

Cardiac Arrest Updates

5

IN THIS CHAPTER

- General Management Considerations
- Circulatory Support
- Defibrillation
- Airway
- Oxygenation
- Ventilation
- Pharmacotherapy
- Systems Issues
- Special Considerations
- Future Directions

Joshua C. Reynolds and Benjamin J. Lawner

Out-of-hospital cardiac arrest (OHCA) represents a profound clinical and public health challenge, both in the United States and across the globe.

Cardiovascular disease, which accounts for one-third of all US deaths, is the most common cause of OHCA.¹

The overall occurrence of OHCA is highest in Australia (113:100,000), but its incidence from presumed cardiac cause is highest in North America (55:100,000).² These events are more likely to stem from cardiac disease in patients older than 35 years, and are more commonly attributable to “noncardiac” causes in patients younger than 35 years.³ In fact, 83% of cardiac arrests occurring in patients younger than 19 years are noncardiac in origin.⁴ Health care providers are notoriously inaccurate in predicting the cause of OHCA, often underestimating noncardiac etiologies.^{5,6}

Epidemiologic data from a large 10-site North American resuscitation research consortium has demonstrated marked regional variations in OHCA-related outcomes.⁷ The median rate of survival to hospital discharge of cardiac arrest victims treated by emergency medical services (EMS) personnel is 8.4% (IQR: 5.4%, 10.4%), with rates ranging from 3.0% to 16.3%. This percentage is significantly higher in patients with ventricular fibrillation (VF) as the initial rhythm. The median rate of survival to hospital discharge in this subpopulation is 22.0% (IQR: 15.0%, 24.4%), with rates ranging from 7.7% to 39.9% across the same geographic locales.

Resuscitation science has evolved greatly since the inception of cardiopulmonary resuscitation (CPR). Guidelines for cardiac arrest resuscitation are updated every 5 years by the International Liaison Committee on Resuscitation (ILCOR), which provides treatment recommendations based on available evidence and expert opinion. ILCOR guidelines then are funneled through national and regional associations (eg, the American Heart Association [AHA]) and packaged as

educational curricula (eg, Basic Life Support [BLS] or Advanced Cardiac Life Support [ACLS]).

Emergency care providers and others tasked with leading resuscitation efforts must be aware of the source material for these curricula and understand the controversies, paradigms, and accumulated evidence behind the latest recommendations.

PEARL

A cardiac cause of cardiac arrest is more likely in patients over 35 years of age.

General Considerations

Cardiac arrest is a dynamic disease. Few other clinical presentations strain the leadership abilities of the emergency care provider to the same degree. Astute clinicians must realize, however, that they are orchestrating only one portion of a larger series of events, each of which directly affects patient outcomes. The achievement of return of spontaneous circulation (ROSC) is only one piece of this resuscitation puzzle.

Layperson recognition of cardiac arrest, activation of the EMS system, and provision of bystander CPR are equally important. In addition, the critical care, inpatient, and rehabilitation phases of treatment play crucial roles in patient survival. This overarching view of cardiac arrest care is embodied in the success of bundled postresuscitation care packages that improve outcomes among patients attaining ROSC.⁸

Circulatory Support

“Pit Crew” CPR

Prompt and effective cardiac arrest management can be difficult in the hectic and potentially austere environments in which it is required. To orchestrate efficient and effective

resuscitation, regimented training and good working relationships between care providers are vitally important. “Pit crew” CPR (Figure 5-1) is an effective strategy for controlling the chaos of resuscitation, which — when bundled into a larger cardiac arrest management plan — can improve patient outcomes.⁹

Just as in motor sports, this technique is centered on a core group of providers with preassigned roles. The responsibility of each caregiver is determined by his or her location and proximity to the patient. For example, the provider at the head is always in charge of the airway, and the provider near the patient’s left shoulder is always tasked with chest compressions. This concept is similar to strategies employed by trauma resuscitation teams.

Mechanical Devices

The management of human factors is one of the most challenging aspects of cardiac arrest resuscitation. With the proliferation of mechanical resuscitation devices, it is tempting to offload certain repetitive tasks to free up additional resources. Chest compressions and ventilations, for example, require a sizable investment of personnel and are prone to a great degree of interoperator variability in quality and effectiveness.

When working together, a mechanical chest compression device and ventilator can deliver sustained, uninterrupted, quality compressions and ventilations without deviating from specified parameters. This essentially eliminates the cognitive burden of constantly verifying the quality of procedure “performance,” allowing the resuscitation leader to focus on detecting and addressing reversible causes. The feasibility of using mechanical CPR as a bridge to computed tomography (CT), cardiac catheterization, and percutaneous cannulation for extracorporeal membranous oxygenation (ECMO) is well demonstrated.¹⁰⁻¹³

PEARLS

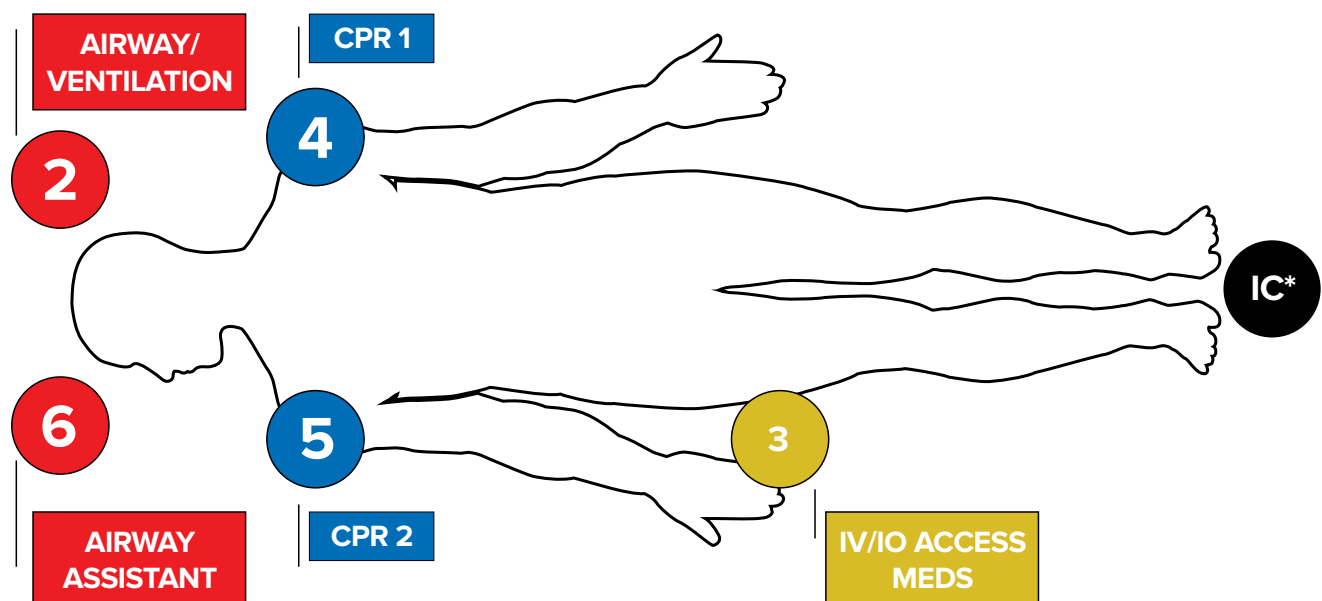
- ✓ Consider offloading repetitive tasks to machines.
- ✓ When considering advanced diagnostic or interventional maneuvers, use a piston-driven or load-distributing band device when performing chest compressions.

The most common devices use either a piston or compression band system to decrease the volume of the thoracic cavity, pushing blood throughout the body. Designed to deliver efficient mechanized compressions comparable to those performed in manual CPR, these tools are timed to work in a 30:2 ratio or at rates suggested by the AHA. In select patients, mechanical CPR devices afford the opportunity for truly astounding resuscitations; however, the same benefits have not been observed in the general cardiac arrest population.¹⁴

A number of studies have been performed to evaluate these devices, but it should be noted that many were sponsored by manufacturers. Studies evaluating CPR metrics, including end-tidal carbon dioxide measurements, cerebral blood flow, and coronary perfusion pressure, demonstrate better results with mechanical CPR devices than with manual CPR.¹⁵⁻¹⁷ Randomized trials and a meta-analysis found a slight trend toward higher rates of ROSC but failed to show an outcome benefit for either technique.¹⁸⁻²¹

Application time appears to be the biggest issue with mechanical methods.^{22,23} In most cases, a hands-off period is needed when applying the device; for an untrained rescuer, this could lead to significant time without compressions. Virtually every manufactured device has some posterior component that demands halting compressions to allow proper placement.

FIGURE 5-1. Pit Crew Model Positional Assignments



Although a number of device-related injuries have been reported, they have not been associated with untoward results.²⁴ Not surprisingly, most of these injuries are similar to those seen with manual CPR (eg, rib fractures, sternal fractures, liver lacerations, and pulmonary contusions). However, these tools typically are applied after some duration of manual CPR, so it is difficult to attribute specific injuries to the equipment alone.

Mechanical devices appear to provide benefit in prolonged resuscitations, during which providers tire; in situations where manual CPR is dangerous or not feasible; and as a bridge to percutaneous coronary intervention (PCI) or mechanical support.^{21,25-27} There is no evidence for their routine use in the undifferentiated cardiac arrest patient.

Compression-Only CPR

Compression-only or hands-only CPR solely employs the chest compression portion of traditional CPR. The AHA suggests this method for lay rescuers, since it is simpler and better received by most people.²⁸ Reports are mixed regarding the efficacy of compression-only CPR performed by professional rescuers and hospital personnel. Some observational studies have suggested that patients whose cardiac arrest stems from a noncardiac cause might fare better with traditional CPR, whereas others report no difference in outcomes between the two techniques.²⁹⁻³² Although data regarding the need for rescue breaths are inconsistent, there is consensus on the need for prompt, effective chest compressions with limited interruptions — a point emphasized by current CPR guidelines.

Continuous CPR

The primary arguments for continuous chest compressions are similar to those for compression-only CPR. The term *continuous chest compressions* usually refers to the initial period of resuscitation, most notably the first 4 to 6 minutes following the loss of pulses. During this initial phase, myocardial and cerebral tissue is most sensitive to decreased blood flow; hypoperfusion during this fragile window will lead to worse outcomes.

It has been well demonstrated that any interruption in chest compressions — even a brief pause for ventilation — decreases coronary perfusion pressure and forward blood flow, which are vital to the heart and brain.³³ Quality, uninterrupted compressions not only perfuse vital organs, but also improve the probability of successful defibrillation. The combination of uninterrupted compressions and a minimal “preshock pause” may improve defibrillation success and neurological outcomes.³⁴

When engaged in continuous compressions, care providers are prevented from employing advanced airway maneuvers or other interventions. The necessary distraction can dilute the focus on quality, minimally interrupted compressions and — at worst — can put patients at risk. A number of studies have questioned the use of advanced airways in cardiac arrest patients during the prehospital phase of care, a strategy that has been linked to poor outcomes.³⁶⁻³⁸ Preclinical studies have found that even the two breaths given during a conventional

30:2 compression cycle increase intrathoracic pressures, decrease venous return, and reduce blood flow to the heart and brain.³⁹ While controversy continues about the best compression-to-breath ratio with a BLS or native airway, continuous compressions (>100 per minute) should be administered after placement of an advanced airway.

Defibrillation

Energy Selection

The original defibrillator was little more than a simple pair of electrodes that conducted 110 volts of alternating current through the exposed heart. Modern external defibrillators are available in a variety of designs with proprietary waveforms (eg, biphasic truncated exponential, pulsed biphasic, rectilinear biphasic, damped sinusoid monophasic, and monophasic truncated exponential) specific to the manufacturer. Most current models employ biphasic waveforms, which require less energy to terminate VF and improve first shock success.^{40,41}

Clinicians should be familiar with the defibrillators available to them and the manufacturers’ recommendations for use. The suggested energy for biphasic defibrillation depends on the manufacturer, varying between 150 and 360 joules.^{43,44} However, concerns have arisen regarding the effectiveness of the recommended first shock energies, prompting some prehospital agencies to implement a “highest dose first” strategy.

Timing of Shock Delivery

Early defibrillation historically has been considered a key link in the “chain of survival” for its vitally important role in minimizing the interval until ROSC.⁴⁵ However, research suggests that defibrillating a myocardium depleted of high-energy phosphates may increase the incidence of post-defibrillation asystole — an observation that begs the question: should chest compressions be performed prior to defibrillation to restore high-energy phosphates and “prime” the myocardium?⁴⁶⁻⁴⁸ Three studies designed to address this question have produced conflicting results. Two failed to demonstrate any benefit of CPR prior to defibrillation, but a third showed a survival benefit in a subgroup of patients for whom EMS response exceeded 4 minutes.⁴⁹⁻⁵¹ A 2011 international randomized trial involving nearly 10,000 patients failed to show a difference in the ability of the two strategies to improve survival rates with good neurological outcomes.⁵²

Minimizing Peri-Shock Pauses

The peri-shock pause begins when compressions are stopped to allow defibrillation and ends when compressions are resumed (*Figure 5-2*). Logistically, this period often includes a rhythm assessment, charging the defibrillator, delivering the defibrillation, and waiting for instructions to resume chest compressions.

The duration of the peri-shock pause is inversely associated with both ROSC and survival; it should be minimized as much as possible.⁵³ Reductions in the use of

this strategy, particularly the preshock component (ie, for rhythm analysis and defibrillator charging), increase the likelihood of survival.⁵⁴

The pit crew-style CPR techniques endorsed by the American Heart Association, including the “Seattle Switch” protocol (Table 5-1), directly address the peri-shock pause. Care providers should communicate with each other to ensure that the device is charging while a compression cycle is finishing. Additionally, using a monitor defibrillator in “manual” mode (as opposed to “AED” mode) may help reduce the preshock pause and improve ROSC.

The primary activities during the postshock pause are rhythm and pulse checks after defibrillation. Notably, myocardial stunning is very common in the period after ROSC.⁵⁵ Even if successfully defibrillated, patients might be hypotensive initially, with weak or absent peripheral pulses. Furthermore, interrupting compressions to perform pulse checks may decrease a patient’s odds of survival.⁵⁶ It is prudent to immediately follow a defibrillation attempt with an additional cycle (2 minutes) of chest compressions to minimize the postshock pause.⁵⁷ The pit-crew techniques discussed above can help facilitate coordination between the care providers.

“Hands-on defibrillation” — essentially continuing compressions while a shock is administered — is an alternative technique for eliminating the peri-shock pause altogether. A compelling study of patients undergoing elective cardioversion with a biphasic defibrillator demonstrated that rescuers, protected only by standard polyethylene gloves, could be in contact with the chest without exposure to dangerous levels of current.⁵⁸ Subsequent preclinical investigations have yielded conflicting results about the level of current to which caregivers are exposed; further study is necessary to determine the safety of this technique over the range of conditions encountered during resuscitation.^{59,60}

Double-Sequence Defibrillation

In some cases of refractory fibrillation, successful restoration of a perfusing rhythm has been achieved through double-sequential defibrillation (ie, the discharge of two defibrillators nearly simultaneously [Figure 5-3]). The technique first was described in the electrophysiology lab as a strategy for terminating persistent atrial fibrillation. Since then, it has been used with some success in correcting out-of-hospital VF.^{61,62}

PEARLS

- ✓ Increased lengths of peri-shock pause are negatively associated with patient survival rates.
- ✓ Be careful and creative in choosing logistic maneuvers so as to minimize hands-off time.

Airway Adjuncts

The two airway adjuncts most commonly available are oropharyngeal and nasopharyngeal devices — both of which have a long history of use, despite the lack of research supporting their utility in human CPR. In typical cases, the insertion of these noninvasive airway adjuncts will maximize the seal during positive-pressure ventilation and mitigate any obstruction caused by the patient’s tongue and oropharyngeal structures. However, inadvertent intracranial insertion of a nasopharyngeal airway has been reported in patients with basal skull fractures.^{63,64}

Cricoid Pressure

Cricoid pressure originally was proposed to reduce gastric inflation during ventilation with a bag-valve mask (BVM); however, the studies that demonstrated its benefits used much higher tidal volumes than those currently recommended.^{65,66} More recent research shows that cricoid pressure hampers

FIGURE 5-2. Schematic of Peri-Shock Pause

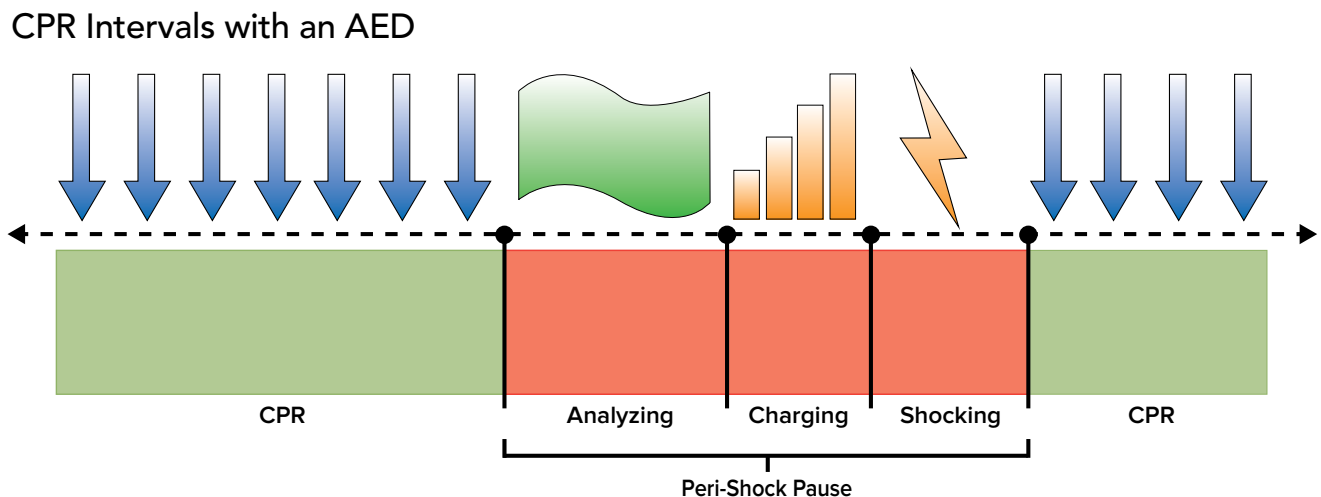


TABLE 5-1. The “Seattle Switch” Procedure

1. At the 1:45 mark, begin thinking about the next defibrillation. Tip: if doing 30:2, the heart rhythm can be seen during ventilations.
2. Ask aloud, “Who is next on chest compressions?” That individual should line up behind the rescuer doing CPR.
3. Precharge the defibrillator without interrupting chest compressions.
4. As soon as the defibrillator begins charging, the BVM should be removed from the patient’s face.
5. Once the defibrillator has charged, announce “Stop CPR.”
6. The provider doing chest compressions should clear out of the way (this is the start of the peri-shock pause).
7. The provider on the monitor should quickly verify that the rhythm is shockable and press “shock.”
8. Once the shock has been delivered (or if the rhythm is nonshockable), announce, “Continue CPR.”
9. A new rescuer should start compressions (this is the end of the peri-shock pause and the start of a new 2-minute cycle).
10. IVs, drugs, and advanced airway procedures are acceptable, provided they do not interfere with expertly performed BLS!
11. Once an advanced airway is in place, deliver asynchronous ventilations every 6 seconds (that’s slow).
12. If the patient fails to respond to pit crew CPR (>5 cycles and still no ROSC), consider switching to another resuscitation system.

the placement of both supraglottic and endotracheal airways, and hinders laryngeal mask airway placement and subsequent ventilation.⁶⁷⁻⁷⁴ The method also increases the time to intubation and reduces laryngoscopic views.⁶⁷⁻⁸² Cricoid pressure should not be applied routinely during airway management in cardiac arrest.

Advanced Airways

Prehospital advanced airway management is a controversial topic beyond the scope of this chapter. There is no clear evidence of its benefit, and the incidence of adverse events during intubation attempts becomes unacceptably high when prehospital personnel do not receive active, ongoing skill training.^{35, 83-88} Whether in the prehospital setting or in the emergency department, prolonged attempts at advanced airway management unnecessarily interrupt chest compressions, especially when acceptable alternatives are available. Evidence is mixed regarding the optimal timing of advanced airway management during cardiac arrest resuscitation; however, earlier airway management (<5 minutes) has been associated with an improved rate of 24-hour survival.⁸⁹

Intubations performed less than 12 minutes into the

resuscitation have been associated with better survival rates than those initiated after 13 minutes.⁹⁰ However, a bundled protocol that includes delayed intubation, passive oxygen delivery via nonbreather mask during CPR, and minimally interrupted chest compressions appears to improve neurological survival to hospital discharge in adults with witnessed OHCA who present with a shockable rhythm.⁹¹

Supraglottic airways are acceptable alternatives to endotracheal intubation during cardiac arrest resuscitation. Ventilation through a variety of these devices results in similar arterial blood gas values compared with traditional BVM ventilation.^{92,93} Additionally, ventilation through a laryngeal mask airway results in less regurgitation (3.5%) than ventilation with a bag-valve mask (12.4%).⁹⁴

Supraglottic airways perform as well as, or better than, endotracheal intubation in terms of insertion success, time to insertion, and ventilation parameters.⁹⁵⁻¹⁰³ They also can serve as rescue devices for difficult/failed intubations in cardiac arrest; however, their routine use, especially in cases of prehospital cardiac arrest, is discouraged.^{1, 96,97,101,104-109} One retrospective study comparing endotracheal intubation with an esophageal-tracheal Combitube found no difference in the rates of ROSC or survival.¹⁰² A 2013 Japanese study of more than 600,000 OHCA events independently linked advanced airway management via endotracheal tube or supraglottic device to worsened neurological outcomes.³⁷

Another retrospective study of more than 10,000 cardiac arrest cases found survival was highest among patients receiving airway management via bag-valve mask. The worst neurological outcomes were found in those who were ventilated with a supraglottic device.³⁶ Given the mixed evidence related to optimal airway management in cardiac arrest, a randomized pragmatic trial of airway management in OHCA (supraglottic airway vs. endotracheal intubation) recently was initiated (NIH: 8793277).

Regardless of the airway management strategy employed, confirmation of advanced airway placement is crucial. The best available standard is continuous waveform capnography, which has 100% sensitivity and 100% specificity in cardiac arrest.^{112,113} If this modality is unavailable, the combination of a colorimetric end-tidal CO₂ detector and clinical assessment is an acceptable alternative. When arrest occurs secondary to a suspected cardiac cause, advanced airway management does not appear to confer a distinct advantage over less invasive techniques such as bag-valve-mask ventilation. Indeed, important considerations with respect to initial airway management include avoiding interruptions in compressions and achieving airway patency.

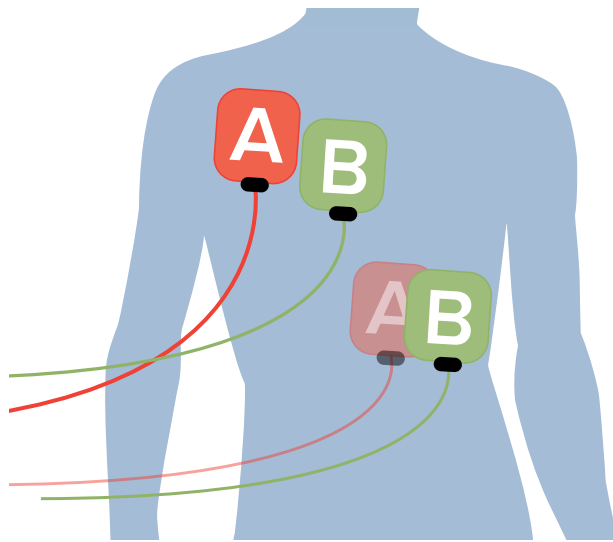
Oxygenation

Current convention dictates oxygenating with 100% fraction of inspired oxygen (FiO₂) during CPR, although preclinical animal research suggests that the higher percentage results in worse neurological outcomes than 21% FiO₂.

Passive oxygenation is one technique that can help

minimize interruptions in chest compressions. It is predicated on cycles of successive chest wall compressions and recoil that generate passive airflow while applying high-flow oxygen via a nonrebreather mask. If the tidal volumes generated are greater than the dead space, oxygenated air is moved into the lungs. If these volumes are insufficient, however, the turbulent mixing of air can result in molecular diffusion and subsequent gas exchange (much like the effects seen in high-frequency oscillatory ventilation).

FIGURE 5-3. Pad Placement for Double-Sequence Defibrillation



A simplified cardiac arrest protocol consisting of passive oxygenation via a nonrebreather mask and continuous chest compressions has been shown to improve rates of neurologically intact survival to hospital discharge in adults with witnessed cardiac arrest and a shockable initial rhythm.^{114,115}

Ventilation

The human data on ventilation parameters during CPR focus solely on respiratory rate and do not address minute ventilation or peak inspiratory pressure. The ventilatory rate frequently is too high during cardiac arrest resuscitation, and the use of real-time CPR feedback devices results in ventilation rates closer to those recommended in the guidelines.⁵⁰ Preliminary animal studies have associated hyperventilation with diminished hemodynamics and survival, but there are no human studies to support the avoidance of hyperventilation.³⁹

End-tidal carbon dioxide (CO₂) monitoring is a noninvasive method of obtaining physiological feedback during resuscitation; increases in CO₂ values typically herald ROSC.^{116,117} Additionally, end-tidal CO₂ values greater than 10 mm Hg during CPR are associated with ROSC,¹¹⁸ whereas those below 10 mm Hg may predict nonsurvival.¹¹⁹⁻¹²⁴ End-tidal CO₂ has not been evaluated specifically as a tool to guide resuscitation interventions in real time.

Pharmacotherapy

General Principles

There is a shifting deemphasis on pharmacological interventions based on a growing body of literature that acknowledges short-term improvements in ROSC but has yet to demonstrate long-term benefits. This lack of treatment effect in clinical studies is in contrast to the benefits observed in preclinical animal trials.¹²⁵ Pharmacotherapy in cardiac arrest originated from a canine model of VF in the 1960s, in which animals receiving epinephrine demonstrated an improved survival rate. The use of epinephrine primarily was intended to boost systemic vascular resistance, leading to increased cardiac preload, thus augmenting the ability of CPR to produce coronary perfusion pressure and end-organ perfusion.¹²⁶ Human investigations have found the same improvements in ROSC or short-term survival, but no resuscitation medication ever has been linked to improvements in survival to hospital discharge or favorable neurological outcomes.

Epinephrine

Despite nearly 50 years of continuous clinical use, there is equipoise regarding epinephrine for cardiac arrest. In recent years, the medication has been associated with a lower survival rate and poor neurological outcomes.¹²⁷⁻¹³⁰ Speculation as to the cause of these unfavorable long-term effects centers on compromised microvascular perfusion, beta-adrenergic-mediated toxicity, and the futility of transient survival in otherwise nonviable patients.¹³¹

The first study to directly investigate the use of epinephrine was a 2009 randomized controlled trial of IV line placement during resuscitation. Patients who received an infusion of the drug experienced a higher rate of ROSC (40%) compared with those who did not (25%); however, the rates of survival to discharge at 1 year did not differ between the groups.¹³² A post-hoc analysis of epinephrine administration yielded a negative association between the drug and good neurological outcomes.¹³³ A more recent propensity-matched, population-based study of more than 400,000 Japanese patients also linked the prehospital administration of epinephrine to an improved rate of ROSC but a decreased rate of survival to hospital discharge with favorable neurological outcomes.¹³⁴

Critics of this work point out variability in the dosing of epinephrine, the timing of its administration, and the post-arrest care of resuscitated patients. The standard dose of epinephrine used in resuscitation (1 mg or 0.05–0.1 mg/kg) was originally derived from a study of 20- to 30-kg dogs. This dose is tremendously supraphysiological and roughly 1,000 times the maximum dose used as a vasopressor in the resuscitation of patients in shock. Several studies in the 1990s explored even higher doses of epinephrine (3–5 mg).¹³⁶⁻¹³⁹ Not surprisingly, most found no improvement in long-term survival. A lower dose (<1 mg) might mitigate concerns regarding toxicity and microvascular compromise.¹³¹

Two recent retrospective studies addressed the timing of

epinephrine administration. In one cohort of more than 3,000 patients who were stratified by the first documented cardiac rhythm, those who received epinephrine within 10 minutes after the emergency call had a higher survival rate and better neurological outcomes than those who received the drug after 10 minutes.¹⁴⁰ Similarly, another study reported improved rates of ROSC and survival if epinephrine was administered within 10 minutes after the onset of cardiac arrest.¹⁴¹ Although the original observational studies of epinephrine were conducted before the era of therapeutic hypothermia and protocolized postarrest care, follow-up studies have addressed these concerns, yielding similar results.^{133,134} A robust, randomized, placebo-controlled trial of epinephrine in cardiac arrest is urgently warranted.

Vasopressin

A potent vasoconstrictor, vasopressin is associated with improved end-organ and cerebral blood flow and lacks the beta toxicity associated with epinephrine. Nonetheless, in head-to-head comparisons, vasopressin alone offers no survival advantage over epinephrine.¹⁴²⁻¹⁴⁴ Furthermore, the combination of the two drugs offers no survival advantage over epinephrine alone.^{145,146} In contrast, a recent trial of vasopressin, epinephrine, and methylprednisolone demonstrated improved survival rates and neurological outcomes.^{147,148} Several confounders (postarrest care protocols that include stress-dose steroids) make it difficult to assess the isolated effects of vasopressin.

Atropine

At best, atropine offers no survival benefit; at worst, it may diminish survival.¹⁴⁹⁻¹⁵⁴ The agent confers no mechanistic advantage during resuscitation from asystole and pulseless electrical activity, so its routine use cannot be recommended.

Antiarrhythmics

Current guidelines recommend the administration of an antiarrhythmic medication if VF or ventricular tachycardia (VT) persists after one defibrillation attempt and 2 minutes of CPR. Amiodarone is the preferred agent, but lidocaine can be given if amiodarone is unavailable. Several studies point to an improved rate of survival to hospital admission in patients receiving amiodarone versus lidocaine for refractory or recurrent VF/VT; however, neither drug has been shown to improve long-term survival or neurological function.^{133,155-157} A three-arm, randomized, blinded, multicenter study of 3,000 OHCA patients with shock-resistant ventricular dysrhythmias found no difference in survival or favorable neurological outcome between patients taking amiodarone, lidocaine, or placebo. A subgroup analysis of patients with witnessed cardiac arrest found that those receiving active drugs (amiodarone or lidocaine) were more likely to survive than those receiving placebo.¹⁵⁸

Systems Issues

Termination of Resuscitation

Advances in resuscitation science continue to shed light on which patient populations are most likely to survive a

cardiac arrest event. Factors consistently linked to survival include prompt bystander CPR, quality uninterrupted chest compressions, and early defibrillation.

In an attempt to develop universally applicable guidelines for the prehospital termination of resuscitation (TOR), a team of researchers prospectively validated a previously established set of rules for BLS providers in a cohort of 2,145 OHCA patients (Table 5-2).¹⁵⁹ These rules demonstrated 100% specificity for recommending transport of potential survivors and a positive predictive value of 100% for death. The predicted transport rate was 46%.

A set of universal set of TOR rules could minimize practice variations among physicians providing online medical control. Established protocols also could improve resource utilization and EMS safety by reducing the number of patients transported to hospitals; however, this reduction could impede the development of new strategies and techniques for managing those currently deemed unresuscitatable. Universal TOR rules also open the possibility for occasional — albeit rare — premature terminations of resuscitation.

Regionalization of Care

Patients in cardiac arrest and those who have been resuscitated should be managed at a regionalized cardiac arrest center. This is not a new model of care for time-sensitive interventions. Trauma, ST-elevation myocardial infarction (STEMI), and acute stroke all take advantage of established, regionalized systems of care that coordinate prehospital units with receiving centers. Several case-control studies have highlighted the effectiveness of bundled postresuscitation care, demonstrating improved results compared with historical controls.^{8,160-165} Typical hospital-based physicians treat postcardiac arrest patients infrequently, given the low rates of resuscitation in communities. Regionalized cardiac arrest centers increase referral volumes and thereby the experience of clinicians.¹⁶⁶ The positive correlation between care providers' experience (or procedural volume) with complex diagnoses (or procedures) and better patient outcomes is well documented.¹⁶⁷

An accumulating body of evidence points to improved outcomes when cardiac arrest patients are treated at regionalized centers.¹⁶⁸ Several studies have described the great influence these transportation decisions can have on outcomes.¹⁶⁹ In one German study, the patients treated in a PCI center were more than 3 times as likely to survive with a favorable neurological outcome. Another study investigated 27,000 Korean patients who were transported to hospitals with CPR in progress.¹⁷⁰

TABLE 5-2. Validated Universal Rules for Prehospital Termination of Resuscitation

No return of spontaneous circulation prior to transport
No shock administered
Arrest not witnessed by EMS personnel

TABLE 5-3. Proposed Clinical Services for Regionalized Cardiac Arrest Centers

Neurological Services

- Induced hypothermia
- Continuous EEG monitoring
- Seizure management
- Neurology consultation
- Neurosurgical consultation
- Cerebral imaging (CT, MRI, perfusion studies)
- Neurophysiological testing (evoked potentials)
- Prognostication services

Critical Care Services

- Ventilator management
- Glucose control
- Goal-directed hemodynamic management

Cardiovascular Services

- Cardiac catheterization/percutaneous coronary intervention
- Coronary artery bypass grafting
- Intraaortic balloon pump
- Cardiovascular mechanical support devices
- Extracorporeal membranous oxygenation (ECMO)
- Transplant surgery consultation
- Electrophysiology consultation
- ICD placement

Other Services

- Physical medicine and rehabilitation consultation
- Physical and occupational therapy
- Social work
- Organ donation
- Outpatient physical and occupational therapy
- Outpatient neurological rehabilitation
- Outpatient psychological services

Even with longer transport intervals, those transferred to high-volume centers were more likely to survive to hospital discharge than those treated in low-volume centers.

One of the common barriers to the implementation of regionalized cardiac arrest care is patient transport. The decision to bypass a local hospital to transport a patient to a more distant resuscitation center is controversial. However, two recent studies indicate that prehospital transfer time does not independently affect patient outcomes after cardiac arrest, suggesting the feasibility of a modest increase in transport intervals.^{172,173} Likewise, patients who achieve ROSC at a local hospital should be strongly considered for interfacility transfer to a regional cardiac arrest center, which also is far likelier to offer organ donation and procurement services for those who do not survive (*Table 5-2*).¹⁷¹

A study of 248 resuscitated patients transferred to tertiary care facilities with a median transport time of 63 minutes found that rearrest was uncommon (6%) and critical events (eg, hypotension and/or hypoxia) affected 23% of patients during transport.¹⁷⁴ Most critical events took place within the first hour of transport, and 27% occurred at the referring facility prior to departure. Patients taking vasopressors were most likely to suffer critical events. When weighing the risk of transport against the overall survival rate (53%) and survival rate of patients suffering a critical event (29%), the researchers found that those referred to a cardiac arrest center from an outlying facility derived benefit, with an acceptable risk of decompensation en route.

Special Populations

Traumatic Cardiac Arrest

Most causes of traumatic cardiac arrest, which historically has carried a dismal prognosis, are related to airway maintenance, thoracic trauma that impedes adequate oxygenation/ventilation, hemorrhage, or intracranial injury. Diagnostic and therapeutic interventions should be tailored to these underlying factors.

KEY POINTS

1. Achieving return of spontaneous circulation is one component of an effective cardiac arrest strategy. Comprehensive resuscitation care requires the engagement of both emergency health care practitioners and the lay public.
2. There is no evidence to support the routine use of mechanical chest compression devices in the prehospital setting for undifferentiated cardiac arrest.
3. In select patients, mechanical chest compression devices provide a bridge to invasive therapies.
4. Although data regarding the need for rescue breaths during CPR are inconsistent, there is consensus on the need for prompt, effective chest compressions with limited interruptions.
5. Know the defibrillator model used in your institution as well as the manufacturer's recommended energy selection.
6. For witnessed arrests with a shockable rhythm, it is reasonable to defibrillate before starting CPR. For unwitnessed arrests with a shockable rhythm, it is reasonable to perform CPR before defibrillating.
7. Increasing lengths of the peri-shock pause are negatively associated with the survival rate.
8. Be careful and creative in choosing logistic maneuvers so as to minimize hands-off time.
9. Cricoid pressure impairs laryngoscopy and the placement of advanced airways; it should not be performed routinely.
10. Evidence for advanced airway management in the setting of out-of-hospital cardiac arrest is lacking. Supraglottic devices and endotracheal intubation have been associated with an increase in mortality rate.

In the setting of traumatic cardiac arrest, the clinician should focus on prompt airway management, empiric chest tube placement, hemorrhage control, the transfusion of blood products, and consideration of resuscitative thoracotomy. Conventional ACLS measures are unlikely to add value in cases of traumatic cardiac arrest. In advanced centers, extracorporeal membranous oxygenation (ECMO) or resuscitative endovascular balloon occlusion of the aorta (REBOA) may be considered for select patients.

Poisoned Patients

Since resuscitation of the critically ill patient often is undertaken without the benefit of a complete medical history, consideration of underlying causes is of prime importance. Certain toxidromes are associated with myocardial depression, lethal arrhythmias, and high fatality rates. In specific cases, the administration of a particular ACLS drug can counteract a poison's deleterious effects. Consider consulting with a regional poison control center when appropriate. (*Also see chapter 16.*)

Pediatric Patients

All providers who perform resuscitation must maintain proficiency in pediatric emergency skills. In children, cardiac arrest typically results from hypoxic insult (as opposed to lethal arrhythmia), so special attention to airway management is of extreme importance when managing these vulnerable patients. In general, pediatric resuscitation emphasizes airway management and the correction of underlying pathology. More detailed information is provided in chapter 25.

The value of quality compressions and BLS cannot be overstated. Lengthy attempts to establish intravenous access are discouraged in favor of quicker modalities such as intraosseous needle insertion. Devices such as the E-Z IO drill (Vidacare, Shavano Park, TX) minimize the technical difficulty of placing a catheter into the bone marrow.

Some tertiary care centers report favorable results with extra-

corporeal membrane oxygenation in victims of refractory arrest.¹⁷⁵ This technology can enhance the resuscitation armamentarium in hospitals with specialized personnel and equipment. Finally, adequate preparation and training are essential. Pediatric supplies must be readily accessible and familiar to all clinicians charged with leading resuscitation. Weight-based drug regimens and color-coded kits containing appropriately sized equipment can minimize stress during an arrest scenario.

Future Directions

Extracorporeal Life Support

Extracorporeal life support (ECLS) — the incorporation of ECMO into cardiac arrest resuscitation — is a resource-intensive therapy that has been deployed successfully to boost neurological survival in select patients suffering OHCA. Japan, which boasts one of the most sophisticated ECLS systems in the world, determines patient eligibility using the following criteria:

- Age 18 to 74 years
- Bystander-witnessed cardiac arrest
- Presumed cardiac etiology
- Less than 15 minutes from collapse until EMS arrival
- Shockable rhythm
- Persistent cardiac arrest on arrival¹⁷⁶

Eligible patients are cannulated percutaneously for ECMO in the emergency department while CPR is in progress. Once life support is initiated, patients are cooled rapidly with the ECMO circuit while receiving urgent coronary angiography, PCI (if indicated), and insertion of an intraaortic balloon pump.

There is a clear stepwise relationship between outcomes and quartiles of the intervals. The optimal cutoffs in the Japanese ECLS system are 55.5 minutes for the collapse-to-ECMO interval and 21.5 minutes for the ECMO-to-34°C (93.2°F) interval. The odds of survival with a positive neurological outcome is 50% or higher when the ECMO-to-34°C (93.2°F) interval is less than 21.5 minutes, regardless of the collapse-to-ECMO interval. A cumulative review of the Japanese ECLS literature through 2011

11. Prehospital airway management should not take precedence over the performance of high-quality uninterrupted chest compressions.
12. Endotracheal tube placement should be confirmed with continuous waveform capnography.
13. After return of spontaneous circulation, oxygenation and ventilation strategies should aim for minimally necessary FiO₂ and normocarbica. There is little evidence to guide these strategies during resuscitation.
14. Indications for resuscitation drugs need to be reevaluated in the context of modern postresuscitation care.
15. Although the routine use of vasopressors can improve the rate of ROSC, there is no evidence that the practice improves survival rates or neurological outcomes. These agents might, in fact, worsen long-term outcomes.
16. Antiarrhythmic medications might offer short-term benefits, but they never have been associated with survival or favorable neurological outcomes.
17. Sodium bicarbonate does not improve outcomes and could be harmful.
18. Calcium, magnesium, and fibrinolytic agents should be reserved for the treatment of an underlying pathology in special cases of cardiac arrest.
19. When geographically feasible, patients with OHCA should be transported to a cardiac arrest center.
20. Patients resuscitated at a local hospital should be evaluated for transfer to a facility capable of the providing the full spectrum of postcardiac arrest care.

found 1,282 patients who experienced OHCA between 1983 and 2008 and received ECLS.¹⁷⁷ Among the 516 patients with available data, 27% survived to hospital discharge. Approximately 50% of the cases resulted in mild or no neurological disabilities. Another propensity-adjusted analysis of ECLS in patients with witnessed OHCA of cardiac origin found a 3-fold improvement in the 90-day neurologically intact survival rate (29% vs. 8%).¹⁷⁸ A randomized comparison of ECLS and traditional resuscitation is being planned by investigators in Prague, Czech Republic.¹⁷⁹

The success of any ECLS program hinges on patient selection and collaboration among prehospital, emergency department, and critical care personnel. ECLS is a resource-intensive endeavor in which successful outcomes are extremely time dependent.

Goal-Directed Intraarrest Resuscitation

Preclinical research and small human studies have explored the possibility of hemodynamic-directed CPR as a model for individually tailored resuscitation.^{126,180-184} In contrast to the “one-size-fits-all” prescription for advanced cardiac life support, hemodynamic-directed CPR attempts to account for an individual patient’s response to resuscitative efforts. This approach requires invasive hemodynamic monitoring and will be best tested in patients who experience an in-hospital cardiac arrest. In theory, CPR metrics and vasopressors can be used to target specific hemodynamic goals such as diastolic blood pressure or coronary perfusion pressure. Targeting these endpoints might reduce vasopressor use, thereby increasing cerebral perfusion pressure and brain tissue oxygenation.

Waveform-Guided Defibrillation

Preclinical data suggest that the VF waveform can be used to guide the timing of defibrillation — the success of which can be predicted using a quantitative analysis of the waveform. Certain waveform characteristics (eg, amplitude, frequency, periodicity) are associated with coronary perfusion pressure and myocardial ATP concentration.¹⁸⁵⁻¹⁸⁷ Many clinicians are familiar with the practice of delaying shock delivery for “fine” VF to provide CPR, improve perfusion of the myocardium, and increase the “coarseness” of the waveform.^{50,188,189} Real-time, automated waveform analysis currently is not available, and the ability of providers to interpret the information has not been studied.

Conclusion

Cardiac arrest is a complex disease. As resuscitation professionals, emergency care providers should move beyond the rote memorization of protocols and understand the science and evidence behind the latest treatment guidelines. In addition, they must be diligent in hunting for treatable causes of cardiac arrest during the brief window afforded by resuscitative measures. Despite technological advances and the maturity of resuscitation science, the priorities of resuscitation remain unchanged.

Careful attention to high-quality minimally interrupted compressions affords patients the best chance for surviving neurologically intact. Intraarrest advanced airway management must not interrupt the delivery of compressions. High-performing prehospital EMS systems have implemented interventions

such as “pit crew” CPR to improve survival and preserve a patient’s functional neurological status through the initiation of compressions, defibrillation, and goal-directed postarrest care.

PEARL

Extracorporeal life support is an option for a subset of patients whose cardiac arrest was witnessed and who receive quality CPR, but are refractory to initial resuscitative measures. ECLS requires a significant investment of time and resources and is feasible only at select centers.

REFERENCES

- Sayre MR, Koster RW, Botha M, et al. Part 5: Adult basic life support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2010;122(16 suppl 2):S298-S324.
- Writing Group Members, Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics — 2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2-220.
- Herlitz J, Svensson L, Engdahl J, et al. Characteristics of cardiac arrest and resuscitation by age group: an analysis from the Swedish cardiac arrest registry. *Am J Emerg Med*. 2007;25:1025-1031.
- Ong ME, Stiell I, Osmond MH, et al. Etiology of pediatric out-of-hospital cardiac arrest by coroner’s diagnosis. *Resuscitation*. 2006;68:335-342.
- Kuisma M, Alaspaa A. Out-of-hospital cardiac arrests of non-cardiac origin: epidemiology and outcome. *Eur Heart J*. 1997;18:1122-1128.
- Kurkciyan I, Meron G, Behringer W, et al. Accuracy and impact of presumed cause in patients with cardiac arrest. *Circulation*. 1998;98:766-771.
- Nichol G, Thomas E, Callaway CW, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA*. 2008;300:1423-1431.
- Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*. 2007;73:29-39.
- Bobrow BJ, Vadeboncoeur TF, Stolz U, et al. The influence of scenario-based training and real-time audiovisual feedback on out-of-hospital cardiopulmonary resuscitation quality and survival from out-of-hospital cardiac arrest. *Ann Emerg Med*. 2013;62:47-56.
- Perkins GD, Brace S, Gates S. Mechanical chest-compression devices: current and future roles. *Curr Opin Crit Care*. 2010;16:203-210.
- Wagner H, Terkelsen CJ, Friberg H, et al. Cardiac arrest in the catheterisation laboratory: a 5-year experience of using mechanical chest compressions to facilitate PCI during prolonged resuscitation efforts. *Resuscitation*. 2010;81:383-387.
- Larsen AI, Hjørnevik AS, Ellingsen CL, Nilsen DW. Cardiac arrest with continuous mechanical chest compression during percutaneous coronary intervention: a report on the use of the LUCAS device. *Resuscitation*. 2007;75:454-459.
- Stub D, Bernard S, Pellegrino V, et al. Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial). *Resuscitation*. 2014 Oct 2. pii: S0300-9572(14)00751-5. doi: 10.1016/j.resuscitation.2014.09.010. [Epub ahead of print]
- Zimmermann S, Rohde D, Marwan M, et al. Complete recovery after out-of-hospital cardiac arrest with prolonged (59 min) mechanical cardiopulmonary resuscitation, mild therapeutic hypothermia and complex percutaneous coronary intervention for ST-elevation myocardial infarction. *Heart Lung*. 2014;43:62-65. doi:10.1016/j.hrtlng.2013.10.011.
- McDonald JL. Systolic and mean arterial pressures during manual and mechanical CPR in humans. *Ann Emerg Med*. 1982;11:292-295.
- Ward KR, Menegazzi JJ, Zelenak RR, et al. Comparison of chest compressions between mechanical and manual CPR by monitoring end-tidal PCO2 during human cardiac arrest. *Ann Emerg Med*. 1993;22:669-674.
- Rubertsson S, Karlsten R. Increased cortical cerebral blood flow with LUCAS; a new device for mechanical chest compressions compared to standard external compressions during experimental cardiopulmonary resuscitation. *Resuscitation*. 2005;65:357-363.
- Rubertsson S, Lindgren E, Smekal D, et al. Mechanical chest compressions and simultaneous defibrillation vs conventional cardiopulmonary resuscitation in out-of-hospital cardiac arrest: the LINC randomized trial. *JAMA*. 2014;311:53-61.
- Axelsson C, Nestin J, Svensson L, et al. Clinical consequences of the introduction of mechanical chest compression in the EMS system for treatment of out-of-hospital cardiac arrest — a pilot study. *Resuscitation*. 2006;71:47-55.
- Smekal D, Johansson J, Huzevka T, Rubertsson S. A pilot study of mechanical chest compressions with the LUCAS device in cardiopulmonary resuscitation. *Resuscitation*. 2011;82:702-706.
- Westfall M, Krantz S, Mullin C, Kaufman C. Mechanical versus manual chest compressions in out-of-hospital cardiac arrest: a meta-analysis. *Crit Care Med*. 2013;41:1782-1789. doi: 10.1097/CCM.0b013e31828a24e3.
- Yost D, Phillips RH, Gonzales L, et al. Assessment of CPR interruptions from transthoracic impedance during use of the LUCAS mechanical chest compression system. *Resuscitation*. 2012;83:961-965.

23. Ong ME, Annathurai A, Shahidah A, et al. Cardiopulmonary resuscitation interruptions with the use of a load-distributing band device during emergency department cardiac arrest. *Ann Emerg Med.* 2010;56:233-241.
24. Krischer JP, Fine EG, Davis JH, Nagel EL. Complications of cardiac resuscitation. *Chest.* 1987;92:287-291.
25. Bonnemeier H, Simonis G, Olivecrona G, et al. Continuous mechanical chest compression during in-hospital cardiopulmonary resuscitation of patients with pulseless electrical activity. *Resuscitation.* 2011;82:155-159.
26. Wyss CA, Fox J, Franzeck F, et al. Mechanical versus manual chest compression during CPR in a cardiac catheterisation setting. *Cardiovascular Med.* 2010;12:92-96.
27. Groggaard HK, Wik L, Eriksen M, et al. Continuous chest compressions during cardiac arrest to facilitate restoration of coronary circulation with percutaneous coronary intervention. *J Am Coll Cardiol.* 2007;50:1093-1094.
28. Sayre MR, Berg RA, Cave DM, et al. Hands-only (compression only) cardiopulmonary resuscitation: a call to action for bystander response to adults who experience out-of-hospital sudden cardiac arrest: a science advisory for the public from the American Heart Association Emergency Cardiovascular Care Committee. *Circulation.* 2008;117:2162-2167.
29. Rea T, Fahrenbruch C, Culley L, et al. CPR with chest compression alone or with rescue breathing. *N Engl J Med.* 2010;363:423-433.
30. Kitamura T, Iwami T, Kawamura T, et al. Bystander-initiated rescue breathing for out-of-hospital cardiac arrests of noncardiac origin. *Circulation.* 2010;122:293-299.
31. Japanese Circulation Society Resuscitation Science Study Group. Chest-compression-only bystander cardiopulmonary resuscitation in the 30:2 compression-to-ventilation ratio era. *Circ J.* 2013;77:2742-2750.
32. Yao L, Wang P, Zhou L, Chen M, et al. Compression-only cardiopulmonary resuscitation vs standard cardiopulmonary resuscitation: an updated meta-analysis of observational studies. *Am J Emerg Med.* 2014;32:517-523.
33. Mader TJ, Paquette AT, Salcido DD, et al. The effect of the preshock pause on coronary perfusion pressure decay and rescue shock outcome in porcine ventricular fibrillation. *Prehosp Emerg Care.* 2009;13:487-494.
34. Kern KB, Ewy GA, Voorhees WD, et al. Myocardial perfusion pressure: a predictor of 24-hour survival during prolonged cardiac arrest in dogs. *Resuscitation.* 1998;16:241-250.
35. Carlson JN, Reynolds JC. Does advanced airway management improve outcomes in adult out-of-hospital cardiac arrest? *Ann Emerg Med.* 2014;64:163-164.
36. McMullan J, Gerecht R, Bonomo J, et al; CARES Surveillance Group. Airway management and out-of-hospital cardiac arrest outcome in the CARES registry. *Resuscitation.* 2014;85:617-622.
37. Hasegawa K, Hiraide A, Chang Y, Brown DF. Association of prehospital advanced airway management with neurologic outcome and survival in patients with out-of-hospital cardiac arrest. *JAMA.* 2013;309:257-266.
38. Shin SD, Ahn KO, Song KJ, et al. Out-of-hospital airway management and cardiac arrest outcomes: a propensity score matched analysis. *Resuscitation.* 2012;83:313-319.
39. Aufderheide TP, Sigurdsson G, Pirralo RG, et al. Hyperventilation-induced hypotension during cardiopulmonary resuscitation. *Circulation.* 2004;109:1960-1965.
40. Schneider T, Martens PR, Paschen H, et al. Multicenter, randomized, controlled trial of 150-J biphasic shocks compared with 200- to 360-J monophasic shocks in the resuscitation of out-of-hospital cardiac arrest victims. Optimized Response to Cardiac Arrest (ORCA) Investigators. *Circulation.* 2000;102:1780-1787.
41. van Alem AP, Chapman FW, Lank P, et al. A prospective, randomised and blinded comparison of first shock success of monophasic and biphasic waveforms in out-of-hospital cardiac arrest. *Resuscitation.* 2003;58:17-24.
42. Kudenchuk PJ, Cobb LA, Copass MK, et al. Transthoracic incremental monophasic versus biphasic defibrillation by emergency responders (TIMBER): a randomized comparison of monophasic with biphasic waveform ascending energy defibrillation for the resuscitation of out-of-hospital cardiac arrest due to ventricular fibrillation. *Circulation.* 2006;114:2010-2018.
43. Stiell IG, Walker RG, Nesbitt LB, et al. BIPHASIC Trial: a randomized comparison of fixed lower versus escalating higher energy levels for defibrillation in out-of-hospital cardiac arrest. *Circulation.* 2007;115:1511-1517.
44. Walsh SJ, McClelland AJ, Owens CG, et al. Efficacy of distinct energy delivery protocols comparing two biphasic defibrillators for cardiac arrest. *Am J Cardiol.* 2004;94:378-380.
45. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: the "chain of survival" concept. A statement for health professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. *Circulation.* 1991;83:1832-1847.
46. Weaver WD, Cobb LA, Dennis D, et al. Amplitude of ventricular fibrillation waveform and outcome after cardiac arrest. *Ann Intern Med.* 1985;102:53-55.
47. Reynolds JC, Salcido DD, Menegazzi JJ. Conceptual models of coronary perfusion pressure and their relationship to defibrillation success in a porcine model of prolonged out-of-hospital cardiac arrest. *Resuscitation.* 2012;83:900-906.
48. Reynolds JC, Salcido DD, Menegazzi JJ. Coronary perfusion pressure and return of spontaneous circulation after prolonged cardiac arrest. *Prehosp Emerg Care.* 2010;14:78-84.
49. Cobb LA, Fahrenbruch CE, Walsh TR, et al. Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA.* 1999;281:1182-1188.
50. Wik L, Hansen TB, Fylling F, et al. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. *JAMA.* 2003;289:1389-1395.
51. Jacobs IG, Finn JC, Oxer HF, et al. CPR before defibrillation in out-of-hospital cardiac arrest: a randomized trial. *Emerg Med Australas.* 2005;17:39-45. Erratum in *Emerg Med Australas.* 2009;21:430.
52. Stiell IG, Nichol G, Leroux BG, et al; ROC Investigators. Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest. *N Engl J Med.* 2011;365:787-797.
53. Cheskes S, Schmicker RH, Christenson J, et al; Resuscitation Outcomes Consortium (ROC) Investigators. Preshock pause: an independent predictor of survival from out-of-hospital shockable cardiac arrest. *Circulation.* 2011;124:58-66.
54. Cheskes S, Schmicker RH, Verbeek PR, et al; Resuscitation Outcomes Consortium (ROC) Investigators. The impact of peri-shock pause on survival from out-of-hospital shockable cardiac arrest during the Resuscitation Outcomes Consortium PRIMED trial. *Resuscitation.* 2014;85:336-342.
55. Zia A, Kern KB. Management of postcardiac arrest myocardial dysfunction. *Curr Opin Crit Care.* 2011;17:241-246.
56. Eftestol T, Sunde K, Steen PA. Effects of interrupting precordial compressions on the calculated probability of defibrillation success during out-of-hospital cardiac arrest. *Circulation.* 2002;105:2270-2273.
57. Rea TD, Helbock M, Perry S, et al. Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: survival implications of guideline changes. *Circulation.* 2006;114:2760-2765.
58. Lloyd MS, Heeke B, Walter PF, Langberg JJ. Hands-on defibrillation: an analysis of electrical current flow through rescuers in direct contact with patients during biphasic external defibrillation. *Circulation.* 2008;117:2510-2514.
59. Neumann T, Gruenewald M, Lauenstein C, et al. Hands-on defibrillation has the potential to improve the quality of cardiopulmonary resuscitation and is safe for rescuers — a preclinical study. *J Am Heart Assoc.* 2012;1:e001313.
60. Deakin CD, Lee-Shrewsbury V, Hogg K, Petley GW. Do clinical examination gloves provide adequate electrical insulation for safe hands-on defibrillation? I: Resistive properties of nitrile gloves. *Resuscitation.* 2013;84:895-899.
61. Alaeddini J, Feng Z, Feghali G, et al. Repeated dual external direct cardioversions using two simultaneous 360-J shocks for refractory atrial fibrillation are safe and effective. *Pacing Clin Electrophysiol.* 2005;28:3-7.
62. Leacock BW. Double simultaneous defibrillators for refractory ventricular fibrillation. *J Emerg Med.* 2014;46:472-474.
63. Schade K, Borzotta A, Michaels A. Intracranial malposition of nasopharyngeal airway. *J Trauma.* 2000;49:967-968.
64. Muzzi DA, Losasso TJ, Cucchiara RF. Complication from a nasopharyngeal airway in a patient with a basilar skull fracture. *Anesthesiology.* 1991;74:366-368.
65. Petito SP, Russell WJ. The prevention of gastric inflation: a neglected benefit of cricoid pressure. *Anaesth Intensive Care.* 1988;16:139-143.
66. Lawes EG, Campbell I, Mercer D. Inflation pressure, gastric insufflation and rapid sequence induction. *Br J Anaesth.* 1987;59:315-318.
67. Asai T, Barclay K, Power I, Vaughan RS. Cricoid pressure impedes placement of the laryngeal mask airway and subsequent tracheal intubation through the mask. *Br J Anaesth.* 1994;72:47-51.
68. Asai T, Barclay K, Power I, Vaughan RS. Cricoid pressure impedes placement of the laryngeal mask airway. *Br J Anaesth.* 1995;74: 521-525.
69. Ansermino JM, Blogg CE. Cricoid pressure may prevent insertion of the laryngeal mask airway. *Br J Anaesth.* 1992;69:465-467.
70. Aoyama K, Takenaka I, Sata T, Shigematsu A. Cricoid pressure impedes positioning and ventilation through the laryngeal mask airway. *Can J Anaesth.* 1996;43:1035-1040.
71. Brimacombe J, White A, Berry A. Effect of cricoid pressure on ease of insertion of the laryngeal mask airway. *Br J Anaesth.* 1993;71: 800-802.
72. Gabbott DA, Sasada MP. Laryngeal mask airway insertion using cricoid pressure and manual in-line neck stabilisation. *Anaesthesia.* 1995;50:674-676.
73. Xue FS, Mao P, Li CW, et al. Influence of pressure on cricoid on insertion ProSeal laryngeal mask airway and ventilation function [in Chinese]. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue.* 2007;19:532-535.
74. Li CW, Xue FS, Xu YC, et al. Cricoid pressure impedes insertion of, and ventilation through, the ProSeal laryngeal mask airway in anesthetized, paralyzed patients. *Anesth Analg.* 2007;104:1195-1198.
75. McNelis U, Syndercombe A, Harper J, Duggan J. The effect of cricoid pressure on intubation facilitated by the gum elastic bougie. *Anaesthesia.* 2007;62:456-459.
76. Harry RM, Nolan JP. The use of cricoid pressure with the intubating laryngeal mask. *Anaesthesia.* 1999;54:656-659.
77. Noguchi T, Koga K, Shiga Y, Shigematsu A. The gum elastic bougie eases tracheal intubation while applying cricoid pressure compared to a stylet. *Can J Anaesth.* 2003;50:712-717.
78. Asai T, Murao K, Shingu K. Cricoid pressure applied after placement of laryngeal mask impedes subsequent fiberoptic tracheal intubation through mask. *Br J Anaesth.* 2000;85:256-261.
79. Snider DD, Clarke D, Finucane BT. The "BURP" maneuver worsens the glottic view when applied in combination with cricoid pressure. *Can J Anaesth.* 2005;52:100-104.
80. Smith CE, Boyer D. Cricoid pressure decreases ease of tracheal intubation using fiberoptic laryngoscopy (WuScope System). *Can J Anaesth.* 2002;49:614-619.
81. Heath ML, Allagain J. Intubation through the laryngeal mask: a technique for unexpected difficult intubation. *Anaesthesia.* 1991;46: 545-548.
82. Levitan RM, Kinkle WC, Levin WJ, Everett WW. Laryngeal view during laryngoscopy: a randomized trial comparing cricoid pressure, backward-upward-rightward pressure, and bimanual laryngoscopy. *Ann Emerg Med.* 2006;47:548-555.
83. Bradley JS, Billows GL, Olinger ML, et al. Prehospital oral endotracheal intubation by rural basic emergency medical technicians. *Ann Emerg Med.* 1998;32:26-32.
84. Sayre MR, Sakles JC, Mistler AF, et al. Field trial of endotracheal intubation by basic EMTs. *Ann Emerg Med.* 1998;31:228-233.
85. Katz SH, Falk JL. Misplaced endotracheal tubes by paramedics in an urban emergency medical services system. *Ann Emerg Med.* 2001;37: 32-37.
86. Jones JH, Murphy MP, Dickson RL, et al. Emergency physician-verified out-of-hospital intubation: miss rates by paramedics. *Acad Emerg Med.* 2004;11:707-709.

87. Wirtz DD, Ortiz C, Newman DH, Zhitomirsky I. Unrecognized misplacement of endotracheal tubes by ground prehospital providers. *Prehosp Emerg Care.* 2007;11:213-218.
88. Timmermann A, Russo SG, Eich C, et al. The out-of-hospital esophageal and endobronchial intubations performed by emergency physicians. *Anesth Analg.* 2007;104:619-623.
89. Wong ML, Carey S, Mader TJ, Wang HE. Time to invasive airway placement and resuscitation outcomes after in-hospital cardiopulmonary arrest. *Resuscitation.* 2010;81:182-186.
90. Shy BD, Rea TD, Becker LJ, Eisenberg MS. Time to intubation and survival in prehospital cardiac arrest. *Prehosp Emerg Care.* 2004;8:394-399.
91. Bobrow BJ, Ewy GA, Clark L, et al. Passive oxygen insufflation is superior to bag-valve-mask ventilation for witnessed ventricular fibrillation out-of-hospital cardiac arrest. *Ann Emerg Med.* 2009;54:656-662.e651.
92. Rumball CJ, MacDonald D. The PTL, Combitube, laryngeal mask, and oral airway: a randomized prehospital comparative study of ventilatory device effectiveness and cost-effectiveness in 470 cases of cardiorespiratory arrest. *Prehosp Emerg Care.* 1997;1:1-10.
93. SOS-KANTO Study Group. Comparison of arterial blood gases of laryngeal mask airway and bag-valve-mask ventilation in out-of-hospital cardiac arrests. *Circ J.* 2009;73:490-496.
94. Stone BJ, Chantler PJ, Baskett PJ. The incidence of regurgitation during cardiopulmonary resuscitation: a comparison between the bag valve mask and laryngeal mask airway. *Resuscitation.* 1998;38:3-6.
95. Frass M, Frenzer R, Rauscha F, et al. Ventilation with the esophageal tracheal Combitube in cardiopulmonary resuscitation: promptness and effectiveness. *Chest.* 1988;93:781-784.
96. Atherton GL, Johnson JC. Ability of paramedics to use the Combitube in prehospital cardiac arrest. *Ann Emerg Med.* 1993;22:1263-1268.
97. Rabitsch W, Schellongowski P, Staudinger T, et al. Comparison of a conventional tracheal airway with the Combitube in an urban emergency medical services system run by physicians. *Resuscitation.* 2003;57:27-32.
98. Rumball C, Macdonald D, Barber P, et al. Endotracheal intubation and esophageal tracheal Combitube insertion by regular ambulance attendants: a comparative trial. *Prehosp Emerg Care.* 2004;8:15-22.
99. Samarkandi AH, Seraj MA, el Dawlatly A, et al. The role of laryngeal mask airway in cardiopulmonary resuscitation. *Resuscitation.* 1994;28:103-106.
100. Staudinger T, Brugger S, Watschinger B, et al. Emergency intubation with the Combitube: comparison with the endotracheal airway. *Ann Emerg Med.* 1993;22:1573-1575.
101. Staudinger T, Brugger S, Roggla M, et al. Comparison of the Combitube with the endotracheal tube in cardiopulmonary resuscitation in the prehospital phase [in German]. *Wien Klin Wochenschr.* 1994;106:412-415.
102. Cady CE, Weaver MD, Pirralo RG, Wang HE. Effect of emergency medical technician-placed Combitubes on outcomes after out-of-hospital cardiopulmonary arrest. *Prehosp Emerg Care.* 2009;13:495-499.
103. Verghese C, Prior-Willeard PF, Baskett PJ. Immediate management of the airway during cardiopulmonary resuscitation in a hospital without a resident anaesthesiologist. *Eur J Emerg Med.* 1994;1:123-125.
104. Deakin CD, Peters R, Tomlinson P, Cassidy M. Securing the prehospital airway: a comparison of laryngeal mask insertion and endotracheal intubation by UK paramedics. *Emerg Med J.* 2005;22:64-67.
105. Calkins TR, Miller K, Langdorf MI. Success and complication rates with prehospital placement of an esophageal-tracheal combitube as a rescue airway. *Prehosp Disaster Med.* 2006;21:97-100.
106. Guyette FX, Wang H, Cole JS. King airway use by air medical providers. *Prehosp Emerg Care.* 2007;11:473-476.
107. Tentillier E, Heydenreich C, Cros AM, et al. Use of the intubating laryngeal mask airway in emergency pre-hospital difficult intubation. *Resuscitation.* 2008;77:30-34.
108. Timmermann A, Russo SG, Rosenblatt WH, et al. Intubating laryngeal mask airway for difficult out-of-hospital airway management: a prospective evaluation. *Br J Anaesth.* 2007;99:286-291.
109. Martin SE, Ochsner MG, Jarman RH, et al. Use of the laryngeal mask airway in air transport when intubation fails. *J Trauma.* 1999;47:352-357.
110. Hasegawa K, Hiraide A, Chang Y, Brown DF. Association of prehospital advanced airway management with neurologic outcome and survival in patients with out-of-hospital cardiac arrest. *JAMA.* 2013;309:257-266.
111. McMullan J, Gerech R, Bonomo J, et al. Airway management and out-of-hospital cardiac arrest outcome in the CARES registry. *Resuscitation.* 2014;85:617-622.
112. Grmec S. Comparison of three different methods to confirm tracheal tube placement in emergency intubation. *Intensive Care Med.* 2002;28:701-704.
113. Silvestri S, Ralls GA, Krauss B, et al. The effectiveness of out-of-hospital use of continuous end-tidal carbon dioxide monitoring on the rate of unrecognized misplaced intubation within a regional emergency medical services system. *Ann Emerg Med.* 2005;45:497-503.
114. Kellum MJ, Kennedy KW, Barney R, et al. Cardiocerebral resuscitation improves neurologically intact survival of patients with out-of-hospital cardiac arrest. *Ann Emerg Med.* 2008;52:244-252.
115. Kellum MJ, Kennedy KW, Ewy GA. Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. *Am J Med.* 2006;119:335-340.
116. Bhende MS, Thompson AE. Evaluation of an end-tidal CO₂ detector during pediatric cardiopulmonary resuscitation. *Pediatrics.* 1995;95:395-399.
117. Sehra R, Underwood K, Checchia P. End tidal CO₂ is a quantitative measure of cardiac arrest. *Pacing Clin Electrophysiol.* 2003;26(part 2):515-517.
118. Grmec S, Kupnik D. Does the Mainz Emergency Evaluation Scoring (MEES) in combination with capnometry (MEESc) help in the prognosis of outcome from cardiopulmonary resuscitation in a pre-hospital setting? *Resuscitation.* 2003;58:89-96.
119. Grmec S, Klemen P. Does the end-tidal carbon dioxide (ETCO₂) concentration have prognostic value during out-of-hospital cardiac arrest? *Eur J Emerg Med.* 2001;8:263-269.
120. Kolar M, Krizmaric M, Klemen P, Grmec S. Partial pressure of end-tidal carbon dioxide successful predicts cardiopulmonary resuscitation in the field: a prospective observational study. *Crit Care.* 2008;12:R115.
121. Levine RL, Wayne MA, Miller CC. End-tidal carbon dioxide and outcome of out-of-hospital cardiac arrest. *N Engl J Med.* 1997;337:301-306.
122. Wayne MA, Levine RL, Miller CC. Use of end-tidal carbon dioxide to predict outcome in prehospital cardiac arrest. *Ann Emerg Med.* 1995;25:762-767.
123. Ahrens T, Schallom L, Bettorf K, et al. End-tidal carbon dioxide measurements as a prognostic indicator of outcome in cardiac arrest. *Am J Crit Care.* 2001;10:391-398.
124. Sanders AB, Kern KB, Otto CW, et al. End-tidal carbon dioxide monitoring during cardiopulmonary resuscitation: a prognostic indicator for survival. *JAMA.* 1989;262:1347-1351.
125. Reynolds JC, Rittenberger JC, Menegazzi JJ. Drug administration in animal studies of cardiac arrest does not reflect human clinical experience. *Resuscitation.* 2007;74:13-26.
126. Paradis NA, Martin GB, Rivers EP, et al. Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. *JAMA.* 1990;263:1106-1113.
127. Herlitz J, Ekström L, Wennerblom B, et al. Adrenaline in out-of-hospital ventricular fibrillation. Does it make any difference? *Resuscitation.* 1995;29:195-201.
128. Behringer W, Kittler H, Sterz F, et al. Cumulative epinephrine dose during cardiopulmonary resuscitation and neurologic outcome. *Ann Intern Med.* 1998;129:450-456.
129. Holmberg M, Holmberg S, Herlitz J. Low chance of survival among patients requiring adrenaline (epinephrine) or intubation after out-of-hospital cardiac arrest in Sweden. *Resuscitation.* 2002;54:37-45.
130. Ong ME, Tan EH, Ng FS, et al. Cardiac Arrest and Resuscitation Epidemiology Study Group. Survival outcomes with the introduction of intravenous epinephrine in the management of out-of-hospital cardiac arrest. *Ann Emerg Med.* 2007;50:635-642.
131. Callaway CW. Epinephrine for cardiac arrest. *Curr Opin Cardiol.* 2013;28:36-42.
132. Olasveengen TM, Sunde K, Brunborg C, et al. Intravenous drug administration during out-of-hospital cardiac arrest: a randomized trial. *JAMA.* 2009;302:2222-2229.
133. Olasveengen TM, Wik L, Sunde K, Steen PA. Outcome when adrenaline (epinephrine) was actually given vs. not given - post hoc analysis of a randomized clinical trial. *Resuscitation.* 2012;83:327-332.
134. Jacobs IG, Finn JC, Jelinek GA, et al. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. *Resuscitation.* 2011;82:1138-1143.
135. Hagihara A, Hasegawa M, Abe T, et al. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. *JAMA.* 2012;307:1161-1168.
136. Brown CG, Martin DR, Pepe PE, et al. A comparison of standard-dose and high-dose epinephrine in cardiac arrest outside the hospital. The Multicenter High-Dose Epinephrine Study Group. *N Engl J Med.* 1992;327:1051-1055.
137. Gueugniard PY, Mols P, Goldstein P, et al. A comparison of repeated high doses and repeated standard doses of epinephrine for cardiac arrest outside the hospital. European Epinephrine Study Group. *N Engl J Med.* 1998;339:1595-1601.
138. Callahan M, Madsen CD, Barton CW, et al. A randomized clinical trial of high-dose epinephrine and norepinephrine vs standard-dose epinephrine in prehospital cardiac arrest. *JAMA.* 1992;268:2667-2672.
139. Stiell IG, Hébert PC, Weitzman BN, et al. High-dose epinephrine in adult cardiac arrest. *N Engl J Med.* 1992;327:1045-1050.
140. Hayashi Y, Iwami T, Kitamura T, et al. Impact of early intravenous epinephrine administration on outcomes following out-of-hospital cardiac arrest. *Circ J.* 2012;76:1639-1645.
141. Kosciak C, Pinawin A, McGovern H, et al. Rapid epinephrine administration improves early outcomes in out-of-hospital cardiac arrest. *Resuscitation.* 2013;84:915-920.
142. Wenzel V, Krismer AC, Arntz HR, et al. European Resuscitation Council Vasopressor during Cardiopulmonary Resuscitation Study Group. A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. *N Engl J Med.* 2004;350:105-113.
143. Stiell IG, Hébert PC, Wells GA, et al. Vasopressin versus epinephrine for in-hospital cardiac arrest: a randomised controlled trial. *Lancet.* 2001;358:105-109.
144. Aung K, Htay T. Vasopressin for cardiac arrest: a systematic review and meta-analysis. *Arch Intern Med.* 2005;165:17-24.
145. Callaway CW, Hostler D, Doshi AA, et al. Usefulness of vasopressin administered with epinephrine during out-of-hospital cardiac arrest. *Am J Cardiol.* 2006;98:1316-1321.
146. Gueugniard PY, David JS, Chanzy E, et al. Vasopressin and epinephrine vs. epinephrine alone in cardiopulmonary resuscitation. *N Engl J Med.* 2008;359:21-30.
147. Mentzelopoulos SD, Zakyntinos SG, Tzoufi M, et al. Vasopressin, epinephrine, and corticosteroids for in-hospital cardiac arrest. *Arch Intern Med.* 2009;169:15-24.
148. Mentzelopoulos SD, Malachias S, Chamos C, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. *JAMA.* 2013;310:270-279.
149. Coon GA, Clinton JE, Ruiz E. Use of atropine for brady-asystolic prehospital cardiac arrest. *Ann Emerg Med.* 1981;10:462-467.
150. Tortolani AJ, Risucci DA, Powell SR, Dixon R. In-hospital cardiopulmonary resuscitation during asystole: therapeutic factors associated with 24-hour survival. *Chest.* 1989;96:622-626.
151. Stiell IG, Wells GA, Hébert PC, et al. Association of drug therapy with survival in cardiac arrest: limited role of advanced cardiac life support drugs. *Acad Emerg Med.* 1995;2:264-273.
152. Engdahl J, Bang A, Lindqvist J, Herlitz J. Can we define patients with no and those with some chance of survival when found in asystole out of hospital? *Am J Cardiol.* 2000;86:610-614.

153. Engdahl J, Bang A, Lindqvist J, Herlitz J. Factors affecting short- and long-term prognosis among 1069 patients with out-of-hospital cardiac arrest and pulseless electrical activity. *Resuscitation*. 2001;51:17-25.
154. van Walraven C, Stiell IG, Wells GA, et al. Do advanced cardiac life support drugs increase resuscitation rates from in-hospital cardiac arrest? The OTAC Study Group. *Ann Emerg Med*. 1998;32:544-553.
155. Kudenchuk PJ, Cobb LA, Copass MK, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med*. 1999;341:871-878.
156. Dorian P, Cass D, Schwartz B, et al. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med*. 2002;346:884-890. Erratum in: *N Engl J Med*. 2002;347:955.
157. Glover BM, Brown SP, Morrison L, et al. Dorian P; Resuscitation Outcomes Consortium Investigators. Wide variability in drug use in out-of-hospital cardiac arrest: a report from the resuscitation outcomes consortium. *Resuscitation*. 2012;83:1324-1330.
158. Kudenchuk PJ, Brown SP, Daya M, et al. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med* 2016;374:1711-1722.
159. Morrison LJ, Verbeek PR, Zhan C, et al. Validation of a universal prehospital termination of resuscitation clinical prediction rule for advanced and basic life support providers. *Resuscitation*. 2009;80:324-328.
160. Gaieski DF, Band RA, Abella BS, et al. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Resuscitation*. 2009;80:418-424.
161. Rittenberger JC, Kelly E, Jang D, et al. Successful outcome utilizing hypothermia after cardiac arrest in pregnancy: a case report. *Crit Care Med*. 2008;36:1354-1356.
162. Knafelj R, Radsel P, Ploj T, Noc M. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. *Resuscitation*. 2007;74:227-234.
163. Wolfum S, Pierau C, Radke PW, et al. Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention. *Crit Care Med*. 2008;36:1780-1786.
164. Oddo M, Schaller MD, Feihl F, et al. From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. *Crit Care Med*. 2006;34:1865-1873.
165. Reynolds JC, Rittenberger JC, Callaway CW. Methylphenidate and amantadine to stimulate reawakening in comatose patients resuscitated from cardiac arrest. *Resuscitation*. 2013;84:818-824.
166. Donnino MW, Rittenberger JC, Gaieski D, et al. The development and implementation of cardiac arrest centers. *Resuscitation*. 2011;82:974-978.
167. Birkmeyer JD, Stukel TA, Siewers AE, et al. Surgeon volume and operative mortality in the United States. *N Engl J Med*. 2003;349:2117-2127.
168. Callaway CW, Schmicker RH, Brown SP, et al. Early coronary angiography and induced hypothermia are associated with survival and functional recovery after out-of-hospital cardiac arrest. *Resuscitation*. 2014;85:657-663.
169. Wnent J, Seewald S, Heringlake M, et al. Choice of hospital after out-of-hospital cardiac arrest - a decision with far-reaching consequences: a study in a large German city. *Crit Care*. 2012;16(5):R164.
170. Cha WC, Lee SC, Shin SD, et al. Regionalisation of out-of-hospital cardiac arrest care for patients without prehospital return of spontaneous circulation. *Resuscitation*. 2012;83:1338-1342.
171. Reynolds JC, Rittenberger JC, Callaway CW; Post Cardiac Arrest Service. Patterns of organ donation among resuscitated patients at a regional cardiac arrest center. *Resuscitation*. 2014;85:248-252.
172. Spaite DW, Bobrow BJ, Vadeboncoeur TF, et al. The impact of prehospital transport interval on survival in out-of-hospital cardiac arrest: implications for regionalization of post-resuscitation care. *Resuscitation*. 2008;79:61-66.
173. Spaite DW, Stiell IG, Bobrow BJ, et al. Effect of transport interval on out-of-hospital cardiac arrest survival in the OPALS study: implications for triaging patients to specialized cardiac arrest centers. *Ann Emerg Med*. 2009;54:256-257.
174. Hartke A, Mumma BE, Rittenberger JC, et al. Incidence of re-arrest and critical events during prolonged transport of post-cardiac arrest patients. *Resuscitation*. 2010;81:938-942.
175. Huang SC, Wu ET, Chen YS, et al. Extracorporeal membrane oxygenation rescue for cardiopulmonary resuscitation in pediatric patients. *Crit Care Med*. 2008;36:1607-1613.
176. Nagao K, Kikushima K, Watanabe K, et al. Early induction of hypothermia during cardiac arrest improves neurological outcomes in patients with out-of-hospital cardiac arrest who undergo emergency cardiopulmonary bypass and percutaneous coronary intervention. *Circ J*. 2010;74:77-85.
177. Morimura N, Sakamoto T, Nagao K, et al. Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: a review of the Japanese literature. *Resuscitation*. 2011;82:10-14.
178. Maekawa K, Tanno K, Hase M, et al. Extracorporeal cardiopulmonary resuscitation for patients with out-of-hospital cardiac arrest of cardiac origin: a propensity-matched study and predictor analysis. *Crit Care Med*. 2013;41:1186-1196.
179. Belohlavek J, Kucera K, Jarkovsky J, et al. Hyperinvasive approach to out-of-hospital cardiac arrest using mechanical chest compression device, prehospital intraarrest cooling, extracorporeal life support and early invasive assessment compared to standard of care. A randomized parallel groups comparative study proposal. "Prague OHCA study." *J Transl Med*. 2012;10:163.
180. Martin GB, Carden DL, Nowak RM, et al. Aortic and right atrial pressures during standard and simultaneous compression and ventilation CPR in human beings. *Ann Emerg Med*. 1986;15:125-130.
181. Sanders AB, Ogle M, Ewy BA. Coronary perfusion pressure during cardiopulmonary resuscitation. *Am J Emerg Med* 1985;3:11-14.
182. Sutton RM, Friess SH, Maltese MR, et al. Hemodynamic-directed cardiopulmonary resuscitation during in-hospital cardiac arrest. *Resuscitation*. 2014;85:983-986.
183. Friess SH, Sutton RM, French B, et al. Hemodynamic directed CPR improves cerebral perfusion pressure and brain tissue oxygenation. *Resuscitation*. 2014;85:1298-1303.
184. Salcido DD, Menegazzi JJ, Suffoletto BP, et al. Association of intramyocardial high energy phosphate concentrations with quantitative measures of the ventricular fibrillation electrocardiogram waveform. *Resuscitation*. 2009;80:946-950.
185. Reynolds JC, Salcido DD, Menegazzi JJ. Correlation between coronary perfusion pressure and quantitative ECG waveform measures during resuscitation of prolonged ventricular fibrillation. *Resuscitation*. 2012;83:1497-1502.
186. Callaway CW, Sherman LD, Mosesso VN Jr, et al. Scaling exponent predicts defibrillation success for out-of-hospital ventricular fibrillation cardiac arrest. *Circulation*. 2001;103:1656-1661.
187. Eftestøl T, Losert H, Kramer-Johansen J, et al. Independent evaluation of a defibrillation outcome predictor for out-of-hospital cardiac arrested patients. *Resuscitation*. 2005;67:55-61.
188. Snyder DE, White RD, Jorgenson DB. Outcome prediction for guidance of initial resuscitation protocol: shock first or CPR first. *Resuscitation*. 2007;72:45-51.