Part 8: Advanced Life Support

2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

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Note From the Writing Group: *Throughout this article, the reader will notice combinations of superscripted letters and numbers (eg, "Cricoid Pressure*[ALS-CPR&A-007B]*"). These callouts are hyperlinked to evidence-based worksheets, which were used in the development of this article. An appendix of worksheets, applicable to this article, is located at the end of the text. The worksheets are available in PDF format and are open access. The topics reviewed by the International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support Task Force are grouped as follows: (1) airway and ventilation, (2) supporting the circulation during cardiac arrest, (3) periarrest arrhythmias, (4) cardiac arrest in special circumstances, (5) identifying reversible causes, (6) postresuscitation care, (7) prognostication, and (8) organ donation. Defibrillation topics are discussed in Part 6.*

The most important developments and recommendations in advanced life support (ALS) since the 2005 ILCOR review are as follows:

- The use of capnography to confirm and continually monitor tracheal tube placement and quality of cardiopulmonary resuscitation (CPR).
- More precise guidance on the control of glucose in adults with sustained return of spontaneous circulation. Blood glucose values >180 mg/dL (>10 mmol/L) should be treated and hypoglycemia avoided.
- Additional evidence, albeit lower level, for the benefit of therapeutic hypothermia in comatose survivors of cardiac arrest associated initially with nonshockable rhythms.
- Recognition that many of the accepted predictors of poor outcome in comatose survivors of cardiac arrest are unreliable, especially if the patient has been treated with therapeutic hypothermia. There is inadequate evidence to recommend a specific approach to prognosticating poor outcome in post–cardiac arrest patients treated with therapeutic hypothermia.
- The recognition that adults who progress to brain death after resuscitation from out-of-hospital cardiac arrest should be considered for organ donation.
- The recommendation that implementation of a comprehensive, structured treatment protocol may improve survival after cardiac arrest.

Airway and Ventilation

Consensus conference topics related to the management of airway and ventilation are categorized as (1) basic airway devices, (2) cricoid pressure, (3) advanced airway devices, (4) confirmation of advanced airway placement, (5) oxygenation, and (6) strategies for ventilation.

Basic Airway Devices

Oropharyngeal and Nasopharyngeal Airways[ALS/BLS-CPR&A-080B]

Consensus on Science

Despite frequent successful use of nasopharyngeal and oropharyngeal airways in the management of nonarrest patients, there are no published data on the use of these airway adjuncts during CPR in humans. When bag-mask ventilation was undertaken with an oral airway and compared with no oral airway, 1 study in anesthetized patients demonstrated higher tidal volumes (LOE 5).[1]

One study of nasopharyngeal airways in anesthetized patients showed that nurses inserting nasopharyngeal airways were no more likely than anesthesiologists to cause nasopharyngeal trauma (LOE 5).[2] One study showed that the traditional methods of sizing a nasopharyngeal airway

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(measurement against the patient's little finger or anterior nares) do not correlate with the airway anatomy and are unreliable (LOE 5).[3] In 1 report, insertion of a nasopharyngeal airway caused some airway bleeding in 30% of cases (LOE 5).[4] Two case reports reported inadvertent intracranial placement of a nasopharyngeal airway in patients with basal skull fractures (LOE 5).[5,6]

Treatment Recommendation

Oropharyngeal and nasopharyngeal airways have long been used in cardiac arrest, despite never being studied in this clinical context. It is reasonable to continue to use oropharyngeal and nasopharyngeal airways when performing bag-mask ventilation in cardiac arrest, but in the presence of a known or suspected basal skull fracture an oral airway is preferred.

Cricoid Pressure[ALS-CPR&A-007B]

In adults and children during ventilation and intubation, does the application and maintenance of cricoid pressure, compared to no cricoid pressure, reduce the incidence of aspiration?

Consensus on Science

No studies addressing the use of cricoid pressure during cardiac arrest were identified. All the identified studies were conducted under anesthesia or in awake volunteers, cadavers, or manikins. (All studies are therefore LOE 5 for cardiac arrest.) Cricoid pressure in nonarrest patients may, to some extent, protect the airway from aspiration, but it may also impede ventilation or interfere with insertion of an advanced airway.

The effect of cricoid presssure on gastric inflation during bag-mask ventilation was examined by 2 adult (LOE 1[7]; LOE 2[8]) and 2 pediatric studies (LOE 2).[9,10] All showed less gastric inflation with cricoid pressure than without, although all of the studies used ventilation volumes higher than those recommended in cardiac arrest.

Nine studies in nonarrest adult subjects undergoing anesthesia showed that cricoid pressure impairs ventilation in many patients, increases peak inspiratory pressures, and causes complete obstruction in up to 50% of patients, depending on the amount of cricoid pressure (in the range of recommended effective pressure) that is applied (LOE 1[7,11–13]; LOE 2[14]; LOE 4[8,15–17]).

One study in anesthetized patients determined that cricoid pressure prevents correct placement and ventilation with the laryngeal tube (LT) (LOE 1).[18] Eight studies in anesthetized adults showed that when cricoid pressure was used before insertion of a laryngeal mask airway (LMA), there was a reduced proportion of LMAs correctly positioned, an increased incidence of failed insertion, and impaired ventilation once the LMA had been placed (LOE 1[19–23]; LOE 2[24–26]). No significant impairment to tracheal intubation was found by 4 LOE-1 studies performed in anesthetized patients,[27–30] while 7 LOE-1 studies[19,31–36] and 1 LOE-2 study[37] did show impairment of intubation with increased time to intubation and decreased intubation success rates. One cadaver study demonstrated a worse laryngoscopic view with the application of cricoid pressure (LOE 5).[38]

Twenty-one manikin studies demonstrated that many providers applied less cricoid pressure than has been shown to be effective (in cadaver studies) whereas many other providers applied more pressure than has been shown to be necessary (and far in excess of the amount of pressure shown to impede ventilation) (LOE 5).[39–59] Four of those studies determined that performance can be improved with training (although many cricoid pressure applications following training remain outside recommended effective pressures).[54–56,59] No study examined if cricoid pressure performance to the required standard could be maintained beyond the immediate post-training period.

Cricoid pressure prevented movement of liquid from the esophagus into the pharynx in 5 cadaver studies (LOE 5)[60–64]; however, in 1 LOE-2 study[65] of 4891 obstetric patients undergoing anesthesia, no significant difference was observed in regurgitation rates between patients who received cricoid pressure and those who did not. There are case reports where prevention of aspiration is ascribed to the application of cricoid pressure (LOE 4)[66–68] and other case reports documenting that aspiration occurs despite the application of cricoid pressure (LOE 4).[69–73]

Treatment Recommendation

The routine use of cricoid pressure to prevent aspiration in cardiac arrest is not recommended. If cricoid pressure is used during cardiac arrest, the pressure should be adjusted, relaxed, or released if it impedes ventilation or placement of an advanced airway.

Knowledge Gaps

Future research should address whether cricoid pressure prevents regurgitation and aspiration, the pressure required to be effective, and effectiveness trials evaluating if it can be done well by responders to a cardiac arrest.

Advanced Airway Devices

The tracheal tube was once considered the optimal method of managing the airway during cardiac arrest. There is considerable evidence that without adequate training or ongoing skills maintenance, the incidence of failed intubations and complications, such as unrecognized esophageal intubation or unrecognized dislodgement, is unacceptably high.[74–79] Prolonged attempts at tracheal intubation are harmful if associated with interruption of chest compressions because this will compromise coronary and cerebral perfusion. Alternatives to the tracheal tube that have been studied during CPR include the bag-mask and supraglottic airway devices, such as the laryngeal mask airway, esophageal-tracheal combitube and laryngeal tube, among others. Studies comparing supraglottic airway to tracheal intubation have generally compared insertion time and ventilation success rates. No study has shown an effect

of the method of ventilation on survival. There are no data to support the routine use of any specific approach to airway management during cardiac arrest. The quality of CPR with various advanced airways was not included in the review for 2010. The best technique depends on the precise circumstances of the cardiac arrest, local guidelines, training facilities, and the competence of the rescuer.

Timing of Advanced Airway Placement[ALS-SAM-062A]

In adult cardiac arrest (prehospital or in-hospital), does an alternate timing for advanced airway insertion (eg, early or delayed), as opposed to standard care (standard position in algorithm), improve outcome (eg, return of spontaneous circulation [ROSC], survival)?

Consensus on Science

One registry study evaluated the impact of timing of advanced airway placement during 25,006 in-hospital cardiac arrests (LOE 2).[80] In this study, earlier time to invasive airway (<5 minutes) was associated with no improvement in ROSC but improved 24-hour survival (NNT=48). In an urban out-of-hospital setting, intubation in <12 minutes was associated with better survival than intubation ≥13 minutes.[81] In an out-of-hospital urban and rural setting, patients intubated during resuscitation had better survival than patients not intubated[82]; whereas in an in-hospital setting, patients requiring intubation during CPR had worse survival.[83] A recent study found that delayed tracheal intubation bundled with passive oxygen delivery and minimally interrupted chest compressions was associated with improved neurologically intact survival after out-of-hospital cardiac arrest in patients with adult, witnessed, ventricular fibrillation (VF)/ventricular tachycardia (VT).[84] The independent contribution of the timing of the advanced airway was not available in the study.

Treatment Recommendation

There is inadequate evidence to define the optimal timing of advanced airway placement during cardiac arrest.

Knowledge Gaps

To advance the science in this area we need to define what is "early" and what is "delayed" placement of advanced airways, the superiority of advanced airways over simple bag-mask ventilation, and whether there is any significant difference between the advanced airway types.

Advanced Airway Versus Ventilation With Bag-Mask[ALS/BLS-CPR&A-088A, ALS/BLS-CPR&A-088B]

In adult cardiac arrest (prehospital, out-of-hospital cardiac arrest [OHCA], in-hospital cardiac arrest [IHCA]), does the use of supraglottic devices, compared with bag-mask alone for airway management, improve any outcomes (eg, increase ventilation, increase oxygenation, reduce hands-off time, allow for continuous compressions, and/or improve survival)?

Consensus on Science

A retrospective case series (LOE 4) comparing a laryngeal mask airway with bag-mask ventilation in cardiac arrest patients demonstrated a regurgitation rate of 3.5% with use of a laryngeal mask airway and 12.4% with use of bag-mask ventilation.[85] When a variety of supraglottic airway devices were compared with bag-mask ventilation in manikin models, 6 studies showed improved ventilation and a decrease in gastric inflation (LOE 5).[86–91] One pseudorandomized and 1 nonrandomized clinical trial (LOE 2) found no difference in arterial blood gas values or survival rates when a variety of supraglottic airway devices were compared to bag-mask ventilation.[92,93] Three studies performed in manikin models of cardiac arrest (LOE 5)[94–96] found that, compared with a bag-mask, the use of a single-use, disposable laryngeal tube to provide ventilation may decrease no-flow times.

Treatment Recommendation

A supraglottic airway device may be considered by healthcare professionals trained in its use as an alternative to bag-mask ventilation during cardiopulmonary resuscitation.

Knowledge Gaps

Further data are needed on the adequacy of ventilation with the various supraglottic airway devices if chest compressions are not interrupted; also needed are comparisons of the various supraglottic airway devices with each other and with bag-mask ventilation when used clinically by inexperienced and by experienced providers.

Tracheal Intubation Versus the Combitube/Laryngeal Mask Airway[ALS/BLS-CPR&A-079A, ALS/BLS-CPR&A-079B]

Consensus on Science

Nine studies compared a variety of supraglottic airway devices with the tracheal tube during cardiac arrest (LOE 1[97]; LOE 2[98–105]) and a further 6 studies compared a variety of supraglottic airway devices with the tracheal tube in patients undergoing anesthesia (LOE 5).[106–111] Overall in these studies the supraglottic airway device performed as well as, or better than, the tracheal tube with respect to successful insertion and/or time to tube insertion or to ventilation. One study retrospectively compared outcomes in cardiac arrest patients treated with an esophageal-tracheal-combitube or tracheal tube and found no difference in ROSC, survival to admission, or survival to discharge (LOE 2).[104] One study compared survival in cardiac arrests managed with a laryngeal mask airway with an historical control group of cardiac arrests managed with a tracheal tube and found that ROSC was significantly higher in the study period (61% versus 36%) (LOE 3).[105]

Eight manikin studies with simulated cardiac arrest (LOE 5)[89,90,96,112–116] and 8 manikin studies without simulated cardiac arrest showed that successful insertion rates and/or time to insertion or to ventilation for a variety of supraglottic airway devices were as good, or better than, for the tracheal tube (LOE 5).[117–124]

Nine studies documented that when a supraglottic airway device is used as a rescue airway after failed tracheal intubation, most patients can be ventilated successfully with the supraglottic airway device (LOE 2[98,99,103]; LOE 3[125–128]; LOE 5[107,129]).

Two studies performed while wearing anti-chemical protective clothing, 1 randomized crossover trial on anesthetized patients, and a pseudorandomized study on manikins found increased time to tracheal tube insertion but not to laryngeal mask airway insertion (LOE 5).[108,117]

Three manikin studies comparing a supraglottic airway device with the tracheal tube during ongoing chest compressions demonstrated decreased time to intubation with the supraglottic airway device, as well as reduced no flow time (LOE 5).[96,112,115] One nonrandomized manikin study found that chest compressions caused only a minor increase in time to tracheal intubation but not to supraglottic airway device insertion (LOE 5).[114]

Treatment Recommendation

Healthcare professionals trained to use supraglottic airway devices may consider their use for airway management during cardiac arrest and as a backup or rescue airway in a difficult or failed tracheal intubation.

Knowledge Gaps

The adequacy of ventilation with supraglottic airway devices during uninterrupted chest compressions is unknown. The performance of the various supraglottic airway devices should be compared with each other and with the tracheal tube when used in cardiac arrest. Use of the supraglottic airway devices by providers of differing experience should also be studied.

Confirming Advanced Airway Placement

Exhaled Carbon Dioxide Detection and Esophageal Detection Devices[ALS-CPR&A-008A, ALS-CPR&A-008B]

In adult cardiac arrest (out-of-hospital [OHCA], in-hospital [IHCA]), does the use of devices (eg, CO_2 detection device, CO_2 analyzer, or esophageal detector device), compared with usual management, improve the accuracy of diagnosis of airway placement?

Consensus on Science

Two studies of waveform capnography (LOE D2) to verify tracheal tube position in victims of cardiac arrest after intubation demonstrated 100% sensitivity and 100% specificity in identifying correct tracheal tube placement.[130,131] One of these studies included 246 intubations in cardiac arrest with 9 esophageal intubations,[130] and the other included 51 cardiac arrests with an overall esophageal intubation rate of 23%,[131] but it is not specified how many of these occurred in the cardiac arrest group. Three studies (LOE D1)[132–134] with a cumulative total of 194 tracheal and 22 esophageal tube placements demonstrated an overall 64% sensitivity and 100% specificity in identifying correct tracheal tube placement when using the same model capnometer (no waveform capnography) on prehospital cardiac arrest victims. The sensitivity may have been adversely affected by the prolonged resuscitation times and very prolonged transport times of many of the cardiac arrest victims studied. Intubation was performed after arrival at hospital and time to intubation averaged more than 30 minutes.

Studies of colorimetric end-tidal CO_2 ($ETCO_2$) detectors (LOE D2[135,136]; LOE D4[137–139]; LOE D5[140,141]), the syringe aspiration esophageal detector device (LOE D1[133]; LOE D4[142]), the self-inflating bulb esophageal detector device (LOE D1),[132–134] and nonwaveform end-tidal CO_2 capnometers (LOE D2[130,143]; LOE D4[137]; LOE D5[141]) showed that the accuracy of these devices is similar to the accuracy of clinical assessment (not uniformly defined across all studies) for confirming the tracheal position of a tracheal tube in victims of cardiac arrest.

Treatment Recommendations

Waveform capnography is recommended to confirm and continuously monitor the position of a tracheal tube in victims of cardiac arrest, and it should be used in addition to clinical assessment (auscultation and direct visualization are suggested).

If waveform capnography is not available, a nonwaveform carbon dioxide detector or esophageal detector device in addition to clinical assessment (auscultation and direct visualization are suggested) is an alternative.

Knowledge Gaps

The relationships between $ETCO_2$, time from arrest, and the response time of emergency medical services (EMS) should be determined so that the meaning of a zero reading on waveform capnography can be understood.

Thoracic Impedance[ALS-CPR&A-006A, ALS-CPR&A-006B]

In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]), does the use of thoracic impedance, compared with usual management, improve the accuracy of diagnosis of airway placement and adequacy of ventilation?

Consensus on Science

Two studies in adults (LOE D5)[144,145] and 1 study in children (LOE D5)[146] in patients undergoing anesthesia demonstrated high sensitivity (0.975 to 1.0) and specificity (0.925 to 1.0) of thoracic impedance in diagnosing tracheal and esophageal intubations. One nonrandomized trial in immediately postmortem patients (LOE D2)[147] demonstrated smaller changes in thoracic impedance with esophageal ventilations than with tracheal ventilations. One study (LOE D2)[148] tested impedance-based ventilation recognition during cardiac arrest with ongoing compressions and was able to detect 90.4% of ventilations with a 95.5% positive predictive value. Two case reports comprising a total of 6 cardiac arrest patients with ongoing CPR (LOE D3;[149] LOE 4[150]) demonstrated disappearance

of ventilation-induced changes in thoracic impedance after esophageal intubation.

The evidence evaluating the use of thoracic impedance in diagnosing adequacy of ventilation is scant. Supportive evidence from 1 animal study (LOE D5)[151] demonstrated that the intensity of the thoracic impedance signal was proportional to the observed tidal volumes. An exploratory study conducted in human cardiac arrest patients (LOE D2)[152] demonstrated a strong correlation between thoracic impedance changes and tidal volume changes in the absence of chest compressions, but large variations in measured impedance coefficients were observed.

Treatment Recommendation

Thoracic impedance may be used as an adjunctive measure to diagnose airway placement in cardiac arrest patients; however, treatment decisions pertaining to the accuracy of airway placement should not be based solely on thoracic impedance measurements until further study has confirmed the utility and accuracy of such measurements in this population.

Knowledge Gaps

More research is needed to clarify the usefulness of thoracic impedance to independently confirm placement of a tracheal tube and adequacy of ventilation during cardiopulmonary resuscitation.

Oxygen

Supplemental Oxygen: 100% vs Titration *ALS-CPR&A-011A*

In adult cardiac arrest (out-of-hospital [OHCA], in-hospital [IHCA]), does the use of titrated oxygen during cardiac arrest, compared with the use of 100% oxygen, improve outcome (eg, ROSC, neurologically intact survival)?

Consensus on Science

There were no adult (>8 years of age) human studies that addressed directly whether titrated oxygen compared with 100% oxygen during CPR affects outcome. Two animal studies (LOE 5)[153,154] that used a fibrillatory model of cardiac arrest suggested that use of 100% oxygen during CPR and for 15 to 60 minutes after ROSC results in worse neurological outcomes compared with normoxic (21% oxygen, room air) resuscitation, whereas 1 animal study (LOE 5)[155] using an asphyxial model documented that ventilation with either 100% oxygen or 21% oxygen during resuscitation did not affect outcome.

Treatment Recommendation

There is insufficient evidence to support or refute the use of a titrated oxygen concentration or constant 21% oxygen (room air) when compared with 100% oxygen during adult cardiac arrest. In the absence of any other data there is no reason to change the current treatment algorithm, which includes use of 100% oxygen during adult cardiac arrest.

Knowledge Gaps

Prospective clinical trials may be warranted to explore constant (including room air) versus titrated oxygen resuscitation approaches during human adult cardiac arrest.

Passive Oxygen vs Positive Pressure Oxygen During CPR *ALS-CPR&A-009A, ALS-CPR&A-009B*

In adults and children in cardiac arrest (out-of-hospital [OHCA], in-hospital [IHCA]), does the use of passive oxygen delivery during CPR, compared with oxygen delivery by positive pressure ventilation, improve outcome (eg, ROSC, survival)?

Consensus on Science

Two studies (LOE 1),[156,157] involving ALS providers in- and out-of-hospital settings, and 2 animal studies (LOE 5)[158,159] suggested that passive oxygen delivery through a Boussignac tube at a flow of 15 L/min associated with continuous chest compressions (with or without active compression-decompression CPR) generated equal or improved gas exchange and hemodynamics, but without improved outcome (ROSC, hospital discharge survival, or neurological outcome), when compared with a standard tracheal tube and positive pressure ventilation.

Four animal models (LOE 5) using different devices or approaches (nasal cannula in the oropharynx,[160] pharyngeal-tracheal lumen airway,[161] and oxygen catheter tip at the level of the carina[162,163]) confirmed an equivalent or better gas exchange and/or hemodynamics, with continuous oxygen inflation compared with standard ventilation.

One swine model (LOE 5)[164] demonstrated equivalent gas exchange and 48-hour survival following 4 minutes VF arrest with passive oxygen supplied via tracheal tube compared with oxygen supplied by positive pressure ventilation.

Two studies (LOE 3)[165,166] of a simplified minimally interrupted cardiac resuscitation (MICR) protocol (concept of cardiocerebral resuscitation), which included passive oxygen delivery via a standard oxygen mask with nonrebreather bag and continuous chest compressions, showed an improvement in neurologically intact survival in adults with bystander-witnessed cardiac arrest and an initially shockable rhythm when controlled with historical controls using standard CPR. Another study (LOE 3)[84] demonstrated better survival with passive oxygen delivery than with bag-mask ventilation. In this study the passive oxygen delivery was included as one intervention in a bundle of different treatment changes in patients with a bystander-witnessed cardiac arrest and an initially shockable rhythm. The relative effect of each component of the treatment bundle, including oxygenation, is unknown.

Treatment Recommendation

There is insufficient evidence to support or refute the use of passive oxygen delivery during CPR to improved outcomes (ROSC, hospital discharge rate, and improve neurological survival) when compared with oxygen delivery by positive pressure ventilation.

Knowledge Gaps
High-quality controlled clinical trials are required to evaluate the relationship between continuous positive airway pressure and important clinical outcomes and comparison with passive oxygen delivery during cardiopulmonary resuscitation.

Strategies for Ventilation

Monitoring Ventilatory Parameters During CPR[ALS-CPR&A-005C]

In adult cardiac arrest (out-of-hospital and in-hospital) with either a protected or unprotected airway, does the monitoring and control of ventilatory parameters (eg, minute ventilation and/or peak pressures), as opposed to standard care (without ventilatory monitoring), improve outcome (eg, ROSC, survival)?

Consensus on Science
There are no studies that directly addressed the relationship between monitoring of minute ventilation and peak pressure during CPR and changes in outcome (other than respiratory rate).

One animal study (LOE 5)[167] showed that hyperventilation was associated with decreased coronary perfusion pressure and decreased survival. The study also demonstrated that hyperventilation during cardiac arrest is common. One animal study (LOE 5)[168] showed that during CPR applying positive end–expiratory pressure (PEEP) up to 10 cm H_2O, in addition to intermittent positive pressure ventilation (IPPV), may improve oxygenation compared with IPPV alone. Another study demonstrated that continuous positive airway pressure with pressure support ventilation (CPAP PSV) during resuscitation also may improve oxygenation and outcome (LOE 5).[169] One study (LOE 3)[170] demonstrated that real-time feedback during CPR compared with no feedback resulted in a delivered ventilation rate closer to that indicated by current guidelines.

Treatment Recommendation
There is insufficient evidence to support or refute the use of peak pressure and minute ventilation monitoring to improve outcome from cardiac arrest. There is indirect evidence that monitoring the respiratory rate with real-time feedback is effective in avoiding hyperventilation and achieving ventilation rates closer to recommended values, but there is no evidence that ROSC or survival is improved.

Knowledge Gaps
Clinical trials evaluating ventilation monitoring during cardiac arrest resuscitation for all outcomes are needed. There is limited information on the accuracy of ventilation rate monitoring in the new defibrillator software that evaluates CPR process measures. This initial work would be helpful to enable controlled trials to determine the optimal ventilation rate associated with survival.

Monitoring Physiological Parameters During CPR[ALS-CPR&A-001A, ALS-CPR&A-001B]

In adult cardiac arrest (out-of-hospital [OHCA], in-hospital [IHCA]), does the use of physiological feedback about CPR quality (eg, end-tidal CO_2 monitoring), compared with no feedback, improve any outcomes (eg, ROSC, survival)?

Consensus on Science
None of the 17 studies that were reviewed evaluated physiological feedback ($ETCO_2$, coronary perfusion pressure, superior vena caval central venous oxygen saturation, bispectral index monitoring) specifically as a tool to guide resuscitation intervention in real time to improve outcomes from cardiac arrest. Eleven studies showed that physiological monitoring values ($ETCO_2$, coronary perfusion pressure, venous oxygen saturation) increased when ROSC was achieved (LOE 4)[171–178,135,179,180] and that they may be an indication of ROSC before it can be seen in vital signs.[181]

Five of the studies found that $ETCO_2$ was accurate for predicting patients who could not be resuscitated; some gave a time frame for that prediction of 20 minutes (LOE 4).[136,174,178,182,183] However, 2 studies documented patients who did not meet the $ETCO_2$ range but who survived (LOE 4).[174,184] Multiple studies by 1 group (LOE 4)[175–177] showed that when $ETCO_2$ exceeded 10 mm Hg, all patients achieved ROSC. In 1 of these studies all the survivors had an initial $ETCO_2$ higher than 10 mm Hg.[176] Similarly, 2 studies showed that if the $ETCO_2$ did not exceed 10 mm Hg, survival was zero (LOE 4).[182,183]

One study showed no correlation between bispectral index (BIS) values during cardiopulmonary resuscitation and ROSC and survival (LOE 4).[185]

Treatment Recommendation
Continuous capnography or capnometry monitoring, if available, may be beneficial by providing feedback on the effectiveness of chest compressions. The prognostic value of end tidal CO_2 is further reviewed in the section on prognostication.[ALS-D&P-014A]

Knowledge Gaps
Animal and human studies evaluating the effects of modification of resuscitation based on physiological feedback would be helpful.

Automatic Transport Ventilators

Automatic Ventilators vs Manual Ventilation During CPR[ALS-CPR&A-010A]

In adults and children in cardiac arrest (out-of-hospital [OHCA], in-hospital [IHCA]) and who have advanced airways in place, does the use of automatic ventilators, compared with manual ventilation, improve outcome (eg, ventilation, oxygenation, reduce hands-off time, allow for continuous compressions and/or improves survival)?

Consensus on Science
One pseudorandomized study suggested that the use of an automatic transport ventilator with intubated patients may

enable the EMS team to perform more tasks while subjectively providing ventilation similar to that provided by hand with a resuscitation bag (LOE 2).[186] One study suggested that the use of an automatic transport ventilator with intubated patients provides oxygenation and ventilation similar to that achieved with a bag-valve device but with no difference in survival (LOE 2).[187]

Treatment Recommendation

There is insufficient evidence to support or refute the use of an automatic transport ventilator over manual ventilation during resuscitation of the cardiac arrest victim with an advanced airway.

Knowledge Gaps

Studies evaluating adequacy of oxygenation, difference between volume and pressure cycled ventilation, and survival and complication rates when comparing manual ventilation versus automatic transport ventilator in cardiopulmonary resuscitation with an advanced airway in place are needed to advance the science in this area.

Supporting the Circulation During Cardiac Arrest

Questions related to circulatory support during cardiac arrest that were discussed during the 2010 Consensus Conference are categorized as (1) timing of drug delivery, (2) vasopressors during cardiac arrest, (3) other drugs during cardiac arrest, (4) intravenous (IV) fluids, and (5) extracorporeal support. It is recognized that the vast majority of studies assessing the effects of drugs on survival have been unable to control for the quality of cardiopulmonary resuscitation. Furthermore most drug evaluations to date have been conducted before recent advances in post–cardiac arrest care, including therapeutic hypothermia. Since most drug trials have, at most, demonstrated only short-term outcome advantage, it may be important to evaluate long-term outcome when these drugs are combined with optimized post–cardiac arrest care. One study (LOE 1)[188] compared the use of IV access and drugs (epinephrine, amiodarone, atropine, vasopressin, without isolating the effect of each individual drug alone), with no IV access and no drugs in adult out-of-hospital CPR without isolating the effect of each individual drug alone, with placebo in adult out-of-hospital CPR and demonstrated improvement in ROSC and survival to hospital and intensive care unit (ICU) admission, but no difference in survival to discharge or neurological outcomes at discharge and at 1-year follow-up; however, that study was not powered to detect clinically meaningful differences in long-term outcome. Similarly 1 study (LOE 3)[189] with a before-and-after design compared various outcomes after out-of-hospital cardiac arrest; it was unable to demonstrate any improvements after introduction of advanced life support (epinephrine, atropine, lidocaine). Neither of these studies was able to isolate outcomes specifically related to individual drug administration.

Timing of Drug Delivery[ALS-SAM-063A, ALS-SAM-063B]

In adult cardiac arrest (out-of-hospital or in-hospital), does an alternate timing for drug delivery (eg, early or delayed), as opposed to standard care (standard position in algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

There are no studies that addressed the order of drug administration. Subgroup analyses from 2 clinical studies reported decreased survival for every minute drug delivery was delayed, measured from call received at EMS dispatch (LOE 4).[190,191] This finding was likely to be biased by a concomitant delay in onset of ALS. In 1 study the interval from the first shock to the injection of the drug was a significant predictor of survival (LOE 4).[190] One animal study reported lower coronary perfusion pressure when delivery of vasopressor was delayed (LOE 5).[192] Time to drug administration was a predictor of ROSC in a retrospective analysis of cardiac arrest in swine (LOE 5).[193]

Treatment Recommendation

There is inadequate evidence to define the optimal timing or order for drug administration. An incomplete review of animal studies suggests that timing of vasopressor administration may affect circulation, and further investigations are important to help guide the timing of drug administration.

Knowledge Gaps

Advancing the science in the timing of drug administration is closely related to the need to conduct placebo-controlled trials to determine the efficacy of some drugs in CPR. The timing of drug administration and route of delivery are important data points to be captured in future studies. Animal models and clinical trials addressing efficacy can also be designed to provide substantial information on how timing and delivery can affect outcome. In the future, inclusion of studies on pharmacokinetics combined with dose response, as well as studies addressing the impact of timing of defibrillation on circulation and drug effect, might better address the question of optimal timing of drug delivery.

Vasopressors[ALS-D-023B]

Despite the continued widespread use of epinephrine and increased use of vasopressin during resuscitation in some countries, there is no placebo-controlled study that shows that the routine use of any vasopressor during human cardiac arrest increases survival to hospital discharge.

In adult patients in cardiac arrest (asystole, pulseless electric activity [PEA], pulseless VT, and VF) (out-of-hospital [OHCA], in-hospital [IHCA]), does the use of vasopressors (epinephrine, norepinephrine, others) or combination of vasopressors, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, ROSC, survival)?

Consensus on Science

One study retrospectively compared epinephrine with no epinephrine for sustained VF and PEA/asystole and found

improved ROSC with epinephrine for both rhythms but no difference in survival (LOE 2).[194] In a large retrospective registry-based study from Sweden (LOE 4) epinephrine was an independent predictor of poor outcome (LOE 4).[195]

Three studies (LOE 1)[196–198] and a meta-analysis (LOE 1)[199] demonstrated no difference in outcomes (ROSC, survival to discharge, or neurological outcome) with vasopressin when compared with epinephrine as a first-line vasopressor in cardiac arrest.

Two studies (LOE 1)[200,201] demonstrated no difference in outcomes (ROSC, survival to discharge, or neurological) comparing epinephrine in combination with vasopressin with epinephrine alone in cardiac arrest.

No study demonstrated a survival benefit with high-dose versus standard-dose epinephrine in cardiac arrest. Two studies (LOE 1)[202,203] reported improvement in ROSC using high-dose epinephrine. One meta-analysis (LOE 1)[204] of pooled data from 5 studies[202,203,205–207] supported improvement in ROSC with high-dose epinephrine but no change in survival outcomes.

Treatment Recommendation

Although there is evidence that vasopressors (epinephrine or vasopressin) may improve ROSC and short-term survival, there is insufficient evidence to suggest that vasopressors improve survival to discharge and neurological outcome. There is insufficient evidence to suggest the optimal dosage of any vasopressor in the treatment of adult cardiac arrest. Given the observed benefit in short-term outcomes, the use of epinephrine or vasopressin may be considered in adult cardiac arrest.

Knowledge Gaps

Placebo-controlled trials to evaluate the use of any vasopressor in adult and pediatric cardiac arrest are needed.

Other Drugs During Cardiac Arrest

There is no convincing evidence that the routine use of other drugs (atropine, amiodarone, lidocaine, procainamide, bretylium, magnesium, buffers, calcium, hormones, or fibrinolytics) during human CPR increases survival to hospital discharge.

Atropine[ALS-D-024B]

In adult patients in cardiac arrest (asystole, PEA, pulseless VT, and VF) (out-of-hospital, in-hospital), does the use of atropine or atropine in combination with other drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, ROSC, survival)?

Consensus on Science

Three studies (LOE 4)[208–210] (total of 12 operating rooms, 2 catheterization laboratories, 2 out-of-hospital cardiac arrest patients, and 4 in-hospital cardiac arrest patients) documented improvement in survival when atropine was given to patients in asystole in combination with epinephrine[208,210] and following induction with succinylcholine and fentanyl.[209] One study documented improvement in ROSC (14% versus 0%) when atropine was given to adults in asystolic out-of-hospital cardiac arrest in combination with epinephrine and sodium bicarbonate, but none survived to discharge (LOE 3).[211]

Three studies suggested that the use of atropine for treatment of cardiac arrest was not associated with any change in survival (LOE 2[212]; LOE 5[213,214]). Four human studies suggested that the use of atropine was associated with poor survival (LOE 4).[83,215–217]

Treatment Recommendation

There is insufficient evidence to support or refute the use of atropine in cardiac arrest to improve survival to hospital discharge.

Knowledge Gaps

Randomized placebo-controlled trials are required to define the role of atropine in PEA and asystolic cardiac arrest.

Lidocaine, Procainamide, Amiodarone, Bretylium, Magnesium[ALS-D-025A, ALS-D-025B]

In adult cardiac arrest (asystole, PEA, pulseless VT, and VF) (out-of-hospital, in-hospital), does the use of antiarrhythmic drugs (lidocaine, procainamide, amiodarone, bretylium, magnesium) or combination with other drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, ROSC, survival)?

Consensus on Science

There was little evidence to suggest a survival-to-discharge advantage with any antiarrhythmic drug used during resuscitation from out-of-hospital or in-hospital cardiac arrest. Two randomized trials demonstrated the benefit of amiodarone over standard of care, which included lidocaine in 80% of cases,[191] or routine use of lidocaine[190] for shock refractory or recurrent VT/VF for the end point of survival to hospital admission, but not to survival to hospital discharge. A retrospective review demonstrated improved survival to admission with lidocaine (compared with standard treatment) for patients in VF out of hospital (LOE 4).[218]

A retrospective review found procainamide was associated with increased survival to 1 hour postarrest in patients with VF in hospital (LOE 4).[214] Four randomized, controlled trials did not show any increase in ROSC or survival when magnesium was compared with placebo for patients in VF in out-of-hospital, ICU, and emergency department (ED) settings (LOE 1).[219–222]

Treatment Recommendation

Amiodarone may be considered for those who have refractory VT/VF, defined as VT/VF not terminated by defibrillation, or VT/VF recurrence in out-of-hospital cardiac arrest or in-hospital cardiac arrest. There is inadequate evidence to support or refute the use of lidocaine in the same settings.

Knowledge Gaps
All the studies to date were done with stacked shocks; it may be helpful to reevaluate the efficacy of amiodarone in the setting of a single-shock defibrillation strategy.

Calcium[ALS-D-026A, ALS-D-026B]

In adult cardiac arrest (asystole, PEA, pulseless VT, and VF) (out-of-hospital, in-hospital), does the use of calcium alone or combination with other drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, ROSC, survival)?

Consensus on Science
Three randomized control trials (LOE 1)[223–225] and 3 cohort studies (LOE 2)[214,217,226] and 1 case series (LOE 4)[227] demonstrated no effect on survival when calcium was given to in-hospital or out-of-hospital cardiac arrest patients. Two adult studies suggest that calcium administration during cardiac arrest was associated with decreased survival to hospital discharge (LOE 2).[217,228]

In VF, calcium did not restore a spontaneous circulation (LOE 4).[227] In 1 study of PEA arrests, calcium demonstrated improved ROSC, without reporting long-term survival, but only in a subgroup of patients with wide QRS (LOE 1).[224] Another study showed improved ROSC and survival to hospital arrival; however, there was no significant effect on survival (LOE 4).[227] Another study showed decreased rate of ROSC in the calcium group (LOE 2).[228] In 2 studies of asystole calcium administration failed to show any improvement in ROSC or survival to hospital discharge (LOE 1).[223,225] One study showed reduced ROSC in the calcium group (LOE 2).[228]

Treatment Recommendation
Routine administration of calcium for treatment of in-hospital and out-of-hospital cardiac arrest is not recommended.

Knowledge Gaps
More data are needed on the administration of calcium for specific circumstances, such as hyperkalemia, documented hypocalcemia, hypermagnesemia, calcium channel blocker overdose, or wide QRS complexes.

Steroid and Hormonal Therapy[ALS-D-027]

During adult cardiac arrest (asystole, PEA, pulseless VT, and VF) (out-of-hospital, in-hospital), does the use of steroid or hormonal therapy (estrogen, progesterone, hydrocortisone, insulin, growth factor, etc.) alone or in combination with other drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, ROSC, survival)?

Consensus on Science
There were no human or animal studies that directly addressed the use of the estrogen, progesterone, insulin, or insulinlike growth factor in cardiac arrest. Early observational studies of the use corticosteroids during cardiac arrest suggested possible benefit (LOE 4).[229,230] One complex randomized pilot study (LOE 1)[231] and 1 nonrandomized human study (LOE 2)[232] suggested benefit with corticosteroids, whereas 1 small, older, human prehospital controlled clinical trial suggested no benefit (LOE 1).[233] One animal study of corticosteroids suggested possible benefit (LOE 5).[234]

Treatment Recommendation
There is insufficient evidence to support or refute the use of corticosteroids alone or in combination with other drugs during cardiac arrest.

Knowledge Gaps
High-quality clinical trials are required to determine if there is a role in cardiopulmonary resuscitation for hormonal therapy with or without vasopressor while controlling for in-hospital use of hormonal therapy postarrest.

Buffers[ALS-D-029A, ALS-D-029C]

In adult cardiac arrest (asystole, PEA, pulseless VT, and VF) (out-of-hospital, in-hospital), does the use of buffering agents alone or combination with other drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, ROSC, survival)?

Consensus on Science
Two studies evaluated buffering agents during CPR (LOE 1).[235,236] Both had limitations but showed no improvement in outcome. Two retrospective cohort studies also showed no benefit in the use of buffering agents during CPR (LOE 2).[237,238] Two studies demonstrated increased ROSC, hospital admission, and survival at hospital discharge with bicarbonate use (LOE 2[239]; LOE 3[240]). Four cohort studies reported that bicarbonate use was associated with poor short- and long-term outcome (LOE 2).[217,241–243]

Treatment Recommendation
Routine administration of sodium bicarbonate for treatment of in-hospital and out-of-hospital cardiac arrest is not recommended.

Knowledge Gaps
There are large differences in direction and effect between results from the laboratory and those derived from clinical trials; therefore, well-designed trials, using bicarbonate or non- CO_2 generating buffers, are necessary to clarify the role of buffers in the treatment of short or prolonged cardiac arrest.

Fibrinolytics[ALS-D-028A, ALS-D-028B]

In adult cardiac arrest, does the use of fibrinolytics alone or in combination with other drugs, compared with not using drugs, improve outcomes?

Consensus on Science
Two studies failed to show any improvement in short- or long-term outcomes with the use of fibrinolytics (LOE

1).[244,245] One study showed an increased risk of intracranial bleeding associated with the routine use of fibrinolytics during cardiac arrest (LOE 1).[245] Seven studies showed benefit from fibrinolytic therapy in the treatment of victims of cardiopulmonary arrest unresponsive to standard therapy; however, those studies had significant limitations (LOE 1[246]; LOE 2[247–250]; LOE 3[251,252]).

Treatment Recommendation
Routine administration of fibrinolytics for the treatment of in-hospital and out-of-hospital cardiac arrest is not recommended. (See "Cardiac Arrest Caused by Pulmonary Embolus" for the treatment of patients with ROSC following suspected pulmonary embolus.)

Knowledge Gaps
The potential role of adjuvant antithrombotic and antiplatelet drugs needs exploration.

IV Fluids During Cardiac Arrest[ALS-D-016A, ALS-D-016B]

In adult cardiac arrest (out-of-hospital, in-hospital), does the use IV fluids, compared with not using fluids (or standard resuscitation), improve outcomes (eg, ROSC, survival)?

Consensus on Science
No published human study directly compared outcome of routine IV fluid administration with no fluid administration during CPR. Two animal studies reported that normothermic fluid infusion during CPR causes a decrease in coronary perfusion pressure (LOE 5),[253,254] and another animal study showed that the coronary perfusion pressure rise with epinephrine during CPR is not improved with the addition of a fluid infusion (LOE 5).[255] Most animal studies of fluid infusion during CPR lack a control group that receives no fluids; without a control group, it is difficult to assess of benefit or harm from fluid therapy (LOE 5).[256–267]

Hypertonic Fluid
One small randomized clinical trial (RCT) in adults found no significant ROSC or survival benefit with hypertonic IV fluid infusion when compared to isotonic IV fluid infusion during CPR (LOE 5).[256] One animal study showed that hypertonic saline improves cerebral blood flow during CPR (LOE 5).[262] Two animal studies found neither benefit nor harm with infusion of hypertonic saline (LOE 5).[260,267]

Chilled Fluid vs Room-Temperature Fluid
Two adult studies (LOE 5)[258,261] and 2 animal studies (LOE 5)[265,266] showed no improvement in ROSC when cold IV fluids (compared with room temperature IV fluids) were infused during CPR. One of the reported animal studies showed that the infusion of cold fluids during CPR caused a decrease in coronary perfusion pressure when compared to no fluids (LOE 5).[268]

Treatment Recommendation
There is insufficient evidence to recommend for or against the routine infusion of IV fluids during cardiac arrest resuscitation.

Knowledge Gaps
Human studies are required that compare outcome with IV fluid administration versus no fluid administration during treatment of VF and non-VF cardiac arrest. Animal models evaluating the hemodynamic effects of IV fluids need to more closely approximate the human model of cardiac arrest with comorbidities and altered physiology.

Extracorporeal Circulatory Support During Cardiac Arrest[ALS-CPR&A-002A, ALS-CPR&A-002B]

In adult cardiac arrest (prehospital, IHCA, OHCA), does the use of rapid deployment extracorporeal membrane oxygenation (ECMO), aortic balloon pump, or emergency cardiopulmonary bypass, compared with standard treatment, increase survival to hospital discharge with favorable neurological outcomes?

Consensus on Science
All the studies on this topic were small and there was a lack of consistency in the management before and after extracorporeal-CPR (ECPR). Three studies documented improvement in outcome in patients <70 years old, without significant comorbid conditions and with potential reversible/correctable conditions, when using ECMO compared with traditional CPR (LOE 2[269,270]; LOE 3[271]). One study demonstrated a 3-month survival of 22.7% for ECPR during out-of-hospital cardiac arrest unresponsive to advance life support after 20 minutes, with 10.6% having a Cerebral Performance Category (CPC) of 1 (LOE 2).[270] However, the ECPR group was more likely to have had a witnessed arrest, received bystander CPR, and be younger (with a mean age of 52 years, compared with 70 years in the standard treatment group).

Treatment Recommendation
There is insufficient evidence to support or refute the routine use of extracorporeal cardiopulmonary resuscitation in cardiac arrest.

Knowledge Gaps
Future research should define the criteria for ECPR after out-of-hospital cardiac arrest and the criteria for ECPR as a bridge to left ventricular assist device (LVAD) or transplant. It is recommended that the intraaortic balloon pump (IABP) and LVADs be included in the list of questions to pursue in 2015.

Antiarrhythmics in the Periarrest Period

Narrow-Complex Tachycardia (Excluding Atrial Fibrillation)[ALS-D-018]

There are 4 options for the treatment of narrow-complex tachycardia in the periarrest setting: electrical conversion, physical maneuvers, pharmacological conversion, or rate control. The choice depends on the stability of the patient and the rhythm. In a hemodynamically unstable patient, narrow complex tachycardia is best treated with electrical cardioversion.

In adult patients with narrow-complex tachycardia (out-of-hospital and in-hospital), does the use of any drug or combination of drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, reversion rates)?

Consensus on Science

Five trials supported the use of adenosine in the treatment of narrow-complex tachycardia (LOE 1).[272–276] Six trials demonstrated the effectiveness of verapamil in conversion to sinus rhythm (LOE 1).[272–275,277,278] The effectiveness of diltiazem in conversion to sinus rhythm is supported by 4 trials (LOE 1).[273,277,279,280] The evidence to support the use of other drugs for conversion to sinus rhythm is limited to a few trials for each drug, including sotalol (LOE 1),[281] amiodarone (LOE 4),[282] propafenone (LOE 1),[283]) and nadolol (LOE 1).[284] The study on nadolol suggested treatment effect on rate as well. There was no evidence of benefit with cibenzoline (LOE 1)[285] or magnesium (LOE 4)[286]; 2 studies reported that the response to magnesium is poor in patients with narrow-complex tachycardia.[287,288] Two studies demonstrated conversion effectiveness of vagal maneuvers (carotid massage and Valsalva) (LOE 2[289]; LOE 4[290]).

Treatment Recommendation

Vagal maneuvers, IV adenosine, verapamil, and diltiazem are recommended as first-line treatment strategies in the termination of narrow-complex tachycardias. Nadolol, sotalol, propafenone, and amiodarone may be considered.

Knowledge Gaps

Future studies should consider evaluating the safety of combining antiarrhythmic drugs and the efficacy of second-line therapies (some β-blockers, digoxin, amiodarone) for termination of narrow-complex tachycardia.

Atrial Fibrillation[ALS-D-017]

In adult patients in atrial fibrillation (prehospital and in-hospital), does the use of any drug or combination of drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, reversion rates)?

Consensus on Science

This topic has been comprehensively reviewed by the European Society of Cardiology, the American Heart Association, and the American College of Cardiology.[291]

Rate Control in Atrial Fibrillation. A systematic review (LOE 1)[292] demonstrated superiority for β-blockers (esmolol, metroprolol, and propranolol) with 70% success in meeting target heart rate or verapamil and diltiazem with 54% success[293] as first-line therapy for rate control in atrial fibrillation without a known accessory pathway and amiodarone when an accessory pathway was known and amiodarone or digoxin when fast atrial fibrillation occurred with heart failure (LOE 1).[292]

Four studies showed benefit for diltiazem in controlling rate in hospital (LOE 1[294–296]; LOE 2[297]), and 1 study for out of hospital (LOE 3).[298] Two studies showed that verapamil is equally effective in rate control for atrial fibrillation (LOE 1).[299,300] Adverse event rates with calcium channel blockers were reported as 18%.[300]

Amiodarone may control rate and rhythm (LOE 1),[301] but significant complications were described in placebo-controlled trials: the risk of adverse events was 26.8% as a pooled estimate, and the most common side effects encountered were phlebitis, bradycardia, and hypotension (LOE 1).[301]

Digoxin is not effective for cardioversion (LOE 1),[302–304] but in some studies it has been shown to have moderate rate controlling properties (LOE 1).[297,303,304]

Rhythm Control of Atrial Fibrillation. Ibutilide has consistently been more effective in converting atrial fibrillation to sinus rhythm when compared with placebo (LOE 1),[305–307] or other antiarrhythmic drugs (LOE 1: sotalol,[308] procainamide,[309] and amiodarone,[310]) and equal to other drugs (LOE 1: flecainide[311]).

Propafenone has been consistently more effective than placebo in converting AF to sinus rhythm (LOE 1),[312–314] but inferior to other drugs (LOE 1: amiodarone,[301] procainamide,[315] and flecainide[316]).

There are also data supporting flecainide (LOE 1)[317–320] and dofetilide (LOE 1)[321,322] for conversion in patients without coronary artery disease.

Data supporting amiodarone for cardioversion are relatively weak (LOE 1)[310,323–325]; however, amiodarone does have rate-controlling properties (LOE 1).[323,326]

Sotalol has consistently been shown to be inferior in conversion compared to other drugs (LOE 1: flecainide[318] and ibutalide[308]), but equal to amiodarone in 1 study (LOE 1).[325]

Most studies showed no conversion benefit for magnesium (LOE 1),[327,328] although 1 meta-analysis showed conversion benefit (LOE 1).[329] Most studies showed a benefit for magnesium in rate control (LOE 1),[295,329,330] although 1 study was neutral for magnesium for rate control (LOE 1).[328]

Quinidine has been shown to have greater conversion than sotalol in 2 studies (LOE 1),[331,332] although this was with greater toxicity. Clonidine has rate-controlling properties compared with placebo (LOE 1).[333,334]

Procainamide has shown increased efficacy in conversion of AF to sinus rhythm when compared with placebo[335] and to propafenone,[315] but appears to be as effective as amiodarone.[336]

Treatment Recommendation
Patients who are hemodynamically unstable with atrial fibrillation should receive prompt electrical cardioversion.

Rate Control in Atrial Fibrillation. Beta-blockers and diltiazem are the drugs of choice for acute rate control in most individuals with atrial fibrillation and rapid ventricular response. Digoxin and amiodarone may be used in patients with congestive heart failure, and amiodarone may also result in cardioversion to normal sinus rhythm. Magnesium and clonidine have rate-controlling effects, though there are fewer data supporting their use.

Rhythm Control of Atrial Fibrillation. Chemical cardioversion can be achieved with ibutilide, dofetilide, and flecainide. Amiodarone can also be used for chemical cardioversion, but it is less effective. Quinidine or procainamide may be useful for cardioversion, but their use is less well established. Propafenone is more effective than placebo but not as effective as amiodarone, procainamide, or flecainide. There is no role for digoxin in chemical cardioversion.

Knowledge Gaps
Future research should address unstable atrial fibrillation and the balance between rate control versus electrical cardioversion versus pharmacological cardioversion. Head-to-head comparisons to find the optimal drug with the best safety profile have not been done.

Wide-Complex Tachycardia

There are 2 options for the treatment of wide-complex tachycardia in the periarrest setting: electrical conversion and chemical conversion. The choice depends on the stability of the patient and the rhythm. In a hemodynamically unstable patient, wide complex tachycardia is best treated with electrical cardioversion.

Monomorphic VT[ALS-D-019-01A, ALS-D-019-01B]

In adult patients in hemodynamically stable monomorphic ventricular tachycardia (out-of-hospital, in-hospital), does the use of any drug or combination of drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, reversion rates)?

Consensus on Science

Procainamide
One unblinded study comparing lidocaine with procainamide (LOE 1)[337] documented an improved reversion rate over lidocaine (1.5 mg/kg) when procainamide (10 mg/kg) was given to adult patients with hemodynamically stable monomorphic ventricular tachycardia (mVT), but without severe congestive heart failure or acute myocardial infarction in the hospital setting. Additional evidence from a case series suggested that procainamide was effective in terminating stable mVT in the hospital setting (LOE 4).[338]

Sotalol
A double-blind study comparing lidocaine with sotalol documented an improved reversion rate over lidocaine (100 mg) when sotalol (100 mg) was given to patients with spontaneous onset hemodynamically stable sustained mVT in the hospital setting (LOE 1).[339]

Amiodarone
The evidence on the effectiveness of amiodarone (150 to 300 mg) in terminating VT is conflicting with reported conversion rates between 20% to 40% based on 1 controlled trial (LOE 1)[340] and 3 case series (LOE 4)[341–343] in patients with coronary artery disease with a low left ventricular ejection fraction in the hospital setting. The use of amiodarone (300 mg) was associated with side effects (primarily hypotension),[341,343] but the effect of these on outcome remains unclear.

Lidocaine
Lidocaine was less effective than sotalol (LOE 1),[339] procainamide (LOE 2),[337] and amiodarone (LOE 2)[340] in terminating VT. Three retrospective analyses showed lidocaine was poorly effective when given to patients with or without a history of myocardial infarction with spontaneous sustained stable VT in the hospital setting (LOE 4).[344–346] One randomized controlled study (LOE 5)[347] and 1 case series (LOE 5)[348] suggested a variable termination of the arrhythmia when lidocaine was injected by paramedics intramuscularly in patients with acute myocardial infarction and VT in the prehospital setting.

Cibenzoline
One case series suggested cibenzoline (70+/−12 mg) may be effective in terminating VT (LOE 4).[349]

Magnesium
One study suggested magnesium was effective in terminating VT (LOE 5).[350]

Adenosine
Adenosine may aid in diagnosing VT, but it will not terminate it (LOE 4).[351,352]

Calcium Channel Blockers
The evidence for the use of calcium channel blockers in VT is conflicting, with most studies opposing their use (LOE 4),[353354,355] but 1 study supported the use as long as coronary disease was not present (LOE 5).[356]

Nifekalant
Two retrospective control studies (LOE 3),[357,358] 1 case series (LOE 4),[359] and 1 other study (LOE 5)[360] suggested that nifekalant improved outcome in patients with shock refractory VF/VT, even though it did not seem to be effective in immediately terminating the arrhythmia.[359]

Preventing recurrence and late conversion in refractory ventricular tachyarrhythmias including mVT:

Amiodarone
Two RCTs (LOE 1) comparing amiodarone with lidocaine[340] or bretylium,[361] 2 double-blind randomized dose-range studies (LOE 4),[362,363] and 5 case series (LOE 4)[364–368] suggested that amiodarone reduced the number of life-threatening arrhythmias (event rate), required shocks, and episodes of symptomatic sustained VT that occurred in patients with recurrent refractory ventricular arrhythmias in hospital.

β-Blockers
A single prospective case series (LOE 4)[369] suggested that recurrent and refractory ventricular arrhythmias were reduced while long- and short-term survival were improved in patients treated with sympathetic blockade (including β-blockers) during electrical storm.

Electrical Cardioversion
Electrical cardioversion at an early stage or as first-line treatment was reasonable based on a prospective case series (LOE 4).[370] Indirect evidence was also provided by 3 case studies (LOE 4).[344,371,372]

Treatment Recommendation
Procainamide is recommended for patients with hemodynamically stable monomorphic ventricular tachycardia (mVT) who do not have severe congestive heart failure or acute myocardial infarction. Amiodarone is recommended for patients with hemodynamically stable mVT with or without either severe congestive heart failure or acute myocardial infarction. Nifekalant (not approved for use in all countries) may be useful in improving outcomes in shock refractory VF/VT even though it did not seem to be effective in immediately terminating the arrhythmia.

Sotalol may be considered for patients with hemodynamically stable sustained mVT, including patients with acute myocardial infarction.

Knowledge Gaps
Overall the evidence for different drugs, in terms of both their efficacy and their side effects, is conflicting, and the evidence supporting the use of drugs such as sotalol and procainamide is limited to just 1 study each. There are no placebo-controlled trials comparing antiarrhythmics, nor are there studies comparing electrical with pharmacological strategy for sustained hemodynamically stable mVT. Future research should define a standard drug therapy to be used as the reference control for scientific advancement in this area.

Undifferentiated Regular Stable Wide-Complex Tachycardia[ALS-D-019-02]

In adult patients with undifferentiated regular stable wide-complex tachycardia (prehospital and in-hospital), does the use of adenosine or adenosine in combination with other drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, reversion rates)?

Consensus on Science
Five studies involving more than 300 patients (LOE 4)[351,352,373–375] demonstrated that adenosine could safely be administered in regular wide-complex tachycardia: it converted wide-complex tachycardia secondary to supraventricular tachycardia to normal sinus rhythm, but rarely terminated VT. One small study showed poor rates of conversion to sinus rhythm in patients known to have VT (LOE 4).[344] No patient in these trials had serious adverse events; however, there are case reports in patients with irregular wide-complex tachycardia (generally pre-excited atrial fibrillation) in whom VF was precipitated by adenosine (LOE 4).[376–379]

Other studies that included lidocaine showed poor rates of conversion to sinus rhythm with lidocaine in patients known to have VT (LOE 4).[344] In 1 study, 11 of 25 patients known to have VT and treated with verapamil developed profound hypotension (LOE 4).[380]

Treatment Recommendation
In undifferentiated regular stable wide-complex tachycardia, IV adenosine may be considered relatively safe, may convert the rhythm to sinus, and may help diagnose the underlying rhythm.

Knowledge Gaps
The science in this area is limited: randomized trials have not been done.

Polymorphic Wide-Complex Tachycardia[ALS-D-020B]

In adult patients in polymorphic wide-complex tachycardia (prehospital and in-hospital), does the use of any drug or combination of drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, reversion rates)?

Consensus on Science
Evidence for benefit from these therapies is limited, mainly anecdotal, extrapolated, or from small, observational studies and based on the presumed mechanism for polymorphic wide-complex tachycardia, which may not always be clinically evident. There are 3 subtypes of polymorphic VT:

1. Polymorphic VT with delayed abnormal repolarization, usually known as torsades de pointes (twisting of the QRS complexes around the baseline), with long QT, as well as "pause-dependent" initiating sequence, and coexisting factors associated with delayed repolarization with 2 subtypes:
   a. Congenital long QT with torsades de pointes
   b. Acquired long QT with torsades de pointes
2. Polymorphic VT caused by ischemia, which usually has a short QT; ischemia often present by history,

clinical picture, and ECG findings of ischemia or infarction
3. Polymorphic VT of unknown cause, usually in the context of severe left ventricular dysfunction with or without congestive heart failure or severe structural heart disease

Familial (Congenital) Long QT (Torsades de Pointes)

Recurrences of polymorphic wide-complex tachycardia associated with congenital long QT may be reduced with IV magnesium, based on extrapolation from a small case series of children (LOE 5)[381]; overdrive pacing (atrial or ventricular); or β-blockers derived from extrapolation from 2 registry case series of secondary prevention in patients with congenital long QT (LOE 5).[382,383] There is virtually no published experience regarding the acute use of these therapies in such patients.

Acquired Long QT (Torsades de Pointes)

Recurrences of polymorphic wide-complex tachycardia associated with acquired or drug-precipitated Long QT may be reduced with IV magnesium, based on 5 studies (LOE 3[384]; LOE 4[385]; LOE 5 (pediatrics)[381]; LOE 5 (animals)[386,387]); overdrive pacing (atrial or ventricular) based on 7 studies (LOE 4[385,388–391]; LOE 5 [extrapolation from secondary prevention in patients with congenital LQTS][382,383]); and IV isoproterenol (when not contraindicated by presence of ischemia or hypertension) is supported by 4 studies (LOE 4[385,388]; LOE 5 (animal)[387,392]) but opposed by 1 study (LOE 4).[389]

Preventing Recurrences of Polymorphic Wide-Complex Tachycardia Secondary to Other Mechanisms

The science on the management of polymorphic wide-complex tachycardia caused by short QT syndrome is limited to case reports involving amiodarone, β-blockers, and quinidine (LOE 4).[393,394]

Polymorphic wide-complex tachycardia associated with acute myocardial ischemia responded to IV β-blockers in a modestly sized study (LOE 3)[369]; however, there was no benefit from IV magnesium in a small study (LOE 3).[384] A LOE-4 study[395] and extrapolation from a small case series suggested that isoproterenol attenuated the ST elevation associated with Brugada syndrome (LOE 5).[396] Extrapolation from 1 case series suggested worsened Brugada ST elevation with class IA antiarrhythmics (LOE 5).[396]

A pediatric case report (LOE 5)[397] and extrapolation from a small case series of secondary prevention using oral β-blockers alone (LOE 5)[398] or in combination with verapamil (LOE 5)[399,400] suggested IV propranolol successfully terminated catecholamine-induced polymorphic wide-complex tachycardia.

Hemodynamically Unstable Polymorphic VT of Unspecified Morphology and Mechanism

Among patients with impaired ventricular function due to structural heart disease (ischemic, valvular, or cardiomyopathy), in the absence of QT prolongation or drug provocation, treatment of hemodynamically unstable VT with IV amiodarone reduced the frequency of recurrent arrhythmias. This evidence rests on extrapolation from 3 prospective RCTs (LOE 5)[361–363] performed in the in-hospital setting but in which VT morphology was not addressed specifically.

Treatment Recommendation

Polymorphic wide-complex tachycardia associated with familial long QT may be treated with IV magnesium, pacing and/or β-blockers; however, isoproterenol should be avoided. Polymorphic wide-complex tachycardia associated with acquired long QT may be treated with IV magnesium. Addition of pacing or IV isoproterenol may be considered when polymorphic wide-complex tachycardia is accompanied by bradycardia or appears to be precipitated by pauses in rhythm. Polymorphic wide-complex tachycardia without long QT may be responsive to IV β-blockers (ischemic VT; catecholaminergic VT) or isoproterenol (Brugada).

Knowledge Gaps

Since the occurrence of these unusual arrhythmogenic mechanisms is rare, randomized clinical trials are unlikely; therefore, future registries may contribute to associations that may guide treatment and advance care.

Bradycardia[ALS-D-022A]

In adult patients in significant bradycardia (out-of-hospital and in-hospital), does the use of any drug or combination of drugs, compared with not using drugs (or a standard drug regimen), improve outcomes (eg, reversion rates)?

Consensus on Science

Four case series (LOE 4) demonstrated that in-hospital transcutaneous pacing had slightly higher success rates for rhythm capture[401] and survival to discharge (18% to 75%)[402–404] compared with survival-to-discharge rates (69%) when transcutaneous pacing was given for out-of-hospital bradycardia (LOE 1).[405] A systematic review supported this survival-to-discharge rate of 15% to 70% in the prehospital setting (LOE 3).[406]

Few studies have compared drugs with transcutaneous pacing for the treatment of bradycardia. A randomized trial of 45 patients (LOE 1)[407] comparing atropine, glycopyrrolate, and transcutaneous pacing in intraoperative patients showed no significant differences in long-term outcomes. Recurrent episodes of bradycardia were less common in the paced group. One feasibility study (LOE 1)[405] compared dopamine with transcutaneous pacing in patients with bradycardia refractory to atropine. There were no differences in outcomes of survival to discharge (70% versus 69%). Enrollment was slow in this feasibility trial because most patients got better with full-dose atropine in

the out-of-hospital setting, making them ineligible for randomization.

One randomized clinical trial (LOE 1),[407] 2 retrospective cohort studies (LOE 4),[408,409] and 2 additional observational studies (LOE 4)[410,411] documented that IV atropine improved heart rate and symptoms and signs associated with bradycardia. An initial dose of 0.5 to 1 mg, repeated as needed to a total of 1.5 to 3 mg, was effective in both in-hospital and out-of-hospital treatment of symptomatic bradycardia. One study (LOE 4)[411] reported that a ≥0.8 mg dose increased the incidence of tachycardia. One other study in 10 healthy volunteers (LOE 5)[412] indicated that a 3-mg dose of atropine produces the maximum achievable increase in resting heart rate. Two studies indicated that atropine may paradoxically cause high-degree atrioventricular (AV) block in patients after cardiac transplantation (LOE 5[413]; LOE 4[414]).

Second-line drug therapy with dopamine (LOE 1)[405] and epinephrine for undifferentiated hemodynamically unstable bradycardia may be successful; it should be tailored according to potential causes in individual patients. For the treatment of bradycardia unresponsive to atropine after inferior myocardial infarction, cardiac transplant, or spinal cord injury, theophylline may be administered (LOE 2[415]; LOE 4[416,417]).

Treatment Recommendation

First-line drug treatment for symptomatic bradycardia is atropine 0.5 to 1 mg IV repeated every 3 to 5 minutes as needed up to 1.5 to 3 mg total. If not effective, then consider epinephrine (2 to 10 μg/min) or dopamine (2 to 10 μg/kg/min). Transcutaneous pacing may be considered when full-dose atropine fails, although it may not be any more effective then second-line drug therapy.

Other second-line choices for symptomatic bradycardia should be tailored according to potential causes. After inferior myocardial infarction, cardiac transplant, or spinal cord injury, theophylline 100 to 200 mg slow injection IV (maximum 250 mg) may be given. Atropine should be used with caution in patients with bradycardia after heart transplant as it may cause paradoxical AV block.

Knowledge Gaps

Randomized trials comparing transcutaneous pacing with pharmacotherapy in hemodynamically unstable bradycardia are required to advance the management. Based on the low incidence of bradycardia that is resistant to atropine these trials may not be pragmatic or possible.

Cardiac Arrest in Special Circumstances

Environmental

Cardiac Arrest Caused by Avalanche[ALS-SC-078B]

For avalanche victims in out-of-hospital cardiac arrest, what factors when present, compared with when absent, are associated with/predict an increased survival to hospital discharge?

Consensus on Science

Time of Burial and Patent Airway. Four studies (LOE P3)[418–421] demonstrated a progressive nonlinear reduction in survival as time of burial lengthened. In 8 studies (LOE P3[419,420,422–425]; LOE P4[426,427]) victims who were buried beyond 35 minutes did not survive if they had an obstructed airway (defined as obstructed by avalanche debris or by other means) on uncovering the head. One study (LOE P5)[428] demonstrated that when breathing in simulated air pockets of different volumes, hypoxia and hypercapnia achieved a steady state after 10 minutes. This finding suggested that long-term survival was possible as long as an air pocket, even as small as 1 L, was present. One study (LOE P5)[429] indicated that deflection of expired air away from an air pocket may slow the development of hypoxia and hypercapnia.

Core Temperature. Two relevant LOE P3-studies in the general hypothermia literature found that survival decreased with core temperatures less than 32°C and reported the use of extracorporeal rewarming only when core temperatures were less than 32°C.[430,431] One relevant LOE P3-study reported a maximum cooling rate of 8°C/hour in buried victims.[432] An avalanche case report described a maximum cooling rate of 9°C/h (LOE P4).[426] Those cooling rates suggested that, at 35 minutes of burial, the core temperature may drop as low as 32°C. Three relevant studies (LOE P3)[423,432,433] and 4 case series or reports (LOE P4)[434,435426,431] recorded ROSC in 22, and survival to hospital discharge in 7 of those 22, buried avalanche victims in cardiac arrest with a core temperature less than 32°C with aggressive rewarming using extracorporeal circulation.

Serum Potassium. A serum potassium of less than 8 mmol/L on hospital admission was found to be predictive of increased ROSC in avalanche burial victims in 1 study (LOE P3)[423] and for increased survival to hospital discharge in 2 studies (LOE P3).[422,432]

Five studies found an inverse correlation between admission potassium concentration and survival to discharge in all-cause hypothermic patients (LOE P3).[430,422,433,436,437] Four studies (LOE P3)[422,432,438,439] found that high potassium values were associated with asphyxia in all hypothermic patients. The highest reported serum potassium value in an avalanche survivor was 6.4 mmol/L,[432] although survival to hospital discharge from all-cause hypothermia with a potassium concentration as high as 11.8 mmol/L has been documented.[440]

Treatment Recommendation

Avalanches occur in areas that are difficult for rescuers to access in a timely manner, and burials frequently involve multiple victims. The decision to initiate full resuscitative measures should be determined by the number of victims

and the resources available, and it should be informed by the likelihood of survival.

Avalanche victims are not likely to survive when they are

- Buried >35 minutes and in cardiac arrest with an obstructed airway on extrication.
- Buried initially and in cardiac arrest with an obstructed airway on extrication, and an initial core temperature of <32°C.
- Buried initially and in cardiac arrest on extrication with an initial serum potassium of >8 mmol/L or more.

Full resuscitative measures, including extracorporeal rewarming, when available, are indicated for all other avalanche victims without evidence of an unsurvivable injury.

Knowledge Gaps

Prospective validation studies of patent airway, core temperature, and serum potassium as prognostic factors among patients in cardiac arrest on extrication and prospective studies on effectiveness of prehospital treatment of nonarrested hypothermic avalanche victims would advance the science of avalanche resuscitation.

Pregnancy[ALS-SC-065]

In pregnant women with cardiac arrest (out-of-hospital or in-hospital), do any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

There are no RCTs evaluating the effect of specialized obstetric resuscitation versus standard care in postarrest pregnant women. Many studies of women not in cardiac arrest document the important physiological changes that occur in pregnancy that may influence treatment recommendations and guidelines for resuscitation of cardiac arrest in pregnancy.

Aortocaval Decompression to Improve Maternal Hemodynamics and Fetal Well-Being. In the nonarrest literature, left lateral tilt improved maternal blood pressure, cardiac output, and stroke volume (LOE 5)[441–443] and improved fetal parameters of oxygenation, nonstress test, and fetal heart rate.[444,445446] While chest compressions in the left lateral tilt position were shown to be feasible in a manikin study,[447] they have been shown to result in less forceful chest compressions than in the supine position.[448] Two studies found no improvement in maternal hemodynamic or fetal parameters in nonarrest patients with 10 to 20° left lateral tilt.[449,450] One study found more aortic compression at 15° left lateral tilt when compared to a full left lateral tilt.[442] In addition, aortic compression has been found to persist at over 30° of tilt;[451] however, the majority of these patients were in labor. Two nonarrest studies found that manual left uterine displacement (which is done with the patient supine) was as good as, or better than, left lateral tilt in relieving aortocaval compression, as assessed by the incidence of hypotension and ephedrine use.[452,453]

Respiratory Considerations. One study documented that the upper airways in the third trimester of pregnancy are smaller (supine mean difference 0.20; 95% confidence interval [CI] 0.06 to 0.35) compared with their postpartum state and to nonpregnant controls (LOE 5).[454] One study found increased intrapulmonary shunting in normal pregnancy at 12.8 to 15.3% compared with the nonpregnant state normal value of 2% to 5% (LOE 5),[455] suggesting a change in the approach to oxygenation demands and in the size of the advanced airway may be physiologically justifiable in maternal cardiac arrest.

Perimortem Caesarean Section. One retrospective cohort study of 55 maternal cardiac arrests evaluated the incidence of perimortem caesarean section after the introduction of a targeted training course and compared it with a historical rate (LOE 4).[456] One systematic review of perimortem caesarean sections documented 38 cases, with 34 surviving infants and 13 maternal survivors at discharge, suggesting that perimortem caesarean section may have improved maternal and neonatal outcomes (LOE 4).[457] At older gestational ages (30 to 38 weeks), infant survival was possible even when delivery was after 5 minutes from the onset of maternal cardiac arrest (LOE 4).[457] One retrospective study concluded that for delivery of infants between 22 to 25 weeks gestational age, neonatal outcome is best at 25 weeks, and there was no infant survival when delivery occurred at 22 weeks (LOE 5).[458]

Changes in Pharmacokinetics. One study documented an increase in glomerular filtration rate, cardiac output, and plasma volume early in the first trimester that starts to return to normal in the end of the third trimester, suggesting that known physiological vascular and fluid changes of pregnancy may respond to fluid resuscitation during maternal cardiac arrest (LOE 5).[459]

Defibrillation. One underpowered case control study reported no difference in transthoracic impedance during pregnancy compared with postpartum, suggesting current energy requirements for adult defibrillation were appropriate (LOE 4).[460]

Positioning. One study indicated that the human wedge technique can provide left lateral tilt and effective external chest compressions in a manikin (LOE 5).[447] However, another study found that the estimation of the degree of table tilt is unreliable and often overestimated, suggesting rescuers are more likely to employ an insufficient amount of tilt to achieve the required hemodynamic benefit (LOE 5).[461] A small study assessed the efficacy of resuscitation at various angles of inclination using a calibrated force transducer (LOE 5).[448] This study found that the maximum possible resuscitative force decreased as the angle of

inclination of the plane increased, from 67% of body weight in the supine position to 36% in the full lateral position. Therefore at an inclination of 27° the maximum resuscitative force for chest compressions was only 80% of the force generated at 0° of inclination (supine). Also at an incline of >30° the patient/manikin tended to roll off the incline plane (LOE 5).[448]

Therapeutic Hypothermia Postarrest. A single case report suggested that post–cardiac arrest hypothermia was used safely and effectively in early pregnancy with fetal heart monitoring and resulted in favorable maternal and fetal outcome after a term delivery (LOE 4).[462]

Treatment Recommendation
There is insufficient evidence to support or refute the use of specialized obstetric resuscitation techniques in maternal cardiac arrest and the use of therapeutic hypothermia in the postarrest period. Treatment may be guided by understanding the physiology of pregnancy, the importance of releasing aortocaval compression, the increased risk for hypovolemia, the compression advantage through positioning, and the value of perimortem caesarean section early in maternal cardiac arrest.

Knowledge Gaps
Research in the area of maternal resuscitation is lacking, and most of the science is extrapolated from nonpregnant women, manikin studies, or case reports. Epidemiological studies are needed to document the incidence of cardiac arrest in pregnancy as there as is a perception that it is increasing because of increased numbers of women with congenital heart conditions who are now having children.

Cardiac Arrest in Morbid Obesity[ALS-SC-074A]

In morbidly obese adult patients with cardiac arrest (out-of-hospital or in-hospital), does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
Evidence from 2 studies did not find a survival difference associated with obesity following out-of-hospital cardiac arrest (LOE 2).[463–465]

Treatment Recommendation
There is insufficient evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for obese patients.

Knowledge Gaps
There is a paucity of research in this area, and studies looking at epidemiology, current variations from the standard protocol, and associated outcomes, as well as simple experimental studies, would be helpful.

Cardiac Arrest Caused by Asthma[ALS-SC-067B]

In adult cardiac arrest due to asthma, does any modification of treatment, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
There are no RCTs that specifically evaluate or compare adjuvant treatment with standard treatment for cardiac arrest in asthmatic patients. Most of the literature comprises case reports and case series.

Evidence from 3 non–cardiac arrest case series involving 35 patients suggests that asthmatic patients are at risk for gas trapping during cardiac arrest, especially if their lungs are ventilated with high tidal volumes and/or rapid rates (LOE 5).[466–468] One volunteer adult study demonstrated that increasing PEEP caused increased transthoracic impedance (LOE 5).[469]

Seven case series involving 37 patients suggested increased ease of ventilation and ROSC with lateral chest compressions at the base of the ribs (LOE 4).[470–476] In a single case report, lateral chest compressions were associated with cardiac arrest and poor cardiac output (LOE 4).[477] Three single case reports (2 intraoperative and 1 ED) involving cardiac arrest caused by asthma suggested improvement in ease of ventilation and ROSC with thoracotomy and manual lung compression (LOE 4).[471,475,476]

Treatment Recommendation
There is insufficient evidence to suggest any routine change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by asthma.

Knowledge Gaps
Several key areas for research include: the role of disconnecting from positive pressure ventilation and the ideal duration of this disconnection; the role of lateral external compression and the timing with respect to chest compressions; the comparison of these techniques and their cumulative advantage; and the role of magnesium infusions and ECMO in cardiac arrest caused by asthma.

Cardiac Arrest Caused by Anaphylaxis[ALS-SC-066A, ALS-SC-066B]

In adult cardiac arrest caused by anaphylaxis, does any modification of treatment, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by anaphylaxis. Evidence is limited to case reports, extrapolations from nonfatal cases, interpretation of pathophysiology, and animal studies.

One human study of a randomized venom immunotherapy trial where 19 of 21 patients became symptomatic and

required emergency treatment suggests that carefully titrated continuous infusion of IV epinephrine in addition to volume infusion may be effective for the treatment of anaphylactic shock (not in cardiac arrest) (LOE 5).[478] One randomized controlled crossover study of animals preshock, but symptomatic with ragweed sensitivity, showed that a continuous IV infusion of 0.01 mg/kg epinephrine maintained a mean arterial pressure at 70% of preshock levels better than no treatment or bolus treatment (LOE 5).[479]

A small case series of patients with anaphylactic shock with or without cardiac arrest suggested that patients who did not respond to standard therapy may benefit from vasopressin (LOE 4).[480,481] A few small case series (LOE 4) have described promising initial findings with α-agonists such as norepinephrine,[482] methoxamine,[483] terlipressin,[484] and metaraminol.[485–487] A few small case reports (LOE 4) of cardiac arrest suggest cardiopulmonary bypass[488,489] or mechanical support of circulation[490] may be helpful in the setting of anaphylaxis.

Several case reports (LOE 4) document the use of a variety of interventions for cardiac arrest caused by anaphylaxis: 6 case reports support high dose α-1 receptor agonists: metaraminol,[485,486] methoxamine,[483,487] and norepinephrine.[482] Other case reports document the use of terlipressin,[484] vasopression,[481] steroids and antihistamines,[491] and cardiopulmonary bypass.[488489]

Treatment Recommendation

There is insufficient evidence to suggest any routine change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by anaphylaxis.

Knowledge Gaps

Future research should consider a comparison between the different IV α-agonists and a comparison of infusion versus bolus doses for cardiac arrest caused by anaphylaxis. The value of secondary therapies such as glucagon, antihistamines, volume infusions, and steroids should be explored.

Drug Overdose and Poisoning

The majority of questions addressing cardiac arrest caused by drug toxicity remain unanswered. Epidemiological studies are required to document the incidence of cardiac arrests caused by drugs, current treatment strategies, and the safety and efficacy of existing treatments. Animal models, controlled clinical trials, and pharmacodynamic studies are needed to advance the treatment of cardiac arrest caused by drugs. Most of the evidence is limited to case reports, extrapolations from nonfatal cases (including severe cardiovascular toxicity cases), and animal studies.

Cardiac Arrest Caused by Local Anesthetic[ALS-SC-073-01A]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by local anesthetic toxicity, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

Local anesthetic toxicity typically occurs in the setting of regional anesthesia, when a bolus of local anesthetic inadvertently enters the arterial or venous system, leading to refractory seizures and/or rapid cardiovascular collapse. There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by local anesthetics (lidocaine). Evidence is limited to case reports involving cardiac arrest and severe cardiovascular toxicity and animal studies.

Five single-case reports describe patients in cardiac arrest attributed to local anesthetic intoxication, who were refractory to advanced life support conventional treatment, but who obtained ROSC soon after treatment with IV lipid emulsion (LOE 4).[492–496] Five single-case reports (LOE 5) describe patients with acute, life-threatening cardiovascular toxicity from local anesthetic intoxication, but who were not pulseless at the time of lipid administration. In 3 cases[497–499] severe cardiovascular toxicity resolved rapidly following IV lipid, but in 2 other cases[500,501] the patient's condition deteriorated to cardiac arrest after IV lipid, although the patients were resuscitated and survived to hospital discharge.

Five controlled animal studies demonstrated that a variety of dosages of IV lipid emulsion were more effective than placebo in models of local anesthetic intoxication with ROSC as the primary outcome (LOE 5).[502–506]

Two controlled animal studies suggested that, in combination with basic life support (BLS), IV lipid emulsion improved the rate of ROSC when compared with vasopressor therapy (vasopressin and epinephrine) (LOE 5).[503,506] Contrasting results were published in 1 controlled animal study that demonstrated a survival advantage with vasopressin and epinephrine over lipid emulsion therapy in a model of asystole induced by low-dose bupivacaine and asphyxia (LOE 5).[507] Two controlled animal studies reported no additional benefit from lipid emulsion infusions when combined with high-dose epinephrine 0.1 mg/kg (LOE 5)[508] and 0.01 and 0.025 mg/kg (LOE 5).[509] Lipid emulsion bolus doses and infusion rates vary across case reports and animal studies. Typical bolus doses were 1 to 3 mL/kg. When infusions were used the typical doses were 0.1 to 0.3 mL/kg/h. A 20% solution of long-chain fatty acid emulsion was used in almost all reports.

Two controlled animal studies showed a survival advantage when cardiac arrest from local anesthetic toxicity was treated with high-dose insulin (1 to 2 U/kg IV bolus) accompanied by glucose and sometimes potassium, compared with basic life support resuscitation alone (LOE 5).[510,511] There were no animal studies comparing this intervention with advanced life support resuscitation.

The use of clonidine (150 μg boluses, repeated as needed) to treat cardiac arrest caused by local anesthetic was described in 1 human case report (LOE 4)[512] while a second case report (LOE 4)[513] was neutral, and a third

(LOE 5),[499] opposed. An animal study demonstrated partial improvement in bupivacaine-induced intracardiac conduction delays following clonidine administration (0.01 mg/kg IV), but nonperfusing rhythms were not studied (LOE 5).[514]

Treatment Recommendation
There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by local anesthetics. Animal studies and case reports suggest severe cardiovascular toxicity or cardiac arrest attributable to local anesthetic intoxication may respond to treatment with IV lipid emulsion.

Knowledge Gaps
Controlled clinical trials and pharmacodynamic studies are needed to advance the treatment of cardiac arrest caused by local anesthetics.

Benzodiazepine Toxicity[ALS-SC-073-02A]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by benzodiazepine toxicity, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
No human studies or reports of any patients who had cardiac arrest solely resulting from benzodiazepine toxicity alone were identified.

Five reports of cardiac arrests resulting from exposure to combinations of medication that included 1 of the benzodiazepines were identified (LOE 4).[515–519] One case report indicated that standard care alone was sufficient to reverse the severe cardiovascular toxicity attributed to an anaphylactic reaction to a benzodiazepine (LOE 5).[520]

One case report described improved outcome when minor cardiovascular toxicity caused by benzodiazepines was treated with flumazenil (LOE 5).[521] Four studies indicated that flumazenil is unlikely to improve hemodynamic function in the setting of benzodiazepine overdose and may complicate other therapy (LOE 5).[518,522–524] Two studies described serious adverse effects such as seizure, arrhythmia, hypotension, and withdrawal syndrome after flumazenil was given to patients presenting with decreased level of consciousness attributed to either benzodiazepine toxicity or an unknown cause (LOE 5).[518,525] These side effects were more common with coingestants (such as tricyclic antidepressant and opioids), chronic benzodiazepine use or abuse, and known seizure disorder.

Treatment Recommendation
There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by benzodiazepines.

Knowledge Gaps
Controlled clinical trials are needed to advance the treatment strategies for the management of cardiac arrest due to benzodiazepine toxicity.

β-Blocker Toxicity[ALS-SC-073-03B]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by β-blocker toxicity, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
There are no RCTs evaluating conventional versus alternative treatment of cardiac arrest caused by β-blockers. Evidence is limited to case reports, extrapolations from nonfatal cases, severe cardiovascular toxicity cases, and animal studies. The wide variety of β-blockers with differing pharmacological and physiochemical profiles makes it difficult to generalize from the limited data available.

In 13 case studies (n=16) of human patients with severe cardiovascular toxicity caused by β-blockers refractory to standard treatment, including vasopressors, the administration of glucagon (50 to 150 μg/kg) was followed by hemodynamic improvement and survival (LOE 5).[526–538]

In 2 animal studies, high-dose insulin infusions (1 U/kg/h) given with glucose supplementation and electrolyte monitoring appeared effective (as measured by rates of improved hemodynamic stability and survival) in the setting of cardiovascular toxicity associated with β-blockers (LOE 5).[539,540] A single human case report documented that high-dose insulin (10 U/kg/h IV), given with glucose supplementation and electrolyte monitoring, was followed by improved hemodynamic stability and survival to hospital discharge in the setting of severe cardiovascular toxicity associated with β-blocker toxicity (LOE 5).[541]

Case reports described the use of phosphodiesterase inhibitors (LOE 5),[542,543] calcium salts (LOE 4),[544] extracorporeal support (LOE 5),[545] intraaortic balloon pumps (LOE 4),[546] and ECMO (LOE 4).[547] Animal studies supported the use of calcium salts (LOE 5)[548] and the phosphodiesterase inhibitor amrinone (LOE 5).[549] Animal studies suggested that dopamine (LOE 5),[550] a combination of dopamine and isoproterenol (isoprenaline) (LOE 5),[551] and milrinone (LOE 5)[552] may decrease the effectiveness of glucagon as an antidote for β-blocker toxicity.

Treatment Recommendation
There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by β-blockers. Animal studies and case reports suggest severe cardiovascular toxicity caused by β-blockers may respond to treatment with IV glucagon, high-dose insulin (with glucose supplementation and electrolyte monitoring), or IV calcium salts in addition to conventional treatment.

Knowledge Gaps
Controlled clinical trials are needed to advance the treatment of cardiac arrest caused by β-blockers. While case reports focus on propranolol toxicity, the different properties of other β-blockers may affect the response to the suggested treatment. Other special interest topics include the use of new and emerging therapies, namely IV lipid infusion and high-dose insulin and the safety and effectiveness of glucagon in combination with new therapies.

Calcium Channel Blocker Toxicity[ALS-SC-073-04B]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by calcium channel blocker toxicity, does use of any specific intervention, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by calcium channel blockers. Evidence is limited to extrapolations from nonfatal case reports of severe cardiovascular toxicity.

In 16 human case series (n=28) high-dose insulin (bolus 0.5 to 2 U/kg followed by 0.5 U/kg/h infusion) given with glucose supplementation and electrolyte monitoring appeared effective (as measured by improved hemodynamic stability 25⁄28 and survival 26⁄28) in the setting of severe cardiovascular toxicity associated with calcium channel blockers (LOE 5).[553–568]

Treatment Recommendation
There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by calcium channel blockers. Case reports suggest severe cardiovascular toxicity caused by calcium channel blockers may respond to treatment with high-dose insulin given with glucose supplementation and electrolyte monitoring in addition to conventional treatment.

Knowledge Gaps
Controlled clinical trials are needed to advance the treatment of cardiac arrest caused by calcium channel blockers. While case reports focus on verapamil toxicity, the different properties of other calcium channel blockers may affect the response to the proposed treatment. Other special interest topics include the use of vasopressin to treat severe cardiovascular toxicity caused by dihyropyridines, the use of combination therapy, sequencing of interventions, and the evaluation of new and emerging therapies, namely IV lipid infusion and calcium sensitizers and nonpharmacological interventions.

Carbon Monoxide Toxicity[ALS-SC-073-05]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by carbon monoxide toxicity, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
Three studies suggested that most patients who develop cardiac arrest from carbon monoxide poisoning will not survive to hospital discharge, regardless of whether hyperbaric oxygen therapy is administered following ROSC (LOE 4).[569–571]

Two studies (LOE 5) suggested that neurological outcomes were improved in patients (all severity excluding cardiac arrest[572]; and mild-to-moderate, excluding loss of consciousness and cardiac instability[573]) who received hyperbaric oxygen therapy for carbon monoxide poisoning. However, 2 studies found no difference in neurologically intact survival (LOE 5).[574,575] Two systematic reviews concluded that improvement in neurologically intact survival following the administration of hyperbaric oxygen to carbon monoxide poisoning patients was possible but unproven (LOE 5).[576,577]

Two studies demonstrated that patients with carbon monoxide toxicity treated with hyperbaric oxygen who developed myocardial infarction have an increased risk of cardiovascular and all-cause mortality lasting at least 7 years after the event (LOE 5).[578,579]

Treatment Recommendation
Patients who develop cardiac arrest caused by carbon monoxide rarely survive to hospital discharge, even if ROSC is achieved; however, hyperbaric oxygen therapy may be considered in these patients because it may reduce the risk of developing persistent or delayed neurological injury. The risks inherent in transporting critically ill postarrest patients to a hyperbaric facility may be significant; it must be weighed against the possibility of benefit on a case-by-case basis. Patients who develop myocardial injury caused by carbon monoxide have an increased risk of cardiac and all-cause mortality lasting at least 7 years after the event; it is reasonable to recommend cardiology follow-up for these patients.

Knowledge Gaps
The epidemiology of cardiac arrest and severe cardiotoxicity caused by carbon monoxide needs further documentation. More precise estimates of the proportion of patients who survive to hospital discharge and who have full neurological recovery following severe carbon monoxide poisoning treated with various interventions are needed. Though challenging, further prospective treatment studies are important and necessary.

Cocaine Toxicity[ALS-SC-073-06B]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by cocaine, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

Cardiac Arrest (Primary Question). There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by cocaine. Evidence is limited to a small case series that demonstrated excellent overall and neurologically intact survival (12/22, 55%) in patients with cocaine-associated cardiac arrest treated with standard therapy (LOE 4).[580]

Severe Cardiotoxicity Caused by Cocaine (Secondary Question). No studies were found that addressed the treatment of severe cardiotoxicity caused by cocaine; however, human studies have evaluated the treatment of cocaine-associated wide-complex tachycardia and ischemic acute coronary syndrome, as well as coronary artery vasospasm caused by cocaine. Thus the benefit or harm of specific agents in cocaine-associated peri-arrest states (defined as severe hypertension, tachycardia, cocaine-induced arrhythmias) is informed by LOE 5-studies (extrapolation for nonarrest patients and, in some cases, cocaine naïve patients).

α-Blockers. A single study demonstrated reversal of cocaine-induced coronary artery vasospasm in the coronary catheterization laboratory with phentolamine (LOE 5).[581]

Benzodiazepines. A single study (LOE 5)[582] of patients with cocaine-associated chest pain demonstrated improved autonomic findings and resolution of chest pain when treated with diazepam. An additional study reported no additional benefit associated with benzodiazepine administration in patients already receiving nitroglycerin (LOE 5).[583]

β-Blockers. A retrospective case series of patients hospitalized for acute coronary syndrome associated with cocaine use suggested that there was a decrease in the incidence of death and nonfatal myocardial infarction with the use of β-blockers (LOE 5).[584] A prospective clinical trial in cocaine-naïve volunteers suggested that propanolol reduced cocaine-induced tachycardia (LOE 5).[585] A prospective clinical trial demonstrated worsening of cocaine-induced coronary artery vasoconstriction following the administration of propanolol to cocaine-naïve research subjects (LOE 5).[586] A retrospective case series of 7 ED and hospitalized patients with cocaine-associated cardiovascular toxicity demonstrated no consistent improvement in hypertension or tachycardia following treatment with esmolol (LOE 5).[587] Three of 7 patients developed apparent adverse effects (hypertension, hypotension, and CNS depression with vomiting).

β-Blockers With Partial α-Adrenergic Antagonism. In a pair of double-blind, crossover studies (LOE 5) of volunteers with a history of crack cocaine use, pretreatment with oral carvedilol[588] or labetolol[589] attenuated the cocaine-induced increases in heart rate and blood pressure compared with placebo, without apparent adverse effect. A prospective clinical trial demonstrated no change in cocaine-induced coronary artery vasoconstriction following the administration of labetolol to cocaine-naïve research subjects (LOE 5).[590]

Calcium Channel Blockers. One study of cocaine-naïve human volunteers demonstrated resolution of cocaine-induced coronary artery vasospasm with verapamil (LOE 5).[591]

Lidocaine. A retrospective case series of 29 patients who received lidocaine in the setting of cocaine-associated myocardial infarction included 8 patients with wide-complex tachycardia (2 sustained, 6 nonsustained) (LOE 5).[592] No patient developed complications and all survived the event.

Morphine. One study of cocaine-naïve human volunteers demonstrated that morphine partially reversed cocaine-induced coronary artery vasospasm (LOE 5).[593]

Nitroglycerin. In a clinical trial of cocaine-naïve volunteers administration of nitroglycerin reversed cocaine-induced coronary artery vasospasm (LOE 5).[594] In a prospective observational study of patients presenting with cocaine-associated acute coronary syndrome, 37/83 (45%) of patients treated with nitroglycerin reported reduction in the severity of chest pain, while 5 patients had other forms of clinical improvement (resolution of ischemia based on ECG, 2; hypertension, 2; or congestive heart failure, 1) (LOE 5).[595]

Treatment Recommendation

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest or cardiotoxicity caused by cocaine. In patients with severe cardiovascular toxicity (defined as severe hypertension, tachycardia, and/or cocaine-induced arrhythmias) it may be reasonable to try drugs known to be effective in acute coronary syndromes: α-blockers (phentolamine), benzodiazepines (lorazepam, diazepam), calcium channel blockers (verapamil), morphine, and sublingual nitroglycerin. The available data do not support the use of 1 drug over another.

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest and cardiotoxicity due to cocaine. Future studies should evaluate the role of sodium bicarbonate and lidocaine and the safety and effectiveness of other antiarrhythmic drugs, such as amiodarone, in the treatment of cocaine-associated VT.

Cyanide Toxicity[ALS-SC-073-07]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by cyanide, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by cyanide. The use of hydroxocobalamin (alone or with sodium thiosulfate) for cardiac arrest caused by cyanide

was suggested by 3 LOE 4-studies.[596–598] The use of hydroxocobalamin (alone or with sodium thiosulfate) in life-threatening cardiovascular toxicity was supported by 7 studies (LOE 5).[596–602]

The use of nitrites plus sodium thiosulfate was suggested by 3 studies, none of which enrolled cardiac arrest patients (LOE 5)[600,603,604]; however, 1 additional study found no benefit to this strategy (LOE 5).[605]

Treatment Recommendation

Patients with severe cardiotoxicity (cardiac arrest, cardiovascular instability, metabolic acidosis, or altered mental status) caused by known or suspected cyanide poisoning should receive cyanide antidote therapy. In addition to standard resuscitation, initial therapy should include a cyanide scavenger (either IV hydroxocobalamin or a nitrite—ie, IV sodium nitrite and/or inhaled amyl nitrite), followed as soon as possible by IV sodium thiosulfate. Hydroxocobalamin and nitrites are equally effective, but hydroxocobalamin may be safer because it does not cause methemoglobin formation or hypotension.

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest and cardiotoxicity caused by cyanide. Comparative studies on antidote therapy and health outcomes including neurological outcomes are required to address the question of which combination of drugs is most effective.

Tricyclic Antidepressant Toxicity[ALS-SC-073-08B]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by tricyclic antidepressants, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

There are no RCTs evaluating conventional versus alternative treatments for cardiac arrest caused by tricyclic antidepressant toxicity. Evidence was limited to 1 small case series of cardiac arrest patients; it demonstrated improvement with the use of sodium bicarbonate and epinephrine (LOE 4).[606] Notably in that case series the prearrest use of physostigmine was a significant potential confounder.

The evidence for the management of cardiotoxicity caused by tricyclic antidepressant was limited to case reports, case series, and animal studies. The use of sodium bicarbonate has been described in 2 case series (LOE 5)[607,608] and 6 animal studies (LOE 5).[609–614] The use of hyperventilation was described in 1 small case series (LOE 5)[615] and 1 animal study (LOE 5).[612] The evidence for the efficacy of specific antidysrhythmics (lidocaine, magnesium, amiodarone, phenytoin) was limited to negative case reports (LOE 5).[612,616–622] Specific vasopressors that have been associated with improvement in the treatment of tricyclic-induced hypotension include norepinephrine (LOE 5),[618,623–625] epinephrine (LOE 5),[611,618,626] dopamine (LOE 5),[625,627,628] and dobutamine (LOE 5).[627] Diazepam improved seizure control and survival in 1 animal study (LOE 5).[627] The use of physostigmine for tricyclic-induced anticholinergic symptoms was not supported by the current literature given the conflicting associations suggested by several case series (LOE 4[613]; LOE 5[608,629,630]). Limited animal research demonstrates a benefit for IV lipid infusions in models of tricyclic toxicity (LOE 5).[631,632] Antitricyclic Fab has been beneficial in animal models of varying degrees of tricyclic cardiotoxicity (LOE 5),[633–638] and 1 small human study (LOE 5)[639] provided evidence of safety and pharmacokinetic advantage; however, clinical benefit has yet to be demonstrated clearly.

Treatment Recommendation

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest or cardiotoxicity caused by tricyclic antidepressants. Because sodium bicarbonate bolus is the mainstay of therapy in the setting of tricyclic-induced cardiac conduction abnormalities, and this treatment strategy should be applied to the postarrest period of care for patients surviving cardiac arrest caused by tricyclic antidepressant toxicity associated with wide QRS complexes. When mechanical ventilation is required, respiratory acidosis should be avoided.

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest and cardiotoxicity caused by tricyclic antidepressants. Future trials exploring novel therapies (Fab, IV lipid infusions) and the use of sodium bicarbonate for hypotension in the absence of cardiac conduction abnormalities would be helpful.

Digoxin Toxicity[ALS-SC-073-09A]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by digoxin, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

There are no RCTs evaluating conventional versus alternative treatments for cardiac arrest caused by digoxin. Evidence is limited to 14 studies demonstrating the usefulness of antidigoxin Fab fragments for severe cardiac glycoside toxicity (LOE 5).[640–653]

Treatment Recommendation

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by digoxin. In adults and children with severe cardiovascular toxicity caused by digoxin and related cardiac glycosides, antidigoxin Fab fragment therapy should be administered.

Knowledge Gaps
Animal models and controlled clinical trials are needed to advance the treatment of cardiac arrest caused by digoxin. Pharmacokinetic and clinical studies would help establish the dosing of antidigoxin Fab fragment for digoxin cardiotoxicity.

Opioid Toxicity[ALS-SC-073-10]

In adult cardiac arrest (prehospital or in-hospital) caused by opioids, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
There are no RCTs evaluating conventional versus alternative treatments for cardiac arrest caused by opioids. Evidence is limited to studies of mild, moderate, and severe cardiovascular toxicity (LOE 5 for cardiac arrest). Evidence from studies assessing other endpoints (efficacy of naloxone), as well as animal studies, support the use of assisted ventilation before giving naloxone in opioid-poisoned patients with severe cardiopulmonary toxicity (LOE 1[654,655]; LOE 3[656]; LOE 4[657–659]; LOE 5[660]).

The use and safety of naloxone is supported by human studies (LOE 4),[657–659,661–664] as well as those assessing other endpoints (alternate routes of administration) (LOE 1[654]; LOE 3[656]; LOE 4[665,666]). Naloxone can be given intravenously (LOE 4),[657,658,662,665] intramuscularly (LOE 1[654]; LOE 4[657,658]), intranasally (LOE 1[654]; LOE 4[665]), and into the trachea (LOE 5).[667]

Treatment Recommendation
There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by opioids. In adults with severe cardiovascular toxicity caused by opioids, ventilation should be assisted using a bag-mask, followed by naloxone, and tracheal intubation if there is no response to naloxone. Naloxone should be given intravenously or intramuscularly. Intranasal or tracheal routes may be used if conditions preclude IV or intramuscular administration.

Knowledge Gaps
Animal models and controlled clinical trials are needed to advance the treatment of cardiac arrest caused by opioids. In particular such studies should determine if naloxone has a role in the resuscitation of the cardiac arrest patient pre- or post-ROSC.

Cardiac Arrest During Coronary Catheterization[ALS-SC-068B, ALS-SC-068C]

In adult cardiac arrest during percutaneous coronary intervention, does use of any specific intervention, as opposed to standard care, improve outcome?

Consensus on Science
There are no RCTs evaluating alternative treatment strategies as opposed to standard care for cardiac arrest during percutaneous coronary intervention (PCI). Evidence is limited to case studies for all interventions.

Mechanical CPR During PCI. Three adult human case reports (LOE 4),[668–670] 2 adult human case series (LOE 4),[671–673] and 1 animal study (LOE 5)[669] reported that the use of a mechanical chest compression device in cardiac arrest during PCI maintained circulation and enabled the procedure to be completed. Although a small proportion of patients in the case series (13/60) survived to hospital discharge, no randomized controlled or comparison study of this intervention has been performed.

Emergency Cardiopulmonary Bypass During PCI. One case study suggested that the use of emergency cardiopulmonary bypass to stabilize and facilitate emergency coronary angioplasty improved the survival of patients who had cardiac arrest during PCI that was unresponsive to advanced life support (LOE 4).[674]

Cough CPR during PCI. Five studies (LOE 4[675–677]; LOE 5[678,679]) supported the use of cough CPR as a temporary intervention to maintain adequate blood pressure and level of consciousness in patients who developed ventricular arrhythmias during PCI[676,677,679] and PCI[678] while definite therapy for malignant arrhythmias was instituted.

Treatment Recommendation
There are insufficient data to support or refute the use of mechanical chest compression, cough CPR, or emergency cardiopulmonary bypass to improve outcome of cardiac arrest during PCI.

Knowledge Gaps
Clinical trials, perhaps initially with historical controls, are needed to advance the treatment of cardiac arrest during PCI.

Cardiac Arrest After Open or Closed Heart Surgery[ALS-SC-069A, ALS-SC-069B, ALS-SC-069C]

In adult cardiac arrest following open (including heart and lung transplantations) and closed heart surgery, does use of any specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science

Resternotomy. Eleven studies documented improvement in outcome in patients with cardiac arrest following cardiac surgery who were treated with resternotomy and internal cardiac compression compared with standard protocol, when administered by experienced personnel in ICUs (LOE 2[680,681]; LOE 4[682–690]). Five studies neither supported nor opposed this finding (LOE 4[691–694]; LOE 5[695]). One study documented that the risk of infection was not significant after resternotomies conducted appropri-

ately outside of the operating room (LOE 4)[689]; whereas 3 studies demonstrated very poor outcomes when resternotomy was performed outside an ICU (LOE 2[680]; LOE 4[686]; LOE 5[695]).

Mechanical Circulatory Support. Six studies supported the use of mechanical circulatory support devices during cardiac arrest following cardiac surgery (LOE 3[690]; LOE 4[696–698]; LOE 5[699,700]). Three studies reported equivocal findings (LOE 5).[701–703] No studies opposed use of mechanical circulatory support. Mechanical circulatory support devices in these studies included extra-corporeal membrane oxygenation or cardiopulmonary bypass.

Graft Damage by Chest Compressions. Two case reports described damage to the heart caused possibly by external chest compressions before resternotomy (LOE 5).[704,705]

Epinephrine. One study reported 2 cases that responded to escalating doses of epinephrine (LOE 4).[706]

Antiarrhythmic Therapy. One study reported 18 cases with VF/VT after cardiac surgery (LOE 4).[707]

Treatment Recommendation
Resternotomy for patients with cardiac arrest following cardiac surgery should be considered in an appropriately staffed and equipped ICU. Resternotomy performed outside these specialized environments has poor results. Chest compressions should not be withheld while preparing for emergency resternotomy. Mechanical circulatory support may be considered in the setting of cardiac arrest following cardiac surgery. There is insufficient evidence to make any recommendations about epinephrine dose, antiarrhythmic use, or any other intervention separate from those recommended in standard protocols.

Knowledge Gaps
Clinical trials are needed to determine the safety and efficacy of mechanical circulatory support devices, chest compressions, and pharmacological adjuncts for the treatment of cardiac arrest after cardiac surgery.

Cardiac Arrest Caused by Cardiac Tamponade[ALS-SC-070B]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by cardiac tamponade, does use of specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
Five studies indicate that echocardiographically guided pericardiocentesis is a safe and effective method of relieving tamponade, especially when used in conjunction with a pericardial drain, and it may obviate the need for subsequent treatment in the operating room (LOE 5).[708–712]

One study documented 39 patients who received prehospital emergency thoracotomy by physicians to treat cardiac arrest from penetrating trauma (LOE 4).[713] Eighteen patients had cardiac tamponade and 4 (22%) survived. Two additional studies indicated that ED thoracotomy may be beneficial in patients who have cardiac arrest associated with cardiac tamponade and may yield improved results over standard needle pericardiocentesis (LOE 4).[714,715] One study indicated that ED thoracotomy may be especially beneficial if gross blood causes clotting and blocking of a pericardiocentesis needle (LOE 2).[716] Two studies indicated that emergency thoracotomy may also be beneficial in patients who have postprocedure complications (LOE 4).[682,717] One study indicated that a more definitive sternotomy or thoracotomy in an operating room may also be beneficial if transportation to the operating room does not introduce significant delay (LOE 5).[718]

Treatment Recommendation
Pericardiocentesis guided by echocardiography should be considered for treatment of cardiac arrest associated with cardiac tamponade while nonimage-guided pericardiocentesis is an acceptable alternative if echocardiography is not available. Placement of a pericardial drain may be beneficial and may obviate the need for subsequent treatment in the operating room. ED thoracotomy and pericardiotomy should be considered as an acceptable alternative to operating room thoracotomy and pericardiotomy for treatment of traumatic cardiac arrest associated with cardiac tamponade, and they can be considered for use in the treatment of nontraumatic cardiac arrest when pericardiocentesis is unsuccessful in relieving cardiac tamponade.

Knowledge Gaps
Clinical trials should include patients with pericardial tamponade secondary to nontraumatic arrest and compare safety and efficacy of needle drainage versus thoracotomy and prehospital versus emergency department versus operating room thoracotomy.

Cardiac Arrest Caused by Pulmonary Embolus[ALS-SC-071B]

In adult cardiac arrest (out-of-hospital or in-hospital) caused by pulmonary embolus, does use of etiology-specific interventions, as opposed to standard care (according to treatment algorithm), improve outcome (eg, ROSC, survival)?

Consensus on Science
One double-blind RCT showed no improvement in survival to discharge with the use of tissue plasminogen activator following cardiac arrest with PEA (LOE 1).[244] One RCT of fibrinolytics showed no difference in short- or long-term (30 days) survival or bleeding in patients randomized to receive tenecteplase or placebo during CPR (LOE 1).[245] Patients with suspected pulmonary embolism were excluded from the study if open fibrinolysis was

possible in the prehospital setting. Thirty-seven cases with suspected pulmonary embolism were randomized in the trial. Of those, 2 of 15 patients survived when treated with tenecteplase compared with no survivors in the 22 patients of the placebo-treated group.[245]

One meta-analysis of 8 retrospective cohort studies with a variety of causes of cardiac arrest (pulmonary embolism, 2 studies; myocardial infarctions, 4 studies; cardiology diseases, 1 study; and nontraumatic etiologies, 1 study) demonstrated an increased rate of ROSC, survival to discharge, and long-term neurological function with fibrinolytic, but it also showed an increased risk of severe bleeding (LOE 2).[719]

Nine studies of patients with presumed pulmonary embolism or all patients with cardiopulmonary arrests showed improvement with fibrinolysis in ROSC and admission to the hospital or ICU, but no improvement in survival to discharge (LOE 1[246]; LOE 2[248,250]; LOE 3[251]; LOE 4[247,720–723]). Three studies showed good neurological function in those who survived after successful fibrinolysis during CPR (LOE 2[719]; LOE 3[722]; LOE 4[721]).

Treatment Recommendation

Fibrinolytic therapy may be considered when pulmonary embolism is suspected as the cause of the cardiac arrest. Routine use of fibrinolytics in undifferentiated cardiac arrest is addressed earlier in "Fibrinolytics."

Knowledge Gaps

The true incidence of pulmonary embolus as a cause of cardiac arrest is not well documented. Surveillance studies of cardiac arrest noting contributing factors and pathological reports may help define the impact on public health of this cause of cardiac arrest.

Cardiac Arrest Caused by Electrolyte Disorders[ALS-SC-076A, ALS-SC-076B]

In adult cardiac arrest (out-of-hospital and in-hospital), does the treatment of electrolyte disturbances (eg, hypokalemia, hyperkalemia, hypomagnesemia, hypermagnesemia, hypocalcemia, or hypercalcemia), as opposed to standard care (according to treatment algorithm, but without treatment of electrolyte disturbances), improve outcome (eg, ROSC, survival)?

Consensus on Science

Magnesium. No studies were identified that addressed specifically the correction of low magnesium concentrations. The presence of a low plasma magnesium concentration was associated with poor prognosis in cardiac arrest patients in 3 studies (LOE 5).[724–726] The use of magnesium in cardiac arrest was supported by 5 case series (LOE 4)[727–731]; however, 5 RCTs (LOE 1)[219–222,732] and a systematic review (LOE 1)[733] found no benefit from the use of magnesium in cardiac arrest.

Calcium. No studies were identified that specifically addressed the treatment of cardiac arrest caused by hypocalcemia or hypercalcemia.

Potassium. There are no randomized trials on the treatment of potassium abnormalities in the setting of cardiac arrest. The management of hypokalemia and hyperkalemia in the setting of cardiac arrest is based on case reports and animal studies. One case series of 2 patients reported the resolution of torsades de pointes with potassium replacement in patients with hypokalemia (LOE 4).[734] Several clinical studies report an association between hypokalemia and the development of VF (LOE 5),[724,735–737] and an animal study reported that hypokalemia lowers the VF threshold (LOE 5).[738] In an animal model of cardiac arrest, it was reported that hyperkalemic animals had a higher rate of survival (LOE 5).[739]

Treatment Recommendation

There are insufficient data to support or refute the routine treatment of electrolyte abnormalities during cardiac arrest resuscitation.

Knowledge Gaps

Epidemiological studies are required to document the incidence of cardiac arrests secondary to electrolyte disturbance. Studies are needed to determine the safety and efficacy of current treatments and electrolyte replacement strategies during cardiac arrest.

Identifying Reversible Causes

Ultrasound During Cardiac Arrest[ALS-CPR&A-003B]

In adult cardiac arrest (out-of-hospital or in-hospital), does the use of ultrasound (including transthoracic and transesophageal echocardiography) during cardiac arrest, compared with standard CPR, improve any outcomes (eg, ROSC, survival)?

Consensus on Science

No studies examined the impact of ultrasound or echocardiography on patient outcomes in cardiac arrest specifically. Three studies examined the prognostic value of the presence or absence of sonographic cardiac motion in cardiac arrest (LOE 4).[184,740,741] One retrospective chart review (LOE 4)[742] and 1 prospective comparison (LOE 4)[743] documented the diagnostic accuracy of transesophageal ultrasound in detecting the cause of circulatory collapse. One study documented the frequency of pulmonary embolism in PEA arrest as detected with transesophageal ultrasound (LOE 4).[744] An additional 2 prospective observational studies examined the use of transthoracic ultrasound by "nonexpert" sonographers to detect pericardial effusion and other causes of PEA (LOE 4[745]; LOE 5[746]).

Three prospective studies examined ultrasound determination of cardiac standstill as a predictor of clinical outcomes and ROSC in patients in cardiac arrest (LOE 4).[184,740,741] Absence of cardiac motion on sonography

during resuscitation of patients in cardiac arrest was highly predictive of death: of the 341 patients from the 3 studies, 218 had no detectable cardiac activity and only 2 of those had ROSC (no data on survival to hospital discharge).

Treatment Recommendation
There is insufficient evidence to support or refute the routine use of ultrasound or echocardiography to guide cardiac arrest resuscitation.

Knowledge Gaps
Future research should address the role ultrasound (both transesophageal and transtracheal) can perform as a targeted intervention (detection of potential causes, guidance of key procedures) during cardiac arrest resuscitation. With increasing emphasis on uninterrupted chest compressions, there is the potential for harm with the use of transthoracic ultrasound because it often requires interruption of compressions and ventilation to acquire adequate images. This is less of a concern with transesophageal or intracardiac echocardiography.

Postresuscitation Care

Postresuscitation Treatment Protocol[ALS-PA-047A, ALS-PA-047B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of comprehensive treatment protocol, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science
There are no RCTs addressing the use of comprehensive treatment protocols after sustained ROSC. Before-and-after studies report increase in survival of comatose patients with sustained ROSC after out-of-hospital cardiac arrest with implementation of a comprehensive treatment protocol (LOE 2[747]; LOE 3[748,749]). Protocols included multiple elements such as hypothermia, glucose control, goal-directed hemodynamic optimization, ventilation, and PCI. The independent effect of each element of the bundle of care could not be established.

Treatment Recommendation
A comprehensive treatment protocol that includes multiple interventions provided in a structured way may improve survival after cardiac arrest.

Knowledge Gaps
Studies are needed to determine whether a comprehensive treatment protocol after cardiac arrest with a sustained ROSC improves short- and long-term outcomes. Future studies should define what interventions other than hypothermia are important inclusions in an effective comprehensive treatment protocol.

Treatment of Precipitating Causes of Cardiac Arrest

Pulmonary Embolism[ALS-PA-046A, ALS-PA-046B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital) diagnosed as pulmonary embolism, does the use of early fibrinolytic therapy with or without thrombectomy, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science
Despite good theoretical reasons why fibrinolysis following cardiac arrest in patients with suspected pulmonary embolism might be beneficial, there is no direct evidence to that effect. Several studies (LOE 5)[251,750] and[247,248,751] and a case series (LOE 4)[752] showed no significant increase in survival to hospital discharge. There was an increase in bleeding complications following fibrinolysis in most of those studies. One study suggested that the risk of major hemorrhage was further increased in patients who have undergone CPR (LOE 5).[247]

Five retrospective reviews demonstrated that pulmonary embolectomy following cardiac arrest had a high mortality rate (LOE 4).[753–757] One case series reported outcomes of 7 patients who had a cardiac arrest caused by pulmonary embolism and who were treated with percutaneous mechanical thrombectomy (LOE 4)[720]; 3 patients also received recombinant tissue plasminogen activator. Only 1 of the 7 patients died and pulmonary perfusion was restored in the majority (85.7%).

Treatment Recommendation
In patients with diagnosed or suspected pulmonary embolism after ROSC following cardiac arrest, there is inadequate evidence to recommend for or against the use of fibrinolytic therapy in addition to heparin. Because the mortality with surgical embolectomy for suspected or diagnosed pulmonary embolism is high if it follows cardiac arrest, it should be avoided in patients who have received CPR. There are few data on percutaneous mechanical thromboembolectomy, but it may be beneficial and may be considered in patients sustaining cardiac arrest from a pulmonary embolism who are not candidates for fibrinolytic therapy.

Knowledge Gaps
Clinical studies directly comparing fibrinolysis, standard therapy, and percutaneous mechanical thromboembolectomy in patients with ROSC following cardiac arrest from confirmed or suspected pulmonary embolism are needed to further advance our knowledge on safety and efficacy.

Ventilation[ALS-PA-053B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of a specific ventilation strategy (including specific CO_2 goal), as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

There were limited studies that addressed alternative ventilation strategies after cardiac arrest. A human study (LOE 2)[758] and studies in animals (LOE 5)[759–762] indicated that hyperventilation reduced cerebral blood flow after cardiac arrest. This cerebral blood flow response to hyperventilation and to hypoventilation may be absent after prolonged cerebral ischemia (LOE 5).[763,764] Avoiding hyperventilation, as part of a bundle of care, improved long-term outcome in humans (LOE 3)[749] and in dogs (LOE 5),[765] but the independent effect of ventilation could not be determined. A single animal study suggested that hyperventilation reduced degenerating neurons (LOE 5).[766,767]

Use of tidal volumes ≤9 mL/kg in patients after cardiac arrest is associated with increased incidence of atelectasis (LOE 3).[768] Manipulation of tidal volume and PEEP are not associated independently with improved survival in cohorts, including cardiac arrest patients (LOE 2[769]; LOE 3[768]).

Treatment Recommendation

After restoration of circulation, routine hyperventilation leading to hypocapnia should be avoided in order to prevent additional cerebral ischemia.

Knowledge Gaps

It is unclear if the changes in cerebral blood flow caused by hypercapnia or hypocapnia are important because there are no studies that relate ventilation strategies to patient-oriented outcomes in patients with sustained ROSC after resuscitation from cardiac arrest.

Controlled Oxygenation[ALS-PA-061A, ALS-PA-061B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of a controlled oxygenation strategy (including specific oxygenation goal), as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

One neutral randomized prospective clinical trial compared ventilation with 30% oxygen or 100% oxygen for the first 60 minutes after ROSC (LOE 1).[770] Mean partial pressure of oxygen in arterial blood (Pao_2) at 60 minutes after ROSC was 14.6±3.3 kPa (110±25 mm Hg) in the 30% oxygen group and 46.5±23.2 (343±174 mm Hg) in the 100% oxygen group. No statistical difference was detected in serum biomarkers of acute brain injury, survival to hospital discharge, or the percent of patients with good neurological outcome (cerebral performance category of 1 or 2) at hospital discharge. However, this study was not adequately powered to detect important differences in survival and cerebral performance category at hospital discharge (n=14 per group). A significant subset of patients in this study (30%) who were ventilated with 30% oxygen after ROSC required increased Fio_2 to maintain a pulse oximetry reading of >95%. The study was underpowered to determine efficacy or harm.

One supportive animal cardiac arrest study demonstrated that ventilation with 100% oxygen (generating Pao_2 > 450 mm Hg) during the first 15 to 60 minutes after ROSC caused neurodegeneration and worse-function neurological outcome when compared with Fio_2 titrated to an arterial pulse oximetry reading between 94% and 96% (LOE 5).[771]

Six supportive animal cardiac arrest studies demonstrated that ventilation with 100% oxygen (generating Pao_2 > 250 to 350 mm Hg) during the first 10 to 60 minutes after ROSC causes increased brain lipid peroxidation, increased metabolic dysfunction (glucose utilization and mitochondrial dysfunction), increased neurodegeneration, and worse-functional neurological outcome when compared to ventilation with room air (LOE 5).[153,154,772–775] These studies reported only short-term evaluation of outcomes (≤24 hours).

One animal study did not detect any difference in outcomes at 72 hours when animals were ventilated with 100% oxygen or room air during CPR and for the first hour after ROSC (LOE 5).[155] Another animal study failed to show any difference in outcome when comparing 2 levels of hypoxic Fio_2 (0.085 and 0.12) with normoxic resuscitation when given for the intra- and early (15 minutes) period after ROSC (LOE 5).[776] The study did not demonstrate a significant difference in neurological assessment scores at 72 hours or in survival. The study also failed to show a significant difference in the serum biomarkers of oxidant injury.

One supporting animal study reported that a Pao_2 of 250 to 350 mm Hg during the first 10 minutes of cardiopulmonary bypass reperfusion after cardiac arrest resulted in worse cardiac function compared to a Pao_2 40 to 90 mm Hg during the same time period (LOE 5).[777] A second animal study found no difference in myocardial function or injury when Pao_2 was gradually increased from 40 mm Hg to 110 mm Hg over the first 15 minutes of cardiopulmonary bypass reperfusion after cardiac arrest compared to initiating reperfusion at 90 to 110 mm Hg (LOE 5).[778]

Treatment Recommendations

There is insufficient clinical evidence to support or refute the use of inspired oxygen concentration titrated to arterial blood oxygen saturation in the early care of cardiac arrest patients following sustained ROSC.

Knowledge Gaps

Prospective randomized controlled clinical trials are needed to compare ventilation with 100% oxygen versus ventilation with inspired oxygen titrated to an arterial blood oxygen saturation goal (possibly 94% to 96%) for the first hour after sustained ROSC. Studies evaluating combined myocardial infarction and cardiac arrest are needed to evaluate the impact of post–cardiac arrest arterial hyperoxemia on cardiovascular outcomes.

Support of the Circulation

Fluid Therapy[ALS-PA-043A, ALS-PA-043C]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital) who have cardiovascular dysfunction, does the use of IV fluids, as opposed to standard care (or other IV fluids), improve outcome (eg, survival)?

Consensus on Science

There are no human studies that compare the use of IV fluids after sustained ROSC in patients with cardiac dysfunction compared with no IV fluids. One small human study used IV fluid (0.9% saline or lactated Ringer's) as part of early goal-directed therapy in post–cardiac arrest syndrome and found an improvement in survival that was not statistically significant (LOE 5).[748] In an additional before-and-after study (LOE 5), IV fluids (0.9% saline, lactated Ringer's, or colloids) were administered as part of a package of care (including PCI and therapeutic hypothermia) that improved survival with favorable neurological outcome in adult patients with sustained ROSC after cardiac arrest (prehospital or in-hospital).[749] The intervention period had a significantly increased positive fluid balance (345 mL versus 2300 mL). Six human studies showed that rapid infusion of fluids (500 mL to 3000 mL of 0.9% saline or lactated Ringer's) to induce therapeutic hypothermia after sustained ROSC produced little evidence of harm (LOE 5).[779–784] One human study showed that the deterioration in oxygenation that occurs after ROSC was not significantly affected by the infusion of cold 0.9% saline (3427 mL ±210 mL) (LOE 5).[785] Three animal studies reported neurological and cardiac protection with the administration of hypertonic fluid compared to normal saline (LOE 5).[786–788] One animal study showed an increase in cerebral blood flow with fluid for hemodilution combined with induced hypertension (LOE 5).[789]

Treatment Recommendation

There is insufficient evidence to support or refute the routine use of IV fluids following sustained ROSC after cardiac arrest. Rapid infusion of cold 0.9% saline or lactated Ringer's appears to be well tolerated when used to induce therapeutic hypothermia. Based on the pathophysiology of post–cardiac arrest syndrome, it is reasonable to use IV fluids as part of a package of post–cardiac arrest care.

Knowledge Gaps

Larger studies are needed to assess optimal fluid strategy for hemodynamic optimization in patients with sustained ROSC after adult cardiac arrest.

Hemodynamic Optimization[ALS-PA-056B]

In adult patients (out-of-hospital and in-hospital) with ROSC after cardiac arrest, does early hemodynamic optimization, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

There are no published RCTs addressing early hemodynamic optimization after cardiac arrest. Only 1 study suggested that the introduction of hemodynamic optimization (fluids, inotropic agents, intra-aortic balloon pump, and reperfusion) as part of a bundle of interventions improved outcome in comparison with historical controls (LOE 3).[749] The independent effect of early hemodynamic optimization was not assessed in this study. A recent study that included early hemodynamic optimization as part of a post–cardiac arrest treatment bundle was not powered to measure a survival benefit (LOE 3).[748]

Treatment Recommendation

Despite limited clinical data, the known pathophysiology of post–cardiac arrest syndrome provides a rationale for titrating hemodynamics to optimize organ perfusion.

Knowledge Gaps

Clinical research is needed to define the optimal targets for hemodynamic optimization and the best strategies to achieve these targets (fluids, vasopressors, inotropes, circulatory support, etc.).

Cardioactive Drugs[ALS-PA-057A]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital) who have cardiovascular dysfunction, does the use of any specific cardioactive drugs, as opposed to standard care (or different cardioactive drugs), improve outcome (eg, survival)?

Consensus on Science

There are no clinical trials that have determined or compared the independent effect of vasopressor and/or inotrope use in the post–cardiac arrest period on cardiovascular dysfunction and/or survival to discharge. Four clinical trials have suggested improved survival to discharge with vasopressor or inotropes, but have been confounded by multiple simultaneous treatments and/or they are underpowered for survival (LOE 3[748,749,790]; LOE 4[791]). Six experimental studies showed improvement in postresuscitation cardiac dysfunction (left ventricular function) with the administration of cardioactive drugs, such as dobutamine or levosimendan, but none have shown that such improvement in function translates into improved survival (LOE 5).[792–797]

Treatment Recommendation

There is insufficient evidence to support or refute the routine use of vasopressors and/or inotropes for improving survival in adult patients with cardiovascular dysfunction after resuscitation from cardiac arrest.

Knowledge Gaps

Specific clinical research is required to investigate whether treatment of post–cardiac arrest cardiovascular dysfunction with vasopressors and/or inotropes will yield incre-

mental beneficial impact on long-term outcomes beyond those achieved with therapeutic hypothermia alone.

Antiarrhythmic Drugs[ALS-PA-058A, ALS-PA-058B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of prophylactic antiarrhythmic drugs, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

No controlled studies addressed specifically and directly the use of amiodarone, lidocaine, or β-blockers early or immediately after resuscitation from cardiac arrest. One uncontrolled retrospective study did not demonstrate an improvement in 6-month survival when amiodarone or lidocaine was given to patients resuscitated from VF or tachycardia during early (first 72 hours) in-hospital postresuscitation care (LOE 4).[798] One single prospective nonrandomized study suggested that recurrent VF was reduced and long- and short-term survival were improved in patients treated with β-blockers during electrical storm (LOE 5).[369] One study reported an incidence of approximately 5% for VF or VT in hospitalized post–cardiac arrest patients (LOE 4).[799] Five RCTs documented consistent improvement in all-cause mortality and sudden death when implantable cardioverter defibrillators were inserted as late, secondary prophylaxis compared with amiodarone or β-blocker administration to patients that survived VF or VT cardiac arrest (LOE 5).[800–804]

Treatment Recommendation

There is no evidence to support or refute continued administration of amiodarone or lidocaine in post–cardiac arrest patients after ROSC.

Knowledge Gaps

The incidence of recurrent ventricular arrhythmias after hospital admission following survival of cardiac arrest and the effect of therapeutic hypothermia on their incidence during the early phase of the postresuscitation period should be further investigated. Studies that specifically address antiarrhythmic drugs during early post–cardiac arrest care are warranted. Furthermore, studies are needed to address the cohort of patients with VF or VT in the field and treated with amiodarone or lidocaine and whether or not and for how long this treatment should be continued after sustained ROSC.

Mechanical Circulatory Support[ALS-PA-060]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital) who have cardiovascular dysfunction, does the use of mechanical circulatory support, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

There are no studies directly addressing the use of mechanical circulatory support in patients with sustained ROSC but who have cardiovascular dysfunction. One human study showed that patients with severe cardiovascular dysfunction who were nonresponsive to standard care can be supported with mechanical chest compressions during PCI (LOE 4)[671]; however, none of these patients survived. One swine study showed worse left ventricular function when an intra-aortic balloon pump was compared with standard treatment including dobutamine in the immediate post–cardiac arrest phase (LOE 5).[796] Five studies of nonarrested patients in cardiogenic shock or severe heart failure showed that left ventricular assist device or continuous aortic flow augmentation improved hemodynamics but not survival (LOE 5).[805–809] Two case series reported the use of the intraaortic balloon pump in patients with severe myocardial dysfunction after sustained ROSC, but the effect was impossible to isolate from other interventions (LOE 4).[749,810]

Treatment Recommendation

There is insufficient evidence to support or refute the use of mechanical circulatory support in post–cardiac arrest patients who have cardiovascular dysfunction.

Knowledge Gaps

RCTs are needed to explore different techniques for mechanical support in patients with severe cardiovascular dysfunction after sustained ROSC.

Temperature Control

Prevention and Treatment of Hyperthermia[ALS-PA-049A]

In adult patients (out-of-hospital or in-hospital) who are comatose after cardiac arrest, does treatment of pyrexia, compared with no temperature intervention, improve outcome (eg, survival)?

Consensus on Science

There are no RCTs evaluating the effect of treatment of pyrexia (defined as ≥37.6°C) compared with no temperature control in patients after cardiac arrest. Eleven studies suggested that there was an association between pyrexia and poor outcomes (LOE 4[811–815]; LOE 5[816–821]). For comparison, patients with cerebrovascular events who developed pyrexia had worsened short- and long-term outcomes (LOE 5).[816–821]

Treatment Recommendation

Patients who develop hyperthermia after cardiac arrest have a worse prognosis. Despite the lack of evidence, it is reasonable to treat hyperthermia if it occurs in the postresuscitation period.

Knowledge Gaps

Clinical trials are needed to determine whether the management of pyrexia after cardiac arrest improves outcomes and what strategy of care produces effective control in this patient population.

Therapeutic Hypothermia[ALS-PA-044]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does therapeutic hypothermia, compared with usual care, improve morbidity or mortality?

Consensus on Science

Who to Cool? All studies of post–cardiac arrest therapeutic hypothermia have included only patients in coma. One trial defined coma as "not responding to verbal commands" (LOE 1).[822] The other trials defined coma similarly, used the Glasgow Coma Score (GCS) ≤8, or did not provide a clear definition.

One randomized trial (LOE 1)[822] and a pseudorandomized trial (LOE 2)[823] demonstrated improved neurological outcome at hospital discharge or at 6 months after hospital discharge in comatose patients after out-of-hospital VF cardiac arrest. Cooling was initiated within minutes to hours after ROSC, and a temperature range of 32 to 34°C was maintained for 12 to 24 hours. Two studies with historical control groups (LOE 3) showed improvement in neurological outcome after therapeutic hypothermia for comatose survivors of VF cardiac arrest.[824,825] One systematic review demonstrated that conventional cooling methods were more likely to reach a best cerebral performance category score of 1 or 2 (5-point scale where 1 is good and 5 is brain death) with a relative risk of 1.55 (99.5% CI 1.22 to 1.96) and more likely to survive to hospital discharge (relative risk of 1.35 95% CI 1.1 to 1.65) compared with standard postresuscitation care (LOE 1).[826]

One small (n=30) randomized trial showed reduced plasma lactate values and oxygen extraction ratios in a group (n=16) of comatose survivors after cardiac arrest with asystole or PEA who were cooled with a cooling cap (LOE 1).[827]

Six studies with historical control groups showed benefit using therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest after all-rhythm arrests (LOE 3).[749,828–832] One study with historical controls showed better neurological outcome after VF cardiac arrest but no difference after cardiac arrest from other rhythms (LOE 3).[833]

Two nonrandomized studies with concurrent controls indicated possible benefit of hypothermia following cardiac arrest from other initial rhythms in- and out-of-hospital (LOE 2).[834,835] One registry study, which included almost 1000 cooled comatose patients following cardiac arrest from all rhythms, showed that survival with good outcome at 6 months was 56% after initial VT/VF, 21% after initial asystole, and 23% after initial PEA (LOE 4).[836]

How to Cool? (See also Implementing Therapeutic Hypothermia in Section 12). Nineteen studies indicated that cooling could be initiated safely with IV ice-cold fluids (30 mL/kg of saline 0.9% or Ringer's lactate) (LOE 3[748,749,825,831,833,837]; LOE 4[779,780,782–785,810,836,838–843]). Six studies indicated that cooling with IV cold saline can be initiated in the prehospital phase (LOE 1[781,844]; LOE 2[845]; LOE 3[261,846]). Thirteen studies documented the use of an intravascular heat exchanger to induce and maintain hypothermia (LOE 2[834,835]; LOE 3[748,749]; LOE 4[782,839,841,847–852]). Twelve studies documented the use of ice packs and either water- or air-circulating blankets to induce and maintain hypothermia (LOE 2[834]; LOE 3[749,825,829,832,833]; LOE 4[748,841,850,853–855]). Seven studies documented the use of ice packs (sometimes combined with wet towels) alone to induce and maintain hypothermia (LOE 2[823]; LOE 3[824,828,830]; LOE 4[847,849,856]). Four studies documented the use of ice packs alone to maintain hypothermia (LOE 3[837]; LOE 4[810,840,843]). Seven studies documented the use of cooling blankets or pads alone to induce and maintain hypothermia (LOE 2[857]; LOE 3[858]; LOE 4[841,859–862]). Eight studies documented the use of water-circulating, gel-coated pads to induce and maintain, or just maintain, hypothermia (LOE 3[749,831]; LOE 4[838,841,842,854,860,863]). One RCT (LOE 1) used a cold-air tent[822] and another used a cooling helmet[827] to induce and maintain hypothermia. In 1 registry study, cooling was maintained with ice packs (17%), air cooling (8%), circulating water blankets (63%), an intravascular cooling device (16%), and other methods (8%) (LOE 4).[836]

When to Cool? One registry-based case series of 986 comatose post–cardiac arrest patients suggested that time to initiation of cooling (median 90 minutes; interquartile range [IQR] 60 to 165 minutes) was not associated with improved neurological outcome postdischarge (LOE 4).[836] A case series of 49 consecutive comatose post–cardiac arrest patients who were intravascularly cooled after out-of-hospital cardiac arrest also documented that time to target temperature (median 6.8 hours; [IQR 4.5 to 9.2 hours]) was not an independent predictor of neurological outcome (LOE 4).[852]

Safe with Percutaneous Coronary Intervention? Five studies indicated that the combination of therapeutic hypothermia and PCI is feasible and safe after cardiac arrest caused by acute myocardial infarction (LOE 3[749,837,864]; LOE 4[810,836]).

Treatment Recommendation

Comatose adult patients (not responding in a meaningful way to verbal commands) with spontaneous circulation after out-of-hospital VF cardiac arrest should be cooled to 32 to 34°C for 12 to 24 hours. Induced hypothermia might also benefit comatose adult patients with spontaneous circulation after out-of-hospital cardiac arrest from a nonshockable rhythm, or cardiac arrest in hospital. Rapid infusion of ice-cold IV fluid 30 mL/kg or ice packs are feasible, safe, and simple methods for initially lowering core temperature up to 1.5oC. When IV fluids are used to induce hypothermia, additional cooling strategies will be required to maintain hypothermia. Limited available evidence suggests that PCI during therapeutic hypothermia is feasible and safe and may be associated with improved outcome.

Knowledge Gaps

Although the data support cooling to 32°C to 34°C, the optimal temperature has not been determined. Furthermore the optimal method, onset, duration and rewarming rate, and therapeutic window remain unknown. Further investigation is also needed to determine the benefit of post–cardiac arrest therapeutic hypothermia after nonshockable cardiac arrest, in-hospital cardiac arrest, and in children. Epidemiological and safety data would help describe the safety and adversity

when cooling is interrupted across the system of care. Clinical and cost comparisons are required of the methods used for inducing and maintaining therapeutic hypothermia in- and out-of-hospital. The safety and efficacy of therapeutic hypothermia during cardiac arrest resuscitation needs to be explored through controlled clinical trials.

Seizure Control[ALS-PA-050A, ALS-PA-050B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of seizure prophylaxis or effective seizure control, as opposed to standard care (no prophylaxis or ineffective seizure control), improve outcome (eg, survival)?

Consensus on Science

No controlled clinical trials directly addressed prophylactic treatment for seizures after cardiac arrest. Five studies documented a 3% to 44% incidence of seizures after sustained ROSC (LOE 4).[749,814,865–867] Two studies reported no difference in neurological outcome after use of single-dose diazepam or magnesium or both; or thiopental given after sustained ROSC (LOE 5).[732,865] There are no studies addressing prompt and aggressive treatment after the first seizure occurring after circulation was restored. Seizures in the postarrest period may be refractory to multiple medications (LOE 4).[866,868] There was no reported difference in the occurrence of seizures after sustained ROSC in patients treated with therapeutic hypothermia or with normothermia care (LOE 5).[749,822]

Treatment Recommendation

There are insufficient data to support or refute the use of specific antiseizure medication in the prevention or treatment of seizures after ROSC.

Knowledge Gaps

Studies need to determine the true incidence of clinical and electrographic seizures in patients after cardiac arrest, particularly in those treated with therapeutic hypothermia.

Clinical trials are required to assess interventions and drugs for the prevention and treatment of seizures. Studies should evaluate whether continuous electroencephalograph (EEG) monitoring to diagnose and treat seizures after cardiac arrest is feasible, interpretable, of prognostic value, and beneficial for patients.

Other Supportive Therapies

Blood Glucose Control[ALS-PA-045A, ALS-PA-045B]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of a specific strategy to manage blood glucose (eg, target range), as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

One human randomized interventional study that prospectively evaluated strict glucose control (72 to 108 mg/dL, 4 to 6 mmol/L]) compared with moderate glucose control (108 to 144 mg/dL, 6 to 8 mmol/L) in patients resuscitated from prehospital cardiac arrest with VF found no survival benefit with strict glucose control (LOE 1).[869] Five retrospective studies in post–cardiac arrest patients suggested an association of higher glucose levels with increased mortality and worse neurological outcomes, but those findings may be related to other factors (LOE 4).[798,814,870–872] Based on those studies, the suggested target ranges for glucose values have been variable. A good randomized trial of intensive glucose control versus conventional glucose control in the largest number of ICU patients to date reported increased mortality in patients treated with intensive glucose control (LOE 5).[873] Two meta-analyses of studies of tight glucose control versus conventional glucose control in critically ill patients showed no significant difference in mortality but found tight glucose control was associated with a significantly increased risk of hypoglycemia (LOE 5).[874,875]

Treatment Recommendation

Strategies to treat hyperglycemia >180 mg/dL (>10 mmol/L) should be considered in adult patients with sustained ROSC after cardiac arrest. Hypoglycemia should be avoided.

Knowledge Gaps

Adequately powered intervention trials of moderate ranges of glucose control in patients who survive cardiac arrest are required.

Steroid Therapy[ALS-PA-048A]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does treatment with corticosteroids, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

Two observational studies (LOE 2)[876,877] and 2 animal studies (LOE 5)[878,879] failed to demonstrate any benefit or harm from the use of steroids after successful resuscitation from cardiac arrest. One small, single-center randomized placebo-controlled trial showed benefit from the use of a package of care consisting of vasopressin and dexamethasone in addition to epinephrine during resuscitation, combined with the treatment of post–cardiac arrest shock with hydrocortisone in the study group (LOE 1).[231] The complex design of this study makes it impossible to determine the independent effect of any interventions on outcome.

Treatment Recommendation

There is insufficient evidence to support or refute the use of corticosteroids for patients with ROSC following cardiac arrest.

Knowledge Gaps

It is important to determine the incidence of adrenal insufficiency after sustained ROSC following cardiac arrest. Clinical trials are needed to determine the effect of exogenous steroids administered after cardiac arrest.

Hemofiltration[ALS-PA-054A]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital) , does the use of hemofiltration as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

One RCT demonstrated no difference in survival or neurological outcome between groups treated with high-volume hemofiltration (200 mL/kg/h for 8 hours) with or without mild hypothermia, and control group without hemofiltration (LOE 1).[880] The combined hemofiltration-only and hemofiltration-plus-hypothermia groups had increased survival at 6 months after cardiac arrest when compared to controls. One study suggested improved survival and neurological outcome in patients treated with high-volume hemofiltration after resuscitation from cardiac arrest (LOE 2).[881]

Treatment Recommendation

There is insufficient evidence to support or refute the use of hemofiltration in patients with sustained ROSC after cardiac arrest.

Knowledge Gaps

Randomized clinical trials are needed comparing hemofiltration to a control group that has similar management of temperature and other confounding protocols of care. It is unknown whether hemofiltration will have different effects in different subgroups of patients.

Neuroprotective Therapy[ALS-PA-055A, ALS-PA-055C]

In adult patients with ROSC after cardiac arrest (out-of-hospital or in-hospital), does the use of neuroprotective drugs, as opposed to standard care, improve outcome (eg, survival)?

Consensus on Science

One small pilot study in witnessed, out-of-hospital cardiac arrests of presumed cardiac etiology showed improved survival at 3 months when therapeutic hypothermia (35°C) and the oral administration of coenzyme Q10 (250 mg followed by 150 mg TID for 5 days) was compared with therapeutic hypothermia alone; however, there was no difference in neurologically intact survival (LOE 1).[859]

Four RCTs (LOE 1) using nimodipine,[882,883] lidoflazine,[884] or diazepam[732] in out-of-hospital cardiac arrest showed no benefits from any of the drugs when compared with standard care. Two RCTs (LOE 1) using thiopental[884] or nimodipine[885] in out-of-hospital cardiac arrest were unable to show any benefits when compared with standard care. A retrospective analysis using glucocorticoids in out-of-hospital cardiac arrest was unable to show any benefits when compared with standard care (LOE 2).[877]

Treatment Recommendation

The value of routine use of coenzyme Q10 in patients treated with hypothermia is not certain. There are insufficient data to recommend for or against the use of neuroprotective drugs (thiopental, glucocorticoids, nimodipine, lidoflazine, or diazepam) alone or as an adjunct to therapeutic hypothermia in comatose cardiac arrest after ROSC.

Knowledge Gaps

Prospective, double-blind RCTs of promising neuroprotective agents alone, in combination, or in combination with therapeutic hypothermia are encouraged.

Specific research and larger clinical trials are required on the use of coenzyme Q10 in patients with therapeutic hypothermia of 33°C on neurologically intact survival.

Prognostication

Prognostication During Cardiac Arrest

End-Tidal CO_2 and Prediction of Outcome[ALS-D&P-014A]

In adult cardiac arrest (out-of-hospital or in-hospital), does the use of end-tidal CO_2 (eg, absolute CO_2 values or changes in waveform), compared with not using end-tidal CO_2, accurately predict outcomes (eg, ROSC, survival)?

Consensus on Science

Thirteen studies (LOE P2[176–178,182,183,886,887]; LOE P3[888] (LOE P5[140,180,889–891]) indicated that higher maximal end-tidal CO_2 levels can predict ROSC. Seven studies demonstrate that end-tidal CO_2 values <10 mm Hg (1.33 kPa) obtained after intubation and during CPR efforts are associated with a low probability of survival from cardiac arrest (LOE P2).[176–178,182,183,886,887] Two prospective human studies demonstrated a significant increase in end-tidal CO_2 when ROSC occurs (LOE 5).[140,180]

Treatment Recommendation

Quantitative measurement of end tidal CO_2 may be a safe and effective noninvasive indicator of cardiac output during CPR and may be an early indicator of ROSC in intubated patients. Although low values of end tidal CO_2 are associated with a low probability of survival, there are insufficient data to support or refute a specific cutoff of end tidal CO_2 at different time intervals as a prognostic indicator of outcome during adult cardiac arrest.

Knowledge Gaps

More well-designed prognostic studies of end tidal CO_2 monitoring designed to measure long-term morbidity, mortality, and neurological survivability are recommended.

In future studies the cause of cardiac arrest should be documented. Use of vasopressors and ventilation rates may lower end-tidal CO_2; and this effect should be controlled in future studies. Evaluation of end-tidal CO_2 for prognosis should be repeated with supraglottic airway devices.

Prognostication After Resuscitation

Clinical Examination[ALS-PA-041]

In adult and pediatric patients who are comatose after cardiac arrest (out-of-hospital or in-hospital), does the use

of the bedside neurological examination, as opposed to standard care, allow accurate prediction of outcome (eg, survival)?

Consensus on Science

In adult patients comatose after cardiac arrest who had not been treated with therapeutic hypothermia, the following parameters predicted poor outcome (CPC 3 or 4, or death) with a false-positive rate (FPR) of 0%: absent vestibulo-ocular reflexes at ≥24 hours [(95% CI 0% to 14%)] (LOE P1)[892,893]; absence of pupillary light *and* corneal reflex at 72 hours [(95% CI 0% to 9%)](LOE P1)[894]; GCS <5 at 48 hours (95% CI 0% to 13%) (LOE P1)[895] and on day 3 (95% CI 0% to 6%) (LOE P2)[896] and a clinical examination score <15 on day 4 [(95% CI 0% to 18%)(LOE P1).[897] However, in 1 study an absent motor response (GCS motor=1) at 72 hours after cardiac arrest predicted poor outcome with a FPR of 5% [(95%CI 2% to 9%]](LOE P1).[894] The presence of myoclonus status in adults was strongly associated with poor outcome (LOE P1[866,894]; LOE P3[868,898]; LOE P4[899]), but rare cases of good neurological recovery have been described and accurate diagnosis was problematic.[900–904]

Treatment Recommendation

There are no clinical neurologic signs that reliably predict poor outcome <24 hours after cardiac arrest. In adult patients who are comatose after cardiac arrest, have *not been treated with hypothermia* and have no confounding factors (eg, hypotension, sedatives or neuromuscular blockers), the absence of both pupillary light and corneal reflex at ≥72 hours reliably predicts poor outcome. Absence of vestibulo-ocular reflexes at ≥24 hours and a GCS motor score of 2 or less at ≥72 hours are less reliable. Other clinical signs, including myoclonus, are not recommended for predicting poor outcome.

Knowledge Gaps

The reevaluation of prognostic indicators during therapeutic hypothermia and in the presence of other confounders needs to be completed to guide current post–cardiac arrest care.

Biochemical Markers[ALS-PA-052A, ALS-PA-052B]

In adult patients who are comatose after cardiac arrest (out-of-hospital or in-hospital), does the use of biochemical markers, as opposed to standard care, allow accurate prediction of outcome (eg, survival)?

Consensus on Science

Serum neuronal-specific enolase (NSE) elevations are associated with poor outcome for comatose patients after cardiac arrest (LOE P1[905,906]; LOE P2[852,894,897,907–920]; LOE P3[921,922]). Although specific cutoff values with a FPR of 0% have been reported, clinical application is limited due to variability in the 0% FPR cutoff values reported among various studies.

Serum S100 elevations are associated with poor outcome for comatose patients after cardiac arrest (LOE P1[905,906]; LOE P2[894,897,907,913,915,917,918,923–928]; LOE P3[921]).

Many other serum markers measured after sustained ROSC have been associated with poor outcome after cardiac arrest, including brain natriuretic peptide (BNP) (LOE P3)[929]vWF (LOE P3)[930] ICAM-1 (LOE P3)[930]; procalcitonin (LOE P2) [924]IL-1ra, RANTES, sTNFRII, IL-6, IL-8 and IL-10 (LOE P3).[931] However, other studies found no relationship between outcome and serum IL-8 (LOE P1),[923] and procalcitonin and sTREM-1 (LOE P3).[932]

Worse outcomes for comatose survivors of cardiac arrest are also associated with increased levels of cerebrospinal fluid (CSF)-CK (LOE P2)[933,934] and cerebrospinal fluid-CKBB (LOE P1[905,906]; LOE P2[908,919,934,935]; LOE P3[936–938]). However, 1 study found no relationship between cerebrospinal fluid-CKBB and prognosis (LOE P2).[939]

Outcomes are also associated with increased cerebrospinal fluid levels of other markers including NSE (LOE P1[906]; LOE P2[915,919]); S100 (LOE P2)[915]LDH, GOT(LOE P2)[908,934]; neurofilament (LOE P3) [940]; and acid phosphatase and lactate (LOE P2).[934] Cerebrospinal fluid levels of β-d-N-acetylglucosaminidase and pyruvate were not associated with the prognosis of cardiac arrest (LOE P2).[934]

Treatment Recommendation

Evidence does not support the use of serum or cerebrosphinal fluid biomarkers alone as predictors of poor outcomes in comatose patients after cardiac arrest with or without treatment with therapeutic hypothermia. Limitations included small numbers of patients and/or inconsistency in cutoff values for predicting poor outcome.

Knowledge Gaps

Future studies should identify and resolve the heterogeneity of cutoff values used to predict poor outcome with a FPR of zero. Studies also must account for confounders that may alter levels or predictive performance of various markers (eg, hypothermia, underlying disease, pregnancy, intra-aortic balloon pump, brain instrumentation, hemodialyisis, or other organ failure). Studies examining whether biomarkers can be used to monitor ongoing injury and response to therapy may be useful.

Electrophysiological Studies[ALS-PA-051A]

In adult patients who are comatose after cardiac arrest (out-of-hospital or in-hospital), does the use of neurological electrophysiological studies, as opposed to standard care, allow accurate prediction of outcome (eg, survival)?

Consensus on Science

Somatosensory evoked potentials measured between 4 hours and 2 weeks after cardiac arrest were associated with poor outcome in 14 studies (LOE P1[893,894,905,941–946]; LOE P2[897]; LOE P3[936,947–949]). In a meta-analysis of patients not treated with therapeutic hypothermia, the absence of cortical N20 response to median nerve stimulation at 24 to 72 hours after

cardiac arrest predicted poor outcome (CPC 3 or 4, or death) with a FPR of 0.7% (95% CI 0.1 to 3.7) (LOE P1).[905]

Abnormal Brain Stem Auditory Evoked Potentials. Abnormal brain stem auditory evoked potentials recorded 1 to 56 days after cardiac arrest in patients not treated with hypothermia predicted poor outcome with a FPR of 0% (95% CI 0 to 14) in 1 LOE P1-study.[942] Abnormal brainstem auditory evoked potentials recorded 55 to 235 minutes after cardiac arrest before initiation of therapeutic hypothermia predicted poor outcome with a FPR of 0% (95% CI 0 to 32) (LOE P1).[950] One study found no predictive value with brainstem auditory evoked potentials (LOE P1).[946] In patients not treated with therapeutic hypothermia, medium-latency auditory evoked potentials predicted poor outcome after cardiac arrest in 1 LOE P1-study with a FPR of 0% (95% C I0 to14)[942] and in 1 LOE P3-study.[948] Auditory N100 and mismatch negativity was also associated with poor outcome in 1 LOE P1-study.[942]

Electroencephalography predicted poor outcome in comatose survivors of cardiac arrest within 1 week after cardiac arrest in 12 studies (LOE P1[893,894,905,941,951–953]; LOE P3[954,955]; LOE P4[956,957]; LOE P5[958]). In a meta-analysis, EEG showing generalized suppression to less than 20μV, burst-suppression pattern associated with generalized epileptic activity, or diffuse periodic complexes on a flat background 12 to 72 hours after sustained ROSC predicted a poor outcome (FPR of 3%, 95% CI 0.9% to 11%) in patients not receiving therapeutic hypothermia (LOE P1).[905]

Treatment Recommendation

No electrophysiological study reliably predicts outcome of comatose patient after cardiac arrest in the first 24 hours treated without therapeutic hypothermia. After 24 hours, bilateral absence of the N20 cortical response to median nerve stimulation predicts poor outcome in comatose cardiac arrest survivors not treated with therapeutic hypothermia. In the absence of confounding circumstances, such as sedatives, hypotension, hypothermia, or hypoxemia, it is reasonable to use unprocessed electroencephalography interpretation (specifically identifying generalized suppression to less than 20 μV, burst suppression pattern with generalized epileptic activity, or diffuse periodic complexes on a flat background) observed between 24 and 72 hours after sustained ROSC to assist the prediction of a poor outcome in comatose survivors of cardiac arrest not treated with hypothermia.

Knowledge Gaps

More data are needed about the performance and timing of somatosensory evoked potentials and electroencephalography criteria for aiding prognostication in patients treated with induced hypothermia.

Imaging Studies[ALS-PA-059]

In adult patients who are comatose after cardiac arrest (out-of-hospital or in-hospital), does the use of imaging studies, as opposed to standard care, allow accurate prediction of outcome (eg, survival)?

Consensus on Science

Magnetic Resonance Imaging. There are no LOE P1- or LOE P2-studies that support the use of magnetic resonance imaging (MRI) to predict outcome of comatose cardiac arrest survivors. Use of MRI to predict outcome is supported by 32 studies (LOE P3[959–963]; LOE P4[964–976]; LOE P5[977–990]). The timing of MRI in these studies ranged from 1 day to 10 months after sustained ROSC. MRI parameters associated with poor outcome included lower gray matter volume, lower hippocampal volume, global cerebral atrophy, higher number of neuroradiologic findings, extensive abnormalities on digital weight imaging, increased lactate on magnetic resonance spectroscopy, hyperintense lesions in basal ganglia, extensive digital weight imaging abnormalities, global apparent diffusion coefficient depression, extensive white matter abnormalities, and cortical laminar enhancement. Overall these studies were limited by small sample sizes, variable time of imaging (many very late in the course of the event), lack of comparison with a standardized method of prognostication, often nonmodern MRI techniques, and early withdrawal of care. One study found that MRI performed on comatose cardiac arrest survivors 1 to 47 days after sustained ROSC did not correlate with outcome (LOE P2).[991] MRI parameters used in this study were leukoaraiosis, cerebral infarcts, and edema. Modern MRI techniques (ie, diffusion-weighted imaging) were not used in this study.

Computed Tomography. There are no LOE P1- or LOE P2-studies that support the use of computed tomography (CT) imaging to predict outcome of comatose cardiac arrest survivors. Use of CT imaging is supported by 22 studies (LOE P3[992]; LOE P4[969, 984, 993-1001]; LOE P5[980, 981, 985, 1002–1006]). The timing of CT in those studies ranged from 1 hour to 20 days after sustained ROSC. CT parameters associated with poor outcome included gray matter to white matter Hounsfield unit ratio $<$1.22, cerebral atrophy (chronic), low cerebral blood flow, low acetazolamide reactivity, bicaudate ratio, low Hounsfield number in putamen and cortex, low density in basal ganglia and thalamus, diffuse mass effect, and global cortical gray matter density. Overall those studies were limited by small sample sizes, variable time of imaging (many very late in the course of the event), lack of comparison with a standardized method of prognostication, and early withdrawal of care. Two LOE P3-studies found that CT did not predict outcome,[954, 1007] and 1 LOE P4-study was neutral in its findings [1008]. The timing of CT in those studies ranged from $<$72 hours to 96 hours after ROSC. CT parameters not associated with poor outcome included normal scans. Overall these studies were limited by small sample sizes, imaging performed too early in the clinical course, nonmodern CT imaging, and early withdrawal of care.

Single photon emission CT (SPECT) is supported by 3 LOE P5-studies[990, 1006, 1009] and is opposed by 1 LOE P2-study.[1010] The timing of SPECT in these studies ranged from 1 to 23 days after sustained ROSC. SPECT parameters associated with poor outcome included diminished cerebral blood flow, particularly frontal and temporal, particularly when persistent on repeated imaging. SPECT parameters not associated with outcome included the anterior-posterior perfusion ratio. These studies were

limited by small sample sizes, variable imaging times, early withdrawal of care, and lack of comparison with a standardized method of prognostication.

Cerebral angiography has been reported by 1 case report (LOE P5).[980] The timing of cerebral angiography was 1 day after sustained ROSC. Cerebral angiography parameters associated with poor outcome included delayed cerebral circulation time.

Transcranial Doppler was evaluated in 1 study (LOE P4).[976] The timing of transcranial Doppler in this study ranged from 4 to 120 hours after ROSC. Transcranial Doppler parameters associated with poor outcome included delayed hyperemia. This study was limited by a small sample size, early withdrawal of care, and lack of comparison with a standardized method of prognostication.

Nuclear Medicine. One case report was supportive of nuclear medicine studies (LOE P5),[985] but the timing of the images after sustained ROSC was not described. Nuclear medicine parameters associated with poor outcome included abnormal tracer uptake in the cerebral cortices. This case report included only a limited description of the findings; it was further limited by lack of comparison with a standardized method of prognostication.

Near-Infrared Spectroscopy. One study of near-infrared spectroscopy was not supportive (LOE P3).[1011] The timing of near-infrared spectroscopy in this study ranged from 6 to 24 hours after sustained ROSC. This study was limited by a small sample size, early withdrawal of care, inclusion of non–cardiac arrest patients, and lack of comparison with a standardized method of prognostication.

Treatment Recommendation

There is insufficient evidence to recommend for or against the routine use of neuroimaging to predict outcome of adult cardiac arrest survivors.

Knowledge Gaps

Adequately powered prospective studies are required to evaluate the accuracy of CT, MRI, or both in prognosticating outcome of comatose cardiac arrest survivors. Prognostication studies should include calculation of FPR with 95% confidence intervals for predicting poor outcome. Outcome prediction should include a comparison with more conventional methods, including clinical examination and electrophysiology (eg, somotosensory evoked potentials). All studies should allow for sufficient time to realize patient recovery, avoiding the bias of self-fulfilling prophecy and premature withdrawal of care. Specific brain structures responsible for coma and recovery after cardiac arrest (eg, thalamus, rostral brainstem) should be a focus of future studies. The optimal timing of neuroimaging after cardiac arrest and the impact of hypothermia should be explored. Prognostic modalities have focused on predicting poor outcome, and the need to identify those with likely good outcome is becoming more important, especially because effective therapies exist. Neuroimaging should be performed in a safe setting for critical patients or be done at the bedside.

Impact of Therapeutic Hypothermia on Accuracy of Post–Cardiac Arrest Prognostication[ALS-PA-040A]

In post–cardiac arrest patients treated with hypothermia, can the same prognostication tools that are used in normothermic patients reliably predict outcome?

Consensus on Science

Two studies (LOE P1)[898,946] provided evidence that status myoclonus (FPR 0%, 95% CI 0% to 40%), absence of corneal and pupillary reflexes at 3 days postsustained ROSC (FPR 0%, 95% CI 0% to 48%), and bilateral absence of N20 peak on somotosensory evoked potentials at 24 hours postsustained ROSC (FPR 0%, 95% CI 0% to 69%) in patients treated with therapeutic hypothermia predict poor outcome. One study evaluated somatosensory evoked potential responses in 112 postarrest patients more then 24 hours after cardiac arrest who were treated with hypothermia and found that 35 of 36 patients with bilateral absent N20 cortical response had a poor outcome (FPR 3%, 95% CI 0% to 14%).[1012] One patient with bilaterally absent N20 and another with a barely detectable N20 had a good recovery; both were evaluated at 3 days post–cardiac arrest (LOE P1).[1012] One LOE P1-study[898] provided evidence that a Glasgow Coma Motor Score of 2 or less at 3 days after sustained ROSC in patients treated with therapeutic hypothermia has a FPR of 14% (95% CI 3% to 44%) for poor outcome. Two studies provided evidence that status epilepticus in postarrest patients treated with hypothermia has a FPR of 7% (95% CI 1% to 25%) to 11.5% (95% CI 3% to 31%) for predicting poor outcome (LOE P2[1013]; LOE P3[955]). One study (LOE P3)[1014] suggested that glial fibrillary acidic protein level >1.0 ng/dL drawn 12 to 48 hours after sustained ROSC predicts poor outcome (defined as CPC score 3 to 5 at 6 months) both in post–cardiac arrest patients treated with normothermia (FPR 0% 95% CI 0% to 27%) or hypothermia (FPR 0% 95% CI 0% to 48%). One study provided evidence that NSE and S-100b protein cutoff values that reliably predict poor outcome are significantly higher in post–cardiac arrest patients treated with hypothermia compared with those not treated with hypothermia (LOE P2).[917] Two studies prospectively measured NSE in cohorts of patients treated with post–cardiac arrest hypothermia and reported cutoff values for 0% FPR (LOE P2)[1015,1016]: 1 study[1015] reported that all patients with a 48-hour NSE value >33 μg/L had a poor outcome (FPR 0%, 95% CI 0% to 23%); the other study[1016] reported that all patients with a 48-hour NSE >28 μg/L had a poor outcome (FPR 0%, 95% CI 0% to 18%). Variability in 0% FPR cutoff values from these derivation cohorts potentially results from variability among assays and performance sites. Two studies examined the utility of bispectral index monitoring in prognosticating poor outcome in post–cardiac arrest patients treated with hypothermia who were under neuromuscular blockade (LOE P1).[953,1017] One study reported that an initial bispectral index monitoring score of ≥22 predicted poor outcome with a FPR of 6% (19 patients having a positive test), and a suppression ratio ≥48 predicted poor outcome with a FPR of 7% [(95% CI 1% to 26%)].[1018] The other study reported that a bispectral index monitoring level of 0 at any time in the first 72 hours after cardiac arrest predicted poor

outcome with a FPR of 0% [0% to 27%].[953] Finally, 1 study (LOE P1)[1019] of 111 post–cardiac arrest patients treated with therapeutic hypothermia attempted to validate prognostic criteria proposed by the American Academy of Neurology.[905] That study demonstrated that clinical examination findings at 36 to 72 hours were unreliable predictors of poor neurological outcome [motor response less than flexion (FPR 16%, 95% CI 6% to 35%); ≥1 brainstem reflexes absent (FPR 8%, 95% CI 2% to 25%); early myoclonus (FPR 4%, 95% CI 1% to 19%), while bilaterally absent N20 peak on somatosensory evoked potentials (FPR 0%, 95% CI 0% to 13%) and unreactive electroencephalogram background (FPR 0%, 95% CI 0% to 13%) were the most reliable. A decision rule derived using that dataset demonstrated that the presence of 2 independent predictors of poor neurological outcome (incomplete recovery brainstem reflexes, early myoclonus, unreactive electroencephalogram, and bilaterally absent cortical somatosensory evoked potentials) predicted poor neurological outcome with a FPR of 0% (95% CI 0% to 14%).

Treatment Recommendation

There is inadequate evidence to recommend a specific approach to prognosticating poor outcome in post–cardiac arrest patients treated with therapeutic hypothermia. There are no clinical neurological signs, electrophysiological studies, biomarkers, or imaging modalities that can reliably predict neurological outcome in the first 24 hours after cardiac arrest. Beyond 24 hours, no single parameter for predicting poor neurological outcome in post–cardiac arrest patients treated with hypothermia is without reported false-positives. Based on limited available evidence, potentially reliable prognosticators of poor outcome in patients treated with therapeutic hypothermia after cardiac arrest include bilateral absence of N20 peak on somatosensory evoked potential ≥24 hours after cardiac arrest or unreactive electroencephalogram background at 36 to 72 hours; and the absence of both corneal and pupillary reflexes >72 hours after cardiac arrest. Limited available evidence also suggests that a Glasgow Coma Motor Score of 2 or less at 3 days after sustained ROSC and the presence of status epilepticus are potentially unreliable prognosticators of poor outcome in post–cardiac arrest patients treated with therapeutic hypothermia. Serum biomarkers such as NSE are potentially valuable as adjunctive studies in prognostication of poor outcome in patients treated with hypothermia, but their reliability is limited by the relatively few patients who have been studied and lack of assay standardization. Given the limited available evidence, decisions to limit care should not be made based on the results of a single prognostication tool.

Knowledge Gaps

Further research is needed to elucidate the impact of therapeutic hypothermia on the accuracy and timing of post–cardiac arrest prognostication tools. Prospective derivation and validation of a clinical decision rule for early prediction of poor outcome in post–cardiac arrest patients treated with or without hypothermia are urgently needed.

Organ Donation[ALS-PA-042A, ALS-PA-042B]

In adult organ recipients, does the use of organs from donors brain dead after cardiac arrest (out-of-hospital or in-hospital), as opposed to the use of donors brain dead not due to cardiac arrest, improve outcome (eg, transplant success)?

Consensus on Science Statements

Three studies suggested no difference in functional outcomes of organs transplanted from patients who were determined to be brain dead as a consequence of cardiac arrest when compared with donors who were brain dead from other causes (LOE 2).[1020–1022]

Treatment Recommendation

Adult patients who progress to brain death after resuscitation from out-of-hospital cardiac arrest should be considered for organ donation.

Knowledge Gaps

Further studies with larger populations and common definitions of outcomes are needed. There is no evidence regarding organ donation from children or adults who are brain dead after resuscitation from an in-hospital cardiac arrest.

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Disclosures

CoSTR Part 8: Writing Group Disclosures

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Bernd W. Bottiger	Uniklinik Köln—MD, DEAA	None	None	None	None	None	None
Clifton W. Callaway	University of Pittsburgh School of Medicine—Associate Professor; *AHA—Work Sheet Editor for 2010 Guidelines. My effort on this project is paid to University of Pittsburgh as a "contracted services agreement," and not paid to me	†Grants to University of Pittsburgh: NHLBI—Resuscitation Outcomes Consortium HRSA—Development and Dissemination of Program Tools for Uncontrolled Donation After Cardiac Death (UDCD)	*Loan of an Arctic Sun cooling device (without disposables) to human physiology laboratory for experiments on hypothermia by Medivance, Inc.	None	†Co-inventor on patent about ventricular fibrillation waveform analysis, licensed by University of Pittsburgh to Medtronic ERS, Inc.	None	None
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Richard E. Kerber	University of Iowa Hospital—Professor of Medicine; Staff Physician	None	None	*Occasional (2–4 times/year) Grand Rounds speaker at other Universities. Usual honorarium is $1,000 for each talk plus expenses. Money to me. Occasional expert witness in legal proceedings; fee is $400/hour plus expenses. These do not involve cardiac drugs or devices. Money to me. I am presently serving on a DSMB for a clinical trial sponsored by Zoll Corp, which manufacture/sells defibrillators and resuscitation devices	*Stock owned in General Electric and Johnson and Johnson. GE makes echocardiographs, which are occasionally used as a diagnostic tool during resuscitation	*I performed a one-time consultation for Philips Defibrillator division earlier this year	*Occasional expert witness in legal cases, usually alleged malpractice. No cardiac drugs or devices at present; I consulted with a law firm defending a manufacturer of Phentermine about 10 years ago
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Eric Lavonas	Denver Health Hospital Authority: A political division of the State of Colorado, DHHA operates a hospital and outpatient clinic system in Denver, CO. DHHA also operates the Rocky Mountain Poison and Drug Center (RMPDC), Denver Public Health, and Denver Emergency Medical Services.—Associate Director, RMPDC	*list of all research grants (previous, current, and pending) germaine to the topics reviewed by ILCOR. All grants are awarded to the Denver Health Hospital Authority. Neither I nor any other DHHA employee derives personal financial benefit from these relationships. I don't get a bonus; My salary is supported by general institutional funds and an unrelated research endowment; my performance evaluation is not related to performance of any of these contracts. Sponsor: Protherics-BTG Project: Study report for the safety and efficacy of CroFab for severe envenomations Related Product: None. However, Protherics-BTG manufactures DigiFab, which is used to treat digoxin poisoning. My role: PI on one portion of the project, collaborator on the rest 2008–2009 (ongoing)	None	None	None	None	None

(*Continued*)

CoSTR Part 8: Writing Group Disclosures, *Continued*

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Robert W. Neumar	University of Pennsylvania—Associate Professor of Emergency Medicine	†Funding Source: NIH/NINDS Grant Number: R21 NS054654 Funding Period 06/01/07 to 06/31/2010 Role on Project: PI Title: Optimizing Therapeutic Hypothermia After Cardiac Arrest Description: The goal is to evaluate the how the onset and duration of therapeutic hypothermia after cardiac arrest impacts survival and neuroprotection	None	None	None	None	None
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Wanchun Tang	Weil Institute of Critical Care Medicine: Non profit research institution—Professor and President	†NIH	None	None	None	None	None
Terry L. Vanden Hoek	The University of Chicago—Associate Professor	*Vanden Hoek, Principal Investigator Department of Defense, Office of Naval Research "Proteomic Development of Molecular Vital Signs: Mapping a Mitochondrial Injury Severity Score to Triage and Guide Resuscitation of Hemorrhagic Shock" 9/6/04 to 4/31/10 $885,639 (this year) research grant awarded to University of Chicago	None	None	None	None	None

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

*Modest.

†Significant.

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Richard A. Bernstein	Northwestern University—Associate Professor	None	None	†Bristol Myers/Sanofi Partnership (Plavix) Boehringer Inelheim Pharmaceuticals (Aggrenox) *Medtronic (Loop recorder—I gave 2 lectures about syncope; a cardiologist who lectured with me discussed some monitoring device,	None	*BMS/Sanofi Partnership (Plavix) Medtronic-Steering Committee for CRYSTAL-AF study	†I have served as an expert witness/medicolegal consultant in cases related to cardiac arrest; none have gone to trial.
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CoSTR Part 8: Worksheet Collaborator Disclosures, *Continued*

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CoSTR Part 8: Worksheet Collaborator Disclosures, *Continued*

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Fulvio Kette	Azienda per I Servizi Sanitari n. 6 "Friuli Occidentale"—Dir Emergency department	None	None	None	None	None	None
Walter Kloeck	Academy of Advanced Life Support Basic and advanced life support training Medical Director	None	None	None	None	None	None
Peter J. Kudenchuk	University of Washington; Professor of Medicine	NIH Resuscitation Outcomes Consortium	None	*Sanofi Aventis *Bristol Myers Squibb *A variety of CME organizations with topics related to arrhythmias/atrial fibrillation	*Sanofi Aventis (modest stock holding)	None	*Expert Witness: Levin Riback Dewsnup, King, Olson Treon, Aquirre, Newman, Norris
Douglas Kupas	Geisinger Health System, Geisinger Clinic Employed as Associate Chief Academic Officer and emergency physician Associate Chief Academic Officer Commonwealth of Pennsylvania, Department of Health Serve as state EMS medical director for the Bureau of EMS Commonwealth EMS Medical Director	None	None	None	None	None	None
Giuseppe La Torre	Self employed	None	None	None	None	None	None
Todd Larabee	Univ Col, Denver School of Med. Assist Prof.	NIH cardiac synch technique for pulseless elect. Activity grant held by Quest PD	None	Sanofi Aventis *Bristol Myers Squibb	*Stock–Sanofi Aventis	None	Levin Riback Dewsnup, King, Olson Treon, Aquirre, newman, Norris
Marion Leary	Hospital of the University of Pennsylvania Center for Resuscitation Science. Nurse Researcher; Medical ICU Critical Care Nurse	†Philips Healthcare grant	†CPR feedback defibrilators were given to us by Philips Healthcare to record CPR quality metrics including $ETCO_2$ and ventilation	*Philips Healthcare in 2008 to speak at NTI	None	*Velomedex in 2008 one time minor consultant fee	None
John Litell	Mayo Clinic Critical Care Fellow	None	None	None	None	None	None
Charles Little	Univ of Colorado, Denver, Assoc Prof Emergency Medicine	None	None	None	None	None	None
David Lobel	Maimonides Med. Center, Emergency Dept attending; Med. Director Prehospital (EMS)	None	None	None	None	None	None
Timothy Mader	Baystate Health; nonprofit healthcare system, Emergency physician	None	None	None	None	None	None
James McCarthy	UTHDC Houston Assist. Prof.	None	None	Intercool 2007	None	None	Expert Brin and Brin
Michael McCrory	Johns Hopkins, Pediatric Intensive Care fellow	None	None	None	None	None	None

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CoSTR Part 8: Worksheet Collaborator Disclosures, *Continued*

Worksheet Collaborator	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
James Menegazzi	University of Pittsburgh Research Professor of Emergency Medicine	†Received significant research grant support from the National Heart, Lung, and Blood Institute	*Received modest research support from Zoll, Medtronic, and Jolife, all in the form of the loan of medical equipment for use in laboratory	None	†Co-inventor of a patented method for analyzing the electrocardiographic waveform during ventricular fibrillation. This method has been licensed by my University to Medtronic. I receive a significant payment from Medtronic, in the form of royalties, via this licensing agreement	None	*In 2009, and in 2010, I lectured at a medical conference in Anchorage, Alaska. While I did not receive an honorarium, my airfare, hotel, and per diem food costs were paid by the Loren Marshall Foundation.
William Meurer	University of Michigan, Assistant Professor Departments of Emergency Medicine and Neurology	None	None	None	None	None	None
Paul Middleton	Ambulance Service of NSW—Medical Director/ Director of Research	None	None	None	None	None	None
Allan Mottram	Univ of Wisc. Emergency Med Division; Assist Prof	NIH potential antidotal therapy for Ca Channel blocker OD	None	None	None	None	None
Eliano P. Navarese	Catholic University of Sacred Heart Cardiologist	None	None	None	None	None	None
Thomas Nguyen	Beth Israel medical center—Attending MD	None	None	None	None	None	None
Marcus Ong	Singapore General Hospital—Consultant	†Research grant from Zoll Medical Corporation for mechanical CPR trial	*Research support (in kind) from Medivance and Alsius for a hypothermia trial	*Honoraria for a lecture on Intraosseous Vascular Access from Vidacare Corp at the Asian Conference on Emergency Medicine 2009 Busan Korea	None	None	None
Andrew Padkin	Royal United Hosp. NHS Trust Bath UK;Healthcare Provider Consultant	None	None	None	None	None	Unpaid editorial board member *Resuscitation J*
Edison Paiva	University of Sao Paulo School of Medicine—Professor	None	None	None	None	None	None
Rod S. Passman	NW Univ Assoc. Prof.	None	None	†GSK *Medtronic	None	Medtronic Steering for CRYSTAL AF	Expert witness
Tommaso Pellis	Santa Maria degli Angeli Hospital—Medical doctor, consultant in Anesthesia, Intensive Care & Emergency Med. Service	None	None	None	None	None	None
Rachel Prout	University Hospitals Bristol NHS Foundation Trust—SpR	None	None	None	None	None	None
Morten Pytte	Oslo University Hospital, Ullevål—MD Attending anesthesiologit	None	None	None	None	None	None
Renee Reid	Virginia Commonwealth University—Emergency Physician	None	None	None	None	None	None
Jon Rittenberger	UPMC, Assist. Prof.	†Zoll Med Fellowship; NIH Road map for Medical Research	None	Sacramento Fire no honorarium; Christopher Fanning Mem. Community Ed. 'The Big Chill'	None	Advisor for Zoll Cool arrest study	None
Will Ross	Royal Melbourne Hosp. Medical intern	None	None	None	None	None	None

(*Continued*)

CoSTR Part 8: Worksheet Collaborator Disclosures, *Continued*

Worksheet Collaborator	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
Sten Rubertsson	Uppsala University/Dept of Surgical Sciences/Anesthesiology and Intensive Care—Professor	None	None	None	None	*Jolife AB, Lund, Sweden Manufacturer of LUCAS device-mechanical chest compressions Consult fees recieved not annually exceeding USD 10.000 I am also a PI for the ongoing LINC trial-a multicenter trial with 2500pts comparing LUCAS concept with manual chest compressions in out of hospital CA. For this I receive no money	None
Malin Rundgren	Region Skane, Lund University Hospital, Department of intensive and peioperative care—Consultant	*8 weeks per year in time from Region Skanes research and development foundation	None	None	None	None	None
Sebastian Russo	University of Goettingen, Germany: Depart. of Anaesthesiology, Emergency and Intensive Care Medicine—Specialist	None	None	None	None	None	None
Tetsuya Sakamoto	Tokyo University—Professor	†Ministry of Health, Labor & Welfare, Jap.	None	None	None	None	None
Claudio Sandroni	Catholic University School of Medicine-Rome: Assistant Professor	None	None	None	None	None	None
Tommaso Sanna	Catholic University of the Sacred Heart—Researcher & cardiologist	None	None	None	None	None	None
Tomoyuki Sato	Physician, Sapporo Municipal General Hospital Department of Emergency Medicine and Critical Care	None	None	None	None	None	None
Sudhakar Sattur	University of Arizona—Assist. Prof.	None	None	None	None	None	None
Andrea Scapigliati	Catholic University of the Sacred Heart—Assistant Professor	None	None	None	None	None	None
Richard Schilling	Physician, Barts and the London NHS Trust	*Medtronic Medical Devices Company, Recipient of research grant	None	*St Jude Medical, medical devices company; *Biosense Webster, medical devices company;	None	None	None
Ian Seppelt	Sydney West Area Health Servcie: Clinical Intensive Care Medicine—Senior Staff Specialist	None	None	None	None	*Sedation Advisory Board in Intensive Care' for Hospira Pharmaceuticals (manufacturers of dexmedetomidine)	None
Fred Severyn	University of Colorado—Emergency Physician	None	None	None	None	*I have been supoenaed several times from Adams county Colorado to testify as expert witness in felony cases in which I provided medical care to a victim of injury/illness—not on my terms, but served as expert witness (or else get hit for contempt of court and go to jail!)	None
Greene Shepherd	University of Georgia, College of Pharmacy—Professor	None	None	*CE talks about calcium channel blocker poisoning (one of my assigned topics) for professional societies. Amounts of honoraria never exceeded $500	None	None	None

(*Continued*)

CoSTR Part 8: Worksheet Collaborator Disclosures, *Continued*

Worksheet Collaborator	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
Richard Shih	Emergency Medical Associates Emergency Medicine Physicain Group Emergency Physician	None	None	None	None	None	None
Markus Skrifvars	Sydney South West Area Health Service—Senior Registrar ICU	†Research grant (15.000 American dollars) from the Laerdal Foundation for Acute Medicine in 2009 for a rearech project on outcome following intensive care of cardiac arrest patients	None	None	None	None	None
Jasmeet Soar	North Bristol NHS Trust—Consultant in Anaesthetics & Intensive Care Medicine	None	None	None	None	None	None
Keichi Tada	Hiroshima Hosp. MD	None	None	None	None	None	None
Sara Tararan	Azienda per i Servizi Sanitari n. 6 ″Friuli Occidentale'RN	None	None	None	None	None	None
Michel Torbey	Medical College of Wisconsin—Associate Professor	None	None	None	None	None	None
Jonathan Weinstock	Tufts Medical Center—Staff Cardiologist	None	None	None	None	None	None
Volker Wenzel	Innsbruck Medical University—Associate Professor and Vice Chair	†Science Foundation Austrian National Bank grant 11448, Vienna, Austria (support for VITRIS. at trauma trial) *German Air Rescue, Filderstadt, Germany Swiss Air Rescue, Zürich, Switzerland Austrian Air Ambulance, Vienna, Austria	†AOP Orphand Drugs, Vienna, Austria, manufacturing of study drugs for VITRIS. at trauma trial Innsbruck Medical University, Department of Anesthesiology, employment of study nurse for VITRIS.at trauma trial	None	None	None	None
Christoph Wiese	Univ of Regensberg Germany,Anes-thesiology	None	None	None	None	None	None
Daniel Wu	Emory University School of Medicine; Assistant Professor	None	None	None	None	None	None
Carolyn Zelop	SFH Dept of Ob/Gyn—Director of MFM/Associate Chair	*I have been an expert witness for VBAC cases	None	None	None	None	None
David Zideman	Imperial College Healthcare NHS Trust—Consultant Anaesthetist; London Olympics 2012—Clinical Lead-EMS	None	None	None	None	None	*Her Majesty's Coroner—Surrey—Less than £1000 (UKP)
Janice Zimmerman	The Methodist Hospital Physician Organization—Head, Critical Care Division	None	None	None	None	None	None

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

*Modest.

†Significant.

Appendix

CoSTR Part 8: Worksheet Appendix

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS/BLS	ALS/BLS-CPR&A-079A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of a supraglottic airway device (I) vs an endotracheal tube (I), improve any outcomes (O).	Supraglottic devices vs intubation	Lauren Berkow	http://circ.ahajournals.org/site/C2010/ALS-BLS-CPR-A-079A.pdf
ALS/BLS	ALS/BLS-CPR&A-079B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of a supraglottic airway device (I) vs an endotracheal tube (I), improve any outcomes (O).	Supraglottic devices vs intubation	Michael Shuster	http://circ.ahajournals.org/site/C2010/ALS-BLS-CPR-A-079B.pdf
ALS/BLS	ALS/BLS-CPR&A-080B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of oropharyngeal airway or nasopharyngeal airway adjuncts (I) compared with no airway adjuncts (C), improve any outcomes (eg. ventilation, oxygenation) (O).	Oropharyngeal and nasopharyngeal adjuncts	Harinder Dhindsa, V. Ramana Feeser, Renee D. Reid	http://circ.ahajournals.org/site/C2010/ALS-BLS-CPR-A-080B.pdf
ALS/BLS	ALS/BLS-CPR&A-088A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of supraglottic devices (I) compared with bag-valve-mask alone for airway management (C), improve any outcomes (eg. ventilation, oxygenation, reduce hands-off time, allow for continuous compressions and/or improves survival) (O).	Supraglottic devices vs BVM	Suzanne R. Davies, Paul M. Middleton	http://circ.ahajournals.org/site/C2010/ALS-BLS-CPR-A-088A.pdf
ALS/BLS	ALS/BLS-CPR&A-088B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of supraglottic devices (I) compared with bag-valve-mask alone for airway management (C), improve any outcomes (eg. ventilation, oxygenation, reduce hands-off time, allow for continuous compressions and/or improves survival) (O).	Supraglottic devices vs BVM	Lauren Berkow, Henry R. Halperin	http://circ.ahajournals.org/site/C2010/ALS-BLS-CPR-A-088B.pdf
ALS	ALS-CPR&A-001A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of physiological feedback regarding CPR quality (eg, End-tidal CO_2 monitoring) (I) compared with no feedback (C), improve any outcomes (eg. ROSC, survival) (O)?	Physiologic feedback (eg, end tidal CO_2) for CPR quality	Blair Bigham	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-001A.pdf
ALS	ALS-CPR&A-001B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of physiological feedback regarding CPR quality (eg, End-tidal CO_2 monitoring) (I) compared with no feedback (C), improve any outcomes (eg. ROSC, survival) (O)?	Physiologic feedback (eg, end tidal CO_2) for CPR quality	Marion Leary	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-001B.pdf
ALS	ALS-CPR&A-002A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P) – does the use of rapid deployment ECMO, Aortic Balloon Pump or emergency cardiopulmonary bypass (I), compared with standard treatment (C), increase survival to hospital discharge with favorable neurologic outcomes (O)?	ECMO, balloon pump etc for CPR	Tetsuya Sakamoto	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-002A.pdf
ALS	ALS-CPR&A-002B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P) – does the use of rapid deployment ECMO, Aortic Balloon Pump or emergency cardiopulmonary bypass (I), compared with standard treatment (C), increase survival to hospital discharge with favorable neurologic outcomes (O)?	ECMO, balloon pump etc for CPR	Michael S. Czekajlo	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-002B.pdf
ALS	ALS-CPR&A-003B	In adult in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of ultrasound (including transthoracic and transesophageal echocardiography) during cardiac arrest (I) compared with standard CPR (C), improve any outcomes (eg. ROSC, survival) (O).	Ultrasound during cardiac arrest	Amanda Hanson	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-003B.pdf
ALS	ALS-CPR&A-005C	In adult cardiac arrest (out-of-hospital and in-hospital) with either a protected and unprotected airway (P), does the monitoring and control of ventilatory parameters (eg. minute ventilation and/or peak pressures) (I) as opposed to standard care (without ventilatory monitoring) (C), improve outcome (O) (eg. ROSC, survival)?	Monitoring ventilatory parameters during CPR	Kate Crewdson	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-005C.pdf
ALS	ALS-CPR&A-006A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of thoracic impedance (I) compared with usual management (C), improve the accuracy of diagnosis of airway placement and adequacy of ventilation (O).	Thoracic impedance to confirm airway placement	F. Javier Garcia-Vega	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-006A.pdf
ALS	ALS-CPR&A-006B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of thoracic impedance (I) compared with usual management (C), improve the accuracy of diagnosis of airway placement and adequacy of ventilation (O).	Thoracic impedance to confirm airway placement	Heather Farley	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-006B.pdf
ALS	ALS-CPR&A-007B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) requiring ventilation and intubation (P), does the application and maintenance of cricoid pressure (I), compared to no cricoid pressure (C), reduce the incidence of aspiration (O)	Cricoid pressure	Michael Shuster	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-007B.pdf
ALS	ALS-CPR&A-008A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of devices (eg. CO_2 detection device, CO_2 analyzer or esophageal detector device) (I) compared with usual management (C), improve the accuracy of diagnosis of airway placement (O)?	Devices to confirm airway placement	Douglas Kupas	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-008A.pdf

(*Continued*)

CoSTR Part 8: Worksheet Appendix, *Continued*

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS	ALS-CPR&A-008B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of devices (eg. CO_2 detection device, CO_2 analyzer or esophageal detector device) (I) compared with usual management (C), improve the accuracy of diagnosis of airway placement (O)?	Devices to confirm airway placement	Ian L. Cash	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-008B.pdf
ALS	ALS-CPR&A-009A	In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of passive oxygen delivery during CPR (I) compared with oxygen delivery by positive pressure ventilation (C), improve outcome (eg. ROSC, survival) (O).	Passive oxygen vs positive pressure oxygen during CPR	Csaba Dioszeghy	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-009A.pdf
ALS	ALS-CPR&A-009B	In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of passive oxygen delivery during CPR (I) compared with oxygen delivery by positive pressure ventilation (C), improve outcome (eg. ROSC, survival) (O).	Passive oxygen vs positive pressure oxygen during CPR	Peter Fenici, Andrea Scapigliati	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-009B.pdf
ALS	ALS-CPR&A-010A	In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) and who have advanced airways in place (P), does the use of automatic ventilators (I) compared with manual ventilation (C), improve outcome (eg. ventilation, oxygenation, reduce hands-off time, allow for continuous compressions and/or improves survival) (O)?	Automatic ventilators vs manual ventilation during CPR	Charles Otto	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-010A.pdf
ALS	ALS-CPR&A-011A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of an FIO_2 titrated to oxygenation during cardiac arrest (I) compared with the use of 100% oxygen (C), improve outcome (eg. ROSC, neurologically intact survival) (O)?	Supplemental oxygen: 100% versus titration	Colin A. Graham	http://circ.ahajournals.org/site/C2010/ALS-CPR-A-011A.pdf
ALS	ALS-D&P-014A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of end-tidal CO_2 (eg, absolute CO_2 values or changes in waveform) (I) compared with not using $ETCO_2$ (C), accurately predict outcomes (eg. ROSC, survival) (O).	End-tidal CO_2 to predict outcome of cardiac arrest	Sadiq S. Bhayani	http://circ.ahajournals.org/site/C2010/ALS-D-P-014A.pdf
ALS	ALS-D-016A	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use intravenous fluids (I) compared with not using fluids (or standard resuscitation (C), improve outcomes (eg. ROSC, survival) (O).	IV fluids during cardiac arrest	Jane A.H. Foster, Jasmeet Soar	http://circ.ahajournals.org/site/C2010/ALS-D-016A.pdf
ALS	ALS-D-016B	In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use intravenous fluids (I) compared with not using fluids (or standard resuscitation (C), improve outcomes (eg. ROSC, survival) (O).	IV fluids during cardiac arrest	Paul A. Jennings	http://circ.ahajournals.org/site/C2010/ALS-D-016B.pdf
ALS	ALS-D-017	In adult patients in atrial fibrillation (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for atrial fibrillation	Steven Kronick, Mark S. Link, Rod S. Passman, Richard Schilling	http://circ.ahajournals.org/site/C2010/ALS-D-017.pdf
ALS	ALS-D-018	In adult patients in narrow complex tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for narrow complex tachycardia	Steven Kronick, Rod S. Passman, Volker Wenzel	http://circ.ahajournals.org/site/C2010/ALS-D-018.pdf
ALS	ALS-D-019–01A	In adult patients in monomorphic (wide complex) tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for monomorphic wide complex tachycardia	Tommaso Pellis	http://circ.ahajournals.org/site/C2010/ALS-D-019–01A.pdf
ALS	ALS-D-019–01B	In adult patients in monomorphic (wide complex) tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for monomorphic wide complex tachycardia	Markus Skrifvars	http://circ.ahajournals.org/site/C2010/ALS-D-019–01B.pdf
ALS	ALS-D-019–02	In adult patients with undifferentiated stable wide complex tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates)(O)?	Drugs for undifferentiated stable wide complex tachycardia	Steven Kronick	http://circ.ahajournals.org/site/C2010/ALS-D-019–02.pdf
ALS	ALS-D-020B	In adult patients in polymorphic (wide complex) tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for polymorphic wide complex tachycardia	Peter J. Kudenchuk	http://circ.ahajournals.org/site/C2010/ALS-D-020B.pdf
ALS	ALS-D-021A	In adult patients in torsades de pointes (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for torsades de pointes	Eliano Pio Navarese, Andrea Scapigliati	http://circ.ahajournals.org/site/C2010/ALS-D-021A.pdf

(*Continued*)

CoSTR Part 8: Worksheet Appendix, *Continued*

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS	ALS-D-022A	In adult patients in significant bradycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O).	Drugs for bradycardia	Thomas Nguyen	http://circ.ahajournals.org/site/C2010/ALS-D-022A.pdf
ALS	ALS-D-023B	In adult patients in cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of vasopressors (epinephrine, norepinephrine, others) or combination of vasopressors (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Vasopressors for cardiac arrest	Todd M. Larabee, Charles M. Little	http://circ.ahajournals.org/site/C2010/ALS-D-023B.pdf
ALS	ALS-D-024B	In adult patients in cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of atropine or atropine in combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Atropine for cardiac arrest	Swee Han Lim	http://circ.ahajournals.org/site/C2010/ALS-D-024B.pdf
ALS	ALS-D-025A	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of antiarrhythmic drugs (lidocaine, procainamide, amiodarone, bretylium, magnesium) or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Antiarrhythmic drugs for cardiac arrest	Marcus Ong	http://circ.ahajournals.org/site/C2010/ALS-D-025A.pdf
ALS	ALS-D-025B	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of antiarrhythmic drugs (lidocaine, procainamide, amiodarone, bretylium, magnesium) or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Antiarrhythmic drugs for cardiac arrest	Mark S. Link, Tommaso Pellis	http://circ.ahajournals.org/site/C2010/ALS-D-025B.pdf
ALS	ALS-D-026A	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of calcium alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Calcium for cardiac arrest	Fulvio Kette, Sara Tararan	http://circ.ahajournals.org/site/C2010/ALS-D-026A.pdf
ALS	ALS-D-026B	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of calcium alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Calcium for cardiac arrest	Jaspinder Ghuman	http://circ.ahajournals.org/site/C2010/ALS-D-026B.pdf
ALS	ALS-D-027	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of steroid or hormonal therapy (estrogen, progesterone, hydrocortisone, insulin, growth factor etc) alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Steroids and hormones for cardiac arrest	Michael Cocchi, Michael Donnino, Ian Seppelt	http://circ.ahajournals.org/site/C2010/ALS-D-027.pdf
ALS	ALS-D-028A	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of fibrinolytics alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Fibrinolytics for cardiac arrest	Michael Parr	http://circ.ahajournals.org/site/C2010/ALS-D-028A.pdf
ALS	ALS-D-028B	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of fibrinolytics alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Fibrinolytics for cardiac arrest	Steven Kronick	http://circ.ahajournals.org/site/C2010/ALS-D-028B.pdf
ALS	ALS-D-029A	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of buffering agents alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Buffering agents for cardiac arrest	James J. McCarthy	http://circ.ahajournals.org/site/C2010/ALS-D-029A.pdf
ALS	ALS-D-029C	In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of buffering agents alone or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O).	Buffering agents for cardiac arrest	Edison Ferreira de Paiva	http://circ.ahajournals.org/site/C2010/ALS-D-029C.pdf
ALS	ALS-PA-040A	In post-cardiac arrest patients treated with hypothermia (P), can the same prognostication tools that are used in normothermic patients (I) reliably predict outcome (O)?	Hypothermia and prognostication	Hans Friberg, Robert Neumar, Malin Rundgren	http://circ.ahajournals.org/site/C2010/ALS-PA-040A.pdf

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CoSTR Part 8: Worksheet Appendix, *Continued*

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS	ALS-PA-041	In adult and pediatric patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of the bedside neurological exam (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?	Bedside neuro exam for prognostication	Romergryko G. Geocadin, Giuseppe La Torre, Claudio Sandroni	http://circ.ahajournals.org/site/C2010/ALS-PA-041.pdf
ALS	ALS-PA-042A	In adult and pediatric organ recipients (P), does the use of organs from donors brain dead after cardiac arrest (prehospital or in-hospital) (I) as opposed to the use of donors brain dead not due to cardiac arrest (C), improve outcome (O) (eg. transplant success?	Organ donation	Claudio Sandroni	http://circ.ahajournals.org/site/C2010/ALS-PA-042A.pdf
ALS	ALS-PA-042B	In adult and pediatric organ recipients (P), does the use of organs from donors brain dead after cardiac arrest (prehospital or in-hospital) (I) as opposed to the use of donors brain dead not due to cardiac arrest (C), improve outcome (O) (eg. transplant success?	Organ donation	Christophe Adrie	http://circ.ahajournals.org/site/C2010/ALS-PA-042B.pdf
ALS	ALS-PA-043A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) who have cardiovascular dysfunction (P), does the use of intravenous fluids (I) as opposed to standard care (or other intravenous fluids) (C), improve outcome (O) (eg. survival)?	IV fluids following cardiac arrest	Jane A.H. Foster, Jasmeet Soar	http://circ.ahajournals.org/site/C2010/ALS-PA-043A.pdf
ALS	ALS-PA-043C	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) who have cardiovascular dysfunction (P), does the use of intravenous fluids (I) as opposed to standard care (or other intravenous fluids) (C), improve outcome (O) (eg. survival)?	IV fluids following cardiac arrest	Hitoshi Kano, Tomoyuki Sato	http://circ.ahajournals.org/site/C2010/ALS-PA-043C.pdf
ALS	ALS-PA-044	In adult patients with ROSC after cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does therapeutic hypothermia (I) compared with usual care (C), improve morbidity or mortality (O)?	Hypothermia following resuscitation	Jerry Nolan, Peter T. Morley	http://circ.ahajournals.org/site/C2010/ALS-PA-044.pdf
ALS	ALS-PA-045A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of a specific strategy to manage blood glucose (eg. target range) (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Glucose control following resuscitation	Jon Rittenberger	http://circ.ahajournals.org/site/C2010/ALS-PA-045A.pdf
ALS	ALS-PA-045B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of a specific strategy to manage blood glucose (eg. target range) (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Glucose control following resuscitation	Janice L. Zimmerman	http://circ.ahajournals.org/site/C2010/ALS-PA-045B.pdf
ALS	ALS-PA-046A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P) diagnosed as pulmonary embolism, does the use of early fibrinolytic therapy (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Fibrinolytics for cardiac arrest	Markus Skrifvars	http://circ.ahajournals.org/site/C2010/ALS-PA-046A.pdf
ALS	ALS-PA-046B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P) diagnosed as pulmonary embolism, does the use of early fibrinolytic therapy (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Fibrinolytics for cardiac arrest	Rachel Prout	http://circ.ahajournals.org/site/C2010/ALS-PA-046B.pdf
ALS	ALS-PA-047A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of comprehensive treatment protocol (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Treatment protocol post resuscitation	Maaret Castrén	http://circ.ahajournals.org/site/C2010/ALS-PA-047A.pdf
ALS	ALS-PA-047B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of comprehensive treatment protocol (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Treatment protocol post resuscitation	Mary Ann Peberdy	http://circ.ahajournals.org/site/C2010/ALS-PA-047B.pdf
ALS	ALS-PA-048A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does treatment with corticosteroids (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Steroids post resuscitation	Andrew Padkin, Kjetil Sunde	http://circ.ahajournals.org/site/C2010/ALS-PA-048A.pdf
ALS	ALS-PA-049A	In adult patients (prehospital or in-hospital) who are comatose after cardiac arrest (P) does treatment of pyrexia (I) compared to no temperature intervention (C) improve outcome (eg. survival).	Fever post resuscitation	Marios Georgiou, Marios Ioannides	http://circ.ahajournals.org/site/C2010/ALS-PA-049A.pdf
ALS	ALS-PA-050A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of seizure prophylaxis or effective seizure control (I) as opposed to standard care (no prophylaxis or ineffective seizure control)(C), improve outcome (O) (eg. survival)?	Seizure prophylaxis post resuscitation	Nabil El Sanadi	http://circ.ahajournals.org/site/C2010/ALS-PA-050A.pdf
ALS	ALS-PA-050B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of seizure prophylaxis or effective seizure control (I) as opposed to standard care (no prophylaxis or ineffective seizure control)(C), improve outcome (O) (eg. survival)?	Seizure prophylaxis post resuscitation	Maaret Castrén	http://circ.ahajournals.org/site/C2010/ALS-PA-050B.pdf
ALS	ALS-PA-051A	In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of neurological electrophysiological studies (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?	EEG post resuscitation	Tommaso Sanna	http://circ.ahajournals.org/site/C2010/ALS-PA-051A.pdf

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CoSTR Part 8: Worksheet Appendix, *Continued*

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS	ALS-PA-052A	In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of biochemical markers (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?	Biomarkers	Tommaso Sanna	http://circ.ahajournals.org/site/C2010/ALS-PA-052A.pdf
ALS	ALS-PA-052B	In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of biochemical markers (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?	Biomarkers	Michel Torbey	http://circ.ahajournals.org/site/C2010/ALS-PA-052B.pdf
ALS	ALS-PA-053B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of a specific ventilation strategy (including specific CO_2 goal) (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Ventilation strategy post resuscitation	Clifton Callaway	http://circ.ahajournals.org/site/C2010/ALS-PA-053B.pdf
ALS	ALS-PA-054A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of a hemofiltration (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Hemofiltration post resuscitation	Wilhelm Behringer	http://circ.ahajournals.org/site/C2010/ALS-PA-054A.pdf
ALS	ALS-PA-055A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of neuroprotective drugs (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Neuorprotective drugs	Michael Holzer	http://circ.ahajournals.org/site/C2010/ALS-PA-055A.pdf
ALS	ALS-PA-055C	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of neuroprotective drugs (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Neuorprotective drugs	Richard A. Bernstein	http://circ.ahajournals.org/site/C2010/ALS-PA-055C.pdf
ALS	ALS-PA-056B	In adult patients (prehospital and in-hospital) with ROSC after cardiac arrest (P), does early hemodynamic optimization (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Hemodynamic support post resuscitation	Michael Fries	http://circ.ahajournals.org/site/C2010/ALS-PA-056B.pdf
ALS	ALS-PA-057A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) who have cardiovascular dysfunction (P), does the use of any specific cardioactive drugs (I) as opposed to standard care (or different cardioactive drugs) (C), improve outcome (O) (eg. survival)?	Cardioactive drugs post resuscitation	Karl B. Kern, Sudhakar Sattur	http://circ.ahajournals.org/site/C2010/ALS-PA-057A.pdf
ALS	ALS-PA-058A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of prophylactic antiarrhythmic drugs (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Antiarrhythmic drugs post resuscitation	Tommaso Pellis	http://circ.ahajournals.org/site/C2010/ALS-PA-058A.pdf
ALS	ALS-PA-058B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of prophylactic antiarrhythmic drugs (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Antiarrhythmic drugs post resuscitation	Mark S. Link	http://circ.ahajournals.org/site/C2010/ALS-PA-058B.pdf
ALS	ALS-PA-059	In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of imaging studies (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?	Imaging studies post resuscitation	Romergryko G. Geocadin, David M. Greer	http://circ.ahajournals.org/site/C2010/ALS-PA-059.pdf
ALS	ALS-PA-060	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) who have cardiovascular dysfunction (P), does the use of mechanical circulatory support (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Mechanical circulatory support post resuscitation	Hitoshi Kano, Sten Rubertsson, Tomoyuki Sato	http://circ.ahajournals.org/site/C2010/ALS-PA-060.pdf
ALS	ALS-PA-061A	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of a controlled oxygenation strategy (including specific oxygenation goal) (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Supplemental oxygen: 100% versus titration	Robert Neumar	http://circ.ahajournals.org/site/C2010/ALS-PA-061A.pdf
ALS	ALS-PA-061B	In adult patients with ROSC after cardiac arrest (prehospital or in-hospital) (P), does the use of a controlled oxygenation strategy (including specific oxygenation goal) (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?	Supplemental oxygen: 100% versus titration (duplicate with 11a?)	Gregory P. Comadira	http://circ.ahajournals.org/site/C2010/ALS-PA-061B.pdf
ALS	ALS-SAM-062A	In adult cardiac arrest (prehospital or in-hospital) (P), does an alternate timing for advanced airway insertion (eg. early or delayed) (I) as opposed to standard care (standard position in algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Advanced airway placement (timing)	Sebastian G. Russo, Christoph H. Wiese, Daniel Wu	http://circ.ahajournals.org/site/C2010/ALS-SAM-062A.pdf
ALS	ALS-SAM-063A	In adult cardiac arrest (prehospital or in-hospital) (P), does an alternate timing for drug delivery (eg. early or delayed) (I) as opposed to standard care (standard position in algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Drug delivery (timing)	James J. Menegazzi, Morten Pytte	http://circ.ahajournals.org/site/C2010/ALS-SAM-063A.pdf

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CoSTR Part 8: Worksheet Appendix, *Continued*

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS	ALS-SAM-063B	In adult cardiac arrest (prehospital or in-hospital) (P), does an alternate timing for drug delivery (eg. early or delayed) (I) as opposed to standard care (standard position in algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Drug delivery (timing)	Elizabeth A. Hunt, Michael C. McCrory	http://circ.ahajournals.org/site/C2010/ALS-SAM-063B.pdf
ALS	ALS-SAM-064B	In adult cardiac arrest (prehospital or in-hospital) (P), initially with a non-shockable rhythm but who develop a shockable rhythm (prehospital or in-hospital) (P), does any specific alteration in treatment algorithm (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Algorithm for transition from shockable to non-shockable rhythm	Masami Ishikawa, Keiichi Tada, Wanchun Tang	http://circ.ahajournals.org/site/C2010/ALS-SAM-064B.pdf
ALS	ALS-SAM-064C	In adult cardiac arrest (prehospital or in-hospital) (P), initially with a non-shockable rhythm but who develop a shockable rhythm (prehospital or in-hospital) (P), does any specific alteration in treatment algorithm (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Algorithm for transition from shockable to non-shockable rhythm	Timothy J. Mader	http://circ.ahajournals.org/site/C2010/ALS-SAM-064C.pdf
ALS	ALS-SC-065	In pregnant patients with cardiac arrest (prehospital or in-hospital) (P), do any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Pregnancy and cardiac arrest	Farida M. Jeejeebhoy, Carolyn M. Zelop	http://circ.ahajournals.org/site/C2010/ALS-SC-065.pdf
ALS	ALS-SC-066A	In adult cardiac arrest due to anaphylaxis (P), does any modification of treatment (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Anaphylaxis and cardiac arrest	Eric Bruder	http://circ.ahajournals.org/site/C2010/ALS-SC-066A.pdf
ALS	ALS-SC-066B	In adult cardiac arrest due to anaphylaxis (P), does any modification of treatment (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Anaphylaxis and cardiac arrest	John Litell	http://circ.ahajournals.org/site/C2010/ALS-SC-066B.pdf
ALS	ALS-SC-067B	In adult cardiac arrest due to asthma (P), does any modification of treatment (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Asthma and cardiac arrest	Barry Brenner, Fred A. Severyn	http://circ.ahajournals.org/site/C2010/ALS-SC-067B.pdf
ALS	ALS-SC-068B	In adult cardiac arrest during PCI (P), does use of any specific intervention (I) as opposed to standard care (acc to treatment algorithm) (C), improve outcome	Cardiac arrest during PCI	Pavan Battu	http://circ.ahajournals.org/site/C2010/ALS-SC-068B.pdf
ALS	ALS-SC-068C	In adult cardiac arrest during PCI (P), does use of any specific intervention (I) as opposed to standard care (acc to treatment algorithm) (C), improve outcome.	Cardiac arrest during PCI	Jonathan Weinstock	http://circ.ahajournals.org/site/C2010/ALS-SC-068C.pdf
ALS	ALS-SC-069A	In adult cardiac arrest following open (including heart and lung transplantations) and closed heart surgery (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Post op cardiothoracic surgery cardiac arrest	Joel Dunning	http://circ.ahajournals.org/site/C2010/ALS-SC-069A.pdf
ALS	ALS-SC-069B	In adult cardiac arrest following open (including heart and lung transplantations) and closed heart surgery (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Post op cardiothoracic surgery cardiac arrest	David Zideman	http://circ.ahajournals.org/site/C2010/ALS-SC-069B.pdf
ALS	ALS-SC-069C	In adult cardiac arrest following open (including heart and lung transplantations) and closed heart surgery (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Post op cardiothoracic surgery cardiac arrest	Peter T. Morley, Will Ross	http://circ.ahajournals.org/site/C2010/ALS-SC-069C.pdf
ALS	ALS-SC-070B	In adult cardiac arrest (prehospital or in-hospital) due to a cardiac tamponade (P), does use of specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Cardiac tamponade	Henry R. Halperin	http://circ.ahajournals.org/site/C2010/ALS-SC-070B.pdf
ALS	ALS-SC-071B	In adult cardiac arrest (prehospital or in-hospital) (P) due to pulmonary embolus (P), does use of etiology specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Pulmonary embolism cardiac arrest	C. Jessica Dine	http://circ.ahajournals.org/site/C2010/ALS-SC-071B.pdf
ALS	ALS-SC-072A	In adult cardiac arrest (prehospital or in-hospital) (P) due to non-cardiac etiology (eg. hemmorhagic shock, hypovolemic shock; septic shock; neurogenic shock) (P), does use of etiology specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Non-cardiac etiology cardiac arrest	Harinder Dhindsa, V. Ramana Feeser, Renee D. Reid	http://circ.ahajournals.org/site/C2010/ALS-SC-072A.pdf
ALS	ALS-SC-073–01A	In adult cardiac arrest (prehospital or in-hospital) due to local anesthetic toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Local anesthesia toxicity	Eric J. Lavonas, John J. Picard, Richard D. Shih	http://circ.ahajournals.org/site/C2010/ALS-SC-073–01A.pdf

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CoSTR Part 8: Worksheet Appendix, *Continued*

Task Force	WS ID	PICO Title	Short Title	Authors	URL
ALS	ALS-SC-073–02A	In adult cardiac arrest (prehospital or in-hospital) due to Benzodiazepine toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Benzodiazepine toxicity	Mohammed Alhelail, Greene Shepherd	http://circ.ahajournals.org/site/C2010/ALS-SC-073–02A.pdf
ALS	ALS-SC-073–03B	In adult cardiac arrest (prehospital or in-hospital) due to Beta blockers toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Beta blocker toxicity	Melissa Givens, Greene Shepherd	http://circ.ahajournals.org/site/C2010/ALS-SC-073–03B.pdf
ALS	ALS-SC-073–04B	In adult cardiac arrest (prehospital or in-hospital) due to Calcium channel blockers toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Calcium channel blocker toxicity	Melissa Givens, Greene Shepherd	http://circ.ahajournals.org/site/C2010/ALS-SC-073–04B.pdf
ALS	ALS-SC-073–05	In adult cardiac arrest (prehospital or in-hospital) due to Carbon monoxide toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Carbon monoxide toxicity	Eric J. Lavonas, David Lobel	http://circ.ahajournals.org/site/C2010/ALS-SC-073–05.pdf
ALS	ALS-SC-073–06B	In adult cardiac arrest (prehospital or in-hospital) due to Cocaine toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Cocaine toxicity	Eric J. Lavonas	http://circ.ahajournals.org/site/C2010/ALS-SC-073–06B.pdf
ALS	ALS-SC-073–07	In adult cardiac arrest (prehospital or in-hospital) due to Cyanide toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Cyanide toxicity	Eric J. Lavonas, David Lobel	http://circ.ahajournals.org/site/C2010/ALS-SC-073–07.pdf
ALS	ALS-SC-073–08B	In adult cardiac arrest (prehospital or in-hospital) due to Cyclic antidepressants toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Tricyclic antidepressant toxicity	Allan R. Mottram	http://circ.ahajournals.org/site/C2010/ALS-SC-073–08B.pdf
ALS	ALS-SC-073–09A	In adult cardiac arrest (prehospital or in-hospital) due to Digoxin/etc toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Digoxin toxicity	Richard D. Shih	http://circ.ahajournals.org/site/C2010/ALS-SC-073–09A.pdf
ALS	ALS-SC-073–10	In adult cardiac arrest (prehospital or in-hospital) due to opioids toxicity (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Opiod toxicity	Mohammed Alhelail, Allan R. Mottram	http://circ.ahajournals.org/site/C2010/ALS-SC-073–10.pdf
ALS	ALS-SC-074A	In morbidly obese adult patients with cardiac arrest (prehospital or in-hospital) (P), does use of any specific interventions (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, survival)?	Morbid obesity	Pavan Battu	http://circ.ahajournals.org/site/C2010/ALS-SC-074A.pdf
ALS	ALS-SC-076A	In adult cardiac arrest (out-of-hospital and in-hospital) (P), does the treatment of electrolyte disturbances (eg. hypo or hyperkalemia, hypo or hyper magnesiemia, hypo and hyper calcemia) (I) as opposed to standard care (according to treatment algorithm, but without treatment of electrolyte disturbances) (C), improve outcome (O) (eg. ROSC, survival)?	Electrolyte disturbances	William J. Meurer	http://circ.ahajournals.org/site/C2010/ALS-SC-076A.pdf
ALS	ALS-SC-076B	In adult cardiac arrest (out-of-hospital and in-hospital) (P), does the treatment of electrolyte disturbances (eg. hypo or hyperkalemia, hypo or hyper magnesiemia, hypo and hyper calcemia) (I) as opposed to standard care (according to treatment algorithm, but without treatment of electrolyte disturbances) (C), improve outcome (O) (eg. ROSC, survival)?	Electrolyte disturbances	Deborah Diercks	http://circ.ahajournals.org/site/C2010/ALS-SC-076B.pdf
ALS	ALS-SC-078B	For avalanche victims in out of hospital cardiac arrest (P), what factors when present (I), compared with when absent (C), are associated with/predict an increased survival to hospital discharge (O)?	Avalanche victims	Jeff Boyd, Hermann Brugger	http://circ.ahajournals.org/site/C2010/ALS-SC-078B.pdf

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KEY WORDS: arrhythmia ■ cardiac arrest ■ cardiopulmonary resuscitation ■ emergency department ■ resuscitation

Part 8: Advanced Life Support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

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