Improving Survival From Cardiac Arrest: A Review of Contemporary Practice and Challenges

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Cardiac arrest is a common and lethal condition frequently encountered by emergency medicine providers. Resuscitation of persons after cardiac arrest remains challenging, and outcomes remain poor overall. Successful resuscitation hinges on timely, high-quality cardiopulmonary resuscitation. The optimal method of providing chest compressions and ventilator support during cardiac arrest remains uncertain. Prompt and effective defibrillation of ventricular arrhythmias is one of the few effective therapies available for treatment of cardiac arrest. Despite numerous studies during several decades, no specific drug delivered during cardiac arrest has been shown to improve neurologically intact survival after cardiac arrest. Extracorporeal circulation can rescue a minority of highly selected patients with refractory cardiac arrest. Current management of pulseless electrical activity is associated with poor outcomes, but it is hoped that a more targeted diagnostic approach based on electrocardiography and bedside cardiac ultrasonography may improve survival. The evolution of postresuscitation care appears to have improved cardiac arrest outcomes in patients who are successfully resuscitated. The initial approach to early stabilization includes standard measures, such as support of pulmonary function, hemodynamic stabilization, and rapid diagnostic assessment. Coronary angiography is often indicated because of the high frequency of unstable coronary artery disease in comatose survivors of cardiac arrest and should be performed early after resuscitation. Optimizing and standardizing our current approach to cardiac arrest resuscitation and postresuscitation care will be essential for developing strategies for improving survival after cardiac arrest. [Ann Emerg Med. 2016;68:678-689.]

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INTRODUCTION

Cardiac arrest affects more than 500,000 US adults each year when both out-of-hospital and inhospital cardiac arrest are included.[1,2] Mortality after out-of-hospital cardiac arrest remains high. Only 25% of patients have a return of spontaneous circulation, and fewer than 10% of patients survive to hospital discharge.[1,3] Better outcomes after inhospital cardiac arrest are attributable primarily to more rapid and effective resuscitation, which achieves return of spontaneous circulation in approximately half of all patients with inhospital cardiac arrest.[2,4] Standardizing basic cardiac resuscitation and postarrest care is crucial for improving cardiac arrest outcomes, with individualized application of advanced therapies. Consensus guidelines are important to standardized care, but when guidelines change, additional evaluations of previously recommended therapies may be necessary.[5,6]

In this review, we will highlight several areas of scientific knowledge applicable to cardiac arrest resuscitation and the early postresuscitation phase for experienced emergency medicine and critical care providers. Specifically, we summarize emerging evidence and key issues for resuscitating patients from cardiac arrest, including recent guideline changes about basic and advanced life support measures,

extracorporeal membrane oxygenator (ECMO) support, new approaches to management of pulseless electrical activity, and initial priorities in postresuscitation care.

INTERVENTIONS

The quality of basic cardiopulmonary resuscitation (CPR) influences the efficacy of other interventions during resuscitation, and delayed or ineffective CPR may negate the potential benefit of concurrent therapies. Consensus guidelines emphasize that rapidly initiated, high-quality chest compressions are the most important intervention for ensuring return of spontaneous circulation and neurologic recovery in persons after cardiac arrest.[5-7] Even brief interruptions in chest compressions during CPR may reduce forward flow and organ perfusion, thus the emphasis on minimizing interruptions in chest compressions.[7] Recent preclinical research suggests that impairments in venous return and cardiac output result from the increase in intrathoracic pressure that accompanies positive-pressure ventilations during CPR.[8] This research has led to advocacy of compression-only CPR during cardiac arrest. Observational studies show better survival after out-of-hospital cardiac arrest in patients who

receive compression-only bystander CPR by laypersons.[9-11] Randomized studies and meta-analyses have not confirmed this benefit, leaving considerable uncertainty about efficacy.[7,12,13] Prolonged compression-only CPR without ventilation may become less effective over time, so perhaps a limited period of compression-only CPR by a bystander may be appropriate immediately after a person collapses, with subsequent initiation of rescue breaths after up to 3 cycles of 30 compressions.[7]

Studies of nearly all other interventions during cardiac arrest have been performed during standard compression/ventilation CPR and might have different efficacy with compression-only CPR. Mechanical devices designed to improve efficiency of chest compression have not consistently improved out-of-hospital cardiac arrest outcomes and are not recommended for routine use.[14-17] Failure of these devices to improve patient outcomes when applied broadly does not exclude a potential benefit during prolonged resuscitation or invasive procedures when rescuer fatigue could compromise quality of CPR.

The only intervention that improves survival after cardiac arrest, despite interrupting chest compressions, is administration of defibrillator shocks for termination of ventricular arrhythmias.[5-7,18] Defibrillator shocks should be delivered as soon as possible and should not be delayed for basic CPR.[7,18] Interruptions in CPR should be as brief as possible during defibrillation and pulse or rhythm checks. Outcomes may be improved when compressions are continued during rhythm analysis and defibrillator charging and then resumed immediately after a shock is delivered.[7,19] Multiple stacked shocks are no longer recommended because of the high first-shock efficacy of biphasic defibrillator shocks and lack of demonstrated benefit of stacked shocks.[7] Eliminating multiple stacked shocks also shortens the interruption of chest compressions.[5-7] Pulseless electrical activity is common after successful defibrillation, so CPR should be continued for another complete cycle after defibrillation, even if organized rhythm is restored.[7,19] A starting defibrillation energy of less than or equal to 200 J biphasic (either the manufacturer's suggested starting or maximum energy) is recommended; subsequent shocks should be delivered at the maximum energy for persistent ventricular arrhythmias or at the previously effective energy for recurrent ventricular arrhythmias.[7] The coarseness of the ventricular fibrillation waveform carries prognostic value during out-of-hospital cardiac arrest because of ventricular fibrillation, but algorithms guided by analysis of the ventricular fibrillation waveform do not improve survival to hospital discharge.[20]

Ventilation with a bag-valve mask or even oxygen delivered by a high-flow face mask can usually maintain adequate pulmonary and arterial oxygen tension during the early phase of CPR. Guidelines do not recommend use of any particular airway device during CPR for unselected patients.[5] Observational studies have shown conflicting outcomes with the use of advanced airways, including supraglottic airways and intubation.[21] Multiple studies suggest worse survival, neurologic outcomes, or both in patients who receive advanced airways during cardiac arrest in the out-of-hospital setting,[22] yet a recent meta-analysis suggested improved outcomes with intubation compared with a supraglottic airway.[23] The time required to deploy advanced airways is a critical element, and prolonged interruptions in CPR are likely to be detrimental. Advanced airways may not be needed early in the course of most adult cardiac arrests that are not caused by airway compromise.[5,9]

There is a paucity of data to support a survival benefit from any individual advanced cardiovascular life support (ACLS) intervention, even when provided early during resuscitation (Table 1).[5] Timely, high-quality CPR, early defibrillation, and optimal postresuscitation care predominantly determine patient outcomes. The efficacy of medications degrades with longer durations of arrest and with poor-quality CPR.[44] Interpretation of clinical trials of these medications is challenging because of heterogeneous resuscitation quality, with negative drug trial results caused by lack of efficacy under ideal circumstances, poor effectiveness in the population studied, or both. Many previous trials could have been underpowered because of low overall survival rates, and future trials should standardize all other aspects of resuscitation quality and postresuscitation care. The efficacy of drug administration in laboratory animal models of cardiac arrest likely differs from that observed in human patients, and thus results may not be easily extrapolated from animals to humans.[45]

Insertion of an intravenous line for administration of medications does not appear to improve outcomes in out-of-hospital cardiac arrest, potentially because of interruptions in CPR, lack of medication efficacy, or both.[24] The availability of rapidly deployable intraosseous line kits suitable for rapid fluid infusion and vasopressor administration has obviated the need for central line placement during arrest in most patients.[46]

The efficacy of medications for ACLS in improving survival during CPR remains uncertain, with some drugs improving return of spontaneous circulation and survival to hospital admission but not survival to hospital discharge (Table 1).[5] Vasopressors remain central to the ACLS algorithm to maintain coronary and cerebral perfusion pressure during CPR, particularly for patients with nonshockable rhythms.[5] Epinephrine has been the standard vasopressor for ACLS for many years despite an absence of

Table 1. Effects of interventions on survival during resuscitation for cardiac arrest.

Intervention	Effect on Outcomes	Best Evidence*
Compressions-only CPR	No benefit	Practice guidelines[12]; randomized trial[13]
Mechanical chest compressions	No benefit	Meta-analysis[14]
Impedance threshold device	No benefit	Meta-analysis[15]
Active compression/decompression	No benefit	Meta-analysis[16]
Delayed vs immediate CPR	No benefit	Meta-analysis[18]
Single vs multiple stacked shocks	No benefit	Practice guidelines[7]
Advanced airway placement	Uncertain	Meta-analysis[23]; observational study[22]
Intravenous line placement	No benefit	Randomized trial[24]
Epinephrine vs placebo	No benefit, possible harm	Meta-analysis[25]; observational studies[26,27]
High vs standard epinephrine dose	No benefit	Meta-analysis[28]
High-dose epinephrine vs high-dose norepinephrine	No benefit	Randomized trial[29]
Epinephrine vs vasopressin	No benefit	Meta-analyses[30,31]
Vasopressin+corticosteroids+epinephrine vs epinephrine alone	Possible benefit	Randomized trial[32]
Amiodarone vs lidocaine	Possible benefit	Meta-analysis[33]
Amiodarone vs nifekalant	Possible benefit	Meta-analysis[33]
Lidocaine vs placebo	Uncertain	Meta-analysis[33]; observational study[34]
Amiodarone vs placebo	No benefit	Meta-analysis[33]
Atropine vs placebo	No benefit	Observational study[35]
Aminophylline vs placebo	No benefit	Randomized trial[36]
Sodium bicarbonate vs placebo	Uncertain	Observational studies[37-39]
Magnesium sulfate vs placebo	No benefit	Practice guidelines[5]
Calcium chloride vs placebo	Uncertain	Practice guidelines[5]
Extracorporeal CPR vs conventional CPR	Possible benefit	Meta-analysis (observational studies)[40]; observational studies[41,42]
Out-of-hospital cooling	No benefit	Meta-analysis[43]

*All meta-analyses include randomized trials unless otherwise noted.

supportive, placebo-controlled, human clinical trials.[5,6,25,47] Randomized studies and meta-analyses have shown increased rates of return of spontaneous circulation with epinephrine versus placebo or with high-dose versus standard-dose epinephrine, without an improvement in overall or neurologically intact survival with any dose of epinephrine.[28,48,49] Observational studies have associated the use of epinephrine and higher epinephrine doses with reduced rates of neurologically intact survival after out-of-hospital cardiac arrest, raising concerns about the safety of epinephrine during ACLS.[26,27] More favorable outcomes might occur with earlier administration of epinephrine, which may facilitate early return of spontaneous circulation.[5] Epinephrine is thought to improve coronary and cerebral perfusion through favorable α-adrenergic effects. It also produces strong cardiac β-adrenergic receptor activation, which may trigger recurrent ventricular arrhythmias and produce reversible myocardial dysfunction, leading to impaired cardiac function after return of spontaneous circulation.[50-52] Because of these concerns, norepinephrine, an α-agonist vasopressor with weaker β-adrenergic effects than epinephrine, was compared with epinephrine in a randomized trial but failed to improve survival after cardiac arrest when used in high doses.[29] Vasopressin increases organ perfusion pressure without harmful β-adrenergic effects and may have greater efficacy during acidemic conditions that impair adrenergic receptor responses. Initial studies showed favorable effects of vasopressin, particularly in patients with asystole,[30] but subsequent studies have failed to show a mortality benefit of vasopressin when added to or substituted for epinephrine during cardiac arrest.[31] Vasopressin has been removed from the most recent guidelines to simplify the ACLS algorithm in the absence of a clear advantage of vasopressin.[5] The addition of vasopressin and corticosteroids to epinephrine during ACLS reduced epinephrine requirements and improved overall and neurologically intact survival in a small randomized trial of inhospital cardiac arrest, warranting further investigation into the role of these agents during CPR.[32] Future studies of vasopressors during CPR should explore lower doses, continuous infusions, or alternative vasopressors with less profound β-adrenergic effects.[24]

For patients with ventricular arrhythmias refractory to at least 1 defibrillator shock, administration of an antiarrhythmic drug may improve efficacy of subsequent shocks and increase the likelihood of return of spontaneous circulation.[33] The evidence showing that antiarrhythmic agents reduce mortality from cardiac arrest is limited, and none of the antiarrhythmic agents studied during cardiac arrest resulted in increased rates of survival to hospital discharge.[33,44] Amiodarone is recommended over lidocaine,

sotalol, and nifekalant because of its greater effectiveness for terminating ventricular arrhythmias, but this has translated only to an improvement in survival to hospital admission and not to hospital discharge.[33,53] A recent, large, multicenter trial of amiodarone, lidocaine, and placebo in shockable out-of-hospital cardiac arrest likewise showed no significant differences in survival to hospital discharge (hospital survival 24.4% with amiodarone, 23.7% with lidocaine, and 21.0% with placebo; P=.08).[44] Unlike patients with unwitnessed out-of-hospital cardiac arrest, those with witnessed out-of-hospital cardiac arrest had modestly lower mortality if they received either antiarrhythmic drug rather than placebo (27.7% and 27.8% versus 22.7%; P<.05), demonstrating that circumstances of arrest can influence efficacy of treatment. Patients receiving amiodarone had higher rates of bradyarrhythmias requiring treatment than did those receiving lidocaine, but they had similar rates of hospital survival. Subsequent use of antiarrhythmic agents after return of spontaneous circulation has been shown in 1 observational study to reduce the risk of recurrent cardiac arrest (20% versus 45%); however, these medications may not be needed when the underlying cause of the ventricular arrhythmia is addressed.[34] Long-term use of antiarrhythmic drugs after cardiac arrest does not improve long-term survival after cardiac arrest (particularly in the context of secondary-prevention defibrillator implantation).[5,54,55] β-Blockers facilitate defibrillation and prevent recurrence of ventricular arrhythmia in animal studies, but human data are lacking, and these drugs may exacerbate hemodynamic instability.[56] Randomized trials do not support routine use of magnesium sulfate as an antiarrhythmic drug.[5]

Evidence supporting the efficacy of other drugs during ACLS is poor. This lack of evidence led to a recent revision in the guidelines, which simplified the algorithm by removing recommendations for atropine and sodium bicarbonate, along with vasopressin.[5] No evidence supports the efficacy of atropine for asystole or bradycardic pulseless electrical activity, although atropine may be used for bradyarrhythmias refractory to epinephrine when increased vagal tone is thought to be a contributing factor.[35] No high-quality evidence supports the efficacy of sodium bicarbonate or calcium chloride for patients with cardiac arrest, and bicarbonate therapy may have adverse effects on acid-base balance, electrolyte levels, cardiac function, and cellular metabolism.[37-39] Anecdotally, calcium and bicarbonate administration may transiently stabilize hemodynamics in refractory shock or prolonged cardiac arrest, but only as a temporizing measure.[37,57] Glover et al[58] did not show improved outcomes with any ACLS medication; increased use of epinephrine, atropine, and

sodium bicarbonate was associated with a decreased likelihood of hospital survival.

Programs that offer support with an ECMO are complex, multidisciplinary endeavors that require substantial advance planning and a clearly defined protocol for patient selection and management; these programs are most suitable for large tertiary care hospitals with heart transplant and left ventricular assist device programs. Venoarterial ECMO during CPR, known as extracorporeal CPR, may provide a pathway to survival in selected patients with refractory cardiac arrest.[5] Extracorporeal CPR maintains organ perfusion while allowing time to reverse the cause of cardiac arrest, bridge a patient to a left ventricular assist device or heart transplant, or both.[5] Observational studies report short-term survival in 27% to 36% of patients who are treated with extracorporeal CPR for refractory cardiac arrest, post–return of spontaneous circulation shock, or both, implying that ECMO may be beneficial in these highly selected patients.[40-42,59] However, selection bias likely exaggerates the favorable outcomes reported in these studies.

Optimal outcomes from extracorporeal CPR may be facilitated by carefully selecting patients most likely to benefit, with explicit criteria to identify patients with reversible causes of cardiac arrest and exclude those with a low likelihood of good neurologic outcome (Table 2). In our opinion, the best outcomes with extracorporeal CPR might be expected for patients with witnessed arrest due to refractory ventricular arrhythmia from a presumed reversible cause, especially in patients who were initially treated with bystander CPR or who had transient return of spontaneous circulation. Extracorporeal CPR should be considered early during ACLS because the probability

Table 2. Indications and relative contraindications of extracorporeal CPR for refractory cardiac arrest.

Indications for ECPR	Relative Contraindications for ECPR
Shockable initial arrest rhythm or nonshockable rhythm with known precipitant	Obvious contraindications for heart transplant or a left ventricular assist device
Presumed reversible cause of arrest	Morbid obesity or peripheral arterial disease
Witnessed arrest with high-quality bystander CPR	Any factor requiring prolonged pauses in CPR to perform cannulation
Duration of pulselessness <15–20 min or transient ROSC with recurrent arrest	Evidence of major, irreversible neurologic injury or poor premorbid functional/neurologic status
Absence of major life-limiting comorbidities (especially endstage, noncardiac organ failure)	Advanced age or severe comorbidities

ECPR, Extracorporeal CPR.

of survival with functional neurologic recovery declines significantly after 15 to 20 minutes of standard CPR.[60] Extracorporeal CPR should generally be combined with emergency coronary angiography and cooling in the absence of an obvious noncardiac arrest cause; recently proposed relative contraindications for coronary angiography after out-of-hospital cardiac arrest may also apply to extracorporeal CPR.[42,61] Difficult femoral cannulation for ECMO can be expected during CPR, particularly in the morbidly obese; this can be a barrier to rapid initiation of extracorporeal CPR, given the need to minimize interruptions in chest compressions. Further research will be needed to optimize outcomes for this approach to refractory cardiac arrest.

The nonshockable rhythms, asystole and pulseless electrical activity, account for an increasing percentage of cardiac arrest episodes and have a markedly worse prognosis than shockable rhythms.[62] Asystole generally reflects the end stage of untreated or refractory cardiac arrest and is associated with dismal outcomes. Pulseless electrical activity is defined by the absence of palpable pulses despite organized cardiac electrical activity and encompasses numerous potential causes (Table 3).[62] It may be the initial arrest rhythm (primary pulseless electrical activity) or may develop during resuscitation of prolonged cardiac arrest from any cause (secondary pulseless electrical activity), especially after defibrillator shocks (postshock pulseless electrical activity) in the presence of prolonged duration of arrest, poor underlying cardiac function, or both.[62] All arrests caused by pulseless electrical activity rhythm have relatively poor outcomes.[62,63] No specific treatment is available for most patients with pulseless electrical activity, so early identification and treatment in the 20% of patients with potentially reversible causes are the only means to achieve return of spontaneous circulation.[35,36,62,64] The causes of pulseless electrical activity have been classically listed as the H's and T's (Table 3), but some authors have developed simpler approaches to its diagnosis.[62,65-67]

Pulseless electrical activity can be broadly divided into reversible states in which the arterial pressure generated by cardiac contraction is inadequate to produce a palpable pulse (termed "pseudo-pulseless electrical activity") and irreversible states of electromechanical dissociation when the electrical activation of the heart fails to produce a mechanical contraction.[62,65-67] Pseudo-pulseless electrical activity is the end stage of any form of profound shock. Desbiens[66] proposed a "3×3 rule," separating reversible causes of pseudo-pulseless electrical activity into 3 underlying categories: hypovolemic, cardiogenic, or obstructive. Obstructive shock was further subdivided into 3 treatable causes: pulmonary embolism, cardiac tamponade, or tension pneumothorax.[66] Metabolic disturbances producing pulseless electrical activity should also be considered, especially hyperkalemia, hypoxemia, and acidosis; less frequent causes of cardiac arrest include hypothermia, hypokalemia, hypoglycemia, and drug overdose (Table 3). Hypoxemia and acidosis typically contribute to persistent or recurrent pulseless electrical activity during prolonged cardiac arrest, although hypoxemia may cause almost 25% of arrests attributed to pulseless electrical activity.[65,66,68,69]

The pulse rate and QRS width on ECG can provide useful clues in regard to the cause of nontraumatic pulseless electrical activity (Figure 1).[62] Reversible causes (pseudo-pulseless electrical activity from profound shock) often produce tachycardia with visible P waves and a narrow QRS complex (tachycardic pulseless electrical activity with a supraventricular rhythm).[65-67] Electromechanical dissociation and irreversible causes of pulseless electrical activity typically manifest bradycardia without visible P waves and a wide QRS complex (bradycardic pulseless electrical activity with a ventricular escape rhythm).[65,67] Causes of wide or slow bradycardic pulseless electrical

Table 3. Traditional approach to causes of pulseless electrical activity (H's and T's).*

H's	T's
Hypoxemia	Toxins/tablets
H+ (acidosis)	Tamponade
Hyperkalemia (hypokalemia not likely)	Tension pneumothorax
Hypovolemia	Thrombosis, coronary (MI)
Hypothermia	Thrombosis, pulmonary embolism
Hypoglycemia (not likely)	Trauma

*Adapted from Link et al.[5] Used with permission.

|	Rapid rate ± P waves	Slow rate, no P waves
Narrow QRS	• Hypovolemia, including trauma/bleeding • Septic/anaphylactic shock • Cardiac tamponade • Pulmonary embolism (usually) • Tension pneumothorax • Dynamic hyperinflation • Cardiogenic shock (variable) • Any other cause of profound shock	• Massive inferior MI (P waves with complete heart block) • Vagal response due to pulmonary embolism or other obstructive shock • Hypothermia (variable)
Wide QRS	• Massive anterior MI • Pulmonary embolism (rarely, in presence of acute RBBB) • Tricyclic antidepressant overdose ± other sodium channel blocker overdoses	• Hyperkalemia • Hypoxemia • Acidosis • Postcountershock PEA • Hypothermia (variable) • Sodium-channel blocker overdose (variable)

Figure 1. Major causes of pulseless electrical activity (PEA) arrest, by QRS width and pulse rate. *MI*, Myocardial infarction; *RBBB*, right bundle branch block; ±, with or without. Data from Myerburg et al,[62] Littmann et al,[65] Desbiens,[66] and Mehta and Brady.[67]

activity include hyperkalemia (expect characteristic ECG changes), sodium channel blocker toxicity (suggested by the clinical scenario), postshock pulseless electrical activity, massive myocardial infarction, hypoxemia, and metabolic causes, such as acidosis, hypothermia, prolonged arrest, and multiorgan failure. Narrow or rapid pulseless electrical activity can progress to wide or slow pulseless electrical activity as metabolic derangements accumulate.[62,65,67] A pronounced vagal response leading to bradycardic pulseless electrical activity with a narrow QRS complex may occur in patients with obstructive shock (including end-stage aortic stenosis or pulmonary hypertension) or inferior myocardial infarction; in theory, atropine could antagonize this response. Acute myocardial infarction is a frequent cause of pulseless electrical activity and an important exception to the narrow or rapid and wide or slow dichotomy—a large, inferior myocardial infarction often produces slow, narrow rhythms from complete heart block, and a large, anterior myocardial infarction often produces rapid, wide rhythms because of interventricular conduction abnormalities with sinus tachycardia.

Littmann et al[65] recommended a therapeutic approach to pulseless electrical activity based on QRS width in addition to vasopressor administration: patients with a narrow QRS complex should be treated with fluid resuscitation while an aggressive search is made for reversible, obstructive causes, and patients with a wide QRS complex should empirically receive calcium chloride (to treat hyperkalemia), sodium bicarbonate (to treat hyperkalemia or sodium channel blocker toxicity), or both.[57,65,69] The absence of a palpable pulse during chest compressions may imply a potential fluid-responsive shock state, such as hypovolemic or obstructive shock. A palpable pulse during chest compressions suggests pump failure from a cardiogenic or metabolic cause.[66]

A subxiphoid or subcostal, echocardiographic, 4-chamber cardiac view can be rapidly obtained from the abdomen during CPR pulse checks to guide resuscitation.[70-72] Identification of electromechanical dissociation (cardiac standstill) during treatment of pulseless electrical activity indicates irreversible myocardial dysfunction with such a low likelihood for achieving return of spontaneous circulation that termination of resuscitation may be considered.[70,73] Cardiac contraction (pseudo-pulseless electrical activity) portends a better prognosis for successful resuscitation.[70,73,74] An echocardiographic differential diagnosis can be quickly generated according to the relative sizes of the cardiac chambers and the presence or absence of a large pericardial effusion.[72] We have condensed the 3 suggested approaches to pulseless electrical activity into 1 algorithm (Figure 2), which is intended for experienced emergency medicine and critical care medicine providers
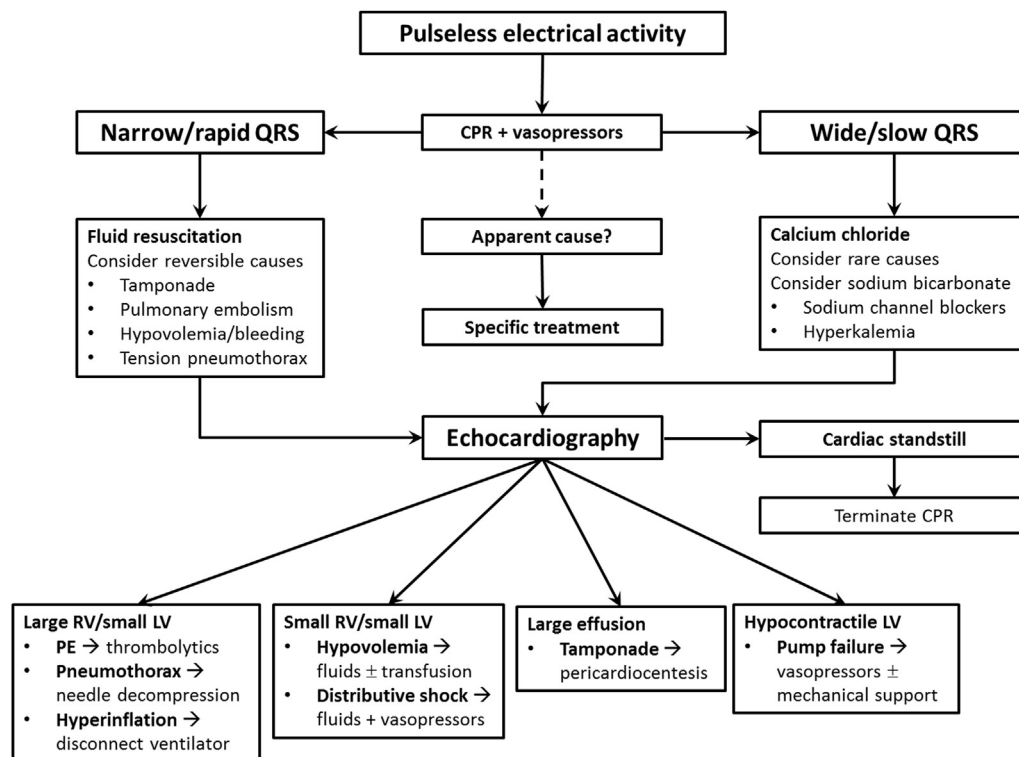
Figure 2. Suggested algorithm for management of PEA arrest. *RV,* Right ventricle; *LV,* left ventricle; *PE,* pulmonary embolism. Data from Littmann et al[65] and Hernandez et al.[72]

working in a hospital-based setting and has not been prospectively validated.[65-67,70] We suggest fluid resuscitation, vasopressors, and a rapid search for reversible causes in narrow or rapid pulseless electrical activity, guided by echocardiography. For wide or slow pulseless electrical activity, consider hyperkalemia or (if history is suggestive) sodium channel blocker toxicity and administer empiric calcium chloride with or without sodium bicarbonate.[57,69]

Patients resuscitated from cardiac arrest remain at high risk of complications, including recurrent arrest, shock, and multiorgan failure. Up to two thirds of patients achieving return of spontaneous circulation after out-of-hospital cardiac arrest or inhospital cardiac arrest die in the hospital.[2-4] Early post–return of spontaneous circulation management should seek to stabilize the patient, identify treatable causes of arrest, and initiate beneficial therapies.[75,76] Attention should be paid to support of the airway, breathing, circulation, and neurologic disability (Figure 3).

Securing an endotracheal tube for airway protection is important for patients who remain obtunded or comatose after return of spontaneous circulation. Ventilator settings should be lung protective, using a tidal volume of 6 to 8 mL/kg (based on ideal body weight), with application of positive end-expiratory pressure to maintain adequate arterial oxygenation.[76] Correction of hypoxemia is important to prevent recurrent arrest, but elevated arterial oxygen levels (hyperoxia) early after return of spontaneous circulation are associated with adverse outcomes.[77] The goal oxygen saturation should be 94% to 98%, rather than 100%.[76] Severe hypercarbia should be avoided, but hypocapnia early after return of spontaneous circulation can provoke cerebral vasoconstriction and is associated with adverse outcomes.[77] End-tidal CO_2 monitoring should be used to achieve normal to slightly elevated $PaCO_2$ levels.[76,77] Chest radiography can confirm endotracheal tube placement and exclude complications of CPR, such as pneumothorax. Insertion of a gastric tube is often appropriate to decompress the stomach and administer medications.

Hypotension and shock are common after return of spontaneous circulation and are associated with adverse outcomes.[52,78] The shock state that follows return of spontaneous circulation is dynamic, progressing from low-output cardiogenic shock caused by postarrest myocardial dysfunction to vasodilated distributive shock with capillary leak caused by a systemic inflammatory response that mimics sepsis.[51,52] Observational studies suggest that early
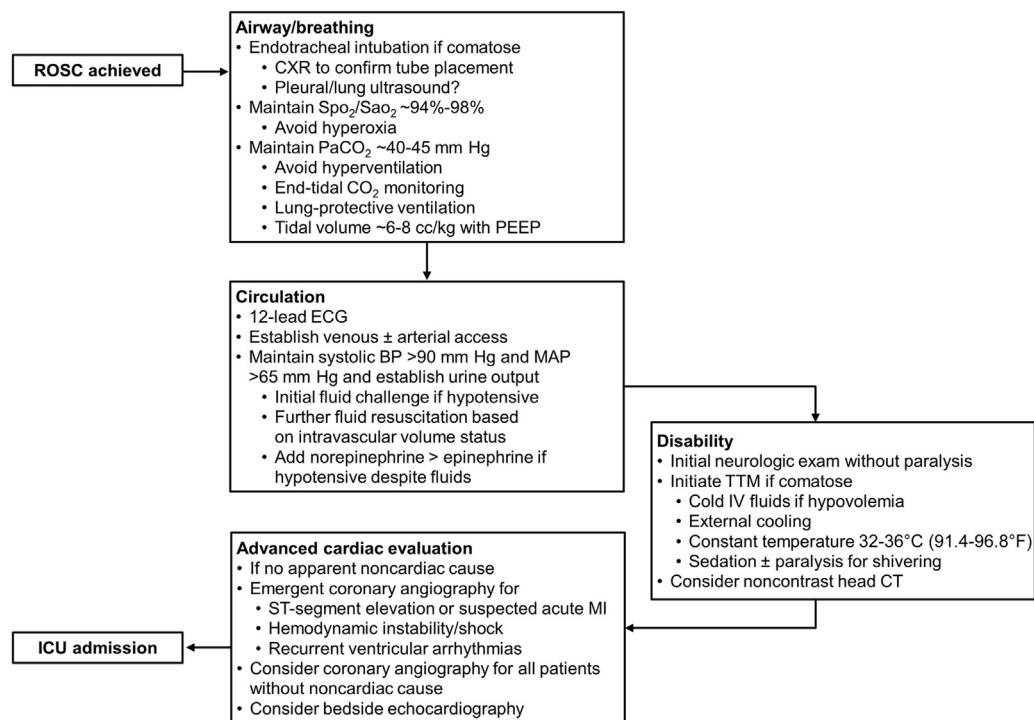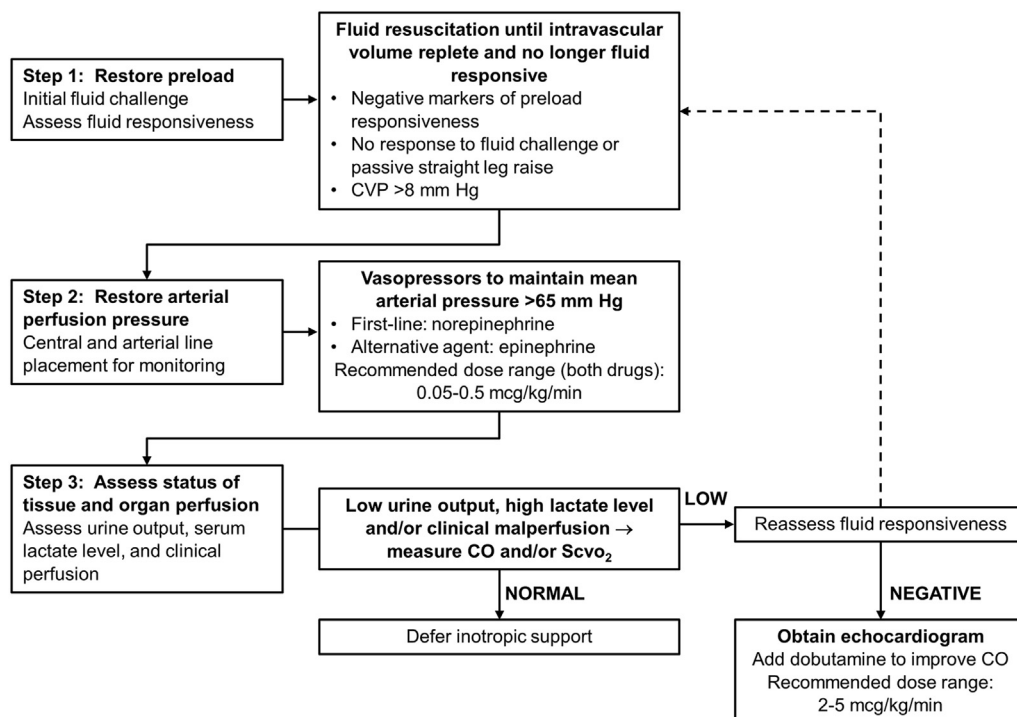

Figure 3. Suggested algorithm for early management of patients after resuscitation from cardiac arrest. *ROSC*, Return of spontaneous circulation; *CXR*, chest radiograph; *PEEP*, positive end-expiratory pressure; *BP*, blood pressure; *MAP*, mean arterial pressure; *TTM*, targeted temperature management; *IV*, intravenous. Data from Callaway et al,[75] Sutherasan et al,[77] and Geri et al.[86]

hemodynamic optimization as part of a postarrest care bundle can improve outcomes, analogous to management of septic shock (Figure 4).[52,79-81] Patients often require fluid resuscitation after return of spontaneous circulation, although this should be guided by measures of preload responsiveness and intravascular volume status to avoid volume overload.[51,52,76] Hypotension refractory to fluids typically responds to vasopressors. Norepinephrine is the first-line vasopressor for shock after return of spontaneous circulation; epinephrine is a useful alternative, but dopamine is more proarrhythmic and therefore not recommended (Figure 4).[52,75,76,82] Guidelines recommend maintaining a systolic blood pressure greater than 90 to 100 mm Hg and a mean arterial pressure greater than 65 mm Hg.[75,76] Observational studies have found that a higher mean arterial pressure early after return of spontaneous circulation is associated with better neurologic outcomes, up to 80 to 100 mm Hg; there is no evidence that increasing vasopressor doses to achieve a higher mean arterial pressure is beneficial.[78,83] Central venous and arterial lines are indicated for most patients to allow hemodynamic monitoring and serial lactate measurements.

Patients with impaired tissue and organ perfusion, shown by an elevated serum lactate level or low urine output, should have their cardiac status assessed. Central venous oxygen saturation can be used as a surrogate measure of cardiac output in patients with organ hypoperfusion after cardiac arrest.[83] Echocardiography can exclude persistent precipitating pathologic issues in patients who are hypotensive after return of spontaneous circulation, including pericardial effusion or evidence of pulmonary embolism. Echocardiography often shows left ventricular systolic dysfunction, but echocardiographic abnormalities do not consistently predict vasopressor requirements or outcomes.[52,84] Inotropic agents should be reserved for patients with objective evidence of organ hypoperfusion coupled with low cardiac output or low central venous oxygen saturation; dobutamine is effective at low doses for reversal of myocardial dysfunction (Figure 4).[52,76] Bradycardia itself generally does not require specific treatment as long as perfusion is adequate. Early resuscitation should restore a normal urine output (>0.5 to 1 mL/kg per hour), with normal or declining serum lactate levels.[85]

Coronary artery disease is the most common trigger for out-of-hospital cardiac arrest and is identified in at least two thirds of patients who are resuscitated and undergo coronary angiography.[61] Twelve-lead ECG should be performed immediately after return of spontaneous circulation in the absence of an obvious noncardiac cause to identify ST-segment elevation myocardial infarction, which

Figure 4. Suggested algorithm for early hemodynamic optimization after resuscitation of a patient from cardiac arrest. *CVP*, Central venous pressure; *CO*, cardiac output. Data from Gaieski et al,[79] Walters et al,[80] and Sunde et al.[81] (Adapted from Jentzer et al.[52] Used with permission.)

is found in 25% to 30% of patients resuscitated from out-of-hospital cardiac arrest.[61,86-88] The sensitivity of ECG for acute myocardial infarction after out-of-hospital cardiac arrest is poor. Approximately one third of patients without ST-segment elevation have unstable coronary artery disease warranting percutaneous coronary intervention, including 10% to 20% without any ischemic ECG changes.[86-88] Because of direct myocardial injury, troponin level elevations are nearly universal after resuscitation from cardiac arrest but lack specificity for coronary occlusion.[89] Emergency coronary angiography (within 2 hours) is recommended for comatose survivors of out-of-hospital cardiac arrest in the presence of ST-segment elevation, suspected acute myocardial infarction, or substantial hemodynamic or electrical instability.[75,90] Coronary angiography may be reasonable independent of the presence of coma for most survivors of out-of-hospital cardiac arrest without an obvious noncardiac cause of arrest, especially for patients with evidence of cardiac dysfunction.[75,90,91] Most patients resuscitated from out-of-hospital cardiac arrest will be comatose, and coma alone should not exclude them from coronary angiography, if indicated.[75] Markers of poor neurologic outcome have been proposed to exclude patients from coronary angiography after out-of-hospital cardiac arrest, but they have not been prospectively validated.[61,92] The optimal medical therapy before coronary angiography for patients with out-of-hospital cardiac arrest caused by a suspected acute myocardial infarction remains uncertain, but in the absence of substantial bleeding should likely include aspirin (rectally or through a nasogastric tube), clopidogrel or ticagrelor (through a nasogastric tube), and intravenous heparin or bivalirudin.[90] Observational studies show a significantly lower mortality in comatose patients who undergo early coronary angiography after out-of-hospital cardiac arrest, especially for those receiving early percutaneous coronary intervention.[86,88,92,93] Pulmonary embolism is an important noncardiac cause of arrest, and computed tomography (CT) angiography of the chest is often appropriate.[76]

Focused neurologic examination should be performed soon after return of spontaneous circulation to determine the need for targeted temperature management, which is indicated for comatose survivors of cardiac arrest who are unable to follow commands.[75,85] It involves maintaining a low body temperature to prevent the secondary neurologic injury that occurs after cardiac arrest.[94] Current guidelines recommend targeted temperature management for essentially all comatose survivors of cardiac arrest, including those with out-of-hospital and inhospital cardiac arrest and with shockable and nonshockable rhythms.[75] Studies have shown

a benefit for providing targeted temperature management compared with not doing so but have not shown a consistent benefit for any particular goal temperature.[94] Current guidelines recommend cooling the patient immediately after return of spontaneous circulation to maintain a stable target temperature between 32°C (89.6°F) and 36°C (96.8°F) for at least 24 hours, followed by fever prevention.[75,76] A lower target temperature of 33°C (91.4°F) does not appear superior to a higher one of 36°C (96.8°F) for any major outcomes or in any major subgroup of out-of-hospital cardiac arrest and may be associated with adverse outcomes in patients with shock.[94-96] Initiation of targeted temperature management should occur as soon as possible after return of spontaneous circulation, even while the patient is still undergoing acute stabilization, diagnostic studies, and therapeutic interventions, such as coronary angiography. Cooling patients before they arrive at the hospital has failed to improve out-of-hospital cardiac arrest outcomes, and empirically administering large volumes of cold intravenous fluids may provoke pulmonary edema.[43,97] The method of cooling does not appear critical for success, but computer-controlled devices offer more stable temperature control.[98] When fluid resuscitation is indicated, cold fluids help achieve faster cooling. Sedation and neuromuscular blockade are often necessary to facilitate targeted temperature management, especially in the presence of shivering; however, neurologic examination is often confounded by these medications, which must be taken into account during assessment of the patient. An emergency noncontrast CT scan of the brain may be appropriate in comatose survivors of out-of-hospital cardiac arrest to exclude relevant intracranial pathologic findings, but it is not essential before emergency coronary angiography in patients without apparent head trauma.[76]

In summary, the mortality rate after cardiac arrest remains high despite incremental refinements of advanced life support strategies and postresuscitation care, which have led to gradual improvements in survival after cardiac arrest over time.[2,99] High-quality early CPR, focusing on chest compressions and early defibrillation, remains the cornerstone of management of cardiac arrest. Few therapies included in advanced life support algorithms have been conclusively shown to improve overall survival or neurologic outcomes, and delivery of these therapies must not compromise CPR quality. Pulseless electrical activity remains a challenging clinical problem, and new approaches to diagnosis and management may provide an opportunity to improve outcomes. Optimal, early postresuscitation management is crucial, and early coronary angiography and hemodynamic stabilization have the potential to improve patient outcomes. Resuscitation of patients from cardiac

arrest remains an important area of research, and future studies will explore new strategies for immediate postresuscitation and early postresuscitation care.

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