

Sudden Cardiac Death

Advances in Resuscitation

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Studies of sudden cardiac death (SCD) demonstrate overwhelmingly poor outcomes regardless of the population or intervention studied. Although SCD is a complex critical illness that is understood poorly, it is clear that outcomes are influenced by timely provision of high-quality, specific interventions.^{1,2} However, there is considerable heterogeneity within this group of patients with regard to the cause of SCD, comorbidities, and duration of the cardiac arrest event that can be difficult to identify during the course of resuscitation.³ These variables can have a significant bearing on outcomes and efficacy of treatment. For example, compression-only bystander cardiopulmonary resuscitation (CPR) may not be ideal for all subgroups of patients experiencing SCD. In addition, a proportion of SCD patients have a significant coronary artery lesion and benefit from percutaneous coronary intervention (PCI). Finally, post-ventricular fibrillation cardiac arrest patients may respond better to therapeutic hypothermia (TH) than those with other rhythms before the return of spontaneous circulation (ROSC).^{4–6}

SCD is a dynamic, time-dependent process, as supported by research on CPR technique, early use of automated external defibrillators (AEDs), and implementation of TH.^{7–9} Weisfeldt and Becker¹⁰ elaborate on this concept in their 3-phase model of resuscitation from ventricular fibrillation cardiac arrest, describing progressive disruption of cardiac electrophysiology, circulation, and metabolism. The electric phase lasts from cardiac arrest through ≈ 4 minutes of resuscitation efforts and is considered the time when defibrillation is most likely to be successful. Herlitz et al¹¹ demonstrated this in a prospective observational study of inpatients with ventricular fibrillation cardiac arrest. Those defibrillated within 3 minutes of collapse had significantly improved survival compared with those defibrillated >12 minutes from collapse. Work by Chan et al¹² demonstrated similar findings, with a significant outcome benefit for inpatients sustaining ventricular fibrillation cardiac arrest who were defibrillated within 2 minutes of their arrest. The critical factor is likely time-dependent deterioration of a shockable ventricular fibrillation rhythm to pulseless electric activity or asystole.^{13,14} Following the electric phase is the circulatory phase, in which CPR with chest compressions gains importance, presumably because the ischemic heart is less responsive to defibrillation. Vilke et al¹⁵ demonstrated higher survival among out-of-hospital ventricular fibrillation cardiac arrest patients with

estimated time from collapse to defibrillation of >4 minutes who received CPR, whereas there was no benefit from CPR in those defibrillated within 4 minutes. In patients receiving bystander CPR before defibrillation, ventricular fibrillation frequency and amplitude have been found to be higher compared with patients not receiving CPR before defibrillation.¹³ At ≈ 10 minutes, significant metabolic dysfunction (the metabolic phase) occurs as a result of global ischemia. The metabolic phase is incompletely defined and poorly understood but generally is considered to involve inflammatory cytokines, lactic acidosis, reactive oxygen species, and reperfusion injury.¹⁰ Patients without ROSC by this time have significantly worse survival.

Early identification and activation of emergency response systems, quality chest compressions, early defibrillation, appropriate advanced cardiac life support, and advanced postresuscitation care are essential to attenuate the time-dependent process of SCD and to improve outcomes.^{16,17} A coordinated regional system of care can promote specialized postresuscitation programs and direct patients to centers prepared to provide optimal care.^{18,19} This article discusses recent advances in resuscitation science for the adult patient experiencing SCD. It focuses on key components of the 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, as well as research published since the new guidelines became available. Highlighted are basic life support (BLS) and CPR, electric therapy, advanced life support, postresuscitation care, and considerations for implementation of these measures.

BLS and CPR

Bystander CPR

The 2010 American Heart Association adult BLS guidelines include several changes intended to increase bystander participation and to reduce time to initiation of chest compressions.¹⁶ The concept of “look, listen, feel” has been removed because it was considered to be inconsistently applied and time-consuming.²⁰ Untrained laypersons are now instructed to begin compression-only CPR because a number of studies have demonstrated bystander compression-only CPR to be equivalent to conventional bystander CPR.^{7,21,22} The algorithm is now simplified, as shown in Figure 1. Two randomized trials demonstrated no benefit for conventional CPR over

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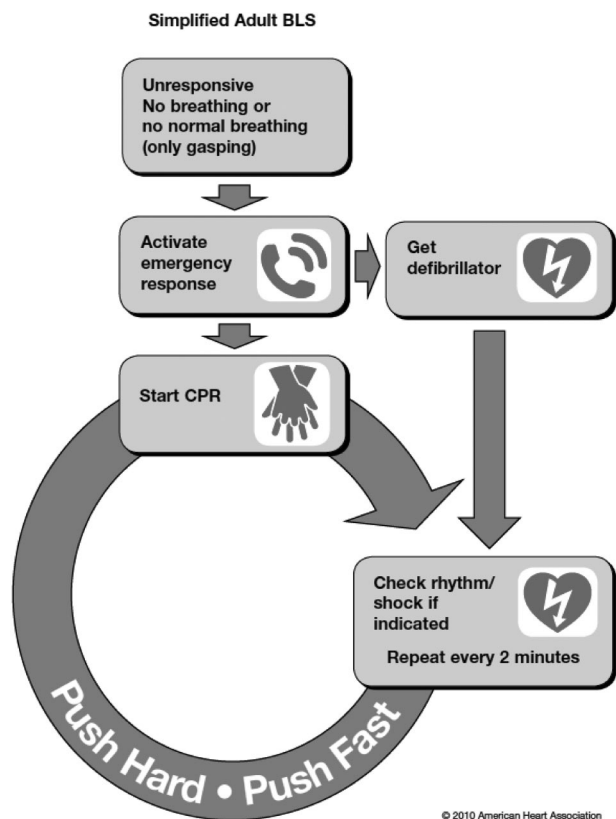
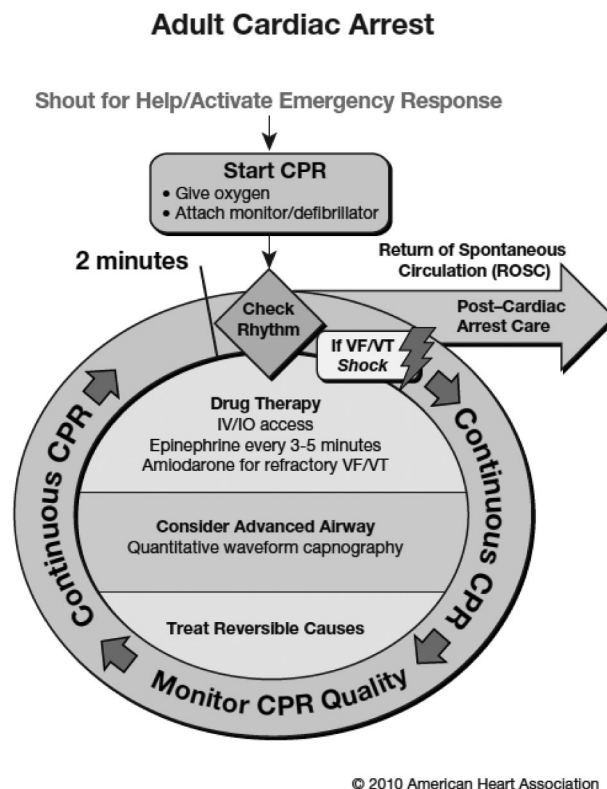


Figure 1. Adult basic life support algorithm. CPR indicates cardiopulmonary resuscitation. Reprinted from Berg et al.¹⁶

compression-only CPR, and a meta-analysis suggested that bystander compression-only CPR was superior to bystander conventional CPR.^{17,18,23} However, since publication of the most recent guidelines, 2 large observational studies demonstrated conventional CPR to be superior in certain subgroups of out-of-hospital cardiac arrest (OHCA): young patients, those with arrest of noncardiac origin, those with delay to CPR initiation, and those with a prolonged arrest of cardiac origin.^{5,7} Although this research is informative, lay rescuers cannot be expected to make such distinctions, and the current AHA CPR protocol should be adhered to for adult patients with SCD. The recommended chest compression depth is now at least 2 inches on the basis of studies that demonstrated improved defibrillation success and short-term outcomes with increased compression depth, and the recommended compression rate is at least 100 per minute.^{16,24,25} In addition to guideline changes, public education and CPR training are paramount because laypersons trained in CPR are significantly more likely to perform CPR.²⁶

Airway and Breathing

For trained rescuers who are comfortable with conventional CPR, airway and breathing considerations are reintroduced, although with a different emphasis.¹⁶ For example, the A-B-C mnemonic has been rearranged to C-A-B to place emphasis on and to reduce delays in providing chest compressions.²⁰ This has been incorporated into the new adult BLS algorithm for healthcare providers, as shown in Figure 2, which emphasizes CPR and defibrillation before any ventilation strate-



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Figure 2. Algorithm for adult basic life support (BLS) for health-care providers. CPR indicates cardiopulmonary resuscitation; VF, ventricular fibrillation; and VT, ventricular tachycardia. Reprinted from Neumar et al.¹⁷

gies.¹⁶ Support for this emphasis is derived from research demonstrating that bystander CPR is a significant predictor of survival in OHCA.²⁷ Evidence from studies of minimally interrupted cardiac resuscitation and cardiocerebral resuscitation supports the new decreased emphasis on pulse checks to promote continuous CPR with minimal interruptions.^{28,29} Beyond the timing of ventilation, care must be taken to avoid excessive ventilation. Observational studies on human cardiac arrest patients have documented this to be a pervasive problem, one that should be considered in the context of animal models of cardiac arrest that demonstrate that excessive ventilation translates to poorer hemodynamics and survival.^{30,31} Strategies to overcome this problem include real-time feedback during CPR, as discussed below, and possibly the use of automated transport ventilators.³² Automated transport ventilators (used in conjunction with advanced airways) may limit human error as a cause of excessive ventilation. However, there is insufficient evidence at this time to routinely recommend this intervention, particularly during active resuscitation.^{33,34}

Quality of CPR

CPR is a learned skill, and retention of proficiency is highly variable so that provision of high-quality CPR is challenging. For instance, laypersons, emergency medical personnel, nurses, and physicians alike often perform CPR poorly in terms of compression rate, depth, and interruptions, as well as allowing for adequate chest wall recoil between compressions and avoidance of hyperventilation.^{35–38} CPR interruptions

occur frequently during patient transport (loading and unloading), rhythm analysis, and preshock and postshock periods.³⁹ A coordinated effort directed toward frequent retraining is essential to maintain skills that otherwise deteriorate rapidly. In addition to optimal training, efforts at real-time feedback may improve the quality of CPR, although the effect on clinical outcomes is less clear. Abella et al³² and Hostler et al⁴⁰ demonstrated better CPR performance when audiovisual feedback was provided, although this did not translate into significant differences in ROSC or survival. Two alternate studies examining real-time feedback, one of which used the addition of weekly debriefing, both improved the quality of CPR and demonstrated better short-term outcomes.^{25,41} Laypersons not trained in CPR may be able to provide effective CPR with assistance from emergency medical system (EMS) dispatchers. Dispatch-assisted CPR has been demonstrated to be safe and to increase the rates of bystander CPR and may improve survival from cardiac arrest.^{42–44}

Alternative CPR techniques include active compression-decompression CPR, the LUCAS mechanical chest compression system, and the ZOLL AutoPulse load-distributing band. These modalities represent unique approaches to improving outcomes from cardiac arrest through modified CPR technique and may prove to be beneficial, particularly with regard to averting provider fatigue and impaired chest compression efficacy. However, this is an active area of research at the present time, and in line with the 2010 AHA guidelines, routine use of these techniques cannot be endorsed or refuted.^{45–50}

Electric Therapies

Out-of-Hospital AED Use

The use of AEDs by laypersons, EMS personnel, and health-care providers has been studied widely for both OHCA and in-hospital cardiac arrest. Early evidence was positive, demonstrating relatively high rates of ROSC and survival to hospital discharge when used by laypersons and emergency personnel for OHCA.^{51,52} Efficacy has been demonstrated in such varied settings as casinos, in airports, and on board passenger aircraft.^{53–55} Recent large population-based studies of public-access defibrillation (PAD) from Japan and the Resuscitation Outcomes Consortium confirm a significant survival benefit in OHCA.^{8,56} Of importance are recent findings by Weisfeldt et al⁵⁷ that shockable rhythms were much more common in patients with witnessed cardiac arrest in public compared with cardiac arrest in the home and that survival to discharge was higher for patients with bystander-applied AED in public compared with at home. Similarly, Bardy et al⁵⁸ found no significant advantage to home AED use in patients with previous anterior wall myocardial infarction who later experienced cardiac arrest in the home. The reason for this discrepancy is not clear and may be related to comorbidities, differences in initial rhythm, delay to recognition of cardiac arrest, or delay to defibrillation among other factors that characterize the home population compared with the public.^{57,59} These data suggest that community-wide approaches to deploy AEDs should focus on arrests in public sites as opposed to those that occur at home.

The small fraction of eligible patients receiving AED defibrillation before EMS arrival in recent studies indicates a need for greater dissemination of this technology and education about its use.^{8,56} A community-wide approach that integrates AED use with early EMS activation, early CPR, timely and skilled advanced life support, and advanced post-cardiac arrest care is advocated.⁶⁰ Work by Rea et al reinforces this concept.⁶¹ Rea et al confirmed a survival advantage for PAD yet noted that the majority of patients receiving PAD were pulseless on EMS arrival and required further advanced care. This highlights the interdependent nature of PAD and EMS and the need for a coordinated system to optimize care of the postarrest patient. An example of such an approach is the Take Heart America program. This initiative aggressively implemented widespread community and EMS education efforts, increased AED deployment, and established cardiac arrest centers to optimize care, including TH and PCI, resulting in a significant improvement in survival to discharge.⁶² Unfortunately, AED use by first responders was not reliably recorded during the study, limiting evaluation of the impact of AEDs in particular.

In-Hospital AED Use

The use of AEDs for in-hospital cardiac arrest seems intuitive given the robust result for out-of-hospital use, and uncontrolled observational studies have documented relatively high rates of ROSC and survival to discharge for hospitals implementing first-responder AED programs.^{63,64} Two more recent studies, particularly those by Chan et al⁶⁵ and Forcina et al,⁶⁶ question the use of in-hospital AEDs. These studies demonstrated no change in in-hospital survival or survival to discharge for shockable rhythms compared with the use of standard defibrillators. This may be explained by advances in resuscitation team proficiency and improved skills with the use of standard defibrillators. Conversely, these investigators found poorer outcomes in patients with nonshockable rhythms, possibly related to the delay in providing chest compression that was caused by AED rhythm analysis; this problem may be ameliorated with the newer generation of AEDs. Other potential causes are multifactorial and may be related to advances in patient care, improved provider training, changes in patient acuity, heterogeneity of resuscitation protocols, evolving approaches to end-of-life care, and advanced directives.⁶⁷

Defibrillator Sequence, Technique, and the Use of Pacing

The importance of the timing of defibrillation in relation to chest compressions was highlighted by Cobb et al.⁶⁸ They had observed a trend toward worse survival from cardiac arrest after implementation of a protocol prioritizing AED application, an observation that prompted a prospective study on the topic. In their study, Cobb et al observed a survival benefit from 90 seconds of CPR before defibrillation compared with a historical period that prioritized AED application. However, they found that the benefit was specific to the subgroup of patients with EMS response intervals of >4 minutes. This finding is supported by subgroup analyses of other studies assessing timing of CPR in relation to defibrillation and a

meta-analysis that indicated that for patients with significant delays to initial response, implementation of chest compressions before defibrillation may be beneficial.^{68–70} This evidence highlights the tension between providing chest compressions and providing early defibrillation in terms of timing and sequence. In practice, the exact duration of cardiac arrest for most SCD patients will be difficult to ascertain; therefore, defibrillation should not be delayed for the sole purpose of providing chest compressions, nor should chest compressions be delayed while obtaining a defibrillator.^{12,71–73}

There is direct evidence concerning 1 shock versus a series of 2 or 3 stacked shocks. Rea et al⁷⁴ investigated this question and found that the initial defibrillation attempt terminated ventricular fibrillation in 83.6% of 481 patients overall and in 92% when biphasic defibrillators were used. A second and third stacked defibrillation attempt terminated ventricular fibrillation in 7.5% and 4.8% of cases, respectively. Of the 332 patients who underwent a second series of defibrillation attempts, ventricular fibrillation was terminated in 86.4%, 6.6%, and 3.6% for the initial, second, and third attempts, respectively. Of note, in this study, defibrillation success was defined as termination of ventricular fibrillation, not the development of a perfusing rhythm. However, the efficacy of the first shock during the initial defibrillation series and the efficacy of the first shock in the second defibrillation series support the recommendation for a 1-shock defibrillation protocol with minimal interruptions in CPR and immediate resumption of chest compressions after defibrillation attempts. Further support is derived from studies of minimally interrupted cardiac resuscitation.^{29,75} These studies compared a protocol for treatment of ventricular fibrillation cardiac arrest that consisted of 1 defibrillation attempt without rhythm reanalysis followed by 2 minutes of CPR to a protocol of up to 3 successive defibrillation attempts followed by a pulse check before resumption of CPR. Survival was increased in the groups treated with the 1-shock protocol, although it should be noted that other variables may have affected the results. For example, interruption of chest compressions is minimized with the 1-shock approach and likely contributed to the positive outcome.

Biphasic waveform defibrillators have been found to be equivalent to or better than monophasic waveform defibrillators. Biphasic waveforms use a reversal of current at a specific time during the defibrillation attempt and require less energy to be successful.⁷⁶ This has been demonstrated under controlled conditions in electrophysiology laboratories.^{77,78} More pertinent to patients experiencing SCD is work demonstrating biphasic waveforms to be equivalent or superior to monophasic waveforms in defibrillating to an organized rhythm.^{28,79} However, evidence is lacking on improved survival in OHCA resulting from the implementation of biphasic defibrillation.

The literature on electric therapy for asystole is somewhat dated. However, it argues against pacing, suggesting that pacing does not improve survival and likely interrupts the provision of CPR.^{80,81} Transcutaneous pacing for asystolic cardiac arrest was not recommended in the 2005 advanced life support guidelines and is not recommended in the 2010 guidelines.^{20,82}

Advanced Cardiovascular Life Support

Advanced cardiovascular life support is a coordinated series of interventions that augment the key BLS components of immediate recognition and activation of the EMS, early CPR, and rapid defibrillation. Advanced cardiovascular life support includes advanced airway management and ventilation strategies, pharmacotherapy, and physiological monitoring.¹⁷

Timing of Airway Interventions

Airway management is difficult in emergency situations such as SCD and is associated with complications for both the in-hospital and out-of-hospital setting.^{83,84} Evidence on the optimal timing and technique for airway management during resuscitation from SCD is insufficient. For in-hospital SCD, intubation within 5 minutes (compared with intubation performed >5 minutes after arrest) has been associated with either worse outcome or a slight increase in 24-hour survival without increased ROSC.^{85,86} Out-of-hospital data are more heterogeneous: Both intubation (regardless of timing) and intubation within 12 minutes have been associated with improved survival in retrospective studies.^{87,88} On the other hand, studies assessing minimally interrupted cardiac resuscitation and passive ventilation suggest that intubation may not be advantageous.^{28,89} In these approaches, an emphasis on chest compressions and defibrillation, rather than on airway and ventilation, has been associated with improved outcomes. As a result, in cases when placement of an advanced airway and ventilation for adult patients with SCD would interfere with CPR and defibrillation, these efforts should be delayed until the patient fails to respond or ROSC occurs.

Airway Management Techniques

When airway management and ventilation are considered in isolation of the other issues discussed above, endotracheal intubation is the ideal intervention. It provides a secure patent airway, protects against aspiration, facilitates complex ventilation and oxygenation strategies, and is a route for drug administration. However, endotracheal intubation requires a high degree of skill and is associated with relatively frequent complications in emergency settings.^{83,84} An alternative approach when an advanced airway is indicated is the supraglottic airway, including the laryngeal tube, esophageal-tracheal double-lumen airway (Combitube), and laryngeal mask airway. The most recent work on out-of-hospital emergency airway management has focused on the laryngeal tube, a single-lumen device that is blindly inserted into the esophagus. A distal cuff seals the esophagus while a proximal cuff seals the upper airway; ports between the cuffs allow oxygenation and ventilation. Laryngeal tube airways have the advantage of ease of training and relatively high rates of successful airway management for both skilled and less skilled providers.^{90,91} These airways have the additional advantage of rapid placement and may result in fewer interruptions in chest compressions.⁹¹ There is less robust support for the laryngeal mask airway, and although the Combitube has been demonstrated to be efficacious in the hands of skilled physicians as an alternative to tracheal intubation, there is evidence that it may be less so when used by minimally trained individuals.^{92,93}

An adjunct to airway and ventilation management is the impedance threshold device (ITD). The ITD is a valve that is connected to an airway device (mask, supraglottic airway, endotracheal tube) and reduces air entry to the lungs during the decompression phase of chest compressions.⁴⁸ It results in negative intrathoracic pressure, improving venous return during CPR. The 2010 AHA guidelines advised that the ITD could be considered for use in adult cardiac arrest by trained personnel.⁴⁸ Two new research studies have been published on the use of ITDs since that time. Aufderheide et al⁹⁴ conducted a randomized multicenter trial assessing the effect of active compression-decompression CPR with ITD versus control patients receiving standard CPR. This study is particularly notable because, in addition to gathering data on survival to hospital discharge, the investigators assessed survival to 1 year with favorable neurological outcome, an outcome that is clearly difficult to achieve. Nonetheless, they demonstrated improved survival to discharge and to 1 year with a favorable neurological condition for the group receiving active compression-decompression CPR and ventilation with ITD. Thigpen et al⁹⁵ prospectively collected data on cardiac arrest patients receiving CPR after implementation of the 2005 AHA guidelines in conjunction with ITD use and compared outcomes with retrospective control subjects resuscitated without ITD and before implementation of the 2005 guidelines. They demonstrated a significant increase in hospital discharge rate in the intervention group. Both studies had confounding variables that do not allow assessment of the ITD alone but provide support for the recommendation that the ITD be considered for use by trained personnel in adult cardiac arrest patients. In addition, to further complicate interpretation of studies with the ITD, the Resuscitation Outcomes Consortium terminated a randomized double-blind study of the ITD because of results that demonstrated no benefit for the device (National Heart, Lung, and Blood Institute press release dated November 6, 2009), the full report of which has not been published.⁹⁶ It should be emphasized that the favorable studies by Thigpen et al⁹⁵ and Aufderheide et al⁹⁴ evaluated the ITD in conjunction with active compression-decompression CPR, whereas the Resuscitation Outcomes Consortium study evaluated the ITD with standard CPR.

Advanced Airway Placement Confirmation and Monitoring

Use of reliable techniques to confirm airway device placement is essential. Clinical assessments including visual confirmation of chest wall expansion, auscultation of bilateral breath sounds, and absence of air sounds over the epigastrium are critical after placement of all types of airway devices. For endotracheal intubation, there is new emphasis on the use of waveform capnography for confirmation and monitoring of tube placement.¹⁷ This is recommended in general; however, some caution is advised in the application of waveform capnography in the SCD patient. The 2 studies that support capnography did not adequately assess its use in patients with SCD. They either had very small numbers of misplaced intubations in cardiac arrest patients or failed to specify whether any of the misplaced endotracheal tubes that were

identified with capnography occurred in the SCD subgroup.^{97,98} Takeda et al⁹⁹ and Tanigawa et al¹⁰⁰ suggested that continuous-waveform capnography identified all esophageal intubations in SCD patients; however, a significant number of tracheal intubations were incorrectly identified as esophageal. Capnography provides an additional modality for confirming proper airway device placement and should be used along with clinical assessment.

Advances in Pharmacotherapy for SCD

Pharmacotherapy for SCD ideally would result in increased ROSC while at the same time having a protective effect on vital organs in the preresuscitation and postresuscitation periods.¹⁰¹ Unfortunately, although current pharmacotherapy for SCD seems to improve short-term outcomes, available evidence does not support improved survival to hospital discharge.¹⁰² Significant advances in drug therapy for SCD are scarce, and recommended changes in therapy are predominantly revised indications for drugs already used clinically for SCD. Along these lines, there are new pharmacological recommendations for the treatment of asystole and the use of antiarrhythmic medication.¹⁷ For instance, atropine is no longer recommended for asystole or pulseless electric activity. The evidence that supported this change is dated and of low quality, but the weight of evidence at the time argued against any benefit in such cases.^{103–105} Since the publication of the 2010 AHA guidelines, a study from the Survey of Survivors of Cardiac Arrest in the Kanto Area (SOS-KANTO) Study Group was published that compared the efficacy of epinephrine and epinephrine plus atropine for patients presenting with pulseless electric activity or asystole. There was no benefit from atropine plus epinephrine compared with epinephrine alone for patients presenting with pulseless electric activity as measured by rate of ROSC, survival to hospital admission, 30-day survival, or 30-day favorable neurological outcome.¹⁰⁶ For patients presenting in asystole, the atropine plus epinephrine group demonstrated increased ROSC and survival to hospital admission but similar 30-day survival and 30-day favorable neurological outcome compared with the epinephrine group.

Amiodarone is now the preferred antiarrhythmic agent for ventricular fibrillation or pulseless ventricular tachycardia.¹⁷ This agent has been demonstrated to be superior to placebo for the treatment of shock-resistant ventricular fibrillation and is more effective than lidocaine for shock-resistant ventricular tachycardia or ventricular fibrillation. Most recently, amiodarone was compared with nifekalant, a class III antiarrhythmic available in Japan.¹⁰⁷ This study demonstrated a trend toward improved defibrillation success and hospital survival for amiodarone and a significant improvement in discharge survival rate compared with nifekalant. One retrospective review suggests an increase in ROSC and survival to admission for lidocaine, although an increased rate of hospital discharge was not demonstrated.¹⁰⁸ Given the evidence in favor of amiodarone, lidocaine should be reserved for cases when amiodarone is not available. As with other pharmacological interventions for SCD, there is no evidence that amiodarone or lidocaine improves survival to hospital discharge compared with standard therapy without these drugs.

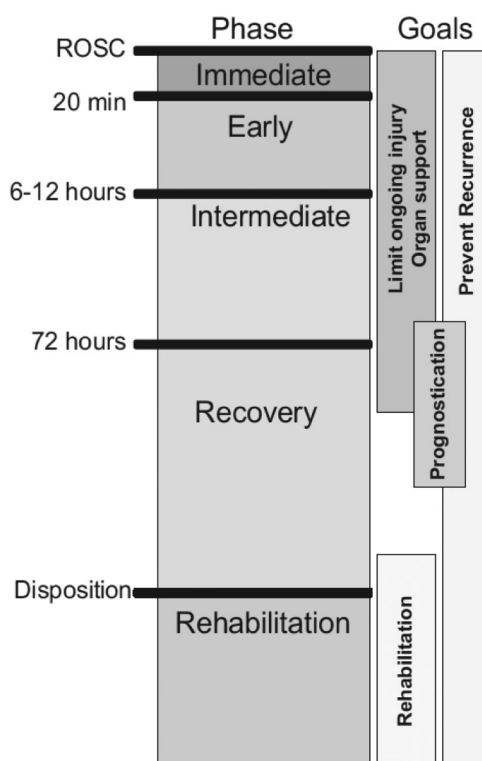


Figure 3. Phases of post-cardiac arrest syndrome. ROSC indicates return of spontaneous circulation. Reprinted from Neumar et al.¹⁰⁹

Post-Cardiac Arrest Care

In 2008, the term post-cardiac arrest syndrome was coined in a consensus statement on post-cardiac arrest care from the International Liaison Committee on Resuscitation.¹⁰⁹ Post-cardiac arrest syndrome refers to the time-dependent complex pathophysiology that follows ROSC from SCD, as diagrammed in Figure 3.¹⁰⁹ Specifically, it refers to brain injury, myocardial dysfunction, and systemic ischemia/reperfusion responses induced by the arrest event, as well as the persistent effects of the precipitating pathology. Specific objectives for the initial and subsequent post-cardiac arrest periods are listed in the Table, as adapted from Peberdy et al.¹⁸ Mortality in the post-cardiac arrest period is extremely high, with most deaths occurring within the first 24 hours, suggesting that an aggressive approach to addressing post-cardiac arrest syndrome is warranted.^{67,110}

Comprehensive Post-Cardiac Arrest Syndrome Care

Significant regional and local variability in post-cardiac arrest outcome has been demonstrated by a number of investigators.^{2,111,112} This may reflect health, racial, or socioeconomic disparities; layperson involvement; or local EMS skill and capacity. However, variability in the hospital volume of post-cardiac arrest patients, specialized capabilities such as PCI or TH, and the quality of post-cardiac arrest care are also likely contributors.

Studies performed in individual institutions have demonstrated that comprehensive multidisciplinary care that pro-

Table. Objectives for the Initial and Subsequent Post-Cardiac Arrest Periods

Initial objectives

- Optimize cardiopulmonary function
- Optimize vital organ perfusion
- Transport to a hospital with a comprehensive post-cardiac arrest treatment system of care including capacity for:
 - Therapeutic hypothermia
 - Acute coronary intervention
 - Goal-directed critical care
 - Neurological care
- Identify and treat precipitating causes
- Prevent recurrent arrest

Subsequent objectives

- Control body temperature
- Identify and treat acute coronary syndromes
- Optimize mechanical ventilation strategies
- Reduce risk of and treat multiorgan injury
- Objectively assess prognosis
- Provide appropriate rehabilitation

Adapted from Peberdy et al.¹⁸

vides these advanced interventions is feasible and significantly improves outcomes. For instance, Gaieski et al.¹¹³ demonstrated successful implementation of a post-cardiac arrest protocol that focused on early goal-directed hemodynamic optimization and TH. In addition, Sunde et al.¹¹⁴ implemented a post-cardiac arrest strategy that included control of hemodynamics, TH, and PCI that resulted in significantly improved survival and neurological status. Although individual hospitals with expertise in post-cardiac arrest care are essential, implementation of coordinated regional systems of care is the foundation on which improvement in outcomes for cardiac arrest patients will occur. The AHA policy statement on regional systems of care for OHCA strongly endorses this concept.¹⁹ The policy statement draws parallels between the cardiac arrest patient and improved patient outcomes seen with regional systems approaches for patients sustaining trauma, ST-segment-elevation myocardial infarction, and stroke. It highlights what is possible for post-cardiac arrest patients and the individual components of post-cardiac arrest care.

Critical Interventions

Key components of a comprehensive approach to post-cardiac arrest care are TH and early PCI. Just as the pathophysiology of SCD and the postresuscitation period are complex, so are the mechanisms theorized to drive the benefits of TH. The preponderance of evidence comes from neuroscience research and includes evidence for reductions in excitatory neurotransmitters, inflammatory cytokines, leukotrienes, free radicals, and inflammatory cells; inhibition of apoptotic neuronal cell death; promotion of neuroprotective growth factors; reduced brain metabolic demand; and suppression of epileptogenic electric activity.¹¹⁵ The strongest indication for TH is in patients after cardiac arrest resulting

from ventricular fibrillation, an indication that was supported by the original reports on TH published in 2002.^{116,117} Subsequent work has confirmed beneficial outcomes in post-ventricular fibrillation cardiac arrest patients and in patients associated with any arrest rhythm.^{118,119} Most recently, van der Wal et al¹²⁰ published a retrospective observational study detailing the effect of TH on post-cardiac arrest patient outcome. In patients with ROSC from both shockable and nonshockable rhythms, TH reduced hospital mortality by 20%. In addition, Dumas et al⁴ provided evidence for a significantly better neurological outcome in patients receiving TH after ventricular fibrillation or pulseless ventricular tachycardia cardiac arrests. In contrast, this benefit was not observed in patients suffering from pulseless electric activity or asystolic cardiac arrest. Thus, the evidence clearly supports the use of TH in patients achieving ROSC after cardiac arrest with shockable rhythms, but the use of TH for those achieving ROSC after nonshockable rhythms requires more investigation.

Roughly half of post-cardiac arrest patients have a significant coronary artery lesion.⁶ The characteristic ECG findings of ST-segment elevation and new left bundle-branch block in these patients are commonly absent.^{121,122} Whereas thrombolytic therapy during cardiac arrest has not been demonstrated to be effective, there is robust support for PCI in the post-cardiac arrest period.^{123,124} PCI has been shown to be associated with increased hospital survival in patients presenting with or without findings of ST-segment-elevation myocardial infarction on ECG.^{6,121} Patients regaining consciousness after SCD associated with ST-segment-elevation myocardial infarction who undergo PCI have been shown to have survival similar to that for those who did not sustain cardiac arrest.¹²⁵ Improved neurological outcomes have been demonstrated, as have long-term outcomes at 6 and 12 months.^{121,126,127}

In the context of providing multidisciplinary care, combining therapeutic TH with early PCI is clearly a challenge. However, several studies have demonstrated that pursuing both modalities is feasible and safe, although the complication of increased bleeding has been noted for patients undergoing both therapies.^{128–130} It is possible to implement both modalities without affecting door-to-balloon time, and the positive outcomes for TH can be maintained.^{131,132} Göthberg et al¹³³ recently studied this in patients who had not sustained cardiac arrest. They randomized 18 ST-segment-elevation myocardial infarction patients to emergent PCI or a combination of TH and emergent PCI. Door-to-balloon time was similar in both groups, and the hypothermia group reached the target core body temperature of $<35^{\circ}\text{C}$ in all patients at the time of reperfusion. Interestingly, the hypothermia group demonstrated a significant reduction in infarct size as measured by cardiac magnetic resonance imaging and cardiac biomarker measurement. Gräsner et al¹³⁴ recently published work on the effect of PCI and TH in OHCA patients who survived to hospital admission. Patients who received TH without PCI demonstrated improved 24-hour survival and neurological outcome. Those treated with PCI but without TH also had favorable outcomes by these measures. In the group who underwent both PCI and TH, binary logistic regression

identified both interventions as associated with improved 24-hour survival. This analysis found PCI to be an independent predictor of favorable neurological outcome, but statistical significance in this regard could not be demonstrated for TH. Of note, a significant proportion of their hypothermia cohort had nonshockable arrest rhythms on their presenting ECG. In light of the work by Dumas et al referenced above, this may be a significant discriminator of those more or less likely to benefit from TH.⁴ Overall, these studies are promising, and there may be incremental benefit from the combination of TH and PCI in post-cardiac arrest patients compared with benefit from the modalities when used in isolation. However, further research is required to identify ideal indications and approaches to managing these patients.

Future of Resuscitation Research

SCD is a major public health problem that has proven refractory to significant advances in healthcare technology and availability. Incremental advances are documented for such interventions as community AED programs, TH and PCI during post-cardiac arrest care. However, advancing care of the SCD patient is a challenging and multifaceted problem. The origin of SCD is highly variable and the pathophysiology of the postarrest state is poorly understood. Pharmacotherapy for the patient in cardiac arrest and in the postarrest period is evolving, yet no new therapeutic options are currently available.¹⁰¹ Improvements in basic and advanced resuscitation techniques are encouraging, yet broad and consistent implementation is lacking, as is the case for postresuscitation care. These challenges are paralleled by obstacles faced in resuscitation research.

Large population-based studies and those facilitated by research consortia are critical to advancing resuscitation care. Studies using large population databases such as those by Kitamura et al⁸ and Rea et al⁶¹ are encouraging. These investigators studied nationwide and regional use of PAD, respectively, and contributed significantly to our understanding of the advantages of PAD programs such as earlier defibrillation, improved outcomes, and the need for a coordinated system that integrates PAD with emergency services. The Resuscitation Outcomes Consortium is a prospectively collected population-based registry of OHCA from regions in the United States and Canada with a collective population of $\approx 23\,000\,000$.¹³⁵ It is a clinical trials network that provides infrastructure and support for cardiopulmonary arrest research.¹³⁶ Data from a registry such as this improve our understanding of community-based resuscitation approaches, enhance our knowledge of the pathophysiology of SCD, and evaluation of the efficacy of interventions. The Resuscitation Outcomes Consortium–Cardiac Arrest has facilitated a large number of resuscitation studies, many of which are referenced in this article. For example, recent publications have included research on out-of-hospital resuscitation variability, real-time feedback during CPR, AED use in the home, and PAD, among many others.^{40,56,57,137}

Recently, a novel approach to resuscitation-related data collection and database management for clinical research was described by Lin et al.¹³⁸ They developed a data dictionary as part of a Web-based data collection form for post-cardiac

arrest TH implemented at 43 Ontario hospitals. A data dictionary provides centralized control over data and data management, implements consistent standardized definitions, and results in improved data validity and reliability.^{138,139} Their tool consisted of 545 variables developed from the Utstein standard, prior studies on TH, and expert opinion. Such an approach may be the ideal tool for studying interventions and outcomes for large numbers of cardiac arrest patients from geographically diverse healthcare organizations.

Beyond the challenges of study design, subject enrollment and data management are considerable regulatory obstacles for resuscitation research, especially with regard to multicenter studies. The experience of the Resuscitation Outcomes Consortium highlights these challenges, as described by Tisherman et al.¹⁴⁰ Multiple regulatory standards must be complied with, including those from the office for Human Research Protections, institutional review boards, and the Food and Drug Administration. Informed consent is not possible in many circumstances related to resuscitation research, yet it is fundamental to the protection of human research subjects, and any exception must be carefully approached. Community consultation and public disclosure are essential, as is an option to opt out of such research. In addition, postenrollment notification and consent are required. The regulatory and ethical issues associated with resuscitation research are significant but not insurmountable; furthermore, compliance is critical to maintain public support of such research as investigators seek to improve outcomes from cardiac arrest.

Conclusions

SCD and care of the post-cardiac arrest patient continue to be formidable challenges. Incremental improvements in outcome are the result of dedicated resuscitation researchers and expert healthcare providers who use the latest evidence to guide care. Key improvements in care of the SCD and post-cardiac arrest patient include refined approaches to CPR, airway and ventilation strategies, and early defibrillation. Advanced interventions such as TH and early PCI build on the foundation of expert basic and advanced life support, further improving outcomes. Regionalized systems that optimize out-of-hospital care and transfer patients to centers with expertise in treating post-cardiac arrest patients such as those seen for trauma and stroke are essential. Support for multi-institutional resuscitation research will facilitate the discovery of new approaches and the refinement of current strategies. Finally, concerted efforts to educate and involve the public, to optimize EMS quality and efficiency, and to implement optimal treatment strategies at community hospitals as in tertiary care centers will ensure that advances in resuscitation science are translated to improved patient outcomes.

Disclosures

None.

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