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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,

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 survival 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 neuro-electrophysiology 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
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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.

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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