, we have identified very-low-quality studies (downgraded for risk of bias and inconsistency) from 9 observational studies[34–41] including 900 ECGs of FP/all positive tests for STEMI recognition ranging from 8% to 40%.

Treatment recommendation

We suggest that in adult patients with suspected STEMI outside of a hospital, nonphysicians may perform ECG interpretation to recognize STEMI in a system where the FP and FN rates are low (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we adopt a balanced approach in between minimizing treatment delays of patients with STEMI and avoiding excess waste of resources resulting from FP system activations.

It is recognized that in many prehospital systems, physicians will not be available on-site, and the evidence indicates that highly trained paramedics and nurses can reliably recognize STEMI. This should occur in an organized system of prehospital care where there is a strong initial education program, ongoing oversight, possible adjunctive computer interpretation, and a quality assurance program.

It is impossible to provide pooled estimates from the reviewed data, because different study methods and/or gold standards have been used. Nonphysician STEMI ECG recognition was not equally reliable across the various reporting systems of care. This may be relevant to the quality of the ECG obtained and the ECG findings but also to the level of training and individual expertise of healthcare providers. Therefore, each system of care should make every effort to assure optimal diagnostic accuracy from healthcare providers by maintaining adequate training programs and meticulous care for quality control. Timely feedback from STEMI receiving centers, including performance benchmarks, prehospital and in-hospital ECGs, and catheterization findings, may be essential in this regard. Diagnostic performance should always be considered in conjunction with local STEMI prevalence as very high or low prevalence rates may lead to unacceptable FP and/or FN rates despite sensitivity and specificity rates that may seem satisfactory as stand-alone values. This may give important clues as to whether nonphysician STEMI interpretation fits best in the setting of a particular system of care in comparison with other existing options of on-site ECG interpretation such as transmission of ECG for interpretation by an experienced provider or computer-assisted interpretation.

Knowledge gaps

- We did not find evaluation of nonphysician ECG interpretation initial and maintenance training programs or measurement of ECG interpretation performance based on specific education or experience.

Prehospital STEMI activation of the catheterization laboratory (ACS 873)

Among adult patients with suspected STEMI outside of a hospital (P), does prehospital activation of catheterization laboratory (I), compared with no prehospital activation of the catheterization laboratory (C), change mortality, major bleeding, stroke, reinfarction (O)?

Introduction

Prompt restoration of coronary flow in the affected area is key to treatment of STEMI. Several system-related strategies have been

developed to minimize system-related delays to reperfusion. For patients with suspected STEMI in the prehospital setting, the above strategies for ECG interpretation are used to ensure prehospital STEMI recognition. Where prehospital fibrinolysis is not possible or appropriate, the focus should then be on prompt patient triage for transfer to the medical institution where the most appropriate treatment would be offered in a timely manner. Advance hospital notification and early activation of the catheterization laboratory can expedite invasive revascularization. This review has focused on the potential of prehospital STEMI activation of the catheterization laboratory to improve patient safety and efficacy outcomes.

Consensus on science

For the critical outcome of 30-day mortality, we have identified moderate-quality evidence (upgraded for large effect size) from 6 observational studies[13,14,16,42–44] enrolling 1805 patients in favor of prehospital activation of the catheterization laboratory over no activation of catheterization laboratory (odds ratio (OR), 0.41; 95% CI, 0.30–0.56) (Fig. 3).

For the important outcome of major bleeding, we have identified very-low-quality evidence (downgraded for imprecision) from 1 observational study[43] enrolling 188 patients showing no benefit of prehospital activation of catheterization laboratory over no activation of catheterization laboratory (OR, 0.68; 95% CI, 0.04–10.68).

For the important outcome of nonfatal stroke, we have identified very-low-quality evidence (downgraded for imprecision) from 1 observational study[13] enrolling 301 patients showing no benefit of prehospital activation of catheterization laboratory over no activation of catheterization laboratory (OR, 0.06; 95% CI, 0.00–1.13).

For the important outcome of nonfatal reinfarction, we have identified very-low-quality evidence (downgraded for imprecision) from 3 observational studies[13,43,44] enrolling 748 patients showing no benefit of prehospital activation of catheterization laboratory over no activation of catheterization laboratory (OR, 0.48; 95% CI, 0.22–1.03).

Treatment recommendation

We recommend that when primary PCI is the planned strategy, that prehospital activation of catheterization laboratory for PPCI is preferred (strong recommendation, very-low-quality evidence) over no prehospital activation.

Values, preferences, and task force insights

In making this recommendation, we place higher value of benefit to patient outcomes over the potential increased resource utilization.

Biomarkers to rule out ACS (ACS 737)

In patients presenting to the ED with chest pain suspected to be of cardiac etiology (P), does a negative troponin test at presentation and 1, 2, 3, and 6 h (I), compared with a positive test (C), exclude the diagnosis of ACS (O)?

Introduction

Troponin has become the most widely used and well-validated diagnostic laboratory test for the diagnosis of myocardial ischemia and is the preferred biomarker for the international definition of myocardial infarction.[45] There have been a variety of biomarkers proposed for the diagnosis of myocardial infarction, including myoglobin, brain natriuretic peptide (BNP), NT-proBNP, D-dimer, C-reactive protein, ischemia-modified albumin pregnancy-associated plasma protein A (PAPP-A), and/or interleukin-6. There is insufficient evidence to support the use of many of these in isolation as primary tests to evaluate patients with symptoms suspicious for cardiac ischemia.[46,47]

The diagnosis of AMI includes the increase and/or decrease in the biomarker troponin; therefore, numerous studies have evaluated the effectiveness of different timelines for ruling in an AMI by using various troponin assays. Many cardiology guidelines have recommended timelines for ruling in AMI. The accuracy and test characteristics of troponins for ruling out an AMI are an area of interest, given the relatively new high-sensitivity troponin tests available.

This evidence review is confined to the use of troponin in the rule out of ACS. Although troponin use to rule out AMI is feasible, non-AMI ACS may not have a rise of troponin, and thus ruling out ACS with only troponin may not be possible. However, troponin in combination with other investigations may be able to identify a group of patients with very low frequency (defined as less than 1%) of MACE in the next 30 days, thus virtually able to rule out or exclude the diagnosis of ACS.

In chest pain patients in the ED, early identification of a group of patients with very low risk of 30-day MACE could substantially decrease the number of chest pain patients admitted to hospital. This use of troponin at specific time intervals with or without other tools may identify the very low risk of patients that can be safely discharged home. These very-low-risk patients may still need additional diagnostic workup for coronary artery disease, but this could be accomplished as outpatients.

This body of evidence reviewed consisted entirely of observational data, because no RCTs were found. In most of these studies, the gold standard for the diagnosis of acute coronary ischemia frequently was a diagnosis of a documented MACE in a given time frame (30 days, 6 months, or 1 year). In the ED setting, one of the most important imperatives is to identify patients in whom ACS can be safely excluded to facilitate timely discharge. Hence, the critical measure of the value of the diagnostic tests is the FN rate, which is the proportion of FNs relative to all patients with ACS (FN/(FN + TP)). The incidence of FN is determined by the prevalence of the relevant disease in the population. So, in patients with ACS, we sought to review the evidence for combining clinical risk stratification tools with the troponin assay to improve the accuracy of ACS identification. This is important, given the many patients who present with chest pain to emergency healthcare providers and the adverse consequences for patients in whom the diagnosis of ACS is missed.

Consensus on science

High-sensitivity cardiac troponin T (Table 1). For the critical outcome of excluding the diagnosis of ACS[1], we have identified very-low-quality evidence (downgraded for selection bias and imprecision) from 1 observational study[48] enrolling 939 patients presenting to the ED with chest pain showing an FN rate (FN/(FN + TP)) of 2.5% if both 0- and 2-hour high-sensitivity cardiac troponin T (hs-cTnT) were less than 99th percentile and the increase was less than 20% without the use of clinical scoring, using the outcome of adjudicated 1-year events.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias and imprecision) from 1 observational study[49a] enrolling 764 patients presenting to the ED with chest pain showing an FN rate (FN/(FN + TP)) of 3.6% if both 0- and 2-hour hs-cTnT were less than 14 ng/L without the use of clinical scoring, using the outcome of 30-day MACE.

High-sensitivity cardiac troponin I. For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias and imprecision) from 1 observational study[49a] enrolling 1635 patients presenting to the ED with symptoms suggestive of ACS showing an FN rate (FN/(FN + TP))

[1] Exclude the diagnosis of ACS defined as less than 1% 30-day MACE.

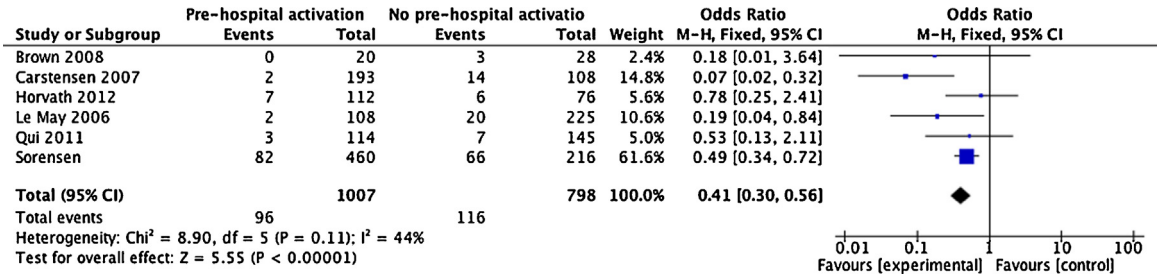

Fig. 3. Thirty-day mortality for prehospital STEMI activation of the catheterization laboratory versus no prehospital activation. Experimental = prehospital STEMI activation of the catheterization laboratory; control = no prehospital STEMI activation of the catheterization laboratory.

Table 1
Troponin and risk stratification to rule out MACE.

Reference	Inclusion criteria	*n*	Measurement	Clinical score	FN/(FN + TP), %	Outcome
Marker: high-sensitivity cardiac troponin T (hs-cTnT)						
Aldous,[48] 2011	Chest pain	939	0- and 2-hour hs-cTnT < 99th percentile and delta <20%	None	2.5	Adjudicated 1-year cardiac event
Parsonage,[49a]2014	Chest pain	764	0- and 2-hour hs-cTnT <14 ng/L	None	3.6	30-day MACE
Marker: high-sensitivity cardiac troponin I (hs-cTnI)						
Cullen,[49b] 2014	Symptoms suggestive of ACS	1635	0- and 2-hour hs-cTnI <99th percentile	Vancouver	0.9	30-day MACE
Cullen,[50] 2013	<12 h of symptoms suggestive of ACS	909	0- and 2-hour hs-cTnI <99th percentile	TIMI score 0 or 1	0.8	30-day MACE
Cullen,[50] 2013	>5 min of chest pressure	1635	0- and 2-hour hs-cTnI <99th percentile	TIMI score 0 or 1	0.8	30-day MACE
Cullen,[50] 2013	<12 h of symptoms suggestive of ACS	909	0- and 2-hour hs-cTnI <99th percentile	TIMI score 0	0	30-day MACE
Cullen,[50] 2013	>5 min of chest pressure	1635	0- and 2-hour hs-cTnI <99th percentile	TIMI score 0	0	30-day MACE
Markers: cardiac troponin I and troponin T (cTnI and cTnT)						
Aldous,[48] 2011	Chest pain	939	0- and 2-hour cTnI <0.056 mcg/L	None	7.8	Adjudicated 1-year cardiac event
Cullen,[49b] 2014	Symptoms suggestive of ACS	1635	0- and 2-hour cTnI <99th percentile	Vancouver	1.2	30-day MACE
Xavier Scheuermeyer,[51] 2014	Symptoms suggestive of ACS	906	0- and 2-hour cTnT <99th percentile	Vancouver	0.8	30-day MACE
Kelly,[52] 2014	>10 min of chest pain	840	0- and 2-hour cTnI <99th percentile	TIMI score 0	0	30-day MACE
Mahler,[53] 2013	Anterior chest pain	1002	0- and 3-hour cTnI <99th percentile	Low risk using an unstructured risk assessment	2.3	30-day MACE
Mahler,[53] 2013	Anterior chest pain	1002	0- and 3-hour cTnI <99th percentile	Low-risk HEART score	0.9	30-day MACE
Mahler,[53] 2013	Anterior chest pain	1002	0- and 3-hour cTnI <99th percentile	Low-risk North American CP score	0	30-day MACE
Hess,[54] 2013	Anterior chest pain	2718	0- and 3- to 6-hour cTnI or cTnT <99th percentile	North American CP score of 0 and age <60 years	1.1	30-day MACE
Hess,[54] 2013	Anterior chest pain	2718	0- and 3- to 6-hour cTnI or cTnT <99th percentile	North American CP score of 0 and age <50 years	0	30-day MACE

ACS indicates acute coronary syndromes; CP, chest pain; FN, false negative; MACE, major adverse cardiac event; TIMI, Thrombolysis in Myocardial Infarction; and TP, true positive.

of 0.9% if both 0- and 2-hour hs-cTnI were less than 99th percentile and met the Vancouver Rule, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias, inconsistency, and imprecision) from 1 observational study[50] enrolling 909 patients presenting to the ED with symptoms suggestive of ACS, finding an FN rate (FN/(FN + TP)) of 0.8% if both 0- and 2-hour hs-cTnI were less than 99th percentile and a Thrombolysis in Myocardial Infarction (TIMI) score of 0 or 1, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias and imprecision) from 1 observational study[50] enrolling 1635 patients presenting to the ED with greater than 5 min of chest pressure showing an FN rate of 0.8% if both 0- and 2-hour hs-cTnI were less than 99th percentile and a TIMI score of 0 or 1, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias, inconsistency, and imprecision) from 1 observational study[50] enrolling 909 patients presenting to the ED with symptoms suggestive of ACS showing an FN rate of 0% if both 0- and 2-hour hs-cTnI were less than 99th percentile and a TIMI score of 0, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias and imprecision) from 1 observational study[50] enrolling 1635 patients presenting to the ED with greater than 5 min of chest pressure showing an FN rate of 0% if both 0- and 2-hour hs-cTnI were less than 99th percentile and a TIMI score of 0, using the outcome of 30-day MACE.

Cardiac troponin I and T. For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence

(downgraded for selection bias and imprecision) from 1 observational study[48] enrolling 939 patients presenting to the ED with chest pain showing an FN rate (FN/(FN + TP)) of 7.8% if both 0- and 2-hour cTnI were less than 0.056 mcg L^{-1} without the use of clinical scoring, using the outcome of adjudicated 1-year cardiac events.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias and imprecision) from 1 observational study[49a] enrolling 1635 patients presenting to the ED with symptoms suggestive of ACS showing an FN rate (FN/(FN + TP)) of 1.2% if both 0- and 2-hour cTnI were less than 99th percentile and met the Vancouver rule, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[51] enrolling 906 patients presenting to the ED with symptoms suggestive of ACS showing an FN rate of 0.8% if 0- and 2-hour cTnT were less than 99th percentile and met the Vancouver rule, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[52] enrolling 840 patients presenting to the ED with greater than 10 min of chest pain showing an FN rate of 0% if 0- and 2-hour cTnI were less than 99th percentile and TIMI risk score of 0, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[53] enrolling 1002 patients presenting to the ED with anterior chest pain showing an FN rate of 0.8% if 0- and 3-hour cTnI were less than 99th percentile and a low-risk unstructured risk assessment, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[53] enrolling 1002 patients presenting to the ED with anterior chest pain showing an FN rate of 0.8% if 0- and 3-hour cTnI were less than 99th percentile and a low-risk HEART score, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[53] enrolling 1002 patients presenting to the ED with anterior chest pain showing an FN rate of 0.8% if 0- and 3-hour cTnI were less than 99th percentile and a low-risk North American CP score, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[54] enrolling 2718 patients presenting to the ED with anterior chest pain and had a troponin ordered showing an FN rate of 1.1% if both 0- and 3–6 h cTnI or cTnT were less than 99th percentile, a North American CP score of 0, and age was less than 60 years, using the outcome of 30-day MACE.

For the critical outcome of excluding the diagnosis of ACS, we have identified very-low-quality evidence (downgraded for selection bias) from 1 observational study[54] enrolling 2718 patients presenting to the ED with anterior chest pain and had a troponin ordered showing an FN rate of 0% if both 0- and 3–6 h cTnI or cTnT were less than 99th percentile, a North American CP score of 0, and age was less than 50 years, using the outcome of 30-day MACE.

Treatment recommendations

We recommend against using hs-cTnT and cTnI alone measured at 0 and 2 h to exclude the diagnosis of ACS* (strong recommendation, very-low-quality evidence).

There is no evidence of using hs-cTnI and cTnT alone to exclude the diagnosis of ACS.

We suggest that negative† hs-cTnI measured at 0 and 2 h may be used together with low-risk patients (low risk defined by Vancouver rule or TIMI score of 0 or 1) to exclude the diagnosis of ACS* (weak recommendation, low-quality evidence).

We suggest negative† cTnI or cTnT measured at 0 and 3 to 6 h may be used together with very-low-risk patients (low risk defined by Vancouver rule, TIMI score of 0, low-risk HEART score, low-risk North American CP rule) to exclude the diagnosis of ACS* (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place higher value on reducing resource utilization by avoiding hospitalization, only if these patients have a very low likelihood of subsequent MACE. We defined the acceptable risk as less than 1% risk of ACS, MACE, or death at 30-day or longer follow-up.

Knowledge gaps

- We encourage further studies to evaluate the combination of troponin and clinical risk scores to determine which patients with chest pain may be safely discharged from the ED.

Therapeutic interventions in ACS

Myocardial reperfusion therapy, by fibrinolysis or primary PCI, is the pivotal treatment of STEMI. The development of STEMI networks during the past decade has improved quick access to reperfusion therapy and led to a reduction of mortality in this setting.[55]

Reperfusion therapy benefits from adjunctive antithrombotic therapy, which, depending on the logistics and organization of emergency medical services, may be provided in the prehospital setting by physicians or in some regions by nurses and paramedics under medical authority. Such therapy includes antiplatelet agents (e.g., aspirin, ADP inhibitors) and anticoagulants (e.g., UFH, enoxaparin, bivalirudin).

The benefit of aspirin administration in STEMI patients is strong, and as there was no significant new research in this area, this question was not prioritized for update in 2015. The administration of aspirin by first aid providers was reviewed in 2015 (see FA 871 and FA 586 in "Part 9: First aid").

Although the administration of ADP-receptor inhibitors is strongly recommended in STEMI (and other) patients, the in-hospital use of these drugs was not addressed in this 2015 publication; however, their prehospital use was reviewed. There were very few studies that evaluated the prehospital versus in-hospital administration of these drugs, and this is a topic requiring further research. Our a priori outcomes did not include stent thrombosis; thus, this was not included in the 2015 consensus on science. However, where post hoc evidence of increased stent thrombosis rates were available, inclusion in treatment recommendations was considered.

The concomitant administration of adjunctive antithrombotic therapy in association with reperfusion therapy is recommended widely based on consistent evidence in international specialty guidelines.[56,57] Nevertheless, whether effort should be undertaken to include such additional therapy in the prehospital management of STEMI patients, particularly in a planned primary PCI strategy, remains to be evaluated and is the subject of this section. Two related questions reviewed the evidence for administration of anticoagulants in the prehospital setting. One reviewed prehospital versus in-hospital use, and the other reviewed prehospital administration of different agents. Interestingly, only UFH has been evaluated directly in a comparison of prehospital versus in-hospital use despite other agents being used in the prehospital setting.

We encourage prospective RCTs on the relative benefits of prehospital versus in-hospital administration of anticoagulants. While stent thrombosis was not an a priori outcome in our evaluations, it remains a major complication of PCI, and, thus, where post hoc evidence of increased stent thrombosis rates were available, this was considered for the treatment recommendations and is discussed further in the comments section.

In addition to the prehospital antiplatelet and anticoagulant treatments for STEMI patients above, this section also includes oxygen supplementation in ACS patients. Although the use of supplementary oxygen (regardless of oxygen saturation) had previously been considered standard of care, its routine use for ACS patients (and postarrest patients, patients with chronic obstructive pulmonary disease, etc) has more recently been questioned. Most of the literature on this topic is relatively old, some before reperfusion therapy for STEMI (1970s) and, thus, this limits its generalizability. These studies also used different nonstandardized outcomes, which limits the ability to combine the studies. Despite these numerous methodological concerns, in 2010 the ILCOR ACS Task Force stated that the routine use of supplementary oxygen in ACS was not recommended. The review did cite gaps in prospective studies of oxygen use in ACS in the modern era. Since 2010, three prospective research studies on the use of supplementary oxygen use in STEMI were started. Therefore, this topic was reviewed for 2015 to update the review with the use of the new GRADE methodology and in anticipation of additional evidence in the near future. At the time of final manuscript preparation, the published results were available for only 1 of these trials. The other 2 studies were not yet published.

Prehospital ADP-receptor antagonists in STEMI (ACS 335)

Among adult patients with suspected STEMI outside of the hospital (P), does prehospital administration of an ADP-receptor antagonist (clopidogrel, prasugrel, or ticagrelor) in addition to usual therapy (I), compared with administration of an ADP-receptor antagonist in-hospital (C), change death, intracranial hemorrhage, revascularization, stroke, major bleeding, reinfarction (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified very-low-quality evidence (downgraded for imprecision and reporting bias) from 3 RCTs[58–60] enrolling 2365 patients showing no additional benefit with prehospital administration of an ADP-receptor antagonist compared with in-hospital administration (OR, 1.58; 95% CI, 0.90–2.78) (Fig. 4).

For the important outcome of major bleeding, we have identified very-low-quality evidence (downgraded for imprecision and reporting bias) from 3 RCTs[58–60] enrolling 2365 patients showing no additional benefit with prehospital administration of an ADP-receptor antagonist compared with in-hospital administration (OR, 1.12; 95% CI, 0.72–1.74).

Treatment recommendation

We suggest that when ADP-receptor antagonists are given to suspected STEMI patients with a planned primary PCI approach, administration can occur in either the prehospital or in-hospital setting, but there is insufficient evidence to change existing practice (very-low-quality evidence, weak recommendation).

Values, preferences, and task force insights

In making this recommendation we place a higher value on not recommending adding complexity to prehospital treatment regimens over uncertain benefits.

There was no difference in mortality or major bleeding with either prehospital or in-hospital administration. We acknowledge, however, that although stent thrombosis was not considered as an outcome a priori, 1 study did report lower early (≤24 h) stent thrombosis rates with prehospital (0.8%) versus in-hospital administration (0%).[60] However, there were no differences in mortality, or their composite ischemic end points in this trial. The relevance of this very rare occurrence of early stent thromobosis in balance with the rare occurrence of additional bleeding if the patient underwent an emergency surgical strategy rather than PCI will need to be elucidated in further studies. Therefore, we find that the relative benefit to administering these agents prehospital versus in-hospital is marginal at best and may be offset by additional harms that could only be evaluated by larger RCTs that include these additional patient-oriented outcomes.

Prehospital anticoagulants versus none in STEMI (ACS 562)

Among adult patients with suspected STEMI outside of hospital transferred for primary PCI (P), does any anticoagulant administered prehospital (e.g., bivalirudin, dalteparin, enoxaparin, fondaparinux, UFH) (I), compared with no anticoagulant administered prehospital (C), change death, intracranial hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 non-RCT[61] enrolling 1702 patients undergoing PPCI for STEMI showing no benefit of prehospital UFH versus in-hospital UFH (OR, 1.07; 95% CI, 0.595–1.924).

For the important outcome of stroke, we have identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 non-RCT[61] enrolling 1702 patients undergoing PPCI for STEMI showing no benefit of prehospital UFH over in-hospital UFH (OR, 0.25; 95% CI, 0.034–3.136).

For the important outcome of myocardial infarction, we have identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 non-RCT[61] enrolling 1702 patients undergoing PPCI for STEMI showing no benefit of prehospital UFH over in-hospital UFH (OR, 0.979; 95% CI, 0.366–2.62).

For the important outcome of major bleeding, we have identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 non-RCT[61] enrolling 1702 patients undergoing PPCI for STEMI showing no benefit of prehospital UFH over in-hospital UFH (OR, 0.699; 95% CI, 0.466–1.047).

There was no direct evidence of other anticoagulant medications administered in the prehospital setting compared with in-hospital setting for STEMI patients.

Treatment recommendation

We suggest that when UFH is given in suspected STEMI patients with a planned primary PCI approach, administration can occur in either the prehospital or in-hospital setting, and there is insufficient evidence to change existing practice (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on not recommending adding complexity to prehospital treatment regimens over uncertain additional benefit.

Prehospital anticoagulants versus UFH in STEMI (ACS 568)

Among adult patients with suspected STEMI outside of a hospital transferred for primary PCI (P), does any anticoagulant prehospital (e.g., bivalirudin, dalteparin, enoxaparin, fondaparinux) (I), compared with UFH prehospital (C), change death, intracranial

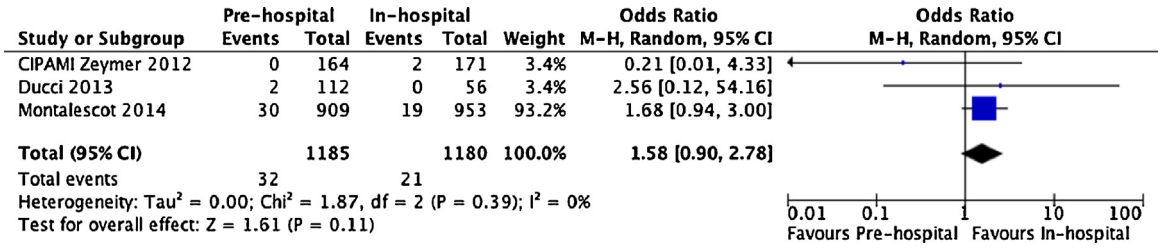

Fig. 4. Thirty-day mortality for prehospital versus in-hospital ADP-antagonist administration. Experimental = prehospital ADP-antagonist administration; control = in-hospital ADP-antagonist administration.

hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?

Consensus on science

Bivalirudin versus UFH RCTs. For the critical outcome of 30-day mortality, we have identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[62] enrolling 2218 patients transferred for PPCI for STEMI showing no benefit of prehospital bivalirudin compared with prehospital UFH (OR, 0.96; 95% CI, 0.59–1.56).

For the important outcome of stroke, we have identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[62] enrolling 2218 patients transferred for PPCI for STEMI showing no benefit of prehospital bivalirudin compared with prehospital UFH (OR, 0.55; 95% CI, 0.2–1.5).

For the important outcome of reinfarction, we have identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[62] enrolling 2218 patients transferred for PPCI for STEMI showing no benefit of prehospital bivalirudin compared with prehospital UFH (OR, 1.95; 95% CI, 0.90–4.22).

For the important outcome of major bleeding, we have identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[62] enrolling 2218 patients transferred for PPCI for STEMI showing a benefit of prehospital bivalirudin compared with prehospital UFH (OR, 0.5; 95% CI, 0.26–0.96).

Bivalirudin Non-RCTs. For the critical outcome of 30-day mortality, we have identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 2 non-RCTs[63,64] enrolling 543 patients transferred for PPCI for STEMI showing no benefit of prehospital bivalirudin compared with prehospital UFH (OR, 0.78; 95% CI, 0.39–1.56).

For the important outcomes of stroke and reinfarction, we have identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 non-RCT[64] enrolling 369 patients transferred for PPCI for STEMI showing no benefit of prehospital bivalirudin over prehospital UFH for stroke (OR, 0.86; 95% CI, 0.12–6.19) or reinfarction (OR, 0.86; 95% CI, 0.17–4.33).

For the important outcome of major bleeding, we have identified very-low-quality evidence (downgraded for indirectness and imprecision) from 2 non-RCTs[63,64] enrolling 543 patients transferred for PPCI for STEMI showing a benefit of prehospital bivalirudin compared with UFH (OR, 0.39; 95% CI, 0.2–0.76).

Enoxaparin Versus UFH. For the critical outcome of 30-day mortality, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[65] enrolling 910 patients transferred for PPCI for STEMI showing no benefit of prehospital enoxaparin compared with prehospital UFH (OR, 0.58; 95% CI, 0.32–1.08).

For the important outcome of stroke, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[65] enrolling 910 patients transferred for PPCI for STEMI showing no benefit of prehospital enoxaparin compared with prehospital UFH (OR, 3.08; 95% CI, 0.32–29.73).

For the important outcome of reinfarction, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[65] enrolling 910 patients transferred for PPCI for STEMI showing no benefit of prehospital enoxaparin compared with prehospital UFH (OR, 0.5; 95% CI, 0.90–4.22).

For the important outcome of major bleeding, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[65] enrolling 910 patients transferred for PPCI for STEMI showing no benefit of prehospital enoxaparin compared with prehospital UFH (OR, 0.61; 95% CI, 0.31–1.20).

Treatment recommendations

We have insufficient confidence in the treatment effect for prehospital administration of bivalirudin compared with prehospital administration of UFH in prehospital-identified STEMI patients to recommend a change in existing practice (weak recommendation, very-low-quality evidence).

We suggest that prehospital enoxaparin may be used as an alternative to prehospital UFH as an adjunct for primary PCI for STEMI (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation regarding bivalirudin, we place a higher value on not recommending new resource allocation for an intervention where the relative benefit is unclear.

In making this recommendation regarding enoxaparin, we place a higher value on recommending agents that may provide benefit with regard to the ease of administration and lack of need for monitoring.

In making these recommendations, it is important to also consider the related review on anticoagulants given to STEMI patients in the prehospital versus in-hospital setting. Only UFH has been evaluated directly in this setting without clear evidence of benefit. We are not recommending that systems implement anticoagulant administration in the prehospital setting. However, in recognizing that some systems are doing this routinely, we conducted this review to look at the relative benefit of one agent over another.

Although stent thrombosis was not considered as an a priori outcome, bivalirudin was strongly associated with the risk of acute stent thrombosis (RR, 6.11; 95% CI, 1.37–27.24).[62] Such association is also consistently reported in other published in-hospital studies and meta-analyses of this agent in patients undergoing PCI.[66,67] While the benefit of bivalirudin over UFH alone in reducing bleeding complications has been shown, this benefit has been challenged by the additional consistent risk of stent thrombosis. This stent thrombosis risk was considered by the task force in making its treatment recommendations.

Supplementary oxygen in ACS (ACS 887)

Among adult patients with suspected ACS and normal oxygen saturation in any setting (prehospital, emergency, or in-hospital)

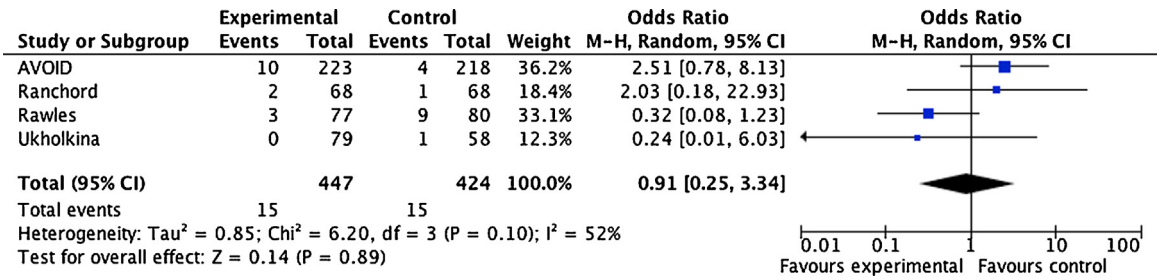

Fig. 5. Mortality in AMI patients when oxygen is withheld compared with routine administration. Experimental = oxygen withholding; control = routine supplementary oxygen.

(P), does withholding oxygen (I), compared with routine supplementary oxygen (C), change death, infarct size, chest pain resolution, ECG resolution (O)?

Consensus on science

For the critical outcome of mortality, we have identified very-low-quality evidence (downgraded for indirectness, heterogeneity, and bias) from 4 RCTs[68–71] enrolling 871 patients showing no benefit (OR, 0.91; 95% CI, 0.25–3.34) when oxygen is withheld compared with routine supplementary oxygen administration (Fig. 5).

For the important outcome of infarct size, we have identified very-low-quality evidence (downgraded for bias, inconsistency, indirectness, and imprecision) from 3 RCTs[68,70,71] enrolling 713 patients showing a small reduction in infarct size when oxygen is withheld compared with routine supplementary oxygen administration. Data from a fourth RCT suggesting increased infarct size when oxygen is withheld could not be used because of incomplete reporting and unvalidated methods.[69] The trial data generated for infarct size are too heterogeneous to enable combined assessment.

For the important outcome of chest pain resolution, we have identified very-low-quality evidence (downgraded for bias, inconsistency, indirectness, and imprecision) from 2 RCTs[68,72] enrolling 199 patients showing no difference when oxygen is withheld compared with routine supplementary oxygen administration.

For the important outcome of ECG resolution, no evidence has been identified in RCTs.

Treatment recommendation

We suggest withholding oxygen in comparison with routine oxygen supplementation in normoxic patients* with ACS† (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on avoiding possible harm when the evidence available suggests no mortality benefit and possible harm in providing routine oxygen supplementation.

We acknowledge the pending results of 2 additional trials addressing this topic. No data were identified for routine administration of oxygen with lower concentrations than those used in the reviewed trials (4–8 L min^{-1} via mask or nasal prongs). Oxygen saturation readings from pulse oximetry should be interpreted with caution, and every effort should be made to recognize and correct patient- or equipment-related factors that might lead to inaccurate results.

Knowledge gaps

We await the pending results of two trials addressing the benefit and safety of administration of supplementary oxygen in ACS patients.

Reperfusion decisions in STEMI

This section addresses the questions of which reperfusion strategy is best under specific circumstances. Which options are available for reperfusion will depend on the local prehospital system and availability of PCI centers. Some prehospital systems include physicians or highly trained personnel that can safely administer prehospital fibrinolysis. Some regions have short transport times to PCI, and STEMI patients can be triaged and transported directly to PCI. The questions in this section consider reperfusion decisions in relation to regional availability (e.g., prehospital fibrinolysis versus ED fibrinolysis or prehospital fibrinolysis versus transport direct for PCI). Table 2 outlines the systematic reviews in this section including the setting where the reperfusion is being made and the intervention versus comparator.

Where there are strong recommendations, regions should consider if these could be implemented safely to provide the same benefits found in the studies. Alternatively, where there are weak recommendations, the current resources and system may determine what option would work best. When reperfusion is the planned strategy, this should occur as soon as possible after diagnosis.

Prehospital fibrinolysis may have advantages when there are long transport times. As the transport time shortens, any expected advantage is lost. These advantages need to be weighed against the resources required to implement this and the alternatives available. Thus, if PCI is available, time to transport to PCI is a more important determinant of the decision. Several of the systematic reviews focused on specific decisions of fibrinolysis versus PCI based on the regional resources or "system."

As fibrinolysis is still a viable option in many systems, some of the reviews addressed whether routine angiography (with PCI if indicated) should be undertaken when fibrinolysis has been administered versus only ischemia-guided (rescue) angiography and in what time frame. These decisions may be dependent on whether PCI is available on-site or via transport.

Although the 2010 CoSTR recommended PCI as the preferred reperfusion strategy for STEMI, the benefit is mostly reflected in lower reinfarction rates, such that fibrinolysis and early transfer for angiography may be a reasonable alternative in settings where access to PCI may be limited or delayed (geographic, resources, time of day).[46] Benefit is less clear if PCI is not performed in high-volume centers by experienced operators. Patient transfer should be within a well-organized system of care including adequate patient surveillance and capability of treating complications such as cardiac arrest.

One of the reviews specifically addressed PCI versus fibrinolysis based on the time from symptoms to provide a summary of the evidence for early presenters versus other time frames. The recommendations depend on any associated delays to PCI and can be used to provide a framework to make decisions for individual systems. Because the other questions did not separately address early presenters or time from symptom onset, this review is key

Table 2
Reperfusion decisions in STEMI: 2015 topics.

	Decision setting	Intervention	Comparator
Prehospital fibrinolysis versus ED fibrinolysis[338]	Prehospital	Prehospital FL	ED FL
Prehospital triage to PCI center versus prehospital fibrinolysis[341]	Prehospital	Prehospital FL	Triage to PPCI
ED fibrinolysis and immediate PCI versus immediate PCI alone[882]	ED	FL + immediate PCI (within 1–4 h)	PPCI
Delayed PCI versus fibrinolysis stratified by time from symptoms[337]	Any setting	PPCI	FL (time dependent)
Transport for PCI versus ED fibrinolysis and transport only for rescue PCI[332]	ED	FL + transport only for rescue PCI	Transport to PCI
ED fibrinolysis and routine early angiography versus transport for PCI[779]	ED	FL + routine transport to PCI	Transport to PCI
ED fibrinolysis and then transport for early angiography versus only rescue PCI[334]	ED	FL + routine transport to PCI	FL + transport only for rescue PCI

ED indicates emergency department; FL, fibrinolysis; PCI, percutaneous coronary intervention; and PPCI, primary percutaneous coronary intervention.

to providing context that can be incorporated into the specific system decisions. These recommendations must be considered in the context of specific patients (gender, age, comorbidities, vascular territory of infarct); some patients have relative contraindications to fibrinolysis and/or may have such little additional benefit from reperfusion that only a low-risk option is beneficial.

The PCI trials excluded patients with contraindications to thrombolysis, high-risk patients who presented with cardiogenic shock, and those in whom femoral vascular access was unobtainable. Patients who were excluded for contraindication to thrombolysis or were in shock usually underwent primary PCI. Fibrinolysis may be relatively or absolutely contraindicated in some patients, making PPCI necessary regardless of the time frame.

Prehospital fibrinolysis versus ED fibrinolysis (ACS 338)

Among adults who are suspected of having STEMI outside of a hospital (P), does prehospital fibrinolysis (I), compared with in-hospital fibrinolysis(C), change death, intracranial hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?

Consensus on science

For the critical outcome of hospital mortality, we have identified moderate-quality evidence (downgraded for imprecision) from 3 RCTs[73–75] enrolling 531 patients showing benefit for prehospital fibrinolysis compared with in-hospital fibrinolysis (OR, 0.46; 95% CI, 0.23–0.93) (Fig. 6).

For the critical outcome of intracranial hemorrhage, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[74,75] enrolling 438 patients showing no additional harm from prehospital fibrinolysis compared with in-hospital fibrinolysis (OR, 2.14; 95% CI, 0.39–11.84).

For the important outcome of bleeding, we have identified low-quality evidence (downgraded for imprecision) from 2 RCTS[74,75] enrolling 438 patients showing no additional harm from prehospital fibrinolysis compared with in-hospital fibrinolysis (OR, 0.96; 95% CI, 0.40–2.32).

For other outcomes (revascularization, reinfarction, and ischemic stroke), no evidence from RCTs was found.

Treatment recommendation

When fibrinolysis is the planned treatment strategy, we recommend using prehospital fibrinolysis in comparison with in-hospital fibrinolysis for STEMI in systems where the transport times are commonly greater than 30 min and can be accomplished by prehospital personnel using well-established protocols, comprehensive training programs, and quality assurance programs under medical oversight (strong recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the reduction of mortality compared with no increased evidence of complications and consideration of the significant resource implications to implement a prehospital fibrinolysis program.

With the advent of more PPCI availability, in some areas the comparison of prehospital fibrinolysis to PPCI is more relevant (see the next systematic review on this topic).

The 3 studies that formed this evidence were all conducted more than 20 years ago. Since those studies showed combined benefit in mortality, no further RCTs have directly addressed this same question. To determine if there was more recent non-RCT evidence that might support or refute these early studies, a post hoc review was done and 1 relevant non-RCT was found from the last 5 years.[76] The review of this study confirmed the inherent risk of bias of a non-RCT. However, the study had similar findings of no greater harm from prehospital fibrinolysis, although it did not show the same potential mortality benefit.

The real advantage of prehospital fibrinolysis is where transport times are greater than 30 min. These RCTs were conducted in healthcare settings with a difference in time between prehospital treatment and in-hospital treatment of 33–52 min. Transport times to hospital were 38–60 min. As the transport time shortens, any expected advantage is lost.

The systems in the included studies included physician and other prehospital professionals who administered fibrinolysis by using well-established protocols, comprehensive training programs, and quality assurance programs under medical oversight.

Prehospital triage to PCI center versus prehospital fibrinolysis (ACS 341)

Among adult patients with suspected STEMI outside of a hospital (P), does direct triage and transport to a PCI center (I), compared with prehospital fibrinolysis (C), change death, intracranial hemorrhage, major bleeding (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified moderate-quality evidence (downgraded for imprecision) from 4 RCTs[77–80] enrolling 2887 STEMI patients showing no differential benefit to either therapy (direct triage and transport to a PCI center compared with prehospital fibrinolysis) (OR, 1.03; 95% CI, 0.72–1.46) (Fig. 7).

For the critical outcome of 1-year mortality, we have identified moderate-quality evidence (downgraded for imprecision) from 2 RCTs[80,81] enrolling 1877 STEMI patients showing no difference

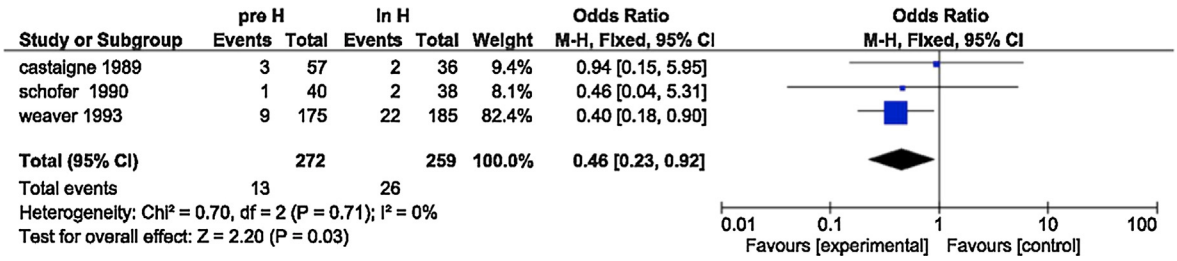

Fig. 6. Hospital mortality for prehospital fibrinolysis versus in-hospital fibrinolysis. Experimental = prehospital fibrinolysis; control = in-hospital fibrinolysis.

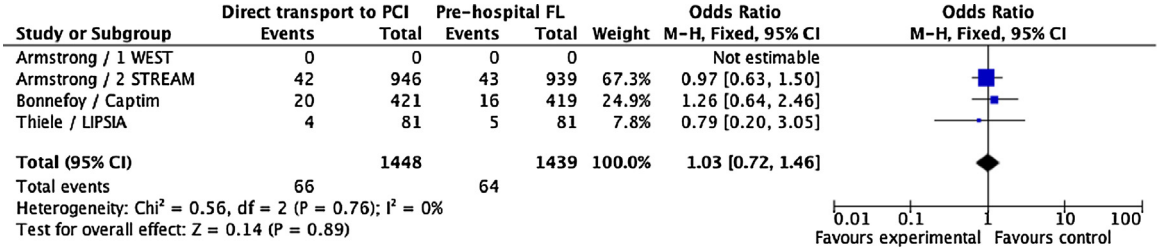

Fig. 7. Thirty-day mortality for prehospital triage to PCI center versus prehospital fibrinolysis. Experimental = prehospital triage to PCI center; control = prehospital fibrinolysis.

between direct triage and transport to a PCI center compared with prehospital fibrinolysis (OR, 0.88; 95% CI, 0.60–1.27).

For the critical outcome of intracranial hemorrhage, we have identified moderate-quality evidence (downgraded for imprecision) from 4 RCTs[77–80] enrolling 2887 STEMI patients showing less harm with direct triage and transport to a PCI center compared with prehospital fibrinolysis (OR, 0.21; 95% CI, 0.05–0.84).

Treatment recommendations

We suggest that where PCI facilities are available in a geographic region, that direct triage and transport for PCI is preferred (weak recommendation, low-quality evidence). There is moderate evidence that mortality is not reduced and low-quality evidence of harm from fibrinolysis.

We suggest that where PCI facilities are not available in a geographic region, that prehospital fibrinolysis is a reasonable alternative to triage and transport directly to PCI.

Values, preferences, and task force insights

In making this recommendation, we are placing a higher value on avoiding iatrogenic harm and a lower value on uncertain benefits on survival. Given the lack of mortality benefit, we are not suggesting the addition of new PCI facilities for this indication and recognize that concentration in fewer high-volume centers may provide better outcomes.

ED fibrinolysis and immediate PCI versus immediate PCI alone (ACS 882)

Among adults who are having STEMI in the ED (P), does fibrinolytic administration combined with immediate PCI (I), compared with immediate PCI alone (C), change death, intracranial hemorrhage, reinfarction, urgent target vessel revascularization, major bleeding (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified moderate-quality evidence (downgraded for imprecision) from 5 RCTs[82–86] enrolling 3533 patients showing no benefit when fibrinolytic administration is combined with immediate PCI versus immediate PCI alone (OR, 1.29; 95% CI, 0.96–1.74) (Fig. 8).

For the critical outcome of intracranial hemorrhage, we have identified moderate-quality evidence (downgraded for imprecision) from 3 RCTs[82,83,86] enrolling 3342 patients showing harm when fibrinolytic administration is combined with immediate PCI versus immediate PCI alone (OR, 7.75; 95% CI, 1.39–43.15) (Fig. 9).

For the important outcome of nonfatal myocardial infarction, we have identified low-quality evidence (downgraded for bias, inconsistency, and imprecision) from 5 RCTs[82–86] enrolling 3498 patients showing no benefit when fibrinolytic administration is combined with immediate PCI versus immediate PCI alone (OR, 1.15; 95% CI, 0.73–1.81).

For the important outcome of target vessel revascularization, we have identified low-quality evidence (downgraded for inconsistency and imprecision) from 4 RCTs[82–84,86] enrolling 3360 patients showing no benefit when fibrinolytic administration is combined with immediate PCI versus immediate PCI alone (OR, 1.16; 95% CI, 0.91–1.47).

For the important outcome of major bleeding, we have identified high-quality evidence from 5 RCTs[82–86] enrolling 3543 patients showing harm when fibrinolytic administration is combined with immediate PCI versus immediate PCI alone (OR, 1.52; 95% CI, 1.05–2.20).

Treatment recommendation

We recommend against the routine use of fibrinolytic administration combined with immediate* PCI, compared with immediate PCI alone in patients with STEMI (strong recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on avoiding harm (intracranial hemorrhage and major bleeding), given that the evidence suggests no mortality benefit for fibrinolytic administration combined with immediate PCI.

Delayed PCI versus fibrinolysis stratified by time from symptoms (ACS 337)

Among patients with STEMI stratified by time from symptom onset to presentation when fibrinolysis is readily available (P), does

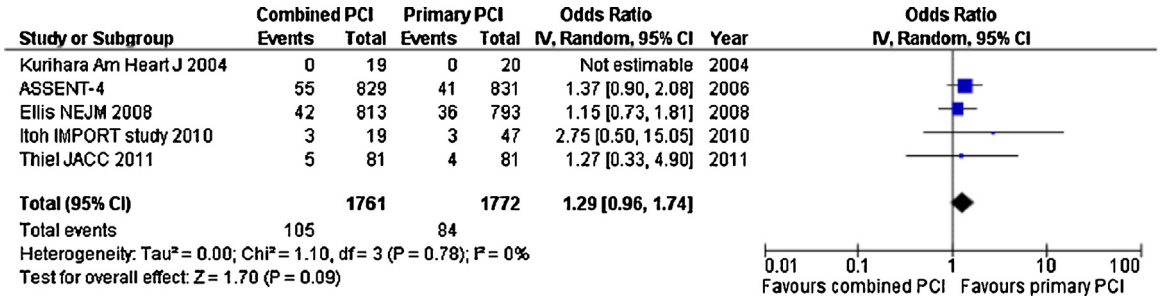

Fig. 8. Thirty-day mortality for ED fibrinolysis and immediate PCI versus immediate PCI alone. Experimental = combined PCI; control = primary PCI.

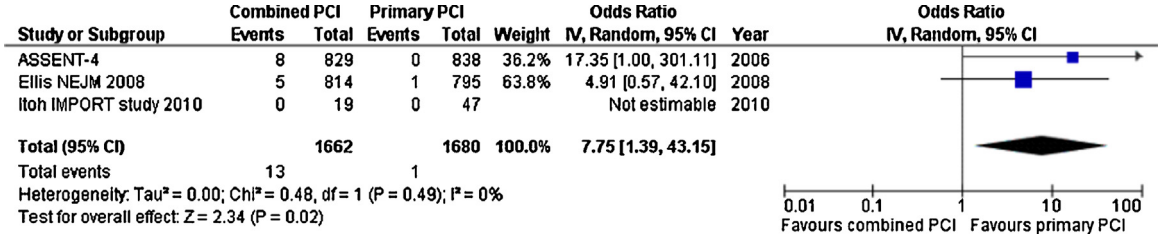

Fig. 9. Intracranial hemorrhage for ED fibrinolysis and immediate PCI versus immediate PCI alone. Experimental = combined PCI; control = primary PCI.

delayed PCI (I), compared with fibrinolysis (C), change mortality, reinfarction, major bleeding, intracranial hemorrhage (O)?

Consensus on science

In STEMI patients presenting less than 2 h after symptom onset in whom immediate PPCI will delay treatment 60–160 min compared with fibrinolysis. For the critical outcome of 30-day mortality, we have identified low-quality evidence (downgraded for indirectness and imprecision) from a combined analysis of 2 RCTs[87] enrolling 646 patients showing greater harm with delayed PPCI compared with fibrinolysis (OR, 2.6; 95% CI, 1.2–5.64).

For the critical outcome of 5-year mortality, we have identified low-quality evidence (downgraded for indirectness and imprecision) from 1 RCT[88] enrolling 449 patients showing greater harm with delayed PPCI compared with fibrinolysis (OR, 2.03; 95% CI, 1.1–4.08).

For the important outcome of reinfarction, we have identified low-quality evidence (downgraded for indirectness and imprecision) from a combined analysis of 2 RCTs[87] enrolling 657 patients showing no difference between delayed PPCI compared with fibrinolysis (OR, 0.43; 95% CI, 0.17–1.1).

For the important outcome of severe bleeding we have identified low-quality evidence (downgraded for indirectness and imprecision) from 1 RCT[89] enrolling 455 patients showing no difference in delayed PPCI compared with fibrinolysis (OR, 0.33; 95% CI, 0.01–8.15).

In STEMI patients presenting 2–6 h after symptom onset in whom PPCI will delay treatment 60–160 min compared with fibrinolysis. For the critical outcome of 30-day mortality, we have identified low-quality evidence (downgraded for indirectness and imprecision) from a combined analysis of 2 RCTs[87] enrolling 508 patients showing no benefit of delayed PPCI over fibrinolysis (1-year mortality OR, 0.85; 95% CI, 0.42–1.74).

For the critical outcome of 5-year mortality, we have found low-quality evidence (downgraded for indirectness and imprecision) from 1 RCT[88] enrolling 367 patients showing no benefit of fibrinolysis over delayed PPCI (OR, 0.99; 95% CI, 0.55–1.77).

For the important outcome of reinfarction, we have identified low-quality evidence (downgraded for indirectness and imprecision) from a combined analysis of 2 RCTs[87] enrolling 511 patients showing no difference (OR, 0.4; 95% CI, 0.13–1.22).

For the important outcome of severe bleeding, we have identified low-quality evidence (downgraded for indirectness and imprecision) from 1 RCT[89] enrolling 375 patients showing greater harm from delayed PPCI compared with fibrinolysis (OR, 8.18; 95% CI, 1.01–66.04).

In STEMI patients presenting 3–12 h after symptom onset in whom PPCI will delay treatment 60–140 min compared with fibrinolysis. For the critical outcome of 30-day mortality, we have identified very-low-quality evidence (downgraded for bias, indirectness, and imprecision) from 1 RCT[90] enrolling 295 patients showing benefit of delayed PPCI (mean fibrinolysis-to-balloon delay of 85 ± 28 min) over immediate fibrinolysis (OR, 0.35; 95% CI, 0.16–0.79).

Other analyses. A reanalysis of the raw data from 16 RCTs comparing 30-day mortality between fibrin-specific fibrinolysis and PPCI[91] has suggested that the acceptable fibrinolysis to PPCI delay varies depending on the patient's baseline risk and presentation delay (low-quality evidence, downgraded for inconsistency and indirectness). Patients with higher risk including Killip class >1, may benefit from PPCI even when there are treatment delays up to 120 min. The acceptable delay may range from 35 min when the risk is low (4%) through to greater than 5 h for high risk (18%). A pragmatic simplification of the formula derived in the analysis has been suggested in the associated editorial: Patients over 65 years of age, and all patients in Killip class greater than 1, should be treated with PPCI.[92] Patients less than 65 years of age in Killip class 1 should have PPCI unless delay is greater than 35 min.

Two observational studies[93,94] used propensity-matched analysis of the national registry of myocardial infarction registry, so they were not included in the original search strategy of RCTs only. The findings suggest an upper time limit for delay of 120 min overall.

Treatment recommendations (Table 3)

In patients with STEMI presenting less than 2 h after symptom onset, when PPCI will result in a delay of greater than 60 min, we suggest fibrinolysis in comparison with PPCI (weak recommendation, low-quality evidence).

Table 3
Most appropriate reperfusion strategy according to time from symptom onset and anticipated treatment delays.

Treatment delays, minutes	Time from symptom onset		
	<2 h	2–3 h	3–6 h[a]
<60	PPCI	PPCI or FL[b]	PPCI
60 to 120	FL[b]	PPCI or FL[b]	PPCI
>120	FL[b]	FL[b]	FL[b]

Patients with higher risk, including Killip class >1, may benefit from PPCI even when there are treatment delays up to 120 min.

[a] If time from symptom onset is greater than 6 h, PPCI is appropriate regardless of treatment delays.

[b] In case of fibrinolytic therapy, immediate transfer to a percutaneous coronary intervention center after fibrinolysis should be considered for cardiac angiography within 3–24 h.

FL indicates fibrinolysis; and PPCI, primary percutaneous coronary intervention.

In patients with STEMI presenting 2–3 h after symptom onset, when PPCI will result in a delay of 60–120 min, we suggest either fibrinolysis or PPCI (weak recommendation, low-quality evidence).

In patients with STEMI presenting 3–12 h after symptom onset, when PPCI will result in a delay of up to 120 min, we suggest PPCI in comparison with fibrinolysis (weak recommendation, very-low-quality evidence).

The evidence does not differentiate the late presenters with long delays to PCI. It is acknowledged that fibrinolysis becomes significantly less effective more than 6 h after symptom onset and, thus, a PPCI may be the ideal option in patients more than 6 h after symptom onset, even if this can only be accomplished with a long delay to PPCI (e.g., more than 120 min).

When long delays to PPCI are anticipated (more than 120 min), a strategy of immediate fibrinolysis followed by routine early (within 3–24 h) angiography and PCI, if indicated, is reasonable (ACS 334).

Values, preferences, and task force insights

In making this recommendation, we place a high priority on the evidence of mortality benefit; however, we acknowledge that geographic and resource factors may limit the availability of PPCI.

Knowledge gaps

Further evidence is required on the maximal treatment delay for PCI versus fibrinolytic therapy by patient characteristics.

ED fibrinolysis and transport only for rescue PCI versus transport for PCI (ACS 332)

Among adult patients with STEMI in the ED (of a non-PCI-capable hospital) (P), does transfer to a PCI center (I), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (C), change short-term survival, stroke, major bleeding, reinfarction (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified moderate-quality evidence (downgraded for serious risk of bias) from 8 RCTs[90,95–101] enrolling 3119 patients showing benefit of transfer without fibrinolysis to a PCI center compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI in the first 24 h (OR, 0.66; 95% CI, 0.50–0.86) (Fig. 10).

For the important outcome of reinfarction, we have identified moderate-quality evidence (downgraded for serious risk of bias) from the same 8 RCTs[90,95–101] enrolling 3119 patients showing benefit of transfer without fibrinolysis to a PCI center compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI in the first 24 h (OR, 0.33; 95% CI, 0.21–0.51).

For the important outcome of stroke, we have identified moderate-quality evidence (downgraded for serious risk of bias) from the same 8 RCTs[90,95–101] enrolling 3119 patients showing benefit of transfer without fibrinolysis to a PCI center compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI in the first 24 h (OR, 0.41; 95% CI, 0.22–0.76).

For the important outcome of major hemorrhage, we have identified very-low-quality evidence (downgraded for serious risk of bias, imprecision, and publication bias) from 2 RCTs[97,100] enrolling 550 patients showing no benefit of transfer without fibrinolysis to a PCI center compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI in the first 24 h (OR, 0.68; 95% CI, 0.20–2.29).

Treatment recommendation

For adult patients presenting with STEMI in the ED of a non-PCI-capable hospital, we recommend emergency transfer without fibrinolysis to a PCI center as opposed to immediate in-hospital fibrinolysis and transfer only for rescue PCI (strong recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we put great weight on the patient benefits of mortality, reinfarction, and stroke with no additional harm in terms of major hemorrhage.

ED fibrinolysis and routine early angiography versus transport for PCI (ACS 779)

Among adult patients with STEMI in the ED of a non-PCI-capable hospital (P), does immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h) (I), compared with transfer to a PCI center (C), change 30-day mortality, stroke, major bleeding, reinfarction (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 2 RCTs[80,102] enrolling 337 patients with STEMI showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 0.84; 95% CI, 0.24–2.98) (Fig. 11).

For the critical outcome of 30-day mortality, we have also identified 1 non-RCT enrolling 1714 patients[103] of very-low-quality evidence (downgraded for risk of bias and imprecision), showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 0.86; 95% CI, 0.48–1.55).

For the critical outcome of intracranial hemorrhage, we have identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from the same 2 RCTs[80,102] enrolling 337 patients with STEMI showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 3.14; 95% CI, 0.13–78.08).

For the important outcome of reinfarction, we have identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from the same 2 RCTs[80,102] enrolling 337 patients with STEMI showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 2.11; 95% CI, 0.51–8.64).

For the important outcome of reinfarction, we also identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 non-RCT enrolling 1714 patients[103] showing no

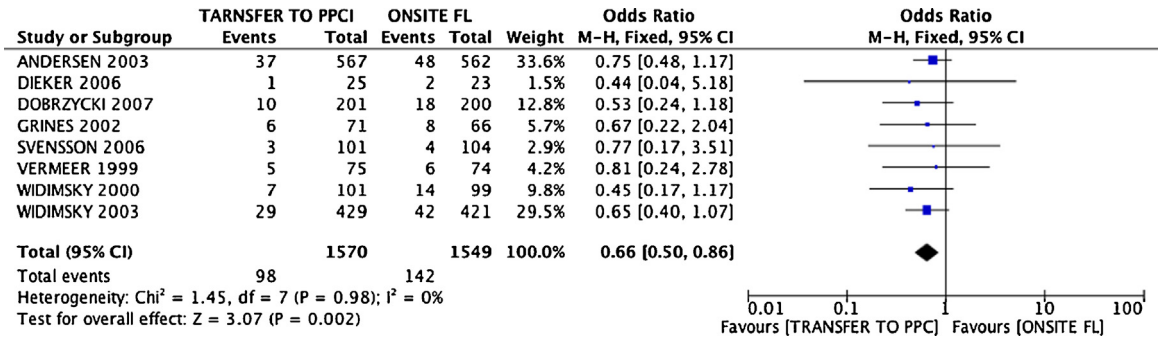

Fig. 10. Thirty-day mortality for ED transport for PCI versus fibrinolysis and transport only for rescue PCI. Experimental = transfer to PCI; control = onsite fibrinolysis. FL indicates fibrinolysis.

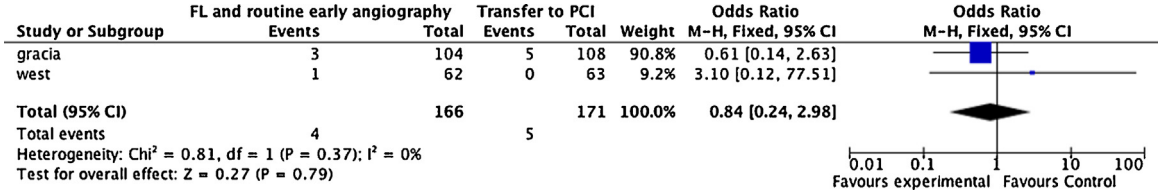

Fig. 11. Thirty-day mortality for ED fibrinolysis and routine early angiography versus transport for PCI. Experimental = ED fibrinolysis and routine early angiography; control = transport for PCI. FL indicates fibrinolysis.

differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 2.2; 95% CI, 0.73–6.61).

For the important outcome of stroke, we have identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from the same 2 RCTs[80,102] enrolling 416 patients with STEMI showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 0.96; 95% CI, 0.06–15.58).

For the important outcome of stroke, we also identified 1 non-RCT enrolling 1714 patients[103] of very-low-quality evidence (downgraded for risk of bias and imprecision) showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 1.52; 95% CI, 0.41–5.67).

For the important outcome of major bleeding, we have identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from the same 2 RCTs[80,102] enrolling 337 patients with STEMI showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 1.33; 95% CI, 0.32–5.47).

For the important outcome of major bleeding, we also identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 non-RCT[103] enrolling 1714 patients with STEMI showing no differential benefit of immediate in-hospital fibrinolysis and routine transfer for angiography compared with transfer to a PCI center (OR, 0.65; 95% CI, 0.26–1.63).

Treatment recommendation

We suggest fibrinolytic therapy with routine transfer for angiography as an alternative to immediate transfer to PCI for patients presenting with STEMI in the ED of a non-PCI-capable hospital (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

This recommendation indicates that either therapy would be appropriate according to the evidence. Fibrinolysis and routine transfer may be appropriate where patients cannot be transferred to a PCI-capable center in a timely manner. Alternatively, transfer to PCI may be appropriate when this can be accomplished quickly or the patient has greater risks with fibrinolysis. Given the lack of mortality benefit, if transport directly to PCI is delayed, fibrinolysis before transport for routine early angiography is a reasonable option. We are not suggesting the addition of new PCI facilities for this indication and recognize that fewer high-volume centers may provide better outcomes.

ED fibrinolysis and then routine early angiography versus only rescue PCI (ACS 334)

Among adult patients with STEMI in the ED (of a non-PCI-capable hospital) who have received immediate in-hospital fibrinolysis (P), does routine transport for angiography at 3–6 h (or up to 24 h) (I), compared with only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (C), change death, intracranial hemorrhage, major bleeding, stroke, reinfarction (O)?

Consensus on science

For the critical outcome of 30-day mortality, we have identified moderate-quality evidence (downgraded for imprecision) from 7 RCTs[80,101,104–108] enrolling 2355 patients showing no differential benefit to either therapy (immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h) (OR, 0.96; 95% CI, 0.64–1.44) (Fig. 12).

For the critical outcome of 1-year mortality, we have identified moderate-quality evidence (downgraded for imprecision) from 6 RCTs[80,104,105,108–110] enrolling 2275 STEMI patients showing no benefit to either therapy (immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h) (OR, 0.54; 95% CI, 0.16–1.89).

For the critical outcome of intracranial hemorrhage, we have identified moderate-quality evidence (downgraded for imprecision) from 6 RCTs[80,104–108] enrolling 2156 STEMI patients, showing no differential harm from either therapy (immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h), compared with immediate in-hospital fibrinolysis and only

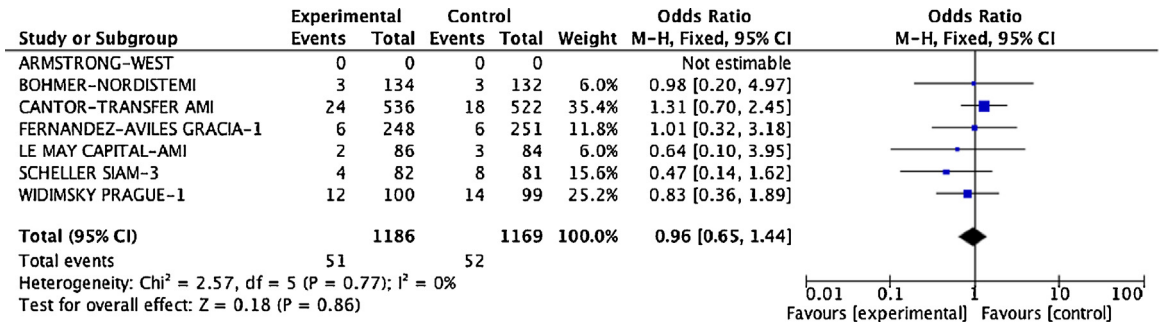

Fig. 12. Thirty-day mortality for ED fibrinolysis and then routine early angiography versus only rescue PCI. Experimental = ED fibrinolysis and then routine early angiography; control = fibrinolysis and only rescue PCI.

transfer for ischemia-driven PCI (rescue PCI) in first 24 h) (OR, 0.71; 95% CI, 0.34–1.44).

For the important outcome of major bleeding, we have identified moderate-quality evidence (downgraded for imprecision) from 6 RCTs[80,104–108] enrolling 2156 STEMI patients showing no differential harm from either therapy (immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h) (OR, 0.88; 95% CI, 0.61–1.27).

For the important outcome of stroke we have identified moderate-quality evidence (downgraded for imprecision) from 4 RCTs[101,104,106,108] enrolling 798 STEMI patients showing no differential harm from either therapy (immediate in-hospital fibrinolysis and routine transfer for angiography at 3 to 6 h (or up to 24 h), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h) (OR, 0.99; 95% CI, 0.39–2.51).

For the important outcome of reinfarction, we have identified moderate-quality evidence (downgraded for risk of bias) from 7 RCTs[80,101,104–108] in 2355 patients of benefit of immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (OR, 0.57; 95% CI, 0.38–0.85).

Treatment recommendation

After fibrinolysis of STEMI patients in the ED (when primary PCI is not available on-site), we suggest transport for early routine angiography in the first 3–6 h (or up to 24 h) rather than only transport for ischemia-guided angiography (weak recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this suggestion, we place a higher value on a measurable benefit in the important outcome of reinfarction despite no apparent benefit in 30-day or 1-year mortality and with no harm from bleeding or stroke. However, there may be circumstances or geography where transfer for angiography within 24 h is particularly difficult or not available. In these cases, the small measurable benefit in reinfarction only may not outweigh any prolonged or difficult transfer.

Knowledge gaps

- The current evidence indicates that PCI at 3–24 h after fibrinolysis reduces reinfarction. The optimal timing within this time window has not been elucidated. Similarly, the optimal management is unclear for patients after fibrinolysis in remote areas where transport to PCI is difficult or prolonged.

Hospital reperfusion decisions after ROSC

There are widely accepted published guidelines surrounding the treatment of STEMI and NSTEMI in the general adult population that are endorsed by the ILCOR community. The evidence used to generate these guidelines did not specifically address patient populations who experienced OHCA and subsequently had ROSC. The management of this patient group, particularly patients having prolonged resuscitation and nonspecific ECG changes, has been controversial because of the lack of specific evidence and significant implications on use of resources.

The majority of patients who have an OHCA have underlying ischemic heart disease. Acute coronary artery occlusion is known to be the precipitating factor in many of these patients. While coronary artery occlusion after cardiac arrest is frequently associated with ECG ST elevation or left bundle branch block, it can also occur in the absence of these findings. In fact, it has been recognized from several large observational series that absence of ST elevation may be associated with acute coronary occlusion in patients with ROSC after OHCA.[111] Similarly, ST elevation after OHCA may be temporary and does not always correlate with an acute coronary artery occlusion.

In 2010, ILCOR completed a single evidence review to examine all adult patients with OHCA and ROSC, inclusive of patients with and without ST elevation. In clinical practice, ACS with and without ST elevation are clinically distinct syndromes that are managed with guidelines that promote specific time to intervention targets for STEMI, while less time-sensitive strategies are recommended for non-ST elevation ACS. For this reason, the evidence review of this topic has been stratified to reflect the need to give guidance specific to each subset (ST elevation and no ST elevation) of the post-OHCA population.

PCI after ROSC with ST elevation (ACS 340)

Among adult patients with ROSC after cardiac arrest with evidence of ST elevation on ECG (P), does emergency cardiac catheterization laboratory evaluation* (I), compared with cardiac catheterization later in the hospital stay or no catheterization (C), change hospital mortality and neurologically favorable survival (O)?

Consensus on science

For the critical outcome of hospital mortality in patients with ROSC after cardiac arrest with ST elevation on ECG, we have identified very-low-quality evidence (downgraded for serious risk of bias and inconsistency and upgraded for large treatment effect) from 15 observational studies[112–126] enrolling 3800 patients showing benefit of emergency cardiac catheterization versus

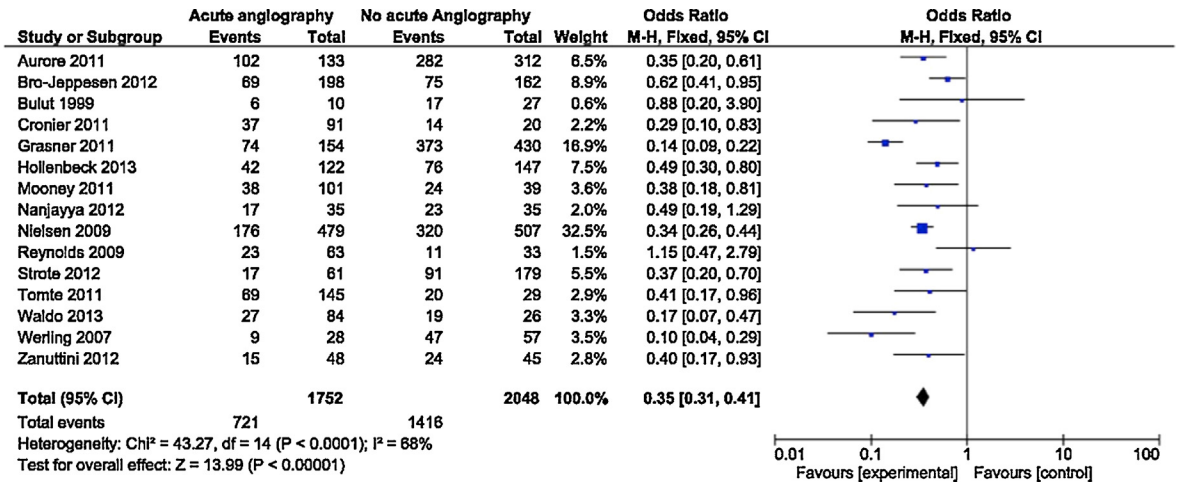

Fig. 13. Hospital mortality for patients with ROSC after cardiac arrest with ST elevation: emergency cardiac catheterization versus delayed or no cardiac catheterization.

cardiac catheterization later in the hospital stay or no catheterization (OR, 0.35; 95% CI, 0.31–0.41) (Fig. 13).

For the critical outcome of neurologically favorable survival in patients with ROSC after cardiac arrest with ST elevation on ECG, we have identified very-low-quality evidence (downgraded for serious risk of bias and inconsistency and upgraded for large treatment effect) from 9 observational studies,[112–114,117,119–122,124] enrolling 2919 patients showing benefit of emergency cardiac catheterization versus cardiac catheterization later in the hospital stay or no catheterization (OR, 2.54; 95% CI, 2.17–2.99).

Treatment recommendation

We recommend emergency[†] cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select[‡] adult patients with ROSC after OHCA of suspected cardiac origin with ST elevation on ECG (strong recommendation, low-quality evidence).

[†]*Time frame for treatment.* The time frame for emergency catheterization has been variably defined in the evidence reviewed. In general, patients were managed to minimize door-to-reperfusion times in a manner similar to the general STEMI patient population. The complexity and heterogeneity of this patient group may delay their resuscitation and management.

[‡]*Patient selection.* The evidence base was nonrandomized case-control studies that were subject to a high level of selection bias. The decision to undertake emergency cardiac catheterization was frequently made at the discretion of the treating physician, and the patient's likelihood of survival is likely to have influenced the decision to undertake the intervention. A variety of factors were more likely to be associated with cardiac catheterization (Table 4): male gender, younger age, ventricular fibrillation as the presenting cardiac arrest rhythm; witnessed arrest; and bystander CPR, being supported with vasopressors or left ventricular assist devices. Those patient characteristics that were less likely to be associated with angiography were diabetes mellitus, renal failure, and heart failure.

Values, preferences, and task force insights

In making this recommendation, we placed a higher value on survival and good neurologic outcome over resource utilization. Although the evidence was low-quality because it involved observational studies of selected patients, the strength of the benefit was large and consistent in numerous studies. Given that the evidence derives from selected patients, this recommendation is not intended to apply to all post-ROSC patients with ST elevation; however, a systematic emergency assessment and consideration of all of these patients is warranted.

We recognize that the capacity to deliver emergency cardiac catheterization is not readily available in all healthcare settings. These recommendations are particularly relevant where primary PCI is available as part of the system of care. We suggest that emergency cardiac catheterization be incorporated in a standardized post-cardiac arrest protocol as part of an overall strategy to improve neurologically intact survival in this patient group. Targeted temperature management is now recommended in patients with ROSC after OHCA. The evidence reviewed demonstrated the feasibility of combining emergency cardiac catheterization and PCI with the early implementation of targeted temperature management.

PCI after ROSC without ST elevation (ACS 885)

Among adult patients with ROSC after cardiac arrest without evidence of ST elevation on ECG (P), does emergency cardiac catheterization laboratory evaluation (I), compared with cardiac catheterization later in the hospital stay or no catheterization (C), change hospital mortality and neurologically favorable survival (O)?

Consensus on science

For the critical outcome of hospital mortality in patients with ROSC after cardiac arrest without ST elevation on ECG, we have identified very-low-quality evidence (downgraded for risk of bias) from 2 observational studies[112,117] enrolling 513 patients showing benefit from emergency cardiac catheterization laboratory evaluation compared with catheterization laboratory evaluation later in the hospital stay or no catheterization (OR, 0.51; 95% CI, 0.35–0.73) (Fig. 14).

For the critical outcome of neurologically favorable survival (CPC 1 or 2) in patients with ROSC after cardiac arrest without ST elevation on ECG, we have identified very-low-quality evidence (downgraded for risk of bias) from 2 observational studies[112,117] enrolling 513 patients showing benefit from emergency cardiac catheterization laboratory evaluation compared with catheterization laboratory evaluation later in the hospital stay or no catheterization (OR, 1.96; 95% CI, 1.35–2.85).

Table 4
Patient characteristics and confounding variables in studies of patients selected for angiography after ROSC with ST elevation1.

	Number of studies	Number of patients	CAG	No/delayed CAG	Risk difference (95% CI)	*P* value
1.2 Male gender	8	1828	0.76	0.64	0.12 (0.0 to 0.19)	0.0002
1.3 Diabetes mellitus	5	870	0.13	0.18	−0.05 (−0.1 to 0.00)	0.05
1.4 Hypertension	5	817	0.37	0.43	−0.06 (−0.12 to 0.01)	0.09
1.5 Renal failure	2	600	0.01	0.06	−0.04 (−0.08 to 0.00)	0.007
1.6 Stroke	2	600	0.05	0.13	−0.8 (−0.18 to 0.02)	0.12
1.7 VF rhythm	7	1472	0.78	0.47	0.31 (0.26 to 0.35)	0.0001
1.8 Witnessed CA	5	1026	0.88	0.83	0.05 (0.01 to 0.09)	0.02
1.9 Bystander CPR	6	1361	0.48	0.44	0.05 (−0.01 to 0.12)	0.10
1.10 Therapeutic hypothermia	3	711	0.66	0.56	0.09 (0.02 to 0.17)	0.01
1.11 LVSD	2	339	0.25	0.01	0.25 (0.18 to 0.31)	<0.0001
1.12 Vasopressors	3	771	0.31	0.13	0.18 (0.12 to 0.25)	<0.0001
1.13 Heart failure	3	739	0.20	0.39	−0.18 (−0.24 to −0.12)	<0.0001

Confounders found in the group that received cardiac angiography (CAG) and no/delayed CAG are reported as frequencies with 95% confidence intervals (CIs) and *P* values. A positive risk difference indicates a higher frequency of confounder variable in patient cohort undergoing early coronary angiography.
CA indicates cardiac arrest; CPR, cardiopulmonary resuscitation; LVSD, left ventricular support device, including aortic balloon pump; and VF, ventricular fibrillation as presenting arrest rhythm.

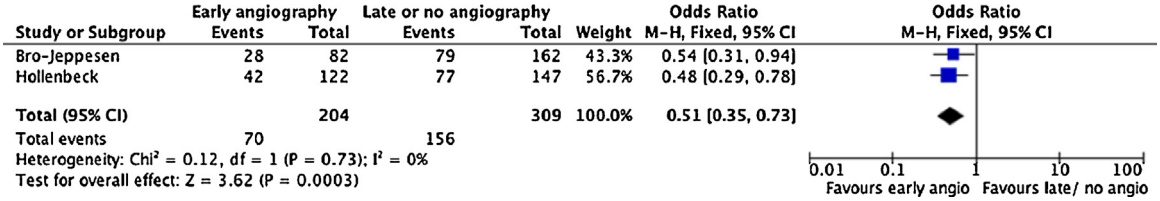

Fig. 14. Hospital mortality for patients with ROSC after cardiac arrest without ST elevation: emergency cardiac catheterization versus delayed or no cardiac catheterization. Experimental = emergency cardiac catheterization; control = delayed or no cardiac catheterization.

Treatment recommendation

We suggest emergency* cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select† adult patients who are comatose with ROSC after OHCA of suspected cardiac origin without ST elevation on ECG (weak recommendation, very-low-quality evidence).

**Time frame for treatment.* In the evidence reviewed, the time frame was variably defined, but patients were managed to minimize door-to-reperfusion times in a manner similar to the general STEMI patient population. The complexity and heterogeneity of this patient group may delay their resuscitation and management.

†*Patient selection.* The evidence base was nonrandomized case-control studies that were subject to a high level of selection bias. Unlike the review pertaining to ST elevation, all of the studies without ST elevation enrolled comatose patients exclusively. The decision to undertake emergency catheterization was frequently made at the discretion of the treating physician. A variety of factors such as patient age, duration of CPR, hemodynamic instability, presenting cardiac rhythm, neurologic status upon hospital arrival, and perceived likelihood of cardiac etiology influenced the decision to undertake the intervention.

Values, preferences, and task force insights

In making this recommendation, we are emphasizing similar values to those outlined above for STEMI. There is a smaller body of evidence for emergency intervention in patients without ST elevation after OHCA with ROSC in comparison to those with ST elevation: The population studied was smaller, the magnitude of the effect was slightly smaller, and the proportion of patients that went on to have PCI was smaller. Therefore, we believed that a weak recommendation was appropriate. We understand that this recommendation represents a departure from most existing guidelines for the treatment of the general population of non-ST elevation ACS patients without OHCA.

Catheterization laboratory evaluation included coronary angiography and early revascularization of acute coronary occlusions or significant stenosis as indicated.

Knowledge gaps

- Further investigation is needed to confirm the benefit seen in the initial 2 observational studies. Ideally, randomized studies would help identify if there are certain subgroups of patients that would benefit most or least from angiography after ROSC.

*Negative troponin value is less than 99th percentile.

*The computer-assisted ECG interpretation can be used as an adjunct or in conjunction with the interpretation of a physician or other trained professional. In this way, recognition of STEMI by the computer interpretation can be verified by individual interpretation, and lack of recognition by the computer would not be used solely to rule out STEMI.

*Exclude the diagnosis of ACS defined as less than 1% 30-day MACE.

†Negative value is less than 99th percentile.

*Two later studies of SpO_2 greater than 93% or 93% to 96%.

†Patients with AMI, excluded previous myocardial infarction, severe chronic obstructive pulmonary disease, respiratory failure, cardiogenic shock, central cyanosis, Spo_2 less than 85%, dyspnea from any other cause.

*In these studies, the time frame from fibrinolysis to PCI ranged from 1 to 4 h.

*Catheterization laboratory evaluation included coronary angiography and early revascularization of acute coronary occlusions or significant stenosis as indicated.

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Chi Keong Ching, Michael Longeway, Catherine Patocka, Vincent Roule, Simon Salzberg, Anthony V. Seto.

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Disclosures.

Disclosure table

2015 CoSTR Part 5: Acute coronary syndromes: writing group disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/honoraria	Expert witness	Ownership interest	Consultant/advisory board	Other
Nikolaos I. Nikolaou	Konstantopouleio General Hospital	None	AMGEN[a]	None	None	None	None	None
Farzin Beygui	CHU Caen	None	AstraZeneca[b]; Daiichi-Sankyo[b]	AstraZeneca[a]; Daiichi-Sankyo Lilly alliance[a]; BMS[a]	None	None	Medtronic[a]; Malinckrodt Pharmaceuticals[a]; AstraZeneca[a]	None
Michelle Welsford	Centre for Paramedic Education and Research, Hamilton Health Sciences Centre	None	None	None	None	None	None	None
Leo Bossaert	University of Antwerp	None	None	None	None	None	None	
Chris Ghaemmaghami	University of Virginia	None	None	None	None	None	None	None
Hiroshi Nonogi	Hospital Deputy, Shizuoka General Hospital	None	None	None	None	None	None	None
Robert E. O'Connor	University of Virginia	None	None	None	None	None	None	None
Daniel R. Pichel	University of Panama	None	None	AstraZeneca[a]; Pfizer[a]; MSD[a]	None	None	None	None
Tony Scott	Waitemata District Health Board	None	None	None	None	None	None	None
Darren L. Walters	The Prince Charles Hospital	None	Cardiac Society Australia and New Zealand[a]	None	None	None	None	None
Karen Woolfrey	University of Toronto	None	None	None	None	None	None	None
								None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

[a] Modest.

[b] Significant.

Appendix A.

Appendix table
CoSTR Part 5: PICO Appendix

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 5	ACS	ACS 332	ED Fibrinolysis and transport only for rescue PCI versus transport for PCI	Among adult patients with STEMI in the ED (of a non-PCI-capable hospital) (P), does transfer to a PCI center (I), compared with immediate in-hospital fibrinolysis and only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (C), change short-term survival, stroke, major bleeding, reinfarction (O)?	Nikolaos Nikolaou, Abdulaziz S. Ali
Part 5	ACS	ACS 334	ED Fibrinolysis and then routine early angiography versus only rescue PCI	Among adult patients with STEMI in the ED (of a non-PCI-capable hospital) who have received immediate in-hospital fibrinolysis (P), does routine transport for angiography at 3–6 h (or up to 24 h) (I), compared with only transfer for ischemia-driven PCI (rescue PCI) in first 24 h (C), change death, intracranial hemorrhage, major bleeding, stroke, reinfarction (O)?	Michelle Welsford, Robert O'Connor
Part 5	ACS	ACS 335	Prehospital ADP-receptor antagonists in STEMI	Among adult patients with suspected STEMI outside of the hospital (P), does prehospital administration of an ADP-receptor antagonist (clopidogrel, prasugrel, or ticagrelor) in addition to usual therapy (I), compared with administration of an ADP-receptor antagonist in-hospital (C), change death, intracranial hemorrhage, revascularization, stroke, major bleeding, reinfarction (O)?	Karen Woolfrey, Daniel Pichel
Part 5	ACS	ACS 336	Prehospital ECG	Among adult patients with suspected STEMI outside of a hospital (P), does prehospital 12-lead ECG with transmission or notification (I), compared with no ECG or no transmission/notification (C), change death, or time to treatment (first medical contact-to-balloon time, first medical contact-to-needle time, door-to-balloon time, door-to-needle time) (O)?	Michelle Welsford, Abdulaziz S. Ali
Part 5	ACS	ACS 337	Delayed PCI versus fibrinolysis stratified by time from symptoms	Among patients with STEMI stratified by time from symptom onset to presentation when fibrinolysis is readily available (P), does delayed PCI (I), compared with fibrinolysis (C), change mortality, reinfarction, major bleeding, intracranial hemorrhage (O)?	Anthony Scott, Hiroshi Nonogi
Part 5	ACS	ACS 338	Prehospital fibrinolysis versus ED fibrinolysis	Among adults who are suspected of having STEMI outside of a hospital (P), does prehospital fibrinolysis (I), compared with in-hospital fibrinolysis(C), change death, intracranial hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?	Chris Ghaemmaghami, Darren Walters
Part 5	ACS	ACS 340	PCI after ROSC with ST elevation	Among adult patients with ROSC after cardiac arrest with evidence of ST elevation on ECG (P), does emergency cardiac catheterization laboratory evaluation* (I), compared with cardiac catheterization later in the hospital stay or no catheterization (C), change hospital mortality and neurologically favorable survival (O)?	Darren Walters, Chris Ghaemmaghami
Part 5	ACS	ACS 341	Prehospital triage to PCI center versus prehospital fibrinolysis	Among adult patients with suspected STEMI outside of a hospital (P), does direct triage and transport to a PCI center (I), compared with prehospital fibrinolysis (C), change death, intracranial hemorrhage, major bleeding (O)?	Michelle Welsford, Michael Longeway
Part 5	ACS	ACS 559	Computer-assisted ECG STEMI Interpretation	Among adult patients with suspected STEMI outside of a hospital (P), does the use of computer-assisted ECG interpretation (I), compared with physician ECG interpretation and/or clinical diagnosis of STEMI (C), change identification of STEMI on an ECG with acceptable rates of FNs to allow earlier identification and FPs, minimizing unnecessary intervention (O)?	Chi Keong Ching, Catherine Patocka
Part 5	ACS	ACS 562	Prehospital anticoagulants versus none in STEMI	Among adult patients with suspected STEMI outside of hospital transferred for primary PCI (P), does any anticoagulant administered prehospital (e.g., bivalirudin, dalteparin, enoxaparin, fondaparinux, UFH) (I), compared with no anticoagulant administered prehospital (C), change death, intracranial hemorrhage, revascularization, major bleeding, stroke, reinfarction (O)?	Farzin Beygui, Vincent Roule
Part 5	ACS	ACS 568	Prehospital anticoagulants versus UFH for STEMI	Among adult patients with suspected STEMI outside of a hospital transferred for primary PCI (P), does any anticoagulants prehospital (eg: bivalirudin, dalteparin, enoxaparin, fondaparinux) (I), compared with UFH prehospital (C), change death, ICH, revascularization, major bleeding, stroke, reinfarction (O)?	Farzin Beygui, Vincent Roule
Part 5	ACS	ACS 737	Biomarkers to Rule Out ACS	In patients presenting to the ED with chest pain suspected to be of cardiac etiology (P), does a negative troponin test at presentation and 1, 2, 3, and 6 h (I), compared with a positive test (C), exclude the diagnosis of ACS (O)?	Robert O'Connor, Michelle Welsford

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 5	ACS	ACS 779	ED fibrinolysis and routine early angiography versus transport for PCI	Among adult patients with STEMI in the ED of a non-PCI-capable hospital (P), does immediate in-hospital fibrinolysis and routine transfer for angiography at 3–6 h (or up to 24 h) (I), compared with transfer to a PCI center (C), change 30-day mortality, stroke, major bleeding, reinfarction (O)?	Nikolaos Nikolaou, Farzin Beygui
Part 5	ACS	ACS 873	Prehospital STEMI Activation of the Catheterization Laboratory	Among adult patients with suspected STEMI outside of a hospital (P), does prehospital activation of catheterization laboratory (I), compared with no prehospital activation of the catheterization laboratory (C), change mortality, major bleeding, stroke, reinfarction (O)?	Karen Woolfrey, Daniel Pichel
Part 5	ACS	ACS 882	ED fibrinolysis and immediate PCI Versus immediate PCI alone	Among adults who are having STEMI in the ED (P), does fibrinolytic administration combined with immediate PCI (I), compared with immediate PCI alone (C), change death, intracranial hemorrhage, reinfarction, urgent target vessel revascularization, major bleeding (O)?	Hiroshi Nonogi, Anthony Scott
Part 5	ACS	ACS 884	Non-physician STEMI ECG interpretation	Among adult patients with suspected STEMI outside of a hospital (P), do nonphysicians (e.g., nurses and paramedics) (I), compared with physicians (C), change identification of STEMI on an ECG with acceptable rates of FNs to allow earlier identification and FPs, minimizing unnecessary angiography (O)?	Chi Keong Ching, Catherine Patocka
Part 5	ACS	ACS 885	PCI After ROSC without ST elevation	Among adult patients with ROSC after cardiac arrest without evidence of ST elevation on ECG (P), does emergency cardiac catheterization laboratory evaluation (I), compared with cardiac catheterization later in the hospital stay or no catheterization (C), change hospital mortality and neurologically favorable survival (O)?	Chris Ghaemmaghami, Darren Walters
Part 5	ACS	ACS 887	Supplementary Oxygen in ACS	Among adult patients with suspected ACS and normal oxygen saturation in any setting (prehospital, emergency, or in-hospital) (P), does withholding oxygen (I), compared with routine supplementary oxygen (C), change death, infarct size, chest pain resolution, ECG resolution (O)?	Anthony Scott, Anthony Seto

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Part 6: Pediatric basic life support and pediatric advanced life support 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆,☆☆

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Introduction

The Pediatric Task Force reviewed all questions submitted by the International Liaison Committee on Resuscitation (ILCOR) member councils in 2010, reviewed all council training materials and resuscitation guidelines and algorithms, and conferred on recent areas of interest and controversy. We identified a few areas where there were key differences in council-specific guidelines based on historical recommendations, such as the A–B–C (Airway, Breathing, Circulation) versus C–A–B (Circulation, Airway, Breathing) sequence of provision of cardiopulmonary resuscitation (CPR), initial back blows versus abdominal thrusts for foreign-body airway obstruction, an upper limit for recommended chest compression rate, and initial defibrillation dose for shockable rhythms (2 versus 4 J kg^{-1}). We produced a working list of prioritized questions and topics, which was adjusted with the advent of new research evidence. This led to a prioritized palate of 21 PICO (population, intervention, comparator, outcome) questions for ILCOR task force focus.

The 2015 process was supported by information specialists who performed in-depth systematic searches, liaising with pediatric content experts so that the most appropriate terms and outcomes and the most relevant publications were identified. Relevant adult literature was considered (extrapolated) in those PICO questions that overlapped with other task forces, or when there were insufficient pediatric data. In rare circumstances (in the absence of sufficient human data), appropriate animal studies were incorporated into reviews of the literature. However, these data were considered only when higher levels of evidence were not available and the topic was deemed critical.

When formulating the PICO questions, the task force felt it important to evaluate patient outcomes that extend beyond return of spontaneous circulation (ROSC) or discharge from the pediatric intensive care unit (PICU). In recognition that the measures must have meaning, not only to clinicians but also to parents and caregivers, longer-term outcomes at 30 days, 60 days, 180 days, and 1 year with favorable neurologic status were included in the relevant PICO questions.

Each task force performed a detailed systematic review based on the recommendations of the Institute of Medicine of the National Academies[1] and using the methodological approach proposed by the Grading of Recommendations, Assessment, Development,

☆ 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations.

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[2] See Acknowledgements for the list of members in Pediatric basic life support and pediatric advanced life support Chapter Collaborators.

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and Evaluation (GRADE) working group.[2] After identifying and prioritizing the questions to be addressed (by using the PICO format)[3] with the assistance of information specialists, a detailed search for relevant articles was performed in each of three online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk-of-bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[4] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[5] and GRADE for observational studies that inform both therapy and prognosis questions.[6]

GRADE evidence profile Tables [7] were then created to facilitate an evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[8] based on the study methodologies and the five core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias).[9]

These evidence profile tables were then used to create a written summary of evidence for each outcome (the consensus on science statements). Whenever possible, consensus-based treatment recommendations were then created. These recommendations (designated as strong or weak) were accompanied by an overall assessment of the evidence and a statement from the task force about the values and preferences that underlie the recommendations.

Further details of the methodology that underpinned the evidence evaluation process are found in "Part 2: Evidence evaluation and management of conflicts of interest."

The pediatric task force included several authors who had produced some of the most important primary work found in the literature. To ensure that there was transparency, and that there was not undue bias, the task force sought opinions as a whole with the interests of the involved author declared at the outset. At face-to-face meetings, this allowed for examination in detail of those papers, producing better understanding of the limitations and interpretation of the work of those authors. Consistent with the policies to manage potential conflicts of interest, participants in discussions with any potential conflicts abstained from any voting on the wording of the consensus on science or treatment recommendations.

External content experts attended the face-to-face meeting in February 2015 in Dallas (ILCOR 2015 International Consensus Conference on CPR and Emergency Cardiovascular Care Science With Treatment Recommendations), providing further independent review beyond that achieved by public consultation. This conference included representation from the World Health Organization (WHO) to add perspective on the global application of the guidelines. These collaborations enhanced participants' understanding of the variability of health care in resource-replete settings, with the realization that the "developed world" has certain parallels to resource-deplete settings. It was clearly understood that the economic classifications of "low-," "middle-," or "high-income country" are inadequate to explain the range of health care available within each country and that the information derived as part of any review of the scientific literature had to be viewed in context of the resources available to appropriately shape local guidelines. The WHO also uses the GRADE assessment process for its guidelines, and similarities were found between ILCOR work and that of the WHO. Thanks must go to the WHO representatives and associated clinicians for their informed and helpful input into discussions about subjects common to both groups.

The values, preferences, and task force insights section after each treatment recommendation section presents the prioritization of outcomes in the decision-making processes and the considerations that informed the direction and strength of the treatment recommendations.[10]

Evidence reviews addressing questions related to the prearrest State

Although survival from pediatric cardiac arrest is improving in many (but not all) parts of the world,[11–13] especially in the in-hospital setting, the recognition and early treatment of infants and children with deteriorating conditions remains a priority to prevent cardiac arrest.

This section contains the following reviews:

- Pediatric medical emergency team (MET) and rapid response team (RRT) (Peds 397).
- Pediatric Early Warning Scores (PEWS) (Peds 818).
- Prearrest care of pediatric dilated cardiomyopathy or myocarditis (Peds 819).
- Atropine for emergency intubation (Peds 821).
- Fluid resuscitation in septic shock (Peds 545).

MET, RRT, and PEWS systems have been widely implemented, and even mandated in many hospitals, but their effectiveness is difficult to measure. The implementation of the afferent (event recognition) and efferent (team response) arms of these systems is intimately related to providing education about the detection and prevention of deterioration with critical illness. There may be a whole system impact as a consequence of developing a MET that leads to change beyond that directly attributable to the MET itself. This may result in an increased awareness of earlier stages of patient deterioration, or increased communication about changes in a patient's condition, so earlier interventions may prevent the need for MET activation. The task force recognized that the PICO questions of MET/RRT and PEWS are related components of an in-hospital safety net and are difficult to evaluate separately.

Pediatric METs and RRTs (Peds 397)

For infants and children in the in-hospital setting (P), does the use of pediatric METs/RRTs (I), compared with not using METs/RRTs (C), change cardiac or pulmonary arrest frequency outside of the intensive care unit (ICU), overall hospital mortality (O)?

Consensus on science

For the critical outcome of cardiac arrest outside the ICU, we identified very-low-quality evidence from seven pediatric observational studies (downgraded for risk of bias, inconsistency, and imprecision). All seven studies showed that the rate of cardiac arrest outside the ICU declined after institution of a MET/RRT system (unadjusted relative risk (RR) less than 1), but none achieved statistical significance.[14–20] There was enough potential variability between the studies (of both patient and healthcare system factors, including the baseline incidence of cardiac arrest) that a decision was made to not pool the data.

For the critical outcome of all arrests (cardiac and respiratory) outside the ICU, we identified very-low-quality evidence from four pediatric observational studies (downgraded for risk of bias and imprecision). One study[21] demonstrated a statistically significant decline ($P = 0.0008$), whereas the other three studies[16,22,23] did not.

For the critical outcome of respiratory arrest, we identified very-low-quality evidence from 1 pediatric observational study[16] (downgraded for risk of bias and imprecision) that observed a decline in respiratory arrests (RR, 0.27; 95% confidence interval (CI), 0.05–1.01; $P = 0.035$).

For the important outcome of cardiac arrest frequency, we identified very-low-quality evidence from one pediatric observational

study[15] (downgraded for risk of bias and imprecision) that was not statistically significant (RR, 0.3; 95% CI, 0–1.04; $P = 0.07$).

For the important outcome of overall hospital mortality, we identified very-low-quality evidence from six pediatric observational studies (downgraded for risk of bias, inconsistency, and imprecision). Three studies[15,17,21] observed a decline in deaths, and three did not.[18,23,24]

Treatment recommendations

We suggest the use of pediatric MET/RRT systems in hospitals that care for children (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the potential to recognize and intervene for patients with deteriorating illness over the expense incurred by a healthcare system committing significant resources to implement a MET/RRT system. We recognize that the decision to use a MET/RRT system should be balanced by the existing resources and capabilities of the institution.

Knowledge gaps

- The amount and quality of evidence in children compared with adults for the role of MET/RRT systems is very low. A major limitation to evaluation of these systems is the low rate of pediatric cardiac arrest and mortality (especially outside the intensive care unit setting), including within the hospitals from which the data in this analysis originate. As such, demonstrating a statistically significant effect after a new implementation is difficult. This is apparent in that most studies demonstrated trends of improving cardiac arrest rate or mortality, although not statistically to significant levels. Use of a more proximate outcome metric, like a critical deterioration event,[25] might further support implementation of a MET/RRT in the pediatric inpatient setting.
- The other major limitation in our analysis is the use of before-and-after studies, with the inherent limitations of unaccounted or confounding variables and inability to develop a comparable control group. Joffe et al[26] demonstrated the potential for risk of bias or confounding variables by comparing the mortality rate at their institution, which did not initiate or organize a MET/RRT, with five published studies (all reviewed here). The reduction in mortality at their institution over the same time period was similar to the published results, illustrating the problems of confounding variables and contemporaneous trends. Quality improvement methodology could be used to regulate the impact of a series of changes that include educational processes, documentation review with feedback systems, and modification of other factors thought to improve the delivery of care.

PEWS (Peds 818)

For infants and children in the in-hospital setting (P), does the use of a PEWS (I), compared with not using a PEWS (O), change overall hospital mortality, cardiac arrest frequency outside of the ICU (O)?

Introduction

PEWS are systems with emphasis on the afferent limb of an emergency response system to detect early clinical deterioration. PEWS assign numeric scores to specific abnormal observations in several clinical domains.

Consensus on science

For the critical outcome of reduced mortality from cardiac arrest, we identified no evidence that showed changes in cardiac arrest rate or mortality outside of the PICU setting.

For the critical outcome of incidence of cardiac arrest, we identified very-low-quality evidence from 1 pediatric observational study (downgraded for risk of bias, indirectness, imprecision, and possible publication bias) reporting that the introduction of PEWS into a hospital with an established MET system was associated with a fall in the incidence of cardiac arrest from 0.15 to 0.12 events/1000 patient days.[27]

Treatment recommendation

The confidence in the estimate of predictive value is so low that the panel decided a recommendation is too speculative.

Knowledge gaps

- A large pediatric, cluster-randomized, multicenter study is currently under way examining the impact of implementing a PEWS.
- Additional outcome measures apart from cardiac arrest rate or hospital mortality are required.
- Does PEWS, independent of other interventions, have an impact on outcomes?
- Future specific research will need to focus on prospective evaluation of different PEWS for identifying and predicting patients at risk for different forms of decompensation, including primary respiratory, circulatory, and neurologic etiologies.

Prearrest care of pediatric dilated cardiomyopathy or myocarditis (Peds 819)

For infants and children with myocarditis or dilated cardiomyopathy and impending cardiac arrest (P), does a specific approach (I), compared with the usual management of shock or cardiac arrest (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; cardiac arrest frequency; ROSC (O)?

Introduction

Although the question was intended to address populations of children with either acute myocarditis or dilated cardiomyopathy, the available relevant literature is limited to acute fulminant myocarditis.

Consensus on science

For the critical outcome of survival to hospital discharge, we identified no evidence that a specific prearrest management strategy in patients with dilated cardiomyopathy or myocarditis shows a benefit.

For the critical outcome of survival to hospital discharge, we identified no evidence that a specific anesthetic technique in patients with dilated cardiomyopathy shows any benefit.

For the critical outcome of survival to hospital discharge, we identified very-low-quality evidence from a pediatric observational study (downgraded for risk of bias and imprecision)[28] of 20 children with acute fulminant myocarditis, which demonstrated that the pre-cardiac arrest use of extracorporeal membrane oxygenation (ECMO) may be beneficial.

Treatment recommendation

The confidence in effect estimates is so low that the panel decided a specific recommendation was too speculative.

Knowledge gaps

- Factors associated with cardiac arrest in patients with dilated cardiomyopathy or myocarditis have not been well studied.
- In addition, the amount and quality of literature addressing the benefits of specific approaches of prearrest care, including anesthetic techniques and the use and/or timing of inotropes and/or inodilator and/or mechanical ventilation and/or ECMO on survival and neurologic outcomes in children with dilated cardiomyopathy or myocarditis is very low. Consequently, these studies could not inform the GRADE evaluation (or subsequent generation of a treatment recommendation) in a substantive way, and ultimately precluded the task force from making a treatment recommendation.

Atropine for emergency intubation (Peds 821)

In infants and children requiring emergency tracheal intubation (P), does the use of atropine as a premedication (I), compared with not using atropine (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 90 days, 180 days, and/or 1 year after event; the incidence of cardiac arrest; survival to hospital discharge; the incidence of peri-intubation shock or arrhythmias (O)?

Introduction

Because emergency intubation may pose a risk of cardiac arrest, this question was designed to determine the utility of routine use of atropine in prevention of an unfavorable outcome.

Consensus on science

For the critical outcome of survival with favorable neurologic outcome, we identified no evidence that addressed any effect on survival when atropine was used for in-hospital emergency intubation.

For the critical outcome of survival to ICU discharge, there was very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric observational study of in-hospital emergency intubation[29] of 264 infants and children supporting the use of atropine preintubation for those patients at more than 28 days of life. The use of atropine preintubation for neonates was not significantly associated with survival to ICU discharge (neonates: propensity score adjusted odds ratio (aOR), 1.3; 95% CI, 0.31–5.10; $P = 0.74$; older children: odds ratio (OR), 0.22; 95% CI, 0.06–0.85; $P = 0.028$).

For the critical outcome of likelihood/incidence of cardiac arrest, we identified no evidence that addressed the effect of atropine use for in-hospital emergency intubation on cardiac arrest.

For the important outcome of likelihood or incidence of shock or arrhythmias, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from two pediatric observational studies. One study of 322 emergency pediatric intubations[30] showed that the use of atropine preintubation was associated with a reduced incidence of any arrhythmia (OR, 0.14; 95% CI, 0.06–0.35), whereas the second study of 143 emergency pediatric intubations[31] failed to find an association between the preintubation use of atropine and a reduced incidence of bradycardia (OR, 1.11; 95% CI, 0.22–5.68).

Treatment recommendation

The confidence in effect estimates is so low that the panel decided a recommendation was too speculative.

Knowledge gaps

The available data are observational and highly confounded. In light of the common use of atropine when intubating acutely ill infants and children, robust prospective studies are needed to identify potential adverse outcomes from the use of atropine and to determine which patients (if any) benefit from its use in reducing short-term complications of intubation (e.g., bradycardia) as well as a critical outcome such as survival.

Fluid resuscitation in septic shock (Peds 545)

Among infants and children who are in septic shock in any setting (P), does the use of restrictive volumes of resuscitation fluid (less than 20 mL kg^{-1}) (I1) when compared with nonrestrictive volumes (greater than or equal to 20 mL kg^{-1}) (C1), or the use of noncrystalloid fluids (I2) when compared with crystalloid fluids (C2), change survival to hospital discharge, need for mechanical ventilation or vasopressor support, complications, time to resolution of shock, hospital length of stay (LOS), ventilator-free days, total intravenous (IV) fluids administered (O)?

Introduction

The task force had difficulty generalizing treatment recommendations for all resource settings and considered different categories to relate underlying pathophysiology with appropriate treatment regimens. Discussion balanced the arguments of delayed bolus fluid therapy until more established signs of shock are present (WHO criteria, hypotension) against the importance of early identification of shock while it is still treatable with available resources.

Consensus on science

For the critical outcome of survival to hospital discharge, for the use of restrictive fluids in sepsis/septic shock, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 pediatric RCT[32] enrolling 147 patients showing no benefit (RR, 0.99; 95% CI, 0.86–1.16), and from 1 observational pediatric study[33] enrolling 34 patients showing no benefit (RR, 0.71; 95% CI, 0.35–1.44). For the use of restrictive fluids in severe malaria, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 pediatric RCTs[34,35] enrolling 106 patients showing no benefit (RR, 1.09; 95% CI, 0.94–1.27). For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[36,37] enrolling 2091 patients showing benefit (RR, 1.05; 95% CI, 1.03–1.07).

For the critical outcome of survival to hospital discharge, for the use of noncrystalloid fluids in sepsis/septic shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[38] enrolling 60 patients showing no benefit (RR, 1.13; 95% CI, 0.77–1.63). For the use of noncrystalloid fluids in severe malaria, we identified no studies. For the use of noncrystalloid fluids in dengue shock syndrome, we identified moderate-quality evidence (downgraded for risk of bias) from 4 pediatric RCTs[39–42] enrolling 682 patients showing no benefit (RR, 0.98; 95% CI, 0.96–1.00). For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2097 patients showing no benefit (RR, 0.99; 95% CI, 0.97–1.03).

For the critical outcome of complications (need for transfusion and diuretic therapy), for the use of restrictive fluids in sepsis/septic shock, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, imprecision) from 1 observational pediatric study[33] enrolling 34 patients showing no benefit (RR, 1.43; 95% CI, 0.71–2.88). For the use of restrictive fluids in severe malaria, we identified low-quality evidence (downgraded for risk of bias

and imprecision) from 2 pediatric RCTs[34,35] enrolling 106 patients showing no benefit (0% versus 5.4%; $P = 0.09$). For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2091 patients showing no benefit (RR, 0.59; 95% CI, 0.3–1.17).

For the critical outcome of complications (need for transfusion and diuretic therapy), for the use of noncrystalloid fluids in sepsis/septic shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[38] enrolling 60 patients showing no benefit (RR, 1.18; 95% CI, 0.48–2.87). For the use of noncrystalloid fluids in severe malaria, we identified very-low-quality evidence (downgraded for imprecision) from 1 observational pediatric study[43] enrolling 52 patients showing no benefit (0% versus 0%). For the use of noncrystalloid fluids in dengue shock syndrome, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 4 pediatric RCTs[39–42] enrolling 682 patients showing no benefit (RR, 1.3; 95% CI, 0.95–1.79). For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2097 patients showing no benefit (RR, 1.17; 95% CI, 0.68–2.02).

For the critical outcome of complications (need for rescue fluid), for the use of restrictive fluids in sepsis/septic shock, we identified no studies. For the use of restrictive fluids in severe malaria, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 pediatric RCTs[34,35] enrolling 106 patients showing harm (17.6% versus 0.0%; $P < 0.005$). For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified no studies.

For the critical outcome of complications (need for rescue fluid), for the use of noncrystalloid fluids in sepsis/septic shock, we identified no studies. For the use of noncrystalloid fluids in severe malaria, we identified no studies. For the use of noncrystalloid fluids in dengue shock syndrome, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 4 pediatric RCTs[39–42] enrolling 655 patients showing no benefit (RR, 0.98; 95% CI, 0.76–1.27). For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2097 patients showing no benefit (RR, 0.49; 95% CI, 0.05–5.49).

For the critical outcome of need for mechanical ventilation or vasopressor support, for the use of restrictive fluids in sepsis/septic shock, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, imprecision) from 1 pediatric RCT[32] enrolling 147 patients showing no benefit (RR, 1.32; 95% CI, 0.91–1.91). For the use of restrictive fluids in severe malaria, we identified no studies. For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" and some but not all signs of shock, we identified no studies.

For the critical outcome of need for mechanical ventilation or vasopressor support, for the use of noncrystalloid fluids in sepsis/septic shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[38] enrolling 60 patients showing no benefit (RR, 1.18; 95% CI, 0.83–1.69). For the use of noncrystalloid fluids in severe malaria, we identified no studies. For the use of noncrystalloid fluids in dengue shock syndrome, we identified no studies. For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified no studies.

For the critical outcome of time to resolution of shock, for the use of restrictive fluids in sepsis/septic shock, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, imprecision) from 1 observational pediatric study[33] enrolling 34 patients showing no benefit (RR, 0.63; 95% CI, 0.39–1.02). For the use of restrictive fluids in severe malaria, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 pediatric RCTs[34,35] enrolling 211 patients showing no benefit (base excess improvement at 8 h: 33% versus 24%; $P = 0.37$ [restrictive versus bolus arms][34]; 42% versus 36%; $P = 0.81$ [restrictive versus bolus arms][35]). For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2091 patients showing harm (RR, 0.76; 95% CI, 0.68–0.85).

For the critical outcome of time to resolution of shock, for the use of noncrystalloid fluids in sepsis/septic shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[38] enrolling 60 patients showing no benefit (RR, 0.96; 95% CI, 0.68–1.38). For the use of noncrystalloid fluids in severe malaria, we identified very-low-quality evidence (downgraded for imprecision) from 1 observational pediatric study[43] enrolling 52 patients showing no benefit (percent change of base deficit ranging from −41% to −19% for noncrystalloid versus −35% to −19% for crystalloid). For the use of noncrystalloid fluids in dengue shock syndrome, we identified moderate-quality evidence (downgraded for imprecision) from 1 pediatric RCT[41] enrolling 222 patients showing benefit (RR, 1.09; 95% CI, 1.00–1.19). For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2097 patients showing no benefit (RR, 1.02; 95% CI, 0.93–1.13).

For the important outcome of total IV fluids administered, for the use of restrictive fluids in sepsis/septic shock, we identified no studies. For the use of restrictive fluids in severe malaria, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[34] enrolling 68 patients showing no benefit in total fluid over the first 8 h (total volume given: 35 mL kg^{-1} versus 48 mL kg^{-1}; $P = 0.14$). For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2091 patients showing no benefit in total fluid over the first 48 h (49 mL kg^{-1} versus 73.9 mL kg^{-1}; $P = 0.7$).

For the important outcome of total IV fluids administered, for the use of noncrystalloid fluids in sepsis/septic shock, we identified no studies. For the use of noncrystalloid fluids in severe malaria, we identified no studies. For the use of noncrystalloid fluids in dengue shock syndrome, we identified moderate-quality evidence (downgraded for imprecision) from 3 pediatric RCTs[39–41] enrolling 632 patients showing no benefit for total volume of initial bolus (mean 31.7 mL kg^{-1} (intervention) versus 40.63 mL kg^{-1} (control), $P = 0.24$; total IV fluids: 134.3 mL kg^{-1} (dextran) versus 134.2 mL kg^{-1} (lactated Ringer's), $P = 0.98$; 100 (66–163) mL/kg (intervention) versus 100 (5–157) mL kg^{-1} (control)). For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[37] enrolling 2097 patients showing no benefit in total fluid over the first 48 h (median 76.2 versus 78.1 mL kg^{-1}, not significant).

For the important outcome of hospital LOS, for the use of restrictive fluids in sepsis/septic shock, we identified no studies. For the use of restrictive fluids in severe malaria, we identified no studies. For the use of restrictive fluids in dengue shock syndrome, we

identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified no studies.

For the important outcome of hospital LOS, for the use of noncrystalloid fluids in sepsis/septic shock, we identified no studies. For the use of noncrystalloid fluids in severe malaria, we identified no studies. For the use of noncrystalloid fluids in dengue shock syndrome, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric RCT[39] enrolling 27 patients showing no benefit (3.55 versus 3.31 ICU days; $P = 0.45$). For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified no studies.

For the important outcome of ventilator-free days, for the use of restrictive fluids in sepsis/septic shock, we identified no studies. For the use of restrictive fluids in severe malaria, we identified no studies. For the use of restrictive fluids in dengue shock syndrome, we identified no studies. For the use of restrictive fluids in "severe febrile illness" with some but not all signs of shock, we identified no studies.

For the important outcome of ventilator-free days, for the use of noncrystalloid fluids in sepsis/septic shock, we identified no studies. For the use of noncrystalloid fluids in severe malaria, we identified no studies. For the use of noncrystalloid fluids in dengue shock syndrome, we identified no studies. For the use of noncrystalloid fluids in "severe febrile illness" with some but not all signs of shock, we identified no studies.

Treatment recommendations

We suggest using an initial fluid bolus of 20 mL kg^{-1} for infants and children with shock, with subsequent patient reassessment, for patients with the following disease states:

- Severe sepsis (weak recommendation, low quality).
- Severe malaria (weak recommendation, low quality).
- Dengue shock syndrome (weak recommendation, low quality).

We suggest against the routine use of bolus intravenous fluids (crystalloids or colloids) for infants and children with a "severe febrile illness" and who are not in shock (weak recommendation, low-quality evidence). Reassessment, regardless of therapy administered, should be emphasized so that deterioration is detected at an early stage.

Values, preferences, and task force insights

In making these recommendations, we place a higher value on allocating resources to the frequent assessment of infants or children with some or all signs of shock and to reassessment of a patient's response to fluid therapy or development of complications over any unproven benefit for critical or important outcomes.

The Pediatric Task Force does not recommend limiting resuscitation fluids for children in septic shock, while still recognizing the importance of information from the Fluid Expansion as Supportive Therapy (FEAST) trial[37] regarding attempts to treat children with "severe febrile illness" with some but not all signs of shock (the FEAST definition of "severe febrile illness" was febrile illness complicated by impaired consciousness [prostration or coma], respiratory distress [increased work of breathing], or both, and with impaired perfusion, as evidenced by 1 or more of the following: a capillary refill time of three or more seconds, lower-limb temperature gradient, weak radial-pulse volume, or severe tachycardia). Specific diseases such as dengue shock syndrome appear to behave differently with respect to response to fluid bolus therapy in comparison with bacterial septic shock. We have grouped our analysis according to the broad types of disease for which we identified evidence on fluid bolus therapy. For further detail as to the fluid composition in each of the cited articles, see the Systematic Evidence Evaluation and Review System (SEERS; Peds 545).

We recognize that the early diagnosis of septic shock and institution of effective therapy is a high priority before collapse of blood pressure with concomitant increased risks of morbidity and mortality. Accurate early diagnosis can be difficult and requires the integration of a range of clinical signs together with consideration of patient- and locality-specific information on prevalent diseases, malnutrition, and other vulnerability (such as severe anemia associated with malaria). "Severe febrile illness" is a modified definition of shock as reported by the FEAST investigators. The pediatric task force is concerned that this expanded definition may include children to whom fluid administration is beneficial.

The management of septic shock may require inotropic therapy and mechanical ventilation in addition to fluids. These modalities are not available in all settings, and we believe that the approach to fluid therapy may need to be modified accordingly. We have avoided the use of "resource-limited settings" in our recommendations because this is difficult to define and can vary greatly, even within individual health systems and small geographic regions.

Knowledge gaps

- Early recognition and treatment of septic shock is required to prevent progression to critical illness, yet most definitions of septic shock require advanced diagnostic or interventions to fulfill the criteria. The FEAST trial is a paradigm-shifting study that highlights the need to not only identify and treat children in septic shock, or in shock from causes other than sepsis, but also avoid the potential complications of fluid therapy in children not in shock.
- There is a need for more studies to define patients with septic shock earlier, as well as the type of monitoring and support of complications of therapy that will impact patient outcomes.

Basic life support care

The major difference between council recommendations for basic life support (BLS) care is the sequence of CPR (C–A–B versus A–B–C) and the upper limit on recommendation for chest compression rate. All other recommendations in this area are similar between councils. Adult BLS currently places greater emphasis on high-quality chest compressions than on the complex interplay of chest compressions and rescue breaths, with the rationale of simplifying lay rescuer education and increasing the rate of bystander CPR. The Pediatric Task Force realized that uniformity of CPR recommendations throughout ages and etiologies would be of added value, but remained convinced that the current evidence does not favor this approach for pediatrics, because asphyxial cardiac arrest represents the majority of pediatric events, which suggests the importance of ventilation as part of effective CPR.

The task force decided to focus on the following areas of BLS cardiac arrest care:

- Sequence of chest compressions and ventilations: C–A–B versus A–B–C (Peds 709).
- Chest compression depth (Peds 394).
- Chest compression–only CPR versus conventional CPR (Peds 414).

Sequence of chest compressions and ventilations: C–A–B versus A–B–C (Peds 709)

Among infants and children who are in cardiac arrest in any setting (P), does the use of a circulation-airway-breathing approach to initial management (I), compared with the use of an

airway-breathing-circulation approach to initial management (C), change ROSC, survival to hospital discharge, survival to 180 days with good neurologic outcome, time to first compressions (O)?

Introduction

In 2010, despite the absence of definitive evidence, some resuscitation councils implemented a C–A–B approach to initiating CPR. Rationale included shortening the time to the initiation of chest compressions and maintaining consistency across pediatric and adult recommendations. Questions remain as to whether the use of the C–A–B approach and the subsequent delay in initiating ventilation impacts outcomes for infants and children in cardiac arrest. The absence of human studies (only manikin studies exist on the topic) led to debate within the task force.

Consensus on science

For the important outcome of time to first chest compression (TFCC), we identified very-low-quality evidence from 3 simulation-based RCTs (all downgraded for imprecision and very serious indirectness), including 2 adult manikin studies[44,45] and 1 pediatric manikin study[46] showing a reduced time to first chest compression with the use of a C–A–B approach as opposed to A–B–C.

Data from 3 simulation-based RCTs showed that TFCC was 18.0 to 24.3 s shorter when using a C–A–B sequence (15.4–25.0 s) as compared with A–B–C (36.0–43.4 s).

Furthermore, data from 2 manikin studies[44,46] showed that time to first ventilation is delayed by only 5.7 to 6.0 s when using a C–A–B sequence (28.4–43.0 s) as compared with A–B–C (22.7–37.0 s).

There were no clinical (human) studies comparing C–A–B versus A–B–C approaches for the initial management of cardiac arrest that addressed the outcomes of ROSC, survival to hospital admission, or survival to 180 days with good neurologic outcome.

Treatment recommendations

The confidence in effect estimates is so low that the panel decided a recommendation was too speculative.

Values, preferences, and task force insights

In considering making a recommendation, the task force placed a higher value on the importance of timely rescue breathing as part of CPR over a strategy that significantly delays ventilation when pediatric cardiac arrest is so commonly asphyxial in nature. Both C–A–B and A–B–C approaches for pediatric resuscitation have supportive arguments. The use of a C–A–B approach will lead to simplification of teaching because adult BLS providers use this strategy. The use of an A–B–C approach recognizes the preponderance of asphyxial etiologies in pediatric cardiac arrest and the importance of early ventilation for infants and children. With the availability of only manikin data on this topic, and with the disparate recommendations previously made by various resuscitation councils, the task force concluded that the recommendation would acknowledge that equipoise exists in councils making different guidelines that stem from either argument.

Knowledge gaps

The only evidence specifically addressing this question is from manikin studies. Clinical studies of surrogate outcomes for the two approaches (e.g., time to first chest compression/breath) would be of use, in addition to critical patient outcomes such as ROSC, survival to discharge, and survival with good functional outcome.

Chest compression depth (Peds 394)

In infants and children receiving chest compressions (in or out of hospital) (P), does the use of any specific chest compression depth (I), compared with the depth specified in the current treatment algorithm (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, complication rate, or intermediate physiological endpoints (O)?

Introduction

The task force decided that providing high-quality CPR to infants and children was of high priority, and, as a result, the ideal depth of compression was addressed as a PICO question.

Consensus on science

For the critical outcomes of survival with good neurologic outcome and survival to hospital discharge, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 pediatric observational study of in-hospital cardiac arrest (IHCA)47 (89 cardiac arrest events) showing that chest compression depths of greater than 51 mm (greater than 2 inches) are associated with statistically significant improvement in outcomes (good neurologic outcome: RR, 3.71; 95% CI, 0.90–15.33; survival to discharge: RR, 3.48; 95% CI, 1.02–11.84).

For the important outcomes of 24-hour survival and ROSC, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 pediatric observational study of IHCA[47] enrolling 89 cardiac arrest events showing that events receiving chest compression of greater than 51 mm are associated with better survival to 24 h (aOR, 10.3; 95% CI, 2.75–38.8; $P < 0.001$) and ROSC (aOR, 4.21; 95% CI, 1.34–13.2; $P = 0.014$).

For the important outcome of physiologic endpoints (a predefined blood pressure target), we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 2 pediatric observational studies of IHCA and out-of-hospital cardiac arrest (OHCA) (6 subjects[48] and 9 subjects[49]) showing that targeting a real-time measured chest compression depth or a subjective anterior–posterior diameter during CPR is not associated with a statistically significant difference in outcome (Sutton[49]: OR, 1.04; 95% CI, 0.63–1.71; and Maher[48]: RR, 6.0; 95% CI, 1.00–35.91).

For the important outcome of complications, we identified no evidence.

Treatment recommendations

We suggest that rescuers compress the chests of infants by at least one third the anterior–posterior dimension, or approximately 1½″ (4 cm). We suggest that rescuers compress the child's chest by at least one third of the anterior–posterior dimension, or approximately 2″(5 cm) (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place a higher value on achieving adequate chest compression depth over the modest risk of exceeding recommended depths and potentially harming the patient. A recently published study of pediatric OHCA (released too late to be incorporated into the GRADE evaluation process) studied associations between chest compression depth and short-term outcomes (i.e., ROSC).[50] Despite the limited pediatric evidence linking chest compression depth to patient outcomes, recently published adult data[51] convincingly demonstrate improved clinical outcomes with the use of deeper chest compressions but also the potential for worse patient outcomes (i.e., increased injuries) with excessive chest compression depths.

Knowledge gaps

- Most of the available pediatric data on this topic originate from a single research center, which may not be representative of all pediatric settings.

- The data are derived from very small patient sample sizes and predominantly from adolescents. There are minimal data generated from infants or young children.
- No out-of-hospital data exist in children, nor are there data about the effect of different surfaces on the adequacy of chest compressions (i.e., most of the data are not adjusted for mattress compression). In intensive care settings, invasive monitoring data (e.g., blood pressure and capnography) at different depths of chest compression would be helpful in guiding future recommendations.
- The need for a consistent approach to the delivery of compressions of adequate depth was commented on in task force discussions, and the use of feedback techniques to enhance BLS delivery was also discussed at the face-to-face task force meetings.

Chest compression—only CPR versus conventional CPR (Peds 414)

Among infants and children who are in cardiac arrest in any setting (P), does compression-only CPR (I), compared with the use of conventional CPR (C), change neurologically intact survival at 1 year, survival to hospital discharge, improved ICU LOS, neurologically intact survival at 30 days (O)?

Introduction

Chest compression—only CPR has been widely adopted in adult BLS training for lay rescuers. Available data, however, suggest that ventilation as part of CPR is critically important for infants and children in cardiac arrest. The task force recognizes that rescuers must possess the knowledge and skills to provide ventilation for pediatric patients, including adolescents, and CPR education must address this issue.

Consensus on science

For the critical outcome of 1-year neurologically intact survival and the important outcome of improved ICU LOS, we identified no data.

For the critical outcome of 30-day neurologically intact survival, we identified low-quality evidence from 2 pediatric observational studies of OHCA ($n = 5170$ patients[52]; $n = 5056$ patients[53]), downgraded for indirectness (dispatcher-assisted CPR), upgraded for effect size, showing that the use of compression-only CPR when compared with conventional CPR is associated with worse 30-day intact neurologic survival (RR, 0.46; 95% CI, 0.34–0.62). Further analysis of these 2 studies (pooled data) demonstrated no benefit in 30-day neurologically intact survival when comparing the use of bystander compression-only CPR with no bystander CPR (RR, 1.21; 95% CI, 0.89–1.65).

For the important outcome of survival to hospital discharge, no pediatric evidence was identified.

Treatment recommendations

We recommend that rescuers provide rescue breaths and chest compressions for pediatric IHCA and OHCA. If rescuers cannot provide rescue breaths, they should at least perform chest compressions (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we place a higher value on the importance of rescue breaths as part of CPR over a strategy that deemphasizes ventilation. The asphyxial nature of most pediatric cardiac arrests necessitates ventilation as part of effective CPR.

Despite the low-quality evidence, the task force advocated for a strong recommendation to provide any CPR (including compression-only) in both in- and out-of-hospital settings; this is preferable to providing no intervention for a child in cardiac arrest. Registry data[52] do show that while infant outcomes are no different whether no CPR or compression-only CPR is attempted, children (older than infants) provided with at least compression-only CPR have better survival and neurologic outcomes compared with those subjects who have no CPR attempted.

Knowledge gaps

- Additional data, separate for the out-of-hospital and in-hospital settings, are needed, because both cited registry-based studies originate from a single region of the world.
- More data on witnessed pediatric arrest are needed, and the potential to capture natural experiments (comparative effectiveness) is high, because different councils are currently using different approaches. There is also the potential to randomize or measure before-and-after effect of dispatcher instructions for compression-only CPR versus chest compressions plus rescue breaths.

Advanced life support during arrest

Advanced life support (ALS) as part of cardiac arrest care builds on high-quality CPR by monitoring a patient's physiology and response to BLS, recognizing and intervening for life-threatening arrhythmias, and optimizing perfusion by medication or mechanical support. Frequent monitoring of the patient's physiologic response to these interventions allows individual titration of care with the goal of optimizing outcome.

Not all patients will respond to standard BLS and ALS care, and escalation to specific interventions for special resuscitation circumstances or advanced rescue therapies depends on the ability to determine which patients are most likely to benefit. Some of these interventions are limited to specific settings due to resource availability (IHCA versus OHCA), and their use must focus on not only short-term outcomes (e.g., ROSC) but also longer-term benefit to the patient (e.g., good functional outcome). All councils currently have similar ALS recommendations, with some differences in recommendation of 2 versus 4 J kg^{-1} initial shock dose for a ventricular fibrillation (VF)/pulseless ventricular tachycardia (pVT) cardiac arrest rhythm.

The task force decided to focus on the following areas of ALS cardiac arrest care:

- Energy doses for defibrillation (Peds 405).
- Invasive blood pressure monitoring during CPR (Peds 826).
- End-tidal carbon dioxide ($ETCO_2$) monitoring during CPR (Peds 827).
- Amiodarone versus lidocaine for shock-resistant VF or pVT (Peds 825).
- Vasopressor use during cardiac arrest (Peds 424).
- Extracorporeal cardiopulmonary resuscitation (ECPR) for IHCA (Peds 407).
- Intra-arrest prognostic factors (Peds 814).

Energy doses for defibrillation (Peds 405)

Among infants and children who are in VF or pVT in any setting (P), does a specific energy dose or regimen of energy doses for the initial or subsequent defibrillation attempt(s) (I), compared with 2 to 4 J kg^{-1} (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; ROSC; termination of arrhythmia (O)?

Introduction

Many of the world's resuscitation councils have different recommendations for defibrillation dosing for pediatric VF or pVT. The task force debated the existing limited (generally low-quality) science, while trying to arrive at consensus on guidelines for energy dosing for first or subsequent defibrillation doses.

Consensus on science

For the critical outcome of survival to hospital discharge, we identified very-low-quality evidence from 3 pediatric observational studies of IHCA and OHCA (downgraded for indirectness, imprecision, and serious risk of bias)[54–56] of 108 subjects showing no advantage to 2 to 4 J kg^{-1} as an initial defibrillation dose over any other specific energy dose (possible absolute effect size range, 18.5%–6.5%).

For the important outcome of termination of VF/pVT. We identified very-low-quality evidence from 2 pediatric observational studies of IHCA[57] and OHCA.[54] Conversion from VF was demonstrated in both studies with either 2 J kg^{-1} [57] or 2–4 J kg^{-1}.[54]

For the important outcome of ROSC, we identified very-low-quality evidence from 1 pediatric observational study of IHCA (downgraded for indirectness, imprecision, and serious risk of bias)[55] of 40 subjects, showing no benefit to a specific energy dose for initial defibrillation ($P = 0.11$). In addition, we identified very-low-quality evidence from 1 pediatric observational study of IHCA (downgraded for imprecision and serious risk of bias)[58] of 285 subjects showing that an initial shock of greater than 3–5 J kg^{-1} is less effective than 1–3 J kg^{-1} (OR, 0.42; 95% CI, 0.18–0.98; $P = 0.04$).

We did not identify any evidence to address the critical outcome of survival at 1 year or the important outcome of harm to patient.

Treatment recommendations

We suggest the routine use of an initial dose of 2–4 J kg^{-1} of monophasic or biphasic defibrillation waveforms for infants or children in VF or pVT cardiac arrest (weak recommendation, very-low-quality evidence).

There is insufficient evidence from which to base a recommendation for second and subsequent defibrillation dosages.

Values, preferences, and task force insights

In making these recommendations, we place a higher value on immediate defibrillation of a shockable rhythm over delaying defibrillation to select a specific dose that is not supported by scientific evidence. In addition, there are differing existing recommendations among the world's resuscitation councils that span the 2 to 4 J kg^{-1} recommendations, without strong evidence for one dose over the other. Practical considerations must be weighed when contemplating a change to pediatric defibrillation guidelines. Considerable challenges exist when attempting to reach and teach a broad spectrum of healthcare personnel using newly created educational materials, as well as the necessary resetting of targets for clinical audit. When faced with limited data, the risk-benefit assessment of changing to a different energy dose may be outweighed by maintaining the current recommendations.

Knowledge gaps

Pediatric evidence to date is observational and biased by multiple confounders (e.g., variable quality of CPR, duration of VF, primary versus secondary VF, monophasic versus biphasic waveforms). The very-low-quality evidence identified by this review highlights the need for further adequately powered RCTs (or high-quality, appropriately powered observational studies) addressing questions such as the effectiveness of:

- An initial shock of 2 versus 4 J kg^{-1}.
- An initial shock of 2–4 J kg^{-1} versus alternative energy doses.
- Subsequent shocks of 2–4 J kg^{-1} versus subsequent shocks using alternative energy doses or regimens.

Current pediatric literature cannot characterize risk of harm, as the data are predominantly registry-based.

Invasive blood pressure monitoring during CPR (Peds 826)

In infants and children undergoing CPR (P), does using invasive hemodynamic monitoring to titrate to a specific systolic/diastolic blood pressure (I), compared with not using invasive hemodynamic monitoring to titrate to a specific systolic/diastolic blood pressure (C), change survival to hospital discharge, 60 days after event, 180 days after event with favorable neurologic outcome, or the likelihood of ROSC or survival to hospital discharge (O)?

Introduction

Children often have a cardiac arrest in settings where invasive blood pressure monitoring (e.g., arterial blood pressure) already exists or is rapidly obtained. This review addressed whether the science exists to recommend using invasively monitored hemodynamics to titrate to higher CPR quality.

Extensive discussion ensued within the task force so as to arrive at the final wording of this PICO question. The "I" or intervention in the PICO question was originally inferred to be the use of invasive monitoring to titrate to improved CPR quality. Some thought that the "I" should refer to a specific numerical blood pressure target to be achieved as part of high-quality CPR. Ultimately, the task force agreed that the review should assess the simpler, broader question restricted to the "use of invasive monitoring," rather than focusing on a specific numeric blood pressure target.

Consensus on science

For the critical outcome of survival to 180 days and good neurologic outcome, we identified no studies. For the critical outcome of survival to 60 days and good neurologic outcome, we identified no studies. For the critical outcome of survival to hospital discharge and good neurologic outcome, we identified no studies.

For the critical outcome of the likelihood of survival to discharge, we identified very-low-quality evidence (downgraded for risk of bias, very serious inconsistency, very serious indirectness, and imprecision) from 2 pediatric animal RCTs[59,60] involving 43 subjects, which showed benefit.

For the important outcome of ROSC, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, very serious indirectness, and imprecision) from 2 pediatric animal RCTs[59,60] involving 43 subjects, which showed benefit.

Treatment recommendations

The confidence in effect estimates is so low that the panel decided a recommendation was too speculative.

Values, preferences, and task force insights

In considering making a recommendation, the task force placed a higher value on establishing and maintaining high-quality CPR over the ability to invasively obtain hemodynamic values by which to further titrate CPR. The potential exists for interruption to and loss of focus on good CPR technique while patients are being invasively instrumented for intra-arterial monitoring. Although we conceptually value optimizing (monitored) hemodynamics during CPR, we recognize the potential for harm to patients by targeting a specific parameter that is informed only by unblinded animal data and subject to important confounding variables. Rescuers in advanced care settings with access to invasive arterial blood pressure monitoring may continue to use targets based on expert consensus recommendations.

Knowledge gaps

- Given the suggestion of a possible effect in these studies, prospective clinical studies and further laboratory studies are needed.

$ETCO_2$ monitoring during CPR (Peds 827)

In infants and children in cardiac arrest (P), does adjustment of chest compression technique to achieve a specific $ETCO_2$ threshold (I), compared with not using $ETCO_2$ to adjust chest compression technique (C), change survival to 180 days with good neurologic outcome, the likelihood of survival to discharge, ROSC (O)?

Introduction

Animal and adult human data exist to support a direct association between $ETCO_2$ and cardiac output. Capnography is used during pediatric cardiac arrest to confirm endotracheal tube placement, and to monitor for ROSC and CPR quality. This review was constructed to determine how $ETCO_2$ monitoring could help improve CPR quality and patient outcomes.

Consensus on science

We did not identify any evidence to address the important outcome of survival to hospital discharge or the critical outcome of neurologically intact survival.

For the important outcome of ROSC, we identified very-low-quality evidence (downgraded for very serious indirectness and imprecision) from 1 pediatric animal RCT study that showed $ETCO_2$-guided chest compressions are as effective as standard chest compressions optimized by marker, video, and verbal feedback.[61]

Treatment recommendations

The confidence in effect estimates is so low that the panel decided a recommendation was too speculative.

Knowledge gaps

- The use of capnography during pediatric cardiac arrest has until now been informed by only animal data and extrapolation from adult observational data.

Amiodarone versus lidocaine for shock-resistant VF or pVT (Peds 825)

In infants and children with shock-refractory VF or pVT (P), does amiodarone (I), compared with lidocaine (C), change survival to hospital discharge, ROSC, recurrence of VF, termination of arrhythmia, risk of complications (e.g., need for tube change, airway injury, aspiration) (O)?

Introduction

Amiodarone has been recommended for the treatment of pediatric VF or pVT arrest. Lidocaine and amiodarone have been used in the treatment of adult VF/pVT cardiac arrest. The task force sought to determine if there was evidence to support 1 antiarrhythmic over the other for the treatment of infants and children with VF or pVT arrest.

Consensus on science

For the critical outcome of survival to hospital discharge, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, indirectness, and possible publication bias) from 1 observational cohort study of pediatric IHCA[62] that failed to show a significant association between the use of either amiodarone or lidocaine and survival to hospital discharge (OR, 0.8; 95% CI, 0.51–1.25).

For the important outcome of ROSC, there was very-low-quality evidence (downgraded for risk of bias, imprecision, indirectness, and possible publication bias) from 1 observational cohort study of pediatric IHCA[62] showing improved ROSC associated with lidocaine use when compared with amiodarone use (50.9% (87/171), ROSC in the amiodarone group and 62.4% (184/295) in the lidocaine group; $P = 0.002$). Use of lidocaine, compared with no lidocaine use, was significantly associated with an increased likelihood of ROSC (aOR, 2.02; 95% CI, 1.36–3).

For the important outcome of survival to hospital admission, there was very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT in adult OHCA[63] showing improved survival to hospital admission with intravenous amiodarone compared with intravenous lidocaine (OR, 2.17; 95% CI, 1.21–3.83; $P = 0.009$).

Treatment recommendation

We suggest that amiodarone or lidocaine may be used for the treatment of pediatric shock–resistant VF/pVT (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the use of pediatric-registry data that demonstrate an uncertain advantage to the use of either drug over the use of adult data. While demonstrating improved outcomes with the use of amiodarone, the literature does so only for short-term outcomes. Cost and availability of the two drugs may also be considerations in making a specific drug choice.

Vasopressor use during cardiac arrest (Peds 424)

Among infants and children in cardiac arrest (P), does the use of no vasopressor (epinephrine, vasopressin, combination of vasopressors) (I), compared with any use of vasopressors (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, ROSC (O)?

Introduction

While the use of vasopressors during cardiac arrest remains controversial, they continue to be recommended by resuscitation councils. Vasopressors are intended to help maintain cerebral perfusion while restoring spontaneous circulation by optimizing coronary blood flow. Vasopressor use comes at a risk of intense vasoconstriction and increased myocardial O_2 consumption. A randomized placebo-controlled trial in adults confirmed improved short-term patient outcomes (i.e., ROSC) but not longer-term patient outcomes with the use of epinephrine during OHCA.[64] This review was structured to ascertain the evidence base for vasopressor use during pediatric cardiac arrest.

Consensus on science

For infants and children in cardiac arrest, there are no studies that directly inform whether the use of no vasopressors (epinephrine, combination of vasopressors), compared with the use of any vasopressors, change survival to 180 days with good neurologic outcome, survival to hospital discharge, or ROSC.

For the critical outcome of survival with good neurologic outcome, we identified very-low-quality evidence (downgraded for indirectness, imprecision, inconsistency, and high risk of bias) from 2 pediatric out-of-hospital observational studies including 74 patients suggesting that the use of vasopressors versus no vasopressors has an uncertain benefit[65,66] (Dieckmann[66]: RR, 2.0; 95% CI, 0.50–7.98).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence (downgraded

for indirectness, imprecision, inconsistency, and high risk of bias) from 2 pediatric out-of-hospital observational studies including 74 patients suggesting that the use of vasopressors versus no vasopressors has an uncertain benefit[65,66] (Dieckmann[66]: RR, 1.67; 95% CI, 0.82–3.41).

For the important outcome of ROSC, we identified very-low-quality evidence (downgraded for indirectness, imprecision, inconsistency, and high risk of bias) from 2 pediatric out-of-hospital observational studies including 74 patients suggesting that the use of vasopressors versus no vasopressors has an uncertain benefit[65,66] (Dieckmann[66]: RR, 0.95; 95% CI, 0.80–1.14).

For all critical and important outcomes, we reviewed and considered a single underpowered adult OHCA RCT that provided very-low-quality evidence (downgraded for very serious indirectness, imprecision, and risk of bias) comparing standard-dose epinephrine to placebo.[64] For the critical outcome of good neurologic outcome and important outcome of survival to discharge, there was uncertain benefit or harm of standard-dose epinephrine compared with placebo. For the important outcomes of survival to hospital admission and ROSC, there was possible benefit of standard-dose epinephrine compared with placebo. (See also adult PICO question 788 in "Part 4: Advanced life support.")

Treatment recommendation

The confidence in effect estimates is so low that the panel decided a recommendation was too speculative.

Values, preferences, and task force insights

In considering making a recommendation, owing to the paucity of pediatric evidence of benefit or harm, the task force placed value on the short-term outcomes of ROSC and survival to hospital admission over uncertainty of the beneficial or harmful effect on long-term survival and neurologic outcome. It is reasonable for providers to use standard-dose epinephrine for pediatric cardiac arrest management.

Knowledge gaps

- If adult studies in OHCA suggest that vasopressor administration is associated with improved ROSC, but with worse survival to hospital discharge and neurologic outcome, then prospective studies of placebo versus epinephrine/vasopressors for pediatric cardiac arrest will be indicated.
- In addition, are there selected resuscitation circumstances (e.g., sudden witnessed adolescent cardiac arrest during exercise, pulmonary hypertension, myocarditis, imminent ECPR rescue) where the potential benefits and harms of administration of vasopressors should be explored?

ECPR for IHCA (Peds 407)

In infants and children with IHCA (P), does the use of ECMO for resuscitation, also called ECPR (I), when compared with conventional resuscitative treatment (CPR without the use of ECMO) (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, or survival to intensive care discharge (O)?

Introduction

Pediatric case series from cardiac arrest registries,[67] an extracorporeal life support registry,[68] and institutional reports[69,70] suggest that ECMO can be safely and effectively used in pediatric resuscitation. This therapy may be associated with added complications for individual patients (e.g., hemorrhage) and significant costs for a healthcare system.[71] The motivation to examine this topic was to provide guidance on the use of ECMO when used with conventional resuscitation measures for the purpose of optimizing survival, recovery, and neurologic outcome from pediatric IHCA. This review did not evaluate the use of ECPR for the purpose of supporting a patient for the end-point of organ donation for transplantation as this may involve different resuscitation goals and targets.

Consensus on science

For the critical outcome of survival at 180 days with favorable neurologic outcome, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 pediatric observational study of IHCA[72] showing no benefit to the use of ECPR when compared with CPR without the use of ECMO (RR, 1.21; 95% CI, 0.67–2.17).

For the critical outcome of survival to hospital discharge, we identified very-low-quality evidence from 4 pediatric observational studies of IHCA[71–74] (downgraded for indirectness, inconsistency, and residual confounding) and very-low-quality evidence from 1 unpublished analysis of a study's public dataset[75] (downgraded for serious risk of residual confounding) showing no benefit to the use of ECPR when compared with CPR without the use of ECMO (RR range, 0.64–1.63). We also identified low-quality evidence (downgraded for indirectness, inconsistency, and residual confounding) from a single pediatric study of IHCA[76] that showed benefit to ECPR when compared with CPR without the use of ECMO (OR, 2.5; 95% CI, 1.3–4.5; $P = 0.007$ in surgical cardiac diagnoses; OR, 3.8; 95% CI, 1.4–5.8; $P = 0.011$ in medical cardiac diagnoses).

Treatment recommendation

We suggest that CPR with ECMO (ECPR) may be considered for infants and children with cardiac diagnoses who have IHCA in settings that allow expertise, resources, and systems to optimize the use of ECMO during and after resuscitation (weak recommendation, very-low-quality evidence).

The confidence in effect estimates is so low that that there is insufficient evidence to suggest for or against the routine use of ECMO with conventional resuscitation (ECPR) in infants and children without cardiac diagnoses who have IHCA (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we value the improved survival of a select patient population (cardiac) over the expense incurred and intensity of resources necessary for universal deployment of ECMO for pediatric IHCA. All of the reports to date are heavily influenced by selection bias of ECPR candidates. There are significant expertise and resource implications for this treatment strategy to be appropriately applied. These should be taken into account before extending the implementation to in-patient settings, including the risk-benefit analysis for patients without cardiac diagnoses as well as those with cardiac conditions, whether or not related to the cause of the cardiac arrest. The task force acknowledged that selection of patients and local practice is highly variable and that further controlled studies are indicated.

Knowledge gaps

- Comparative studies in pediatric IHCA or OHCA receiving resuscitation with and without ECMO are lacking.
- The quality of CPR (quality of perfusion of cerebral and systemic circulations) before and during ECMO cannulation has not been studied in the pediatric setting.
- The optimal timing of initiation of ECMO during pediatric resuscitation measures in general has not been studied; both minimal interval and maximal intervals have not been established (studies are needed to establish these thresholds).
- The optimal timing of ECMO initiation during resuscitation measures in select populations such as patients with deep hypothermic

out-of-hospital arrest, pulmonary emboli, and high-risk, complex, congenital heart disease (e.g., in single-ventricle physiology) has not been established.
- The optimal anatomic vascular access for ECMO cannulation (neck versus femoral versus central) during resuscitation for optimal neuro- and cardio-protection has not been studied.
- The effect of co-interventions delivered during ECMO initiation and circulatory support (e.g., therapeutic hypothermia) has not been studied in the pediatric IHCA population.
- Interventions that warrant further evaluation also include the following: targeted temperature management (TTM) and rate of rewarming, blood flow rate on reperfusion, pulsatile versus nonpulsatile flow, oxygenation and carbon dioxide targets, hemodilution (associated with crystalloid circuit prime), hemofiltration, concurrent mechanical ventilation, inotropes and vasoactive strategies, thrombolytics or steroids.
- Studies incorporating functional outcomes are urgently needed.
- Application of alternative study designs to patient-level randomization study designs to evaluate benefit is needed, such as cluster-randomized trials or prospective observational with Bayesian methodology. Several centers have adopted the use of ECMO in resuscitation as standard practice in pediatric IHCA in selected pediatric populations. Random allocation of ECMO for resuscitation at an individual patient level presents several challenges, that decrease the feasibility of traditional RCT designs, suggesting that alternative study designs may need to be considered to minimize bias to compare interventions and generate clinical evidence to inform practice. Studies on the ethical frameworks applied or informed consent processes used with ECMO for resuscitation are also missing.

One of the largest obstacles identified in conducting traditional patient-level RCTs is that, in some healthcare settings, the perceived utility of ECMO may make those studies difficult to undertake (perceived absence of equipoise). Nonetheless, selection bias is prevalent, and the evidence base is limited. The task force suggests that, particularly in settings or countries where these services are available, this knowledge would be of considerable value.

Intra-arrest prognostic factors (Peds 814)

Among infants and children during cardiac arrest (P), does the presence of any specific intra-arrest prognostic factors (I), compared with the absence of these factors (C), change survival to 180 days with good neurologic outcome; survival to 60 days with good neurologic outcome; survival to hospital discharge with good neurologic outcome; survival to 30 days with good neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?

Introduction

If resuscitation resources (human and technical) are to be used appropriately, those patients who are most likely to benefit should ideally be identified before or early during active CPR. This review was structured to determine what evidence exists to allow for prognostication by rescuers during pediatric cardiac arrest.

Consensus on science

OHCA: age greater or less than 1 year. For the important outcome of 30-day survival with good neurologic outcome, we identified low-quality evidence for prognostic significance (downgraded for serious risk of bias and upgraded for moderate effect size) from 1 pediatric observational study of OHCA (5158 subjects)[52] in which age greater than 1 year was associated with improved survival when compared with age less than 1 year (relative risk (RR), 2.4; 95% CI, 1.7–3.4).

For the important outcome of 30-day survival, we identified very-low-quality evidence for prognostic significance (downgraded for serious risk of bias) from 1 pediatric observational study of OHCA (5158 subjects)[52] in which age greater than 1 year (versus age less than 1 year) was associated with improved survival (RR, 1.5; 95% CI, 1.3–1.8).

For the important outcome of survival to hospital discharge, we identified low-quality evidence for prognostic significance (downgraded for serious imprecision and upgraded for moderate effect size) from 1 pediatric observational study of OHCA (621 subjects)[77] in which age greater than 1 year (versus age less than 1 year) was significantly associated with improved outcome (RR, 2.7; 95% CI, 1.3–5.7). We identified very-low-quality evidence for prognostic significance (downgraded for very serious risk of bias and serious imprecision) from 2 pediatric observational OHCA studies[78,79] enrolling a total of 738 children that failed to show any significant difference in outcomes in patients older than 1 year when compared with patients younger than 1 year (Young[78]: RR, 1.3; 95% CI, 0.8–2.1; Moler[79]: RR, 1.4; 95% CI, 0.8–2.4).

OHCA: shockable versus nonshockable rhythms. For the important outcome of 30-day survival with good neurologic outcome, we identified low-quality evidence for prognostic significance (downgraded for serious risk of bias and upgraded for large effect size) from 1 pediatric observational study of OHCA (5170 subjects)[52] that found that VF as an initial rhythm compared with the combined rhythm group of pulseless electrical activity (PEA)/asystole was associated with improved survival (RR, 4.4; 95% CI, 3.6–5.3).

For the important outcome of 30-day survival, we identified moderate-quality evidence for prognostic significance (downgraded for serious risk of bias and upgraded for large effect size) from 1 pediatric observational study of OHCA (5170 subjects)[52] that found that VF as an initial rhythm compared with the combined rhythm group of PEA/asystole was associated with improved survival (RR, 9.0; 95% CI, 6.7–12.3).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence for prognostic significance (downgraded for very serious risk of bias and serious imprecision and upgraded for moderate effect size) from 2 pediatric observational studies of OHCA,[77,79] enrolling a total of 504 children, that found VF/pVT as an initial rhythm was significantly associated with improved outcome compared with the combined rhythm group of PEA/asystole (Atkins[77]: RR, 4.0; 95% CI, 1.8–8.9; and Moler[79]: RR, 2.7; 95% CI, 1.3–5.6). We identified very-low-quality evidence for prognostic significance (downgraded for very serious risk of bias) from 1 pediatric observational study of OHCA (548 subjects)[78] that failed to show a survival difference between VF/pVT as an initial rhythm when compared with the combined rhythm group of PEA/asystole (RR, 1.3; 95% CI, 0.5–3.0).

OHCA: duration of CPR. For the important outcome of survival to hospital discharge and survival to 1 year, we identified very-low-quality evidence for prognostic significance (downgraded for very serious risk of bias and serious imprecision and upgraded for large effect size) from 3 pediatric observational OHCA studies[78–80] enrolling a total of 833 children, showing a higher likelihood of survival with shorter duration of CPR. CPR for less than 20 min was associated with improved 1-year survival in 1 study (RR, 6.6; 95% CI, 2.9–14.9),[80] while median durations of 16 (interquartile range (IQR), 10–30) and 19 (IQR, 3.5–28.5) minutes were associated with survival to hospital discharge in 2 studies.[78,79]

IHCA: age greater or less than 1 year. For the important outcome of survival to hospital discharge, we identified low-quality evidence for prognostic significance from 1 pediatric observational IHCA study (3419 subjects)[12] that showed that age greater than 1 year

when compared with age less than 1 year was associated with lower survival to discharge (RR, 0.7; 95% CI, 0.6–0.8). There was low-quality evidence (not downgraded) from 1 pediatric observational study[81] of 502 subjects, and very-low-quality evidence (downgraded for very serious risk of bias and imprecision) from 2 pediatric observational IHCA studies[73,82] enrolling a total of 444 children subjects, that did not show a statistically significant difference for age greater than 1 year versus age less than 1 year.

For the critical outcome of survival to hospital discharge with good neurologic outcome, there was very-low-quality evidence (downgraded for very serious risk of bias) for prognostic significance from 1 pediatric observational IHCA study (464 subjects)[83] that did not show a difference for age greater than 1 year when compared with age less than 1 year (RR, 0.7; 95% CI, 0.4–1.0).

IHCA: shockable versus nonshockable rhythms. For the important outcome of survival to hospital discharge, there was low-quality evidence (not downgraded) for prognostic significance from 1 pediatric observational IHCA study (280 subjects)[81] showing that the presence of an initial arrest rhythm of VF/pVT when compared with asystole/PEA was associated with improved outcomes (RR, 1.6; 95% CI, 1.1–2.4). There was low-quality evidence (not downgraded) for prognostic significance from 1 pediatric observational study[12] (2903 subjects) that did not show statistical significance to the initial arrest rhythm (RR, 1.1; 95% CI, 1.0–1.3).

For the important outcome of 1-year survival, there was very-low-quality evidence (downgraded for very serious risk of bias and imprecision) for prognostic significance from 1 pediatric observational IHCA study (37 subjects)[84] that the initial arrest rhythm of VF/pVT when compared with asystole/PEA was not statistically significant (RR, 2.2; 95% CI, 0.7–6.5).

IHCA: duration of CPR. For the important outcome of 30-day survival, there was very-low-quality evidence (downgraded for very serious risk of bias and imprecision) for prognostic significance from 1 pediatric observational IHCA study (129 subjects)[85] that showed shorter duration of resuscitation events was associated with improved outcomes (adjusted relative risk (aRR), 0.95; 95% CI, 0.91–0.98 for each elapsed minute of CPR).

For the important outcome of survival to hospital discharge, there was very-low-quality evidence (downgraded for very serious risk of bias and imprecision) for prognostic significance from 1 observational study of pediatric IHCA (103 subjects)[86] that showed shorter duration of resuscitation events was associated with improved survival (aRR, 5.8; 95% CI, 1.3–25.5). Low-quality evidence (not downgraded) from 1 observational study of pediatric IHCA (3419 subjects)[12] showed shorter duration of resuscitation events (10 [IQR, 4–25] minutes versus 25 [IQR, 12–45] minutes) was associated with improved survival. This same study found significantly improved outcomes for surgical cardiac patients compared with general medical patients for all durations of resuscitation times (OR range, 2.2–3.7). Very-low-quality evidence (downgraded for very serious risk of bias) from 1 observational study of pediatric IHCA (330 subjects)[82] showed shorter duration of resuscitation events (8 [IQR, 3–19] minutes versus 13 [IQR, 5–31] minutes) was associated with improved survival (8 (IQR, 3–19) min versus 13 (IQR, 5–31) min). Very-low-quality evidence (downgraded for imprecision) from 1 observational study of pediatric IHCA (451 subjects),[81] when comparing resuscitation durations of less than 20 min to greater than 20 min, failed to show outcome differences that were statistically significant (RR, 0.8; 95% CI, 0.3–2.1).

For the critical outcome of survival to hospital discharge with good neurologic outcome, there was low-quality evidence from 1 observational study of pediatric IHCA (3419 subjects)[12] that showed that shorter duration of resuscitation was associated with improved survival to discharge with good neurologic outcome among surgical cardiac patients when compared with general medical patients for all durations of resuscitation (OR range, 2.0–3.3).

We did not identify enough evidence to address the critical outcomes of survival to 180 days with good neurologic outcome, or survival to 60 days with good neurologic outcome.

We did not identify any evidence to address the important outcomes of survival only at 60 days, 180 days.

Treatment recommendation

We suggest that for infants and children in cardiac arrest in the in-hospital setting, the use of predictors of positive patient outcome, such as patient age less than 1 year and the initial presence of a shockable rhythm, be used to assist prognostic decisions (weak recommendation, very-low-quality evidence for prognostic significance).

We suggest that for infants and children in cardiac arrest in the out-of-hospital setting, the use of predictors of positive patient outcome, such as age greater than 1 year or VF/pVT as an initial rhythm, be considered to assist prognostic decisions (weak recommendation, very-low-quality evidence for prognostic significance).

The confidence in estimates for the use of duration of resuscitation as a predictor of patient outcome in the in- or out-of-hospital setting is so low that the panel decided a recommendation was too speculative.

Values, preferences, and task force insights

In making this recommendation, we value the potential for individual children to have functional outcomes from cardiac arrest, despite the presence of individual poor prognostic factors, over the certainty of death associated with premature cessation of resuscitative efforts. We note that the measurement and reporting of quality of CPR, in addition to duration of CPR, confounds the attempt to define a cutoff duration. It is prudent for clinicians to use multiple patient factors and clinical observations and tests to help guide prognostication and decision-making during resuscitation, to avoid "self-fulfilling prophecies" of futility.

Knowledge gaps

- Large prospective studies of the association of pediatric cardiac arrest risk factors with outcomes are needed for rescuers to accurately predict successful outcomes and, in particular, to guide decisions on termination of resuscitation. In addition to age, arrest rhythm, and duration of resuscitation, other prognostic variables include but are not limited to illness etiology, initiating event (drowning, trauma, drug overdose, etc), and location of resuscitation (operating suite, ICU, emergency department). Studies need to be performed that maintain similar resuscitation protocols to reduce the risk of bias from changing treatment strategies, including post-ROSC care.

Post-ROSC care

The postresuscitation care section focuses on specific interventions and predictive factors to optimize the recovery of children after cardiac arrest and ROSC.

While the scope of postresuscitation syndrome care is broad, the Pediatric Task Force limited their evidence review to six topics. These are highlighted in Table 1 and include the following:

- Post-ROSC TTM (Peds 387).
- Post-ROSC Pao_2 (Peds 544).
- Post-ROSC ventilation (Peds 815).
- Post-ROSC fluid/inotropes (Peds 820).
- Post-ROSC electroencephalography (EEG) (Peds 822).
- Post-ROSC predictive factors (Peds 813).

Table 1
Postarrest checklist.

	Peds	ALS
Oxygenation and ventilation		
• Measure oxygenation and target normoxemia.		
• Avoid hypoxia.		
• Measure $Paco_2$, and target a clinically appropriate value.		
• Avoid hypocapnia.		
Hemodynamic monitoring		
• Monitor blood pressure.		
• Set hemodynamic goals during postresuscitation care		
• Use parenteral fluids and/or inotropes or vasopressors to maintain a systolic blood pressure greater than the fifth percentile.		
Targeted temperature management		
• Measure and monitor core temperature; prevent and treat fever.		
• In children, apply TTM (32 °C–34 °C or 36 °C–37.5 °C) for at least 24 h if unresponsive after ROSC.		
• In adults, select and maintain a constant target temperature between 32 °C and 36 °C if unresponsive after ROSC; if used, apply for at least 24 h.		
• Prevent fever after rewarming.		
Neuromonitoring		
• Treat clinical seizures.		
• Do not routinely use pharmacologic prophylaxis for seizures.		
Glucose control		
• Measure glucose.		
• Avoid hypoglycemia.		
• In adults, follow standard glucose control protocols.		
Prognosis		
• Always consider multiple modalities (clinical and other) over any single predictor factor.		
• EEG may be useful within the first seven days.		
• Somatosensory evoked potentials may be useful after 72 h.		
• Blood biomarkers may be measured repeatedly over 72 h.		
• Neuroimaging such as CT in the initial hours and MRI during the first six days may be valuable.		
• Remember that assessments may be modified by TTM or induced hypothermia.		

ALS indicates advanced life support; CT, computed tomography; EEG, electroencephalography; MRI, magnetic resonance imaging; ROSC, return of spontaneous circulation; and TTM, targeted temperature management.

Post-ROSC TTM (Peds 387)

Among infants and children who are experiencing ROSC after cardiac arrest in any setting (P), does the use of TTM (e.g., therapeutic hypothermia) (I), compared with the use of normothermia (C), change survival to hospital discharge, ICU LOS (O)?

Consensus on science

For the critical outcome of neurologic function at 1 year, we identified moderate-quality evidence (downgraded for imprecision) from 1 RCT of pediatric OHCA,87 involving 260 infants and children, that failed to show a significant difference in the proportion of patients receiving a score higher than 70 at 1 year (27/138 versus 15/122; RR, 1.54; 95% CI, 0.85–2.76), when comparing patients who received TTM to either 33 °C or 36.8 °C (Vineland Adaptive Behavioral Scale, 2nd edition).

For the critical outcome of survival to 6 months with good neurologic outcome, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric observational multicenter study of IHCA and OHCA[88] involving 79 patients that failed to show a significant difference in functional outcome (specifically Pediatric Cerebral Performance Category [PCPC], 4–6; aOR, 2.00; 95% CI, 0.45–9.01) with the use of TTM.

For the critical outcome of survival to hospital discharge with good neurologic outcome, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric observational study of asphyxial IHCA and OHCA[89] of 24 patients that failed to show significantly improved outcomes (PCPC, 1–2) with the use of TTM (RR, 1.77; 95% CI, 0.92–3.40).

For the critical outcome of survival to 6 months, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric observational multicenter study of IHCA and OHCA[88] involving 79 patients that failed to show a significant difference in outcome (aOR, 1.99; 95% CI, 0.45–8.85).

For the critical outcome of survival to 30 days, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 pediatric observational multicenter study of IHCA and OHCA[88] involving 79 patients that failed to show a significant difference in outcome (aOR, 2.50; 0.55–11.49).

For the critical outcome of survival to hospital discharge, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 2 pediatric observational studies, 1 with both in-hospital and out-of-hospital asphyxial cardiac arrest[89] of 42 patients, that showed improved outcomes with the use of TTM (RR, 1.69; 95% CI, 1.04–2.74) and a single-center observational study of pediatric OHCA,[90] involving 73 children over a 6-year period, that did not show a difference in survival at discharge from hospital (13/38 TTM versus 8/35 standard temperature management (STM); $P = 0.28$).

For the important outcome of survival to 1 year, we identified moderate-quality evidence (downgraded for imprecision) from 1 RCT of pediatric OHCA,[87] involving 287 patients, that failed to show a difference when comparing patients who received TTM to either 33 °C or 36.8 °C (57/151, 33 °C group; 39/136, 36.8 °C group; RR, 1.29; 95% CI, 0.93–1.79).

For the important outcome of PICU LOS, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 3 pediatric observational studies of IHCA and OHCA[88,90,91] involving 79, 181, and 73 patients, respectively. Two of these studies failed to show any difference in PICU LOS (Doherty[88]: TTM median LOS was 16 (IQR, 4–30.5) days compared with 9 (IQR 5–22.5) days; $P = 0.411$; Fink[91]: mean PICU LOS was TTM 20 ± 47.7 days versus normothermia 20.1 ± 35.9 days; $P = 0.5$). One study[90] found that the LOS was longer for those treated with TTM than without TTM (i.e., median duration of 4.1 (IQR, 3.0–6.8) days as compared with 1.3 (IQR, 0.5–6.7) days; $P < 0.001$). The authors attributed this difference to more interventions in the TTM group and to withdrawing treatment later than in patients without TTM.

Treatment recommendation

We suggest that for infants and children with OHCA, TTM be used in the post–cardiac arrest period. While the ideal target temperature range and duration are unknown, it is reasonable to use either hypothermia (32 °C–34 °C) or normothermia (36 °C–37.5 °C) (weak recommendation, moderate-quality evidence).

For pediatric survivors of IHCA, the confidence in effect estimates for the use of TTM is so low that the task force decided that a recommendation was too speculative.

Values, preferences, and task force insights

In making this recommendation, the task force preferred the use of a targeted temperature of 32 °C to 34 °C as opposed to the normothermic range, based on the fact that while the Therapeutic

Hypothermia After Pediatric Cardiac Arrest (THAPCA) study did not show success for the primary outcome (neurologic status at 1 year), it was underpowered to show a significant difference for survival, for which the lower 95% CI approached 1, with the Kaplan-Meier survival curves showing a tendency toward better outcomes at the lower temperature ranges. Furthermore, the task force noted that hyperthermia occurs frequently in the postarrest period, and that this is potentially harmful and should be avoided. There were insufficient data on IHCA patients, who may represent a different population. The provision of TTM to an individual patient can be resource intensive. These resources, the associated expertise necessary to deliver and maintain TTM, and the presence of appropriate systems of critical care are required to provide optimal post-ROSC care. The task force noted that the application of TTM may require sedation, analgesia, and neuromuscular blockade that will modify neurologic assessment.

Knowledge gaps

- The THAPCA OHCA trial suggests that, when comparing the use of TTM and temperature targets of 33 °C or 36.8 °C, there is no difference in terms of mortality or neurologic functioning at 1 year after event. This suggests that equipoise exists for further study, including specific target temperatures, time to target temperature, and duration of TTM. There is a requirement to monitor the long-term outcomes of post-ROSC children who undergo either TTM or STM, to establish the associated risks and benefits. It remains unclear as to whether certain subpopulations of cardiac arrest patients, such as those with IHCA, may benefit from TTM. The results are awaited from a multicenter study of TTM for pediatric IHCA (THAPCA, in-hospital study arm).[92] The RCTs are registered on www.clinicaltrials.gov (Trial NCT00880087, Therapeutic Hypothermia to Improve Survival After Cardiac Arrest in Pediatric Patients-THAPCA-IH (In Hospital) Trial). See also THAPCA.gov.
- There is insufficient information available on the possible complications associated with TTM or cooling.

Post-ROSC Pao_2 (Peds 544)

Among infants and children with ROSC after cardiac arrest (in- or out-of-hospital setting) (P), does the use of a targeted Pao_2 strategy (I), compared with a strategy of no targeted Pao_2 (C), change ICU LOS, survival to 180 days with good neurologic outcome, survival to hospital discharge, survival to ICU discharge, survival to 6 months (O)?

Introduction

Animal studies and some observational adult data suggest that post-ROSC exposure to elevated levels of tissue Po_2 may worsen postresuscitation syndrome. In the absence of prospective studies of post-ROSC oxygenation, the task force was reliant on retrospective cohort studies that evaluated differing post-ROSC Pao_2 levels and looked for association with outcomes.

Consensus on science

For the critical outcome of **s**urvival to hospital discharge with good neurologic outcome, we identified very-low-quality evidence from 1 observational study[93] of 153 pediatric IHCA and OHCA survivors (downgraded for indirectness, imprecision, and very serious risk of bias) showing no association between post-ROSC normoxemia or hyperoxemia and benefit or harm (RR, 1.27; 95% CI, 0.86–1.90).

For the critical outcome of survival to 6 months, we identified very-low-quality evidence from 1 observational study[94] of 64 pediatric IHCA and OHCA survivors to PICU admission (downgraded for indirectness, imprecision, and very serious risk of bias) showing no association between post-ROSC normoxemia or hyperoxemia and benefit or harm (RR, 1.09; 95% CI, 0.81–1.46).

For the critical outcome of survival to hospital discharge, we identified very-low-quality evidence from 1 observational study[95] of 164 pediatric IHCA survivors (downgraded for indirectness, imprecision, and very serious risk of bias) showing no association between post-ROSC normoxemia or hyperoxemia and benefit or harm (RR, 1.25; 95% CI, 0.76–2.05).

For the important outcome of survival to PICU discharge, we identified very-low-quality evidence from 1 observational study[96] of 1427 pediatric IHCA and OHCA survivors to PICU admission (downgraded for indirectness and very serious risk of bias) showing no association between post-ROSC normoxemia or hyperoxemia and benefit or harm (RR, 1.08; 95% CI, 0.95–1.23).

Treatment recommendation

We suggest that rescuers measure Pao_2 after ROSC and target a value appropriate to the specific patient condition. In the absence of specific patient data, we suggest rescuers target normoxemia after ROSC (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

Accurate targeting of post-ROSC normoxemia might be achievable and acceptable in the in-hospital setting, but its use in the prehospital setting has not been studied and is not without risk of inadvertent patient hypoxemia. Any titration of oxygen delivery to children after ROSC must be balanced against the risk of inadvertent hypoxemia stemming from overzealous weaning of Fio_2. Further challenges for pediatrics include identifying what the appropriate targets should be for specific patient subpopulations (e.g., infants and children with cyanotic heart disease).

Knowledge gaps

- The data from the four observational studies cited derive from a diverse patient population (IHCA versus OHCA, different etiologies of cardiac arrest, different patient populations) that has been exposed to variable doses of post-ROSC oxygen (Fio_2 and duration of exposure), and has reported association with different outcomes. In addition, the timing of the evaluation of post-ROSC arterial oxygen tension varied widely between and even within studies. Attempts should be made to investigate a larger and more homogenous patient population, through a multi-institutional study design, with a defined duration of exposure to a set Fio_2, and with predefined patient outcomes.

Post-ROSC ventilation: $Paco_2$ goals (Peds 815)

Among infants and children with ROSC after cardiac arrest in any setting (P), does ventilation to a specific $Paco_2$ target (I), compared with ventilation to no specific $Paco_2$ target (C), change survival with favorable neurologic outcome, survival to 180 days with good neurologic outcome, survival to 30 days with good neurologic outcome, the likelihood of a good quality of life after discharge from the hospital, survival to hospital discharge, survival to 30 days, survival to 60 days, survival to 6 months, survival to ICU discharge (O)?

Introduction

The post-ROSC period may be associated with altered cardiocerebral interaction, and high ventilation tidal volumes and intrathoracic pressures may affect cardiopulmonary interaction. A low Pco_2 may affect vascular tone, affecting pulmonary and cerebral blood flow, blood volume, and compartmental pressures. Cerebral vascular autoregulation may be abnormal after ROSC.

Consensus on science

There are no studies specifically comparing ventilation to a predetermined $Paco_2$ target in children after cardiac arrest. Furthermore, there are no studies in the prehospital setting.

Part A: hypercapnia versus normocapnia. For the critical outcome of survival to hospital discharge with favorable/functional neurologic outcome (assessed with PCPC 1–2 or no change from baseline before cardiac arrest), we identified very-low-quality evidence from 1 pediatric observational study of IHCA and OHCA (downgraded for indirectness, imprecision, and serious risk of bias[93]) involving 195 survivors to at least 6 h after arrest that there was no association between hypercapnia ($Paco_2$ greater than 50 mm Hg) and outcome (RR, 0.76; 95% CI, 0.50–1.16).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence from 1 pediatric observational study of IHCA (downgraded for inconsistency, indirectness, imprecision, and serious risk of bias[95]) involving 223 subjects showing that worse outcomes were associated with hypercapnia ($Paco_2$ 50 mm Hg or greater) than when the $Paco_2$ was less than 50 mm Hg (RR, 0.48; 95% CI, 0.27–0.86).

Part B: hypocapnia versus normocapnia. For the critical outcome of survival to hospital discharge with favorable/functional neurologic outcome (assessed with PCPC 1–2 or no change with baseline before cardiac arrest), we identified very-low-quality evidence from 1 pediatric observational study of IHCA and OHCA (downgraded for indirectness, imprecision, and serious risk of bias[93]), involving 195 survivors to at least 6 h postarrest, that failed to show an association between hypocapnia ($Paco_2$ less than 30 mm Hg) and outcome (RR, 0.70; 95% CI, 0.43–1.14).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence from 1 pediatric observational study of IHCA (downgraded for inconsistency, indirectness, imprecision, and serious risk of bias[95]), involving 223 subjects, that failed to show an association between hypocapnia ($Paco_2$ less than 30 mm Hg) and outcome (RR, 0.83; 95% CI, 0.46–1.51).

Treatment recommendation

We suggest that rescuers measure $Paco_2$ after ROSC and target a value appropriate to the specific patient condition, although the confidence in effect estimates is so low that the panel decided a recommendation for a specific $Paco_2$ target was too speculative.

Knowledge gaps

- No studies demonstrate better outcomes with ventilation to any specific $Paco_2$ in pediatric patients with ROSC. The upper and lower limits at which $Paco_2$ becomes harmful are unknown. Hypocapnia during the postarrest period is associated with worse outcome in adult studies. Although mild hypercapnia may have some neuroprotective effect in adult studies, this has not been observed in the pediatric population. We recognize that the criteria for normocapnia may be context-specific (prehospital versus in-hospital) and disease dependent. We do not have pediatric evidence for or against $Paco_2$ targets in patients treated with therapeutic hypothermia. For the subgroup of adult patients being treated with therapeutic hypothermia after ROSC, neither hypocapnia nor hypercapnia was associated with benefit.
- It is not known whether patients undergoing "permissive hypercapnia" as a lung-protective ventilator strategy before cardiac arrest may benefit from maintaining an elevated $Paco_2$.

Post-ROSC fluid/inotropes (Peds 820)

In infants and children after ROSC (P), does the use of parenteral fluids and inotropes and/or vasopressors to maintain targeted measures of perfusion such as blood pressure (I), as compared with not using these interventions (C), change patient satisfaction; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; harm to patient (O)?

Introduction

Shock occurs commonly in infants and children after ROSC. This review was structured to study the evidence base that would allow identification of an appropriate post-ROSC blood pressure to avoid shock as well as the best interventions (intravenous fluid versus inotropes/vasopressors) to achieve that blood pressure.

Consensus on science

For the critical outcome of survival to hospital discharge with good neurologic outcome, we identified very-low-quality evidence from 1 pediatric observational study of IHCA and OHCA (downgraded for risk of bias, indirectness, and imprecision[97]) involving 367 children, showing worse outcomes when subjects experienced systolic blood pressures less than fifth percentile for age after ROSC (RR, 0.78; 95% CI, 0.62–0.99).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence from 3 pediatric observational studies of IHCA and OHCA (downgraded for risk of bias, inconsistency, indirectness, and imprecision[97–99]) involving a total of 615 subjects, showing worse outcomes when children experienced hypotension after ROSC. Significant heterogeneity (I-squared value 0.87) did not support pooling the data from these 3 studies (Topjian[97]: OR, 0.62; 95% CI, 0.41–0.93; Lin[98] OR, 0.10; 95% CI, 0.03–0.32; and Lin[99] OR, 0.07; CI, 0.02–0.25).

For the important outcome of harm to patient, we identified no evidence.

Treatment recommendations

We recommend that for infants and children after ROSC, parenteral fluids and/or inotropes or vasopressors should be used to maintain a systolic blood pressure of at least greater than the fifth percentile for age (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on avoiding mortality and progressive organ failure from the effects of hypotension than on unknown harms that may be associated with the use of fluids, inotropes, or vasopressors. Although the measurement of blood pressure has limitations in determining perfusion of vital organs, it is a practical and valued measurement of hemodynamic status. The task force made a strong recommendation despite the weakness of the available evidence, owing to the intuitive need to avoid hypotension where there is a likely association with reduced perfusion of vital organs.

Knowledge gaps

- All evidence was observational, so while associations can be made between hypotension and outcomes, the potential remains that unrecognized/unadjusted confounders might be contributing to these associations.
- Other knowledge gaps include the following:

- The optimal strategy to avoid hypotension (i.e., the relative use of parenteral fluids versus inotropes and/or vasopressors) in children post-ROSC after cardiac arrest is currently unclear.
- The optimal perfusion endpoints to target have yet to be defined but could include systolic blood pressure, mean blood pressure, measures of cardiac output, and/or other markers of perfusion such as serum lactate.
- The optimal time period during which targeted measures of perfusion should be considered remains unclear.
- It is unclear whether any harm to the patient or adverse effects may arise as a result of use of parenteral fluids and inotropes and/or vasopressors to maintain targeted measures of perfusion.
- It is unknown if there are subgroups of children who respond differently to components of the intervention, such as cardiac patients or trauma patients who may be particularly sensitive to preload status and changes in afterload.

Post-ROSC EEG (Peds 822)

For infants and children who have had cardiac arrests in the in-hospital or out-of-hospital setting (P), does any use of neuroelectrophysiology information (EEG) (I), compared with none (C), predict survival at 1 year with good neurologic outcome, survival to 180 days with good neurologic outcome, survival to 60 days with good neurologic outcome, survival to 6 months, survival to 30 days with good neurologic outcome, survival to hospital discharge with good neurologic outcome, survival with favorable neurologic outcome, survival to hospital discharge (O)?

Introduction

This review was undertaken to determine if abnormalities on EEG or electrophysiological testing, which are common after ROSC, could be used to help predict the outcomes of infants and children after cardiac arrest.

Consensus on science

For the important outcome of survival to hospital discharge with good neurologic outcome, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, imprecision, and publication bias) for prognostic significance from 2 pediatric observational studies of IHCA and OHCA[100,101] enrolling 68 subjects, showing that an EEG performed within the first 7 days after cardiac arrest and demonstrating a continuous and reactive tracing is associated with a higher likelihood of good neurologic outcome at hospital discharge (RR, 4.18; 95% CI, 2.25–7.75), compared with an EEG demonstrating a discontinuous or isoelectric tracing being associated with a higher likelihood of poor neurologic outcome at hospital discharge (RR, 2.19; 95% CI, 1.51–3.77).

We did not identify any evidence to address the critical outcome of survival to 180 days or 1 year with good neurologic outcome.

Treatment recommendations

We suggest that the use of EEG within the first 7 days after pediatric cardiac arrest may assist in prognostication (weak recommendation, very-low-quality evidence).

The confidence in predictive estimates for the use of EEG alone as a predictor after pediatric IHCA and OHCA is so low that the panel decided a recommendation to use EEG alone to make decisions is too speculative.

Values, preferences, and task force insights

We place greater value on preserving opportunities for recovery than on limiting therapy based on insufficiently studied prognostic tools that might be used in isolation.

Knowledge gaps

- As none of the studies blinded clinicians to EEG results, a high risk of bias exists. The use of an investigation that has not been validated as a prognostic tool may affect the clinical course and create "self-fulfilling prophecies," leading to a worse outcome.
- The data from these two limited studies derive from a relatively limited patient sample that may not be representative of the broader pediatric population. Although IHCA and OHCA and different etiologies of cardiac arrest were included, both studies were single-center studies from the same institution. Attempts should be made to incorporate multicenter study samples as well as examine a standardized approach to EEG analysis (standardization of background analysis, timing of EEG after cardiac arrest).
- A well-defined consensus on classification of EEG background would be informative.
- Multicenter prospective studies that include longer-term outcomes would be valuable.

Post-ROSC Predictive Factors (Peds 813)

Among infants and children with return of circulation (P), does the presence of any specific factors (I), compared with the absence of those factors (C), change survival to 180 days with good neurologic outcome; survival to 60 days with good neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to 30 days with good neurologic outcome; survival to hospital discharge with good neurologic outcome (O)?

Introduction

The purpose of this review was to determine whether the presence of any specific variable after resuscitation (such as blood or serum biomarkers and clinical examination) could assist in predicting outcomes for children and infants after ROSC.

Consensus on science

For the critical outcome of survival to 180 days with good neurologic outcome, we identified very-low-quality evidence for prognostic significance (downgraded for imprecision and risk of bias) from 1 pediatric observational prospective cohort study of IHCA and OHCA,[102] enrolling 43 children showing that reactive pupils at 24 h after ROSC is associated with improved outcomes (RR, 5.94; 95% CI, 1.5–22.8).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence for prognostic significance (downgraded for imprecision and risk of bias, but with moderate dose-response relationship) from 4 pediatric observational studies of IHCA and OHCA,[79,82,101,103] enrolling a total of 513 children showing that pupils reactive to light 12–24 h after ROSC is associated with improved outcomes (RR, 2.3; 95% CI, 1.8–2.9).

For the important outcome of survival to hospital discharge with good neurologic outcome, we identified very-low-quality evidence for prognostic significance (downgraded for risk of bias and imprecision, but with a moderate effect size) from 2 pediatric observational studies of IHCA and OHCA,[101,103] enrolling a total of 69 children showing that pupils reactive to light before hypothermia or 24 h after ROSC is associated with improved outcomes (OR, 3.0; 95% CI, 1.4–6.5).

For the important outcomes of survival to hospital discharge and hospital discharge with good neurologic outcome, we identified very-low-quality evidence for prognostic significance (downgraded for risk of bias and imprecision) from 2 pediatric observational studies of IHCA and OHCA,[102,104] enrolling a total of 78 children showing that lower neuron-specific enolase (NSE) or S100B serum levels at 24, 48, and 72 h are associated with an increased likelihood of improved outcomes ($P < 0.001$ to $P < 0.02$).

For the important outcome of survival to hospital discharge, we identified very-low-quality evidence for prognostic significance (downgraded for imprecision and risk of bias) from 1 pediatric observational study of IHCA and OHCA,[105] enrolling 264 children showing that lower serum lactate levels at 0 to 6 h ($P < 0.001$) and 7 to 12 h ($P < 0.001$) after ROSC are associated with improved outcomes.

Treatment recommendations

We suggest that practitioners use multiple variables when attempting to predict outcomes for infants and children after cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

We place greater value on preserving opportunities for recovery than on limiting therapy based on as-yet-unvalidated prognostic tools.

Knowledge gaps

- Multiple knowledge gaps exist.
- What is the effect of evolving post-ROSC care (TTM, hypotension/cardiovascular function, etc) on markers of prognostication?
- In addition, causes of cardiac arrest and differences in arrest location may have an effect on our ability to use post-ROSC factors in prognostication.
- Prospective blinded studies are needed to validate the use of prognostic factors; otherwise, these unvalidated factors may create "self-fulfilling prophecies" of poor outcomes.

Disclosures

2015 CoSTR Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support: Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Ian K. Maconochie	St. Mary's Hospital	None	None	None	None	None	None	None
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Amelia G. Reis	Inter-American Heart Foundation	None	None	None	None	None	None	None
Naoki Shimizu	Tokyo Metropolitan Children's Medical Centre	Governmental grant[a]	None	None	None	None	None	None
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Remigio Veliz Pintos	Inter-American Heart Foundation	None	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

[a] Modest.

[b] Significant.

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Appendix A.

CoSTR Part 6: PICO Appendix

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 6	Peds	Peds 387	Post-ROSC TTM	Among infants and children who are experiencing ROSC after cardiac arrest in any setting (P), does the use of TTM (e.g., therapeutic hypothermia) (I), compared with the use of normothermia (C), change survival to hospital discharge, ICU LOS (O)?	Ian Maconochie, Mark Coulthard
Part 6	Peds	Peds 394	Chest compression depth	In infants and children receiving chest compressions (in or out of hospital) (P), does the use of any specific chest compression depth (I), compared with the depth specified in the current treatment algorithm (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, complication rate, or intermediate physiological endpoints (O)?	Gabrielle Nuthall, Fernanda Sá
Part 6	Peds	Peds 397	Pediatric METs and RRTs	For infants and children in the in-hospital setting (P), does the use of pediatric METs/RRTs (I), compared with not using METs/RRTs (C), change cardiac or pulmonary arrest frequency outside of the ICU, overall hospital mortality (O)?	Kee Chong Ng, Dianne Atkins
Part 6	Peds	Peds 405	Energy doses for defibrillation	Among infants and children who are in VF or pVT in any setting (P), does a specific energy dose or regimen of energy doses for the initial or subsequent defibrillation attempt(s) (I), compared with 2–4 J kg^{-1} (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; ROSC; termination of arrhythmia (O)?	Robert Bingham, Stuart Dalziel
Part 6	Peds	Peds 407	ECPR for IHCA	In infants and children with IHCA (P), does the use of ECMO for resuscitation, also called ECPR (I), when compared with conventional resuscitative treatment (CPR without the use of ECMO) (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, or survival to intensive care discharge (O)?	Anne-Marie Guerguerian, Ericka Fink
Part 6	Peds	Peds 414	Chest compression—only CPR versus conventional CPR	Among infants and children who are in cardiac arrest in any setting (P), does compression-only CPR (I), compared with the use of conventional CPR (C), change neurologically intact survival at 1 year, survival to hospital discharge, improved ICU LOS, neurologically intact survival at 30 days (O)?	Jonathan Duff, Dominique Biarent
Part 6	Peds	Peds 424	Vasopressor use during cardiac arrest	Among infants and children in cardiac arrest (P), does the use of no vasopressor (epinephrine, vasopressin, combination of vasopressors) (I), compared with any use of vasopressors (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, ROSC (O)?	Vinay Nadkarni, David Kloeck
Part 6	Peds	Peds 544	Post-ROSC Pao_2	Among infants and children with ROSC after cardiac arrest (in- or out-of-hospital setting) (P), does the use of a targeted Pao_2 strategy (I), compared with a strategy of no targeted Pao_2 (C), change ICU LOS, survival to 180 days with good neurologic outcome, survival to hospital discharge, survival to ICU discharge, survival to six months (O)?	Allan de Caen, Amelia Reis
Part 6	Peds	Peds 545	Fluid resuscitation in septic shock	Among infants and children who are in septic shock in any setting (P), does the use of restricted volumes of resuscitation fluid (I1) when compared with nonrestricted volumes (C1), or the use of noncrystalloid fluids (I2) when compared with crystalloid fluids (C2), change survival to hospital discharge, need for mechanical ventilation or vasopressor support, complications, time to resolution of shock, hospital length of stay (LOS), ventilator-free days, total intravenous (IV) fluids administered (O)?	Richard Aickin, Peter Meaney
Part 6	Peds	Peds 709	Sequence of chest compressions and ventilations: C–A–B versus A–B–C	Among infants and children who are in cardiac arrest in any setting (P), does the use of a circulation-airway-breathing approach to initial management (I), compared with the use of an airway-breathing-circulation approach to initial management (C), change ROSC, survival to hospital discharge, survival to 180 days with good neurologic outcome, time to first compressions (O)?	Naoki Shimizu, Christoph Eich
Part 6	Peds	Peds 813	Post-ROSC predictive factors	Among infants and children with return of circulation (P), does the presence of any specific factors (I), compared with the absence of those factors (C), change survival to 180 days with good neurologic outcome; survival to 60 days with good neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to 30 days with good neurologic outcome; survival to hospital discharge with good neurologic outcome (O)?	Thomaz Bittencourt Couto, Marc Berg
Part 6	Peds	Peds 814	Intra-arrest prognostic factors	Among infants and children during cardiac arrest (P), does the presence of any specific intra-arrest prognostic factors (I), compared with the absence of these factors (C), change survival to 180 days with good neurologic outcome; survival to 60 days with good neurologic outcome; survival to hospital discharge with good neurologic outcome; survival to 30 days with good neurologic outcome; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year (O)?	Audrey Shibata, Steve Schexnayder
Part 6	Peds	Peds 815	Post-ROSC ventilation: $PaCo_2$ goals	Among infants and children with ROSC after cardiac arrest in any setting (P), does ventilation to a specific $PaCo_2$ target (I), compared with ventilation to no specific $PaCo_2$ target (C), change survival with favorable neurologic outcome, survival to 180 days with good neurologic outcome, survival to 30 days with good neurologic outcome, the likelihood of a good quality of life after discharge from the hospital, survival to hospital discharge, survival to hospital discharge, survival to 30 days, survival to 60 days, survival to 6 months, survival to ICU discharge (O)?	Javier Urbano, Janice Tijssen

Appendix A (*Continued*)

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 6	Peds	Peds 818	PEWS	For infants and children in the in-hospital setting (P), does the use of a pediatric early warning score (I), compared with not using a pediatric early warning score (C), change overall hospital mortality, Cardiac arrest frequency outside of the ICU (O)?	Alexis Topjian, Antonio Rodriguez-Nunez
Part 6	Peds	Peds 819	Prearrest care of pediatric dilated cardiomyopathy or myocarditis	For infants and children with myocarditis or dilated cardiomyopathy and impending cardiac arrest (P), does a specific approach (I), compared with the usual management of shock or cardiac arrest (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; cardiac arrest frequency; ROSC (O)?	Graeme MacLaren, Ravi Thiagarajan
Part 6	Peds	Peds 820	Post-ROSC fluid/inotropes	In infants and children after ROSC (P), does the use of parenteral fluids and inotropes and/or vasopressors to maintain targeted measures of perfusion such as blood pressure (I), as compared with not using these interventions (C), change patient satisfaction; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; harm to patient (O)?	Melissa Parker, Takanari Ikeyama
Part 6	Peds	Peds 821	Atropine for emergency intubation	In infants and children requiring emergency tracheal intubation (P), does the use of atropine as a premedication (I), compared with not using atropine (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 90 days, 180 days, and/or 1 year after event; the incidence of cardiac arrest; survival to hospital discharge; the incidence of peri-intubation shock or arrhythmias (O)?	Gene Ong, Jos Bruinenberg
Part 6	Peds	Peds 822	Post-ROSC EEG	For infants and children who have had cardiac arrests in the in-hospital or out-of-hospital setting (P), does any use of neuroelectrophysiology information (EEG) (I), compared with none (C), predict survival at 1 year with good neurologic outcome, survival to 180 days with good neurologic outcome, survival to 60 days with good neurologic outcome, survival to 6 months, survival to 30 days with good neurologic outcome, survival to hospital discharge with good neurologic outcome, survival with favorable neurologic outcome, survival to hospital discharge (O)?	Stuart Friess, Corsino Rey
Part 6	Peds	Peds 825	Amiodarone versus lidocaine for shock-resistant VF or pVT	In children and infants with shock-refractory VF or pVT (P), does amiodarone (I), compared with lidocaine (C), change survival to hospital discharge, ROSC, recurrence of VF, termination of arrhythmia, risk of complications (e.g., need for tube change, airway injury, aspiration) (O)?	Dianne Atkins, Mary McBride, Brad Marino
Part 6	Peds	Peds 826	Invasive blood pressure monitoring during CPR	In children and infants undergoing CPR (P), does using invasive hemodynamic monitoring to titrate to a specific systolic/diastolic blood pressure (I), compared with not using invasive hemodynamic monitoring to titrate to a specific systolic/diastolic blood pressure (C), change survival to hospital discharge, 60 days after event, 180 days after event with favorable neurologic outcome, or the likelihood of ROSC or survival to hospital discharge (O)?	Tia Raymond, Jonathan Egan
Part 6	Peds	Peds 827	$ETCO_2$ monitoring during CPR	In infants and children in cardiac arrest (P), does adjustment of chest compression technique to achieve a specific $ETCO_2$ threshold (I), compared with not using $ETCO_2$ to adjust chest compression technique (C), change survival to 180 days with good neurologic outcome, the likelihood of survival to discharge, ROSC (O)?	Remigio Veliz, Monica Kleinman

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Part 7: Neonatal resuscitation 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆,☆☆

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Introduction

Newborn transition

The transition from intrauterine to extrauterine life that occurs at the time of birth requires timely anatomic and physiologic adjustments to achieve the conversion from placental gas exchange to pulmonary respiration. This transition is brought about by initiation of air breathing and cessation of the placental circulation. Air breathing initiates marked relaxation of pulmonary vascular resistance, with considerable increase in pulmonary blood flow and increased return of now-well-oxygenated blood to the left atrium and left ventricle, as well as increased left ventricular output. Removal of the low-resistance placental circuit will increase systemic vascular resistance and blood pressure and reduce right-to-left shunting across the ductus arteriosus. The systemic organs must equally and quickly adjust to the dramatic increase in blood pressure and oxygen exposure. Similarly, intrauterine thermostability must be replaced by neonatal thermoregulation with its inherent increase in oxygen consumption.

Approximately 85% of babies born at term will initiate spontaneous respirations within 10–30 s of birth, an additional 10% will respond during drying and stimulation, approximately 3% will initiate respirations after positive-pressure ventilation (PPV), 2% will be intubated to support respiratory function, and 0.1% will require chest compressions and/or epinephrine to achieve this transition.[1–3] Although the vast majority of newborn infants do not require intervention to make these transitional changes, the large number of births worldwide means that many infants require some assistance to achieve cardiorespiratory stability each year.

Newly born infants who are breathing or crying and have good tone immediately after birth must be dried and kept warm so as to avoid hypothermia. These actions can be provided with the baby lying on the mother's chest and should not require separation of mother and baby. This does not preclude the need for clinical assessment of the baby. For the approximately 5% of newly born infants who do not initiate respiratory effort after stimulation by drying, and providing warmth to avoid hypothermia, 1 or more of the following actions should be undertaken: providing effective ventilation with a face mask or endotracheal intubation, and administration of chest compressions with or without intravenous medications or volume expansion for those with a persistent heart

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[2] The members of the Neonatal resuscitation Chapter Collaborators are listed in the Acknowledgments section.

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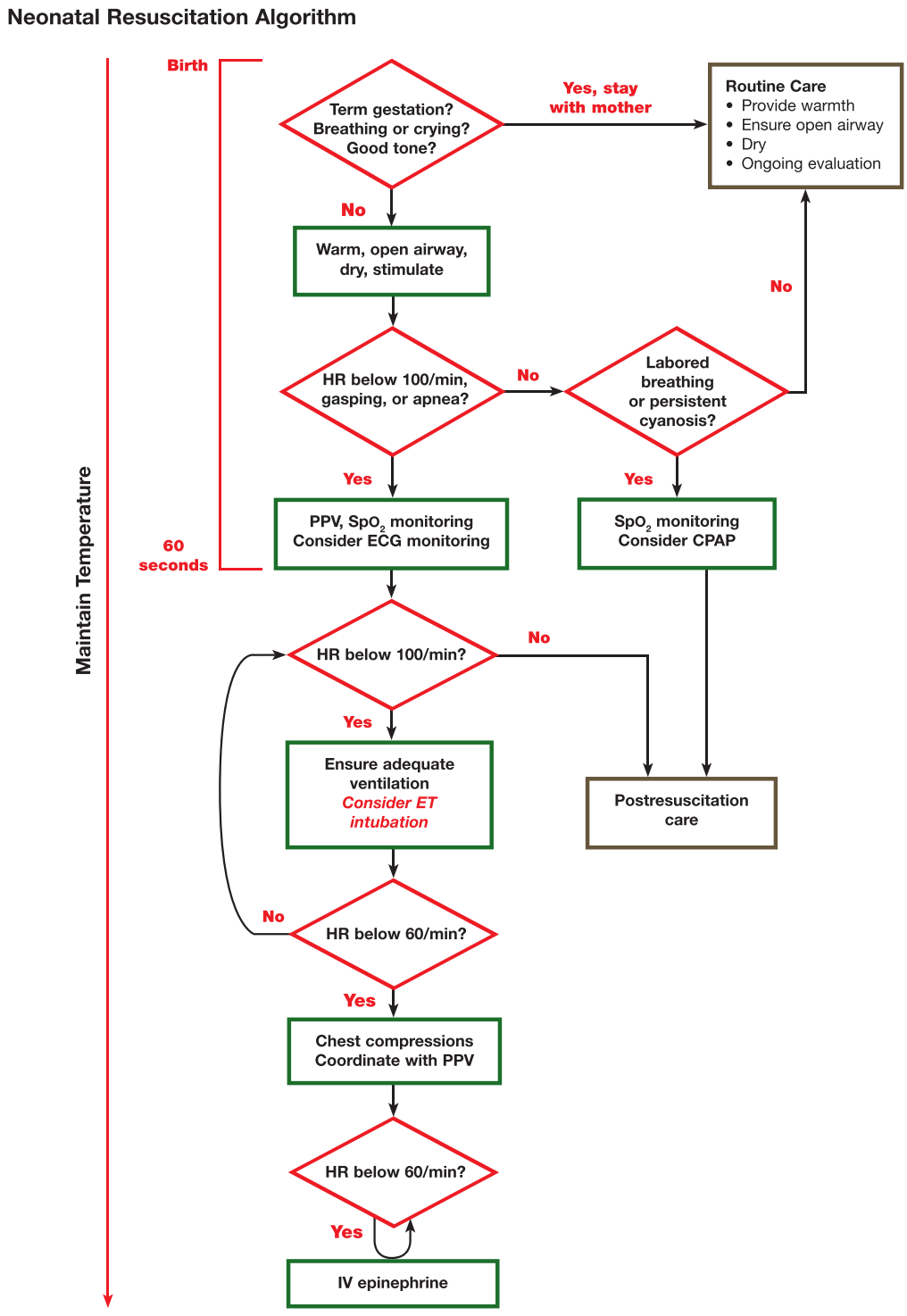

Fig. 1.

rate less than 60/min or asystole, despite strategies to achieve effective ventilation (Fig. 1).

The 2 vital signs that are used to identify the need for an intervention as well as to assess the response to interventions are heart rate and respirations. Progression down the algorithm should proceed only after successful completion of each step, the most critical being effective ventilation. A period of only approximately 60 s after birth is allotted to complete each of the first 2 steps, i.e., determination of heart rate and institution of effective ventilation. Subsequent progression to the next step will depend on the heart rate and respiratory response.

Evidence evaluation

GRADE

The task force performed a detailed systematic review based on the recommendations of the Institute of Medicine of the National Academies[4] and using the methodological approach proposed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group.[5] After identification and prioritization of the questions to be addressed (using the PICO [population, intervention, comparator, outcomes] format),[6] with the assistance of information specialists, a detailed search for relevant

articles was performed in each of 3 online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk of bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials,[7] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[8] and GRADE for observational studies that inform both therapy and prognosis questions.[9]

GRADE is an emerging consensus process that rates quality of evidence and strength of recommendations along with values and preferences. GRADE evidence profile tables[10] were created to facilitate an evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high (where one has high confidence in the estimate of effect as reported in a synthesis of the literature), moderate (where one has moderate confidence, but there may be differences from a further elucidated truth), low (where one has low confidence in the estimate of the effect that may be substantially different from the true effect), or very low (where it is possible that the estimate of the effect is substantially different from the true effect).[11] These categorizations were based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness (i.e. the population studied was not the same as that for which the guideline will be used), imprecision of effect estimates, and other considerations (including publication bias).[12] Randomized studies start as high quality but may be downgraded for methodological quality, whereas observational or cohort studies start off as low quality and can be further downgraded or upgraded depending on methodical quality or positive outcome effect.

Guideline users have to determine how much they can trust that a recommendation will produce more favorable rather than unfavorable consequences. The strength of a recommendation reflects a gradient in guidance, with a clearer expectation for adherence with strong recommendations (identified by the words *we recommend*) and lesser insistence in weak recommendations (identified by the words *we suggest*). In addition, the direction of effect may be in favor of or against the recommendation. GRADE points to several factors that may influence the strength of a recommendation, including the risk-benefit balance, quality of evidence, patient values and preferences, and, finally, costs and resource utilization. If confidence in these values and preferences is high and variability is low, it is more likely that the recommendation will be strong (and vice versa). Recommendations, whether strong or weak, have different implications for patients, healthcare professionals, or healthcare management.

Generation of topics

After publication of the 2010 International Consensus on Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care Science With Treatment Recommendations (CoSTR),[13–15] it was apparent that several unclear and contentious delivery room resuscitation issues remained. In 2012, the Neonatal Task Force published an article titled "Neonatal Resuscitation: In Pursuit of Evidence Gaps in Knowledge,"[16] in which the major gaps in knowledge were identified. The following critical randomized studies were proposed with the goal for completion before the ILCOR 2015 International Consensus Conference on CPR and Emergency Cardiovascular Care Science With Treatment Recommendations:

- Prophylactic postdelivery endotracheal suctioning versus no suctioning in a depressed baby with meconium
- Comparison of different saturation percentiles to use for targeting supplementary oxygen delivery in uncompromised and compromised premature infants
- Comparison of prolonged versus conventional inspiratory times to determine if the former is more effective in establishing functional residual capacity (FRC) and increasing the heart rate
- Studies to determine the optimum technique for maintaining the temperature of very low birth weight (VLBW) infants from the time of delivery through admission to intensive care

One small randomized study has addressed the question of prophylactic endotracheal suctioning in the depressed baby with meconium[17] (see NRP 865), and 1 randomized trial of sustained inflation (SI) has recently been published[18] (see NRP 804). Additional studies addressing these critical questions are ongoing but were not available for the 2015 CoSTR review.

To achieve the goal of identifying a series of relevant questions, the Neonatal Task Force group comprising 38 members and representing 13 countries met for the first time in May 2012 in Washington, DC. At that meeting, a series of questions were identified, researched, culled, and eventually refined into 26 questions at subsequent meetings by using the GRADE approach. One additional question, related to the accurate and timely detection of heart rate immediately after birth, was identified in December 2014 as a major gap in knowledge and was introduced as a late-breaking PICO question. The meetings since May 2012 included 3 ILCOR group meetings (in Vienna, October 2012; Melbourne, April 2013; and Banff, April 2014) and neonatal-specific ILCOR meetings (in Denver, CO, May 2013; Washington, DC, December 2013; Vancouver, Canada, May 2014; and Washington, DC, December 2014).

The literature was researched and consensus was reached on the following issues:

- Optimal assessment of heart rate (NRP 898)
- Delayed cord clamping in preterm infants requiring resuscitation (NRP 787)
- Umbilical cord milking (NRP 849)
- Temperature maintenance in the delivery room (NRP 589)
- Maintaining infant temperature during delivery room resuscitation (NRP 599)
- Warming of hypothermic newborns (NRP 858)
- Babies born to mothers who are hypothermic or hyperthermic in labor (NRP 804)
- Maintaining infant temperature during delivery room resuscitation—intervention (NRP 793)
- Continuous positive airway pressure (CPAP) and intermittent positive-pressure ventilation (IPPV) (NRP 590)
- Sustained inflations (NRP 809)
- Outcomes for positive end-expiratory pressure (PEEP) versus no PEEP in the delivery room (NRP 897)
- T-piece resuscitator and self-inflating bag (NRP 870)
- Intubation and tracheal suctioning in nonvigorous infants born through meconium-stained amniotic fluid (MSAF) versus no intubation for tracheal suctioning (NRP 865)
- Oxygen concentration for resuscitating premature newborns (NRP 864)
- 2-Thumb versus 2-finger techniques for chest compression (NRP 605)
- Chest compression ratio (NRP 895)
- Oxygen delivery during CPR—neonatal (NRP 738)
- Laryngeal mask airway (NRP 618)
- Newborn infants who receive PPV for resuscitation, and use of a device to assess respiratory function (NRP 806)
- Use of feedback CPR devices for neonatal cardiac arrest (NRP 862)
- Limited resource-induced hypothermia (NRP 734)

- Delivery room assessment for less than 25 weeks and prognostic score (NRP 805)
- Apgar score of 0 for 10 min or greater (NRP 896)
- Predicting death or disability of newborns of greater than 34 weeks based on Apgar and/or absence of breathing (NRP 860)
- Resuscitation training frequency (NRP 859)
- Neonatal resuscitation instructors (NRP 867)

Neonatal algorithm

There was considerable debate with regard to modifying the algorithm. The first debate related to the necessity of a timeline. Many thought that a 30-s time rule was unreasonable and not evidenced based. On the other hand, because this is a global document, others advocated strongly that a reminder to assess and intervene if necessary, within 60 s after birth, should be retained to avoid critical delays in initiation of resuscitation. Thus, more than 95% of newly born infants will start breathing spontaneously or in response to stimulation within approximately 30 s.[1] If apnea persists PPV should be initiated within 60 s. As a compromise, the 30-s time point has been removed. Given the importance of hypothermia as a predictor of mortality and evidence from multiple studies that moderate hypothermia (temperature less than 36 °C) can be avoided with simple intervention strategies, the new algorithm contains a running line reminding providers to maintain thermoregulation throughout the immediate newborn period.

Initial assessment and intervention

ECG/EKG in comparison to oximetry or auscultation for the detection of heart rate (NRP 898)

In babies requiring resuscitation (P), does electrocardiography (ECG/EKG) (I), compared with oximetry or auscultation (C), measure heart rate faster and more accurately (O)?

Introduction

Neonatal resuscitation success has classically been determined by detecting an increase in heart rate through auscultation. Heart rate also determines the need for changing interventions and escalating care. However, recent evidence demonstrates that auscultation of heart rate is inaccurate and pulse oximetry takes several minutes to achieve a signal and also may be inaccurate during the early minutes after birth. This PICO question is intended to review the evidence regarding how best to determine heart rate after birth.

Consensus on science

For the important outcomes of **fast and accurate measurement of heart rate** in babies requiring resuscitation, we have identified

- Very-low-quality evidence from 5 nonrandomized studies enrolling 213 patients showing a benefit of ECG compared with oximetry[19–23]
- Very-low-quality evidence from 1 nonrandomized study enrolling 26 patients showing a benefit of ECG compared with auscultation[24]

The available evidence is from nonrandomized studies, downgraded for indirectness and imprecision.

Treatment recommendation

In babies requiring resuscitation, we suggest the ECG can be used to provide a rapid and accurate estimation of heart rate (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

There was much discussion and heated debate about the use of ECG to determine heart rate. Although the data suggest that the ECG provides a more accurate heart rate in the first 3 min, there were no available data to determine how outcomes would change by acting (or not acting) on the information. Important issues were raised about inappropriate interventions being implemented based on a falsely low heart rate by pulse oximetry or auscultation that might be avoided if the heart rate could be determined by ECG. It was pointed out that pulse oximetry is still very important for the measurement of saturation values to define supplementary oxygen needs. Introducing ECG leads in the delivery room will take time, as will acquiring methods to rapidly apply electrodes. In view of these findings of false-positive readings by conventional means, we have no data on when to advise appropriate actions for bradycardia detected by the conventional measures such as pulse oximetry or auscultation. Some transient bradycardia may be normal and be reflective of timing of cord clamping. More studies are needed.

Knowledge gaps

- Studies delineating differences in interventions and/or patient outcomes based on ECG versus pulse oximetry measurements
- Studies of heart rate in VLBW infants requiring resuscitation and in relationship to timing of cord clamping
- Improved technology for rapid application of ECG

Delayed cord clamping in preterm infants requiring resuscitation (intervention) (NRP 787)

In preterm infants, including those who received resuscitation (P), does delayed cord clamping (greater than 30 s) (I), compared with immediate cord clamping (C), improve survival, long-term developmental outcome, cardiovascular stability, occurrence of intraventricular hemorrhage (IVH), necrotizing enterocolitis, temperature on admission to a newborn area, and hyperbilirubinemia (O)?

Introduction

In the past 50 years, the umbilical cords of babies born preterm have generally been cut soon after birth, so that the newborns can be transferred immediately to the neonatal team. However, there is recent evidence that a delay of clamping by 30–60 s after birth results in a smoother transition, particularly if the baby begins breathing before the cord is cut. In both animal and human models, the delay is associated with increased placental transfusion, increased cardiac output, and higher and more stable neonatal blood pressure. There is controversy about how long it is appropriate to delay clamping if the baby is perceived to require resuscitation.

Consensus on science

For the critical outcome of **infant death**, we identified very-low-quality (downgraded for imprecision and very high risk of bias) evidence from 11 randomized clinical trials enrolling 591 patients showing no benefit to delayed cord clamping (odds ratio [OR], 0.6; 95% confidence interval [CI], 0.26–1.36).[25–35]

For the critical outcome of **severe IVH**, we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 5 randomized clinical trials enrolling 265 patients showing no benefit to delayed cord clamping (OR, 0.85; 95% CI, 0.20–3.69).[26,27,31,32]

For the critical outcome of **periventricular hemorrhage (PVH)/IVH**, we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 9 randomized

clinical trials enrolling 499 patients showing benefit of delayed cord clamping (OR, 0.49; 95% CI, 0.29–0.82).[26,27,29–35]

For the critical outcome of **neurodevelopment**, we did not identify any evidence.

For the critical outcome of **cardiovascular stability** as assessed by mean blood pressure at birth, we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 2 randomized clinical trials enrolling 97 patients showing higher blood pressure associated with delayed cord clamping (mean difference [MD], 3.52; 95% CI, 0.6–6.45).[29,31]

For the critical outcome of **cardiovascular stability** as assessed by mean blood pressure at 4 h after birth, we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 3 randomized clinical trials enrolling 143 patients showing increased mean blood pressure at 4 h of age after delayed cord clamping (MD, 2.49; 95% CI, 0.74–4.24).[25,31,32]

For the critical outcome of **cardiovascular stability** as assessed by blood volume, we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 2 randomized clinical trials enrolling 81 patients showing benefit of delayed cord clamping (MD, 8.25; 95% CI, 4.39–12.11).[35,36]

For the critical outcome of **temperature**, on admission we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 4 randomized clinical trials enrolling 208 patients showing no statistically significant benefit from delayed cord clamping (MD, 0.1; 95% CI, −0.04 to 0.24).[29,31,32,34]

For the important outcome of **need for transfusion**, we identified very-low-quality evidence from 7 randomized clinical trials enrolling 398 patients showing less need for transfusion after delayed cord clamping (OR, 0.44; 95% CI, 0.26–0.75).[28–30,32,34–36]

For the important outcome of **necrotizing enterocolitis**, we identified very-low-quality evidence (downgraded for imprecision and very high risk of bias) from 5 randomized clinical trials enrolling 241 patients showing lower incidence of necrotizing enterocolitis (OR, 0.3; 95% CI, 0.19–0.8).[29,31–34]

For the important outcome of **hyperbilirubinemia** and peak bilirubin concentrations (mmol/L), we identified moderate-quality evidence from 6 randomized clinical trials enrolling 280 patients showing higher peak bilirubin value in those neonates with delayed cord clamping (MD, 16.15; 95% CI, 6.13–26.17).[29–33,35]

For the important outcome of **treated hyperbilirubinemia** (need for phototherapy), we identified low-quality evidence from 1 randomized clinical trial enrolling 143 patients showing no statistically significant difference (relative risk [RR], 1.29; 95% CI, 1.00–1.67).[35]

Treatment recommendation

We **suggest** delayed umbilical cord clamping for preterm infants not requiring immediate resuscitation after birth (weak recommendation, very-low-quality evidence).

There is insufficient evidence to recommend an approach to cord clamping for preterm infants who do receive resuscitation immediately after birth, because many babies who were at high risk of requiring resuscitation were excluded from or withdrawn from the studies.

Values, preferences, and task force insights

Overall, the quality of evidence for the question was very low. Despite drawing evidence from randomized controlled trials, the small sample size in most trials and the associated imprecision limited the quality of evidence for all outcomes of interest. Although 2 larger observational trials were considered, the quality and size of effect were not sufficient to influence the conclusions. The quality of evidence for necrotizing enterocolitis and hyperbilirubinemia was limited by inconsistent definitions of the outcome, and inconsistent thresholds for treatment with phototherapy across studies.

- **Balance of consequences** favors delayed cord clamping, as desirable consequences *probably outweigh* undesirable consequences in most settings. The results of randomized controlled trials and nonrandomized observational studies with comparison groups were generally consistent. However, small and sick infants who received immediate resuscitation were generally excluded from the available randomized controlled trials, so data are very limited for this group at highest risk for physiologic instability, complications of prematurity, and mortality who may also realize highest benefit or harm from the intervention.
- **Preferences (parents')** favor delayed clamping, which has received strong popular support through social media and Internet sites. The advantages of delayed cord clamping assume heightened importance in resource-limited settings where specialty care for preterm neonates may be limited. Improving initial cardiovascular stability with maintenance of temperature and lower risk of morbidities such as necrotizing enterocolitis and severe intracranial hemorrhage may offer significant survival advantages, even where neonatal intensive care is not available. In areas where maternal anemia is prevalent, iron supplementation is limited, and a safe blood supply is often unavailable, the reduction in need for transfusion and improved blood volume at birth may have increased significance.

A major debate surrounded the issue as to whether the quality of the studies was low or very low. Overall, the group thought that downgrading the evidence as suggested by the GRADE tool was not reasonable, given that this was one of the areas with the most randomized trial data. However, eventually based on the GRADE criteria, it was necessary to classify most of the outcomes as very-low-quality evidence. It was noted that the existing studies enrolled very few extremely premature infants and very few who received resuscitation. The group was unanimous in stressing the need for additional research, which parallels a Cochrane review reflecting similar sentiments of a need for more high-quality evidence. Some members questioned how to reconcile with obstetric guidelines, which has an out clause for babies requiring resuscitation.[37]

Knowledge gaps

- Results of ongoing large randomized controlled trials
- Comparison of delayed versus immediate cord clamping among preterm infants who receive resuscitation with PPV
- Comparison of delayed cord clamping with cord milking
- Outcome data of high importance, such as long-term neurodevelopment
- Need for resuscitative intervention at delivery
- Hyperbilirubinemia among high-risk populations

Umbilical cord milking—intervention

In very preterm infants (28 weeks or less) (P), does umbilical cord milking (I), in comparison with immediate umbilical cord clamping (C), affect death, neurodevelopmental outcome at 2–3 years, cardiovascular stability, i.e. need for pressors, need for fluid bolus, initial mean blood pressure, IVH (any grade, severe grade), temperature on admission, hematologic indices (initial hemoglobin, need for transfusion), hyperbilirubinemia, need for phototherapy, or need for exchange transfusion (O)?

Introduction

There is some evidence that "milking" of the umbilical cord from the placental side toward the newborn may have a similar

effect to delayed cord clamping (i.e. increased placental transfusion, improved cardiac output, and increased neonatal blood pressure). If correct, this would offer a more rapid alternative to delayed clamping of the cord.

Consensus on science

For the critical outcome of **death**, we found low-quality evidence (downgraded for very serious imprecision) from 3 randomized clinical trials[38–40] showing that there is no difference in death (OR, 0.76; 95% CI, 0.25–2.29).

For the critical outcome of **cardiovascular stability**, we found low-quality evidence (downgraded for imprecision) from 2 randomized studies[38,39] showing that the initial mean blood pressure was 5.43 mm Hg higher (range, 1.98–8.87 mm Hg) in the group receiving umbilical cord milking.

For the critical outcome of **IVH**, we found low-quality evidence (downgraded for very serious imprecision) from 2 randomized clinical trials[38,40] showing a reduction of IVH (all grades: OR, 0.37; 95% CI, 0.18–0.77) but no difference (from 1 randomized clinical trial[38] in severe IVH; OR, 0.44; 95% CI, 0.07–2.76) (low-quality evidence, downgraded for very serious imprecision) when umbilical cord milking was performed.

For the critical outcome of **neurologic outcome at 2–3 years**, we did not identify any evidence to address this.

For the important outcome of **hematologic indices**, we found low-quality evidence (downgraded for imprecision) from 2 randomized clinical trials[38,39] showing that cord milking increased the initial hemoglobin level (MD, 2.27 g/dL; 95% CI, 1.57–2.98 g/dL) and low-quality evidence (downgraded for imprecision) from 3 randomized clinical trials[38–40] showing that cord milking decreased transfusion (OR, 0.2; 95% CI, 0.09–0.44).

For the important outcome of **temperature**, we found low-quality evidence (downgraded for very serious imprecision) from 1 randomized clinical trial[39] showing that the temperature of the milking group was not different on admission.

For the important outcome of **bilirubin** indices, we found low-quality evidence (downgraded for very serious imprecision) showing that the maximum bilirubin measurement (3 randomized clinical trials[38–40]) and use of phototherapy (1 study[40]) was not different between groups.

Treatment recommendation

We **suggest against** the routine use of cord milking for infants born at 28 weeks of gestation or less, because there is insufficient published human evidence of benefit. Cord milking may be considered on an individual basis or in a research setting, as it may improve initial mean blood pressure and hematologic indices and reduce intracranial hemorrhage. There is no evidence for improvement in long-term outcomes (weak recommendation, low-quality evidence).

All studies included in this evidence review milked 20 cm of umbilical cord toward the umbilicus 3 times while the infant was held at the level of the introitus or below the level of the placenta before cord clamping.

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the unknown safety profile and less value on the simplicity/economy of this intervention.

Much of the deliberations focused on the wording of the treatment recommendation. The first recommendation proposed was, "We suggest that cord milking, as opposed to immediate cord clamping, be performed at delivery for VLBW infants." A second recommendation was, "We suggest that cord milking, as opposed to immediate cord clamping, may be performed at delivery for VLBW but should not be regarded as a standard of care." A third recommendation was, "We suggest that cord milking, as opposed to immediate cord clamping, may be performed at delivery for VLBW to improve initial mean blood pressure, hematologic indices, and IVH (Grades 1 and 2)." However, concerns were raised related to the absence of evidence pertinent to long-term outcomes and, in particular, neurologic outcome. Moreover, there was serious imprecision in the data. These factors led to the final treatment recommendation.

Knowledge gaps

- Evidence regarding neurodevelopmental outcomes for cord milking compared with immediate cord clamping is necessary.
- Comparison of delayed cord clamping with cord milking
- Multiple studies of cord milking in this population are under way at this time, and additional data will be available in 2020.

Temperature

It has been known for more than a century that preterm babies who become hypothermic after birth have a higher mortality than those who remain normothermic.[41] The association between hypothermia and neonatal mortality and morbidity, including respiratory distress syndrome, metabolic derangements, IVH, and late-onset sepsis, has long been recognized, with premature infants being particularly vulnerable (see below). Specifically, moderate hypothermia (temperature less than 36 °C) at birth has been recognized as an independent risk factor for death in premature infants.[42,43]

These relationships reflect the fact that the premature infant is at very high risk of net heat loss because of a large surface area-to-volume ratio and increased evaporative fluid losses from the skin. Strategies introduced to minimize heat loss include use of occlusive wrapping, exothermic warming mattress, warmed humidified resuscitation gases, polyethylene caps, and increasing delivery room temperature, and have met with varying success. A by-product of these interventions to prevent hypothermia is more-frequent hyperthermia (temperature greater than 37.5 °C). Hyperthermia (temperature greater than 37.5 °C) also increases the risk for neonatal mortality and morbidity in both term and preterm infants. This section will review the importance of maintaining temperature in a goal range, interventions to minimize heat loss at delivery, how quickly a low temperature should be raised into a normal range, the impact of maternal hyperthermia and hypothermia on the newborn, and strategies to avoid hypothermia in the resource-limited setting.

Temperature maintenance in the delivery room—prognosis (NRP 589)

In nonasphyxiated babies at birth (P), does maintenance of normothermia (core temperature 36.5 °C or greater and 37.5 °C or less) from delivery to admission (I), compared with hypothermia (less than 36 °C) or hyperthermia (greater than 37.5 °C) (C), change survival to hospital discharge, respiratory distress, survival to admission, hypoglycemia, intracranial hemorrhage, or infection rate (O)?

Consensus on science

For the critical outcome of **mortality**, there is evidence from 36 observational studies of increased risk of mortality associated with hypothermia at admission[42–77] (low-quality evidence but upgraded to moderate-quality evidence due to effect size, dose–effect relationship, and single direction of evidence). There is evidence of a dose–effect relationship on mortality, suggesting an increased risk of at least 28% for each 1° below 36.5 °C body temperature at admission[42,43] and dose-dependent effect size.[42,43,48,66]

One small randomized clinical trial[78] (very-low-quality evidence, downgraded for indirectness and serious imprecision) showed a reduction in adverse events, including death, intracranial hemorrhage, necrotizing enterocolitis, and oxygen dependence with improved temperature management, but 3 randomized controlled trials[79–81] (low-quality evidence, downgraded for indirectness and imprecision) did not show any significant improvement in mortality with significantly improved temperature control. Four observational studies[60,61,63,82] (very-low-quality evidence, downgraded for indirectness and imprecision) did not find any improvement in mortality with improved admission temperatures, but they were not sufficiently powered for this outcome.

For the critical outcome of **IVH**, 8 observational studies (very-low-quality evidence, downgraded for risk of bias and indirectness) show hypothermia (temperature less than 36 °C) in preterm infants is associated with an increased likelihood of developing IVH.[48,55,66,83–87] Eight observational studies (low-quality, downgraded for indirectness) found no association between hypothermia and IVH.[43,60,61,88–92]

For the important outcome of **respiratory issues**, there is evidence from 9 observational studies[44,48,50,67,83,93–96] (low-quality evidence) showing an association between hypothermia and respiratory disease. One large randomized controlled trial[79] (low-quality evidence, downgraded for imprecision and risk of bias) found a reduction in pulmonary hemorrhage associated with improved admission temperature (OR, 0.57; 95% CI, 0.35–0.94). Eight observational studies (very-low-quality evidence) have shown an improvement in respiratory outcomes after improved admission temperature maintenance.[44,49,51,63,72,84,93,95] Two of these have shown a decrease in respiratory support with improved temperature maintenance.[93,96] Two observational studies (very-low-quality evidence, downgraded for indirectness and imprecision) did not show any association.[43,60]

For the serious outcome of **hypoglycemia**, there were seven observational studies (very-low-quality, downgraded for risk of bias and indirectness) showing a significant association between hypothermia (less than 36 °C) and hypoglycemia.[44,67,70,97–100] Two of these studies, using historical controls, showed improved glycemic control with improved normothermia.[44,99]

For the serious outcome of **late sepsis**, 2 observational studies (very-low-quality evidence, downgraded for risk of bias and indirectness) indicated an association between hypothermia on admission and late sepsis.[43,101] One observational study (low-quality, downgraded for risk of bias and indirectness) found no association after multivariate analysis.[66]

For the serious outcome of **survival to admission**, there is no published evidence addressing any effect of delivery room hypothermia upon survival to admission.

For the serious outcome of **admission hyperthermia**, there is no published evidence about newborn hyperthermia at admission.

Treatment recommendations

Admission temperature of newly born nonasphyxiated infants is a strong predictor of mortality and morbidity at all gestations. It should be recorded as a predictor of outcomes as well as a quality indicator (strong recommendation, moderate-quality evidence).

We recommend that the temperature of newly born nonasphyxiated infants be maintained between 36.5 and 37.5 °C after birth through admission and stabilization (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making these statements, we place a higher value on the strong association of inadvertent hypothermia with mortality, the apparent dose effect, the single direction of the evidence, the universal applicability, and the evidence for intervention improving respiratory outcomes over the lack of modern evidence for intervention changing mortality.

The group thought that this question should change to a prognostic one. A recurring question is whether some of the babies stay cold because of intrinsic factors. However, there are data that hypothermia upon admission impacts mortality through at least the first 6 months. It was suggested that a low temperature may also be related to the quality of care and environment. Most studies reviewed used an axillary temperature but some older studies utilized a rectal temperature. The relative benefits of one over the other were not assessed in this PICO. The task force felt that an axillary temperature should be used in the delivery room but that on admission it should be left to individual regional practice.

Knowledge gaps

- Further studies are required to find if improved admission temperature improves mortality and other outcomes.

Maintaining infant temperature during delivery room resuscitation—intervention

Among preterm neonates who are under radiant warmers in the hospital delivery room (P), does increased room temperature, thermal mattress, or another intervention (I), compared with plastic wraps alone (C), reduce hypothermia (less than 36 °C) on admission to neonatal intensive care unit (NICU) (O)?

Introduction

A variety of strategies have been suggested to maintain a preterm infant's temperature; it is unknown which of these strategies is/are most effective. This PICO question was intended to identify the strategies and techniques that might be most effective.

Consensus on science

Thermal mattress plus plastic wrap plus radiant warmer (I) versus plastic wrap plus radiant warmer. For the critical outcome of **hypothermia** (temperature less than 36.0 °C) at NICU admission, we identified low-quality evidence (downgraded for serious risk of bias) from 1 randomized controlled trial[102] enrolling 72 preterm infants of less than 32 weeks of gestation showing no benefit to addition of a thermal mattress to the use of plastic wrap and radiant warmer (RR, 1.89; 95% CI, 0.18–19.95). Four observational studies (low-quality evidence, downgraded for serious risk of bias)[82,103–105] including 612 patients of less than 32 weeks of gestation showed benefit to the addition of the thermal mattress (OR, 0.27; 95% CI, 0.18–0.42).

For the important outcome of **hyperthermia** (temperature greater than 38.0 °C) at admission, we have identified low-quality evidence (downgraded for serious risk of bias) from the same randomized controlled trial[102] and 4 observational studies[82,103,105,106] including 426 patients showing no harm from the thermal mattress (RR, 3.78; 95% CI, 0.86–16.60 and OR, 6.53; 95% CI, 0.80–53.30).

Environmental temperature 26 °C or greater plus plastic wrap plus radiant warmer (I) versus plastic wrap plus radiant warmer (C). For the critical outcome of **hypothermia** (temperature less than 36.0 °C) at NICU admission, we identified no studies addressing this intervention alone.

For the important outcome of **hyperthermia** (temperature greater than 38.0 °C) at admission, we identified low-quality evidence (downgraded for serious risk of bias) from 1 observational study[107] including 40 patients of less than 29 weeks of gestation showing no harm from increasing the environmental temperature **26 °C or greater** (OR, 8.45; 95% CI, 0.37–182.58).

Heated and humidified gases plus plastic wrap plus radiant warmer (I) versus plastic wrap plus radiant warmer (C). For the critical outcome of **hypothermia** (temperature less than 36.0 °C) at NICU admission, we identified very-low-quality evidence (downgraded for serious risk of bias) from 1 randomized controlled trial[78] enrolling 203 patients of less than 32 weeks of gestation showing no benefit (RR, 0.64; 95% CI, 0.31–1.35), and 1 observational study (low-quality evidence)[108] including 112 patients of less than 33 weeks of gestation showing benefit to the use of heated and humidified gases and to the use of plastic wrap and the radiant warmer (OR, 0.20; 95% CI, 0.08–0.47).

For the important outcome of **hyperthermia** (temperature greater than 38.0 °C) at admission, we identified low-quality evidence (downgraded for serious risk of bias) from the same observational study[108] showing no harm (OR, not estimable).

Total body and head plastic wrap plus radiant warmer (I) versus body plastic wrap plus radiant warmer (C). For the critical outcome of **hypothermia** (temperature less than 36.0 °C) at NICU admission, we identified very-low-quality evidence (downgraded for serious risk of bias) from 1 randomized controlled trial[109] enrolling 100 patients of less than 29 weeks of gestation showing no benefit to the addition of wrapping (RR, 0.60; 95% CI, 0.24–1.53).

For the important outcome of **hyperthermia** (temperature greater than 38.0 °C) at admission, we identified low-quality evidence (downgraded for serious risk of bias) from the same randomized controlled trial[109] showing no harm (RR, 0.33; 95% CI, 0.01–7.99).

Combination of interventions (environmental temperature 23–25 °C plus plastic wrap without drying plus cap plus thermal mattress plus radiant warmer) versus plastic wrap plus radiant warmer (C). For the critical outcome of **hypothermia** (temperature less than 36.0 °C) at admission, we identified very-low-quality evidence (downgraded for serious risk of bias) from 4 observational studies[93,95,96,110] enrolling 9334 patients of less than 35 weeks of gestation showing benefit from using a combination of interventions (i.e. environmental temperature 23–25 °C plus plastic wrap without drying plus cap plus thermal mattress plus radiant warmer; OR, 0.40; 95% CI, 0.35–0.46).

For the important outcome of **hyperthermia** (temperature greater than 38.0 °C) at admission, we have identified low-quality evidence (downgraded for serious risk of bias) from 3 observational studies[93,95,110] enrolling 8985 patients showing no harm to the combination of interventions (OR, 1.12; 95% CI, 0.82–1.52).

Treatment recommendations

Among newly born preterm infants of less than 32 weeks of gestation under radiant warmers in the hospital delivery room, we suggest using a combination of interventions, which may include environmental temperature 23–25 °C, warm blankets, plastic wrapping without drying, cap, and thermal mattress to reduce hypothermia (temperature less than 36.0 °C) on admission to NICU (weak recommendation, very-low-quality evidence).

We suggest that hyperthermia (greater than 38.0 °C) be avoided due to the potential associated risks (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

We place value on the large numbers enrolled in the observational studies and consistent direction of effect.

Because many of the studies used multiple strategies, it was not possible to identify the different specific interventions, that are effective in maintaining temperature. There was concern whether the recommendation should be so strong when the CIs for hyperthermia (0.80–53.30) comprising 3 studies are so wide, raising the potential chance for harm. A strong recommendation was made because of the large numbers in the studies and the consistent direction of effect. There was concern about 1 randomized thermal mattress trial, which was stopped for safety issues because of hyperthermia. However, this is the only study that has demonstrated an adverse effect with small numbers, suggesting some unclear negative (possible environmental) effect. In the treatment recommendation, it was suggested to add the words *may include* after the word *combination*.

Knowledge gaps

- Although a combination of interventions (increasing environmental temperature, warm blankets, thermal mattress, and cap) linked to quality improvement initiatives are effective in reducing hypothermia (less than 36 °C) on NICU admission among newly born preterm infants of less than 32 weeks of gestation who are under radiant warmers and plastic wrap, the contribution of each intervention (increasing environmental temperature, thermal mattress, heated and humidified gases, and cap) remains to be established.

Warming of hypothermic newborns—intervention (NRP 858)

In newborns who are hypothermic (temperature less than 36.0 °C) on admission (P), does rapid rewarming (I), compared with slow rewarming (C), change mortality rate, short and long-term neurologic outcome, hemorrhage, episodes of apnea and hypoglycemia, or need for respiratory support (O)?

Introduction

Neonates are at high risk for becoming hypothermic during resuscitation. Some early teaching for rewarming these neonates has suggested that slow rewarming is preferable over faster so as to avoid complications such as apnea and arrhythmias. This PICO question is intended to review the recent evidence on this issue.

Consensus on science

We identified 2 randomized trials[111,112] and 2 observational studies[113,114] comparing rapid (greater than 0.5 °C/h) versus slow (less than 0.5 °C/h) rewarming strategies for hypothermic newborns (less than 36.0 °C) on admission. All studies were dated (the most recent study was published 28 years ago) and conducted in different settings (2 in low-resource countries and 2 in high-resource countries); enrolled patients had different baseline characteristics (postnatal age, gestational age, proportion of outborn/inborn, degree of hypothermia). The quality of the studies was very poor in terms of number of enrolled patients, inclusion criteria, randomization methods, study design, and outcome measures.

For the critical outcome of **mortality**, we identified low-quality evidence (downgraded for serious risk of bias) from 1 randomized clinical trial[112] including 30 patients showing no benefit (RR, 0.88; 95% CI, 0.36–2.10) and 2 observational studies[113,114] including 99 patients showing benefit in favor of a rapid rewarming strategy (OR, 0.23; 95% CI, 0.06–0.83).

For the critical outcome of **convulsions/seizures**, we identified very-low-quality evidence (downgraded for serious risk of bias) from 1 randomized clinical trial[112] including 30 patients showing no benefit to rapid versus slow rewarming (RR, 0.88; 95% CI, 0.14–5.42).

For the critical outcome of **hemorrhage/pulmonary hemorrhage**, we identified very-low-quality evidence (downgraded for serious risk of bias) from 1 randomized clinical trial[112] including 30 patients and 1 observational study[113] including 38 patients showing no benefit to rapid versus slow rewarming (RR, 1.31; 95% CI, 0.26–6.76 and OR, 0.16; 95% CI, 0.02–1.50, respectively).

For the important outcome of **need for respiratory support**, we identified very-low-quality evidence (downgraded for serious risk of bias) from 1 observational study[114] including 56 patients showing benefit in a slower over a rapid rewarming strategy (OR, 7.50; 95% CI, 2.14–26.24).

For the important outcome of **episodes of hypoglycemia**, we identified very-low-quality evidence (downgraded for serious risk of bias and very serious imprecision) from 1 randomized controlled trial[111] including 36 patients and 1 observational study[114] including 56 patients showing no benefit to rapid versus slow rewarming (RR, 0.11; 95% CI, 0.01–1.81 and OR, 0.21; 95% CI, 0.01–4.06, respectively).

For the important outcome of **episodes of apnea**, we identified very-low-quality evidence (downgraded for serious risk of bias and very serious imprecision) from 2 randomized clinical trials[111,112] including 66 patients showing no benefit to rapid versus slow rewarming (RR, 0.44; 95% CI, 0.04–4.32).

Treatment recommendation

The confidence in effect estimates is so low that a recommendation for either rapid (0.5 °C/h or greater) or slow rewarming (0.5 °C/h or less) of unintentionally hypothermic newborns (T° less than 36 °C) at hospital admission would be speculative.

Values, preferences, and task force insights

It was considered important to distinguish the warming of infants where hypothermia is iatrogenic after birth, which in general is of a short duration, from hypothermia that is therapeutic and has been intentionally induced over 72 h. The latter rewarming is generally recommended to be slow.

Knowledge gaps

- Attempts should be made to study a more homogenous patient population with specific inclusion criteria stratified by gestational and postnatal age, severity of hypothermia on admission, and common outcome measures.
- Addressing these factors with attention to power of the study by using a multicenter study design will generate useful data on which to base decisions on the rewarming strategy for hypothermic newborns.

Babies born to mothers who are hypothermic or hyperthermic in labor—prognosis (NRP 804)

In newborn babies (P), does maternal hypothermia or hyperthermia in labor (I), versus normal maternal temperature (C), result in adverse neonatal effects (O)? Outcomes include mortality, neonatal seizures, and adverse neurologic states.

Introduction

There is substantial literature from observational studies indicating an association between maternal hyperthermia and neonatal mortality and morbidity (see NRP 589). However, the mechanisms linking these associations remain unclear. In addition, the impact of maternal hypothermia on neonatal outcome remains unclear. This PICO question attempts to address this issue.

Consensus on science

Maternal hyperthermia. For the critical outcome of **mortality**, we identified low-quality evidence from 2 nonrandomized clinical trials (downgraded for risk of bias) showing an increased risk with maternal hyperthermia.[115,116]

For the important outcome of **neonatal seizures**, we identified low-quality evidence from 7 nonrandomized clinical trials (downgraded for risk of bias) showing an increased risk with maternal hyperthermia.[115–121]

For the important outcome of **adverse neurologic states** (encephalopathy), we identified low-quality evidence from 4 nonrandomized clinical trials (downgraded for risk of bias) showing an increased risk with maternal hyperthermia.[122–125]

Maternal hypothermia. For the critical outcome of **mortality** and the important outcomes of **seizures or adverse neurologic states (encephalopathy)**, we identified very-low-quality evidence from 5 randomized clinical trials (downgraded for very serious indirectness) that showed no significant risk of these outcomes with maternal hypothermia.[126–130] However, the above studies did not specifically examine these outcomes.

There are no studies of neonatal outcomes after interventions to keep mothers normothermic.

Treatment recommendations

Although maternal hyperthermia is associated with adverse neonatal outcomes, there is insufficient evidence to make a recommendation regarding the management of maternal hyperthermia.

There is insufficient evidence to make a treatment recommendation about maternal hypothermia.

Values, preferences, and task force insights

There was discussion as to whether this is a prognostic versus a therapeutic question. The worksheet authors used observational studies, because the randomized clinical trials did not focus on the outcomes targeted. There was discussion as to whether it was possible to separate hypothermia from the cause of hypothermia.

Knowledge gaps

- There are no randomized controlled trials of neonatal outcomes after interventions to keep mothers normothermic.
- Do interventions to achieve normothermia in mothers who are hyperthermic decrease risk of adverse outcomes for newborns? (Lack of randomized clinical trials)
- Do interventions to achieve normothermia in mothers who are hypothermic decrease risk of adverse outcomes for newborns? (Lack of critical/important outcomes)

Maintaining infant temperature during delivery room resuscitation—intervention (NRP 793)

In newborn infants (greater than 30 weeks of gestation) in *low-resource settings* during and/or after resuscitation/stabilization (P), does drying and skin-to-skin contact or covering with plastic (I), compared with drying and no skin-to-skin or use of radiant warmer or incubator (C), change body temperature (O)?

Introduction

The ability to maintain temperature in a resource-limited setting after birth is a significant problem (see NRP 589), with a dose-dependent increase in mortality for temperatures below 36.5 °C. Moreover, premature infants demonstrated a 12-fold increase in mortality compared with term babies. Therefore, avoiding hypothermia at birth would seem to be a relatively simple intervention to reduce mortality.

Consensus on science

Plastic wraps with or without skin drying and swaddling compared with cot or crib with or without initial use of radiant warmer. For the important outcome of **normothermia or preventing hypothermia** during resuscitation, we could not find any studies reporting on use of plastic bags. During transition (from birth to 1–2 h after delivery),

we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 3 randomized clinical trials[131–133] enrolling 409 newborns of greater than 30 weeks of gestation, showing either a reduction in incidence of hypothermia with plastic after drying[131,132] (RR, 0.77; 95% CI, 0.65–0.90) or no difference in temperature[133] with plastic with or without drying compared with cot bed or open crib and swaddling with or without initial use of radiant warmer.

Skin-to-skin contact versus cot or crib with or without use of radiant warmer.

- During transition (birth to 1–2 h after delivery), we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 7 randomized clinical trials[134–140] enrolling 600 newborns of greater than 30 weeks of gestation showing a reduction in the number of babies with hypothermia when nursed with skin-to-skin contact after delivery[134,136,137,140] or similar body temperatures[135,138,139] when compared with cot or crib and swaddling with or without initial use of radiant warmer.

Skin-to-skin contact versus incubator. For the important outcome of **normothermia or preventing hypothermia** during resuscitation, we could not find any studies reporting on skin-to-skin contact. During transition (birth to 1–2 h after delivery), we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 2 randomized clinical trials[136,141] enrolling 66 newborns of greater than 30 weeks of gestation showing reduction in incidence of hypothermia by about 90%[141] or a 50% reduction in drop in body temperature[136] with skin-to-skin contact compared with incubator.

Treatment recommendations

There are no data examining the use of plastic wrap during resuscitation/stabilization. To maintain body temperature or prevent hypothermia during transition (birth to 1–2 h of life), we suggest that after a well newborn infant of greater than 30 weeks of gestation has been dried, his or her trunk and limbs may be put in a clean food-grade plastic bag and swaddled compared with open crib or cot and swaddling (weak recommendation, very-low-quality evidence).

There are no data on skin-to-skin contact during resuscitation/stabilization. To maintain normal body temperature or prevent hypothermia during transition (birth to 1–2 h after delivery), we suggest well newborns of greater than 30 weeks of gestation be nursed with skin-to-skin contact or kangaroo mother care compared with a cot/open crib and swaddling or incubator (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this suggestion on plastic wrap, we considered the decrease in hypothermia with plastic. However, clean plastic may not be available and could be costly, and use of unclean plastic may lead to infections.

In making this suggestion on skin-to-skin contact, we valued the prevention of hypothermia by using a free and effective intervention.

An issue was raised about the quality and the safety of occlusive wrap, and the suggestion was made to include food-grade quality. The question was raised with regard to the availability of thermometers.

Knowledge gaps

- The feasibility of skin to skin during resuscitation
- Using plastic with or without drying during resuscitation

Ventilation

The respiratory management of the newly born infant in part depends on whether the infant is making some respiratory effort or not. In the breathing term or preterm infant, application of CPAP may be sufficient to augment endogenous effort. In the absence of respiratory effort, establishment of FRC may be more difficult to establish in some cases. In the term infant, positive inflating pressure may be sufficient to establish FRC, whereas in other cases PEEP and/or an SI may be helpful. In this section, we will review the evidence for the use of CPAP in the spontaneously breathing infant, and the use of SI and/or PEEP in the nonbreathing infant. This section will also examine the important question of whether a nonbreathing infant delivered in the presence of MSAF needs to be intubated for suctioning or not. Finally, the starting oxygen concentration in a premature newborn will be reviewed.

CPAP and IPPV—intervention (NRP 590)

In spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room (P), does the use of CPAP (I), compared with intubation and IPPV (C), improve outcome (O)?

Introduction

CPAP was introduced to neonatology in the 1970s for treatment of respiratory distress syndrome. However, because of equipment limitations, this treatment modality was not part of the early recommendations for neonatal resuscitation at birth. Over the past decade, the use of CPAP rather than the immediate intubation and ventilation for preterm babies who do not breathe well spontaneously after birth has been explored. Initially, this controversy was also complicated by the common teaching that babies born very preterm (less than 32 weeks of gestation) should be intubated electively at birth for the purpose of administering surfactant. There was also a concern that the use of CPAP in the delivery room might lead to a higher incidence of pneumothorax. Several randomized controlled studies have tested these concerns, which prompted the following 2 PICO analyses.

Consensus on science

For the critical outcome of **death or bronchopulmonary dysplasia**, we identified moderate-quality evidence (downgraded for risk of bias) from 3 randomized clinical trials[142–144] enrolling 2358 preterm infants born at less than 30 weeks of gestation showing potential benefit to starting treatment with CPAP in the first 15 min after birth (RR, 0.91; 95% CI, 0.83–1.00).

For the critical outcome of **death**, we identified moderate-quality evidence (downgraded for risk of bias, imprecision) from the same 3 randomized clinical trials[142–144] showing no benefit to starting treatment with CPAP (RR, 0.82; 95% CI, 0.66–1.03). However, we recognize that while the point estimate would suggest potential for benefit, the confidence intervals cross unity to 1.03, suggesting that the potential for harm is minimal.

For the critical outcome of **bronchopulmonary dysplasia**, we identified moderate-quality evidence (downgraded for indirectness) from the same 3 randomized clinical trials[142–144] showing no benefit to starting treatment with CPAP (RR, 0.92; 95% CI, 0.82–1.03). However, we recognize that while the point estimate would suggest potential for benefit, the confidence intervals cross unity to 1.03, suggesting that the potential for harm is minimal.

For the critical outcome of **air leak**, we identified very-low-quality evidence (downgraded for inconsistency and very serious imprecision) from the same 3 randomized clinical trials[142–144]

showing no benefit to starting treatment with CPAP (RR, 1.24; 95% CI, 0.91–1.69).

For the critical outcome of **severe IVH**, we identified very-low-quality evidence (downgraded for inconsistency and serious imprecision) from the same 3 randomized clinical trials[142–144] showing no benefit to starting treatment with CPAP (RR, 1.09; 95% CI, 0.86–1.39).

For the important outcome of **necrotizing enterocolitis**, we identified moderate-quality evidence (downgraded for imprecision) from the same 3 randomized clinical trials[142–144] showing no benefit to starting treatment with CPAP (RR, 1.19; 95% CI, 0.92–1.55).

For the important outcome of **severe retinopathy of prematurity**, we identified low-quality evidence (downgraded for very serious imprecision) from 2 randomized clinical trials[143,144] enrolling 1359 infants showing no benefit to starting treatment with CPAP (RR, 1.03; 95% CI, 0.77–1.39).

Treatment recommendation

For spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room, we suggest initial use of CPAP rather than intubation and IPPV (weak recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this suggestion, we recognize that the absolute reduction in risk of adverse outcome associated with starting with CPAP is small and that infants recruited to the trials had a high rate of treatment with antenatal steroids but we value the less invasive approach.

CPAP was introduced in the 2010 CoSTR[13–15] as an option to be considered for babies who are breathing, but breathing with difficulty. The previous recommendation had been to simply administer blow-by oxygen. The current PICO question did not address the option of using no support. There was a consensus that, in the absence of contrary evidence, administration of CPAP, with or without supplementary targeted oxygen, is preferable in this situation if resources permit.

Knowledge gaps

- The balance of risks and benefits of this approach in infants who have not received antenatal steroids is unknown.
- A further trial of CPAP versus intubation and IPPV in high-risk preterm infants at lower gestations is required to determine the risks and benefits more clearly. It is not clear whether there is a significant effect on mortality. The CIs for the other morbidities of prematurity leave open the possibility that any benefit in relation to bronchopulmonary dysplasia might still be balanced by a small increase in risk of severe IVH or necrotizing enterocolitis.
- The utility of using an intubation-surfactant-extubation sequence (INSURE) approach[145] to facilitate early stabilization on CPAP soon after birth has been compared with CPAP alone in at least 2 trials. This should be the subject of a future worksheet.

Ventilation strategies in the delivery room

The most effective method for establishing an FRC in the fluid-filled lung of a newborn who does not breathe spontaneously has been debated for many decades. In the 1980s, Vyas et al.[146] suggested a technique of administering an SI of up to 5 s in duration. Both standard IPPV with or without PEEP and inflation breaths up to 3 s in duration are currently initial strategies advocated to initiate ventilation (Neonatal Resuscitation Program, European Resuscitation Council). Several recent animal studies have suggested that a longer SI may be beneficial for short-term respiratory outcomes. The following 3 PICO analyses reflect an in-depth analysis of the different strategies that have been suggested for this initial establishment of FRC after birth.

Sustained inflations—intervention (NRP 809)

In term and preterm newborn infants who do not establish spontaneous respiration at birth (P), does administration of 1 or more pressure-limited sustained lung inflations (I), compared with intermittent PPV with short inspiratory times (C), change Apgar score at 5 min, establishment of FRC, requirement for mechanical ventilation in first 72 h, time to heart rate greater than 100/min, rate of tracheal intubation, overall mortality (O)?

Consensus on science

For the critical outcome of need for **mechanical ventilation** in the first 72 h after birth, low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 3 randomized clinical trials enrolling 404 newborns showed significant benefit of sustained lung inflations.[18,147,148] In addition, very-low-quality evidence (downgraded for variability of interventions in SI and control populations) from 2 cohort studies with a total of 331 patients also showed benefit of sustained lung inflations as compared with intermittent PPV with short inspiratory times.[18,149] One randomized clinical trial[151] was excluded from analysis due to methodological concerns pertaining to differences in the various interventions between the study groups of which sustained lung inflation was merely one.

For the critical outcome of **mortality**, low-quality evidence (downgraded for indirectness and imprecision) from 3 randomized clinical trials enrolling 404 newborns[18,147,149] and very-low-quality evidence (downgraded for variability of interventions in sustained lung inflation and control populations) from 2 cohort studies with a total of 331 patients showed no benefit as compared with IPPV with short inspiratory times.[18,147,149]

For the critical outcome of **bronchopulmonary dysplasia**, low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 3 randomized clinical trials enrolling 404 patients showed no benefit.[18,147,149] Very-low-quality evidence (downgraded for variability of interventions in SI and control populations) from 2 cohort studies with a total of 331 patients showed significant benefit of sustained lung inflations as compared with IPPV with short inspiratory times.[18,149]

For the critical outcome of **air leak**, low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 3 randomized clinical trials enrolling 404 newborns[18,147,148] and very-low-quality evidence (downgraded for variability of interventions in SI and control populations) from 2 cohort studies with a total of 331 patients showed no effect of sustained lung inflation as compared with IPPV with short inspiratory times.[147,148]

For the important outcome of **Apgar score**, there was no difference between groups in any studies reviewed.[18,147–149]

For the important outcome of **need for intubation**, very-low-quality evidence (downgraded for lack of controls) from 1 cohort study[18] showed that the need in the delivery room was significantly lower in infants who received an SI compared with conventional management.

For the important outcome of heart rate greater than 100/min, no evidence was found.

For the important outcome of **establishment of FRC**, no evidence was found.

For the important outcome of **Fio_2 in the delivery room**, no evidence was found.

For the important outcome of **chest compressions in the delivery room**, no evidence was found.

Additional comments:

- No human studies evaluated time to heart rate greater than 100/min, establishment of FRC, FIO_2 in the delivery room, or need for chest compressions in the delivery room.
- In a small case series of 9 asphyxiated term infants (very-low-quality evidence), a prolonged initial inflation of 5 s produced a 2-fold increase in FRC compared with historic controls.[146]
- Comparison of all studies (randomized clinical trials and cohort) was compromised due to the heterogeneity of methodology, i.e. wide differences in duration of the initial SI (5–20 s) as well as the peak inspiratory pressure (20–30 cm H_2O) and use of a variety of interface devices to deliver the SI (endotracheal tube, face mask, or nasopharyngeal tube). Three studies repeated the initial sustained lung inflation once,[18,149,150] 1 at a higher positive inflating pressure,[18] whereas 1 study repeated the SI twice with increasing positive inflating pressure.[148]
- No studies compared the efficacy of a single SI with multiple SIs.
- Animal studies of the effects of SI on alveolar recruitment have shown in lambs[151] and preterm rabbits[152] more uniform lung inflation and better lung compliance, if animals received an SI before initiation of mechanical ventilation. However, a study by Klopping-Ketelaars[153] showed no benefit after an initial SI in preterm lambs, and another study showed that stepwise increases in PEEP resulted in better overall lung mechanics than treatment with an initial SI.[154]

Treatment recommendation

We **suggest against** the routine use of initial SI (greater than 5 s duration) for preterm infants without spontaneous respirations immediately after birth, but an SI may be considered in individual clinical circumstances or research settings (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, and in the absence of long-term benefits, we place a higher value on the negative aspect involving lack of clarity as to how to administer sustained lung inflations versus the positive findings of a reduced need for intubation at 72 h.

Although the studies reviewed showed that administration of an SI reduced the need for mechanical ventilation in the first 72 h of life, the use of SI did not change the incidence of important long-term outcomes related to lung function, including risk of bronchopulmonary dysplasia or overall mortality. Studies thus far are likely underpowered for these outcomes.

There was much debate about the use of SI. The methods used in delivering SI varied among studies. It was stressed that different devices varied in their ability to generate pharyngeal pressures. Moreover, a recent animal study suggests that there may be unintended glottis closure associated with SI. There was also concern that the current wording of the treatment recommendation may be viewed by some as limiting the potential for future clinical studies.

Evidence evaluators were asked to decide whether to include the te Pas article.[155] The decision was made to exclude it because of multiple confounding interventions. It was thought that more detail in the consensus on science was needed to reflect that studies used SI ranging from 5 to 25 s. There was debate about the use of the wording *suggest against*. Several members were in favor of using this term, because there is insufficient evidence regarding how to administer sustained lung inflation, how many such breaths should be applied, or whether it should be used with or without PEEP. It is difficult to extrapolate from animal data, because the animals in the studies were nonbreathing and had tracheostomies, so that the anatomy, physics, and physiology are different. Although there was consensus agreement on the current wording, it was noted that individual councils may choose to interpret the recommendations differently.

Knowledge gaps

- The duration of an SI, the appropriate peak initial inflation pressure, the number of SIs to be administered, and an early measure of response remain unclear.
- Further studies are essential to determine the optimal pressure and duration of SI that would allow the establishment of FRC while minimizing the risk of barotrauma in the newly born infant and long-term morbidity.

Outcomes for PEEP versus no PEEP in the delivery room—intervention (NRP 897)

In preterm/term newborn infants who do not establish respiration at birth (P), does the use of PEEP as part of the initial ventilation strategy (I), compared with no PEEP (C), improve Apgar score at 5 min, intubation in the delivery room, chest compressions in the delivery room, heart rate greater than 100/min by 2 min of life, time for heart rate to rise above 100/min, air leaks, oxygen saturation/oxygenation, FIO_2 in the delivery room, mechanical ventilation in the first 72 h, bronchopulmonary dysplasia, survival to discharge (O)?

Introduction

In the 2010 CoSTR, new recommendations were introduced regarding the use of CPAP for babies exhibiting breathing difficulty and for using PEEP whenever IPPV was required. But problems have continued because of an inability of self-inflating bags to reliably deliver PEEP, and self-inflating bags are the most common devices used for neonatal resuscitation worldwide. This PICO question and the one immediately following (NRP 870) were constructed to examine the value of using one device over another and the need for PEEP when administering IPPV during resuscitation.

Consensus on science

For the critical outcome of **mortality before discharge**, we identified low-quality evidence from 2 randomized trials of 596 preterm newborns showing no benefit (RR, 0.616; 95% CI, 0.274–1.382) to providing PEEP compared with no PEEP (downgraded for serious imprecision and risk of bias).[156,157]

For the critical outcome of **chronic lung disease**, we identified moderate-quality evidence from 2 randomized trials of 596 preterm newborns showing no benefit (RR, 1.153; 95% CI, 0.711–1.871) to providing PEEP as compared with no PEEP (downgraded for imprecision and risk of bias).[156,157]

For the critical outcome of **need for cardiac drugs or chest compressions in the delivery room**, we identified low-quality evidence from 2 randomized trials of 596 preterm newborns showing no benefit (RR, 1.468; 95% CI, 0.550–3.917) to providing PEEP as compared with no PEEP[156,157] (downgraded for imprecision and risk of bias).

For the important outcome of **oxygen saturation at 5 min after birth**, we identified moderate-quality evidence from 1 randomized trial of 80 preterm newborns showing no benefit ($P = 0.55$) to providing PEEP (median Spo_2, 49%; interquartile range [IQR], 25–90%) versus not providing PEEP (median Spo_2, 59%; IQR, 33–66%) (downgraded for imprecision and risk of bias).[156]

For the important outcome of **maximum concentration of oxygen used during resuscitation**, we identified low-quality evidence from 1 randomized trial of 516 preterm newborns showing moderate benefit ($P = 0.005$) to providing PEEP (mean, 48%; standard deviation [SD], 0.2) versus not providing PEEP (mean, 53%; SD, 0.2).[157]

For the important outcome of **heart rate greater than 100/min at 2 min of age**, we identified low-quality evidence from 1 randomized trial of 516 preterm newborns showing no benefit to providing PEEP versus not providing PEEP (RR, 1.656; 95% CI, 0.938–2.923) (downgraded for imprecision and risk of bias).[157]

For the important outcome of **time for heart rate to rise to greater than 100/min**, we identified moderate-quality evidence from 1 randomized trial of 516 preterm newborns showing no benefit to providing PEEP (median, 1 min; IQR, 0.5–1.8) versus not providing PEEP (median, 1 min; IQR, 0.5–1.9) (downgraded for imprecision and risk of bias).[157]

For the important outcome of **need for intubation in the delivery room**, we identified moderate-quality evidence from 2 randomized trials of 596 preterm newborns showing no benefit (RR, 1.208; 95% CI, 0.907–1.609) to providing PEEP (downgraded for imprecision and risk of bias)[156,157] versus not providing PEEP.

For the important outcome of **need for mechanical ventilation in the first 72 h**, we identified low-quality evidence from 1 randomized trial of 80 preterm newborns showing no benefit (RR, 0.317; 95% CI, 0.093–1.086) to providing PEEP (downgraded for imprecision and risk of bias) versus not providing PEEP. We identified only 1 randomized clinical trial that included term infants,[157] which provided insufficient data to address this question as a secondary outcome measure in a subgroup analysis (very-low-quality evidence, downgraded for serious imprecision and risk of bias).

For the important outcome of **pulmonary air leaks**, we identified low-quality evidence from 2 randomized trials of 596 preterm newborns showing no benefit (RR, 1.401; 95% CI, 0.414–4.735) to providing PEEP (downgraded for imprecision and risk of bias)[156,157] versus not providing PEEP.

For the important outcome of **Apgar score less than 6 at 5 min**, we identified moderate-quality evidence from 1 randomized trial of 516 preterm newborns showing no benefit to providing PEEP (RR, 0.813; 95% CI, 0.472–1.402) (downgraded for imprecision and risk of bias)[157] versus not providing PEEP.

For the less-important outcome of **Apgar score at 5 min**, we identified moderate-quality evidence from 1 randomized trial of 80 preterm newborns showing no benefit ($P = 0.18$) to providing PEEP (median, 7; IQR, 6–8) versus no PEEP (median, 7; IQR, 6–9) (downgraded for imprecision and risk of bias).[156]

Treatment recommendations

We suggest using PEEP ventilation for premature newborns during delivery room resuscitation (weak recommendation, low-quality evidence).

We cannot make any recommendation for term infants because of insufficient data.

Values, preferences, and task force insights

In making this suggestion, we are considering the small reduction in maximum oxygen concentration needed during resuscitation with 5 cm H_2O PEEP compared with those not receiving PEEP shown in 1 human study, and considering the evidence from animal studies (see NRP 809). Interpretation of human studies is further complicated by varying interfaces (e.g., face mask versus endotracheal tube) and methods of generating PEEP (e.g., self-inflating bags with PEEP valve versus T-piece resuscitator).

Only 1 study was available to indirectly address the specific PICO question,[157] where a subgroup comparison was applied. Good animal studies are available but are classified as low levels of evidence from the point of applicability due to indirectness (see NRP 809). There was concern that the evidence based on the GRADE criteria was regarded as low quality. There was a major struggle to come up with a recommendation when the evidence was weak. The only positive effect found was a 5% change in FIO_2 (see comments after NRP 870).

Knowledge gaps

- Properly powered, well-designed randomized trials specifically addressing important outcomes for the effects of PEEP in the delivery room are necessary.
- It remains unclear as to the optimal level of PEEP to use.
- The question of static PEEP versus dynamic PEEP needs to be delineated.
- Differential effects of PEEP at different gestational ages and for different pathologies remain to be determined.

T-piece resuscitator and self-inflating bag—intervention (NRP 870)

In newborns (preterm and term) receiving ventilation (PPV) during resuscitation (P), does using a T-piece resuscitator with PEEP (I), compared with using a self-inflating bag without PEEP (C), achieve spontaneous breathing sooner and/or reduce the incidence of pneumothorax, bronchopulmonary dysplasia, and mortality (O)?

Introduction

The T-piece resuscitator has replaced the self-inflating and flow-inflating bag in many institutions. One major reason for this change has been the inability of the self-inflating bag to deliver either CPAP or PEEP reliably. Advantages of the T-piece include ease of use and ability to deliver CPAP, PEEP, and/or IPPV. However, it also requires a pressurized-gas source to drive the device. This PICO question is intended to review the evidence of the utility of self-inflating bags versus T-piece resuscitators.

Consensus on science

For the following consensus on science statements, the analysis is based on all patients ($n = 80$) from 1 study[156] and from a subgroup analysis ($n = 453$) in a second study.[157]

For the critical outcome of **death before discharge**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 randomized clinical trials[156,157] enrolling 532 patients showing no benefit to the use of a T-piece resuscitator as compared with a self-inflating bag (OR, 0.68; 95% CI, 0.31–1.56).

For the critical outcome of **bronchopulmonary dysplasia**, which was only assessed for infants of less than 1500 g, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 randomized clinical trials[156,157] enrolling 151 patients showing no benefit to the use T-piece resuscitator as compared with self-inflating bag (OR, 0.92; 95% CI, 0.59–1.43).

For the critical outcome of **air leaks**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 randomized controlled trials[156,157] enrolling 532 patients showing no benefit to the use of T-piece resuscitator as compared with self-inflating bag (OR, 1.72; 95% CI, 0.51–5.78).

For the important outcome of **achieving spontaneous breathing** or **reducing intubation in delivery room**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and inconsistency) from 2 randomized clinical trials[156,157] enrolling 532 patients showing no benefit to the use of T-piece resuscitator as compared with self-inflating bag (OR, 0.80; 95% CI, 0.59–1.07).

Treatment recommendation

There is insufficient evidence, so the recommendation of one device over another would be purely speculative because the confidence in effect estimates is so low.

Values, preferences, and task force insights

The current studies suggest a benefit to using PEEP to assist establishment of an FRC during transition of the fluid-filled lung to an air-breathing organ. However, the evidence to date is not sufficiently compelling to recommend against using a self-inflating bag (in which reliable administration of PEEP is not achievable with current devices) during neonatal resuscitation, particularly in regions where pressurized gases are not readily available. PEEP is recommended when the facilities and equipment permit it to be given reliably (approximately 5 cm H_2O).

Knowledge gaps

- One cluster randomized controlled trial[157] showed benefit of using T-piece resuscitator for achieving spontaneous breathing in the late preterm (mean gestational age 36 weeks) population. Further research in this population would be important.
- There are no studies comparing the flow-inflating bag to either the self-inflating bag or the T-piece resuscitator (with or without PEEP) for neonatal resuscitation. Theoretically, the flow-inflating bag should be similar to the T-piece resuscitator, although ease of use may prove it to be less effective.
- Studies comparing the flow-inflating bag to the other 2 devices would be helpful.

Intubation and tracheal suctioning in nonvigorous infants born through MSAF versus no intubation for tracheal suctioning—intervention (NRP 865)

In nonvigorous infants at birth born through MSAF (P), does tracheal intubation for suctioning (I), compared with no tracheal intubation (C), reduce meconium syndrome or prevent death (O)?

Introduction

For more than 30 years, it has been recommended that newborns with MSAF should receive endotracheal intubation, with tracheal suctioning using the endotracheal tube as a suction device. Approximately 15 years ago, as a result of a multicenter randomized clinical trial, the recommendation was restricted to babies who appeared to have respiratory compromise at birth (i.e. were nonvigorous). It remains controversial as to whether even nonvigorous babies benefit from this procedure. This PICO question is intended to address this issue.

Consensus on science

For the critical outcome of **mortality and/or meconium aspiration syndrome** (MAS), we identified 1 randomized study involving 122 infants (low-quality evidence, downgraded for risk of bias and imprecision)[17] comparing tracheal intubation for suctioning versus no tracheal intubation for suctioning in nonvigorous infants showing no benefit to suctioning in either reduced mortality and/or MAS.

For the critical outcome of **mortality and/or MAS**, we identified very-low-quality evidence from 3 studies[158–160] including 12 389 MSAF infants showing higher incidence of MAS in depressed infants (268/1022, 26%) who had tracheal intubation for suctioning compared with vigorous infants (34/11 367, 0.3%) who were not intubated (downgraded for indirectness).

For the critical outcome of **mortality and/or MAS**, we identified evidence from 7 very-low-quality observational studies[161–167] demonstrating improved survival and lower incidence of MAS when infants (including depressed and/or vigorous infants) born through MSAF were intubated for tracheal suctioning (downgraded for indirectness and inconsistency).

For the critical outcome of **mortality and/or MAS**, we identified evidence from 9 very-low-quality observational studies[158–160,168–173] demonstrating no improvement in survival and/or incidence of MAS (including depressed and/or vigorous infants) when infants born through MSAF were intubated for tracheal suctioning (downgraded for indirectness).

Treatment recommendation

There is insufficient published human evidence to suggest routine tracheal intubation for suctioning of meconium in nonvigorous infants born through MSAF as opposed to no tracheal intubation for suctioning.

Values, preferences, and task force insights

In making this suggestion, we place value on both harm avoidance (delays in providing bag-mask ventilation, potential harm of the procedure) and the unknown benefit of the intervention of routine tracheal intubation and suctioning.

Routine suctioning of nonvigorous infants is more likely to result in delays in initiating ventilation, especially where the provider is unable to promptly intubate the infant or suction attempts are repeated. In the absence of evidence of benefit for suctioning, the emphasis should be on initiating ventilation within the first minute of life in nonbreathing or ineffectively breathing infants.

Much of the deliberations focused on the wording of the treatment recommendation. There were 3 different treatment recommendation options. First "We suggest against the routine intubation of nonvigorous infants born through MSAF." Second "We suggest that routine tracheal intubation for suctioning of meconium in nonvigorous infants should not be considered as a standard of care but may be considered a reasonable alternative to no tracheal intubation in some settings." Third "We suggest that routine tracheal intubation for suctioning of meconium in nonvigorous infants should not be considered as a standard of care but may be considered a reasonable alternative to no tracheal intubation if a meconium plug is suspected." There was concern that the legal profession could misinterpret the term *standard of care*. Consensus was reached on the final treatment recommendation.

Knowledge gaps

- Tracheal intubation or no tracheal intubation for suctioning in nonvigorous infants: Is there a benefit or harm?

Oxygen concentration for resuscitating premature newborns—intervention (NRP 864)

Among preterm newborns (less than 37 weeks of gestation) who receive PPV in the delivery room (P), does the use of high O_2 (50–100%) as the ventilation gas (I), compared with low concentrations of O_2 (21–30%) (C), decrease mortality, decrease bronchopulmonary dysplasia, decrease retinopathy, decrease IVH (O)?

Introduction

The fact that high oxygen concentrations can be toxic to the newly born lungs has been recognized in all CoSTR statements since 2000. The original studies examined only 21% oxygen versus 100% and led to a recommendation that blended oxygen be used to titrate the concentration to achieve an oxygen saturation that is reflective of what healthy babies born at term experience (i.e. targeted saturation). There has been an ongoing controversy as to what the initial oxygen concentration should be. Babies born at term should be started in air (21%), but there has been uncertainty as to whether the preterm baby should be started in a high concentration (50–100%) versus low concentration (21–30%) of oxygen while the pulse oximetry is being attached. This PICO question was intended to examine only the starting concentration of administered oxygen, not the targets.

Consensus on science

For the critical outcome of **mortality before discharge**, we found moderate-quality evidence from 7 randomized clinical trials enrolling 607 subjects showing no benefit to beginning resuscitation with high-oxygen as compared with low-oxygen concentration (RR, 1.48; 95% CI, 0.8–2.73). The quality of evidence was downgraded for imprecision.[174–180] When limited to randomized clinical trials with concealed allocation and oxygen targeting as a cointervention, we found moderate-quality evidence from 5 trials enrolling 468 subjects showing no benefit to beginning resuscitation with a high-oxygen concentration as compared with low-oxygen concentration (RR, 1.33; 95% CI, 0.68–2.62). The quality of evidence was downgraded for imprecision.[175,177–180] We found very-low-quality evidence from 1 cohort study including 125 subjects showing no benefit to beginning resuscitation with high-oxygen as compared with low-oxygen concentration (RR, 1.31; 95% CI, 0.41–4.24). The quality of evidence was downgraded for serious imprecision.[181]

For the critical outcome of **bronchopulmonary dysplasia**, we found low-quality evidence from 5 randomized trials enrolling 502 subjects showing no benefit to beginning resuscitation with a high-oxygen as compared with low-oxygen concentration (RR, 1.08; 95% CI, 0.59–1.98). The quality of evidence was downgraded for inconsistency and imprecision.[175,177–180]

For the critical outcome of **intraventricular hemorrhage**, we found moderate-quality evidence from 4 randomized clinical trials enrolling 400 subjects showing no benefit to beginning resuscitation with a high-oxygen as compared with low-oxygen concentration (RR, 0.90; 95% CI, 0.47–1.72). The quality of evidence was downgraded for imprecision.[175,178–180]

For the important outcome of **retinopathy of prematurity**, we found moderate-quality evidence from 3 randomized trials enrolling 359 subjects showing no benefit to beginning resuscitation with a high- as compared with low-oxygen concentration (RR, 1.28; 95% CI, 0.59–2.77). The quality of evidence was downgraded for imprecision.[175,178,179]

Treatment recommendations

We **recommend against** initiating resuscitation of preterm newborns (less than 35 weeks of gestation) with high supplementary oxygen concentrations (65–100%).

We **recommend initiating resuscitation** with a low-oxygen concentration (21–30%) (strong recommendation, moderate-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place value on not exposing preterm newborns to additional oxygen without proven benefit for critical or important outcomes. Our preference for each outcome, therefore, was to describe the risk of high-oxygen relative to low-oxygen concentration. In all studies, irrespective of whether air or high oxygen including 100% was used to initiate resuscitation, by the time of stabilization most infants were in approximately 30% oxygen. We recognize that all but 1 included study allowed adjustment of oxygen concentration based on pulse oximetry and/or heart rate response.

Concerns were expressed about the practical implications of recommending separate and simultaneous monitoring of both heart rate and oxygen saturation, although accurate measurements of both variables are important (see NRP 898). The chosen range for the low oxygen starting point (21–30%) was also questioned, but the available articles defined it. Whether the high oxygen should be greater than 60% was also discussed.

Knowledge gaps

- The most appropriate time-specific oxygen targets for premature newborns need to be defined.
- Neurodevelopmental outcomes for preterm newborns resuscitated with low- and high-oxygen concentrations need to be determined.

Circulatory support

Circulatory support focused on the most effective method of delivering chest compressions and included comparison of the 2-thumb versus the 2-finger techniques as well as comparing various compression-to-ventilation ratios. During the evidence evaluation in 2010, it was decided to continue recommending a chest compression-to-ventilation ratio of 3:1 as opposed to 15:2 or 30:2, predominantly because profound bradycardia or asystole in the newly born period is invariably secondary to an asphyxial rather than a primary cardiac event. Evidence in this review was sought to determine whether there was any recent evidence to change this recommendation. Moreover, factors important to the ergonomics of CPR for enhancing blood flow during chest compressions were identified. The evidence below summarizes these findings.

2-Thumb versus 2-finger techniques for chest compression—intervention (NRP 605)

In neonates receiving cardiac compressions (P), does the use of a 2-thumb technique (I), compared with a 2-finger technique (C), result in return of spontaneous circulation (ROSC), improved neurologic outcomes, improved survival, improved perfusion and gas exchange during CPR, and decreased compressor fatigue (O)?

Introduction

Two different techniques for administering chest compressions during resuscitation of neonates have been suggested: 2 thumbs, with fingers surrounding the lateral and posterior chest, versus 2 fingers placed vertically on the lower sternum. This PICO question is intended to evaluate which technique is preferable.

Consensus on science

For the critical outcomes of **time to ROSC**, **survival rates**, or **neurologic injury**, we found no data.

For the critical outcome of **improved perfusion and gas exchange during CPR**, we identified low-quality evidence from 9 randomized controlled trials (downgraded for indirectness and imprecision)[182–190] and 6 nonrandomized controlled trials (downgraded for indirectness, imprecision, and high risk of bias)[191–196] identifying higher blood pressure generation with the 2-thumb versus the 2-finger method.

For the important outcome of **compressor fatigue**, we identified low-quality evidence from 4 randomized controlled trials (downgraded for indirectness and imprecision), with 2[183,197] identifying less fatigue with the 2-thumb versus the 2-finger technique, and 2 studies finding no difference.[189,198]

New compression methods:

- **Thumb and index finger (TIF)**[199] compared the new method versus the 2-thumb and 2-finger methods on manikins. Cardiac compressions lasted for only 5 min while recording rate, hand location, depth, incomplete recoil, excessive depth, and error rate during CPR. Two-thumb and TIF had less decay in "suitable chest compressions" over the 5 min compared with the 2-finger method.

- **Adhesive glove**[200] compared using the adhesive glove with conventional CPR in 4 groups, including an infant group in a manikin model. The 2-thumb method was used as standard in the infant group versus adhesive 2-thumb method. The theory is that the glove enables active compression-decompression. Rate, compression, and decompression depth were measured. No differences in fatigue variables were found amongst groups. Results showed more active decompression with the adhesive glove group.

Summary: No evidence was found supporting the new thumb and index finger technique as superior to the 2-thumb method. The adhesive glove enhanced active decompression but did not reduce fatigue.

Other issues:

- **Does the CPR technique cause fractures?** Franke[201] performed a 10-year retrospective survey to determine whether the 2-thumb technique causes rib fractures. All infants received CPR plus chest X-rays. Median age was 9 days.

Summary: There was no evidence of rib fractures in any case.

- **Best location on the sternum**: Using 4 assessment methods over a wide age range of infants,[202] it was confirmed that the heart lies under the lower third of the sternum. In addition, blood pressure readings were higher when cardiac compressions were applied to the lower versus the middle third of the sternum. Use of the infant computed tomography (CT) scan data (mean age, 4.4 months) and adult thumb side-by-side measurements on manikins[203] confirmed that the left ventricle lies mostly under the lower quarter of the sternum. No functional data were collected to confirm better outcomes if compressions focused on that area. An assumption was made that the lower third of the sternum was the best position for compressions.[204]
- **Term and preterm babies**: Correct positioning on the chest was determined to be much better with the 2-thumb method in both groups of babies, although incorrect placements were found for both techniques in infants less than 1500 g. Chest X-ray analysis of term and preterm babies[205] found the heart to be under the lower third of the sternum. Chest CT scans of infants (mean age, 4.7 months), compared with adult thumb measurements on a manikin, comparing the 2-thumb method side by side or superimposed,[206] demonstrated that the side-by-side method increases the likelihood of other organs (lungs and liver) being under the points of compressions application. A manikin study looked at fatigue levels with the 2-thumb technique, comparing side-by-side or superimposed thumb position[207] demonstrated that the superimposed thumb technique generated higher simulated blood pressure and pulse pressure but had a higher fatigue-rating score. Physiologic indices of fatigue showed no difference between groups. CT scans of the chest to compare thumb (side-by-side)/fingers measurements placed on manikins were conducted to determine which method avoided compressing other structures when using the lower third of the sternum.[208] Both methods compress other structures, but the 2-thumb method (side-by-side) performs better than the two finger method. The accuracy of using the nipple line to the xiphisternum landmarks for 2-finger chest compression was examined by Clements.[209] They concluded that this method could result in abdomen and xiphisternum compression in all infants and suggested an alternate method of determining position.

Summary: The lower one third of the sternum remains the best location to press over the newborn heart. Superimposed thumbs may be the better technique.

Treatment recommendations

We suggest that chest compressions in the newborn should be delivered by the 2-thumb, hands-encircling-the-chest method as the preferred option (weak recommendation, very-low-quality evidence).

We suggest that chest compressions should be delivered over the lower third of the sternum (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

None are noted.

Knowledge gaps

- No studies of any kind regarding the most critical outcomes were available.
- No data from good transitional models were found.
- There are very limited human neonatal data.

Chest compression ratio—intervention (NRP 895)

In neonates receiving cardiac compressions (P), do other ratios (5:1, 9:3, 15:2, synchronous, etc.) (I), compared with 3:1 compressions to ventilations (C), increase survival rates, improve neurologic outcomes, improve perfusion and gas exchange during CPR, decrease time to ROSC, decrease tissue injury, or decrease compressor fatigue (O)?

Introduction

Chest compressions administered in a ratio of 3 compressions to 1 ventilation have been recommended for resuscitation of neonates at birth. The concept has been that newborns are born with lungs filled with fluid, much of which is absorbed directly across the alveolar membrane with the first few breaths. If a newborn is compromised sufficiently to prevent spontaneous breathing, resulting in bradycardia or cardiac arrest, successful resuscitation must achieve adequate lung aeration and ventilation to reverse an asphyxial pathophysiology. Thus, the focus of newborn resuscitation efforts must be primarily aimed at establishing ventilation first and cardiac support second. This PICO question is meant to identify which compression-to-ventilation ratio will be most effective at achieving this.

Consensus on science

Animal studies demonstrate no advantage to higher compression-to-ventilation ratios (very-low-quality evidence, downgraded for potential bias, indirectness, and imprecision) regarding

- **Short-term survival** (2 randomized controlled trials including 54 pigs)[210,211]
- **Gas exchange during CPR** (2 randomized controlled trials including 54 pigs)[210,211]
- **Time to ROSC** (2 randomized controlled trials including 54 pigs)[210,211]
- **Markers of tissue injury** (lung/brain) (2 randomized controlled trials including 54 pigs)[212,213]

There was no evidence identified to address the critical issue of **neurologic outcome**.

Manikin studies demonstrated a disadvantage to higher compression-to-ventilation ratios (5:1, 9:3, 15:2)

(very-low-quality evidence, downgraded for potential bias, imprecision, and indirectness) with regard to

- **Compressor fatigue** (better depth of compression, less decay in depth over time; 1 randomized controlled trial including 32 resuscitation providers)[214]
- **Minute ventilation** (1 randomized controlled trial including 32 resuscitation providers)[214]
- A single manikin study demonstrated higher minute ventilation for asynchronous compressions (120 compressions: 40 ventilations) compared with 3:1 (90 compressions: 30 ventilations) (1 randomized controlled trial including 2 resuscitation providers with 5 different sessions per treatment arm)[215]

Treatment recommendation

We suggest continued use of a 3:1 compression-to-ventilation ratio for neonatal CPR (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

We prefer to retain our prior recommendation of 3:1 compression-to-ventilation ratio for neonatal CPR, because there is no compelling evidence suggesting a benefit to other ratios for the newborn. Since asphyxia is the predominant cause of cardiovascular collapse in the newborn, effective resuscitation requires significant focus on ventilation. In addition, we value consistency in the resuscitation algorithm and education programs unless new evidence drives the change.

All studies were done in young posttransitioned piglets (no human or animal data in a transitioning model). Since there is no evidence in either a human or animal with fluid-filled lungs, we need to be clear when communicating with other groups (pediatrics and basic life support providers) that neonates have unique cardiopulmonary physiology, prompting our unique 3:1 ratio.

Some may not agree, but the values and preferences statement expresses why we still favor a 3:1 ratio.

Knowledge gaps

- Specific research is required, such as clinical and appropriate animal model studies.
- We need neonatal human data.
- How many compressions in a row are required to achieve forward blood flow and adequate coronary perfusion pressure during newborn asphyxial arrest?
- How many interposed ventilations are needed to achieve and maintain normocapnia during cardiac compressions due to newborn asphyxial arrest?
- Asynchronous technique deserves more investigation.
- Is ventilation adequate with SI cardiac compressions?
- How should we limit interruptions in compressions to assess efficacy?

Oxygen delivery during CPR (neonatal)—intervention (NRP 738)

In neonates receiving cardiac compressions (P), does 100% O_2 as the ventilation gas (I), compared with lower concentrations of oxygen (C), increase survival rates, improve neurologic outcomes, decrease time to ROSC, or decrease oxidative injury (O)?

Introduction

Neonatal resuscitation has historically focused on achieving adequate oxygenation as quickly as possible. Recently, it has been recognized that excessive oxygen administration can be toxic. Current guidelines recommend starting resuscitation with low inspired oxygen and then increasing inspired oxygen as necessary as guided by pulse oximetry. However, once the resuscitation has reached the need for chest compressions, it has been suggested to increase the F_{IO_2}. This PICO question is intended to consider evidence to determine if this is the correct or incorrect practice.

Consensus on science

For the critical outcome of **ROSC**, we found 8 animal studies (lambs/pigs/rats)[216–223] all demonstrating no advantage to 100% over 21% during CPR (very-low-quality evidence, downgraded for bias and indirectness).

For the critical outcome of **survival**, we found 8 of 9 animal studies (lambs/pigs/rats) reporting on survival demonstrated no advantage to 100% over 21% during CPR.[216–223] However, 1 study (mouse) of 9 studies evaluating this outcome found an advantage to 100% O_2[224] (very-low-quality evidence, downgraded for potential bias, inconsistency, and indirectness). All studies combined showed 80/100 (80%) versus 74/102 (73%) survival for 100% O_2 versus air (not different). Eight studies with no advantage showed 70/77 (91%) versus 71/79 (90%) survival. One study with advantage for 100% showed 10/23 (43%) versus 3/23 (13%) survival ($P = 0.02$).

For the critical outcome of **neurologic outcome**, we found 4 animal studies (pigs/rats/mice)[218,221,222,224] reporting on neurologic outcome with varying results (very-low-quality evidence, downgraded for potential bias, inconsistency, indirectness, and imprecision). One demonstrated no difference in neurologic deficits at 72 h, and ischemic neurons in hippocampal were not different.[218] One demonstrated worse 4-h neurologic examination in the 100% O_2 group.[221] One demonstrated more hippocampal apoptosis in the 100% O_2 group.[222] One demonstrated more rapid restoration of cerebral blood flow but no difference in histologic brain injury scores.[224]

For the critical outcome of **oxidative injury**, we found 10 animal studies reported on oxidative injury with varying results[212,213,216,219–223,225–227] (very-low-quality evidence, downgraded for potential bias, inconsistency, and indirectness). Six studies (pigs/mice) demonstrated no difference in various oxidative injury markers,[212,213,219–221,224] 3 (lambs/rats) demonstrated more oxidative damage from using 100% O_2 including apoptosis,[216,222,226] and a pig study reported less striatal and hippocampal apoptosis with 100% O_2 compared with 21% O_2.[227]

Treatment recommendation

There are no human data to inform this question.

Despite animal evidence showing no advantage to the use of 100% oxygen, by the time resuscitation of a newborn baby has reached the stage of chest compressions, the steps of trying to achieve ROSC using effective ventilation with low-concentration oxygen should have been attempted. Thus, it would seem prudent to try increasing the supplementary oxygen concentration (Good Practice Guidance).

If used, supplementary oxygen should be weaned as soon as the heart rate has recovered (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

Although most of the available animal evidence suggests that resuscitation using air during neonatal chest compressions is feasible and that 100% O_2 as the resuscitation gas may increase oxidative injury, we remain concerned that we have no human data to prove feasibility and none of the animal studies have evaluated use of room-air CPR for more than brief asystole. We value balancing the desire to prevent ongoing hypoxic injury in these profoundly asphyxiated neonates with the desire to prevent subsequent hyperoxic injury.

This was a much-debated topic. In the case of hypotension and bradycardia, the experimental evidence is clear: You only need to

use room air. Thus, in this case, we are making the recommendation independent of the evidence. Perhaps, we say, "Despite no evidence, for the following reasons, we recommend. . .." In training scenarios, once chest compressions are started, failing to turn up O_2 is a common error of the learner. But is it a serious error? The indirectness does not inform the recommendation. We are not even following low-level animal evidence. We are making a conscious decision to take no notice of the evidence. Can we say why this group values giving oxygen for asystole? The task force considered the option of making a neutral recommendation (with either 21% or 100% O_2) and allowing councils to decide what to do. Is this a place where we do not want to suggest air or oxygen? We have no data, but we need to say something.

Knowledge gaps

- Specific research is required, i.e. studies in good transitional animal model of asphyxia-induced severe bradycardia or asystole and any neonatal human data.

Assist ventilation devices and CPR feedback devices

There are numerous techniques used and advocated to ventilate effectively. In addition there are devices used to assess respiratory function and to provide feedback during CPR. The following reviews were undertaken to assess the role of alternative techniques to ventilate effectively when intubation is not feasible or unsuccessful and to ascertain the evidence of feedback devices on resuscitation skill performance and outcomes.

Laryngeal mask airway—intervention (NRP 618)

In newborn infants at near term (greater than 34 weeks) or term who have indications for intermittent positive pressure for resuscitation (P), does use of a laryngeal mask as a primary or secondary device (I), compared with mask ventilation or endotracheal intubation (C), improve response to resuscitation or change outcome (O), including indicators of neonatal brain injury, achieving stable vital signs, increasing Apgar scores, long-term outcomes, reducing the need for subsequent intubation, or neonatal morbidity and mortality?

Introduction

Endotracheal intubation is the most difficult skill to learn and teach in neonatal resuscitation. The laryngeal mask has recently been suggested as an alternative, either as a primary device, replacing face-mask ventilation, or as a secondary device for failed or not-possible endotracheal intubation. This PICO question is intended to review the evidence for the utility and efficacy of the laryngeal mask for neonatal resuscitation.

Consensus on science

For comparison of laryngeal mask airway to face mask as a **primary device** (i.e. use of laryngeal mask ventilation rather than bag-mask ventilation for infants at term requiring PPV for resuscitation) we identified 3 randomized controlled trials enrolling a total of 469 patients:

- For the critical outcome of **achieving vital signs**, we identified low-quality evidence (downgraded for very serious risk of bias) from 2 small randomized clinical trials and 1 large quasi-randomized clinical trial[228–230] showing that the laryngeal mask was more effective than the face mask (OR, 11.43; 95% CI, 4.01–32.58).
- For the critical outcome of **need for subsequent endotracheal intubation after failed laryngeal mask or face mask**, we identified low-quality evidence (downgraded for very serious risk of bias) from the same randomized clinical trials[228–230] showing that the laryngeal mask was more effective than the face mask (OR, 0.13; 95% CI, 0.05–0.34).
- For the critical outcome of **increasing Apgar score**, we have identified low-quality evidence from the same randomized controlled trials (downgraded for very serious risk of bias); the method of reporting precluded analysis of this outcome.
- We did not identify any evidence to address the critical outcomes of **indicators of brain injury** or **long-term outcomes**.
- For the important outcome of **morbidity** (gastric distention or vomiting), we identified low-quality evidence (downgraded for imprecision and very serious risk of bias) from the same randomized clinical trials[228–230] showing no difference for any variable between the laryngeal mask and the face mask (OR, 5.76; 95% CI, 0.7–47.32).

For comparison of laryngeal mask to endotracheal tube as a **secondary device** (i.e. laryngeal mask or intubation when bag-mask ventilation has failed) for infants at term requiring PPV for resuscitation, we identified the following evidence (1 randomized clinical trial with 40 patients)[231]:

- For the critical outcome of **achieving vital signs or successful resuscitation**, we identified very-low-quality evidence (downgraded for imprecision, risk of bias) from 1 randomized clinical trial[231] showing that laryngeal mask airway was as effective as the endotracheal tube.
- For the critical outcome of **need for subsequent endotracheal intubation after failed** bag-mask ventilation, we identified very-low-quality evidence (downgraded for imprecision, risk of bias) from the same randomized clinical trial[231] showing that the laryngeal mask was as effective as the endotracheal tube.
- For the critical outcome of **increasing Apgar score**, we identified very-low-quality evidence (downgraded for imprecision and risk of bias) from the same randomized clinical trial[231]; the method of reporting precluded analysis of this outcome.
- For the critical outcome of **mortality**, we identified very-low-quality evidence (downgraded for imprecision and risk of bias) from the same randomized clinical trial[231] showing no difference between the laryngeal mask or the endotracheal tube.
- We did not identify any evidence to address the critical outcome of indicators of **brain injury** or **long-term neurologic outcomes** comparing laryngeal mask airway or endotracheal tube as a secondary device.
- For the important outcome of **morbidity**, we identified very-low-quality evidence (downgraded for imprecision and risk of bias) from the same randomized clinical trial[231] showing more trauma to tissue when comparing laryngeal mask versus endotracheal tube (OR, 2.43; 95% CI, 0.51–11.51).

Treatment recommendations

We suggest the laryngeal mask may be used as an alternative to tracheal intubation during resuscitation of the late-preterm and term newborn (more than 34 weeks) if ventilation via the face mask is unsuccessful (weak recommendation, low-quality evidence).

In the unusual situation where intubation is not feasible after failed PPV, the laryngeal mask is recommended for resuscitation of the late-preterm and term newborn (more than 34 weeks) (strong recommendation, good clinical practice).

Values, preferences, and task force insights

In making these recommendations, we place a moderate value in the proven safety and feasibility for a laryngeal mask to provide ventilation in newborns while recognizing the necessity for more studies in other clinical settings (e.g., premature infant). We also

place high value on the idea that an alternative airway is a potentially lifesaving intervention when face-mask ventilation has failed and/or endotracheal intubation is unsuccessful or not feasible. There is now reasonable evidence to add a recommendation for the late-preterm infant.

Knowledge gaps

- The effectiveness and safety of laryngeal mask airway compared with mask ventilation as the primary interface in term and preterm infants; insertion technique, which model, and how to teach its use

Newborn infants who receive PPV for resuscitation, and use of a device to assess respiratory function—diagnostic (NRP 806)

In newborn infants who receive PPV for resuscitation (P), does use of a device to assess respiratory function with or without pressure monitoring (I), compared with no device (C), change survival to hospital discharge with good neurologic outcome, IVH, time to heart rate greater than 100/min, bronchopulmonary dysplasia, pneumothorax (O)?

Introduction

Resuscitation of babies at birth often involves assisting ventilation with positive-pressure devices. Current guidelines for this technique have always involved recommending a specific pressure range to inflate the lungs. Recent research has indicated that excessive pressure can seriously injure the lungs, particularly in babies born preterm, and some have advocated that resuscitation guidelines should be based on volume rather than pressure. It has also been suggested that measuring exhaled CO_2 might indicate adequate ventilation. Devices for measuring both of these variables have been developed. This PICO question is meant to assess the advisability of recommending their use during resuscitation.

Consensus on science

Flow and volume monitoring. For the critical outcome of **survival to hospital discharge** and **IVH**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pilot randomized controlled trial enrolling 49 babies showing no benefit.[232]

For the critical outcome of time to heart rate greater than 100/min and neurologically intact survival, we found no evidence.

For the important outcome of **bronchopulmonary dysplasia** and **pneumothorax**, we found no evidence.

Capnography. For the critical outcome of **survival to hospital discharge and IVH**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pilot randomized clinical trial enrolling 48 babies showing no evidence.[233]

For the critical outcome of time to heart rate greater than 100/min and neurologically intact survival, we found no evidence.

For the important outcome of **bronchopulmonary dysplasia and pneumothorax**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 pilot randomized clinical trial enrolling 48 babies showing no evidence.[233]

Treatment recommendations

Although a feasible technique, we **suggest against** the routine use of flow and volume monitoring for babies who receive PPV at birth, until more evidence becomes available (weak recommendation, low-quality evidence).

Although a feasible technique, we **suggest against** the routine use of capnography for babies who receive PPV at birth, until more evidence becomes available (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

We should consider revising future PICO questions to embrace new technologies for more reasonable outcomes and benchmarks rather than death and disability. It was stressed that it is important to point out the human factors piece of the equation. The devices are only as useful as how well the human care provider can interface with and incorporate them appropriately into care. Another point raised is that we have process outcomes, but do they impact actual performance? Do we need this to be a more stepwise approach? What other process outcomes should be included? In the future, we need to look at device design, types of alarms (visual or audio, color, font, etc.). If this were a medication, we would suggest against something with such resource implications.

Knowledge gaps

- There is a need for large studies powered for important clinical outcomes to determine the role of flow and volume monitoring and capnography in improving response to and outcomes of newborn resuscitation.
- There is a need for further research to determine whether routine use of flow and volume monitoring for task training in newborn resuscitation improves training or clinical outcomes.
- There is a need for specific research to determine whether continuous monitoring of flow and volume or exhaled CO_2 levels compete with other essential auditory and visual cues that need to be appreciated and responded to by resuscitation teams.

Use of feedback CPR devices for neonatal cardiac arrest—diagnostic (NRP 862)

In asystolic/bradycardic neonates receiving cardiac compressions (P), does the use of feedback devices such as end-tidal carbon dioxide ($ETCO_2$)monitors, pulse oximeters, or automated compression feedback devices (I), compared with clinical assessments of compression efficacy (C), decrease hands-off time, decrease time to ROSC, improve perfusion, increase survival rates, or improve neurologic outcomes (O)?

Introduction

The current measure for determining successful progress in neonatal resuscitation is to assess the heart rate response. Other devices such as CO_2 monitoring and pulse oximetry have been suggested as more sensitive measures. This PICO question is designed to determine the current evidence regarding this issue.

Consensus on science

For the critical outcomes of improved perfusion, decreased time to ROSC, decreased hands-off time, increased survival rates, or improved neurologic outcomes, we found no specific data.

Increased exhaled CO_2: Five small observational studies (2 piglet posttransitioned models),[234,235] 2 dog posttransitioned models[236,237] (these latter 2 articles were the identical sample of dogs and data but published in separate journals), and 1 human study[238] of very low quality (downgraded for indirectness and risk of bias) assessed the $ETCO_2$ levels associated with the onset or presence/absence of ROSC.

- One piglet study[234] and the dog studies[236,237] associated the presence of decreased time to ROSC with an $ETCO_2$ of 27–28 mm Hg. CPR in these studies was started after 5–10 min of cardiac arrest.
- One piglet study[235] associated the presence of a heart rate greater than 60/min with an $ETCO_2$ of 14 mm Hg (sensitivity, 93%; specificity, 81%). CPR was started at onset of asystole.
- One human study covered a wide age range of children, 1 week to 10 years.[238] The majority were out-of-hospital arrests. $ETCO_2$

levels in all patients who did not attain ROSC never rose above 15 mm Hg.

Treatment recommendation

In asystolic/bradycardic neonates, we **suggest against** the routine reliance on any single feedback device such as $ETCO_2$ monitors or pulse oximeters for detection of ROSC until more evidence becomes available (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

Several questions were raised: Should detection of ROSC be the only real outcome for the question because identifying this is the first step to recovery? Thus, it is a critical tool for determining if your actions are effective or if you need to consider other interventions. Was there a need to rate the effectiveness of the equipment as the critical outcome, or is the effect on the patient what is important? Does the device measure what it is supposed to measure? What about human factors issues? Can providers effectively use the equipment? Does it impact outcome?

Knowledge gaps

- There is a need for large studies powered for important clinical outcomes to determine the role of flow and volume monitoring and capnography in improving response to and outcomes of newborn resuscitation.
- There is a need for further research to determine whether routine use of flow and volume monitoring for task training in newborn resuscitation improves training or clinical outcomes.
- There is a need for specific research to determine whether continuous monitoring of flow and volume or exhaled CO_2 levels compete with other essential auditory and visual cues that need to be appreciated and responded to by resuscitation teams.

Postresuscitation management

ILCOR previously reviewed postresuscitation strategies that focused on glucose control and the implementation of therapeutic hypothermia to minimize or avoid reperfusion injury from intrapartum hypoxia–ischemia in well-resourced settings. For this cycle, we only reviewed the potential role of therapeutic hypothermia to minimize or avoid reperfusion injury from intrapartum hypoxia–ischemia where resources are limited.

Limited-resource-induced hypothermia—intervention (NRP 734)

In term infants with moderate/severe hypoxic–ischemic encephalopathy managed in resource-limited countries (P), does therapeutic hypothermia to core temperature of approximately 33.5 °C for 72 h delivered by passive hypothermia and/or ice packs (I), versus standard therapy (C), improve the rates of death, neurodevelopmental impairments at 18 months to 2 years (O)?

Introduction

Therapeutic hypothermia has been shown to reduce mortality and morbidity in term and near-term newborns who have had a hypoxic–ischemic insult and are at risk for evolving encephalopathy. This therapy has generally been restricted to developed countries where resources and regional systems permit the therapy to be administered under a strict protocol. This PICO question is intended to determine if therapeutic hypothermia can practically and effectively be practiced in countries with limited resources.

Consensus on science

For the critical outcome of **death or disability**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 2 randomized controlled trials[239,240] enrolling 338 infants showing benefit to the use of therapeutic hypothermia (OR, 0.43; 95% CI, 0.26–0.7).

For the critical outcome of **death to latest follow-up**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 4 randomized controlled trials[239–242] enrolling 416 infants showing no benefit to the use of therapeutic hypothermia (OR, 0.72; 95% CI, 0.44–1.16).

Treatment recommendations

We suggest that newly born infants at term or near-term with evolving moderate-to-severe hypoxic–ischemic encephalopathy in low-income countries and/or other settings with limited resources may be treated with therapeutic hypothermia (weak recommendation, low-quality evidence).

Cooling should only be considered, initiated, and conducted under clearly defined protocols with treatment in neonatal care facilities with the capabilities for multidisciplinary care and availability of adequate resources to offer intravenous therapy, respiratory support, pulse oximetry, antibiotics, anticonvulsants, and pathology testing. Treatment should be consistent with the protocols used in the randomized clinical trials in developed countries, i.e. cooling to commence within 6 h, strict temperature control at 33–34 °C for 72 h and rewarming over at least 4 h.

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the demonstrated effectiveness of simple cooling methods and the lack of harm associated with these methods over the paucity of evidence specific to resource-limited settings.

It is difficult to define a low-resource setting. Even within a country (e.g., India) resources may vary widely. Simple methods of cooling are successful in lowering body temperature. There was a concern that passive cooling may not be so harmless (e.g., extreme hypothermia, inappropriate hypothermia). Low-resource areas do not have nursing care to monitor the babies closely.

Knowledge gaps

- Further adequately powered randomized controlled trials of simple methods of cooling in resource-limited settings are required to improve the quality of evidence relating to this question.
- Specific regional guidelines should take account of public health system priorities for allocation of available resources and the availability of sufficient nursing and ancillary resources to safely and effectively deliver cooling therapy in the facility.

Discontinuing resuscitation

Deciding how long resuscitative efforts should continue in a newly born infant with no heart rate and/or absent respirations with a very low heart rate after sustained resuscitative efforts remains a critically important and difficult management decision. In recent years, long-term outcomes have shown some improvement.

Delivery room assessment for less than 25 weeks and prognostic score (NRP 805)

In extremely preterm infants (less than 25 weeks) (P), does delivery room assessment with a prognostic score (I), compared with gestational age assessment alone (C), change survival to 18–22 months (O)?

Introduction

Antenatal assignment of prognosis for survival and/or disability of the neonate born extremely preterm has generally been made on the basis of gestational age alone. Recently, scoring systems for including additional variables such as gender, use of maternal antenatal steroids, and multiplicity have been developed in an effort to improve prognostic accuracy. This PICO question was developed to examine the utility of these systems.

Consensus on science

There is no evidence that addresses the clinical prospective use of prognostic scoring (the use of composite survival data using gestational age and other parameters) in infants of less than 25 weeks of estimated gestational age.

There is increasing retrospective evidence that prognostic accuracy is improved by using additional information such as birth weight, appropriateness of weight for gestational age, use of maternal antenatal steroids, multiplicity, and gender[243–247] (low-quality evidence), but there are no prospective studies showing the postnatal effect of such improved accuracy in predicting outcome.

Treatment recommendation

There is insufficient evidence to support the prospective use of any delivery room prognostic score presently described over estimated gestational age assessment alone in preterm infants of less than 25 weeks of gestation. No score has been shown to improve the ability to estimate the likelihood of survival through either 30 days or in the first 18–22 months after birth.

In individual cases, when constructing a prognosis for survival at gestations below 25 weeks, it is reasonable to consider variables including perceived accuracy of gestational age assignment, the presence or absence of chorioamnionitis, and the level of care available for location of delivery. It is also recognized that decisions about appropriateness of resuscitation below 25 weeks of gestation will be influenced by region-specific guidelines established by regional resuscitation councils.

Values, preferences, and task force insights

In making this statement, we put a higher value on the lack of evidence for a generalizable prospective approach changing important outcomes over improved retrospective accuracy and locally validated counseling policies. For antenatal counseling, the most useful data would give outcome figures for babies alive at the onset of labor, not just those born alive or admitted to the neonatal intensive care unit. In reality, many are already using such extended data in antenatal counseling to try to provide parents and healthcare professionals with the most accurate estimates for mortality (and morbidity).

It would obviously be preferable if there were studies to show that using such data can prospectively improve the outcome for these babies: Does using the most accurate information have a positive influence on the difficult decisions made about whether intensive care should be implemented?

There was agreement to amend the treatment recommendation to include consideration of possible inaccuracy of gestational age assessment, as well as to include evaluation for chorioamnionitis, and level of subsequent care that may be available. A question was raised with regard to the fact that we included weights in previous statements about prognosis; however, those were taken out to allow councils to make independent recommendations. Should antenatal steroids be mentioned in the treatment recommendation? The list may become exhaustive as more factors are added (e.g., gender).

Knowledge gaps

- Insufficient or absent data concerning timing of death, i.e. early versus later death
- Lack of information on factors other than gestational age known before birth
- Limited information on use of combined antenatal and postnatal information
- Inability to fully distinguish between outcomes driven by practice (e.g., belief that mortality is universal below a certain gestational age), surrogate decision making by parents, and physiologic limitations

Apgar score of 0 for 10 min or longer—prognosis (NRP 896)

In infants with a gestational age of 36 weeks or greater and an Apgar score of 0 for 10 min or longer, despite ongoing resuscitation (P), what is the rate of survival to NICU admission and death or neurocognitive impairment at 18–22 months (O)?

Introduction

There has been an ongoing controversy as to how long after one has been attempting resuscitation after birth, and a heart rate cannot be detected, should one continue or discontinue resuscitation efforts. The balance must be between ceasing too early, when ROSC and long-term survival may still be achievable, and continuing too long, when ROSC may occur, but early death or an unacceptable degree of neurologic injury may have occurred. The Apgar score of 0 has classically been the criterion, because it indicates no detectable signs of life. The recommended duration of resuscitative efforts after birth has variously been 15, and more recently 10 min, after birth.

The controversy has been generated from the following uncertainties: (1) It is often not clear whether resuscitation efforts have taken place throughout the 10-min period, (2) There may be questions about whether the score has indeed been 0 throughout the 10 min and not just at 10 min, and (3) Have resuscitation efforts been optimal throughout the 10 min? Recently, the 10-min guideline has been subjected to further controversy, with published reports from therapeutic hypothermia trials of an increasing number of intact survivors after 10 min of an Apgar score of 0.

Consensus on science

For the critical outcome of **death up to 22 months**, very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 6 studies encompassing 8 case series showed that 75 of 129 infants (58%) with an estimated gestational age of 36 weeks or greater and an Apgar score of 0 at 10 min of life died before 22 months of age.[248–253] Results from 3 of these studies performed after 2009 that included nested observational series of cases from 3 randomized clinical trials of therapeutic hypothermia and a series of infants who received therapeutic hypothermia outside a randomized trial (low-quality evidence, downgraded for risk of bias) found that 46 of 90 infants (51%) with an Apgar score of 0 at 10 min died before 22 months of age.[250,251,253]

For the critical outcome of **death or moderate/severe neurodevelopmental impairment** at 22 months of age or older, 6 studies (very-low-quality evidence, downgraded for risk of bias, inconsistency, indirectness, and imprecision) showed this outcome in 106 of 129 infants (85%) with a gestational age of 36 weeks or greater and an Apgar score of 0 at 10 min of life.[248–253] Results from 3 of these studies performed after 2009 (very-low-quality evidence, downgraded for risk of bias, inconsistency, indirectness, and imprecision) that included nested observational series in randomized clinical trials of therapeutic hypothermia and series of infants who received therapeutic hypothermia showed that this adverse

outcome occurred in 68 of 90 infants (76%) with an Apgar score of 0 at 10 min. Among the 44 survivors of these studies, 22 (50%) survived without major/moderate disabilities. Among the 56 cooled infants in these studies, 15 (27%) survived without major/moderate disabilities[250,251,253] (very-low-quality evidence, downgraded for risk of bias).

No studies differentiated between severe and moderate disability.

None of the studies described the resuscitation procedures that were provided.

Treatment recommendation

An Apgar score of 0 at 10 min is a strong predictor of mortality and morbidity in late-preterm and term infants. We suggest that, in babies with an Apgar score of 0 after 10 min of resuscitation, if the heart rate remains undetectable, it may be reasonable to stop resuscitation; however, the decision to continue or discontinue resuscitative efforts should be individualized. Variables to be considered may include whether the resuscitation was considered to be optimal, availability of advanced neonatal care, such as therapeutic hypothermia, specific circumstances before delivery (e.g., known timing of the insult), and wishes expressed by the family (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this statement in infants of 35 weeks or greater with an Apgar score of 0 for 10 min or longer, the likelihood of dying or having severe or moderate developmental disabilities at 18–24 months is very high. Studies that included 69 infants with an Apgar score of 0 at 10 min after birth who were successfully resuscitated and randomly assigned to hypothermia or normothermia, and case series of 21 additional infants who were managed with therapeutic hypothermia, suggest improvement in outcome compared with previously reported cohorts. Among these 90 infants, 45 (50%) died and 22 (24%) survived without major or moderate disability at 18–24 months. However, the number of infants with no heart rate at 10 min who died in the delivery room is unknown.

This topic resulted in a long and spirited debate. A question was raised as to how can we say that we should consider stopping with a 24% possibility of survival without major handicap? Is 10 min sufficient time to make this decision? It was suggested not to use the word *adequate*, because the resuscitation was not assessed. What would the adults do with 20% chance of survival? However, it was pointed out that it is not a 20% chance, because not all babies got to cooling. Someone advocated using the term *discontinue* instead of *withdraw*. The term *adequate* caused a lot of debate. What do we mean by it? Can it be clearer? Concern was expressed that providers will likely not use science to guide the decisions for this situation and will likely use their own judgment. Parents tend to choose continuation even when the data are presented to them. The decision to continue or discontinue should be based on consultation with the family. The optimal way to restore circulation can be in the qualifier. An Apgar score of 0 at 10 min is a strong predictor of disability at all gestations.

Knowledge gaps

The major flaw in the available scientific evidence regarding outcome of term neonates with asystole after 10 min of adequate resuscitation is the absence of data regarding

- Number of infants born in the study centers or the transferring centers with asystole at 10 min who were not actively resuscitated (in the hypothermia studies many were transfers)
- Number of infants born in the study or the transferring centers with asystole at 10 min in whom delivery room resuscitation was attempted and unsuccessful
- Data regarding the quality and extension of resuscitation of these infants
- Only a prospective international registry with all needed information of infants with asystole/heart rate less than 60/min after 10 min of adequate resuscitation may provide evidence of sufficient scientific merit to answer this prognostic question

Predicting death or disability of newborns of greater than 34 weeks based on Apgar and/or absence of breathing—prognosis (NRP 860)

In newborn infants of greater than 34 weeks of gestation, receiving PPV at birth in settings where resources are limited (P), does presence of heart rate with no spontaneous breathing or Apgar scores of 1–3 at greater than 5 min predict mortality or morbidity or cerebral palsy (O)?

Introduction

The Apgar score is intended to be a retrospective predictor of outcome, particularly at 5 min of age. It has been suggested that an Apgar score of 0 at 10 min of age is an indication to consider discontinuing resuscitation efforts (see NRP 896), but there have been no other levels of Apgar assessment by which one might make discontinuation decisions, such as Apgar score of 3 or less at 20 min. This PICO question is intended to review the recent evidence regarding these additional predictors.

Consensus on science

Apgar score at 20 min. For all the outcomes, we could not find studies that reported on individual Apgar scores (1, 2, or 3) beyond 10 min. One very-low-quality study (downgraded for indirectness) reported on Apgar scores at 20 min but included patients with an Apgar score of 0.[254] This study reported that in babies weighing greater than 2500 g with an Apgar score of 0–3 at 20 min, the mortality was 59%, and 57% of survivors developed cerebral palsy.

Apgar score at 10 min. For the critical outcome of **death**, we identified low-quality evidence (downgraded for imprecision) from 2 randomized studies involving babies who participated in induced-hypothermia studies.[251,255] One study[251] reported mortality of 64%, 47%, and 39% for Apgar score of 1, 2, and 3, respectively, with an OR of 1.42 (95% CI, 1.19–1.69) at 18–22 months. The other study[255] reported outcomes from the same study, but at 6–7 years. Babies with Apgar scores of 1, 2, and 3 had mortality rates of 67%, 43%, and 27%, respectively, if they were managed with induced hypothermia and 63%, 57%, and 62% if they were not cooled.

For the critical outcome of **moderate/severe disability**, we identified low-quality evidence (downgraded for imprecision) from 2 randomized studies involving babies who participated in induced hypothermia studies,[251,255] one[251] reporting the outcome in 50%, 63%, and 38% for Apgar scores of 1, 2, and 3, respectively, with an OR of 1.30 (95% CI, 1.06–1.58) at 18–22 months. The other study[255] reported at 6–7 years of life that 100%, 75%, and 9% of babies with Apgar score of 1, 2, and 3, respectively, had moderate/severe disability if managed with induced hypothermia and 67%, 67%, and 71% if not managed with hypothermia, although the sample size was small.

No spontaneous respiration. For the critical outcome of **death**, we identified very-low-quality evidence (downgraded for imprecision) from 2 observational studies[256,257] that time to spontaneous respiration of more than 30 min was associated with 52–77% mortality.

For the critical outcome of **cerebral palsy** or **abnormal neurologic findings**, we identified very-low-quality evidence (downgraded for imprecision)[256–258] that time to respiration of more than 30 min was associated with 35% cerebral palsy and 67–100% abnormal neurologic findings.

For the critical outcome of **death and/or moderate-to-severe disability**, we identified very-low-quality evidence (downgraded for imprecision) from 2 observational studies[259,260] that time to spontaneous respiration of 10–19 min and more than 20 min was associated with this outcome in 56% and 88% of patients, respectively,[259] and time to spontaneous breathing of 30 min or more was a predictor of this outcome (OR, 2.33; 95% CI, 1.27–4.27).

Treatment recommendation

Absence of spontaneous breathing or an Apgar score of 1–3 at 20 min of age in babies of greater than 34 weeks of gestation but with a detectable heart rate are strong predictors of mortality or significant morbidity. In settings where resources are limited, we suggest that it may be reasonable to stop assisted ventilation in babies with no spontaneous breathing despite presence of heart rate or Apgar score of 1–3 at 20 min or more (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this statement, in infants of greater than 34 weeks with an Apgar score of 0, 1, 2, or 3 for 20 min or more, the likelihood of dying or having severe or moderate developmental disabilities at 18–24 months is very high. Importantly, each of the studies reviewed was conducted in a resource setting where therapeutic hypothermia was likely to be available (see NRP 734).

Perhaps there is a publication bias when those babies who did not respond at 20 min are not included in the numbers. The question was raised, if the prognosis is the same, why would we recommend something different for resource-limited settings? A response was that in resource-limited regions, there will likely not be the regional systems and postresuscitation neonatal intensive care facilities and subspecialty personnel that were available in the recent studies reviewed in the Consensus on Science. If such facilities are available, this treatment recommendation may be less applicable.

Knowledge gaps

- No studies identified from low-resource settings
- Outcome of babies with delayed onset of breathing who are managed with induced hypothermia in low-resource settings.
- Outcome of babies with gasping or irregular breathing and a heart activity at 20 min of life.

Educational techniques for teaching, assessing, and maintaining resuscitation knowledge and skills

Resuscitation training frequency (NRP 859)

For course participants including (a) trainees and (b) practitioners (P), does frequent training (I), compared with less frequent training (annual or biennial) (C), change all levels of education or practice, prevention of adverse outcomes, overall mortality, scenario performance, medical knowledge, psychomotor performance, provider confidence, course satisfaction (O)?

Introduction

Training in the cognitive, technical, and behavioral skills necessary for successful neonatal resuscitation has historically been conducted at varying intervals of time, and there is little evidence to support the use of one interval over another. As an example, the national steering committee of the US Neonatal Resuscitation Program has recommended that trainees complete the program once every 2 years, but in the United Kingdom, 4 years is the recommended interval; there is no objective evidence to validate these intervals. It is intuitive that individual trainees will require different training intervals to facilitate optimal acquisition and maintenance of different skills. This PICO question is intended to update the evidence as to what may be the most effective strategy.

Consensus on science

Sixteen studies were identified that have investigated this PICO question. Ten randomized controlled studies[261–270] and 6 nonrandomized controlled trials[271–276] were identified for inclusion.

The evidence for frequency of resuscitation training is very low quality (downgraded for high risk of bias, inconsistency, and imprecision), with the exception of studies of psychomotor performance, which are of moderate quality (downgraded for risk of bias). Meta-analyses were greatly limited by the heterogeneity between studies of training frequency, educational interventions, and outcomes.

For the critical outcome of **patient outcomes**, 2 studies[271,275] of very low quality (downgraded for high risk of bias, inconsistency, and imprecision) looked at endotracheal intubation success. Both studies included psychomotor skill training on an airway simulator, and Nishisaki[275] included simulation-based training. There was no significant difference in first-time intubation success (RR, 0.879; 95% CI, 0.58–1.33) or any intubation success (RR, 0.87; 95% CI, 0.65–1.17) between the providers who were exposed to frequent training and controls.

For the important outcome of **prevention of adverse events**, the Nishisaki study also included the important outcome of prevention of adverse outcomes and airway injury as a secondary outcome. No significant difference was seen between groups (RR, 1.097; 95% CI, 0.747–1.612).[275]

For the important outcome of **performance in simulation**, 3 studies[264,267,273] of very low quality (downgraded for high risk of bias, inconsistency, and imprecision) investigated the important outcome of performance in simulated scenarios using both validated and nonvalidated evaluations. In all studies, subjects in the intervention groups trained more frequently than controls. The range of time between initial course completion and first additional training session was 1–4 months. The educational interventions were heterogeneous, including independent and facilitated practice on airway simulators,[264] didactic lectures, skill station practice, mock codes,[273] and periodic review of course material and case-based study.[267] Kovacs[264] and Stross[267] found no significant difference between frequent and infrequent practice with respect to simulation-based performance. Only 1 of these studies (Nadel[273]) offered quantitative data: After averaging of multiple outcomes, there was a trend to improved performance in those exposed to increased frequency of training compared with controls (RR, 1.51; 95% CI, 0.971–2.35).

For the important outcome of **psychomotor performance**, there were 8 studies[261,262,266,267,269,273,274,276] of moderate quality (downgraded for risk of bias) that evaluated the important outcome of impact of frequent training on psychomotor performance, demonstrated on a task trainer or simulator. With the exception of O'Donnell[276] and Stross[267] (which were neutral to the question), studies demonstrated improvements in psychomotor performance with no negative effect. The range of time between course completion and first additional training session was 1 week to 6 months. The educational interventions were again heterogeneous. Psychomotor task trainers were used to achieve competency in a specific technical skill, including practice on a chest compression task trainer (Niles[274]), neonatal airway management task trainer (Ernst[262]), or a CPR task trainer where both chest compressions and ventilation were emphasized.[261,266,276] The study

by Stross[267] included periodic review of course material and case-based study.[267] The educational intervention in the Nadel[273] study used didactic lectures, skill station practice, and mock codes. Although 8 studies were identified, only 1 randomized[273] and 2 observational studies[267,276] with dichotomous quantitative data were included in the analysis. The 1 randomized study[273] demonstrated a significant improvement in psychomotor skills in subjects in the intervention group when compared with controls. One randomized study[266] with multiple outcomes showed significantly improved performance of the important outcomes of manual ventilation volume and chest compression depth after practice every 3 months. However, an improvement in psychomotor skills in the intervention groups was not seen when 3 studies[267,273,276] were included in a meta-analysis after averaging of scores (RR, 1.38; 95% CI, 0.87–2.2).

For the important outcome of **knowledge**, 5 studies[263,268,270,273,276] of very low quality (downgraded for high risk of bias, inconsistency, and imprecision) investigated the relationship between frequent training and the important outcome of acquisition of medical knowledge assessed by written tests or oral exams. Studies by Nadel,[273] O'Donnell,[260] and Turner[254] demonstrated sustained knowledge with refreshers when compared with controls, whereas Kaczorowski[263] and Su[252] were neutral to the question. The educational interventions for these studies have been described previously except for 2 studies: Su used a knowledge exam and mock resuscitation at 6 months, and the Kaczorowski[263] study included subjects in the intervention groups either watching a newborn resuscitation education video or hands-on practice. The range of time between course completion and first additional training session was 1–6 months. Although 5 studies were identified, only 2 had quantitative data.[270,273] The analysis of the 2 observational studies was not possible because it was difficult to average the means ± SDs and then pool the 2 studies for a meta-analysis. The Nadel[273] study found a significant improvement in knowledge with more frequent training in a short answer test (mean scores 73 ± 11 versus 60 ± 10; $P = 0.0003$). The Turner[254] study showed significant improvement in 2 out of 3 test scores in the intervention group (mean scores 7.1 versus 6.2 and 29.0 versus 25.8, respectively; $P < 0.05$ in both cases). O'Donnell[260] demonstrated lower test scores in the control group than in the intervention group ($P < 0.04$).

For the nonimportant outcome of **provider confidence**, Montgomery[265] found that subjects who practiced CPR for 6 min every month were more likely than controls to report that they felt confident (RR, 1.60; 95% CI, 1.27–2.01), and Nadel[273] found improved confidence in both leadership and technical skills.

No study demonstrated a negative or detrimental effect from more frequent training. Publication bias was difficult to assess.

Treatment recommendation

We suggest that training should be recurrent and considered more frequently than once per year. This retraining may be composed of specific tasks and/or behavioral skills, depending on the needs of the trainees (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In drawing our conclusions, we place value on improved psychomotor skills, knowledge, and provider confidence during more-frequent training versus less-frequent training (and versus the established and unproven practice of training every 1–2 years).

The debate included the fact that the PICO question does not specify that it is resuscitation training, although the search did restrict itself to this. Should the costs of training be addressed? However, it was noted that it was hard to comment on cost based on studies, because the interventions themselves were so different. Could the follow-up programs be briefer and more focused on needs? What is best for the patient? What is the cost to the child and family when the patient does not receive adequate resuscitation? What is a technical proficiency program? How do we achieve it? There is no assessment of translation of increased training to improved outcomes. We need data to show that improved education is worth the staff time. The PICO question specifically avoided looking at studies about decay of knowledge and skills.

Knowledge gaps

- Although some outcomes are of critical importance, the quality of evidence is very low. Serious methodological flaws occur, such as lack of randomization, multiple primary outcomes with inadequate sample size and power analysis, lack of blinding, controls that consist of no educational intervention resulting in a comparison of training to no training, insufficiently validated evaluation tools, and significant heterogeneity of outcomes and interventions.
- There is a need for well-designed and well-powered clinical trials, possibly cluster randomized, that answer key questions with critical outcomes: How frequently should learning occur? What type of intervention is most effective? What validated tools are available to measure educational outcomes?
- How do high-opportunity versus low-opportunity environments differ in their need for frequent training?
  - Did we take experience into account?
  - What about knowledge, skills, and behaviors?
  - Are patient outcomes lacking?
  - Is cost impact lacking?
  - Is high-frequency, low-dose training effective?
  - Decay and boosting rates?
  - Should we add "within the constraints of local resources"?
  - Reinforcement from other domains, for example

Neonatal resuscitation instructors (NRP 867)

In neonatal resuscitation instructors (P), does formal training on specific aspects of how to facilitate learning (I), compared with generic or nonspecific training (C), change clinical outcome, improve all levels of education or practice (O)?

Introduction

Around the world, millions of healthcare professionals bear the responsibility for resuscitating neonates in the delivery room, and they must not only acquire the necessary cognitive, technical, and behavioral skills but also maintain them over time, often for decades. The precise roles and mandatory skills of the instructors charged with training healthcare professionals have yet to be defined, and thus how to best prepare instructors to fulfill these roles and acquire these skills is not yet objectively described. It is intuitive that training of instructors should be based on specific learning objectives targeting the specific instructor skills that are necessary to facilitate the acquisition of specific skills in specific populations of learners. Comprehensive assessment of resuscitation instructor training requires identification and development of (1) objective markers of performance for instructors, (2) appropriate objective markers of performance for the trainees who are trained by the instructors, and (3) objective markers of patient outcome that are directly related to how well they were resuscitated. This PICO question is intended to identify literature that is pertinent to these and other issues involving the preparation of instructor of neonatal resuscitation.

Consensus on science

For the critical outcome of **improvement in patient outcome**, we identified no evidence.

For the critical outcome of **improvement in learner performance** in the real clinical environment, we identified very-low-quality evidence from 1 randomized clinical trial[277] (downgraded for indirectness, risk of bias, and imprecision) that providing structured self-reflection and peer group feedback to psychiatry registrars improved their students' performance of standardized psychiatric interviews.

For the critical outcome of **improvement in learner performance in educational settings**, we identified very-low-quality evidence (downgraded for indirectness, imprecision, and risk of bias) from 1 randomized clinical trial[278] in which 18 emergency medicine instructors were randomly assigned to 2 intervention groups and trained 193 medical students. The study found that learners trained by instructors who underwent a 2-day teacher training course focused on education principles performed at an equal or lower level of proficiency in technical skills when compared with those trained by instructors who did not attend the 2-day course.

For the critical outcome of **improvement in all levels of education or practice**, we identified low-quality evidence (downgraded for indirectness and bias) from 5 randomized clinical trial[278–282] enrolling 271 participants (not estimable). Several studies did note at least temporary deterioration in instructor performance after commencement of new instructor training intervention.

For the critical outcome of **improvement in clinical outcome**, we identified no evidence.

For the important outcome of **improvement in instructor performance**, we identified very-low-quality evidence (downgraded for indirectness and bias) from 5 randomized clinical trials[278–282] and 2 nonrandomized trials.[283,284] No meaningful numerical summary of the results of these studies could be performed. These studies indicate that preparation of instructors produces inconsistent results in terms of instructor performance. While it does seem that written and verbal feedback, delivered in a constructive and timely manner, often produces improvement in instructor performance, in other instances posttraining deterioration in aspects of instructor performance was seen, at least initially.

Treatment recommendation

We suggest that training of resuscitation instructors incorporate timely, objective, structured, individually targeted verbal and/or written feedback (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

While common sense dictates that instructors be properly prepared before engaging learners, it is clear that such instruction must be based on specific learning objectives targeting the specific skills that are necessary to facilitate learning. Definitions of these skills will require collaboration with colleagues in fields such as human factors and ergonomics who have experience in examining human performance in high-risk domains (similar to the delivery room) rather than relying solely on those with expertise in traditional education settings such as the classroom.

Deliberations of the task force and writing group

The PICO question may be too global/broad. Perhaps we need to be more specific in the future. We may need to move away from dependence on traditional methodologies and look to those industries where adults are trained to be proficient in specific tasks. Instructors need to know how to do specific tasks and give feedback to improve performance. Perhaps we have made instructors poor trainers. People who develop curricula need to address this critical deficit. How do we teach task proficiency? That is what is most needed.

Knowledge gaps

- How is optimal instructor performance defined?
- What are the skills necessary to achieve this?
- What are the optimal methods for selection of candidate instructors, initial skill acquisition by instructors, ongoing maintenance of instructor skill, and (objective and subjective) assessment of instructor skill?

2010 PICO questions not reviewed in 2015

- Suctioning (other than meconium)
- Inflation pressures
- Face mask characteristics
- CO_2 detectors to confirm endotracheal tube placement
- Epinephrine dose and route
- Volume expansion
- Sodium bicarbonate
- Glucose
- Therapeutic hypothermia
- Personnel needs at elective cesarean delivery
- Briefing and debriefings during learning activities

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Disclosures. 2015 CoSTR Part 7: neonatal resuscitation: writing group

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/honoraria	Expert witness	Ownership interest	Consultant/advisory board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

[a] Modest.

[b] Significant.

Appendix A. CoSTR Part 7: PICO Appendix

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 7	NRP	NRP 589	Temperature maintenance in the delivery room—prognosis	In nonasphyxiated babies at birth (P), does maintenance of normothermia (core temperature 36.5 °C or greater and 37.5 °C or less) from delivery to admission (I), compared with hypothermia (less than 36 °C) or hyperthermia (greater than 37.5 °C) (C), change survival to hospital discharge, respiratory distress, survival to admission, hypoglycemia, intracranial hemorrhage, or infection rate (O)?	Jonathan Wyllie, Jeffrey Perlman
Part 7	NRP	NRP 590	CPAP and IPPV—intervention	In spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room (P), does the use of CPAP (I), compared with intubation and IPPV (C), improve outcome (O)?	Tetsuya Isayama, Ben Stenson
Part 7	NRP	NRP 599	Maintaining infant temperature during delivery room resuscitation—intervention	Among preterm neonates who are under radiant warmers in the hospital delivery room (P), does increased room temperature, thermal mattress, or another intervention (I), compared with plastic wraps alone (C), reduce hypothermia (less than 36 °C) on admission to neonatal intensive care unit (NICU) (O)?	Daniele Trevisanuto, Maria Fernanda de Almeida
Part 7	NRP	NRP 605	Thumb versus 2-finger techniques for chest compression—intervention	In neonates receiving cardiac compressions (P), does the use of a 2-thumb technique (I), compared with a 2-finger technique (C), result in return of spontaneous circulation (ROSC), improved neurologic outcomes, improved survival, improved perfusion and gas exchange during CPR, and decreased compressor fatigue (O)?	Myra Wyckoff, Lindsay Mildenhall
Part 7	NRP	NRP 618	Laryngeal mask airway—intervention	In newborn infants at near term (greater than 34 weeks) or term who have indications for intermittent positive pressure for resuscitation (P), does use of a laryngeal mask as a primary or secondary device (I), compared with mask ventilation or endotracheal intubation (C), improve response to resuscitation or change outcome (O), including indicators of neonatal brain injury, achieving stable vital signs, increasing Apgar scores, long-term outcomes, reducing the need for subsequent intubation, or neonatal morbidity and mortality?	Edgardo Szyld, Enrique Udaeta

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 7	NRP	NRP 734	Limited-resource–induced hypothermia—intervention	In term infants with moderate/severe hypoxic–ischemic encephalopathy managed in resource-limited countries (P), does therapeutic hypothermia to core temperature of approximately 33.5 °C for 72 h delivered by passive hypothermia and/or ice packs (I), versus standard therapy (C), improve the rates of death, neurodevelopmental impairments at 18 months to 2 years (O)?	Peter Davis, Jeffrey Perlman
Part 7	NRP	NRP 738	Oxygen delivery during CPR (neonatal)—intervention	In neonates receiving cardiac compressions (P), does 100% O_2 as the ventilation gas (I), compared with lower concentrations of oxygen (C), increase survival rates, improve neurologic outcomes, decrease time to ROSC, or decrease oxidative injury (O)?	Myra Wyckoff, Lindsay Mildenhall
Part 7	NRP	NRP 787	Delayed cord clamping in preterm infants requiring resuscitation (intervention)	In preterm infants, including those who received resuscitation (P), does delayed cord clamping (greater than 30 seconds) (I), compared with immediate cord clamping (C), improve survival, long-term developmental outcome, cardiovascular stability, occurrence of intraventricular hemorrhage (IVH), necrotizing enterocolitis, temperature on admission to a newborn area, and hyperbilirubinemia (O)?	Masanori Tamura, Susan Niermeyer
Part 7	NRP	NRP 793	Maintaining infant temperature during delivery room resuscitation—intervention	In newborn infants (greater than 30 weeks of gestation) in low-resource settings during and/or after resuscitation/stabilization (P), does drying and skin-to-skin contact or covering with plastic (I), compared with drying and no skin-to-skin or use of radiant warmer or incubator (C), change body temperature (O)?	Sithembiso Velaphi, Hege Ersdal, Nalini Singhal
Part 7	NRP	NRP 804	Babies born to mothers who are hypothermic or hyperthermic in labor—prognosis	In newborn babies (P), does maternal hypothermia or hyperthermia in labor (I), versus normal maternal temperature (C), result in adverse neonatal effects (O)? Outcomes include mortality, neonatal seizures, and adverse neurologic states	Henry Lee, Marilyn Escobedo
Part 7	NRP	NRP 805	Delivery room assessment for less than 25 weeks and prognostic score	In extremely preterm infants (less than 25 weeks) (P), does delivery room assessment with a prognostic score (I), compared with gestational age assessment alone (C), change survival to 18 to 22 months (O)?	Steven Ringer, Steve Byrne
Part 7	NRP	NRP 806	Newborn infants who receive PPV for resuscitation, and use of a device to assess respiratory function—diagnostic	In newborn infants who receive PPV for resuscitation (P), does use of a device to assess respiratory function with or without pressure monitoring (I), compared with no device (C), change survival to hospital discharge with good neurologic outcome, IVH, time to heart rate greater than 100/min, bronchopulmonary dysplasia, pneumothorax (O)?	Helen Liley, Vishal Kapadia
Part 7	NRP	NRP 809	Sustained inflations—intervention	In term and preterm newborn infants who do not establish spontaneous respiration at birth (P), does administration of 1 or more pressure-limited sustained lung inflations (I), compared with intermittent PPV with short inspiratory times (C), change Apgar score at 5 min, establishment of FRC, requirement for mechanical ventilation in first 72 h, time to heart rate greater than 100/min, rate of tracheal intubation, overall mortality (O)?	Jane McGowan, David Boyle
Part 7	NRP	NRP 849	Umbilical cord milking—intervention	In very preterm infants (28 weeks or less) (P), does umbilical cord milking (I), in comparison with immediate umbilical cord clamping (C), affect death, neurodevelopmental outcome at 2–3 years, cardiovascular stability, i.e. need for pressors, need for fluid bolus, initial mean blood pressure, IVH (any grade, severe grade), temperature on admission, hematologic indices (initial hemoglobin, need for transfusion), hyperbilirubinemia, need for phototherapy, or need for exchange transfusion (O)?	Marya Strand, Takahiro Sugiura
Part 7	NRP	NRP 858	Warming of hypothermic newborns—intervention	In newborns who are hypothermic (temperature less than 36.0 °C) on admission (P), does rapid rewarming (I), compared with slow rewarming (C), change mortality rate, short and long-term neurologic outcome, hemorrhage, episodes of apnea and hypoglycemia, or need for respiratory support (O)?	Cheo Yeo, Daniele Trevisanuto
Part 7	NRP	NRP 859	Resuscitation training frequency	For course participants including (a) trainees and (b) practitioners (P), does frequent training (I), compared with less frequent training (annual or biennial) (C), change all levels of education or practice, prevention of adverse outcomes, overall mortality, scenario performance, medical knowledge, psychomotor performance, provider confidence, course satisfaction (O)?	Chris Colby, Khalid Aziz
Part 7	NRP	NRP 860	Predicting death or disability of newborns of greater than 34 weeks based on Apgar and/or absence of breathing—prognosis	In newborn infants of greater than 34 weeks of gestation, receiving PPV at birth in settings where resources are limited (P), does presence of heart rate with no spontaneous breathing or Apgar scores of 1–3 at greater than 5 min predict mortality or morbidity or cerebral palsy (O)?	Sithembiso Velaphi, Nalini Singhal, Hege Ersdal
Part 7	NRP	NRP 862	Use of feedback CPR devices for neonatal cardiac arrest—diagnostic	In asystolic/bradycardic neonates receiving cardiac compressions (P), does the use of feedback devices such as end-tidal carbon dioxide ($ETCO_2$) monitors, pulse oximeters, or automated compression feedback devices (I), compared with clinical assessments of compression efficacy (C), decrease hands-off time, decrease time to ROSC, improve perfusion, increase survival rates, or improve neurologic outcomes (O)?	Lindsay Mildenhall, Takahiro Sugiura

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 7	NRP	NRP 864	Oxygen concentration for resuscitating premature newborns—intervention	Among preterm newborns (less than 37 weeks of gestation) who receive PPV in the delivery room (P), does the use of high O_2 (50–100%) as the ventilation gas (I), compared with low concentrations of O_2 (21–30%) (C), decrease mortality, decrease bronchopulmonary dysplasia, decrease retinopathy, decrease IVH (O)?	Gary Weiner, Douglas McMillan
Part 7	NRP	NRP 865	Intubation and tracheal suctioning in nonvigorous infants born through MSAF versus no intubation for tracheal suctioning—intervention	In nonvigorous infants at birth born through MSAF (P), does tracheal intubation for suctioning (I), compared with no tracheal intubation (C), reduce meconium syndrome or prevent death (O)?	Sithembiso Velaphi, Jeffrey Perlman
Part 7	NRP	NRP 867	Neonatal resuscitation instructors	In neonatal resuscitation instructors (P), does formal training on specific aspects of how to facilitate learning (I), compared with generic or nonspecific training (C), change clinical outcome, improve all levels of education or practice (O)?	Helen Liley, Louis Halamek
Part 7	NRP	NRP 870	T-piece resuscitator and self-inflating bag—intervention	In newborns (preterm and term) receiving ventilation (PPV) during resuscitation (P), does using a T-piece resuscitator with PEEP (I), compared with using a self-inflating bag without PEEP (C), achieve spontaneous breathing sooner and/or reduce the incidence of pneumothorax, bronchopulmonary dysplasia, and mortality (O)?	Yacov Rabi, Han Suk Kim
Part 7	NRP	NRP 895	Chest compression ratio—intervention	In neonates receiving cardiac compressions (P), do other ratios (5:1, 9:3, 15:2, synchronous, etc) (I), compared with 3:1 compressions to ventilations (C), increase survival rates, improve neurologic outcomes, improve perfusion and gas exchange during CPR, decrease time to ROSC, decrease tissue injury, or decrease compressor fatigue (O)?	Qi Feng, Myra Wyckoff
Part 7	NRP	NRP 896	Apgar score of 0 for 10 min or longer—prognosis	In infants with a gestational age of 36 weeks or greater and an Apgar score of 0 for 10 min or longer, despite ongoing resuscitation (P), what is the rate of survival to NICU admission and death or neurocognitive impairment at 18–22 months (O)?	Ruth Guinsburg, Jane McGowan
Part 7	NRP	NRP 897	Outcomes for PEEP versus no PEEP in the delivery room—intervention	In preterm/term newborn infants who do not establish respiration at birth (P), does the use of PEEP as part of the initial ventilation strategy (I), compared with no PEEP (C), improve Apgar score at 5 min, intubation in the delivery room, chest compressions in the delivery room, heart rate greater than 100/min by 2 min of life, time for heart rate to rise above 100/min, air leaks, oxygen saturation/oxygenation, FIO_2 in the delivery room, mechanical ventilation in the first 72 h, bronchopulmonary dysplasia, survival to discharge (O)?	Yacov Rabi, Colm O'Donnell
Part 7	NRP	NRP 898	ECG/EKG (I) in comparison to oximetry or auscultation for the detection of heart rate	In babies requiring resuscitation (P), does electrocardiography (ECG/EKG) (I), compared with oximetry or auscultation (C), measure heart rate faster and more accurately (O)?	Marya Strand, Hege Ersdal

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Part 8: Education, implementation, and teams 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations☆

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Introduction

Current evidence demonstrates considerable variability in cardiac arrest survival in and out of hospital and, therefore, substantial opportunity to save many more lives.[1–3] The Formula for Survival[4] postulates that optimal survival from cardiac arrest requires high-quality science, education of lay providers and healthcare professionals, and a well-functioning Chain of Survival[5] (implementation).

The Education, Implementation, and Teams (EIT) Task Force of the International Liaison Committee on Resuscitation (ILCOR) set out to define the key PICO (population, intervention, comparator, outcome) questions related to resuscitation education (including teamwork skills) and systems-level implementation that would be reviewed by 2015. The selection of questions was supported through the use of an online anonymous task force member–only voting process where the results were considered in the ultimate consensus decisions of the task force. Topics from the 2010 evidence review process were scrutinized for relevance, the potential to improve outcomes, and the likelihood of new evidence being published since 2010. Finally, PICO questions for which the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) process was not as well developed at the time of PICO selection were deferred until at least after the 2015 cycle. We planned to reduce the total number of PICO questions reviewed to provide more in-depth and evidence-based reviews of the included questions. New topics were determined on the basis of the evolving literature and changes in resuscitation practice. Input on the selection of PICO questions was sought from the general public through the ILCOR website and from ILCOR member resuscitation councils through their council chairs and individual task force members.

The GRADE process

The EIT Task Force performed detailed systematic reviews based on the recommendations of the Institute of Medicine of the National Academies[6] and using the methodological approach proposed by the GRADE Working Group.[7] After identification and prioritization of the questions to be addressed (using the PICO format),[8] with the assistance of information specialists, a detailed search for relevant articles was performed in each of 3 online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk of bias assessment for each of the

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included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[9] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[10] and GRADE for observational studies that inform both therapy and prognosis questions.[11]

GRADE Evidence Profile tables[12] were then created to facilitate an evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[13] based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias).[14]

These evidence profile tables were then used to create a written summary of evidence for each outcome (the Consensus on Science statements). Whenever possible, consensus-based treatment recommendations were then created. These recommendations (designated as strong or weak) were accompanied by an overall assessment of the evidence and a statement from the task force about the values and preferences that underlie the recommendations.

Further details of the methodology that underpinned the evidence evaluation process are found in "Part 2: Evidence Evaluation and Management of Conflicts of Interest."

To our knowledge, this is the first time that GRADE has been applied on a large scale to education literature in health. Detailed review of the evidence, the Consensus on Science statements, and treatment recommendations occurred within the task force, and most final recommendations reflect the consensus of the task force. In some instances, the task force could not reach consensus and a vote was required; greater than 50% agreement was adequate for standard decisions on wording, and 70% agreement was required for treatment recommendations that were discordant with the quality of evidence.

The EIT Task Force spent considerable time deliberating on the scoring of the importance of outcomes according to the GRADE approach, particularly with respect to educational studies. In contrast to clinical studies, where direct patient outcomes are commonly measured, in educational research, which often include manikin studies, participant learning outcomes are very common. After considerable task force discussion, for education PICO questions, patient-related outcomes and actual performance in the clinical setting were deemed the critical outcomes, with learning-related outcomes (immediate and longer retention) classed as important. Kirkpatrick's classic model of Program Evaluation[15] as well as McGaghie's[16] T1 to T3 for simulation research both align with the notion that patient-related (and system-related) outcomes are more relevant than transfer of learning from the education programs to the clinical environment, which in turn is more important than isolated demonstration of learning in a training setting. Recognizing the considerable body of evidence demonstrating a decay of resuscitation skills within weeks to months after a course, long-term retention of learning was considered a more robust outcome than learning assessed at the time of the training. Similarly, resuscitation is considered a (psychomotor or leadership/teamwork) skill; therefore, "skills" were considered to be higher-level outcomes than "knowledge." The published resuscitation education literature and subsequent GRADE analysis were frequently limited by the heterogeneous nature of the interventions (with frequent downgrades for inconsistency) and the quality of the assessment tools (outcome measures). In keeping with systematic review methodology, meta-analysis was conducted in specific PICO questions only when studies of similar design, interventions, and target populations reported comparable outcomes.

The EIT Task Force reviewed 17 PICO questions, which was a reduction of 15 questions from 2010. The questions selected included the following:

Basic Life Support Training

- Cardiopulmonary resuscitation (CPR) instruction methods (self-instruction versus traditional) (EIT 647)
- Automated external defibrillator (AED) training methods (EIT 651)
- Timing for basic life support (BLS) retraining (EIT 628)
- Resource-limited settings (EIT 634)
- BLS training for high-risk populations (EIT 649)
- Compression-only CPR training (EIT 881)

Advanced Life Support Training

- Precourse preparation for advanced life support (ALS) courses (EIT 637)
- High-fidelity manikins in training (EIT 623)
- Team and leadership training (EIT 631)
- Timing for advanced resuscitation training (EIT 633)

Implementation

- Implementation of guidelines in communities (EIT 641)
- Cardiac arrest centers (EIT 624)
- Social media technologies (EIT 878)
- Measuring performance of resuscitation systems (EIT 640)
- CPR feedback devices in training (EIT 648)
- Debriefing of resuscitation performance (EIT 645)
- Medical emergency teams (METs) for adults (EIT 638)

Summary of new treatment recommendations

The following is a summary of the most important new reviews or changes in recommendations for education, implementation, and teams since the last ILCOR review, in 2010:

Training

- High-fidelity manikins may be preferred to standard manikins at training centers/organizations that have the infrastructure, trained personnel, and resources to maintain the program.
- CPR feedback devices (providing directive feedback) are useful for learning psychomotor CPR skills.
- One- to 2-year retraining cycles are not adequate to maintain competence in resuscitation skills. The optimal retraining intervals are yet to be defined, but more frequent training may be helpful for providers likely to encounter a cardiac arrest.

Systems Level

- You can't improve what you can't measure, so systems that facilitate performance measurement and quality improvement initiatives are to be used where possible.
- Data-driven performance-focused debriefing can help improve future performance of resuscitation teams.
- Out-of-hospital cardiac arrest (OHCA) victims should be considered for transport to a specialist cardiac arrest center as part of a wider regional system of care.
- There have been advances in the use of technology and social media for notification of the occurrence of suspected OHCA and sourcing of bystanders willing to provide CPR.

BLS training

BLS is foundational in the care of cardiac arrest victims. For the OHCA victim, the goal is to increase rates of bystander CPR and

deliver prompt defibrillation, because these are the major determinants of the community Chain of Survival. Unfortunately, only a minority of cardiac arrest victims actually receive bystander CPR, and it is difficult for potential rescuers to overcome barriers such as panic, fear of harming the victim, concern about the rescuers' inability to perform CPR correctly, physical limitations, fear of liability or infection, or in some instances the victim's characteristics.[17] Recent training in CPR,[17–19] along with dispatcher-assisted CPR,[20,21] may help overcome these barriers and save more lives. For healthcare professionals, it is the quality of CPR delivered that is critical, because poor compliance with recommended guidelines has been associated with lower survival.[22,23] Suboptimal CPR is common[24] but should be considered a preventable harm, and quality improvement processes should be implemented to try to minimize its occurrence.

The ILCOR EIT Task Force chose the following PICO questions as part of the review of BLS training:

- Video- or computer-assisted self-instruction versus traditional courses
- Alternate methods to train in AED use
- Timing of BLS retraining

An additional PICO question on the use of CPR feedback devices in training was also conducted and is documented later in this article, along with the corresponding PICO questions on the use of feedback devices in clinical practice (BLS 361) and the use of feedback devices as part of the quality improvement process (EIT 640).

CPR instruction methods (self-instruction versus traditional) (EIT 647)

Among students who are taking BLS courses in an educational setting (P), does video or computer self-instructions (I), compared with traditional instructor-led courses (C), change survival, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

No studies addressed the critical outcomes of **skill performance in actual resuscitations** or **survival of patients**.

For the important outcome of **cognitive knowledge**, we have identified low-quality evidence (downgraded for serious risk of bias and imprecision) from 4 RCTs with a total of 370 students showing no differences between self-instruction and instructor-led course (using a multiple-choice questionnaire at course conclusion and at 2 months to 1 year).[25–28]For the important outcome of **skill performance at course conclusion**, we have identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 9 RCTs[25,29–36] and 1 randomized cluster-controlled trial[37] with a total of 2023 students showing no differences between self-instruction and instructor-led courses based on failure to pass total performance evaluation by instructors using checklists (relative risk [RR], 1.09; 95% confidence interval [CI], 0.66–1.83).

For the important outcome of **skill performance at 1 year**, we have identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs with a total of 234 students showing no differences between self-instruction and traditional instruction based on failure to pass the total performance evaluation by instructors using checklists (RR, 0.91; 95% CI, 0.61–1.35).[28,38]

Treatment recommendations

We suggest that video and/or computer-based self-instruction with synchronous or asynchronous hands-on practice may be an effective alternative to instructor-led courses (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

Despite heterogeneity in the delivery of video and/or computer-based instruction and in the evaluation methods among different studies, we make this recommendation based on the absence of differences in the outcomes between self-instruction versus instructor-led courses. In making this recommendation, we place higher value on the potential reduction in time and resources with self-instruction, which could translate to increased CPR training.

The EIT Task Force recognized the considerable heterogeneity in the interventions on self-instruction (computer versus video assisted; with or without hands-on practice) and challenge with lumping them together (ie, a poorly designed computer-based learning activity is very different from a well-designed one), yet they are grouped together in the GRADE process. Nonetheless, the task force developed consensus that this was an important PICO question that had the potential to increase the number of lay providers available to respond to cardiac arrests and potentially the subsequent survival for victims in a time- and resource-wise manner.

Knowledge gaps

- Do students receiving self-instruction courses have better skill performance in actual resuscitations and further improve the rate of return of spontaneous circulation (ROSC) and survival to hospital discharge of patients when compared with those receiving traditional courses?
- The teaching material of the video or the computer and different type of self-instruction teaching courses might affect the learning effect.

AED training methods) (EIT 651)

Among students who are taking AED courses in an educational setting (P), does any specific training intervention (I), compared with traditional lecture/practice sessions (C), change clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge, use of AEDs (O)?

Consensus on science

No study addressed the critical outcomes of **skill performance in an actual resuscitation** or **patient outcome**.

All studies for this PICO question were manikin based, and all participants were adults.[16,36,37,39–42] The included studies used manikin-based scenarios as the standard method for assessment, and end points did not extend beyond skill retention after 6 months. Substantial heterogeneity was found for interventions and controls, and for time points of assessment. Except for 2 studies[40,41] none investigated AED training in isolation. All other studies address the whole sequence of BLS together with AED related outcomes.

To account for the nature of training, 4 subquestions were specified. For both groups of lay providers and healthcare providers, the question was subdivided into (a) self-instruction without (or with minimal) instructor involvement versus a traditional instructor-led course, and (b) self-instruction combined with instructor-led versus a traditional course.

For lay providers

For the subquestion of *self-instruction without (or with minimal) instructor involvement* versus *a traditional instructor-led course*, we identified low-quality evidence (downgraded for indirectness)

addressing the important outcome of skill retention after 2 to 6 months.[16,36,40,41]

For 2 of the investigated DVD-based teaching methods, the RR to pass the overall test directly after the course was only 0.36 (95% CI, 0.25–0.53), and 0.35 (95% CI, 0.24–0.51) if compared with instructor-led training.[40] No significant difference was found 2 months after training when comparing a computer-learning-only course to instructor-led training.[16] No significant difference was reported for AED performance (time to first shock and AED placement) for a video self-learning intervention of 30 minutes in comparison with instructor-led training of 3 to 4 hours.[36] Training for senior citizens (video self-training of 11 minutes plus 45 minutes of manikin training plus minimal instructor) was not significantly different compared with the control group. This study also suggests a saving of resources by the alternative training method.[41]

For the subquestion of *self-instruction combined with instructor-led versus traditional courses*, we identified low-quality evidence (downgraded for indirectness) addressing the important outcomes of **skill retention after 2 months** for the following 2 studies:

- Interactive computer session of 45 minutes plus 45 minutes of instructor-based practice led to results comparable with those from a traditional course of the same duration.[16] AED skills remained rather stable over 2 months, while CPR skills deteriorated significantly.
- A 9-minute DVD plus manikin training plus scenario training was inferior to traditional training, with an RR to pass the overall test of 0.55, which increased to 0.84 after 2 months.[40] This may indicate a potential learning effect of the short postcourse test.

For healthcare providers

For the subquestion of *self-instruction without (or with minimal) instructor involvement versus traditional instructor-led courses*, we identified very-low-quality evidence (downgraded for indirectness and imprecision) addressing the important outcome of **skill performance at end of course, or 2 weeks after completion**.

Isolated self-instructed training was as efficient as traditional training, but testing was limited to the end of the course.[37] No differences were found between groups, but significant time (and financial) savings were reported.[39] However, the sample size was very small. Another study showed worse results for theory-only training, but this study was flawed because the control group was inadequate.[42]

For the subquestion of *self-instruction combined with instructor-led versus traditional courses*, we identified low-quality evidence (downgraded for indirectness) for the important outcomes of skill performance at end of course, or 2 weeks after completion. Training time was reduced while performance was only slightly reduced. A 40-minute skills lab training plus instructor was associated with a higher rate of mistakes in AED operations.[37] In another study, no differences were found between groups, but significant time (and financial) savings were reported in the self-instruction combined with instructor-training group[39]; however, the sample size was very small.

Treatment recommendation

For lay providers learning AED skills, we suggest that self-instruction combined with short instructor-led training may replace longer traditional courses (weak recommendation, low-quality evidence).

For healthcare providers learning AED skills, we suggest that self-directed training (as short as 40 minutes) may be used in place of traditional training (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place value on pragmatic considerations such that if instructor-led training is not available, then self-directed training (or no training at all ["just do it"]) is an acceptable pragmatic option to use AED as stated in the *2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations* (CoSTR).[18,19]

Very little research was conducted on AED teaching outside of the context of a (standard) BLS course (only 2 studies[40,41] reported on that setting). All data were extracted from studies in the context of BLS teaching.

The ILCOR 2010 CoSTR stated that laypeople and healthcare providers could use an AED without training[16,43,44] and that untrained individuals could deliver a shock with an AED.[45–47] The current systematic review investigated whether a specific training intervention in an educational setting changed clinical or learning outcomes.

The original intent was to produce a single consensus on science with treatment recommendations based on a single PICO question. As the literature was reviewed, it became clear that there was marked heterogeneity in populations studied and the types of interventions, so multiple subsections were developed with multiple treatment recommendations.

Knowledge gaps

- Properly powered studies are needed where the primary outcome is AED use in the clinical setting and patient outcomes are considered.
- The optimal duration of AED training is still unclear.
- The effectiveness and optimal timing of brief refresher training should be evaluated.
- The most suitable methods to train children/adolescents need to be determined.

Timing for BLS retraining (EIT 628)

Among students who are taking BLS courses (P), does any specific interval for update or retraining (I), compared with standard practice (ie, 12 or 24 monthly) (C), change patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

For critical outcomes of **patient outcome** and **skill performance during actual resuscitation**, we found no published evidence.

For the important outcome of **skill performance 3 to 12 months after initial training**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 3 RCTs[48–50] and 2 non-RCTs[51,52] evaluating the effects of additional updates or retraining compared with standard practice (12–24 monthly). The heterogeneous nature of the studies prevented pooling of data. Two studies (1 RCT and 1 non-RCT) evaluated the effect of high-frequency, low-dose training (6 minutes monthly practice and every-2-weeks video reminder) after standard BLS courses and demonstrated benefit on CPR performance (compression depth, 40.3 ± 6.6 versus 36.5 ± 7.7 mm)[50] and on time to shock delivery (time [mean ± SD], 60.0 ± 12.9 versus 73.6 ± 22 s).[52] Two other RCTs and 1 non-RCT conducting a variety of retraining and evaluating 5 to 6 months after the retraining showed no benefit on chest compression quality or time to shock delivery.[48,49,51]

For the important outcome of **cognitive knowledge**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 1 RCT[48] demonstrating

improved self-reported confidence score (96 versus 92; $P = 0.038$) after additional traditional BLS retraining and 1 non-RCT[52] demonstrating increased willingness to perform CPR (RR, 0.62; 95% CI, 0.40–0.96) after high-frequency, low-dose training (every-2-weeks video reminder).[52]

Studies evaluating BLS skill retention demonstrated rapid decay in BLS skills (eg, chest compression quality and time to defibrillation) within 3 to 12 months after initial training.[18,19]

Treatment recommendations

There is insufficient evidence to recommend the optimum interval or method for BLS retraining for laypeople.

Because there is evidence of skills decay within 3 to 12 months after BLS training and evidence that frequent training improves CPR skills, responder confidence, and willingness to perform CPR, we suggest that individuals likely to encounter cardiac arrest consider more frequent retraining (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place emphasis on the need for individuals and organizations to determine the importance of BLS skill maintenance, based on their local context and the feasibility of more frequent training.

The search strategy for this PICO question focused on lay providers, but the results were considered to be generalizable. The EIT Task Force debated at length whether to recommend a specific interval for retraining, but opted to leave this to the discretion of the organizations involved because the only evidence is that CPR skills decay before the currently recommended 12- to 24-month retraining intervals.

Knowledge gaps

- There is limited evidence evaluating the effect of shorter intervals between BLS courses
- High-frequency, low-dose training shows some promise, and could potentially enhance BLS training and reduce skill decay. More studies are needed to confirm the role of such training.
- There is significant heterogeneity of initial training, timing and contents of retraining, and outcomes among current studies. There is a need for development of guidelines to ensure uniform testing and reporting in BLS training and simulation research.

Basic life support: other considerations

There are several issues that impact the optimal design and implementation of BLS training within communities. The ILCOR EIT Task Force chose to focus on PICO questions that aligned with the GRADE methodology for intervention questions and that could have a relatively immediately impact to help save more lives or could identify important knowledge gaps that require further research.

For 2015, the ILCOR EIT Task Force chose to focus on

- Educational approaches to resuscitation training in resource-limited settings
- Focused training of likely rescuers for high-risk populations
- The impact of training communities to use compression-only CPR

Resource-limited settings (EIT 634)

Among students who are taking BLS or ALS courses in a resource-limited educational setting (P), does any educational approach (I), compared with other approaches (C), change clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

For the critical outcomes of **change in clinical outcome** and **skill performance in actual resuscitations** and the important outcome of **skill performance at 1 year**, we found no evidence in low-resource settings.

For the important outcome of **skill performance at time of course conclusion and 1 year**, we found very-low-quality evidence (downgraded for serious risk of bias, imprecision, and possible publication bias) from 2 RCTs.[53,54] One study tested cognitive and skill retention 3 weeks after ALS refresher training in 3 arms, namely simulation (traditional course format) versus multimedia (computer-based learning) and self-directed reading.[53] In another study, students were tested at 3 and 6 months after training.[54] This study involved BLS training in a traditional course format versus limited instruction (larger student-to-instructor ratio) and self-directed computer-based learning. All modalities were shown to be equivocal or to have mixed but not constant benefit over traditional format.

For the important outcome of **skill performance at course conclusion**, we identified 6 RCTs[53–58] and 1 observational study.[59] Studies varied significantly in the subject taught from BLS to ALS, range of participants (paramedic students, medical students in various stages of training, nursing staff, general healthcare providers), duration of course, and training methods. Educational strategies included traditional course format versus computer-based learning, telemedicine, self-directed reading, limited instruction (larger student-to-instructor ratio), 4-stage skill teaching, video instruction, and video-based group feedback. Studies ranged from very-low-quality evidence[53] (downgraded for serious risk of bias and imprecision) to moderate-quality evidence[55–58] (downgraded for imprecision).

Because the outcome of **skill performance** in all 7 studies[53–59] demonstrated equivocal or minimal benefit in skill performance compared with traditional course format, we suggest the possibility of using other training methods for teaching BLS or ALS. However, the heterogeneity of the studies makes it unclear what this alternative method might be (weak recommendation, low-quality evidence).

For the important outcome of **cognitive knowledge**, we identified 4 RCTs: 2 were of very low quality (downgraded for serious risk of bias, imprecision, and possible publication bias),[53,54] 1 was of low quality (downgraded for risk of bias and imprecision),[57] and 1 was of moderate quality (downgraded for imprecision).[55] These studies differed in the teaching methods used to compare cognitive outcome, including simulation (traditional course format), multimedia (computer-based learning), self-directed reading, limited instruction (larger student-to-instructor ratio), and self-directed computer-based learning. In comparing traditional course format to alternative teaching strategies for BLS or ALS training, there were some studies showing slight cognitive knowledge benefit of various teaching strategies, but no constant benefit over the traditional method, and no studies could be pooled together to strengthen a recommendation or quality of evidence.

All of the RCTs included few participants. Therefore, we suggest the possibility of using alternative educational strategies (weak recommendation, low-quality evidence).

Treatment recommendations

We suggest that alternative instructional strategies would be reasonable for BLS or ALS teaching in low-income countries (weak recommendation, very-low-quality evidence). The optimal strategy has yet to be determined.

Values, preferences, and task force insights

In making this recommendation, we consider that cost of and access to training may play a large role in the ability of healthcare workers to receive training in BLS and ALS in low-income countries.

Some of the alternative techniques for BLS or ALS teaching identified in this review may be less expensive and require less instructor resource than a traditional teaching format, and may enable wider dissemination of BLS and ALS training in low-income countries.

The heterogeneity of the content taught (eg, BLS versus ALS), the learner populations, and the different instructional methods studied in resource-limited settings were challenging to summarize as a single systematic review. As the body of evidence develops, this PICO question may benefit from subdivision across content taught, learner populations, and instructional methods.

Knowledge gaps

- Educational resources vary from one country to another. From the studied data in low-resource settings, there is no one-size-fits-all approach, and therefore, specific educational strategies need to be developed and tested for specific low-resource countries and settings.

Basic life support training for high-risk populations (EIT 649)

For people at high risk of OHCA (P), does focused training of likely rescuers (eg, family or caregivers) (I) compared with no such targeting (C), change survival with favorable neurologic outcome at discharge, ROSC, bystander CPR performance, number of people trained in CPR, willingness to provide CPR (O)?

Consensus on science

We found 32 studies relating to CPR training in likely rescuers (eg, family or caregivers) of high-risk OHCA groups. These studies used varying methods for CPR training and assessment of outcomes.

In brief, there is insufficient evidence on patient outcomes to support or refute the use of training interventions in high-risk groups.[60–70] Existing evidence on educational outcomes suggest likely rescuers are willing to be trained,[63,71–77] are likely to share training with others,[71,74,75,78–80] are unlikely to seek training on their own,[63,79] and, after training, are competent in BLS skills and/or knowledge.[33,71,73,74,78,81–90]

For the critical outcomes of **survival with favorable neurologic outcome at discharge and ROSC**, we have identified low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 3 RCTs[60,61,64] and very-low-quality evidence (downgraded for risk of bias) from 8 non-RCTs.[63,65–70,62] The heterogeneous nature of the studies prevents pooling of data. In individual studies, there were insufficient numbers of events, with significant loss to follow-up, to be confident in the direction of the survival estimates, particularly for adult cardiac patients.

The 3 RCTs followed high-risk patients for subsequent OHCA events and survival as secondary outcomes, so were not adequately powered for these outcomes.[60,61,64] One study reported 4 out-of-hospital deaths in 65 adult cardiac patients at 6 months (2/24 in the control group and 2/41 in the CPR-trained group).[61] A larger study, which was subject to high loss to follow-up, documented 13 OHCA events among high-risk children within 12 months after training of parents and other caretakers; all of these children were successfully resuscitated, and all were in the trained groups, with no events reported in the control group.[64] The third RCT reported 71 OHCA events in the home among 7001 adult high-risk patients with training (CPR or CPR with AED); survival was 12%, with an indirect comparison made to 2% survival for OHCA events in the home from the literature.[60]

Eight non-RCTs were of very-low-quality evidence.[63,65–70,91] The majority of these studies relied on self-reported outcomes and were subject to high loss to follow-up or small sample sizes. One study documented higher survival rates for OHCA events in centers offering CPR training for high-risk children (28/41, 46%) when compared with centers offering no training (0/24, 0%); however, it is not reported whether the parents of OHCA children in either group had any CPR training, including the CPR training offered.[66] Two studies trained the parents of high-risk infants.[33,69] The first study reported 75% survival for 8 OHCA events,[24] all with good or stable neurologic status, and the second study reported 100% for 7 OHCA events.[59] Among adult cardiac patients, who were followed-up for varying durations after training, there were very few OHCA events: 1 very small study ($n = 33$) reported no events or deaths[70]; 3 studies report single OHCA events during follow-up after training, all of whom died[63,67,68]; and 1 study reported 14 OHCA events and 12 deaths among 97 OHCA survivors after training (CPR or CPR with AED).[65]

For the important outcome of **bystander CPR performance—subsequent utilization of skills**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[61,64] and very-low-quality evidence (downgraded for risk of bias) from 7 non-RCTs.[63,66–70,91] The heterogeneous nature of the studies prevents pooling of data. In individual studies, there were too few events, with significant loss to follow-up, to be confident in the direction of the estimates, particularly for adult cardiac patients.

The 2 RCTs followed patients for OHCA events and bystander CPR.[61,64] One study found bystander CPR was not performed in any of the 4 adult OHCA cardiac-related deaths (2 in control, 2 in intervention).[61] The other study reported 13 OHCA events in high-risk infants, all of whom received CPR by trained parents, with no OHCAs occurring in the control group.[64]

Seven non-RCTs followed patients for OHCA events and determined whether bystander CPR was performed.[63,66–70,91] One study documented higher bystander CPR rates for OHCA events in centers offering CPR training to parents of high-risk children (28/41, 68%) compared with centers providing no training (0/24, 0%), but it is not reported whether the parents in either group were CPR trained.[66] Two studies documented bystander CPR rates of 100% for 13 OHCA events in high-risk infants (bystander CPR status for 1 additional event was unknown).[69,91] In 2 small studies of adult cardiac patients, there were single OHCA events, and trained individuals were either not present at the time[67] or physically unable to perform CPR.[68] A larger study describes CPR-trained family members using CPR on 4 occasions; 3 were successful.[63]

For the important outcome of **CPR skills performance and retention**, we identified moderate-quality evidence (downgraded for risk of bias) from 3 RCTs[33,71,81] and very-low-quality evidence (downgraded for risk of bias) from 12 non-RCTs.[73,74,78,82–90] Although these studies used different methods for CPR training and assessment, they consistently report competent CPR performance and/or knowledge immediately after training,[33,73,78,81–90] which is usually retained in the short term[71,73,85,88] but declines over longer periods of follow-up without retraining or reminders.[84]

For the important outcome of **number of people trained**, we identified low-quality evidence (downgraded for risk of bias and indirectness) from 2 RCTs[71,79] and very-low-quality evidence (downgraded for risk of bias) from 4 non-RCTs.[74,75,78,80] The heterogeneous nature of the studies prevents pooling of data, but overall the data suggest that family members and caregivers are unlikely to seek training on their own[63,79] but, when trained, are likely to share the training with others.[71,74,75,78]

The 2 RCTs examined the question from different perspectives.[71,79] The first study reported CPR kit sharing rates

by trained family members of cardiac patients, with a mean of 2.0 (SD ± 3.4) additional family members in the continuous chest compression CPR group versus a mean of 1.2 (SD ± 2.2) in the conventional CPR group ($P = 0.03$).[71] In the second study, adult cardiac patients were more likely to follow prescribed advice by a physician to purchase a CPR training kit than to take a traditional CPR class ($P = 0.0004$), although few followed any advice (12/77 purchased a CPR training kit, and 0/79 underwent CPR training through a traditional CPR class).[79]

Five non-RCTs also used different methods to examine the question.[63,74,75,78,80] One study targeted 190 OHCA survivors, with 50 of 101 responding, and 20 patients and 71 family members and friends were subsequently trained.[80] In 1 study, free mass CPR training sessions were provided, and an increase in those attending training because of heart disease after a targeted recruitment campaign (5.6% to 13.2%) was documented. In 1 study,[78] 49% shared a CPR DVD with family and/or friends, and in another,[75] 79% shared the kit with at least 2 family members/friends. One study documented that only 18% of untrained family members sought training on their own in the follow-up period of 21 ± 6 months.[63]

For the important outcome of **willingness to provide CPR**, we identified moderate-quality evidence (downgraded for risk of bias) from 2 RCTs[71,76] and very-low-quality evidence (downgraded for risk of bias) from 6 non-RCTs.[63,72–75,77] The heterogeneous nature of the studies prevents pooling of data, but there was a strong signal toward willingness to provide CPR if required in all studies.

Two RCTs[71,76] were identified as moderate quality of evidence. The first RCT documented that trainees in the continuous chest compression CPR group were more likely to rate themselves as very comfortable with the idea of using CPR skills in actual events than were the conventional CPR trainees (34% versus 28%; $P = 0.08$).[71] The second RCT found that the majority "would absolutely" be willing to perform CPR if required.[76]

Very-low-quality evidence was identified from 6 non-RCTs.[63,72–75,77] In 3 of the studies,[63,72,74] the vast majority of trained individuals stated they would use CPR if needed (79%–99%), and 1 study reported that all subjects felt neutral to somewhat confident in their comfort with providing CPR.[75] One study reported that 98% of those trained stated that they "agreed" or that they "maybe" would perform first aid (including CPR) correctly at 1-year follow-up.[72] Another study found a slight decrease in comfort level with CPR use within 6 months after training.[75]

Treatment recommendations

We recommend the use of BLS training interventions that focus on high-risk populations, based on the willingness to be trained and the fact that there is low harm and high potential benefit (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place higher value on the potential benefits of patients receiving CPR by a family member or caregiver, and the willingness of this group to be trained and to use skills if required. We place lesser value on associated costs and the potential that skills may not be retained without ongoing CPR training. Because cardiac arrest is life threatening, the likelihood of benefit is high relative to possible harm.

Knowledge gaps

There is a need for

- Higher-quality research
- Adequately powered studies reporting critical clinical outcomes
- Studies examining the cost-effectiveness of CPR training for family members of high-risk patients
- Studies examining innovative CPR training versus conventional CPR training (versus no training)
- Studies with standardized/objective methods of assessment for CPR performance (real-time data recording)

Compression-only CPR training (EIT 881)

Among communities that are caring for patients in cardiac arrest in any setting (P), does teaching compression-only CPR (I), compared with conventional CPR (C), change survival rates, bystander CPR rates, willingness to provide CPR (O)?

Consensus on science

For the critical outcome of **neurologically intact survival at hospital discharge**, we found very-low-quality evidence (downgraded for serious imprecision) from 2 observational studies (n = 1767)[92,93] that documented survival to hospital discharge for adults receiving bystander CPR from the same statewide database; one reported on events of cardiac origin,[92] and the other reported on events of noncardiac origin.[93] Both studies demonstrated no difference in neurologically intact survival (odds ratio [OR], 1.41; 95% CI, 0.92–2.14).

For the critical outcome of **bystander CPR rates**, we found very-low-quality evidence (downgraded for serious imprecision and serious risk of bias) from 1 observational study, which showed a higher proportion of bystander CPR performed with compression-only CPR than with conventional CPR over the 5-year study period (34.3% versus 28.6%).[92]

For the important outcome of **willingness to perform CPR**, we found very-low-quality evidence (downgraded for very serious risk of bias, very serious indirectness, and serious imprecision) from 1 randomized trial documenting that family members of hospitalized adults who were given a compression-only CPR training kit were more likely to express willingness to perform CPR (34%) than family members given a conventional CPR training kit, but this difference did not achieve statistical significance (28%; OR, 1.30; 95% CI, 0.85–1.98).[71]

Treatment recommendation

We suggest that communities may train bystanders in compression-only CPR for adult OHCA as an alternative to training in conventional CPR (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we took into account that willingness to perform bystander CPR in the community may be increased when compression-only CPR is offered as an alternative technique.[94–97] Accordingly, communities should consider existing bystander CPR rates and other factors, such as local epidemiology of OHCA and cultural preferences, when deciding on the optimal community CPR training strategy.

Compression-only CPR instruction has been proposed for several reasons, including overcoming barriers to providing CPR, simplicity in delivery so that all lay providers are able to provide CPR, ease of instruction, etc. Recognizing that a proportion of cardiac arrests are caused by asphyxia (eg, drowning or with cardiac arrests involving children) and in these cases compression-only CPR may not be as effective as conventional CPR, the EIT Task Force suggests that communities consider epidemiology of cardiac arrest in their locale, their bystander CPR response rates, and cultural preferences along with this systematic review to decide on their optimal community CPR training strategy.

Knowledge gaps

- Studies with patient survival outcomes and bystander CPR rates are needed.

Advanced life support training

ALS training was established in the mid-1970s. Since this time, the courses have evolved in design and have been implemented in many different countries, training healthcare workers throughout the world. Unfortunately, the literature suggests that without ongoing education the skills learned in these courses are lost over a period of months.[17,98] There are also increasing pressures from administrators to justify the time and costs of training away from the clinical workplace.

This section addresses issues associated with ALS training and key PICO questions that could supplement learning and retention of resuscitation skills. If effective and transferable to the clinical environment, these interventions have the potential to improve healthcare worker performance and help save lives.

The questions reviewed include

- The use of precourse preparation to determine if it improves learning and clinical performance (EIT 637)
- The use of high-fidelity manikins (EIT 623)
- The effect of leadership and team training (EIT 631)
- Determine if there is any evidence for an alternate retraining interval to affect learning and performance of healthcare workers (EIT 633)

Precourse preparation for advanced life support courses (EIT 637)

Among students who are taking ALS courses in an educational setting (P), does inclusion of specific precourse preparation (eg, eLearning and pretesting) (I), compared with no such preparation (C), change survival rates, skill performance in actual resuscitations, cognitive knowledge, skill performance at course conclusion, skill performance at 1 year, skill performance at time between course conclusion and 1 year (O)?

Consensus on science

For the important outcomes of **skill performance at course conclusion and cognitive knowledge**, we identified moderate-quality evidence (downgraded for indirectness) from 1 RCT enrolling a total of 572 participants showing no benefit for 1 specific format of precourse preparation (skill: mean difference, −0.5; 95% CI, −2.81 to 1.81; knowledge: difference in pass rates, 1.8%; $P = 0.4$)[98a]. The study did not evaluate the impact of precourse preparation on face-to-face or overall course time (eg, when used as part of a blended learning program).

Treatment recommendation

The confidence in effect estimates is so low that the task force decided a specific recommendation for or against precourse preparation in ALS courses was too speculative.

Values, preferences, and task force insights

There is considerable ambiguity about the definition of precourse learning, particularly because some larger published studies have used a blended learning model (independent electronic learning coupled with a reduced-duration face-to-face course) resulting in similar learning outcomes and substantial cost savings. In the end, the EIT Task Force decided to focus purely on precourse preparation and remove studies with hybrid training programs.

Knowledge gaps

- There is a need for more research in this area, in particular precourse preparation with limited-resource requirements.
- This research needs to be conducted across various groups. Studies could include different courses, different course participant groups (eg, physicians, nurses, EMTs), and different precourse preparation methodologies (eg, manuals, testing, self-directed learning).

High-fidelity manikins in training (EIT 623)

Among participants undertaking ALS training in an education setting (P), does the use of high-fidelity manikins (I), compared with the use of low-fidelity manikins (C), change patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

For the important outcome of **skill performance at 1 year**, we identified low-quality evidence (downgraded for very serious risk of bias) from 1 RCT enrolling a total of 86 participants showing no benefit for high-fidelity training compared with low-fidelity training (standardized mean difference [SMD], 0; 95% CI, −0.42 to 0.42).[99]

For the important outcome of **skill performance between course conclusion and 1 year**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT enrolling a total of 47 participants showing no benefit for high-fidelity training compared with low-fidelity training (SMD, 0.08; 95% CI, −0.49 to 0.65).[100]

For the important outcome of **skill performance at course conclusion**, we identified very-low-quality evidence (downgraded for risk of bias, inconsistency and imprecision) from 12 RCTs, enrolling a total of 726 participants showing a moderate benefit for high-fidelity training compared with low-fidelity training (SMD, 0.60; 95% CI, 0.17–1.03).[99–110] This was supported by very-low-quality evidence (downgraded for inconsistency and imprecision) from 1 non-RCT enrolling a total of 34 participants, which trended in the same direction (SMD, 0.50; 95% CI, −0.19 to 1.18).[111]

For the important outcome of **knowledge at course conclusion**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 8 RCTs enrolling a total of 773 participants showing no benefit for high-fidelity training compared with low-fidelity training (SMD, 0.15; 95% CI, −0.05 to 0.34).[100–103,108,109,112,113] This was supported by very-low-quality evidence (downgraded for inconsistency and imprecision) from 1 non-RCT enrolling a total of 34 participants showing no benefit for high-fidelity training (SMD, 0.26; 95% CI, −0.42 to 0.93).[111]

Treatment recommendations

We suggest the use of high-fidelity manikins when training centers/organizations have the infrastructure, trained personnel, and resources to maintain the program (weak recommendations based on very-low-quality evidence).

If high-fidelity manikins are not available, we suggest that the use of low-fidelity manikins is acceptable for standard ALS training in an educational setting (weak recommendations based on low-quality evidence).

Values, preferences, and task force insights

In making these recommendations, we took into account the well-documented, self-reported participant preference for high-fidelity manikins (versus low-fidelity manikins) and the likely impact of this preference on willingness to train.[98] We considered

the positive impact of skill acquisition at course completion, as well as the lack of evidence of sustained impact on the learner. We also considered the relative costs of high- versus low-fidelity manikins.

High-fidelity manikins can provide physical findings, display vital signs, physiologically respond to interventions (via computer interface), and enable procedures to be performed on them (eg, bag-mask ventilation, intubation, intravenous cannulation).[114] When considering physical realism, these high-fidelity manikins are more expensive but are increasingly more popular with candidates and faculty.

Determining the treatment recommendation for this PICO question was challenging because of the marginal benefits for the intervention. In reviewing the science, it was clear that there was a benefit to high-fidelity manikins but less clear whether the incremental costs justified the added expenses.

Knowledge gaps

Future research should

- Explore methods for teaching resuscitation educators how to optimally use high-fidelity simulation to enhance educational outcomes
- Determine the effect of the various different aspects of fidelity (manikin, environment, emotional engagement, etc.) on educational outcomes
- Determine the relative importance of debriefing in simulation-based education for ALS courses
- Assess the impact on clinical outcomes and measure performance outcomes extending beyond the end of the course
- Include adequately powered RCTs with sufficient sample size to detect the desired effect in each of the key outcomes

Team and leadership training (EIT 631)

Among students who are taking ALS courses in an educational setting (P), does inclusion of specific leadership or team training (I), compared with no such specific training (C), change patient outcomes, bystander CPR performance, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

For the critical outcome of **patient survival**, we found no randomized clinical trials but found very-low-quality evidence (downgraded for risk of bias and indirectness) from 2 observational studies.[115,116] One study documented an increase in hospital survival from pediatric cardiac arrest over a 4-year period after implementation of a hospital-wide mock code program, which included team training.[115] The other study documented reduced severity-adjusted surgical mortality in 74 hospitals in the United States that had implemented a surgical team training program, compared with 34 hospitals that had not introduced such a program.[116]

For the critical outcome of **skill performance in actual resuscitation**, we found very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from a single RCT that randomly assigned 32 internal medicine residents to receive simulation training with a focus on the role of the resuscitation team leader versus no additional training; there was no effect on CPR quality during actual resuscitation of patients.[117] We also found very-low-quality evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 2 observational studies.[118,119]

For the important outcome of **skill performance at 4 months to 1 year** (patient tasks), we found very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 2 randomized trials[110,120] that showed that team or leadership training improved CPR hands-on time and time to initiation of various patient tasks at follow-up assessment.

For the important outcome of **skill performance at 4 months to 1 year** (teamwork performance), we found low-quality evidence (downgraded for bias and imprecision) from a single randomized trial[110] and very-low-quality evidence (downgraded for risk of bias) from a single observational study[121] that showed more frequent teamwork behaviors demonstrated in the teamwork-trained learners at follow-up assessment.

For the important outcome of **skill performance at 4 months to 1 year** (leader performance), we found moderate-quality evidence (downgraded for risk of bias) from a single randomized trial[120] and very-low-quality evidence (downgraded for risk of bias and imprecision) from a single observational study[122] that showed more frequent leadership behaviors demonstrated in the leadership-trained learners at follow-up assessment.

For the important outcome of **skill performance at course conclusion** (patient tasks) (assessed with time to completion of various patient tasks), we found low-quality evidence (downgraded for risk of bias and imprecision) from 8 randomized trials[110,120,123–128] and very-low-quality evidence (downgraded for risk of bias and indirectness) from 4 observational studies[128–131] that showed that team or leadership training improved CPR hands-on time and time to initiation of various patient tasks at course conclusion. A dose-response gradient was found.

For the important outcome of **skill performance at course conclusion** (teamwork performance) (assessed with teamwork score), we found low-quality evidence (downgraded for risk of bias and imprecision) from 6 randomized studies[110,123–125,127,132] and very-low-quality evidence (downgraded for risk of bias, indirectness, inconsistency, and imprecision) from 3 observational studies[121,130,133] that showed that teamwork-trained learners demonstrated more frequent teamwork behaviors at course conclusion.

For the important outcome of **skill performance at course conclusion** (leader performance), we found low-quality evidence (downgraded for risk of bias and imprecision) from 4 randomized studies[120,126,128,134] and very-low-quality evidence (downgraded for indirectness and imprecision) from 2 observational studies[122,131] that showed that leadership-trained learners demonstrated more frequent leadership behaviors at course conclusion.

For the important outcome of **cognitive knowledge**, we found no evidence.

Treatment recommendations

We suggest that team and leadership training be included as part of ALS training for healthcare providers (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we have placed emphasis on the potential benefit, lack of harm, and high level of acceptance of team and leadership training and lesser value on associated costs.

There are many ways that leadership and team behavior training can be delivered. As such, there was considerable heterogeneity in the studies analyzed. It was recognized that there are multiple variables other than direct instruction on a life support course that contribute to the development of leadership skills. There are numerous studies from outside the medical literature that could have been included, but these were considered not to be directly relevant to the PICO.

Knowledge gaps

- Studies relating team and leadership training to patient outcome are lacking.

Timing for advanced resuscitation training (EIT 633)

Among students who are taking ALS courses in an educational setting (P), does any specific interval for update or retraining (I), compared with standard practice (ie, 12 or 24 monthly) (C), change/improve patient outcomes, skill performance in actual resuscitations, skill performance between course completion and 1 year; skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

For the important outcome heading of **skill performance at 1 year**, there were 4 studies[135–138] using a variety refresher techniques and unique outcome measures.

The refreshers included a simulation-enhanced booster 7 to 9 months after the course, a commercially available eLearning tool used monthly, mail-outs of information related to course objectives or a patient management problem every 3 months, or in situ monthly simulation for 6 months. The outcome measures respectively used in the 4 studies were a validated procedural skills and teamwork behavior assessment tool; a previously validated composite score of a written test and cardiac arrest simulation test (CASTest); mock arrest, compression, and ventilation performance with no evidence provided of validity/reliability of the tools; and the change in score on the previously validated Clinical Performance Tool (CPT) and Behavioral Assessment Tool (BAT).

One study used simulation boosters and demonstrated benefit from the refresher in procedural skills and teamwork behavior scores (very-low-quality evidence, downgraded for indirectness and imprecision).[138] The studies that used periodic eLearning and mailings (very-low-quality evidence, downgraded for indirectness and imprecision) demonstrated no benefit from the refreshers except in the performance on mock arrests. Only 1 of the studies related directly to the research question comparing frequent refreshers to standard retraining intervals, using manikin-based simulation[137]; this study documented better scores on the CPT and equivalent outcomes for the BAT while using less total time of retraining: 4.5 versus 7.5 hours (low-quality evidence, downgraded for imprecision).

For the important outcome of **skill performance beyond course completion and before 1 year**, there was 1 study that compared a single refresher using video and self-guided practice or a single 2-hour hands-on session with no retraining[139]; it showed no benefit for the refresher (very-low-quality evidence, downgraded for serious bias, indirectness, and imprecision).

For the important outcome of **knowledge**, there were 4 studies[139a] using a variety of refresher techniques, such as simulation-enhanced booster, video and self-guided practice, knowledge examination, and mock resuscitation training or mail-outs as described above. The assessment tools varied from those with no reported validity/reliability evidence to well-described psychometrics in 1 study.[139a] There was no benefit of refresher training (very-low-quality evidence, downgraded for serious bias, indirectness, and imprecision).

Treatment recommendations

Compared with standard retraining intervals of 12 to 24 months, we suggest that more frequent manikin-based refresher training for students of ALS courses may be better to maintain competence (weak recommendation, very-low-quality evidence). The optimal frequency and duration of this retraining is yet to be determined.

Values, preferences, and task force insights

In making this recommendation, we consider the rapid decay in skills after standard ALS training to be of concern for patient care. Refresher training, in the form of frequent low-dose in situ training using manikins, offers promise.[137] The potential cost savings of integrating these sessions into daily workflow rather than removing staff for standard refresher training may be important, as might a reduced total time of retraining. More recent literature in resuscitation demonstrates improved learning from "frequent, low-dose" compared with "comprehensive, all-at-once" instruction and a learner preference for this format.[140]

Ultimately, the question to be asked is, how frequently should training be delivered? As yet, there is no definitive answer to this question because it is dependent on the type of training. For example, it has been shown in another systematic review (EIT 623) that the use of different types of manikins can lead to improved outcomes in the short term. However, there is a paucity of published literature, so there was no consensus within the task force about an overall specified time interval.

Knowledge gaps

- To date, studies addressing this PICO question are of relatively poor quality and limited in sample size, without the use of consistent high-quality assessment tools.
- Larger, multicenter studies might be important to answer this important educational question, particularly to determine optimal retraining time periods and cost-effectiveness of this model.
- Can initial spaced instruction alter the decay of ALS skills?
- What is the relationship between clinical exposure and skill maintenance?

Implementation

The resuscitation literature is heterogeneous in its methods, quality, and results. Studies conducted decades apart or in different settings often demonstrate conflicting findings, making comparisons difficult; yet resuscitation councils are required to develop evidence-based guidelines for organizations to implement. Past guideline rollouts have demonstrated that implementation is neither easy nor straightforward and can take years to accomplish.[141] The barriers to implementing a guideline within an organization may delay its entry into practice by years, and modifying caregiver behaviors can take years longer.[141–143] Recognizing this, publishing clinical practice guidelines is not sufficient without including a discussion of how to implement them.

Implementation: what we should do versus what we say we will do

It remains unclear which strategies best translate knowledge into practice. Several barriers delayed implementation of the 2005 resuscitation guidelines among member organizations of the Resuscitation Outcomes Consortium, including delays in training providers, obtaining training materials and instructors, reprogramming defibrillators, changing regulatory frameworks, obtaining agreement from physician leadership, and conflicting research interests.[143] Similar delays were also demonstrated in Europe.[142]

This section addresses issues associated with systems of care for managing cardiac arrest both in- and out- of the hospital; the use of evolving technologies to implement resuscitation; and the use of feedback at the training, individual patient, and systems levels. The section is also premised on the belief that resuscitation outcomes will improve if guideline-based care is implemented and

that measurement of actual performance is a necessary component of resuscitation system improvement.

The questions reviewed include

- Implementation of guidelines in communities (EIT 641)
- Cardiac arrest centers (EIT 624)
- Social media technologies (EIT 878)
- Measuring performance of resuscitation systems (EIT 640)
- CPR feedback devices in training (EIT 648)
- Debriefing of resuscitation performance (EIT 645)
- MET for adults (EIT 638)

Implementation of guidelines in communities (EIT 641)

Within organizations that provide care for patients in cardiac arrest in any setting (P), does implementation of resuscitation guidelines (I), compared with no such use (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, bystander CPR performance, ROSC (O)?

Consensus on science

For the critical outcome of survival to 180 days with good neurologic outcome, we found no data.

For the critical outcome of **survival to hospital discharge**, we identified very-low-quality evidence (downgraded for imprecision, risk of bias, and indirectness) from 11 observational studies. Seven studies showed that implementation of resuscitation guidelines improved survival (RR, 1.25; 95% CI, 1.16–1.35),[144–150] and 4 studies were neutral.[141,142,151,152]

For the important outcome of **ROSC**, we identified very-low-quality evidence (downgraded for imprecision, risk of bias, and indirectness) from 10 observational studies. Seven studies showed that implementation of resuscitation guidelines improved ROSC (RR, 1.15; 95% CI, 1.11–1.20),[144–150] and 3 studies were neutral.[142,151,152]

For the important outcome of **CPR performance**, we identified very-low-quality evidence (downgraded for imprecision, risk of bias, and indirectness) from 4 observational studies that implementation of resuscitation guidelines improved the hands-off ratio of emergency medical services CPR performance (mean 0.28 versus 0.42).[142,145,149,150]

Treatment recommendations

We recommend implementation of resuscitation guidelines within organizations that provide care for patients in cardiac arrest in any setting (strong recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this (discordant) recommendation, we placed a high value on the notion that cardiac arrest care requires coordination of time-sensitive interventions and often involves care providers who have not worked together before, potentially from multiple agencies or departments; guidelines may facilitate coordinated action. Despite the very low quality of evidence, the direction of effect is consistent, and pooled data are statistically significant and clinically meaningful. A discordant recommendation is justified because cardiac arrest is life threatening and the likelihood of benefit is high relative to possible harm.[153] We recognize that most of the authors of the 2015 CoSTR are involved in writing resuscitation guidelines and that this should be considered a potential intellectual conflict of interest.

Knowledge gaps

- The optimal treatment components of resuscitation guidelines are unknown.
- The optimal methods for knowledge translation are unknown.
- The optimal methods for implementation are unknown.

Cardiac arrest centers (EIT 624)

Adults and children in OHCA (P), does transport to a specialist cardiac arrest center (I), compared with no directed transport (C), change neurologically intact survival at 30 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, hospital admission, ROSC (O)?

Consensus on science

There were no RCTs identified that specifically addressed this question. Of the 26 observational studies included in the evidence review, there was only 1 prospective study where survival outcomes in OHCA patients transported to a critical care medical center were compared with those transported to a non–critical care hospital.[154] There were 10 observational studies that compared OHCA patient survival outcomes between hospitals based on various hospital characteristics such as hospital type, hospital size, hospital location, and OHCA case volume.[155–164] Six observational studies compared OHCA patient survival outcomes before and after the implementation of a regionalized system of postresuscitation care.[165–170] Six observational studies compared patient survival outcomes based on transport time to the hospital and/or direct versus indirect transport to a major center.[171–176] One observational study compared OHCA patient outcomes across hospitals in those patients who received early coronary angiography or reperfusion and induced hypothermia versus those who did not.[156] Two observational studies did not report any of the patient survival outcomes of interest and hence do not appear in the summary below.[177,178] Heterogeneity in study design and inclusion criteria precluded meta-analyses.

For the critical outcome of **neurologically intact survival**, we have identified very-low-quality evidence (downgraded for significant risk of bias and indirectness) from 12 observational studies enrolling more than 23,000 patients.[154,156,158,163,165,167–170,172–174] Three studies examined neurologic intact survival at 30 days.[154,170,173] The other 9 studies reported survival to hospital discharge with good neurologic outcome.[178a] There was an association between improved neurologic intact survival and patient transport to specialist cardiac arrest centers. The key study reported improved 30-day neurologically favorable survival (Cerebral Performance Category ≤ 2) in OHCA patients transported to a critical care medical center compared with a non–critical care hospital (6.7% versus 2.8%; OR, 2.47; 95% CI, 2.02–3.01; $P < 0.001$).[154]

For the important outcome of **survival**, we identified very-low-quality evidence (downgraded for significant risk of bias and indirectness, with heterogeneity in reported hospital factors associated with differences in patient survival) from 21 studies with more than 120 000 patients. Three studies examined survival at 30 days,[159,161,173] 18 studies with more than 120 000 patients reported survival to hospital discharge,[155–160,163,164,166,168–172,174–176] and 1 study reported survival at 4.6 years.[162]

There was an association with survival and transport to a cardiac arrest center; however, the specific hospital factors most related to patient outcome were inconsistent in these studies.

Treatment recommendation

We suggest that OHCA patients should be considered for transport to a specialist cardiac arrest center as part of wider regional system of care for management of patients with OHCA (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we recognize the development of cardiac arrest centers may be considered as a health improvement initiative, as has been performed for other critical conditions, including myocardial infarction, stroke, and major trauma, without the evidence of randomized trials.

Knowledge gaps

- What are the precise differences in postresuscitation care received at cardiac arrest centers compared with non–cardiac arrest centers?
- The safe journey time or distance for patient transport under various conditions is unknown.
- The essential treatments that a cardiac resuscitation center should offer need to be defined.
- What is the role of secondary transport from receiving hospital to a regional center?
- Is there sufficient clinical equipoise to conduct an RCT of standard care versus transport to a cardiac resuscitation center?

Social media technologies (EIT 878)

For OHCA (P), does having a citizen CPR responder notified of the event via technology or social media (I), compared with no such notification (C), change survival to hospital discharge with good neurologic outcome, survival to hospital discharge, hospital admission, ROSC, bystander CPR rates, time to first compressions (O)?

Consensus on science

We did not identify any evidence to address the critical outcomes. We identified 1 RCT that addressed the important outcome of bystander CPR rates.

For the outcome of **bystander CPR rates**, we identified high-quality evidence from 1 RCT[178b] involving a mobile-phone positioning system which alerted lay responders within 500 m of a suspected OHCA, demonstrating a rate of bystander-initiated CPR of 62% (188 of 305 patients) in the intervention group versus a rate of 48% (172 of 360 patients) in a control group which did not receive such alerts, with an absolute difference of 14% (95% CI, 6–21; $P < 0.001$).

For the outcome of **time to first shock**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 case series (n = 76) involving text-message alerts to lay responders within 1000 m of a suspected cardiac arrest demonstrating a median call to first shock time of 8 minutes (interquartile range, 6:35–9:49 minutes).[179] In the same study, the median time from call to first shock when emergency medical services personnel arrived first was 10:39 minutes (interquartile range, 8:18–13:23 minutes).

For the outcome of **first responder on scene**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 case series involving computer-generated phone calls and text messages to lay responders within 500 m of a suspected cardiac arrest, demonstrating that responders notified via this system arrived first in 44.6% of suspected cardiac arrest episodes, compared with emergency medical services providers in 55.4% of the episodes.[180]

Treatment recommendation

We suggest that individuals in close proximity to a suspected OHCA episodes who are willing and able to perform CPR be notified of the event via technology or social media (weak recommendation, moderate quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place value on the time-sensitive benefit of CPR and AED use in OHCA and the limitations of optimized emergency medical services systems to improve response times. We also recognize that there are individuals willing and able to provide BLS in most communities and these novel technologies can engage these individuals in the response to cardiac arrest outside the hospital. Although the evidence available to support this treatment recommendation is sparse, the relative benefits versus harms are judged to be in favor of the recommendation. Research into the effectiveness of these interventions is justified and required.

Knowledge gaps

- What is the impact of notified versus unnotified bystander responses on clinically meaningful patient outcomes such as survival to hospital discharge with good neurologic outcome, survival to hospital discharge, survival to hospital admission, and ROSC?
- What is the impact of notified versus unnotified bystander responses on bystander CPR rates and time to first compressions?

Measuring performance of resuscitation systems (EIT 640)

Among resuscitation systems caring for patients in cardiac arrest in any setting (P), does a performance measurement system (I), compared with no system (C), change survival to hospital discharge, skill performance in actual resuscitations, survival to admission, system-level variables (O)?

Consensus on science

For the critical outcome **survival to hospital discharge—OHCA**, we identified very-low-quality evidence (downgraded for indirectness, imprecision, and inconsistency) from 4 observational studies enrolling 6983 patients.[181–184] One of these studies contributed a disproportional number of patients (6331).[181] Heterogeneity prevented calculating a pooled effect and limited our confidence in the individual effects. Individual effects appear weakly in favor of quality measurement.

For the critical outcome of **survival to hospital discharge—in-hospital cardiac arrest (IHCA)**, we identified low-quality evidence (downgraded for indirectness, imprecision, and inconsistency) from 2 observational studies enrolling 318 patients showing no benefit in survival to hospital discharge (data cannot be pooled).[185,186] One study showed a modest improvement in neurologic outcomes.[186] There was very-low-quality evidence (downgraded for indirectness, imprecision, and inconsistency) from 3 observational time-series studies enrolling 105 003 patients.[187–189] One of these studies contributed a disproportional number of patients (104 732).[187] Heterogeneity prevented calculation of a pooled effect. Individual effects were in favor of quality measurement in 2 studies[187,188] and showed no effect for the third study.[189]

For the important outcome of **chest compression depth**, we have identified very-low-quality evidence (downgraded for risk of bias and inconsistency) from 3 observational studies enrolling 990 patients.[182,185,186] Heterogeneity prevented calculating a pooled effect and limited our confidence in the individual effects. Individual effects appear weakly in favor of quality measurement.

For the important outcome of **chest compression rate**, we identified very-low-quality evidence (downgraded for risk of bias and inconsistency) from 6 observational studies, enrolling 1020 patients in 4 of the studies, and an unreported number in 2 others.[182–186,189] Heterogeneity prevented calculating a pooled effect and limited our confidence in the individual effects. Three of the studies appear to weakly favor quality measurement, whereas 3 showed no effect.

For the important outcome of **other system variables**, very-low-quality evidence (downgraded for risk of bias, indirectness) from 1 human observational study shows defibrillator-equipped resource response time decreased to 5.3 minutes from 6.7 minutes when an optimization strategy was implemented.[181] Across studies, the direction of the effect was consistent, and at times the effect size was large and statistically significant. There is no evidence that data collection and feedback are deleterious to patients in any way.

Treatment recommendation

We suggest the use of performance measurement and quality improvement initiatives in organizations that treat cardiac arrest (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place greater value on the potential for lives saved and the idea that you can only improve what you can measure, and lesser value on the costs associated with performance measurement and quality improvement interventions.

Once new guidelines have been approved and frontline providers trained, their real-life integration is often overlooked. Assessing clinical performance and using a system to continuously assess and improve quality can improve compliance with guidelines.

Knowledge gaps

There is a need to

- Identify the most appropriate approach to measure performance
- Better understand the influence of local community and organizational characteristics

CPR feedback devices in training (EIT 648)

Among students who are taking BLS or ALS courses in an educational setting (P), does CPR feedback device use (I), compared with no use of CPR feedback devices (C), change/improve patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?

Consensus on science

For the critical outcomes of **improvement of patient outcomes and skill performance at actual resuscitation**, we found no evidence that examined the use of feedback devices.

For the important outcome of **skill performance at 1 year**, we found 5 studies (low-quality evidence downgraded for imprecision, inconsistency, and risk of bias) that retested subjects after a period of time (6 weeks to 12 months) and showed substantial decay in skills irrespective of whether a feedback device was used.[50,191,192,211,214] Meta-analysis was not possible.

For the important outcome of **skill performance at course conclusion**, we found 28 low-quality studies (downgraded for risk of bias, imprecision, and indirectness) that demonstrated some limited improvement in CPR quality.[50,191–217] Compression depth, compression rate, chest recoil, hand placement, hands-off time, and ventilation were used as markers of CPR quality. Heterogeneous reporting prevented some meta-analyses.

There were 23 directive feedback studies[50,191–207,212–216] showing that in comparison with no feedback devices, the use of feedback devices

- Had no effect on mean depth (SMD, −0.10; 95% CI, −0.58 to 0.39; $P = 0.70$).
- Increased the number of participants able to compress to the correct depth (OR, 3.47; 95% CI, 2.55–4.73; $P < 0.001$).
- Was associated with a compression rate closer to 100/min, and increased number of subjects compressed at the correct rate (OR, 4.10; 95% CI, 2.81–6.00; $P < 0.001$).
- Volume and rate of ventilations improved in the majority of studies.
- Hand placement was not shown to improve (1.38; 95% CI, 0.88–2.15; $P = 0.16$), but recoil was (OR, 1.63; 95% CI, 1.10–2.42; $P = 0.02$).

Five tonal guidance studies improved compression rate (OR, 1.72; 95% CI, 1.13–2.64; $P = 0.01$).[208–211,217] One study showed statistically significantly reduced mean compression depth, but this may not be clinically significant (39.3 ± 9.5 mm to 35.8 ± 8.2 mm; $P < 0.01$).[208] Two other studies showed a nonsignificant increase in the proportion of participants unable to perform compressions to adequate depth (OR, 1.23; 95% CI, 0.87–1.74; $P = 0.24$).[209,210] Two neonatal studies showed improved compliance with chest compression rates and manual inflation rates, but results were limited to certain pieces of music ("Radetzkymarsch"[211] and ABBA's "SOS"[217]).

For the important outcome of **improvement of cognitive knowledge**, we found no evidence that examined the use of feedback devices.

Treatment recommendation

We suggest the use of feedback devices that provide directive feedback on compression rate, depth, release, and hand position during training (weak recommendation, low-quality evidence). If feedback devices are not available, we suggest the use of tonal guidance (examples include music or metronome) during training to improve compression rate only (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

Unfortunately, several of the tonal studies identified compression depth decreasing as the participant focused on the rate. The positive effect of real-time feedback devices on CPR performance was found only at the end of training.

In making these recommendations, a higher value was placed on the potential of improving CPR performance over the potential costs. Used by BLS instructors, these real-time feedback adjuncts can provide accurate participant performance information to give effective feedback during training.[202]

Real-time directive feedback devices provide immediate feedback on performance, including depth, rate, hand placement, and release. Guidance feedback devices are tonal devices that only prompt rate.

Knowledge gaps

- The effectiveness of different types of feedback is unknown.
- What is the role of instructors in combination with the use of real-time feedback devices?
- The effect of real-time feedback on performance of ventilations (currently limited by available technology) is unknown.
- The effect of real-time feedback on psychomotor skill retention, attainment of cognitive knowledge, performance in actual resuscitations, and patient outcomes is unknown.

Debriefing of resuscitation performance (EIT 645)

Among rescuers who are caring for patients in cardiac arrest in any setting (P), does briefing or debriefing (I), compared with no briefing or debriefing (C), change survival, skill performance in actual resuscitations, improve quality of resuscitation (eg, reduce hands-off time), cognitive knowledge (O)?

Consensus on science

There were no RCTs and no studies comparing briefing as the sole intervention. Data from 2 in-hospital observational before-after studies, 1 in adults[185] and 1 in pediatrics,[186] involving a total 318 patients and 2494 epochs of chest compressions demonstrate improved outcomes after implementation of a data-driven, performance-focused debriefing program for resuscitation team members using CPR-quality defibrillator transcripts.

For the critical outcome of **survival with favorable neurologic outcome at discharge in in-hospital cardiac arrest (IHCA)**, very-low-quality data (downgraded for imprecision) demonstrated an improvement with debriefing from 28.8% to 50.0% (RR, 1.73; 95% CI, 1.04–2.43).

For the critical outcome of **survival to hospital discharge**, very-low-quality evidence (downgraded for inconsistency) yielded an insignificant improvement from 17% to 18.8% (RR, 1.35; 95% CI, 0.81–2.1).

For the critical outcome of **ROSC**, low-quality evidence associated the intervention with an increase of 54.7% to 66.5% (RR, 1.25; 95% CI, 1.06–1.41).

For the critical outcomes of **compression depth and compression rate within target range**, moderate-quality data (upgraded for strong association) demonstrated an improvement for both (RR, 1.18; 95% CI, 1.15–1.21 and RR, 1.25; 95% CI, 1.21–1.29, respectively).

For these same outcomes in the out-of-hospital setting, the quality of evidence was further downgraded for indirectness, resulting in very-low-quality evidence for the 3 survival outcomes and low-quality evidence for the 2 process outcomes.

Treatment recommendations

We recommend data-driven, performance-focused debriefing of rescuers after IHCA in both adults and children (strong recommendation, low-quality evidence). We suggest data-driven, performance-focused debriefing of rescuers after OHCA in both adults and children (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making the discordant recommendation for IHCA, we have placed a high value on the consistency and precision of the improvement in CPR quality and short-term survival as the proximal end points of the educational intervention. We have placed a lesser value on the potential costs of implementation.

Knowledge gaps

- The benefit of data-driven, performance-focused debriefing for OHCA is unknown.
- The ideal format in which data-driven, performance-focused debriefing is delivered is unknown.
- The proper source of objective data for data-driven, performance-focused debriefing (eg, CPR-quality transcript, video) needs to be determined.
- The optimal duration of data-driven, performance-focused debriefing is unknown.
- The most effective interval between event and data-driven, performance-focused debriefing remains to be determined.

Medical emergency teams (MET) for adults (EIT 638)

Among adults who are at risk for cardiac or respiratory arrest in the hospital (P), does use of the Early Warning Score (EWS)/response teams/MET systems (I), compared with no such responses (C), change survival to hospital discharge, in-hospital incidence of cardiac/respiratory arrest, survival to hospital discharge with good neurologic outcome (O)?

Consensus on science

For the critical outcome of **survival to hospital discharge**, we have found low-quality evidence (downgraded for risk of bias and inconsistency) from 2 RCTs[218,219] and very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 33 non-RCTs.[220–252] Of the 2 RCTs, one demonstrated no significant difference between control hospitals (functioned as usual) and intervention hospitals (introduced a MET team) for both unadjusted ($P = 0.564$; Diff, −0.093; 95% CI, −0.423 to 0.237) and adjusted ($P = 0.752$; OR, 1.03; 95% CI, 0.84–1.28) survival.[218] The other study demonstrated a significant difference between control wards and intervention wards (introduction of a critical care outreach service) with all patients (OR, 0.70; 95% CI, 0.50–0.97), and matched randomized patients (OR, 0.52; 95% CI, 0.32–0.85).[219] Of the 33 nonrandomized studies reporting mortality, no studies reported statistically significant worse outcomes for the intervention; 15 studies with no adjustment demonstrated no significant improvement[220–234]; 6 studies with no adjustment demonstrated significant improvement[235–240]; 1 study with no adjustment reported on rates, which improved with MET, but did not report on significance[241]; 1 study with no adjustment demonstrated significant improvement for medical patients but not surgical patients (combined significance not reported)[242]; 4 studies with adjustment demonstrated significant improvement both before and after adjustment[243,244,250,252]; 2 studies with adjustment demonstrated no significant improvement both before and after adjustment[245,246]; 2 studies with adjustment demonstrated significant improvement before adjustment but not after adjustment[247,251]; 1 study with adjustment demonstrated significant improvement before adjustment but not after adjustment[27]; 1 study that reported on both unexpected mortality and overall mortality showed significant improvement both before and after adjustment for unexpected mortality but no significant improvement both before and after adjustment for overall mortality[249]; and 1 before-after study that presented "after" data for unexpected mortality in 3 separate time bands demonstrated significant improvement in time band 3 before adjustment and in time bands 2 and 3 after adjustment.[248] The heterogeneous nature of the studies prevents pooling of data; however, there is a suggestion of improved hospital survival in those hospitals that introduce a MET service, and a suggestion of a dose-response effect, with higher-intensity systems (eg, higher MET calling rates, senior medical staff on MET teams) being more effective.

For the critical outcome of **in-hospital incidence of cardiac/respiratory arrest**, we found low-quality evidence (downgraded for risk of bias and indirectness) from 1 RCT[218] and very-low-quality evidence (downgraded for risk of bias, inconsistency, and indirectness) from 31 further non-RCTs.[220,221,224,225,227–230,232–247,249,250,253–256] For the 1 RCT,[218] no significant difference between control hospitals and intervention hospitals, both unadjusted ($P = 0.306$; Diff, −0.208; 95% CI, −0.620 to 0.204) and adjusted ($P = 0.736$; OR, 0.94; 95% CI, 0.79–1.13), was demonstrated. Of the 31 observational studies reporting on cardiac arrest rates, 1 before-after study using an aggregated weighted scoring system (Modified Early Warning Score [MEWS]) reported significantly higher cardiac arrest rates in MEWS bands 3 to 4 after intervention, but not in MEWS bands 0 to 2 or 5 to 15, and overall cardiac arrest rate significance was not reported[232]; 7 studies with no adjustment demonstrated no significant improvement in cardiac arrest rates after the introduction of a MET system[224,225,228–230,233,234]; 15 studies with no adjustment demonstrated significant improvement in cardiac arrest rates after the introduction of a MET system[220,221,227,235,236,238,239,241–244,247,253–256]; 4 studies with adjustment demonstrated significant improvement in cardiac arrest rates after the introduction of a MET system both before and

after adjustment[237,240,250,252,256]; 1 study with contemporaneous controls demonstrated no significant improvement in cardiac arrest rates after the introduction of a MET system both before and after adjustment[246]; 1 study with adjustment demonstrated significant improvement before adjustment for whole of hospital and non–intensive care unit (ICU) cardiac arrest rates, but only for non-ICU cardiac arrest rates after adjustment[245]; and 1 before-after study that presented "after" unadjusted data for cardiac arrest in 3 separate time bands demonstrated significant improvement in time bands 2 and 3.[249] The heterogeneous nature of the studies prevents pooling of data. However, there is a suggestion of a reduced incidence of cardiac/respiratory arrest in those hospitals that introduce a MET service, and a suggestion of a dose-response effect, with higher-intensity systems (eg, higher MET calling rates, senior medical staff on MET teams) being more effective.

Treatment recommendations

We suggest that hospitals consider the introduction of an EWS/response team/MET system to reduce the incidence of IHCA and in-hospital mortality (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

This recommendation places a high value on the outcomes—the prevention of IHCA and death—relative to the likely substantial cost of the system. Such a system should provide a system of care that includes (a) staff education about the signs of patient deterioration; (b) appropriate and regular vital signs monitoring of patients; (c) clear guidance (eg, via calling criteria or early warning scores) to assist staff in the early detection of patient deterioration; (d) a clear, uniform system of calling for assistance; and (e) a clinical response to calls for assistance. The best method for the delivery of these components is unclear.[98] The "Recommended Guidelines for Monitoring, Reporting, and Conducting Research on Medical Emergency Team, Outreach, and Rapid Response Systems: An Utstein-Style Scientific Statement"[257] should be used by hospitals to collect the most meaningful data to optimize system interventions and improve clinical outcomes.

Knowledge gaps

- What are the ideal components of the "afferent limb" of a rapid response system, eg, which vital signs, observations, and/or laboratory parameters, and with what frequency?
- What are the ideal components of an education program in the recognition of a deteriorating patient?
- What is the ideal mechanism for escalation for assistance (eg, conventional escalation versus automated electronic escalation)?
- What is the ideal makeup of the efferent limb (the response team)?

Disclosures

2015 CoSTR Part 8: Education, implementation, and teams: writing group disclosures.

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Judith C. Finn	Curtin University	NHMRC (Australia)†	None	None	None	None	None	None
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Robert Frengley	Waikato District Health Board	None	None	None	None	None	None	None
Robert Greif	Universitätsspital Anesthesiology and Pain Medicine	Departmental Grants*	None	None	None	None	None	Journal Trends in Anesthesia and Critical Care; Editor in chief*
Taku Iwami	Kyoto University Health Service	None	None	None	None	None	None	None
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

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Appendix A.

CoSTR Part 8: PICO Appendix.

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 8	EIT	EIT 623	High-Fidelity Manikins in Training	Among participants undertaking ALS training in an education setting (P), does the use of high-fidelity manikins (I), compared with the use of low-fidelity manikins (C), change patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Adam Cheng, Andy Lockey
Part 8	EIT	EIT 624	Cardiac Arrest Centers	Adults and children in OHCA (P), does transport to a specialist cardiac arrest center (I), compared with no directed transport (C), change neurologically intact survival at 30 days, survival to hospital discharge with good neurologic outcome, survival to hospital discharge, hospital admission, ROSC (O)?	Judith Finn, Dion Stub
Part 8	EIT	EIT 628	Timing for BLS Retraining	Among students who are taking BLS courses (P), does any specific interval for update or retraining (I), compared with standard practice (ie, 12 or 24 monthly) (C), change patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Taku Iwami, Theresa Olasveengen
Part 8	EIT	EIT 631	Team and Leadership Training	Among students who are taking ALS courses in an educational setting (P), does inclusion of specific leadership or team training (I), compared with no such specific training (C), change patient outcomes, bystander CPR performance, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Koen Monsieurs, Elaine Gilfoyle
Part 8	EIT	EIT 633	Timing for Advanced Resuscitation Training	Among students who are taking ALS courses in an educational setting (P), does any specific interval for update or retraining (I), compared with standard practice (ie, 12 or 24 monthly) (C), change/improve patient outcomes, skill performance in actual resuscitations, skill performance between course completion and 1 year; skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Matthew Ma, Chih-wei Yang, Farhan Bhanji
Part 8	EIT	EIT 634	Resource-Limited Settings	Among students who are taking BLS or ALS courses in a resource-limited educational setting (P), does any educational approach (I), compared with other approaches (C), change clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, cognitive knowledge (O)?	David Kloeck, Traci Wolbrink
Part 8	EIT	EIT 637	Precourse Preparation for Advanced Life Support Courses	Among students who are taking ALS courses in an educational setting (P), does inclusion of specific precourse preparation (eg, eLearning and pretesting) (I), compared with no such preparation (C), change survival rates, skill performance in actual resuscitations, cognitive knowledge, skill performance at course conclusion, skill performance at 1 year, skill performance at time between course conclusion and 1 year (O)?	Andy Lockey, Mary Mancini, John Billi

Continued

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 8	EIT	EIT 638	Medical Emergency Teams for Adults	Among adults who are at risk for cardiac or respiratory arrest in the hospital (P), does use of the Early Warning Score (EWS)/response teams/MET systems (I), compared with no such responses (C), change survival to hospital discharge, in-hospital incidence of cardiac/respiratory arrest, survival to hospital discharge with good neurologic outcome (O)?	Mary Mancini, Robert Frengley
Part 8	EIT	EIT 640	Measuring Performance of Resuscitation Systems	Among resuscitation systems caring for patients in cardiac arrest in any setting (P), does a performance measurement system (I), compared with no system (C), change survival to hospital discharge, skill performance in actual resuscitations, survival to admission, system-level variables (O)?	Blair Bigham, Robert Schultz
Part 8	EIT	EIT 641	Implementation of Guidelines in Communities	Within organizations that provide care for patients in cardiac arrest in any setting (P), does implementation of resuscitation guidelines (I), compared with no such use (C), change survival to 180 days with good neurologic outcome, survival to hospital discharge, bystander CPR performance, ROSC (O)?	Jon Rittenberger, Theresa Olasveengen, Patrick Ko
Part 8	EIT	EIT 645	Debriefing of Resuscitation Performance	Among rescuers who are caring for patients in cardiac arrest in any setting (P), does briefing or debriefing (I), compared with no briefing or debriefing (C), change survival, skill performance in actual resuscitations, improve quality of resuscitation (eg, reduce hands-off time), cognitive knowledge (O)?	Robert Greif, Dana Edelson
Part 8	EIT	EIT 647	CPR Instruction Methods (Self-Instruction Versus Traditional)	Among students who are taking BLS courses in an educational setting (P), does video or computer self-instructions (I), compared with traditional instructor-led courses (C), change survival, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Ming-Ju Hsieh, Matthew Ma, Judy Young
Part 8	EIT	EIT 648	CPR Feedback Devices in Training	Among students who are taking BLS or ALS courses in an educational setting (P), does CPR feedback device use (I), compared with no use of CPR feedback devices (C), change improve patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge (O)?	Joyce Yeung, Mary Ann McNeil
Part 8	EIT	EIT 649	Basic Life Support Training for High-Risk Populations	For people at high risk of OHCA (P), does focused training of likely rescuers (eg, family or caregivers) (I) compared with no such targeting (C), change survival with favorable neurologic outcome at discharge, ROSC, bystander CPR performance, number of people trained in CPR, willingness to provide CPR (O)?	Janet Bray, Marion Leary
Part 8	EIT	EIT 651	AED Training Methods	Among students who are taking AED courses in an educational setting (P), does any specific training intervention (I), compared with traditional lecture/practice sessions (C), change clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, cognitive knowledge, use of AEDs (O)?	Jan Breckwoldt, Henrik Fischer
Part 8	EIT	EIT 878	Social Media Technologies	For OHCA (P), does having a citizen CPR responder notified of the event via technology or social media (I), compared with no such notification (C), change survival to hospital discharge with good neurologic outcome, survival to hospital discharge, hospital admission, ROSC, bystander CPR rates, time to first compressions (O)?	Zuzana Triska, Steven Brooks
Part 8	EIT	EIT 881	Compression-Only CPR Training	Among communities that are caring for patients in cardiac arrest in any setting (P), does teaching compression-only CPR (I), compared with conventional CPR (C), change survival rates, bystander CPR rates, willingness to provide CPR (O)?	Jonathan Duff, Aaron Donoghue

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Part 9: First aid
2015 International Consensus on First Aid Science with Treatment Recommendations☆

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Introduction

Definition of first aid

The International Liaison Committee on Resuscitation (ILCOR) First Aid Task Force first met in June 2013. Comprising nominated members from around the globe appointed by each ILCOR member organization, the task force members first agreed to the goals of first aid and produced a definition of first aid as it might apply to the international setting. Task force members considered an agreed-upon definition essential for the subsequent development of research questions, evidence evaluation, and treatment recommendations.

First aid is defined as the **helping behaviors** and **initial care** provided for an acute illness or injury. First aid can be initiated by anyone in any situation.

A *first aid provider* is defined as someone trained in first aid who should

- Recognize, assess, and prioritize the need for first aid
- Provide care by using appropriate competencies
- Recognize limitations, and seek additional care when needed

The goals of first aid are to preserve life, alleviate suffering, prevent further illness or injury, and promote recovery.

This definition of first aid addresses the need to recognize injury and illness, the requirement to develop a specific skill base, and the need for first aid providers to simultaneously provide immediate care and activate emergency medical services (EMS) or other medical care as required. First aid assessments and interventions should be medically sound and based on evidence-based medicine or, in the absence of such evidence, on expert medical consensus. The scope of first aid is not purely scientific, as both training and regulatory requirements will influence it. Because the scope of first aid varies among countries, states, and provinces, the treatment recommendations contained herein may need to be refined according to circumstances, need, and regulatory constraints.

One difference between this 2015 definition and that used for the 2010 process is that the task force did not restrict first aid to "assessments and interventions that can be performed. . .with minimal or no equipment." We acknowledge that, in most cases, equipment might not be available to first aid providers, particularly for bystanders and lay providers. However, the First Aid Task Force noted that, in some countries, supplementary first aid supplies now include inexpensive and compact pulse oximeters, glucose meters, and other adjuncts never before considered to be in the realm of first aid. In the 2015 treatment recommendations, we have striven to remain true to the "minimal or no equipment" approach, but recognize that addition of equipment, used by those trained to use and maintain it, may enhance care.

The task force strongly believes that education in first aid should be universal: everyone can and should learn first aid.

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[2] The members of the First Aid Chapter Collaborators are listed in the Acknowledgments section.

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How and why topics were chosen

In the autumn of 2012, ILCOR approved the First Aid Task Force as a fully participating task force in the 2015 ILCOR international evidence evaluation and appointed 2 international co-chairs. In the spring of 2013, each member council of ILCOR nominated individuals for membership in the First Aid Task Force. In addition to the co-chairs, 11 task force members were appointed, representing the ILCOR member organizations of the American Heart Association (AHA), the European Resuscitation Council (ERC), the Heart and Stroke Foundation of Canada, the Australian Resuscitation Council, the InterAmerican Heart Foundation, and the Resuscitation Council of Asia. Members included physicians specializing in anesthesia, critical care/resuscitation, emergency medicine, cardiology, internal medicine, and pediatric emergency medicine, as well as paramedics specializing in prehospital care guideline development, specialists in first aid course education and curriculum development, and a specialist in first aid evidence evaluation methodology and guideline development.

The task force convened in June 2013 to review the topics and questions that were evaluated in 2005 and 2010, past research questions formulated in the PICO style (population, intervention, comparator, outcomes) that were never completed, and the new questions that had been submitted since 2010 to the task force, and a priority list created. Topics were reviewed for areas of controversy, known additional new science, and subject matter not previously evaluated. Task force members created a priority list for review, and the top 10 priority-ranked PICO questions were assigned. After the successful commencement of the workflow, the task force co-chairs added a further 12 PICO questions, including 5 new questions, 1 derived question, and 6 that had been previously reviewed. Selected PICO questions that had been previously reviewed were, in some cases, reworded to facilitate literature searches, and outcomes were decided upon by group consensus.

Evidence reviewers were recruited through a call for volunteers distributed by ILCOR to stakeholder organizations around the world. More than 30 individual reviewers were assigned to topics, usually by preference or expertise, but avoiding any direct conflicts of interest. In general, 2 evidence reviewers were assigned to each PICO, supervised by a member of the task force designated as the task force question owner. Evidence reviewers included physicians with diverse specialties including emergency medicine, EMS, wilderness medicine, critical care, cardiology, occupational medicine, toxicology, anesthesia, pediatric emergency medicine, public health, and epidemiology, as well as paramedics, nurse practitioners and first aid education specialists with experience in guideline and curriculum development, and professional evidence evaluation and methodology experts.

The evidence evaluation process

For the 2015 international evidence evaluation process, the AHA developed a new Web-based information and documentation platform, the Systematic Evidence Evaluation and Review System (SEERS), to support the ILCOR systematic reviews and to capture the data in reusable formats. This Web-based system facilitated structured reviews in a consistent format that would support the ultimate development of science summaries and evidence-based treatment recommendations.

Each task force performed a detailed systematic review based on the recommendations of the Institute of Medicine of the National Academies,[1] using the methodological approach proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[2] After identifying and prioritizing the PICO questions to be addressed,[3] and with the assistance of information specialists, a detailed search for relevant articles was performed in each of 3 online databases (PubMed, Embase, and the Cochrane Library).

By using detailed inclusion and exclusion criteria, articles were screened for further evaluation. The reviewers for each question created a reconciled risk of bias assessment for each of the included studies, using state-of-the-art tools: Cochrane for randomized controlled trials (RCTs),[4] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[5] and GRADE for observational studies that inform both therapy and prognosis questions.[6]

GRADE evidence profile tables[7] were then created to facilitate an evaluation of the evidence in support of each of the critical and important outcomes. The quality of the evidence (or confidence in the estimate of the effect) was categorized as high, moderate, low, or very low,[8] based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias).[9]

The GRADE evidence profile tables were then used to create a written summary of evidence for each outcome (the consensus on science statements). Whenever possible, consensus-based treatment recommendations were then created. These recommendations (designated as strong or weak) were accompanied by an overall assessment of the evidence and a statement from the task force about the values and preferences that underlie the recommendations. Strong recommendations use the words "we recommend," and weak recommendations use the words "we suggest."

Further details of the methodology that underpinned the evidence evaluation process are found in "Part 2: Evidence Evaluation and Management of Conflicts of Interest."

The learning curve for use of the GRADE evidence evaluation methodology was steep and resulted in a total of 22 PICO questions, including 6 new questions, being completed by the task force before the ILCOR 2015 International Consensus Conference on CPR and ECC Science With Treatment Recommendations in February 2015. The remaining topics not reviewed for 2015 have since been reprioritized, with the addition of several new questions that were identified during the ILCOR 2015 work process.

Very little research has been conducted in first aid, and most of the recommendations are extrapolations from research in the prehospital or hospital setting. The selected methodology for evaluation of the literature led to the elimination of lower-quality data from animal studies, case series, and case reports, except for topics where no human studies were identified that met the inclusion criteria. These more stringent requirements led to the inclusion of studies with a higher initial quality of evidence, but most studies were eventually downgraded due to indirectness for the first aid setting. The gaps in knowledge have been identified by the evidence reviewers and summarized at the end of each treatment recommendation. It is our hope that these knowledge gaps will be filled through future research. In the absence of evidence-based medicine to support a treatment recommendation, the task force has made many recommendations based on expert opinion, perceived best practice, and the principle of "do no harm."

PICO questions reviewed

First Aid for Medical Emergencies

- Recovery position (FA 517)
- Optimal position for shock (FA 520)
- Oxygen administration for first aid (FA 519)
- Bronchodilator use for asthma with difficulty breathing (FA 534)
- Stroke recognition[3] (FA 801)

[3] Topics not previously reviewed.

Aspirin for Chest Pain
- Aspirin for chest pain: administration[4] (FA 871)
- Aspirin for chest pain: early compared with late (FA 586)

Epinephrine for Anaphylaxis and Treatment of Hypoglycemia, Exertion-Related Dehydration, and Chemical Eye Injuries
- Second dose of epinephrine for anaphylaxis (FA 500)
- Hypoglycemia treatment[5] (FA 795)
- Exertion-related dehydration and oral rehydration (FA 584)
- Eye chemical injury: irrigation (FA 540)

First Aid for Trauma Emergencies
- Control of bleeding (FA 530)
- Hemostatic dressings (FA 769)
- Use of a tourniquet (FA 768)
- Straightening of an angulated fracture (FA 503)
- First aid treatment for an open chest wound[6] (FA 525)
- Cervical spinal motion restriction (FA 772)
- Concussion[7] (FA 799)
- Cooling of burns (FA 770)
- Wet compared with dry burn dressing (FA 771)
- Dental avulsion (FA 794)

Education
- First aid training[8] (FA 773)

First aid for medical emergencies

Important medical topics reviewed for 2015 include use of supplementary oxygen for purposes other than patients with chest pain, positioning for shock and recovery, use of bronchodilators for asthmatics with acute shortness of breath, use of a second dose of epinephrine for anaphylaxis, and the administration of aspirin for chest pain. The exhaustive ILCOR literature search, with the help of information specialists and the more rigorous GRADE methodology, led to a few additional recommendations as well as differences in strength of recommendations.

- No evidence was found to support a change in current practice for the use of supplementary oxygen by first aid providers.
- The position recommended for the patient in shock remains the supine position, although there is some evidence suggesting passive raising of the legs between 30° and 60° may have a transient (7 min or less) benefit (Modified).
- There is a change in recommendations for the position of a normally breathing, unresponsive person. Because a potential need has been shown for advanced airway management in the supine position compared with a lateral recumbent position, we are now recommending that the lateral recumbent position be used as a "recovery" position (Modified).
- Assisting with the administration of inhaled bronchodilators is recommended for asthmatics with acute shortness of breath (Unchanged).
- Although questions remain about the ability of a first aid provider to recognize anaphylaxis, the use of a second dose of epinephrine via an autoinjector is beneficial when a first dose fails to improve symptoms. Adverse effects were not reported in studies included, although this may reflect the administration of epinephrine with an autoinjector, thus limiting opportunity for an inadvertent overdose injection (Modified).
- The use of aspirin for chest pain has been previously reviewed; however, the task force agreed that this topic should be looked at again in light of the newly implemented GRADE methodology and the emergence of newer medications used for acute myocardial infarction (MI). Thus, the original question asking if aspirin should be administered for patients with MI was reviewed, followed by a review of the early (i.e., prehospital) use of aspirin for chest pain versus delayed (i.e., in-hospital) administration of aspirin (Modified).
- A new review topic is the use of stroke assessment systems to aid with recognition of stroke, with findings that will have enormous implications for first aid and public health. This review found a significant decrease in time between symptom onset and arrival at a hospital or emergency department with the use of these assessment tools; use of such tools may reduce the degree of damage from stroke when treatment is initiated early (New).
- A new review looks at use of oral dietary sugars for mild symptomatic hypoglycemia in diabetics. The studies for this review administered various forms of dietary sugars, such as specific candies, dried fruit strips, juice, or milk, in a dose-equivalent amount compared with glucose tablets, to diabetics with symptomatic hypoglycemia who were conscious and able to swallow and follow commands. It was concluded that, as a group, dietary sugar products were not as effective as glucose tablets for relief of hypoglycemia, but all studied forms showed benefit and potential usefulness in cases where glucose tablets are not available (New).

Recovery position (FA 517)

Among adults who are breathing and unresponsive outside of a hospital (P), does positioning in a lateral, side-lying, recovery position (I), compared with supine position (C), change overall mortality, need for airway management, the incidence of aspiration, the likelihood of cervical spinal injury, complications, incidence of cardiac arrest (O)?

Introduction

In 2010, the treatment recommendation for this topic stated that there was no evidence that moving an individual into a recovery position was beneficial. It also stated that if an individual with a suspected cervical spine injury had to be turned onto his or her side, the high arm in endangered spine (HAINES) position seemed to be safer.[10] An extensive literature search and use of GRADE methodology resulted in some studies from the 2010 review being excluded from the 2015 review and other newly identified studies being included. The revised 2015 recommendations reflect this rigorous evidence evaluation process.

Although some studies included in this review showed no benefit to a recovery position over a supine position, there were studies that demonstrated significant benefit in terms of maintaining an open airway. The task force thought a priority outcome for any recovery position would be maintenance of an open airway.

Consensus on science

Lateral, side-lying recovery position compared with supine position. For the critical outcome of **the incidence of aspiration**, we identified very-low-quality evidence (downgraded for imprecision) from 1 observational study with a total of 142 patients[11] found in the left lateral decubitus or supine position demonstrating no benefit to being in the left lateral position (relative risk [RR], 0.93; 95% confidence interval [CI], 0.55–1.58). The same observational study had a total of 132 patients found in the right lateral decubitus or supine position and demonstrated no benefit to being in the right lateral position (RR, 1.15; 95% CI, 0.67–1.96).

For the critical outcome of **need for airway management**, only studies with indirect measures of potential need for airway management were identified, including measures of total airway

[4] Topics derived from existing questions.
[5] Topics not previously reviewed.
[6] Topics not previously reviewed.
[7] Topics not previously reviewed.
[8] Topics not previously reviewed.

volume and stridor scores. Very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 observational study with 17 patients[12] demonstrated the benefit of the lateral position by increasing total airway volume (mean difference [MD], 2.7; 95% CI, 0.88–4.52), and very-low-quality evidence (downgraded for indirectness, and imprecision) from 1 observational study with 30 patients[13] demonstrated the benefit of the lateral position by decreasing stridor score (MD, −0.9; 95% CI, −1.21 to −0.59).

HAINES modified recovery position compared with lateral recovery position. For the critical outcome of the **likelihood of cervical spinal injury**, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 observational study with 2 healthy volunteers[14] demonstrating less overall lateral cervical spine flexion with the HAINES position (MD, −17; 95% CI, −21.39 to −12.62), no difference in lateral flexion of the upper cervical spine with the HAINES position (MD, −4.5; 95% CI, −11.7 to 2.7), and less lateral flexion of the lower cervical spine with the HAINES position (MD, −12.5; 95% CI, −21.52 to −3.47). We have also identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 observational study with 10 cadavers with surgically created cervical instability[15] demonstrating no difference in linear translation between the HAINES recovery position and the 1992 ERC lateral recovery position in terms of medial/lateral movement (MD, −1.1; 95% CI, −5.17 to 2.97), compression/distraction (MD, −1.06; 95% CI, −3.7 to 1.58), or anterior/posterior movement (MD, −0.24; 95% CI, −2.96 to 2.48).

Left lateral position compared with right lateral position. For the critical outcome of **the incidence of aspiration**, we identified very-low-quality evidence (downgraded for imprecision) from 1 observational study with a total of 50 patients[11] who were found in the left lateral decubitus or right lateral decubitus position, demonstrating no benefit to the left versus the right lateral position (RR, 0.82; 95% CI, 0.42–1.6).

1992 ERC recovery position compared with old left lateral, Semiprone Resuscitation Council (UK) recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for imprecision) from 1 observational study with 6 healthy volunteers[16] demonstrating no difference in either position in terms of venous occlusion (RR, 5; 95% CI, 0.29–86.44), arterial insufficiency with venous occlusion (RR, 5; 95% CI, 0.29–86.44), or left arm discomfort (RR, 7; 95% CI, 0.44–111.92).

1997 Resuscitation Council (UK) recovery position compared with 1992 ERC recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 100 healthy volunteers[17] demonstrating less pain/discomfort with the 1992 ERC recovery position (RR, 3.25; 95% CI, 1.81–5.83).

AHA Semiprone recovery position compared with 1992 ERC recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 40 healthy volunteers placed in 1 or both of the positions[18] demonstrating less discomfort with the AHA recovery position (RR, 0.36; 95% CI, 0.14–0.95).

Morrison, Mirakhur, and Craig recovery position compared with Rautek recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 20 healthy volunteers placed in 1 or both of the positions[18] demonstrating no difference in discomfort between the positions (RR, 1.25; 95% CI, 0.47–3.33).

AHA Semiprone recovery position compared with Morrison, Mirakhur, and Craig recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 30 healthy volunteers placed in 1 or both of the positions[18] demonstrating no difference in discomfort between the positions (RR, 0.4; 95% CI, 0.14–1.17).

AHA Semiprone recovery position compared with Rautek recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 30 healthy volunteers placed in 1 or both of the positions[18] demonstrating no difference in discomfort between the positions (RR, 0.5; 95% CI, 0.16–1.59).

1992 ERC recovery position compared with Morrison, Mirakhur, and Craig recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 30 healthy volunteers placed in 1 or both of the positions[18] demonstrating no difference in discomfort between the positions (RR, 1.1; 95% CI, 0.53–2.23).

1992 ERC recovery position compared with Rautek recovery position. For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 observational study with 30 healthy volunteers placed in 1 or both of the positions[18] demonstrating no difference in discomfort between the positions (RR, 1.38; 95% CI, 0.58–3.24).

We did not identify any evidence to address the critical outcome of overall mortality or the important outcome of incidence of cardiac arrest.

Treatment recommendation

We suggest that first aid providers position individuals who are unresponsive and breathing normally into a lateral, side-lying recovery (lateral recumbent) position as opposed to leaving them supine (weak recommendation, very-low-quality evidence).

There is little evidence to suggest the optimal recovery position.

Values, preferences, and task force insights

Due to the low-quality evidence, it was difficult to make a recommendation as to the best recovery position. In terms of the HAINES position versus the standard left lateral position, the task force chose to put more value in the outcomes of a study that included cadavers with surgically created cervical spine instability over a study involving 2 healthy volunteers. We discussed the need for guideline developers to clearly address situations in which a first aid provider should not move a person into a recovery position, such as in the presence of pelvic or spinal injury.

Finally, discussions were held about the quality of breathing being used to help determine when it is appropriate to move an individual into the recovery position. The qualifying term “breathing normally” was included in the treatment recommendation so as to avoid the situation where a first aid provider recognizes that an individual is breathing and moves them into a recovery position when in fact chest compressions should be initiated.

Knowledge gaps

- Given the poor and outdated evidence available, further research is needed as to the best recovery position.
- When should a first aid provider not move a person into the recovery position?

Optimal position for shock (FA 520)

Among adults and children who receive first aid for shock (P), does positioning of the patient (I), compared with not positioning the patient (C), change overall mortality, complications, incidence of cardiac arrest, vital signs, hospital length of stay (O)?

Introduction

Similar to many topics reviewed for 2015, the reviewers for this PICO question were challenged by the paucity of good-quality scientific studies and the need to extrapolate data from studies in normotensive volunteers or from studies designed to determine fluid responsiveness in hypotensive intensive care unit patients. The diversity of positions studied and the varying time intervals between change of position or maintenance in a position created difficulty with interpreting results. Results often differed for the same position between studies. The supine position remains a basic position that the First Aid Task Force thinks is the most appropriate position for an individual with signs or symptoms of shock.

Consensus on science

After application of inclusion and exclusion criteria, 1 RCT and 5 observational trials were included in evidence evaluation. For the critical outcome of **vital signs**, we identified 1 RCT and 5 observational trials.

In normotensive subjects (P), passive leg raising to 60° for 5 min (I) compared with supine position (C). We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[19] enrolling 43 subjects (12 healthy subjects and 31 subjects with heart disease) showing no significant changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), or heart rate (HR).

In normotensive subjects with blood loss (P), passive leg raising to 45° for 5 min (I) compared with supine position for 5 min (C). We identified low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[20] enrolling 27 normotensive subjects with 500 mL blood loss, showing no benefit from passive leg raising (PLR) with a nonsignificant change in mean arterial blood pressure (MAP) but a benefit from PLR, with a significant

- Increase in thoracic bioimpedance cardiac index (MD, 0.8; 95% CI, 0.75–0.85)
- Increase in stroke index (SI) (MD, 15.00; 95% CI, 14.46–15.54)
- Decrease in HR (MD, −3; 95% CI, −3.56 to −2.44)

Subjects without blood loss showed a significant increase in cardiac index with PLR (MD, 0.3; 95% CI, 0.12–0.72) but no significant change in MAP or difference in HR.

In normotensive subjects with blood loss (P), standing for 5 min (I) compared with supine position (C) for 5 min. We identified low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[21] enrolling 27 normotensive subjects with 500 mL blood loss, showing a nonsignificant increase in MAP.

The standing position showed a statistically significant decrease in cardiac index compared with supine position (MD, −0.3; 95% CI, −0.38 to −0.22), and an increase in HR (MD, 22; 95% CI, 20.84–23.16).

In normotensive subjects (P), supine position for 3 min followed by PLR to 60° for 20 s (I) compared with supine position (C) for 3 min. We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[21] enrolling 10 normotensive subjects showing a benefit from the supine position plus PLR, with a significant increase in both cardiac output (CO) (MD, 0.6; 95% CI, 0.48–0.72) and stroke volume (SV) (MD, 7; 95% CI, 2.93–11.07).

In normotensive subjects (P), supine position for 3 min followed by PLR to 60° for 7 min (I) compared with supine position for 3 min (C). We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[21] enrolling 10 normotensive subjects showing no significant difference in MAP, CO, or HR. Thus, improvements in CO and SV seen with PLR at 20 s disappeared by 7 min.

In normotensive subjects (P), PLR to 60° for 1 min (I) compared with supine position (C). We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[22] enrolling 125 normotensive subjects. No cardiovascular benefit was shown for PLR to 60° for 1 min.

In hypotensive patients (P), PLR to 45° (I) for 2 min compared with semirecumbent (head at 45°) for 2 min (C). We identified low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 RCT[23] enrolling 35 hypotensive subjects. No difference was found in HR, but a statistically significant benefit with PLR was demonstrated with

- An increase in MAP (median difference 7 higher, CI not estimable)
- An increase in SBP (median difference 12 higher, CI not estimable)
- An increase in central venous pressure (CVP) (median difference 2 higher, CI not estimable)

In hypotensive patients (P), supine position (C) for 2 min compared with semirecumbent (head at 45°) for 2 min (I). We identified low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 RCT[23] enrolling 35 hypotensive subjects. Placing patients in the supine position for 2 min compared with a semirecumbent 45° position failed to show any benefit for MAP, SBP, or HR. A significant increase in CVP was reported with transfer from semirecumbent to supine position (median difference 1 higher, CI not estimable).

In hypotensive patients (P), PLR to 45° for 2 min (I) compared with supine for 2 min (C). We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 RCT[23] enrolling 35 hypotensive subjects. No difference was noted for HR, but a statistically significant benefit with PLR was shown with

- An increase in MAP (median difference 5 higher, CI not estimable)
- An increase in systolic arterial pressure (SAP) (median difference 8 higher, CI not estimable)
- An increase in CVP (median difference 1 higher, CI not estimable)

In hypotensive patients (P), supine position for 4 min (C) compared with PLR to 45° for 4 min (I). We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[24] enrolling 15 hypotensive

subjects. No statistically significant difference in MAP or HR was shown between the supine position and PLR to 45° for 4 min. A statistically significant decrease in SAP was found for change in position from PLR to supine (MD, −4; 95% CI, −16.88 to 8.88) and for diastolic arterial pressure (DAP) (MD, −3; 95% CI, −14.81 to 8.81).

In hypotensive patients (P), PLR to 45° for 4 min (I) compared with supine for 4 min (C). We identified very-low-quality evidence (downgraded for inconsistency, indirectness, and imprecision) from 1 observational study[24] enrolling 15 hypotensive subjects. There was no statistically significant difference in MAP or HR between PLR to 45° for 4 min and the supine position for 4 min. Statistically significant benefit with PLR was found for SAP (MD, 7; 95% CI, −10.89 to 24.89) and DAP (MD, 3.0; 95% CI, −8.47 to 14.47).

We did not identify any evidence to address the critical outcomes of complications, incidence of cardiac arrest, overall mortality, or length of hospital stay.

Treatment recommendation

We suggest first aid providers place individuals with shock in the supine position as opposed to the upright position (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In regard to other positions studied, a review of the evidence suggests clinical equipoise in the first aid setting. For individuals with shock who are in the supine position and with no evidence of trauma, the use of PLR may provide a transient (less than 7 min) but statistically significant improvement in HR, MAP, cardiac index, or stroke volume. The clinical significance of this transient improvement is uncertain; however, no study reported adverse effects due to PLR.

Because improvement with PLR is brief and its clinical significance uncertain, this position is not recommended, although it may be appropriate in some first aid settings as a temporizing measure while awaiting more advanced emergency medical care. Studies included used PLR ranging between 30° and 60° elevation. An optimal degree of elevation was not identified.

- Categories of hypotensive shock in studies included with this review were septic shock, cardiogenic shock, and hypovolemic shock.
- In making these recommendations, we place increased value on the potential but uncertain clinical benefit of improved vital signs and cardiac function by positioning an individual with shock in the supine position or supine with PLR position over the risk of movement to effect a change in position.
- The Trendelenburg position was excluded from evaluation in this review due to the inability or impracticality of first aid providers to place a person into the Trendelenburg position in an out-of-hospital setting.

Knowledge gaps

Well-designed studies are needed to assess

- Clinical effects of position change in hypotensive patients
- Effect of position change in patients without fluid responsiveness
- Adverse effects of position change

Oxygen administration for first aid (FA 519)

Among adults and children who exhibit symptoms or signs of shortness of breath, difficulty breathing, or hypoxemia outside of a hospital (P), does administration of supplementary oxygen (I), compared with no administration of oxygen (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; shortness of breath; time to resolution of symptoms; or therapeutic endpoints (e.g., oxygenation and ventilation) (O)?

Introduction

Administration of supplementary oxygen is traditionally considered essential for individuals presenting with shortness of breath, difficulty breathing, or hypoxemia. In certain circumstances, oxygen supplementation might have potential adverse effects that complicate the disease course or even worsen clinical outcomes. In this PICO question, we sought to determine the impact of oxygen supplementation, as compared with no oxygen supplementation, on outcomes of patients who have shortness of breath, difficulty breathing, or hypoxemia.

This review differs from the 2010 review in the targeted population. In 2015, we focus on adults and children who exhibit signs and symptoms of shortness of breath, difficulty breathing, or hypoxemia in the out-of-hospital setting. In addition, we attempt to identify specific medical conditions that may benefit from supplementary oxygen administration by first aid providers. We excluded chest pain from the conditions evaluated for potential use of oxygen. Oxygen administration for individuals with chest pain due to acute coronary syndrome is separately reviewed by the ACS task force and described in "Part 5: Acute Coronary Syndromes."

Consensus on science

For the critical outcomes of **survival** and **therapeutic endpoints as measured by a composite of death, need for assisted ventilation, and respiratory failure**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 retrospective observation study[25] enrolling 232 patients with acute exacerbation of chronic obstructive pulmonary disease showing no benefit from supplementary oxygen administration (odds ratio [OR], 1.4; 95% CI, 0.6–2.9).

For the important outcome of **shortness of breath**, we identified very-low-quality evidence (downgraded for inconsistency and serious indirectness) from 1 RCT[26] enrolling 14 terminal cancer patients with dyspnea and hypoxemia showing benefit with supplementary oxygen administration (MD in visual analog scale score, −20.5; 95% CI, −27.6 to −13.5), and low-quality evidence (downgraded for inconsistency and indirectness) from 1 meta-analysis[27] and 4 RCTs[26,28–30] enrolling 134 advanced cancer patients with dyspnea without hypoxemia who did not show benefit from supplementary oxygen administration (standardized MD, −0.09; 95% CI, −0.22 to 0.04, $P = 0.16$).

For the important outcome of **oxygen saturation**, we identified moderate-quality evidence (downgraded for indirectness) from 3 RCTs, 1 enrolling 14 terminal cancer patients with dyspnea and hypoxemia[26] (MD in oxygen saturation, 8.6%; 95% CI, 7.0–10.3), 1 enrolling 6 patients with dyspnea and hypoxemia[29] (MD in oxygen saturation, 10.0%; 95% CI, 6.3–13.7), and 1 enrolling 51 advanced cancer patients with dyspnea[28] (mean increase in oxygen saturation, air 0.94% versus oxygen 5.43%; $P < 0.001$), all showing benefit with supplementary oxygen.

For the important outcome of **complete relief of decompression injury** after first recompression, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 retrospective observation study[31] enrolling 2231 patients with decompression injury from a registry database showing benefit from first aid supplementary oxygen administration (OR, 1.5; 95% CI, 1.2–1.8).

We did not identify any evidence to address the outcomes of survival, survival with favorable neurologic outcomes, or time to resolution of symptoms.

Treatment recommendation

No recommendation; the confidence in effect estimate is so low that the task force thinks a recommendation to change current practice is too speculative.

Values, preferences, and task force insights

In this review, the administration of supplementary oxygen was found to be of some benefit in the following specific circumstances:

- Advanced cancer patients who exhibit symptoms or signs of shortness of breath (dyspnea) and signs of hypoxia
- Individuals with decompression injury

The use of supplementary oxygen should be limited to individuals with specific training in oxygen administration.

Public commenting requested an oxygen saturation target for this review. We did not evaluate flow rates, but patients with hypoxemia in the included studies were provided supplementary oxygen that helped them reach normoxemia.

Knowledge gaps

- Is oxygen beneficial to all patients with shortness of breath or dyspnea with diverse etiologies?
- Does administration of oxygen improve survival in patients presenting with shortness of breath or hypoxemia?

Bronchodilator use for asthma with difficulty breathing (FA 534)

Among adults and children in the prehospital setting who have asthma and are experiencing difficulty in breathing (P), does bronchodilator administration (I), compared with no bronchodilator administration (C), change time to resolution of symptoms, time to resumption of usual activity, complications, harm to patient, therapeutic endpoints (e.g., oxygenation and ventilation), need for advanced medical care (O)?

Introduction

The 2005 review of asthma and bronchodilator therapy noted that the incidences of severe asthma and deaths from asthma are increasing and found bronchodilator therapy for wheezing to be safe and effective.[32] Although evidence in 2005 was extrapolated from prehospital and hospital studies, the potential benefit of decreased mortality led to the recommendation that first aid rescuers assist with administration of bronchodilator therapy for asthmatics with acute shortness of breath.

The use of bronchodilators in the first aid setting can take many forms, ranging from assisting someone with their bronchodilator to administering a bronchodilator as part of an organized response team with medical oversight. This review did not compare methods of bronchodilator therapy but sought evidence for or against patient outcomes with all inhaled bronchodilator therapies that might be used for acute asthma exacerbations.

Consensus on science

After application of inclusion and exclusion criteria, the search strategy yielded 8 double-blind RCTs,[33–40] 2 observational studies,[41,42] and 1 meta-analysis.[43] It is important to note that all of these trials involved administration of the bronchodilators in a healthcare setting (prehospital EMS setting, emergency department, or in-hospital setting); because none involved administration by first aid providers in a typical first aid setting, all have been downgraded for indirectness.

Regarding the critical outcome of **time to resolution of symptoms**, 2 RCTs were found. Very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 RCT[33] with 28 participants aged 3 months to 2 years showed benefit in reduction of respiratory rate (MD, 5.1; 95% CI, 0.45–9.75), wheezing score (MD, 0.8; 95% CI, 0.36–1.24), accessory muscle score (MD, 0.85; 95% CI, 0.45–1.23), and total clinical score (MD, 2.5; 95% CI, 1.06–3.94) when treatment (albuterol/salbutamol nebulization) was compared with placebo. Low-quality evidence (downgraded for imprecision and indirectness) from another RCT[34] with 17 participants aged 18 to 41 years showed benefit in reduction of time to subjective improvement in dyspnea in participants treated with fast-acting β_2-adrenergic agonists (formoterol or salbutamol dry-powdered inhaler) compared with placebo dry-powdered inhaler or the slow-acting β_2-agonist (salmeterol dry-powdered inhaler). This study also demonstrated a reduction in time to return to baseline symptoms in the fast-acting β_2-adrenergic agonist group compared with the placebo or slow-acting β_2-agonist groups (MD indeterminable).

Regarding the critical outcome of time to resumption of usual activity, there were no human trials found.

Regarding the important outcome of **complications**, very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[33] with 28 participants aged 3 months to 2 years failed to demonstrate a significant difference in mean HR between participants treated with nebulized albuterol/salbutamol and those treated with placebo (MD, 7; 95% CI, −9.6 to 23.6). Very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from a second RCT[35] comprising 11 participants aged between 9 and 16 years failed to demonstrate a difference in mean HR or mean blood pressure when albuterol/salbutamol metered-dose aerosol was compared with placebo. A total of 4 patients on the albuterol/salbutamol days reported tremors, compared with 6 on the placebo days. All tremors were “fine” in quality. Very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from a third RCT[36] comprising 100 patients with an average age of 33 years failed to demonstrate a significant difference in potassium, SBP or DBP, tremor, headache, nervousness, weakness, palpitations, or dry mouth between the albuterol/salbutamol metered-dose aerosol given once group (T0), compared with every 30 min for 4 doses group (T30), compared with every 60 min for 2 doses group (T60). There was a statistically significant difference in mean HR change between the T30 compared with T0 groups, where the T30 group’s HR (beats per minute [BPM]) increased and the T0 group’s decreased (MD, 9.2; 95% CI, 3.51–14.93). Very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from an observational study[41] comprising 52 participants with an average age of 33.6 years failed to demonstrate a significant difference in respiratory rate and HR between the treatment group (nebulized isoetharine) and the control group. One participant in the treatment group reported headache and 2 participants in the control group reported headache or nausea (MD undeterminable).

Regarding the important outcome of harm to patient, there were no human trials found.

Regarding the important outcome of **therapeutic endpoints** (e.g., oxygenation and ventilation), 1 RCT[35] with very-low-quality evidence (downgraded for bias, imprecision, and indirectness) showed benefit in an improvement in percentage maximal achievable forced expiratory volume over 1 s (FEV1) and forced vital capacity (FVC) at 60 min when comparing inhaled albuterol/salbutamol metered-dose aerosol or isoproterenol metered-dose aerosol to placebo and at 360 min (MD undeterminable). A second RCT[37] with very-low-quality evidence (downgraded for bias, imprecision, and indirectness) enrolled 134 participants with an average age of 8.3 years, which demonstrated a statistically significant improvement in FEV1 after initial treatment dose (day 0) for levalbuterol/salbutamol and albuterol/salbutamol compared with placebo (33.1%, 29.6% versus 17.8%; $P < 0.05$).

Very-low-quality evidence (downgraded for serious indirectness and imprecision) from a third RCT[36] involving 100 patients demonstrated a statistically significant improvement in FEV1 when albuterol/salbutamol metered-dose aerosol was given every 30 min for 4 doses (T0, 30, 60, 90) or every 60 min for 2 doses (T0, 60) compared with when albuterol/salbutamol metered-dose aerosol was given once at T0 (MD undeterminable). Very-low-quality evidence (downgraded for serious indirectness and imprecision) was identified in another RCT[38] enrolling 17 patients ranging in age from 18 to 41 years, who demonstrated a more rapid return to 85% of baseline FEV1 when treated with formoterol dry-powdered inhaler or albuterol/salbutamol dry-powdered inhaler compared with placebo (7.2 and 6.5 min versus 34.7 min, respectively). This study also showed benefit by demonstrating an increase in FEV1 at 60 min with formoterol, albuterol/salbutamol, and salmeterol all by dry-powdered inhaler compared with placebo (46.2%, 42.2%, and 41.2% versus 31.5%, respectively) (MD undeterminable).

Further very-low-quality evidence (downgraded for risk of bias, very serious indirectness, and imprecision) was identified from an RCT[39] enrolling 26 patients between 7 and 16 years of age, which showed a benefit in median recovery time to 95% of baseline FEV1 of 5.0 min for formoterol dry-powdered inhaler versus 44 min with placebo (MD undeterminable). Very-low-quality evidence (downgraded for very serious risk of bias, imprecision, and very serious indirectness) from an RCT[40] enrolling 17 patients with an average age of 10.3 years demonstrated that formoterol dry-powdered inhaler and albuterol/salbutamol dry-powdered inhaler resulted in a mean recovery time to within 90% of baseline FEV1 that was shorter than that of placebo (8.3 min and 13.2 min versus 36.1 min, respectively) (MD undeterminable). Very-low-quality evidence (downgraded for risk of bias, very serious imprecision, and indirectness) from an RCT[33] showed an increase in arterial oxygen saturation in nebulized albuterol/salbutamol treated patients compared with those who were treated with placebo (MD of 1.6, 0.28, and 2.92, respectively). Very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[41] demonstrated an improvement in percent recovery of peak expiratory flow rate (PEFR) when patients were treated with nebulized isoetharine compared with placebo (MD, 55.3; 95% CI, 25.4–85.2). Very-low-quality evidence (downgraded for risk of bias and indirectness) from a second observational study[42] enrolling 208 participants with an average age of 43.7 years showed a reduction in first posttreatment PEFRs of less than 120 L/min in the cohort given prehospital nebulized albuterol compared with a historic control (RR, 0.75; 95% CI, 0.58–0.98). In addition, the patient condition on arrival at the emergency department was not as severe in the prehospital nebulized albuterol group versus control (RR, 0.79; 95% CI, 0.64–0.98).

Regarding the low priority outcome of **need for advanced medical care**, very-low-quality evidence (downgraded for risk of bias, very serious indirectness, and imprecision) from 1 RCT[36] showed a benefit with a significant association between early, frequent use of albuterol/salbutamol metered-dose aerosol and fewer subsequent albuterol/salbutamol metered-dose aerosol treatments. Participants who received 30-minute or 60-minute albuterol/salbutamol metered-dose aerosol compared with a single dose placebo at study start required less subsequent bronchodilation after study end at 120 min (20.6%, 23.5%, and 42.4%, respectively; $P < 0.05$).

Very-low-quality evidence (downgraded for very serious risk of bias, imprecision, and indirectness) from an observational study[42] showed no benefit, by failing to demonstrate a difference in length of emergency department stay when patients were administered prehospital nebulized albuterol/salbutamol compared with those who were not. Very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from a meta-analysis[43] failed to demonstrate a difference in clinical outcome or patient disposition in those patients treated with nebulized ipratropium bromide and nebulized albuterol/salbutamol compared with those treated with nebulized albuterol/salbutamol alone.

Treatment recommendation

When an individual with asthma is experiencing difficulty breathing, we suggest that trained first aid providers assist the individual with administration of a bronchodilator (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place higher value in an intervention that may reduce mortality in a life-threatening situation over the risk of potential adverse effects. This review found evidence that use of a bronchodilator in asthmatics with acute difficulty breathing is effective for reducing wheezing, dyspnea, and respiratory rate, while improving measures of effectiveness such as FEV1 or PEFR, and with few reported side effects.

As with the 2005 review and as noted above, no studies of bronchodilator administration in the first aid setting met the inclusion criteria; therefore, studies were used from the EMS and hospital settings. While these studies support the use of bronchodilators for asthmatics with difficulty in breathing, caution is required in extrapolating our findings to a first aid recommendation.

The task force recognizes that first aid providers may be limited in their abilities to administer or assist with bronchodilator therapy due to clinical governance and local regulations. In addition, this recommendation must be appropriately operationalized by first aid organizations with due consideration to the setting and scope of practice in which the first aid is being applied.

Knowledge gaps

- What is the optimal bronchodilator for administration?
- What is the optimal dose of bronchodilator?
- How should this bronchodilator be administered?
- Is there evidence that prehospital use of bronchodilators for asthmatics with acute shortness of breath reduces mortality?

Stroke recognition (FA 801)

Among adults with suspected acute stroke (P), does the use of a rapid stroke scoring system or scale (I), compared with standard first aid assessment (C), change time to treatment (e.g., door to drug), recognition of acute injury or illness, discharge with favorable neurologic status, survival with favorable neurologic outcome, or increased public/layperson recognition of stroke signs (O)?

Introduction

The use of stroke assessment systems has become widespread by EMS and other healthcare providers to identify individuals with possible stroke, but in many countries, it is often not an educational component of first aid courses. In some regions, simple stroke assessment systems have been the focus of recent public campaigns, with the objective of raising public awareness of the signs of stroke and minimizing delays in recognition, diagnosis, and definitive treatment. This review evaluated the outcomes related to use of stroke assessment systems and showed reduced time to recognition of stroke with most stroke assessment systems, more accurate recognition of stroke, and increased public/layperson recognition of signs of stroke.

The task force discussed the need to identify the relative sensitivities and specificities of each included stroke assessment system to discern which may be most useful in the first aid setting. The ideal stroke assessment system for use by first aid providers would have high sensitivity, thereby "casting a wide

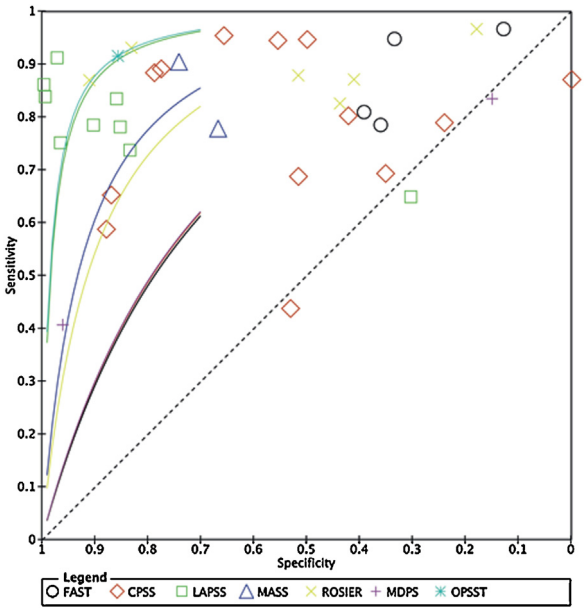

Fig. 1. Summary receiver operating characteristic plot of stroke screening systems.

net" to identify possible stroke victims. Additional benefit may be gained if a stroke assessment system with both high sensitivity and specificity is used by those with advanced training (such as EMS providers). Thus, this review identified stroke assessment systems that may be preferred, based on sensitivity and specificity, to aid those developing guidelines for stroke recognition in various first aid and out-of-hospital settings (Figs. 1 and 2).

Consensus on science

For the critical outcome of **time to treatment**, we identified 6 studies with 6 different stroke assessment systems studied:

1. For the Face (facial drooping), Arm (arm weakness), Speech (speech difficulty), Time (time to call 9-1-1/EMS) (FAST) scale (measured as number of patients with time from symptom onset to hospital arrival within 3 h), we identified moderate-quality evidence from 1 observational study[44] enrolling 356 patients showing benefit where 48.2% patients who had the scale applied arrived within 3 h compared with 14.6% who did not have the scale applied (RR, 3.3; 95% CI, 2.29–4.75).
2. For the Kurashiki Prehospital Stroke Scale (KPSS; measured as number of patients with time from symptom onset to hospital arrival within 3 h), we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational study[45] enrolling 430 patients showing benefit where 62.9% patients who had the scale applied arrived within 3 h compared with 52.3% who did not have the scale applied (RR, 1.2; 95% CI, 1.01–1.43). In the same study, the mean time was 2.1 h for those who had a stroke screening scale applied compared with 2.7 h for those who did not have a stroke screening scale applied (MD, −0.6; 95% CI, −2.45 to 1.25).
3. For the Ontario Prehospital Stroke Scale (OPSS; measured as number of patients with time from symptom onset to hospital arrival within 3 h), we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational study[46] enrolling 861 patients showing no significant benefit where 52.3% patients who had the scale applied arrived within 3 h compared with 47.2% who did not have the scale applied (RR, 1.1; 95% CI, 0.96–1.28).
4. For the Los Angeles Prehospital Stroke Screen (LAPSS; measured in minutes from symptom onset to emergency department arrival time), we identified low-quality evidence from 1 observational study[47] enrolling 1027 patients showing a mean time of 356 min for those who had a stroke screening scale applied compared with 359 min for those who did not have a stroke screening scale applied (SMD, 0.11; 95% CI, 0.02–0.24).
5. For the Cincinnati Prehospital Stroke Scale (CPSS; measured with EMS on-scene time), we identified low-quality evidence (downgraded for risk of bias) from 1 observational study[48] enrolling 308 patients showing no benefit, as the mean on-scene time was 17 min for those who had a stroke screening scale applied compared with 19 min for those who did not have a stroke screening scale applied (MD, −2.00; 95% CI, −3.34 to 0.66).
6. For the Face, Arm, Speech, Time, Emergency Response (FASTER) protocol (measured with symptom onset to emergency department arrival [door] time), we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational study[49] enrolling 115 patients showing no significant benefit where the mean time was 59 min for those who had a stroke screening scale applied compared with 76 min for those who did not have a stroke screening scale applied ($P = 0.180$).

For the important outcome of **recognition of stroke** (interventional studies, outcome defined as definitive stroke diagnosis or administration of thrombolytic/fibrinolytic; the publications varied in the term used), we identified 4 observational studies of 4 different stroke scales:

1. For FAST (measured as number of patients with confirmed stroke or transient ischemic attack), we identified moderate-quality evidence from 1 observational study[44] enrolling 356 patients showing benefit where 48.2% patients who had the scale applied were diagnosed compared with 14.6% who did not have the scale applied (RR, 3.3; 95% CI, 2.29–4.75).
2. For KPSS (measured as number of patients who received fibrinolytic), we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational study[45] enrolling 430 patients showing no benefit where 13.7% patients who had the scale applied were diagnosed compared with 14.4% who did not have the scale applied (RR, 0.95; 95% CI, 0.59–1.53).
3. For the FASTER scale (measured as number of patients who received thrombolytic), we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational study[49] enrolling 34 patients showing benefit where 19.1% patients who had the scale applied received fibrinolytic compared with 7.5% who did not have the scale applied (RR, 0.87; 95% CI, 0.78–0.98).
4. For CPSS (measured with patients who received fibrinolytic), we identified moderate-quality evidence from 1 observational study[50] enrolling 308 patients showing benefit where 45.7% patients who had the scale applied received fibrinolytic compared with 2.1% who did not have the scale applied (RR, 22.2%; 95% CI, 7.14–69.1).

For the important outcome of **recognition of stroke** (diagnostic studies, outcome defined as correct stroke diagnosis), we identified low-quality evidence (all downgraded for risk of bias) from 22 observational studies[44,46–48,51–68] enrolling a total of 30 635 patients, studying 8 different stroke screening assessment systems, showing diagnostic performance across all stroke screening systems of sensitivity ranging from 0.41 to 0.97 and specificity ranging from 0.13 to 1.00. These studies were divided into subgroups based on whether the stroke scales included glucose measurement or not. For studies that included stroke scales with glucose measurement (LAPSS, OPSS, KPSS, and Recognition of Stroke in the

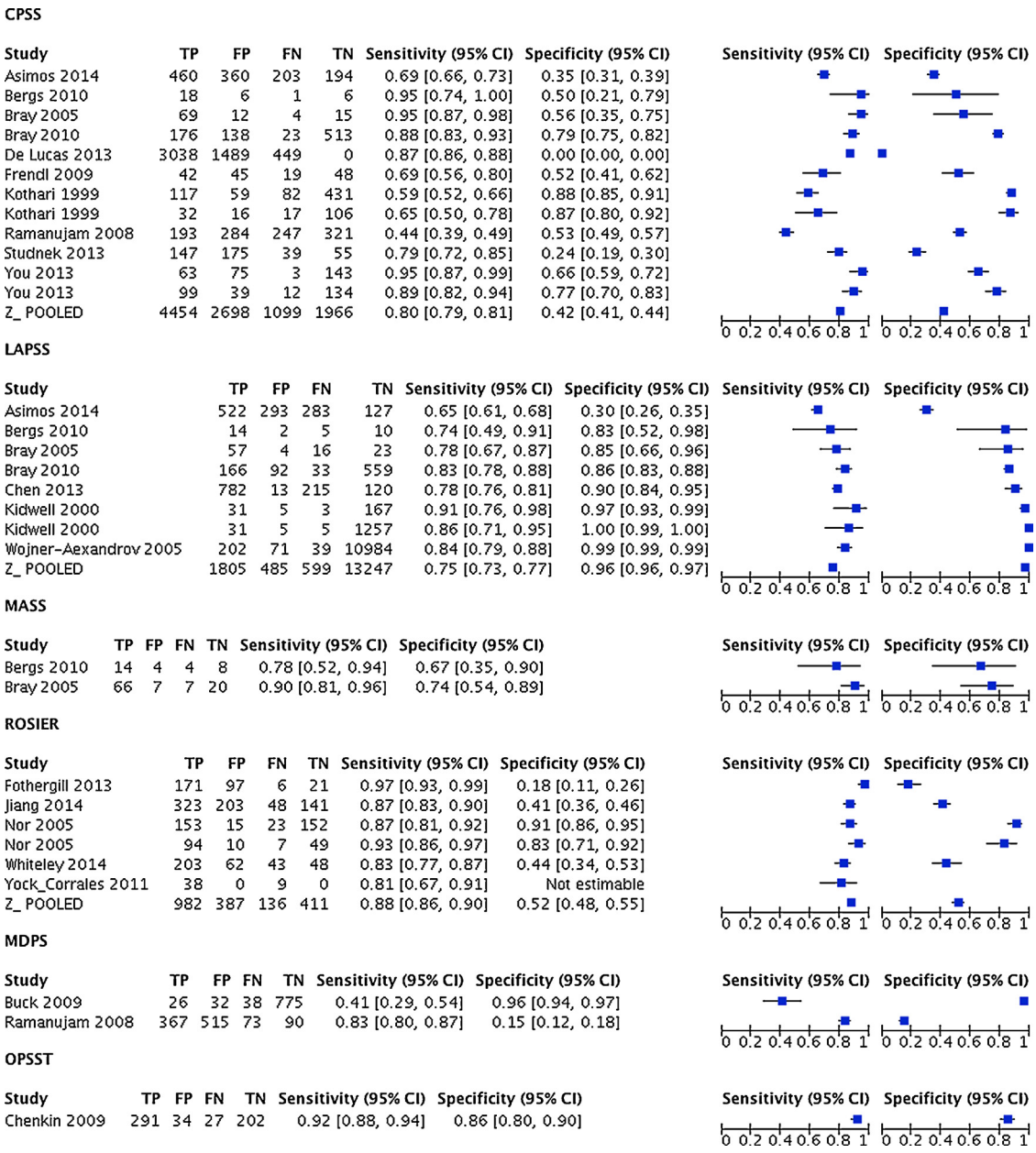

Fig. 2. Forest plot of stroke assessment systems.

Emergency Room [ROSIER]), the pooled sensitivity was 0.84 (95% CI, 0.82–0.85) and pooled specificity was 0.97 (95% CI, 0.97–0.97), compared with stroke scales without glucose measurement (FAST, Melbourne Ambulance Stroke Screen [MASS], Los Angeles Motor Scale [LAMS], CPSS, Medical Priority Dispatch System [MPDS]), which have pooled sensitivity of 0.82 (95% CI, 0.81–0.83) and pooled specificity of 0.48 (95% CI, 0.46–0.49).

For the important outcome of **increased public/layperson recognition of signs of stroke**, very-low-quality evidence (downgraded for risk of bias) from 1 human study[69] enrolling 72 participants (members of the public) showed benefit where 76.4% of participants (55/72) were able to identify signs of stroke before training on a stroke screening assessment system compared with 94.4% (68/72) immediately after training (OR, 5.25; 95% CI, 1.67–16.52), and 96.9% of participants (63/65) were able to identify the signs of stroke 3 months after training (OR, 2.07; 95% CI, 0.36–11.69).

Treatment recommendation

We recommend that first aid providers use stroke assessment systems (such as FAST or CPSS) for individuals with suspected acute stroke (strong recommendation, low-quality evidence).

We suggest the use of FAST or CPSS stroke assessment systems (weak recommendation, low-quality evidence).

We suggest the use of stroke assessment systems that include blood glucose measurement, when available, such as LAPSS, OPSS, ROSIER, or KPSS, to increase specificity of stroke recognition (weak recommendation, low-quality evidence).

In the absence of a glucometer, we suggest the use of FAST or CPSS stroke assessment systems compared with MASS, LAMS, or MPDS (weak recommendation, low-quality evidence).

The literature search was rerun in January 2015 to capture the most updated evidence possible. Two additional studies were added[51,59] and incorporated into the consensus on science and GRADE tables, both supporting this treatment recommendation.

Values, preferences, and task force insights

In making this recommendation, we place increased value on the benefits of early stroke recognition, which could lead to early treatment to minimize potentially devastating neurologic injury.

Training first aid providers in stroke assessment systems outweighs the risks, largely limited to false-positive identification by first aid providers. The cost of the intervention is estimated to be low.

In this review of the literature, the stroke assessment systems include various components, such as looking for specific signs and obtaining blood glucose levels. Our review found that stroke assessment systems that included blood glucose measurement had similar sensitivity and increased specificity to accurately identify stroke compared with those systems that did not include glucose measurement. We recognize that first aid providers may or may not have access to a properly calibrated glucose measurement device. Although use of these devices is not a standard component of first aid, glucose measurement devices are commonly available among the public.

Ideal stroke assessment systems for first aid use are accurate, have few steps, are easily understood and remembered, and take minimal time to complete. Those developing local guidelines for first aid providers can use the results of this review to determine if the benefit of increased specificity with systems that include glucose measurement would be desirable in their settings, compared with using simpler stroke assessment systems that do not include glucose measurement, which have similar sensitivity but lower specificity.

Knowledge gaps

More research is required to determine how much training is needed and what type of training should be used to enable first aid providers to correctly apply stroke assessment systems and to compare the accuracy of use of stroke assessment systems by first aid providers to the accuracy of use of stroke assessment systems by healthcare providers. Research is also required to determine accuracy of assessment and its effect on survival and neurologic status at discharge. In addition, future research could include investigating direct transport to specified stroke centers when a stroke assessment system measurement is positive (bypassing community/small emergency departments).

Aspirin for chest pain

Chest pain is one of the common symptoms of acute MI. Antiplatelet agents such as aspirin play a large role in management. In 2010, the first aid treatment recommendation stated that the administration of aspirin to individuals with chest discomfort was recommended.

In 2015, 2 PICOs were generated, 1 simply looking at the administration of aspirin and the other looking at the timing of this administration. The first PICO sought to determine if the administration of aspirin in the setting of MI was beneficial. Subsequently, the second PICO was used to determine if there was a difference in outcomes when aspirin is given early, in the first hours after symptom onset by a first aid provider, or later, in the setting of chest pain symptoms due to suspected acute MI. This same PICO was also used to see if there would be benefit to early administration of aspirin to adults with chest pain of unclear etiology.

Aspirin for chest pain: administration (FA 871)

Among adults experiencing chest pain due to suspected MI (P), does administration of aspirin (I), compared with no administration of aspirin (C), change cardiovascular mortality, complications, adverse effects, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay (O)?

Introduction

This 2015 PICO question asks if administration versus no administration of aspirin changed outcomes in the setting of suspected acute MI. There are no major changes from what has been stated in previous treatment recommendations.

Consensus on science

For the critical outcome of **cardiovascular mortality (at 5 weeks)**, we identified high-quality evidence from 1 RCT[70] enrolling 17 187 patients with acute MI showing benefit to aspirin (162.5 mg, enteric-coated) administration (RR, 0.79; 95% CI, 0.73–0.87).

For the critical outcome of **cardiovascular mortality (at 3 months)**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[71] enrolling 100 patients with acute MI showing no benefit to aspirin (100 mg, capsule) administration (RR, 0.83; 95% CI, 0.4–1.75).

For the critical outcome of **cardiovascular mortality (at 28 days)**, we identified low-quality evidence (downgraded for risk of bias and indirectness) from 1 RCT[72] enrolling 1705 patients with acute MI showing no benefit to aspirin (300 mg, capsule) administration (RR, 0.98; 95% CI, 0.81–1.19).

For the critical outcome of **cardiovascular mortality (in-hospital)**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[73] with a total of 22 572 patients with acute MI showing benefit to aspirin (500 mg, oral or intravenous loading dose; 100 mg, oral; maintenance recommended) administration (RR, 0.33; 95% CI, 0.31–0.35).

For the critical outcome of **adverse effects (bleeding)**, we identified high-quality evidence from 1 RCT[70] enrolling 16 981 patients with acute MI showing adverse effects (minor bleeding) with aspirin (162.5 mg, enteric-coated) administration (RR, 1.25; 95% CI, 1.04–1.51).

For the critical outcome of **adverse effects (allergic reaction)**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[74] with 219 patients with suspected acute MI showing no adverse effects (allergic reaction) with aspirin (dose not available) administration (unable to calculate RR as there was no control group).

For the critical outcome of **complications**, we identified high-quality evidence from 1 RCT[70] enrolling 16 981 patients with acute MI showing benefit to aspirin (162.5 mg, enteric-coated) administration (RR, 0.62; 95% CI, 0.52–0.73). We also found very-low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 RCT[71] enrolling 100 patients with acute MI showing benefit to aspirin (100 mg, capsule) administration (RR, 0.11; 95% CI, 0.05–0.98).

We identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[73] with a total of 22 572 patients with acute MI showing no benefit to aspirin (500 mg oral or intravenous loading, 100 mg oral maintenance recommended) administration (RR, 1.05; 95% CI, 0.78–1.42).

For the critical outcome of **incidence of cardiac arrest**, we identified high-quality evidence from 1 RCT[70] enrolling 16 981 patients with acute MI showing benefit to aspirin (162.5 mg, enteric-coated) administration (RR, 0.87; 95% CI, 0.79–0.96).

For the important outcome of **infarction size**, we identified very-low-quality evidence (downgraded for bias, imprecision, and indirectness) from 1 RCT[71] enrolling 89 patients with acute MI showing no benefit to aspirin (100 mg, capsule) administration (MD, −161; 95% CI, −445.57 to 230.57).

We did not identify any evidence to address the important outcomes of cardiac functional outcome or length of hospital stay.

Treatment Recommendation

We recommend the administration of aspirin to adults with chest pain due to suspected MI (strong recommendation, high-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on decreasing mortality and decreased complications of MI over the risks of adverse effects, such as bleeding.

Public comments for this question requested a suggestion for the optimal aspirin dose and form. Our PICO question was not designed to look at changes in outcomes based on various doses of aspirin, as all the articles selected for review compared administration to no administration, as opposed to 1 dose compared with another. Due to the heterogeneity in study design in the articles that were included in this review, the dose and form (e.g., chewable or nonchewable, enteric-coated or nonenteric coated) of aspirin varied, and no recommendation could be made regarding the optimal dose or form of aspirin administered. Where available, the dose of aspirin used for each study has been identified in the consensus on science statement.

Knowledge gaps

- Is aspirin safe if given to patients with chest pain who are not having an MI?
- Is aspirin safe when given by a first aid provider?
- Is there high-quality evidence to indicate that the administration of aspirin after MI is time critical?

Aspirin for chest pain: early compared with late (FA 586)

Among adults who are experiencing chest pain outside of a hospital (P), does early administration of aspirin (I), compared with later administration of aspirin (C), change cardiovascular mortality, complications, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay, chest pain resolution (O)?

Introduction

This 2015 PICO question asked if early administration versus later administration of aspirin changes outcomes, which is different wording from the focus of the 2010 review. The recommendation in 2015 differs from that in 2010 as a result of the intent of the PICO question, as well as the studies identified after using the rigorous literature search techniques and reviewed through the GRADE process.

Consensus on science

In this review, early administration of aspirin is defined as prehospital or administration in the first hours from onset of symptoms of MI (i.e., median 1.6 h in 1 study).[75]

For the critical outcome of **cardiovascular mortality (at 7 days)**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 2 observational studies[75,76] with a total of 2122 patients with acute MI showing benefit to early aspirin administration (RR, 0.37; 95% CI, 0.23–0.62).

For the critical outcome of **cardiovascular mortality (at 30 days)**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 2 observational studies[75,76] with a total of 2122 patients with acute MI showing benefit to early aspirin administration (RR, 0.45; 95% CI, 0.3–0.68).

For the critical outcome of **cardiovascular mortality (at 5 weeks)**, we identified low-quality evidence (downgraded for indirectness) from 1 RCT[70] enrolling 8587 patients with acute MI showing no benefit to aspirin (162.5 mg, enteric-coated) administration within 2 h of symptom onset (RR, 0.92; 95% CI, 0.76–1.11).

For the critical outcome of **cardiovascular mortality (at 1 year)**, we identified very-low-quality evidence (downgraded for indirectness) from 1 observational study[75] with 1200 patients with acute MI showing benefit to early aspirin (160 mg, oral) administration (RR, 0.47; 95% CI, 0.29–0.77).

For the critical outcome of **complications**, we identified very-low-quality evidence (downgraded for indirectness) from 1 observational study[76] with a total of 922 patients with acute MI showing no increase in complication rate with early aspirin (greater than 200 mg, chewable) administration (RR, 0.61; 95% CI, 0.46–0.81). We also identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[75] with a total of 1200 patients with acute MI demonstrating an increase in complications (such as re-ischemia) in the group that received early aspirin (160 mg, oral) administration (RR, 1.22; 95% CI, 1.09–1.37).

For the critical outcome of **incidence of cardiac arrest**, we identified very-low-quality evidence (downgraded for indirectness) from 1 observational study[76] with a total of 922 patients with acute MI showing no benefit to early aspirin (greater than 200 mg, chewable) administration (RR, 0.82; 95% CI, 0.56–1.2) and very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[75] with a total of 1200 patients with acute MI demonstrating an increased incidence of cardiac arrest in the group that received early aspirin (160 mg, oral) administration (RR, 1.53; 95% CI, 1.13–2.09).

We did not identify any evidence to address the important outcomes of cardiac functional outcome, infarct size, or hospital length of stay or the low importance outcome of chest pain resolution.

Treatment recommendation

We suggest the early administration of aspirin by first aid providers to adults with chest pain due to suspected MI (weak recommendation, very-low-quality evidence).

There is no evidence for the early administration of aspirin by first aid providers to adults with chest pain of unclear etiology.

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the benefits of aspirin, such as decreased mortality from MI, which outweigh possible risks of complications.

The task force discussed concerns about first aid providers being able to differentiate chest pain of cardiac origin from other causes of chest discomfort. With any treatment recommendations naming a particular clinical pathology, such as in this case with MI or chest pain of cardiac origin, it is very important that guidelines or educational materials clearly indicate what signs and symptoms the first aid provider should look for to recognize that clinical presentation.

Knowledge gaps

- Is aspirin safe if given to patients with chest pain of other etiologies, particularly gastrointestinal?
- Is it safe for a first aid provider to administer 1 dose of aspirin?
- Is there any high-quality evidence demonstrating that there is a critical time window for the administration of aspirin after the onset of acute MI in terms of reducing morbidity and mortality?
- Is the prehospital administration of aspirin required if the patients are fast tracked to percutaneous coronary intervention (PCI)?

Epinephrine for anaphylaxis and treatment of hypoglycemia, exertion-related dehydration, and chemical eye injuries

This section includes the topics of a second dose of epinephrine for anaphylaxis and first aid treatment of hypoglycemia in diabetics, exertion-related dehydration, and chemical injuries of the eye.

Second dose of epinephrine for anaphylaxis (FA 500)

Among adults and children experiencing severe anaphylaxis requiring the use of epinephrine (P), does administration of a second dose of epinephrine (I), compared with administration of only 1 dose (C), change resolution of symptoms, adverse effects, complications (O)?

Introduction

In 2010, evidence evaluation regarding effectiveness of administration of a second dose of epinephrine for anaphylaxis concluded that there was insufficient evidence to make a recommendation regarding the routine first aid administration of a second dose of epinephrine. Use of a more rigorous literature search strategy and of the GRADE methodology for the 2015 review provided additional scientific evidence that has resulted in a change in the treatment recommendation.

The question's specific focus was on the benefit of a second dose of epinephrine for severe anaphylaxis when signs and symptoms fail to respond to an initial dose. For the purpose of this review, if a study provided data for epinephrine administered after a first dose, unless the study specified that a second dose was given as part of a protocol, it was presumed that doses administered after a first dose were administered due to failure to respond.

Consensus on science

For the critical outcome of **resolution of symptoms**, we identified very-low-quality evidence (downgraded for risk of bias and confounding) from 9 observational studies[77–85] showing benefit for giving a second dose (or multiple doses) of epinephrine to patients not responding to a first dose (RR, 1.16; 95% CI, 1.13–1.20).

In addition, for the critical outcome of **resolution of symptoms**, we identified very-low-quality evidence (downgraded for risk of bias) from 1 observational study[86] showing no significant difference between the percentage of resolved reactions in an ambulance service routinely using 2 doses of epinephrine versus an ambulance service using a single dose (RR, 0.97; 95% CI, 0.9–1.04).

We did not identify any evidence to address the critical outcomes of adverse effects or complications.

Treatment recommendation

We suggest a second dose of epinephrine be administered by autoinjector to individuals with severe anaphylaxis whose symptoms are not relieved by an initial dose (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place a higher value on the resolution of life-threatening symptoms, such as airway compromise, breathing difficulty, and circulatory collapse, over the potential risk of adverse effects from an unnecessary second injection.

When caring for a person with anaphylaxis, first aid providers should always call for EMS (eg, 9-1-1 or 1-1-2) rescue service.

Public comments and discussion on this topic centered on issues of dosing, interval time for a second dose, and the possibility of adverse effects should epinephrine be inadvertently administered to a person not experiencing anaphylaxis. This evidence review did not evaluate the time interval between doses of epinephrine or the optimal dose. However, literature included in the review suggests that a second dose of epinephrine may be administered 10 to 15 min after the initial dose.[80]

While the included studies did not identify any adverse effects, selection bias might have prevented those effects from being identified. Adverse effects have previously been reported in the literature when epinephrine is administered in the incorrect dose or via inappropriate routes, such as the intravenous route. Use of autoinjectors by first aid providers may minimize the opportunity for incorrect dosing of epinephrine.

Knowledge gaps

In 2010, first aid worksheet 303B attempted to define if or can "the First Aid Provider Appropriately Recognize the Signs and Symptoms of Anaphylaxis." The task force did not address this PICO question in 2015, and thus the question "How can a first aid provider determine that a victim needs additional epinephrine?" remains.

- What should the time interval be between doses of epinephrine?
- Would a higher concentration (0.5 mg) recommended for standard therapy versus the injectable syringe dose (0.3 mg) be more effective and decrease the need for additional doses in the EMS setting?
- Should an initial injection be administered in the early stages of anaphylaxis, before the onset of severe symptoms?

Hypoglycemia treatment (FA 795)

Among adults and children with symptomatic hypoglycemia (P), does administration of dietary forms of sugar (I), compared with standard dose (15–20 g) of glucose tablets (C), change time to resolution of symptoms, risk of complications (e.g., aspiration), blood glucose, hypoglycemia, hospital length of stay (O)?

Introduction

This is a new topic for the 2015 consensus on science.

Because glucose tablets may not be readily available in all first aid settings, this task force performed a review to evaluate the effectiveness of dietary (i.e., food source) sugars compared with glucose tablets for the management of symptomatic hypoglycemia.

The literature search for this review identified 5 studies that compared glucose tablets to various commercial sugar-containing dietary products. The named commercial products cited in the consensus on science and in the treatment recommendation were specifically included in evaluated studies and are not particularly endorsed by the First Aid Task Force. To our knowledge, none of the product manufacturers contributed to or were involved with the identified studies. Two tables listing the specific sugar content for each studied product are provided to assist with guideline development (Tables 1 and 2).

Consensus on science

Dietary sugars (I) compared with glucose tablets (C). For the critical outcome of **time to resolution of symptoms**, none of the 4 studies identified[87–90] showed that any form of dietary sugar or glucose tablets improved the blood glucose before 10 min.

For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we identified low-quality evidence (downgraded for risk of bias and imprecision) from 3 randomized controlled studies[88–90] with pooled data from 502 diabetic patients treated with dietary sugars (sucrose, fructose, orange juice, jelly beans, Mentos, and milk) and 223 treated with glucose tablets (15–20 g)

Table 1
Major dietary sugars with about 20 g carbohydrate from sugar and number of people with improvement in hypoglycemia within 15 min.

Type of food or fluid	Carbohydrates per serving	Measure representing 20 g carbohydrates[a]	Clinical relief 15 min or less after ingestion
Glucose tablets	Varies	Varies	194/223 (87.0%)
Sucrose (Skittles)[b]	0.9 g/candy	20–25 candies	150/177 (84.7%)
Fructose (fruit leather, e.g., Stretch Island)[c]	10 g/strip	2 strips	111/165 (67.3%)
Orange juice (unsweetened, from concentrate)[d]	1 g/10 mL	200 mL	35/50 (70.0%)
Jelly beans[d]	1.1 g/jelly bean	15–20 jelly beans	33/45 (73.3%)
Mentos[e]	2.8 g/mint	5–10 mints	44/48 (91.7%)
Whole milk[f]	21.75 g/mL	435 mL	Not reported

[a] These measurements may differ from those in the evaluated studies, because the amount was not standardized across studies.
[b] Manufacturer label.
[c] One study[88] used fruit leather under the trade name Fruit to Go (Kelowna, British Columbia, Canada). We were unable to find the nutritional information for this fruit leather, so we substituted another brand, Stretch Island Cherry Flavor (Stretch Island Fruit Co, La Jolla, CA); http://www.stretchislandfruit.com/en_US/Products.html, accessed February 2, 2015.
[d] http://onlinelibrary.wiley.com/doi/10.1002/pdi.953/pdf.
[e] Manufacturer label.
[f] Brodows, 1984.[87]

that showed a benefit with glucose tablets, with slower resolution of symptoms 15 min after diabetic patients were treated with dietary sugars compared with glucose tablets (RR, 0.89; 95% CI, 0.83–0.96).

For the important outcome of **blood glucose** (diabetic patients with at least a 20-mg/dL increase of blood glucose by 20 min), we found very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[87] with 13 diabetic patients treated with dietary sugars and 9 treated with glucose tablets that showed a benefit with glucose tablets, with fewer diabetic patients demonstrating a 20-mg/dL increase in blood glucose level 20 min after treatment when treated with dietary sugars compared with glucose tablets (RR, 0.3; 95% CI, 0.1–0.85). For the critical outcome of time to resolution of symptoms, the important outcome of risk of complications (e.g., aspiration), and the low-priority outcome of hospital length of stay, there were no human trials found.

Sucrose (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we found low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[88,90] with pooled data from 177 diabetic patients treated with sucrose (165 with sucrose candy [Skittles] and 12 with sucrose tablets) and 171 treated with glucose tablets that showed no difference in their effects on blood glucose. Sucrose (either as sucrose candy [Skittles] or sucrose tablets) and glucose tablets were equivalent in providing clinical relief of hypoglycemia 15 min after ingestion (RR, 0.99; 95% CI, 0.91–1.07). For the important outcome of **blood glucose** (mean change in blood glucose [mmol/L] after 15 min), we found low-quality evidence (downgraded for risk of bias and imprecision) from 1 randomized controlled study[90] with 6 diabetic patients treated with sucrose (dissolved in water) and 6 treated with glucose tablets that showed a benefit to glucose administration, with the MD (mmol/L) in blood glucose 15 min after ingestion lower with sucrose (dissolved in water) than glucose tablets (MD, −0.9; 95% CI, −1.78 to −0.02). A second arm of this same study with 6 diabetic patients treated with sucrose (chewed) and 6 treated with glucose tablets showed no benefit, with the MD (mmol/L) in blood glucose 15 min after ingestion similar between sucrose (chewed) and glucose tablets (MD, 0.3; 95% CI, −0.8 to 1.41). For the critical outcome of time to **resolution of symptoms**, the important outcome of risk of complications (e.g., aspiration), and the lower-priority outcome of hospital length of stay, there were no human trials found.

Fructose (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we found low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[88] with 165 diabetic patients treated with fructose (Fruit to Go) and 165 treated with glucose tablets that showed benefit with glucose, with a lower incidence of resolution of symptoms 15 min after treatment for diabetic patients treated with fructose compared with glucose tablets (RR, 0.77; 95% CI, 0.68–0.86). For the critical outcome of time to resolution of symptoms, the important outcomes of risk of complications (e.g., aspiration) and blood glucose, and the low-priority outcome of hospital length of stay, there were no human trials found.

Orange juice (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we found very-low-quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from 2 RCTs[89,90] with the pooled data of 50 diabetic patients treated with orange juice and 58 treated

Table 2
Type of dietary sugar representing 15 g of carbohydrates and Number of People With Improvement in Hypoglycemia Within 15 Min.

Type of dietary sugar	Carbohydrates per serving	Measure representing 15 g carbohydrates[a]	Clinical relief 15 min or less after ingestion
Glucose tablets	Varies	Varies	194/223 (87.0%)
Glucose solution[a,b]	1 g/10 mL	150 mL	5/6 (83.3%)
Glucose gel[a,c]	15 g of glucose in 40 g of 40% dextrose gel	15 g	2/6 (33.3%)
Cornstarch hydrolysate[a,d]	15 g cornstarch	15 g	4/5 (80%)

[a] Glucose solution, glucose gel, and hydrolysate were evaluated in 1 study.[90]
[b] 15 g of glucose dissolved in 150 mL of water.
[c] Hypostop, Novo Industries.
[d] 15 g of cornstarch hydrolysate containing 2%–3% glucose, 6%–8% maltose, 89%–92% oligosaccharides and polysaccharides, and 0.15% protein (Glucides 19, Roquette Freres, Lestrem, France) diluted in 150 mL of water.

with glucose tablets that showed no difference in the resolution of symptoms 15 min after treatment for diabetic patients treated with orange juice compared with glucose tablets (RR, 0.84; 95% CI, 0.69–1.02). For the important outcome of **blood glucose**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[90] with 6 diabetic patients treated with orange juice and 6 treated with glucose tablets that showed no benefit with glucose tablets, with the MD (mmol/L) in blood glucose 15 min after ingestion lower with orange juice than with glucose tablets (MD, −0.7; 95% CI, −1.55 to −0.15). Very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[87] with 8 diabetic patients treated with orange juice and 9 treated with glucose tablets showed no difference in a diabetic patient's likelihood of having a 20-mg/dL increase in blood glucose level 20 min after treatment with orange juice compared with glucose tablets (RR, 0.48; 95% CI, 0.18–1.26). For the critical outcome of time to **resolution of symptoms**, the important outcome of risk of complications (e.g., aspiration), and the low-priority outcome of hospital length of stay, no human trials were found.

Jelly beans (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief less in 15 min or less), we found very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[89] with 45 diabetic patients treated with jelly beans and 52 treated with glucose tablets that showed no difference in the resolution of symptoms 15 min after treatment, whether diabetic patients were treated with jelly beans or glucose tablets (RR, 0.85; 95% CI, 0.69–1.04). For the critical outcome of time to resolution of symptoms, the important outcomes of risk of complications (e.g., aspiration) and blood glucose, and the low-priority outcome of hospital length of stay, no human trials were found.

Mentos (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we found very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[89] with 48 diabetic patients treated with Mentos and 52 treated with glucose tablets that showed no difference in the resolution of symptoms 15 min after treatment, whether diabetic patients were treated with Mentos or glucose tablets (RR, 1.06; 95% CI, 0.92–1.21). For the critical outcome of time to resolution of symptoms, the important outcomes of risk of complications (e.g., aspiration) and blood glucose, and the low-priority outcome of hospital length of stay, no human trials were found.

Milk (I) compared with glucose tablets (C). For the important outcome of **blood glucose** (diabetic patients with at least a 20-mg/dL increase of blood glucose by 20 min), we found very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[87] that included 5 diabetic patients treated with whole milk and 9 treated with glucose tablets, showing no difference in likelihood of a 20-mg/dL increase in blood glucose level 20 min after treatment, whether diabetic patients were treated with milk or glucose tablets (RR, 0.11; 95% CI, 0.01–1.62). For the critical outcome of time to **resolution of symptoms**, the important outcomes of risk of complications (e.g., aspiration) and hypoglycemia, and the low-priority outcome of hospital length of stay, no human trials were found.

Glucose gel (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[90] that included 6 diabetic patients treated with glucose gel and 6 treated with glucose tablets, finding no difference in the resolution of symptoms 15 min after treatment (RR, 0.5; 95% CI, 0.14–1.77).

For the critical outcome of time to resolution of symptoms, the important outcomes of risk of complications (e.g., aspiration) and blood glucose, and the low-priority outcome of hospital length of stay, no human trials were found.

Glucose solution (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[90] that included 6 diabetic patients treated with glucose solution and 6 treated with glucose tablets, finding no difference in the resolution of symptoms 15 min after treatment (RR, 1.25; 95% CI, 0.64–2.44).

For the critical outcome of time to resolution of symptoms, the important outcomes of risk of complications (e.g., aspiration) and blood glucose, and the low-priority outcome of hospital length of stay, no human trials were found.

Cornstarch hydrolysate (I) compared with glucose tablets (C). For the important outcome of **hypoglycemia** (clinical relief in 15 min or less), we found very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[90] that included 5 diabetic patients treated with cornstarch hydrolysate 15 g and 6 treated with glucose tablets, finding no difference in the resolution of symptoms 15 min after treatment (RR, 1.20; 95% CI, 0.59–2.45).

For the critical outcome of time to resolution of symptoms, the important outcomes of risk of complications (e.g., aspiration) and blood glucose, and the low-priority outcome of hospital length of stay, no human trials were found.

The following dietary sugars were evaluated in the included studies:

- **Skittles:** ~90 g carbohydrate per 100 g, sugar (sucrose) corn syrup, partially hydrogenated soybean oil, fruit juice from concentrate (grape, strawberry, lemon, lime, orange), citric acid, dextrin, natural and artificial flavors, gelatin, food starch–modified coloring, ascorbic acid
- **Fruit to Go:** apple pure concentrate; apple, cherry, and elderberry juice concentrates; wild berry concentrate (concentrated cherry, raspberry, blueberry, cranberry and boysenberry juices, natural flavor); citrus pectin; natural flavor; lemon juice concentrate
- **Mentos:** 2.8 g carbohydrate in each mint (71% glucose and 29% oligosaccharides), 91.6 g carbohydrate per 100 g, 69.3 g sugar per 100 g, sugar, glucose syrup (corn), reconstituted fruit juices (strawberry, orange, lemon; 2.5%), hydrogenated vegetable oil (coconut), acid (citric acid), rice starch, thickeners (gum arabic, gellan gum, flavorings, glazing agent [carnauba wax]), emulsifier (sucrose esters of fatty acids), colors
- **Glucose gel:** 15 g of glucose in 40 g of 40% dextrose gel (Hypostop, Novo Industries)
- **Glucose solution:** 15 g of glucose dissolved in 150 mL of water
- **Cornstarch hydrolysate:** 15 g of cornstarch hydrolysate containing 2% to 3% glucose, 6% to 8% maltose, 89% to 92% oligosaccharides and polysaccharides, and 0.15% protein (Glucides 19, Roquette Freres, Lestrem, France) diluted in 150 mL of water.

Treatment recommendation

We recommend that first aid providers administer glucose tablets for treatment of symptomatic hypoglycemia in conscious individuals (strong recommendation, low-quality evidence). We suggest that if glucose tablets are not available, various forms of dietary sugars such as Skittles, Mentos, sugar cubes, jelly beans, or orange juice can be used to treat symptomatic hypoglycemia

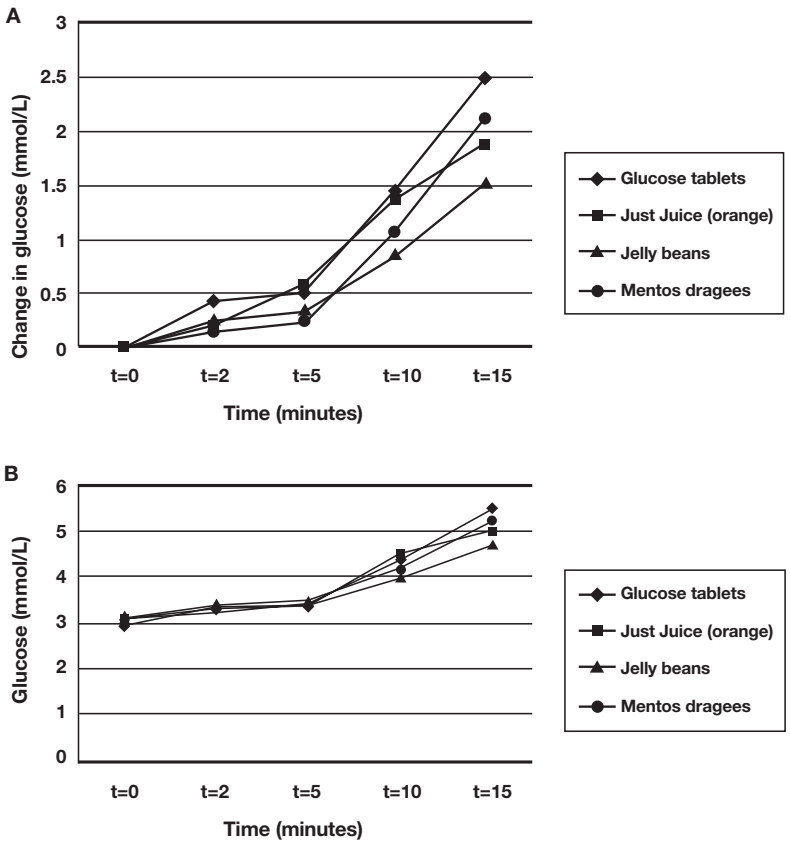

Fig. 3. Change in blood glucose from baseline for 4 treatment groups. **A**, Mean change in blood glucose from baseline by time for 4 treatment groups ($P = 0.034$ at 10 minutes and $P = 0.005$ at 15 minutes, respectively, between groups). **B**, Mean blood glucose by time for 4 treatment groups ($P = 0.099$ at 10 minutes and $P = 0.026$ at 15 minutes, respectively, between groups). From McTavish L, Wiltshire E. Effective treatment of hypoglycemia in children with type 1 diabetes: a randomized controlled clinical trial. *Pediatr Diabetes*. 2011;12:381–7.[89]

in conscious individuals (weak recommendation, very-low-quality evidence).

There is insufficient evidence to make a recommendation on the use of whole milk, cornstarch hydrolysate, and glucose solution, or glucose gels as compared with glucose tablets for the treatment of symptomatic hypoglycemia.

Values, preferences, and task force insights

In making this recommendation, we acknowledge the likelihood that glucose tablets will not always be available and that other dietary sugars are often more accessible.

In the 4 studies, most individuals had symptom improvement 10 to 15 min after treatment.

A rerun of the original literature search was performed in January 2015. No new studies were identified that subsequently altered the treatment recommendation.

This review generated a number of excellent questions within the ILCOR task forces and via public commenting. Several of the comments asked if alternative forms of candy or dietary sugars could be substituted for those listed in the tables. Although alternative dietary sugars and candy may be effective in treating hypoglycemia, the forms of sugars listed in this review are the specific dietary sugars that have been evaluated, with the specific amount used (i.e., number of candies or amount of orange juice) equating to glucose 15 to 20 g. Those who commented also asked if there is any harm from giving more than the tested amount of dietary sugars. While this review did not look at adverse effects of administering more sugar than needed, it is well known that providing more sugar than needed to diabetics with symptomatic hypoglycemia can lead to "overshooting" of blood glucose goals, which, when repeated over time, may be as harmful as recurrent episodes of hypoglycemia.

Concern was expressed over administration of oral sugars to diabetics with symptomatic hypoglycemia, particularly if they have altered mental status. The recommendations made by this task force apply to individuals with symptomatic hypoglycemia *who are conscious*, *able to follow commands*, and *able to swallow*. If these criteria are not present, oral treatment should be withheld because there is risk of aspiration, and EMS (eg, 9-1-1 or 1-1-2) rescue services should be contacted.

The evidence reviewers for this topic were asked if some guidance could be provided in terms of the time required for resolution of symptoms of hypoglycemia after treatment using dietary sugar supplements as tested, to help determine when a repeat treatment may be necessary. For all tested dietary sugars, blood glucose levels did not improve substantially until 10 to 15 min after treatment (Fig. 3).

Glucose gels and paste are not directly equivalent to oral glucose tablets in terms of dosing and absorption, and, therefore, we did not include them in the control arm of this review. Instead, these agents were included as interventions compared with glucose tablets, with the finding of a single study with a very small number of subjects, showing them to be suboptimal as compared with oral glucose tablets. The task force strongly believes that further studies are needed with glucose gels and paste to determine if they are absorbed through the buccal mucosa or sublingually (versus swallowed), and to determine any dose equivalence to glucose tablets. We are aware of studies evaluating dextrose spray, gel, or paste for neonates or children, but without a glucose tablet comparison; thus, these studies were excluded from this review.

Table 3
Effectiveness/beneficial effects of various rehydration solutions.

Fluid	PICO outcome	Studies (RCT/Obs)	Subjects	Benefit CE	No difference	Benefit water	Total outcomes
12% CE	Volume/hydration status	1 (1/0)	30	1			1
5%–8% CE	Volume/hydration status	8 (5/3)	204	10	5		15
5%–8% CE	Vital signs	3 (2/1)	86		5		5
5%–8% CE	Hyperthermia	1 (1/0)	36		1		1
5%–8% CE	Hyponatremia	1 (1/0)	18	3			3
5%–8% CE	Advanced medical care	1 (1/0)	18	3			3
5%–8% CE	Patient satisfaction	2 (1/1)	50		8		8
3%–4% CE	Volume/hydration status	3 (3/0)	66	3			3
3%–4% CE	Patient satisfaction	2 (2/0)	36	1	3		4
Coconut water	Volume/hydration status	3 (3/0)	60	3	1		4
Coconut water	Patient satisfaction	2 (2/0)	44	2	2	1	5
3% Na + coconut water	Volume/hydration status	1 (1/0)	20	3			3
3% Na + coconut water	Patient satisfaction	1 (1/0)	20	1			1
Coconut water (conc)	Volume/hydration status	1 (1/0)	12	1	1		2
Coconut water (conc)	Vital signs	1 (1/0)	24		1		1
Coconut water (conc)	Patient satisfaction	1 (1/0)	24			2	2
Green tea–4.2% CE	Blood glucose	1 (0/1)	48	1			1
Lemon tea–CE	Volume/hydration status	1 (0/1)	26		2		2
Lemon tea–CE	Vital signs	1 (0/1)	26		1		1
Lemon tea–CE	Patient satisfaction	1 (0/1)	26		2	4	6
Chinese tea–caffeine	Volume/hydration status	1 (1/0)	20		4		4
2% Milk	Volume/hydration status	1 (1/0)	22	2			2
2% Milk + Na/K	Volume/hydration status	1 (1/0)	22	2			2

CE indicates carbohydrate–electrolyte; conc, from concentrate; K, potassium; Na, sodium; Obs, observational; PICO, population, intervention, comparator, outcome; and RCT, randomized controlled trials.

Knowledge gaps

More evidence and well-designed studies are needed regarding

- Complications associated with various oral hypoglycemia treatment options
- Hospital length of stay for various oral hypoglycemia treatment options
- Other dietary forms of sugars that patients or providers may have readily available (e.g., high-fructose syrup drinks or soda pop soft drinks)
- Glucose gels, pastes, and spray
- Dietary sugar snacks containing gelatin (jelly beans, jelly lollies, or candies), honey, and sweetened condensed milk

Exertion-related dehydration and oral rehydration (FA 584)

Among adults and children with exertion-related dehydration (P), does drinking oral carbohydrate-electrolyte (CE) liquids (I), compared with drinking water (C), change volume/hydration status, vital signs, development of hyperthermia, development of hyponatremia, need for advanced medical care, blood glucose, patient satisfaction (O)?

Introduction

A review of this topic was performed in 2010 and concluded that CE beverages are recommended for rehydration of individuals who become dehydrated through sweating in hot climates and/or exercise. For the 2015 review, the task force used an extensive literature search combined with GRADE methodology, resulting in a much larger number of included studies. In addition, we included several alternative beverages with varying CE content compared with water. The authors of some included studies noted that a relatively lower urine volume is considered an indicator for increased intravascular volume during the immediate postexercise rehydration period.[86,89,91] The physiologic basis of this relates to a fall in plasma osmolality and sodium concentration with plain water ingestion after exercise, which stimulates urine production and reduces the stimulus to drink, both of which delay the rehydration process. Addition of sodium chloride to plain water has been shown to increase fluid intake while reducing urine output. Thus, for this review, a lower urine output in the first several hours after ingestion of studied fluids is considered a beneficial effect for rehydration. The rehydration index is an indication of how much of the fluid ingested was actually used in body weight restoration,[92,93] with a lower number reflecting a higher amount of ingested fluid used in body weight restoration.

Consensus on science

After the application of inclusion and exclusion criteria to the 1751 initial citations, a total of 12 studies were included. A summary of the evidence from these 12 studies is provided (Table 3).

12% CE solution (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[91] with 30 subjects showing a benefit with the use of CE solution, with increased fluid retention (%) at 2 h after exercise (MD, 16.1; 95% CI, 7.45–24.75).

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, and development of hyponatremia, or the important outcomes of blood glucose, need for advanced medical care, and patient satisfaction.

5% to 8% CE solution (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 8 studies including 204 subjects showing an overall benefit to 5% to 8% CE solution compared with water in 10 of 15 outcomes, and 5 of 15 showing no difference:

- Very-low-quality evidence (downgraded for imprecision) from 1 observational study[94] with 38 subjects showing at 2 h after hydration no difference for body weight loss (kg) with CE solution compared with water, a benefit with CE solution with increased rehydration (%) (MD, 8; 95% CI, 6.09–9.91), and a benefit with CE solution for increased blood volume response (%) (MD, 2.8; 95% CI, 2.26–3.34).
- Moderate-quality evidence (downgraded for imprecision) from 1 RCT[95] with 18 subjects showing no benefit for CE solution

compared with water for rehydration (%) at 4 h after hydration (MD, −1.6; 95% CI, −11.12 to 7.92).

- Very-low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[91,96] with 54 subjects showing no difference in fluid retention (%) at 2 h after hydration for CE solution compared with water; low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[96,97] with 44 subjects showing a benefit of CE solution for increased fluid retention (%) at 3 h (MD, 15.6; 95% CI, 12.44–18.8); very-low-quality evidence (downgraded for imprecision) from 1 observational study[98] with 26 subjects showing a benefit with CE solution for increased fluid retention (%) at 3 h (MD, 21.7; 95% CI, 9.89–33.51); very-low-quality evidence (downgraded for imprecision) from 1 observational study[99] with 26 subjects showing a benefit with CE solution for increased fluid retention (%) at 4 h (MD, 22; 95% CI, 9.6–34.4); low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[100] with 22 subjects showing no difference in fluid retention (%) at 4 h.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[97] with 20 subjects showing a benefit with CE solution compared with water with decreased mean urine volume by weight (g) between 1 and 2 h after hydration (MD, −175; 95% CI, −206.37 to −143.63) and a benefit of CE solution with decreased mean urine volume between 2 and 3 h after hydration (MD, −41; 95% CI, −64.27 to −17.73); very-low-quality evidence (downgraded for imprecision) from 1 observational study[94] with 38 subjects showing at 2 h after hydration a benefit with CE solution with decreased mean urine volume (mL) (MD, −160; 95% CI, −198.15 to −121.85); very-low-quality evidence (downgraded for imprecision) from 1 observational study[98] with 26 subjects showing a benefit with CE solution with decreased mean urine volume (mL) at 3 h after hydration (MD, −465.3; 95% CI, −700.73 to −229.87); low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[100] with 22 subjects showing no difference for mean urine volume (mL) at 4 h after hydration; and very-low-quality evidence (downgraded for imprecision) from 1 observational study[99] with 26 subjects showing a benefit with CE solution with decreased mean urine volume (mL) at 4 h after hydration (MD, −277; 95% CI, −458.26 to −95.74).
- Very-low-quality evidence (downgraded for imprecision) from 1 observational study[98] with 26 subjects showing no difference in plasma volume change (%) at 3 h after hydration with CE solution; 1 observational study of very-low-quality evidence[99] (downgraded for imprecision) with 26 subjects showing a benefit with CE solution with increased plasma volume change (%) at 4 h (MD, 11; 95% CI, 9.42–12.58).

For the critical outcome of **vital signs**, we identified the following:

- Very-low-quality evidence (downgraded for imprecision) from 1 observational study[99] with 26 subjects showing no significant difference for HR (BPM) at 1 h after hydration and at 3 h after hydration with CE solution.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[101] with 36 subjects showing no difference in HR (BPM) 20 min after hydration or respiratory rate (BPM) 20 min after hydration with CE solution.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 subjects showing no benefit with CE solution for HR (BPM) at 3 h after hydration (MD, 7; 95% CI, −0.02 to 14.02).

For the critical outcome of **development of hyperthermia**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[101] with 36 subjects showing no difference in core temperature (°C) after hydration with CE solution compared with water.

For the critical outcome of **development of hyponatremia** (a potential complication of endurance exercise), we identified moderate-quality evidence (downgraded for imprecision) from 1 RCT[95] with 18 subjects showing an increased serum sodium (mmol/L) at 2 h after hydration (MD, 3; 95% CI, 2.08–3.92), at 3 h (MD, 3; 95% CI, 2.08–3.92), and at 4 h after hydration (MD, 4; 95% CI, 3.08–4.92) with CE solution compared with water.

We did not identify any evidence to address the important outcome of need for advanced medical care.

For the important outcome of **patient satisfaction**, we identified the following:

- Very-low-quality evidence (downgraded for imprecision) from 1 observational study[95] with 26 subjects showing no difference in abdominal discomfort ratings (1–10) with CE solution compared with water at 2, 3, and 4 h after hydration, and no difference in stomach fullness ratings (1–10) at 2, 3, or 4 h after hydration.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 participants showing no difference in stomach upset ratings (1–5) at 2 or 3 h after hydration with CE solution compared with water.

We did not identify any evidence to address the important outcome of blood glucose.

3% to 4% CE solution (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified the following:

- Low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[92,93] with 36 subjects showing no difference in the rehydration index for CE solution compared with water.
- Very-low-quality evidence (downgraded for risk of bias and imprecision) from 3 RCTs[91–93] with 66 subjects showing a benefit with CE solution with increased fluid retention (%) at 2 h after hydration (MD, 8.97; 95% CI, 7.54–10.4).
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[93] with 20 subjects showing a benefit of CE solution with decreased cumulative urine output (mL) at 2 h into the hydration period (MD, −174.5; 95% CI, −220.89 to −128.11).

For the important outcome of **patient satisfaction**, we identified the following:

- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[93] with 20 subjects showing no difference for nausea scores (1–5) at 90 min after hydration with CE solution, and low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[92,93] with 36 subjects showing no difference for nausea scores (1–5) at 2 h for CE solution compared with water.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[93] with 20 subjects showing no difference for stomach upset scores (1–5) at 90 min after hydration with CE solution compared with water, and low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[92,93] with 36 subjects showing a benefit with CE solution with a decrease in stomach upset scores (1–5) at 2 h after hydration (MD, −0.3; 95% CI, −0.45 to 0.16).

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, and development of hyponatremia, or the important outcomes of blood glucose and need for advanced medical care.

Coconut water (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified the following:

- Low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[92,93] with 36 subjects showing no difference in rehydration index for coconut water compared with water.
- Very-low-quality evidence (downgraded for risk of bias and imprecision) from 3 RCTs[92,93,96] with 60 subjects showing a benefit with coconut water with increased fluid retention (%) at 2 h after hydration (MD, 5.81; 95% CI, 4.35–7.27), and very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 subjects showing no difference in fluid retention (%) at 3 h after hydration with coconut water compared with water.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[93] with 20 subjects showing a benefit with coconut water with decreased cumulative urine output (mL) at 2 h into the hydration period (MD, −76.9; 95% CI, −120.34 to −33.46) compared with water.

For the important outcome of **patient satisfaction**, we identified the following:

- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[93] with 20 subjects showing no difference for nausea scores (1–5) with coconut water compared with water at 90 min after hydration and at 2 h.
- Low-quality evidence (downgraded for risk of bias and imprecision) from 1 randomized trial[93] with 20 subjects showing a benefit with coconut water with a decrease in stomach upset scores (1–5) at 90 min after hydration (MD, −0.4; 95% CI, −0.54 to −0.26), very-low-quality evidence (downgraded for risk of bias and imprecision) from 2 RCTs[93,96] with 44 subjects showing benefit with coconut water with a decrease in stomach upset scores (1–5) at 2 h after hydration (MD, −0.41; 95% CI, −0.55 to −0.28), and very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 subjects showing no benefit with coconut water with an increase in stomach upset scores (1–5) at 3 h after hydration with the coconut water compared with water (MD, 1.84; 95% CI, 1.08–2.6).

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, or development of hyponatremia, or the important outcomes of blood glucose or need for advanced medical care.

3% sodium plus coconut water (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[93] with 20 subjects showing a benefit with 3% sodium plus coconut water compared with water, with a decreased rehydration index (MD, −0.7; 95% CI, −0.81 to −0.59), a benefit with 3% sodium plus coconut water with increased retained fluid (%) at 2 h after hydration (MD, 10.5; 95% CI, 9.09–11.91), and a benefit with 3% sodium plus coconut water with decreased urine volume (mL) at 2 h after hydration (MD, −150.3; 95% CI, −187.39 to −113.21).

For the important outcome of **patient satisfaction**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 randomized trial[93] with 20 subjects showing a benefit with 3% sodium plus coconut water compared with water, with less nausea (1–5) at 90 min after hydration (MD, −0.2; 95% CI, −0.38 to −0.02).

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, and development of hyponatremia, or the important outcomes of blood glucose or need for advanced medical care.

Coconut water from concentrate (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 subjects showing no difference in mean fluid retention at 120 min after exercise (MD, 10.7; 95% CI, −6.39 to 27.79) for coconut water from concentrate compared with water, but higher mean fluid retention with coconut water at 180 min after exercise (MD, 17; 95% CI, 0.86–33.14).

For the critical outcome of **vital signs**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 subjects showing no difference in mean HR (BPM) at 180 min after exercise with coconut water from concentrate compared with water.

For the important outcome of **patient satisfaction**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[96] with 24 subjects showing no difference in mean stomach upset score (1–5) for coconut water from concentrate compared with water at 120 min (MD, 1.84; 95% CI, 0.91–2.77) and at 180 min (MD, 1.47; 95% CI, 0.6–2.34).

We did not identify any evidence to address the critical outcomes of development of hyperthermia or development of hyponatremia, or the important outcomes of blood glucose or need for advanced medical care.

Green tea-based 4.2% CE solution (I) compared with water (C). For the important outcome of **blood glucose**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[102] with 48 subjects showing that a green tea-based 4.2% CE solution was associated with increased mean glucose (mg/dL) at 2 h after hydration compared with water (MD, 6.9; 95% CI, 1.59–12.21).

We did not identify any evidence to address the critical outcomes of volume/hydration status, vital signs, development of hyperthermia, and development of hyponatremia, or the important outcomes of need for advanced medical care and patient satisfaction.

Lemon tea-based 12% CE (t-CE) solution (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified of very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[99] with 26 subjects showing no difference in mean retained fluid (%) at 4 h after hydration (MD, 6; 95% CI, −5.15 to 17.15) with t-CE solution compared with water and no difference in mean urine volume (mL) at 4 h after hydration.

For the critical outcome of **vital signs**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[99] with 26 subjects showing no difference in mean HR (BPM) at 60 min after hydration with t-CE solution compared with water.

For the important outcome of **patient satisfaction**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[99] with 26 subjects showing no difference in mean abdominal discomfort scores (1–10) at 120 min after hydration with t-CE, no benefit with t-CE with an increase in abdominal discomfort scores at 180 min (MD, 1.3; 95% CI, 0.69–1.91), and no benefit with t-CE compared with water with an increase in abdominal discomfort at 240 min; also, there was no difference for mean stomach fullness scores (1–10) with t-CE solution at 120 min after hydration, and no significant difference for mean stomach fullness scores with t-CE solution at 180 min or at 240 min as compared with water.

We did not identify any evidence to address the critical outcome of development of hyperthermia and development of hyponatremia, or the important outcome of blood glucose and need for advanced medical care.

Chinese tea plus caffeine (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[97] with 20 subjects showing no difference with Chinese tea plus caffeine compared with water in mean total body water loss (%), no difference in mean fluid retention (%) at 3 h after hydration, and no significant difference in mean urine volume by weight (g) between 60 and 120 min or between 120 and 180 min after hydration.

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, or development of hyponatremia, or the important outcomes of blood glucose, need for advanced medical care, or patient satisfaction.

Milk (2% fat) (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[100] with 22 subjects showing a benefit with milk (2% fat) compared with water at 4 h after hydration for fluid retention (%) (MD, 33; 95% CI, 24.64–41.36) and for urine volume (mL) (MD, −594; 95% CI, −742.34 to −445.66).

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, or development of hyponatremia, or the important outcomes of blood glucose, need for advanced medical care, or patient satisfaction.

Milk (2% fat) plus high sodium (Na^+) and potassium (K^+) concentration (I) compared with water (C). For the critical outcome of **volume/hydration status**, we identified low-quality evidence (downgraded for risk of bias and imprecision) from 1 RCT[100] with 22 subjects showing a benefit with milk (2% fat) with high Na^+/K^+ concentration compared with water at 4 h after hydration for fluid retention (%) (MD, 36; 95% CI, 29.64–42.36) and benefit with urine volume (mL) (MD, −655; 95% CI, −773.26 to −536.74). We recognize that this beverage is not a standard commercial product.

We did not identify any evidence to address the critical outcomes of vital signs, development of hyperthermia, or development of hyponatremia, or the important outcomes of blood glucose, need for advanced medical care, or patient satisfaction.

Treatment recommendation

We suggest that first aid providers use 3% to 8% CE drinks for treating exertion-related dehydration. If 3% to 8% CE drinks are not available or not tolerated, alternative beverages for rehydration include water, 12% CE solution, coconut water, 2% milk, tea, tea-CE, or caffeinated tea beverages (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we recognize that first aid providers are commonly recruited to assist at first aid stations located at sporting and challenge events and that exercise-induced dehydration is a common problem. It may not be possible to determine the exact quantity or percent of fluid loss in the first aid setting.

Public comment was made about the potential mortality associated with ingestion of water only during ultramarathons. The reviewers for this PICO question specifically looked at sodium levels reported after rehydration in the included studies and agreed that oral rehydration with CE liquids may assist in preventing hyponatremia, although this review did not specifically address exercise-associated hyponatremia. In addition, all included trials conducted exercise in a controlled environment and time period. Extreme events such as ultramarathons were not included in the evidence evaluation.

Knowledge gaps

How can a first aid provider determine the amount of liquid required for rehydration?

Eye chemical injury: irrigation (FA 540)

Among adults and children who have a chemical or other unknown substance enter the conjunctival sac (P), does irrigation with isotonic saline, balanced salt solution, or other commercial eye irrigation solutions (I), compared with irrigation with water (C), change tissue healing, functional recovery, pain, complications, time to resumption of usual activity, restoration to the preexposure condition, time to resolution of symptoms (O)?

Introduction

The 2010 review of eye injuries focused on irrigation of eyes after exposure to an unknown toxic substance, with a recommendation to use copious amounts of water unless a specific antidote is available. For 2015, the First Aid Task Force looked at which solutions might be compared with water for the management of ocular injuries from chemicals or other substances. This use of water as a comparator made the literature search extremely difficult, and no human comparative trials were identified. Thus, animal studies were later introduced into the search strategy, and 1 comparative animal study met all our inclusion criteria.

Consensus on science

Saline (I) compared with water (C). For the critical outcome of **pH level**, studied as maximum pH of the anterior chamber after alkali application to the cornea, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 in vivo observational animal study[103] using the eyes of 16 rabbits divided into 4 groups of 4 rabbits (8 eyes) in which twice normal sodium hydroxide (2 N NaOH) was applied to the corneas, demonstrating benefit (i.e., in reduction of the high, alkaline pH) with irrigation using water, including

- A statistically significant higher maximum pH when irrigating with 0.5 L of 0.9% normal saline versus 0.5 L of tap water (MD, 0.62; 95% CI, 0.25–0.99)
- A statistically significant higher maximum pH when irrigating with 1.5 L of 0.9% normal saline versus 0.5 L tap water (MD, 0.57; 95% CI, 0.035–1.105)
- A statistically significant higher maximum pH when irrigating with 0.5 L of 0.9% normal saline versus 1.5 L of tap water (MD, 0.5; 95% CI, 0.119–0.881)

No significant difference in maximum pH was found after irrigation using 1.5 L of 0.9% normal saline versus 1.5 L of tap water (MD, 0.45; 95% CI, −0.09 to 0.994).

We did not identify any evidence to address the outcomes of intraocular penetration, risk of secondary glaucoma, corneal thickness (swelling), or intraocular pressure.

Treatment recommendation

We suggest that first aid providers use continuous, large volumes of clean water for irrigation of chemical eye injuries (weak recommendation, very-low-quality evidence).

We did not identify any studies evaluating the use of irrigation for other substances entering the eye comparing irrigation solutions with water.

Values, preferences, and task force insights

In making this recommendation, we value the preservation of vision.

We recommend that the local poison center be called to assist with identification of any chemical involved in an ocular injury. Because of the dangers associated with chemical eye injuries, a healthcare professional should evaluate these injuries immediately.

Public comments expressed concern that our recommendation could be made based on a single animal study. This is a valid concern. However, although the included animal study is of a very-low-quality evidence, it is important because it demonstrates the extreme caustic nature of an alkali injury to the cornea and the need to irrigate with large volumes of water. The included study showed persistently high pH levels of the alkali-injured corneas at 3 h after irrigation with 1.5 L of either saline or water. Thus, based on this single study, we again recommend continuous irrigation of corneal injuries caused by alkaline substances with clean or tap water and to continue until a healthcare professional evaluates the injury and determines that the pH of the eye has returned to normal.

Knowledge gaps

Well-designed studies are needed to evaluate

- Irrigation with commercial eye-rinsing solutions versus tap water (controlled trial)
- Comparison between different types of commercial eye-rinsing solutions and tap water, including irrigation times
- Civilian first aid setting
- Control for confounders, type of toxin, or other substance

First aid trauma emergencies

Important trauma topics reviewed for 2015 included the first aid management of hemorrhage, angulated fractures, open chest wounds, burns (cooling of burns and burn dressings), and dental avulsion. Two additional important trauma topics were cervical spinal motion restriction and the recognition of concussion by first aid providers.

The correct management of hemorrhage and the enhancement of hemostasis in the first aid setting are essential to maintaining the circulating blood volume in acute trauma. Three PICO reviews focused on critical interventions for severe bleeding:

- There was inadequate evidence to support the use of proximal pressure points or limb elevation to control bleeding. The use of localized cold therapy is suggested for closed bleeding in extremities to aid hemostasis, but there was no evidence to support this therapy for open bleeding (Revised).
- The use of hemostatic dressings in first aid is supported when standard first aid hemorrhage control (e.g., direct wound pressure) fails to control severe bleeding or cannot be applied (Revised).
- Similarly, the evidence supports the use of tourniquets in the civilian setting when standard first aid hemorrhage control (e.g., direct wound pressure) fails to control severe external limb bleeding (Revised).

The task force recognized that the use of hemostatic dressings and tourniquets will have cost and training implications. However, the task force thought that these costs would be moderate and justified considering the benefit of maintaining circulating blood volume in the management of trauma.

- There was no evidence to support the straightening of an angulated fracture in the first aid situation, and the task force did not make a recommendation. The task force recognized the need to protect the victim from further injury by splinting the fracture in position to reduce pain or to enable safe extrication and transportation (Revised).
- The application of an occlusive dressing or device by first aid providers to an open chest wound may lead to an unrecognized tension pneumothorax. The task force suggested that these wounds be left open with local control of bleeding rather than risk occlusion (New).
- There is a growing body of scientific evidence showing complications related to use of cervical collars. When combined with concern for potential secondary injury due to neck movement during attempts to apply a collar, this has led to a suggestion (weak recommendation) against the use of cervical collars by first aid providers. The task force acknowledges that first aid providers may not be able to distinguish between high- and low-risk criteria for spinal injuries, and recognizes the possible need for alternative methods of cervical spine motion restriction or stabilization, but these were not formally reviewed. The task force believes that formal spinal motion restriction in high-risk individuals is best accomplished by trained emergency medical rescuers or healthcare professionals (Revised).
- The recognition of concussion after head trauma is a common challenge of first aid. No simple concussion scoring system was found that would assist the first aid provider in making this important diagnosis; however, there are more advanced scoring systems for use by healthcare professionals (New).
- The correct first aid management of burns is critical to their eventual outcome. Cooling burns is a widespread first aid practice, but it is only supported by low-quality scientific evidence. No evidence was found as to the preferred method of cooling, the temperature of the coolant, or the duration of cooling. It was recommended that active cooling begin as soon as possible by using cool or nonfreezing water or cooling adjuncts such as gel pads (Revised).
- A comparison of wet dressings with dry dressings for thermal burns yielded no recommendation. There were no studies comparing plastic wrap, considered a dry dressing, with a wet dressing (Revised).
- It is widely recommended that an avulsed tooth be replanted immediately in the conscious victim. However, first aid providers may not have the skills or the willingness to undertake this procedure. This review suggests a series of commercially available storage solutions and simple household mediums, when available, for the short-term storage of an avulsed tooth until reimplantation can be accomplished (New).

Control of bleeding (FA 530)

Among adults and children with bleeding (P), does application of localized cold therapy, elevation of extremity, and/or application of pressure over proximal pressure points (I), compared with direct pressure alone (C), change overall mortality, hemostasis, major bleeding, complications, hospital length of stay (O)?

Introduction

For 2015, this review compared direct pressure with either localized cold therapy (such as a cold pack), elevation of an extremity, or proximal pressure points. The absence of literature on all interventions except localized cold therapy, and the interpretive caution required when generalizing results from hospital to first aid settings, limited the treatment recommendations.

Consensus on science

For the critical outcome of mortality, we identified no evidence.

For the critical outcome of **hemostasis**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[104] showing a benefit in the reduction of femoral hematoma formation in post-PCI patients receiving cold pack (vasoconstriction) compared with sandbags (compression). This study enrolled 50 patients and reported a statistically significant reduction in femoral hematoma formation, but no quantitative data were provided to calculate the MD and CI. The publication included an illustration suggesting that cold compression reduced the size of the hematoma by approximately 20 cm^2 over 180 min in the cold compression group and by less than approximately 10 cm^2 in the compression-only group.

For the critical outcome of **major bleeding**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT,[105] which enrolled 80 patients who underwent total knee arthroplasty and reported an MD in calculated total body blood loss in the cold compression group of 610 mL (95% CI, 415.6–804.4) and an MD in extravasation of 357 mL (95% CI, 184.6–529.3).

For the important outcome of **complications**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 RCT[105] showing a nonsignificant reduction in complications of the occurrence of deep vein thrombosis in the cold compression group (1/60 knees) compared with the non–cold compression group (2/40 knees).

For the important outcome of hospital length of stay, we identified no evidence.

Treatment recommendation

We suggest that localized cold therapy with or without pressure may be beneficial in hemostasis for closed bleeding in extremities (weak recommendation, very-low-quality evidence).

There is inadequate evidence to make a treatment recommendation concerning the use of proximal pressure points, localized cold therapy for external bleeding, or the elevation of an extremity for control of bleeding.

Values, preferences, and task force insights

In making this weak recommendation, we do so cautiously because we are generalizing results from the healthcare setting to the first aid setting.

Public comments on this topic expressed concern about the application of localized cold therapy to pediatric patients and the risk of hypothermia. The task force thought that local application of cold therapy to an area of closed bleeding, such as a bruise or hematoma, is intended to be directed at a relatively small, limited-size injury and would not result in hypothermia (e.g., an instant cold pack applied to a bruise).

Knowledge gaps

There is a paucity of literature comparing different bleeding-control strategies commonly used by first aiders. Studies assessing the relative effectiveness of cold therapy, elevation of an extremity, and proximal pressure in addition to manual compression in the first aid setting are needed, as are studies assessing the effectiveness of combining these strategies with other interventions such as hemostatic agents and tourniquets. In addition, further research exploring how much pressure is required to control bleeding by using a proximal pressure point is required to determine if this is feasible by a first aid provider.

Hemostatic dressings (FA 769)

In patients with severe external bleeding (P), does the application of topical hemostatic dressings plus standard first aid (I), compared with standard first aid alone (C), change overall mortality, vital signs, hemostasis, complications, blood loss, major bleeding, incidence of cardiac arrest (O)?

Introduction

Hemostatic dressings are commonly used to control bleeding in the surgical and military settings. Early-generation powder or granular hemostatic agents were poured directly into the wound and were associated with exothermic reactions that could exacerbate tissue injury. These products have improved in recent years, and hemostatic agent–impregnated dressings are now believed to be associated with fewer adverse effects. Their use in the civilian setting is becoming more common.

The objective of this review was to evaluate the current evidence for the use of hemostatic dressings and to identify if their use by first aid providers can be safely recommended.

Consensus on science

For the critical outcome of **overall mortality**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 human case series[106] enrolling 26 patients, demonstrating that 7.7% of patients with hemostatic dressings (2/26) died (no comparison group). We also identified very-low-quality evidence (downgraded for indirectness) from 7 animal RCT studies[107–113] showing benefit, where 29.1% (25/86) of subjects who were treated with hemostatic dressings died, compared with 65.8% (54/82) who were not treated with hemostatic dressings (RR, 0.44; 95% CI, 0.31–0.64).

For the critical outcome of **hemostasis**, very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 4 human case series[106,114–116] enrolling 130 participants demonstrated that hemostasis occurred in 90.8% of participants (118/130) (no comparison group). We also identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 3 animal studies[112,113,117] showing benefit where hemostasis occurred in 74.2% (23/31) who were treated with hemostatic dressings, compared with 50% (13/26) who were not treated with hemostatic dressings (RR, 1.48; 95% CI, 0.96–2.30).

For the critical outcome of **complications**, very-low-quality evidence (downgraded for indirectness and imprecision) from 4 human case series studies[106,114–116] enrolling 96 participants demonstrated that complications from hemostatic dressings occurred in 3% of participants (3/96) (no comparison group).

For the important outcome of **time to bleeding cessation**, very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 human case series[114] demonstrated that 73% of participants (25/34) achieved hemostasis in under 3 min after a hemostatic dressing was applied (no comparison group).

Treatment recommendation

We suggest hemostatic dressings be used by first aid providers when standard first aid hemorrhage control (including direct pressure with or without a dressing) cannot control severe external bleeding (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place increased value on the benefits of hemostasis, which outweigh the risks (including infection and/or burns). The cost of the intervention is moderate.

This PICO question specifically addressed hemostatic dressings and does not apply to other agents (such as granules) that may be applied alone or followed by a gauze dressing.

A rerun of the literature search performed in January 2015 found no new studies that would change the treatment recommendation or strength of recommendation.

The 2010 consensus on science treatment recommendation stated that application of topical hemostatic agents to control life-threatening bleeding not controlled by standard techniques was "reasonable," although the best agents and the conditions under which it should be applied were not known. For 2015, it remains unclear when hemostatic dressings compared with other interventions, such as direct pressure with or without gauze dressing and/or tourniquets, should be used for the control of severe bleeding. However, the task force thinks that hemostatic dressings may be of greatest use in severe external bleeding in locations where a tourniquet cannot be applied, or when a tourniquet is not available and standard hemorrhage control (direct pressure with or without gauze dressing) is not effective. Effective use of hemostatic dressings requires that first aid providers be trained in proper application techniques.

Knowledge gaps

More research is required to establish how much training is required and what type of training should be used for first aid providers to apply hemostatic dressings to bleeding wounds, what should be used, and when it should be used. Specific questions include

- Which specific hemostatic dressings should be used by first aid providers?
- In humans, how do hemostatic dressings compare with properly applied standard first aid for effective bleeding cessation, time to cessation, and complications?
- How do hemostatic dressings compare with tourniquet application by first aid providers?
- Compared with standard hemorrhage control, does the use of hemostatic dressings lead to differences in mortality in humans?

Use of a tourniquet (FA 768)

Among adults and children with severe external limb bleeding (P), does the application of a tourniquet (I), compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, blood loss, incidence of cardiac arrest (O)?

Introduction

Tourniquets have been used in military settings for severe external limb bleeding for many years. Various types of tourniquets have been used, including improvised and commercially available devices. Until recently, there have been little data from the use of tourniquets in the civilian setting to establish their safety and effectiveness, and their use has remained controversial.

In 2010, the evidence was reviewed for the following questions: When direct pressure fails to stop bleeding, does the application of a tourniquet improve outcome? In which circumstances is the application of a tourniquet appropriate? At that time, no studies were found on the use of tourniquets to control hemorrhage in a civilian setting by first aid providers. However, evidence was reviewed from military settings. In civilian settings, tourniquets were only recommended for control of extremity hemorrhage if direct pressure is not adequate or possible (e.g., multiple injuries, inaccessible wounds, multiple victims). Further, specifically designed tourniquets were found to be superior to improvised ones, but they could be used only with proper training. There was insufficient evidence to determine how long a tourniquet could remain in place safely.

The objective of the 2015 question was to review the current evidence in the prehospital setting on the use of tourniquets for control of severe external limb bleeding compared with standard hemorrhage control (such as direct pressure with or without a dressing) alone. Evaluated studies were from both civilian EMS and military settings and included a mix of commercial, improvised, and unspecified types of tourniquets. The evidence remains unclear regarding which type of tourniquet (improvised or commercially available) or specific brand of tourniquet is most effective. The body of literature on this topic is continuously growing and includes large civilian series, but controlled studies with a comparison group are lacking.

Consensus on science

For the critical outcome of **hemostasis**, we identified low-quality evidence from 1 human study[118] with a comparison group enrolling 70 patients showing benefit where 83% of those who had a tourniquet applied (35/42) achieved hemostasis compared with 61% of those who did not have a tourniquet applied (17/28) (RR, 10.54; 95% CI, 6.55–16.96), and very-low-quality evidence (downgraded for risk of bias and indirectness) from 6 human case series[69,119–123] enrolling a total of 750 patients demonstrating that 74.7% of patients who had a tourniquet applied (560/750) achieved hemostasis (MD not estimable because control group was lacking).

For the critical outcome of **mortality**, we identified low-quality evidence (downgraded for risk of bias) from 3 human studies[118,124,125] with a comparison group enrolling 1768 patients showing no difference, where 12% of patients who had a tourniquet applied (91/791) died compared with 9% of patients who did not have a tourniquet applied (89/977) (RR, 1.08; 95% CI, 0.82–1.43) and 7 very-low-quality evidence (downgraded for risk of bias) human case series[120–122,126–129] enrolling 903 patients, where 10% of those patients who had a tourniquet applied (92/903) died.

For the critical outcome of **vital signs**, we identified low-quality evidence (downgraded for risk of bias) from 3 human studies with a comparison group[118,124,125] enrolling 1642 participants demonstrating no benefit, with an MD in HR of 3 BPM more (95% CI, 0.21–6.91) if a tourniquet was applied, and low-quality evidence (downgraded for risk of bias and imprecision) from 2 human studies with a comparison group[118,124] enrolling 284 participants demonstrating no benefit, with an MD in SBP of 9 mm Hg less (95% CI, −14.13 to −3.43) if a tourniquet was applied.

For the critical outcome of **complications**, low-quality evidence (downgraded for risk of bias and imprecision) from 1 human study with a comparison group[118] enrolling 165 patients showed benefit to tourniquet application, where 6% of patients who had a tourniquet applied (6/67) had complications compared with 9% who did not have a tourniquet applied (9/98) had complications (RR, 0.19; 95% CI, 0.06–0.55), and very-low-quality evidence (downgraded for risk of bias and imprecision) from 4 human case series studies[121,122,126,128] enrolling 846 patients documented that complications from tourniquets occurred in 4.3% of patients (36/846).

Treatment recommendation

We suggest first aid providers use a tourniquet when standard first aid hemorrhage control (including direct pressure with or without a dressing) cannot control severe external limb bleeding (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place increased value on the benefits of hemostasis, which outweigh the risks (such as compartment syndrome, nerve palsy, or secondary amputation). The cost of the intervention is moderate.

The tourniquets used in the studies evaluated included a mix of improvised and commercial devices. The maximum length of time for leaving a tourniquet in place was not reviewed.

The literature search was rerun in January 2015, and 2 additional studies were added to the consensus on science and GRADE table, 1 from the military setting[125] and 1 from the civilian EMS setting,[121] both supporting our treatment recommendation.

The task force believes that application of a tourniquet will be most effective and safe if the provider is trained with the type(s) of tourniquet to be used and if the tourniquet is applied properly and rapidly. Other situations when a tourniquet might be used instead of direct pressure were discussed. Such situations are thought to include mass casualty incidents, an unsafe scene, a complex or prolonged transfer, inability to access an injury, and caring for someone with multiple injuries requiring triage of injuries.

A major finding in this review is that the rate of adverse events with tourniquet application is low, and the rate of successful hemostasis is high. However, we did not find a relationship between the application of tourniquet and improved survival.

Knowledge gaps

More research is required to establish how much training is required and what type of training should be used for first aid providers to apply tourniquets to bleeding wounds.

Specifically research should focus on

- Tourniquet use versus no tourniquet versus double tourniquet
- Use in the civilian setting
- Control for confounders, such as concurrent use of hemostatic dressings
- For major external bleeding, a prospective registry study would be useful, including a comparison between types of tourniquets and between commercial tourniquets, and including injury severity, provider types, time to surgery, etc.
- Can instructions be given by EMS dispatchers?

Straightening of an angulated fracture (FA 503)

Among adults and children who receive first aid for an angulated long bone fracture (P), does realignment of the fracture prior to splinting (I), compared with splinting as found (C), change neurologic injury, vascular injury, splinting, pain, time to medical transportation (O)?

Introduction

Angulated extremity fractures vary in etiology and outcomes. In some circumstances, the degree of angulation of a long bone fracture may limit the ability to splint the extremity or to move the patient. We sought to learn what outcomes may result from attempts to gently realign a severely angulated fracture to facilitate splinting or transportation. Understanding outcomes from first aid procedures will help in developing training.

Consensus on science

For the question of straightening an angulated fracture, compared with splinting as found, the literature search initially returned 458 citations. After application of inclusion and exclusion criteria by title and abstract (inclusion: care provided before definitive treatment; exclusion: hospital settings, use of analgesics), 9 studies were identified for full review. Upon full review, all 9 studies were excluded because they did not completely meet criteria for inclusion; thus, no evidence was found to address the critical outcomes of neurologic injury, vascular injury, or splinting, nor was there evidence for the important outcome of pain.

There is no published evidence for or against the realignment of angulated long bone fractures as a first aid procedure in terms of neurologic or vascular injury, pain, or time to medical transportation outcomes.

Treatment recommendation

No recommendation; we found no evidence regarding the risks and benefits of straightening an angulated fracture by first aid providers.

Values, preferences, and task force insights

Consistent with the first aid principle of preventing further harm, and based on training and circumstance, providers may need to move an injured limb or person. In such situations, first aid providers should protect the victim, which includes splinting in a way that limits pain, reduces the chance for further injury, and facilitates safe and prompt transport.

Knowledge gaps

As ethical and practical considerations prohibit RCTs, high-quality non-RCTs comparing realignment versus nonrealignment are important. Describing confounders is important for developing future outcomes to be studied. If or when realignment is appropriate, what instructions or training might be given to first aid providers to optimize outcomes?

First aid treatment for an open chest wound (FA 525)

Among adults and children who are being treated for an open chest wound outside of a hospital (P), does occlusive bandage application or occlusive device (I), compared with a nonocclusive dressing (C), change or improve survival, respiratory arrest, oxygen saturation, vital signs, the rate of cardiac and respiratory arrests, improve therapeutic endpoints (oxygenation and ventilation) (O)?

Introduction

This is a new PICO question for 2015. The management of an open chest wound in the out-of-hospital setting is challenging. The most worrisome issue is the improper use of an occlusive dressing or device that potentially could lead to a tension pneumothorax. In this PICO question, we sought to compare the effects of an occlusive measure as opposed to a nonocclusive measure in individuals being treated for an open chest wound. Occlusion was the complete sealing of the wound, and nonocclusion was the maintenance of an open wound in communication with ambient air. In this review, we included animal studies because human comparative studies could not be identified.

Consensus on science

For the critical outcome of **respiratory arrest**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 animal study[130] showing benefit from using a nonocclusive device (RR, 0.059; 95% CI, 0.004–0.874).

For the critical outcome of **oxygen saturation**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 animal study[130] showing benefit from using a nonocclusive device ($P < 0.05$, MD and CI not available).

For the important outcome of **therapeutic endpoint (tidal volume)**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 animal study[130] showing benefit from using a nonocclusive device in tidal volume (mL) (MD, 34.7; 95% CI, 28.8–40.6 mL).

For the important outcome of **vital signs**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from the same animal study[130] showing benefit from using a nonocclusive device in HR (BPM) (MD, −32.0; 95% CI, −42.8 to 21.2) and respiratory rate (respirations per minute) (MD, 3.0; 95% CI, 1.5–4.5). Finally, for the important outcome of **vital signs**, we also identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from the same animal

study[130] showing no significant benefit from using a nonocclusive device in MAP (mm Hg) (MD, 4.6; 95% CI, −0.4 to 9.6).

We did not identify any evidence to address the critical outcome of survival. We did not identify any evidence to address the important outcome of rate of cardiac and respiratory arrests.

Treatment recommendations

We suggest against the application of an occlusive dressing or device by first aid providers to individuals with an open chest wound (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place higher value on the avoidance of the potential life-threatening complication of tension pneumothorax, compared with other risks associated with an open chest wound.

Public comments expressed concern about making a recommendation based solely on a single animal study. The task force took into consideration the potential life-threatening complication of an unrecognized tension pneumothorax associated with the use of an occlusive dressing or device in the first aid setting. In addition, the review recognized the long-standing accepted clinical practice of treating a tension pneumothorax by creating and maintaining an open communication between the pneumothorax and ambient air.

Furthermore, while this will require a change for some in current teaching, there was recognition of the practicality and acceptance in the first aid setting of leaving an open chest wound exposed to ambient air without a dressing or seal.

The task force discussed the reality that many dressings, both initially and over time, may themselves produce inadvertent partial or full occlusion and that this needs to be recognized as a serious potential complication.

Knowledge gaps

- Does the application of nonocclusive dressings or chest seals to patients with open chest wounds outside of a hospital improve survival and the rates of cardiac arrest and respiratory arrest (out-of-hospital or in-hospital)?
- Do nonocclusive chest seals differ in effects as compared with nonocclusive dressings?
- Does the application of nonocclusive devices delay the activation or transportation of EMS?

Cervical spinal motion restriction (FA 772)

Among adults and children with suspected blunt traumatic cervical spinal injury (P), does cervical spinal motion restriction (I), compared with no cervical spinal motion restriction (C), change neurologic injury, complications, overall mortality, pain, patient comfort, movement of the spine, hospital length of stay (O)?

Introduction

For more than 30 years, the cervical collar has been routinely applied by healthcare providers for patients with suspected cervical spine injury, with the aim of avoiding additional injury due to movement of the victim. However, there is no good quality evidence available showing clinical benefit of this intervention for injured patients, and this practice is based primarily on expert consensus and tradition. The 2010 consensus on science for the topic of spinal immobilization noted that there were no published studies to support or refute the benefit of spinal immobilization by first aid providers.[10] For 2015, the task force evaluated all available evidence focused on the use of cervical collars and/or sandbags relevant for patients with blunt traumatic cervical spinal injury.

Consensus on science

Cervical spinal motion restriction was defined as the reduction or limitation of cervical spinal movement. This definition may not be consistent with definitions used in some countries or by some organizations. Spinal stabilization was defined as the physical maintenance of the spine in a neutral position before applying spinal motion restriction devices. This evaluation was limited to mechanical cervical immobilization devices accessible to first aid providers, including cervical collars and sandbags with tape, but did not include spine boards.

(Semi)rigid collar (I) compared with no collar (C). For the critical outcome of **neurologic injury**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 nonrandomized study[131] with 5138 motorcycle crash victims, showing no difference in neurologic injury (no significant difference according to the article; however, we were unable to calculate the MD and CI, because the mean and standard deviation (SD) of the intervention and control group were not reported).

For the critical outcome of **complications (intracranial pressure)**, we identified low-quality evidence from 5 nonrandomized studies[132–136] with 107 patients in total, showing increased intracranial pressure with the use of a cervical collar (MD [mm Hg], 4.69; 95% CI, 1.95–7.43; MD [mm H20], 20.48; 95% CI, 5.62–35.33). We also identified very-low-quality evidence (downgraded for indirectness) from 1 nonrandomized study[137] with 42 healthy volunteers showing increased intracranial pressure (MD [internal jugular vein cross-sectional area], 0.19; 95% CI, 0.05–0.33) with the application of a cervical collar.

For the critical outcome of **complications (tidal volume)**, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 nonrandomized study[138] with 38 patients, showing no decrease in tidal volume (a significant decrease was reported in the publication; however, we were unable to calculate the CI because the SD of the intervention and control group was not reported).

For the important outcome of **cervical spine movement**, we identified low-quality evidence from 1 nonrandomized study[139] with 18 head-injured children showing no significant limitation of flexion (MD, −2.20; 95% CI, −7.75 to 3.35). For the same outcome, we also identified very-low-quality evidence (downgraded for indirectness) from 13 nonrandomized studies[140–152] with 457 cadavers or healthy volunteers showing significant decrease in flexion, extension, lateral bending, axial rotation, and flexion/extension (flexion: MD, −12.50; 95% CI, −13.13 to −11.87; extension: MD, −0.91; 95% CI, −1.18 to −0.64; lateral bending: MD, −1.99; 95% CI, −2.33 to −1.65; axial rotation: MD, −4.73; 95% CI, −5.16 to −4.3; flexion/extension: MD, −19.13; 95% CI, −19.89 to −18.36]). Seven additional studies[153–159] were not included in the final analysis because they were missing data (mean and/or SD of intervention and control group not reported).

For the important outcome of **patient comfort**, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 nonrandomized study[158] with 26 healthy volunteers, showing no change in patient comfort score.

We did not identify any evidence to address the important outcomes of overall mortality and pain and the less important outcome of hospital length of stay.

Soft collar (I) compared with no collar (C). For the important outcome of **cervical spine movement**, we identified very-low-quality evidence (downgraded for indirectness) from 3 nonrandomized studies[140,147,151] with 36 cadavers or healthy volunteers showing a significant decrease in flexion and axial rotation (flexion: MD, −3.04; 95% CI, −5.64 to −0.4; axial rotation: MD, −9.07; 95% CI, −14.17 to −3.96). The same studies showed no significant

difference in terms of limiting extension, flexion/extension, and lateral bending.

We did not identify any evidence to address the critical outcomes of neurologic injury and complications; the important outcomes of overall mortality, pain, and patient comfort; and the less important outcome of hospital length of stay.

Sand bags and tape (I) compared with no motion restriction (C). For the important outcome of **cervical spine movement**, we identified very-low-quality evidence (downgraded for indirectness) from 1 nonrandomized study[140] with 25 healthy volunteers showing a significant decrease in flexion, extension, axial rotation, and lateral bending (flexion: MD, −35.60; 95% CI, −38.69 to −32.51; extension: MD, −6; 95% CI, −9.53 to −2.47; axial rotation: MD, −73.30; 95% CI, −75.99 to −70.61; lateral bending: MD, −19.40; 95% CI, −21.62 to −17.18).

We did not identify any evidence to address the critical outcomes of neurologic injury and complications; the important outcomes of overall mortality, pain, and patient comfort; and the less important outcome of hospital length of stay.

Treatment recommendations

We suggest against the use of cervical collars by first aid providers (weak recommendation, very-low-quality evidence).

Values, preferences, and task force insights

Consistent with the first aid principle of preventing further harm, the potential benefits of applying a cervical collar do not outweigh harms such as increased intracranial pressure and the consequences of unnecessary neck movement.

We recognize that first aid providers might not be able to discriminate between high- or low-risk individuals. We also recognize the potential value of manual stabilization in certain circumstances, but this was not evaluated in this review.

Task force discussion about this review included the recognition that, although evidence from the few studies that are available comes primarily from healthy volunteers and cadavers, there is a growing body of evidence demonstrating harmful effects, such as the development of raised intracranial pressure. In addition, there was concern expressed that the process for application of a cervical collar by a first aid provider to an individual with cervical spinal trauma could result in further injury. Application of a cervical collar requires training and regular practice to be performed properly, and such training may not be a component of every first aid course curriculum. Another important discussion topic was whether a first aid provider is able to distinguish between high- and low-risk injury criteria. As a result of these concerns and the consensus on science findings, the task force suggests against the routine application of cervical collars by first aid providers.

Knowledge gaps

More evidence is needed on manual stabilization (using hands/knees to restrict motion), trauma patients in the prehospital setting, high-risk versus low-risk patients, other forms of physical cervical spinal stabilization, and implementation and education. A review of the adverse effects as a consequence of application of a cervical collar could be interesting in the future.

Concussion (FA 799)

Among adults and children with suspected head injury without loss of consciousness (P), does use of a simple concussion scoring system (I), compared with standard first aid assessment without a scoring system (C), change time to recognition of the deteriorating patient, the likelihood of a poor neurologic outcome, survival to 30 days with good neurologic outcome, need for advanced medical care, time to medical transportation, or likelihood of differentiating between minor head contusion and more serious concussion (O)?

Introduction

This is a new topic for the 2015 consensus on science.

First aid providers are commonly faced with the need to identify concussion. The identification of concussion can be complex, and if concussion is missed, this can lead to a delay in receiving proper postconcussion advice and a delay in formal assessment and definitive treatment that can result in life-changing or even life-threatening consequences.

The task force sought to evaluate the effectiveness of early clinical recognition of concussion by first aid providers using a simple scoring system.

Consensus on science

For the critical outcome of **likelihood of differentiating between minor head contusion and more serious concussion (brain injury)**, we identified very-low-quality evidence (downgraded for risk of bias and indirectness) from 1 observational study[160] with 19 408 patients in a trauma registry using a secondary analysis of rescoring prehospital Glasgow Coma Scale (GCS) scores showing no significant difference between a simple derived motor score versus the GCS score to determine brain injury.

For the important outcome of **need for advanced medical care** (neurosurgical intervention and emergency tracheal intubation), we identified very-low-quality evidence (downgraded for imprecision) from 1 nonrandomized study[160] with 19 408 patients in a trauma registry using a secondary analysis of rescoring the prehospital GCS scores showing no significant difference between a simple derived motor score versus the GCS score for neurosurgical intervention (MD, 0.04; 95% CI, 0.01–0.09) and the need for emergency tracheal intubation (MD, 0.05; 95% CI, 0.01–0.11).

For the critical outcome of change in time to recognition of the deteriorating patient, for the important outcomes of survival to 30 days with good neurologic outcome, and for the likelihood of a poor neurologic outcome, we did not identify any evidence.

Treatment recommendations

No recommendation; we acknowledge the role that a simple, validated, single-stage concussion scoring system could play in the first aid provider's recognition and referral of victims of suspected head injury. However, review of the available literature shows no evidence regarding the application of such scoring systems by the first aid provider.

Values, preferences, and task force insights

Failure to properly recognize concussion can result in delay or absence of referral for definitive evaluation and care or inappropriate release to activity, which has the potential to worsen outcomes. We did identify concussion assessment tools currently recommended for use in sports medicine, but these require a 2-stage assessment, before competition and after concussion, and were thought to be inappropriate for use in the standard first aid setting.

Our extensive search strategy yielded 1837 publications, but subsequent review resulted in the selection of only 1 published manuscript. Despite the finding of 1 prehospital scientific publication supporting a simplified motor score, it was decided that this single article, a retrospective observational study where prehospital GCS scoring extracted from an urban Level 1 trauma registry was rescored by using a 3-point simplified motor score and compared with 4 hospital-based outcomes, did not formally address the PICO question and was in itself a very weak level of scientific evidence.

Many of the studies identified in our literature search used the adult and pediatric GCS to grade concussion. The GCS was

designed as a tool for use by advanced prehospital and hospital care providers, and it is not commonly used by first aid providers. The task force thought that this was not an appropriate tool to be used by first aid providers to assess concussion.

Our search and analysis did not identify any evidence to support or refute the use of a simplified scoring system, such as Sport Concussion Assessment Tool (SCAT); the GCS; or Alert, responds to Voice, responds to Pain, Unresponsive Scale (AVPU), versus standard first aid without a scoring system. It was thought that the serious consequences of not recognizing concussion in the first aid environment warranted an approach whereby any individual with a head injury and any alteration of level of consciousness requires immediate evaluation by an advanced healthcare provider or at a hospital.

Knowledge gaps

- There is a need for a clearer definition of concussion supported by clinical data that can be used to support assessment made in the first aid environment.
- There is a need for RCTs to access the efficacy of scoring systems as used by non–healthcare professionals in prehospital environments.
- There is a need for RCTs to assess the efficacy of SCAT in the clinical environment and whether it can be applied to nonsport environments.

Cooling of burns (FA 770)

Among adults and children with thermal injuries (P), does active cooling of burns (I), compared with passive cooling (C), change pain, complications, wound healing, need for advanced medical care, patient satisfaction, rates of fasciotomy, depth or breadth of burn (O)?

Introduction

The evidence for the first aid care of thermal injuries is limited. For this review, we focused on human studies that used active forms of cooling, defined as any method undertaken to decrease local tissue temperature. Limited evidence was found to support cooling of thermal injuries for decreasing the depth of burns, decreasing the need for advanced medical care, and improving healing times. It remains unclear what effect cooling may have on the potential for contamination or infection.

Consensus on science

After application of inclusion and exclusion criteria, the search strategy yielded 1 single-blind RCT and 5 observational studies. One of the observational studies was withdrawn from publication due to inconsistencies in data and was, therefore, withdrawn from the evidence review, leaving a total of 5 studies for inclusion.[161–165]

For the critical outcome of **pain**, 1 RCT and 1 observational study were found. Low-quality evidence (downgraded for risk of bias) from a single RCT[161] with 24 subjects showed no benefit in reduction of tactile pain measurements in cooled versus noncooled first-degree burns (MD undeterminable). Low-quality evidence (downgraded for risk of bias) from a prospective observational study[162] with 48 subjects showed no benefit in reduction of pain at 2, 4, and 24 h in patients with active cooling of burns caused by electric cardioversion versus those without cooling (MD undeterminable).

For the important outcome of **depth of burn**, 1 RCT and 3 observational studies were found. Low-quality evidence (downgraded for risk of bias) from a single RCT[161] with 24 subjects showed no difference in the amount of erythema between cooled and noncooled burns (MD undeterminable). Low-quality evidence (downgraded for risk of bias) from a prospective observational study[162] with 48 patients showed a reduction in the number and depth of burns in those with cooling versus those without (12.5% versus 83.3%) (RR, 0.15; 95% CI, 0.05–0.44). Very-low-quality evidence (downgraded for indirectness) from a retrospective observational study[163] with 695 patients reported an association between superficial burns and cooling and between deep burns and a lack of cooling (33.2% versus 48.5%) (RR, 0.68; 95% CI, 0.55–0.85). Very-low-quality evidence (downgraded for risk of bias) from a third observational study[164] with 268 patients found no benefit in reducing depth of burns, as measured by the need for skin grafting, in the cooling versus control group (9.4% versus 10.7%; RR, 0.88; 95% CI, 0.35–2.21).

Regarding the important outcome of **need for advanced medical care**, 3 observational studies were identified. Very-low-quality evidence (downgraded for risk of bias) from 1 observational study[164] with 268 patients showed no reduction in the need for advanced medical care after scald burns (including number of follow-up visits and need for scar management) for patients who received 20 min or more of cooling versus those who did not (scar management 20.8% versus 20.9%; RR, 0.99; 95% CI, 0.55–1.78). Very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from another observational study[165] comprising 125 patients showed an association between the use of water for first aid cooling of burns and decreased average length of hospital stay (10.3 days versus 5.3 days) for patients with less than 20% body surface area burns. It also showed a higher percentage of inpatient stays of less than 10 days in patients receiving first aid cooling of burns with water (88.5% versus 67.2%) (RR, 1.32; 95% CI, 1.09–1.6). In this study, adequate cooling time was defined as 10 min or more. Very-low-quality evidence (downgraded for indirectness and imprecision) from a third prospective observational study[166] enrolling 244 patients showed a benefit of cooling by demonstrating that a community and media campaign that increased use of first aid cooling for burns from 40% to 59% was associated with a decreased percentage of burns requiring hospital admission (64.4% precampaign versus 35.8% postcampaign) (RR, 0.55; 95% CI, 0.42–0.73).

Regarding the important outcome of **wound healing**, 1 observational study was found. Very-low-quality evidence (downgraded for risk of bias) from a single observational study[164] showed no benefit in reducing re-epithelialization time for patients who received 20 min or more of cooling versus those who did not (MD undeterminable).

Regarding the critical outcome of **complications**, and the low-priority outcomes of patient satisfaction and rates of fasciotomy, there were no human trials found.

Treatment recommendations

We recommend that first aid providers actively cool thermal burns (strong recommendation, low-quality evidence).

Values, preferences, and task force insights

In making this recommendation, we place higher value on decreased burn depth over the potential risk of infection or hypothermia.

- Method/temperature of cooling: Forms of active cooling evaluated in this review included cool/cold nonfreezing water and mechanical devices (e.g., cold probes, cooled gel pads), but there is no evidence to recommend a specific temperature or method of cooling.
- Time of cooling: Literature from this review suggests that active cooling should take place as soon as possible for a minimum of 10 min.

The risk of hypothermia from cooling large burns or in special populations is also unknown and was a topic of discussion within the task force.

Knowledge gaps

- When is a burn sufficiently large that cold application creates risk of hypothermia?
- What is the optimal temperature of cold application for cooling burns?
- What is the optimal cooling duration?

Wet compared with dry burn dressings (FA 771)

Among adults and children with thermal injuries (P), does the use of a wet dressing (I), compared with dry dressing (C), change complications, pain, tissue healing, need for advanced medical care, patient satisfaction, rates of fasciotomy (O)?

Introduction

"Wet" and "dry" dressings were difficult to define for this review. After careful consideration of the PICO wording and the various available dressings that may be applied to a burn, the First Aid Task Force thought that this question would benefit from a future revision to one that compares specific dressings, rather than an arbitrary wet or dry categorization.

Consensus on science

There are no studies directly evaluating wet versus dry dressings in the first aid context. All studies were performed in a healthcare professional setting, and caution should be used in generalizing findings to the first aid situation.

For the critical outcome of **complications (infection)**, we identified low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 RCT enrolling 104 subjects with superficial burns[167] showing benefit with application of honey compared with silver sulfadiazine–impregnated gauze dressings, with resolution of infection at 7 days (RR, 12.40; 95% CI, 4.15–37.00). A second RCT enrolling 100 patients with partial thickness burns[168] found benefit with application of honey compared with potato peel dressings, with resolution of infection at 7 days (absolute risk reduction, 0.90; 95% CI, 0.74–0.95).

We also identified very-low-quality evidence (downgraded for risk of bias and imprecision) from a non-RCT[169] with 262 enrolled patients with partial thickness burns of less than 15% total body surface area, evaluating the difference in infection rates with a topical, nonpenetrating antibacterial agent (Polysporin, wet; $n = 102$); a topical, penetrating antibacterial agent (silver sulfadiazine, wet; $n = 58$); and a petrolatum gauze dressing (Xeroform, dry; $n = 112$). This study showed no statistically significant difference in infection rate for the silver sulfadiazine wet dressings compared with the dry Xeroform dressing or for the Polysporin wet dressing compared with the dry Xeroform dressing.

For the critical outcome of **complications** (hypergranulation tissue, postburn contracture, or hypertrophic scar), we identified low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 RCT[167] showing benefit for honey dressings compared with silver sulfadiazine–impregnated gauze dressings (RR, 0.13; 95% CI, 0.03–0.52).

For the important outcome of **tissue healing**, we identified low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 RCT[167] showing benefit with honey (wet) compared with (dry) silver sulfadiazine–impregnated gauze dressing. This study enrolled 104 subjects and showed a decreased mean duration of time to healing when a honey dressing was used (MD, −7.80; 95% CI, −8.78 to −6.63). In addition, further low-quality evidence (downgraded for risk of bias, imprecision, and indirectness) from 1 RCT[168] enrolling 100 subjects also showed a decreased mean duration of time to healing with honey (wet) compared with (dry) potato peel dressings (MD, −5.80; 95% CI, −6.68 to −4.92).

We did not identify any evidence to address the important outcome of pain and the less important outcomes of need for advanced medical care, patient satisfaction, and rates of fasciotomy.

Treatment recommendations

No recommendation; there is insufficient evidence to show any benefits of wet compared with dry dressings applied to thermal burns in the prehospital setting.

Values, preferences, and task force insights

Studies included in this review evaluated out-of-hospital use of dressings and assumed that cooling had taken place before a dressing was applied. Public comment was made about the use of plastic wrap for burns. Plastic wrap (a dry dressing) was included in the search strategy, but no comparative studies to a wet dressing were identified.

Knowledge gaps

Further research is needed on the use of burn dressings in the prehospital setting. Specifically, it is unknown what type of dressing is optimal for use by first aid providers.

Dental avulsion (FA 794)

Among adults and children with an avulsed permanent tooth (P), does storage of the tooth in any solution prior to replantation (I), compared with storage in whole milk or the patient's saliva (C), change success of reimplantation, tooth survival or viability, infection rate, pain, malfunction (eating, speech), color of the tooth (O)?

Introduction

Immediate reimplantation of an avulsed tooth is thought by the dental community to result in the greatest chance of tooth survival. The First Aid Task Force believes that, in reality, few first aid providers have the skills or willingness to attempt this painful procedure, especially without protection from exposure to blood or possible sharp bone spicules. Therefore, if an avulsed tooth is not immediately reimplanted, the priority is to quickly transfer the patient and the avulsed tooth to a healthcare professional capable of reimplanting the tooth. Placing the avulsed tooth in a temporary storage solution such as milk or saliva has been reported to extend the viability of the tooth before reimplantation. This PICO question evaluates the effectiveness of alternative solutions to whole milk or saliva.

Consensus on science

We did not identify any evidence to address the important outcomes of infection rate, pain, malfunction, and cosmetic outcome.

Egg white (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 2 randomized studies[170,171] with 10 extracted teeth in each study, showing benefit in 1 study[170] (MD, 91.80; 95% CI, 90.53–93.07 for cell viability after 1 h of immersion; MD, 90.00; 95% CI, 87.87–92.13 for cell viability after 2 h of immersion) and not showing any benefit in the other study[171] (MD, −4.03; 95% CI, −10.39 to 2.33 for cell viability after 1 h of immersion; MD, 15.74; 95% CI, −9.76 to 41.24 after 3 h of immersion).

Ricetral (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study[172] with 20 extracted teeth, showing benefit (MD, 44.3; 95% CI, 12.82–75.78) for cell viability after 45 min of immersion.

Coconut water (I) compared with milk (C). For the critical outcome of viability, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study[173] with 30 extracted teeth, showing benefit (MD, 339.4; 95% CI, 331.65–347.15) for cell viability after 45 min of immersion.

Lactobacillus reuteri *Solution (I) Compared With Milk (C).* For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 observational study[174] with 12 extracted teeth, but the MD for cell viability was not estimable (median difference 116 000).

Saliva and thereafter Hank's balanced salt solution (I) compared with saliva and thereafter milk (C). For the critical outcome of viability, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 observational study[175] with 10 extracted teeth. The study found a lower MD for cell viability (MD 1% lower) after 30 min and a higher MD (MD, 2.4% higher) after 60 min, but the CI was not estimable.

Saliva (I) compared with saliva and thereafter milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 observational study[175] with 10 extracted teeth. The study found a lower MD for cell viability (MD, 8.4% lower after 30 min, 2% lower after 60 min), but the CI was not estimable.

Eagle's medium (aMEM) (I) compared with saliva and thereafter milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 observational study[175] with 10 extracted teeth. The study found a higher MD for cell viability (MD, 5% higher after 30 min, 12.5% higher after 60 min), but the CI was not estimable.

EGCG (epigallocatechin-3-gallate) (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study[176] with 20 extracted teeth, showing no benefit (MD, 0.1; 95% CI, −0.09 to 0.28) for cell viability after 2 h of immersion.

Tap water (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 observational study,[177] but the MD for cell viability was not estimable (mean percentage of 45.17 ± 12.03 SD for intervention group compared with the mean percentage of 90.59 ± 3.77 SD for control group).

Propolis 10% (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study[171] with 10 extracted teeth, showing benefit for cell viability after 1 h of immersion (MD, 14.73; 95% CI, 9.53–19.93), and for cell viability after 3 h of immersion (MD, 45.33; 95% CI, 21.73–68.93).

Propolis 50% (I) compared with milk (C). For the critical outcome of viability, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 2 randomized studies[171,178] with 24 and 10 extracted teeth, showing benefit for cell viability after 45 min of immersion (MD, 1 192 290; 95% CI, 720 274.12–1 664 305.28), for cell viability after 1 h of immersion (MD, 13.96; 95% CI, 4.9–23.02), and for cell viability after 3 h of immersion (MD, 29.36; 95% CI, 2.37–56.35).

Propolis 100% (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study[178] with 24 extracted teeth, showing benefit for cell viability after 45 min of immersion (MD, 1 077 710; 95% CI, 266 920.68–1 888 499.32).

Phosphate buffered saline (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study[179] with 10 extracted teeth, showing no benefit for cell viability after 30 min of dry time followed by a 15-minute immersion (MD, 8.31; 95% CI, −0.09 to 16.71), but showing benefit for cell viability after both 60 min (MD, 8.76; 95% CI, 4.03–13.49) and 90 min of dry time (MD, −5.17; 95% CI, −9.93 to −0.41) followed by a 15-minute immersion.

Saline (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 1 randomized study with 24 extracted teeth[178] showing no benefit for cell viability after 45 min of immersion (MD, −143 540; 95% CI, −210 604.01 to −76 475.99). We identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 observational study[180] with 24 teeth in which benefit for cell viability was not shown after 2 h of immersion (MD, −161 000; 95% CI, −362 186.91 to 40 186.91). We identified very-low-quality evidence (downgraded for indirectness and imprecision) from 2 other observational studies[174,177] in which the MD for cell viability was not estimable (median difference 376 000; mean percentage of 77.8 ± 2.92 SD for intervention group versus mean percentage of 90.59 ± 3.77 SD for control group).

For the critical outcome of **viability** (periodontal healing), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[181] with 25 avulsed teeth showing no benefit (RR, 0.99; 95% CI, 0.48–2.04).

For the critical outcome of success of reimplantation (replacement resorption and extraction due to replacement resorption), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[181] with 25 avulsed teeth showing no benefit (RR, 1.07; 95% CI, 0.33–3.46; and RR, 0.89; 95% CI, 0.09–8.50, respectively).

Hank's balanced salt solution (I) compared with milk (C). For the critical outcome of **viability**, we identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 4 randomized studies[170–173] including 10 to 30 extracted teeth, showing benefit for cell viability after 45 min of immersion (MD, 261.13; 95% CI, 249.7–272.56),[173] for cell viability after 45 min of immersion (MD, 64.2; 95% CI, 32.59–95.81),[172] for cell viability after 1 h of immersion (MD, 93.4; 95% CI, 91.81–94.99),[170] for cell viability after 2 h of immersion (MD, 89.8; 95% CI, 87.95–91.65),[170] and for cell viability after 3 h of immersion (MD, 25.59; 95% CI, 1.13–50.05).[171] We identified very-low-quality evidence (downgraded for risk of bias, indirectness, and imprecision) from 3 studies[171,176,178] that did not show benefit for cell viability after 45 min of immersion (MD, 22 090; 95% CI, −64 812.53 to 108 992.53[178]; MD, 0.85; 95% CI, −9.31 to 7.61[171]; MD, 0.05; 95% CI, −0.16 to 0.25[176]). We identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 study, from which the MD for cell viability was not estimable (mean percentage of

87.04 ± 5.7 SD for intervention group versus mean percentage of 90.59 ± 3.77 SD for control group).[177]

Another's saliva (I) compared with storage in the patient's mouth (C). For the critical outcome of **viability** (pulpal healing), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[182] with 10 avulsed teeth, showing no benefit (RR, 1; 95% CI, 0.08–11.93).

Saline (I) compared with saliva (C). For the critical outcome of **viability** (pulpal and periodontal ligament healing), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 2 observational studies[182,183] with 24 and 66 avulsed teeth, showing no benefit (RR, 0.6; 95% CI, 0.18–1.97 for pulpal healing and RR, 0.67; 95% CI, 0.21–2.15 for periodontal ligament healing).

Storage in another person's mouth (I) compared with storage in the patient's mouth (C). For the critical outcome of **viability** (periodontal ligament healing), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[183] with 18 avulsed teeth, showing no benefit (RR, 1; 95% CI, 0.27–3.96).

Dentosafe box compared with milk. For the critical outcome of **viability** (periodontal healing), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[181] with 24 avulsed teeth showing no benefit (RR, 1.33; 95% CI, 0.74–2.40).

For the critical outcome of **success of replantation** (replacement resorption and extraction due to replacement resorption), we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[181] with 24 avulsed teeth showing no benefit (RR, 0.40; 95% CI, 0.06–2.87 and RR, 1.00; 95% CI, 0.11–9.44, respectively).

Treatment recommendations

We suggest the use of Hank's Balanced Salt Solution, propolis, egg white, coconut water, or ricetral in comparison with whole milk as a temporary storage solution for an avulsed tooth that cannot be immediately reimplanted (weak recommendation, very-low-quality evidence). The solutions used and the order of priority for tooth storage are listed in Table 4.

We suggest the use of whole milk in comparison with saline as a temporary storage solution for an avulsed tooth if none of the above solutions are available (weak recommendation, very-low-quality evidence).

There is insufficient evidence for or against temporary storage of an avulsed tooth in saliva compared with alternative solutions.

Values, preferences, and task force insights

In making this recommendation, we recognize that survival of an avulsed tooth requires that it must be reimplanted as soon as possible, but this procedure may not be possible in the first aid setting. The use of a suitable temporary storage solution for an avulsed tooth should not delay efforts at reimplantation, but it may aid in the survival of the tooth before reimplantation.

No treatment recommendation was formulated regarding the use of phosphate-buffered saline (PBS) as a storage solution, as in the PBS study there was a dry time from 60 to 90 min, which is not representative of a typical situation. However, this could be relevant for settings where it is not possible to immediately store the tooth in a storage solution.

Table 4
Composition of Temporary storage solutions for avulsed tooth, in order of preference.[a]

Temporary storage solution	Composition
Hank's balanced salt solution	Group of salts rich in bicarbonate ions: 0.14 g/L $CaCl_2$, 0.40 g/L KCl, 0.06 g/L KH_2PO_4, 0.10 g/L $MgCl_2$-$6H_20$, 0.10 g/L $MgSO_4$-$7H_2O$, 8.00 g/L NaCl, 0.35 g/L $NaHCO_3$, 0.048 g/L Na_2HPO_4, 1.00 g/L glucose, 0.01 g/L phenol red
Propolis	Resinous mixture that honey bees collect from tree buds, sap flows, or other botanical sources
Egg white	
Coconut water	Clear liquid from young green coconuts
Ricetral	Sodium chloride, sodium citrate, potassium chloride, extruded rice
Whole milk	
Saline	Sodium chloride: 9.0 g/L NaCl; home-made saline: dissolving approximately half a teaspoon of table salt into 240 mL of clean tap water
Phosphate-buffered saline	Water-based salt solution containing sodium phosphate, sodium chloride: 8.0 g/L NaCl, 0.2 g/L KCl, 1.44 g/L Na_2HPO_4, 0.24 g/L KH_2PO_4

[a] Based on the evidence alone, it was not possible to decide which solution will result in the longest tooth survival. The order of preference proposed in this table is based on the evidence evaluated, availability, and feasibility.

Knowledge gaps

- There is a lack of observational studies with avulsed teeth (instead of extracted teeth), measuring tooth viability (not cell viability), and success of replantation.
- In a future PICO question, reimplanting the tooth in the mouth (in dental socket) versus storage in a temporary storage medium could be compared.
- Is training in dental reimplantation for first aid providers feasible and effective?

Education

Education in first aid continues to be a topic with few scientific studies. In the 2010 review of educational topics, no evidence was found to support or recommend any method of evaluating or monitoring a first aid trainee's educational progress or the specific frequency of retraining to retain skills and knowledge.[10] The task force decided to investigate the basic question, "Is there documented evidence of benefit in terms of patient outcomes as a result of first aid training?"

Many questions remain, and research is desperately needed, particularly in the realm of teaching techniques for first aid and methods to evaluate the retention of skills.

First aid training (FA 773)

Among adults and children receiving first aid (P), does care from a trained first aid provider (I), compared with care from an untrained person (C), change survival rates, recognition of acute injury or illness, prevent further illness or injury (i.e., harm), time to resolution of injury, the likelihood of harm (e.g., infection), time to resolution of symptoms (O)?

Introduction

In the ILCOR 2015 review process, *first aid* is defined as the **helping behaviors** and **initial care** provided for an acute illness or injury. Training is, therefore, an essential core element of the practice of first aid. The task force thought that it was important to verify the impact of both formal and informal first aid training of individuals and communities.

Consensus on science

For the critical outcome of **increased survival rates** from trauma, we identified low-quality evidence (downgraded for risk of bias) from 1 observational study[184] enrolling 1341 patients showing a reduced mortality rate among patients initially managed by trained first aid providers of 9.8% (32/325) compared with 15.6% (158/101) for patients without trained first aid support (OR, 0.59; 95% CI, 0.40–0.89).

For the important outcome of **time to resolution of symptoms**, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 observational study[174] with 125 subjects with burns of less than 20% total body surface area showing benefit from first aid training, with 88.5% of patients who received first aid treatment of cooling the burn with water requiring hospitalization of less than 10 days, compared with only 67.2% who received no treatment requiring less than 10 days' hospitalization (RR, 0.35; 95% CI, 0.16–0.76).

For the important outcome of **preventing further injury**, we identified very-low-quality evidence (downgraded for indirectness and imprecision) from 1 observational study[175] with 244 patients (121 precampaign, 123 postcampaign) with acute burn injury treated either before or after a burn first aid treatment public education campaign, showing benefit with burn first aid treatment by reduction of the percent of those burned requiring inpatient wound care or surgery from 64.2% (78/121) precampaign compared with 35.6% (44/123) postcampaign (OR, 0.307; 95% CI, 0.18–0.52).

Furthermore, we identified very-low-quality evidence (downgraded for risk of bias and imprecision) from 1 observational study[185] with 39 subjects without formal/advanced medical training who performed reduction of shoulder dislocations in a wilderness environment. This study found no statistically significant difference in the rate of successful reduction by laypersons without first aid training (17/24, 70.8%) compared with the successful reduction rate when individuals with either wilderness first aid or first responder training were present or performed the reduction (11/15, 73%; OR, 0.88; 95% CI, 0.21–3.74).

For the critical outcome of recognition of acute injury or illness, and the important outcome of the likelihood of harm, there were no studies identified.

Treatment recommendations

We suggest that education and training in first aid is undertaken to improve morbidity and mortality from injury and illness (weak recommendation, low-quality evidence).

Values, preferences, and task force insights

Positive outcomes were identified in both public health campaigns for specific injuries and course-based training for general trauma. Although no other formal PICO questions related to first aid education were evaluated, the review of stroke assessment systems (above) incidentally discovered that training of lay providers in a stroke assessment system led to improved ability to identify the signs of a stroke when assessed immediately after training (94.4% in those trained versus 76.4% in untrained lay providers), and that 96.9% of the trained lay providers were able to identify signs of stroke when assessed 3 months after training.[69] This study supports the recommendation in this review, and specifically shows that public health campaigns aimed at first aid for specific illnesses and injuries, as well as course-based first aid training, can positively impact outcomes of morbidity and mortality.

Knowledge gaps

Individual domains of first aid (e.g., recognizing an emergency, calling for additional help, specific skills such as direct pressure) have not been studied as to what contributes to a victim's health outcomes. Future reviews comparing first aid education modalities and context of first aid settings may contribute to developing training guidelines. Additionally, the period of time between a first aid provider's initial training and refreshing those first aid skills to maintain competency needs to be identified. Along with patient outcomes, public health outcomes and cost-analysis of training versus no training may help prioritize resources. These questions and opportunities for research can also be valuable as new modalities emerge for learning (e.g., social media or just-in-time).

Disclosures

2015 CoSTR Part 9: First Aid: Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
David A. Zideman	Imperial College Healthcare NHS Trust	None	None	None	None	None	None	None
Eunice M. Singletary	University of Virginia	None	American Red Cross[a]	None	None	None	None	None
Ian E. Blanchard	University of Calgary	None	None	None	None	None	None	None
Wei-Tien Chang	National Taiwan University Hospital	Research grants from government and university hospital[a]	None	None	None	Patent for Leverage-assisted ACD CPR device[a]	None	None
Emmy D. J. De Buck	Belgian Red Cross-Flanders	None	None	None	None	None	None	Belgian Red Cross-Flanders[a]
Rita A. Herrington	Indiana University	None	None	None	None	None	None	None
Natalie A. Hood	Monash Medical Centre	None	None	None	None	None	None	None
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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
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David S. Markenson	Sky Ridge Medical Center	None	American Red Cross[a]	None	None	None	None	None
Jeffrey L. Pellegrino	Kent State University	None	None	None	None	None	None	None
Janel M. Swain	Emergency Health Services	None	None	None	None	None	None	None
Hyuk Jun Yang	Gachon University	None	None	None	None	None	None	None
Consultant								
Jeff A. Woodin	Tualatin Valley Fire & Rescue	None	None	None	None	None	American Heart Association[b]	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

[a] Modest.

[b] Significant.

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Appendix A.

CoSTR Part 9: PICO Appendix

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 9	First Aid	FA 500	Second Dose of Epinephrine for Anaphylaxis	Among adults and children experiencing severe anaphylaxis requiring the use of epinephrine (P), does administration of a second dose of epinephrine (I), compared with administration of only 1 dose (C), change resolution of symptoms, adverse effects, complications (O)?	Athanasios Chalkias, Barbara Caracci, Emmy De Buck
Part 9	First Aid	FA 503	Straightening of an Angulated Fracture	Among adults and children who receive first aid for an angulated long bone fracture (P), does realignment of the fracture prior to splinting (I), compared with splinting as found (C), change neurologic injury, vascular injury, splinting, pain, time to medical transportation (O)?	Ryan Fringer, Catherine Patocka
Part 9	First Aid	FA 517	Recovery Position	Among adults who are breathing and unresponsive outside of a hospital (P), does positioning in a lateral, side-lying, recovery position (I), compared with supine position (C), change overall mortality, need for airway management, the incidence of aspiration, the likelihood of cervical spinal injury, complications, incidence of cardiac arrest (O)?	Janel Swain, S Seitz
Part 9	First Aid	FA 519	Oxygen Administration for First Aid	Among adults and children who exhibit symptoms or signs of shortness of breath, difficulty breathing, or hypoxemia outside of a hospital (P), does administration of supplementary oxygen (I), compared with no administration of oxygen (C), change survival with favorable neurologic/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; shortness of breath; time to resolution of symptoms; or therapeutic endpoints (e.g., oxygenation and ventilation) (O)?	Michael Nemeth, Chih-Hung Wang
Part 9	First Aid	FA 520	Optimal Position for Shock	Among adults and children who receive first aid for shock (P), does positioning of the patient (I), compared with not positioning the patient (C), change overall mortality, complications, incidence of cardiac arrest, vital signs, hospital length of stay (O)?	Anthony Handley, Luis Lojero-Wheatley, Justin DeVoge

Appendix A (*Continued*)

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 9	First Aid	FA 525	First Aid Treatment for an Open Chest Wound	Among adults and children who are being treated for an open chest wound outside of a hospital (P), does occlusive bandage application or occlusive device (I), compared with a nonocclusive dressing (C), change or improve survival, respiratory arrest, oxygen saturation, vital signs, the rate of cardiac and respiratory arrests, improve therapeutic endpoints (oxygenation and ventilation) (O)?	Wei-Tien Chang, Kyee Han
Part 9	First Aid	FA 530	Control of Bleeding	Among adults and children with bleeding (P), does application of localized cold therapy, elevation of extremity, and/or application of pressure over proximal pressure points (I), compared with direct pressure alone (C), change overall mortality, hemostasis, major bleeding, complications, hospital length of stay (O)?	Richard Bradley, Jae-Hyug Woo
Part 9	First Aid	FA 534	Bronchodilator Use for Asthma with Difficulty Breathing	Among adults and children in the prehospital setting who have asthma and are experiencing difficulty in breathing (P), does bronchodilator administration (I), compared with no bronchodilator administration (C), change time to resolution of symptoms, time to resumption of usual activity, complications, harm to patient, therapeutic endpoints (e.g., oxygenation and ventilation), need for advanced medical care (O)?	Andrew MacPherson, Nathan Charlton, Ian Blanchard
Part 9	First Aid	FA 540	Eye Chemical Injury: Irrigation	Among adults and children who have a chemical or other unknown substance enter the conjunctival sac (P), does irrigation with isotonic saline, balanced salt solution, or other commercial eye irrigation solutions (I), compared with irrigation with water (C), change tissue healing, functional recovery, pain, complications, time to resumption of usual activity, restoration to the preexposure condition, time to resolution of symptoms (O)?	Ralph Shenefelt, L. Kristian Arnold, Janel Swain
Part 9	First Aid	FA 584	Exertional Dehydration and Oral Rehydration	Among adults and children with exertion-related dehydration (P), does drinking oral carbohydrate-electrolyte (CE) liquids (I), compared with drinking water (C), change volume/hydration status, vital signs, development of hyperthermia, development of hyponatremia, need for advanced medical care, blood glucose, patient satisfaction (O)?	Rita Herrington, Amy Kule, Jestin Carlson
Part 9	First Aid	FA 586	Aspirin for Chest Pain (Early vs. Late)	Among adults who are experiencing chest pain outside of a hospital (P), does early administration of aspirin (I), compared with later administration of aspirin (C), change cardiovascular mortality, complications, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay, chest pain resolution (O)?	Janel Swain, Thomas Evans
Part 9	First Aid	FA 768	Use of a Tourniquet	Among adults and children with severe external limb bleeding (P), does the application of a tourniquet (I), compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, blood loss, incidence of cardiac arrest (O)?	Jan Jensen, Michael Reilly
Part 9	First Aid	FA 769	Hemostatic Dressings	In patients with severe external bleeding (P), does the application of topical hemostatic dressings plus standard first aid (I), compared with standard first aid alone (C), change overall mortality, vital signs, hemostasis, complications, blood loss, major bleeding, incidence of cardiac arrest (O)?	Jan Jensen, Richard Bradley
Part 9	First Aid	FA 770	Cooling of Burns	Among adults and children with thermal injuries (P), does active cooling of burns (I), compared with passive cooling (C), change pain, complications, wound healing, need for advanced medical care, patient satisfaction, rates of fasciotomy, depth or breadth of burn (O)?	Natalie Hood, Nathan Charlton
Part 9	First Aid	FA 771	Wet Compared With Dry Burn Dressings	Among adults and children with thermal injuries (P), does the use of a wet dressing (I), compared with dry dressing (C), change complications, pain, tissue healing, need for advanced medical care, patient satisfaction, rates of fasciotomy (O)?	Emmy De Buck, Ian Blanchard
Part 9	First Aid	FA 772	Cervical Spinal Motion Restriction	Among adults and children with suspected blunt traumatic cervical spinal injury (P), does cervical spinal motion restriction (I), compared with no cervical spinal motion restriction (C), change neurologic injury, complications, overall mortality, pain, patient comfort, movement of the spine, hospital length of stay (O)?	Tessa Dieltjens, Jeff Woodin
Part 9	First Aid	FA 773	First Aid Training	Among adults and children receiving first aid (P), does care from a trained first aid provider (I), compared with care from an untrained person (C), change increase survival rates, recognition of acute injury or illness, prevent further illness or injury (i.e., harm), time to resolution of injury, the likelihood of harm (e.g., infection), time to resolution of symptoms (O)?	Jeffrey Pellegrino, Danita Koehler
Part 9	First Aid	FA 794	Dental Avulsion	Among adults and children with an avulsed permanent tooth (P), does storage of the tooth in any solution prior to replantation (I), compared with storage in whole milk or the patient's saliva (C), change success of reimplantation, tooth survival or viability, infection rate, pain, malfunction (eating, speech), color of the tooth (O)?	Nele Pauwels, Bryan Kitch

Appendix A (*Continued*)

Part	Task force	PICO ID	Short title	PICO question	Evidence reviewers
Part 9	First Aid	FA 795	Hypoglycemia Treatment	Among adults and children with symptomatic hypoglycemia (P), does administration of dietary forms of sugar (I), compared with standard dose (15–20 g) of glucose tablets (C), change time to resolution of symptoms, risk of complications (e.g., aspiration), blood glucose, hypoglycemia, hospital length of stay (O)?	Jestin Carlson, Susanne Schunder-Tatzber
Part 9	First Aid	FA 799	Concussion	Among adults and children with suspected head injury without loss of consciousness (P), does use of a simple concussion scoring system (I), compared with standard first aid assessment without a scoring system (C), change time to recognition of the deteriorating patient, the likelihood of a poor neurologic outcome, survival to 30 days with good neurologic outcome, need for advanced medical care, time to medical transportation, or likelihood of differentiating between minor head contusion and more serious concussion (O)?	Richard Rusk, Christina Gruber
Part 9	First Aid	FA 801	Stroke Recognition	Among adults with suspected acute stroke (P), does the use of a rapid stroke scoring system or scale (I), compared with standard first aid assessment (C), change time to treatment (e.g., door to drug), recognition of acute injury or illness, discharge with favorable neurologic status, survival with favorable neurologic outcome, or increased public/layperson recognition of stroke signs (O)?	Pascal Cassan, Jeffrey Ferguson, Daniel Meyran
Part 9	First Aid	FA 871	Aspirin for Chest Pain: Administration	Among adults experiencing chest pain due to suspected MI (P), does administration of aspirin (I), compared with no administration of aspirin (C), change cardiovascular mortality, complications, adverse effects, incidence of cardiac arrest, cardiac functional outcome, infarct size, hospital length of stay (O)?	Thomas Evans, Janel Swain

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