Part 9: Post–Cardiac Arrest Care

2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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There is increasing recognition that systematic post–cardiac arrest care after return of spontaneous circulation (ROSC) can improve the likelihood of patient survival with good quality of life. This is based in part on the publication of results of randomized controlled clinical trials as well as a description of the post–cardiac arrest syndrome.[1–3] Post–cardiac arrest care has significant potential to reduce early mortality caused by hemodynamic instability and later morbidity and mortality from multiorgan failure and brain injury.[3,4] This section summarizes our evolving understanding of the hemodynamic, neurological, and metabolic abnormalities encountered in patients who are initially resuscitated from cardiac arrest.

The initial objectives of post–cardiac arrest care are to

- Optimize cardiopulmonary function and vital organ perfusion.
- After out-of-hospital cardiac arrest, transport patient to an appropriate hospital with a comprehensive post–cardiac arrest treatment system of care that includes acute coronary interventions, neurological care, goal-directed critical care, and hypothermia.
- Transport the in-hospital post–cardiac arrest patient to an appropriate critical-care unit capable of providing comprehensive post–cardiac arrest care.
- Try to identify and treat the precipitating causes of the arrest and prevent recurrent arrest.

Subsequent objectives of post–cardiac arrest care are to

- Control body temperature to optimize survival and neurological recovery
- Identify and treat acute coronary syndromes (ACS)
- Optimize mechanical ventilation to minimize lung injury
- Reduce the risk of multiorgan injury and support organ function if required
- Objectively assess prognosis for recovery
- Assist survivors with rehabilitation services when required

Systems of Care for Improving Post–Cardiac Arrest Outcomes

Post–cardiac arrest care is a critical component of advanced life support (Figure). Most deaths occur during the first 24 hours after cardiac arrest.[5,6] The best hospital care for patients with ROSC after cardiac arrest is not completely known, but there is increasing interest in identifying and optimizing practices that are likely to improve outcomes (Table 1).[7] Positive associations have been noted between the likelihood of survival and the number of cardiac arrest cases treated at any individual hospital.[8,9] Because multiple organ systems are affected after cardiac arrest, successful post–cardiac arrest care will benefit from the development of system-wide plans for proactive treatment of these patients. For example, restoration of blood pressure and gas exchange does not ensure survival and functional recovery. Significant cardiovascular dysfunction can develop, requiring support of blood flow and ventilation, including intravascular volume expansion, vasoactive and inotropic drugs, and invasive devices. Therapeutic hypothermia and treatment of the underlying cause of cardiac arrest impacts survival and neurological outcomes. Protocolized hemodynamic optimization and multidisciplinary early goal-directed therapy protocols have been introduced as part of a bundle of care to improve survival rather than single interventions.[10–12] The data suggests that proactive titration of post–cardiac arrest hemodynamics to levels intended to ensure organ perfusion and oxygenation may improve outcomes. There are multiple specific options for acheiving these goals, and it is difficult to distinguish between the benefit of protocols or any specific component of care that is most important.

A comprehensive, structured, multidisciplinary system of care should be implemented in a consistent manner for the treatment of post–cardiac arrest patients (Class I, LOE B). Programs should include as part of structured interventions therapeutic hypothermia; optimization of hemodynamics and gas exchange; immediate coronary reperfusion when indicated for restoration of coronary blood flow with percutaneous coronary intervention (PCI); glycemic control; and neurological diagnosis, management, and prognostication.

Overview of Post–Cardiac Arrest Care

The provider of CPR should ensure an adequate airway and support breathing immediately after ROSC. Unconscious

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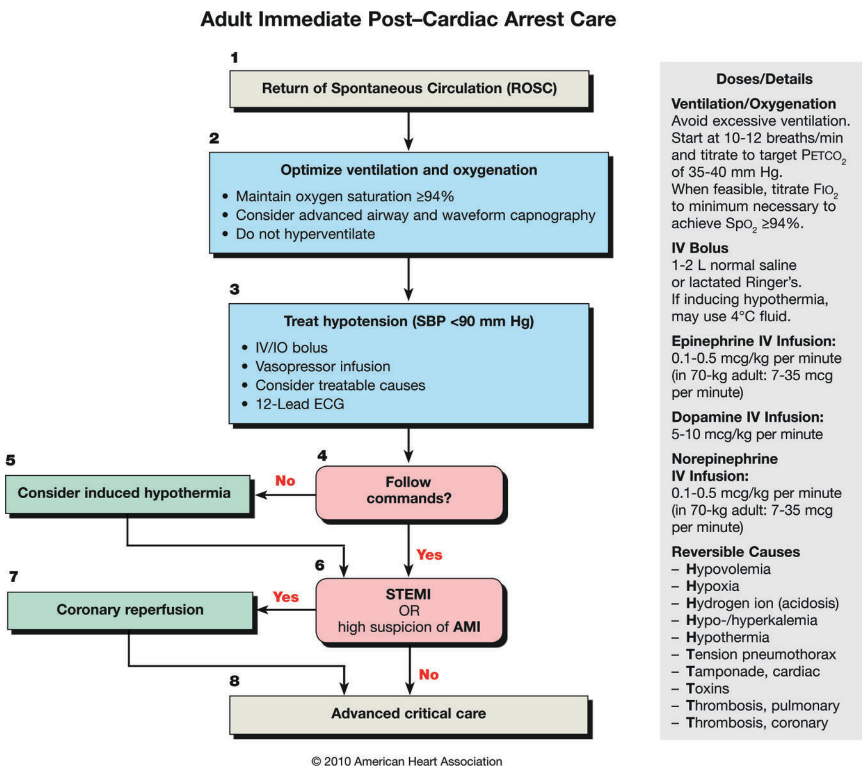

Figure. Post–cardiac arrest care algorithm.

patients usually require an advanced airway for mechanical support of breathing. It may be necessary to replace a supraglottic airway used for initial resuscitation with an endotracheal tube, although the timing of replacement may vary. Methods for securing an advanced airway are discussed in Part 8.1: "Airway Management," but several simple maneuvers deserve consideration. For example, rescuers and long-term hospital providers should avoid using ties that pass circumferentially around the patient's neck, potentially obstructing venous return from the brain. They should also elevate the head of the bed 30° if tolerated to reduce the incidence of cerebral edema, aspiration, and ventilatory-associated pneumonia. Correct placement of an advanced airway, particularly during patient transport, should be monitored using waveform capnography as described in other sections of the *2010 AHA Guidelines for CPR and ECC*. Oxygenation of the patient should be monitored continuously with pulse oximetry.

Although 100% oxygen may have been used during initial resuscitation, providers should titrate inspired oxygen to the lowest level required to achieve an arterial oxygen saturation of ≥94%, so as to avoid potential oxygen toxicity. It is recognized that titration of inspired oxygen may not be possible immediately after out-of-hospital cardiac arrest until the patient is transported to the emergency department or, in the case of in-hospital arrest, the intensive care unit (ICU). Hyperventilation or "overbagging" the patient is common after cardiac arrest and should be avoided because of potential adverse hemodynamic effects. Hyperventilation increases intrathoracic pressure and inversely lowers cardiac output. The decrease in Pa_{CO_2} seen with hyperventilation can also potentially decrease cerebral blood flow directly. Ventilation may be started at 10 to 12 breaths per minute and titrated to achieve a P_{ETCO_2} of 35 to 40 mm Hg or a Pa_{CO_2} of 40 to 45 mm Hg.

The clinician should assess vital signs and monitor for recurrent cardiac arrhythmias. Continuous electrocardiographic (ECG) monitoring should continue after ROSC, during transport, and throughout ICU care until stability has been achieved. Intravenous (IV) access should be obtained if not already established and the position and function of any intravenous catheter verified. IV lines should be promptly established to replace emergent intraosseous access achieved during resuscitation. If the patient is hypotensive (systolic blood pressure <90 mm Hg), fluid boluses can be considered. Cold fluid may be used if therapeutic hypothermia is elected. Vasoactive drug infusions such as dopamine, norepinephrine, or epinephrine may be initiated if necessary and titrated to achieve a minimum systolic blood pressure of ≥90 mm Hg or a mean arterial pressure of ≥65 mm Hg.

Brain injury and cardiovascular instability are the major determinants of survival after cardiac arrest.[13] Because therapeutic hypothermia is the only intervention demonstrated to improve neurological recovery, it should be considered for any patient who is unable to follow verbal commands after ROSC. The patient should be transported to a facility that reliably provides this therapy in addition to coronary reperfusion (eg, PCI) and other goal-directed postarrest care therapies.

Overall the most common cause of cardiac arrest is cardiovascular disease and coronary ischemia.[14,15] Therefore, a 12-lead ECG should be obtained as soon as possible to detect ST elevation or new or presumably new left bundle-branch block. When there is high suspicion of acute myocardial infarction (AMI), local protocols for treatment of AMI and coronary reperfusion should be activated. Even in the absence of ST elevation, medical or interventional treatments may be considered for treatment of ACS[14,16,17] and should not be deferred in the presence of coma or in conjunction with

Table 1. Multiple System Approach to Post–Cardiac Arrest Care

Ventilation	Hemodynamics	Cardiovascular	Neurological	Metabolic
• Capnography	• Frequent Blood Pressure Monitoring/Arterial-line	• Continuous Cardiac Monitoring	• Serial Neurological Exam	• Serial Lactate
• Rationale: Confirm secure airway and titrate ventilation	• Rationale: Maintain perfusion and prevent recurrent hypotension	• Rationale: Detect recurrent arrhythmia	• Rationale: Serial examinations define coma, brain injury, and prognosis	• Rationale: Confirm adequate perfusion
• Endotracheal tube when possible for comatose patients	• Mean arterial pressure $\geq$65 mm Hg or systolic blood pressure $\geq$90 mm Hg	• No prophylactic antiarrhythmics	• Response to verbal commands or physical stimulation	
• P_{ETCO_2} $\sim$35–40 mm Hg		• Treat arrhythmias as required	• Pupillary light and corneal reflex, spontaneous eye movement	
• $Paco_2$ $\sim$40–45 mm Hg		• Remove reversible causes	• Gag, cough, spontaneous breaths	
• Chest X-ray	• Treat Hypotension	• 12-lead ECG/Troponin	• EEG Monitoring If Comatose	• Serum Potassium
• Rationale: Confirm secure airway and detect causes or complications of arrest: pneumonitis, pneumonia, pulmonary edema	• Rationale: Maintain perfusion	• Rationale: Detect Acute Coronary Syndrome/ST-Elevation Myocardial Infarction; Assess QT interval	• Rationale: Exclude seizures	• Rationale: Avoid hypokalemia which promotes arrhythmias
	• Fluid bolus if tolerated		• Anticonvulsants if seizing	• Replace to maintain K >3.5 mEq/L
	• Dopamine 5–10 mcg/kg per min			
	• Norepinephrine 0.1–0.5 mcg/kg per min			
	• Epinephrine 0.1–0.5 mcg/kg per min			
• Pulse Oximetry/ABG	...	• Treat Acute Coronary Syndrome	• Core Temperature Measurement If Comatose	• Urine Output, Serum Creatinine
• Rationale: Maintain adequate oxygenation and minimize Fio_2	...	• Aspirin/heparin	• Rationale: Minimize brain injury and improve outcome	• Rationale: Detect acute kidney injury
• Spo_2 $\geq$94%	...	• Transfer to acute coronary treatment center	• Prevent hyperpyrexia >37.7°C	• Maintain euvolemia
• Pao_2 $\sim$100 mm Hg	...	• Consider emergent PCI or fibrinolysis	• Induce therapeutic hypothermia if no contraindications	• Renal replacement therapy if indicated
• Reduce Fio_2 as tolerated	...		• Cold IV fluid bolus 30 mL/kg if no contraindication	
• Pao_2/Fio_2 ratio to follow acute lung injury	...		• Surface or endovascular cooling for 32°C–34°C×24 hours	
	...		• After 24 hours, slow rewarming 0.25°C/hr	
• Mechanical Ventilation	...	• Echocardiogram	• Consider Non-enhanced CT Scan	• Serum Glucose
• Rationale: Minimize acute lung injury, potential oxygen toxicity	...	• Rationale: Detect global stunning, wall-motion abnormalities, structural problems or cardiomyopathy	• Rationale: Exclude primary intracranial process	• Rationale: Detect hyperglycemia and hypoglycemia
• Tidal Volume 6–8 mL/kg	...			• Treat hypoglycemia (<80 mg/dL) with dextrose
• Titrate minute ventilation to P_{ETCO_2} $\sim$35–40 mm Hg $Paco_2$ $\sim$40–45 mm Hg	...			• Treat hyperglycemia to target glucose 144–180 mg/dL
• Reduce Fio_2 as tolerated to keep Spo_2 or Sao_2 $\geq$94%	...			• Local insulin protocols
	...	• Treat Myocardial Stunning	• Sedation/Muscle Relaxation	• Avoid Hypotonic Fluids
	...	• Fluids to optimize volume status (requires clinical judgment)	• Rationale: To control shivering, agitation, or ventilator desynchrony as needed	• Rationale: May increase edema, including cerebral edema
	...	• Dobutamine 5–10 mcg/kg per min		
	...	• Mechanical augmentation (IABP)		

hypothermia. Concurrent PCI and hypothermia are safe, with good outcomes reported for some comatose patients who undergo PCI.

Patients who are unconscious or unresponsive after cardiac arrest should be directed to an inpatient critical-care facility with a comprehensive care plan that includes acute cardiovascular interventions, use of therapeutic hypothermia, standardized medical goal-directed therapies, and advanced neurological monitoring and care. Neurological prognosis may be difficult to determine during the first 72 hours, even for patients who are not undergoing therapeutic hypothermia. This time frame for prognostication is likely to be extended in patients being cooled.[18] Many initially comatose survivors of cardiac arrest have the potential for full recovery such that they are able to lead normal lives.[1,2,19] Between 20% and 50% or more of survivors of out-of-hospital cardiac arrest who are comatose on arrival at the hospital may have good one-year neurological outcome.[1,2,11] Therefore, it is important to place patients in a hospital critical-care unit where expert care and neurological evaluation can be performed and where appropriate testing to aid prognosis is available and performed in a timely manner.

Attention should be directed to treating the precipitating cause of cardiac arrest after ROSC. The provider should initiate or request studies that will further aid in evaluation of the patient. It is important to identify and treat any cardiac, electrolyte, toxicological, pulmonary, and neurological precipitants of arrest. The clinician may find it helpful to review the H's and T's mnemonic to recall factors that may contribute to cardiac arrest or complicate resuscitation or postresuscitation care: hypovolemia, hypoxia, hydrogen ion (acidosis of any etiology), hyper-/hypokalemia, moderate to severe hypothermia, toxins, tamponade (cardiac), tension pneumothorax, and thrombosis of the coronary or pulmonary vasculature. For further information on treating other causes of cardiac arrest, see Part 12: "Special Resuscitation Situations."

Targeted Temperature Management

Induced Hypothermia

For protection of the brain and other organs, hypothermia is a helpful therapeutic approach in patients who remain comatose (usually defined as a lack of meaningful response to verbal commands) after ROSC. Questions remain about specific indications and populations, timing and duration of therapy, and methods for induction, maintenance, and subsequent reversal of hypothermia. One good randomized trial[1] and a pseudorandomized trial[2] reported improved neurologically intact survival to hospital discharge when comatose patients with out-of-hospital ventricular fibrillation (VF) cardiac arrest were cooled to 32°C to 34°C for 12 or 24 hours beginning minutes to hours after ROSC. Additional studies with historical control groups show improved neurological outcome after therapeutic hypothermia for comatose survivors of VF cardiac arrest.[20,21]

No randomized controlled trials have compared outcome between hypothermia and normothermia for non-VF arrest. However, 6 studies with historical control groups reported a beneficial effect on outcome from use of therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest associated with any arrest rhythm.[11,22–26] Only one study with historical controls reported better neurological outcome after VF cardiac arrest but no difference in outcome after cardiac arrest associated with other rhythms.[27] Two nonrandomized studies with concurrent controls[28,29] indicate a possible benefit of hypothermia after in- and out-of-hospital cardiac arrest associated with non-VF initial rhythms.

Case series have reported the feasibility of using therapeutic hypothermia after ROSC in the setting of cardiogenic shock[23,30,31] and therapeutic hypothermia in combination with emergent PCI.[32–36] Case series also report successful use of fibrinolytic therapy for AMI after ROSC,[37,38] but data are lacking about interactions between fibrinolytics and hypothermia in this population.

The impact of the timing of initiating hypothermia after cardiac arrest is not completely understood. Studies of animal models of cardiac arrest showed that short-duration hypothermia (≤1 hour) achieved <10 to 20 minutes after ROSC had a beneficial effect that was lost when hypothermia was delayed.[39–41] Beyond the initial minutes of ROSC and when hypothermia is prolonged (>12 hours), the relationship between the onset of hypothermia and the resulting neuroprotection is less clear.[42,43] Two prospective clinical trials in which hypothermia was achieved within 2 hours[2] or at a median of 8 hours (interquartile range [IQR] 4 to 16 hours)[1] after ROSC both demonstrated better outcomes in the hypothermia-treated than the normothermia-treated subjects. Subsequent to these studies, one registry-based case series of 986 comatose post–cardiac arrest patients[35] suggested that time to initiation of cooling (IQR 1 to 1.8 hours) and time to achieving target temperature (IQR 3 to 6.7 hours) were not associated with improved neurological outcome after discharge. A case series of 49 consecutive comatose post–cardiac arrest patients[44] cooled intravascularly after out-of-hospital cardiac arrest also documented that time to target temperature (median 6.8 hours [IQR 4.5 to 9.2 hours]) was not an independent predictor of neurological outcome.

The optimal duration of induced hypothermia is at least 12 hours and may be >24 hours. Hypothermia was maintained for 12[2] or 24 hours[1] in the studies of out-of-hospital patients presenting in VF. Most case series of adult patients have reported 24 hours of hypothermia. The effect of a longer duration of cooling on outcome has not been studied in adults, but hypothermia for up to 72 hours was used safely in newborns.[45,46]

Although there are multiple methods for inducing hypothermia, no single method has proved to be optimal. Feedback-controlled endovascular catheters and surface cooling devices are available.[47–49] Other techniques (eg, cooling blankets and frequent application of ice bags) are readily available and effective but may require more labor and closer monitoring. As an adjunct, iced isotonic fluid can be infused to initiate core cooling but must be combined with a follow-up method for maintenance of hypothermia.[50–52] Although a theoretical concern is that rapid fluid loading could have adverse cardiopulmonary effects such as pulmonary edema, 9 case series indicate that cooling can be initiated safely with IV ice-cold fluids (500 mL to 30 mL/kg of saline 0.9% or Ringer's lactate).[51–59] One human case series[56] showed that the deterioration in oxygenation that often occurs after ROSC was not significantly affected by the infusion of cold fluids (3427 mL ± 210 mL). Two randomized controlled trials,[60,61] one study with concurrent controls,[62] and 3 case series[63,64] indicate that cooling with IV cold saline can be initiated safely in the prehospital setting.

Clinicians should continuously monitor the patient's core temperature using an esophageal thermometer, bladder catheter in nonanuric patients, or pulmonary artery catheter if one is placed for other indications.[1,2] Axillary and oral temperatures are inadequate for measurement of core temperature changes, especially during active manipulation of temperature for therapeutic hypothermia,[65,66] and true tympanic temperature probes are rarely available and often unreliable.

Bladder temperatures in anuric patients and rectal temperatures may differ from brain or core temperature.[66,67] A secondary source of temperature measurement should be considered, especially if a closed feedback cooling system is used for temperature management.

A number of potential complications are associated with cooling, including coagulopathy, arrhythmias, and hyperglycemia, particularly with an unintended drop below target temperature.[35] The likelihood of pneumonia and sepsis may increase in patients treated with therapeutic hypothermia.[1,2] Although these complications were not significantly different between groups in the published clinical trials, infections are common in this population, and prolonged hypothermia is known to decrease immune function. Hypothermia also impairs coagulation, and any ongoing bleeding should be controlled before decreasing temperature.

In summary, we recommend that comatose (ie, lack of meaningful response to verbal commands) adult patients with ROSC after out-of-hospital VF cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours (Class I, LOE B). Induced hypothermia also may be considered for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIb, LOE B). Active rewarming should be avoided in comatose patients who spontaneously develop a mild degree of hypothermia (>32°C [89.6°F]) after resuscitation from cardiac arrest during the first 48 hours after ROSC. (Class III, LOE C).

Hyperthermia

After resuscitation, temperature elevation above normal can impair brain recovery. The etiology of fever after cardiac arrest may be related to activation of inflammatory cytokines in a pattern similar to that observed in sepsis.[68,69] There are no randomized controlled trials evaluating the effect of treating pyrexia with either frequent use of antipyretics or "controlled normothermia" using cooling techniques compared to no temperature intervention in post–cardiac arrest patients. Case series[70–74] and studies[75–80] suggest that there is an association between poor survival outcomes and pyrexia ≥37.6°C. In patients with a cerebrovascular event leading to brain ischemia, studies[75–80] demonstrate worsened short-term outcome and long-term mortality. By extrapolation this data may be relevant to the global ischemia and reperfusion of the brain that follows cardiac arrest. Patients can develop hyperthermia after rewarming posthypothermia treatment. This late hyperthermia should also be identified and treated. Providers should closely monitor patient core temperature after ROSC and actively intervene to avoid hyperthermia (Class I, LOE C).

Organ-Specific Evaluation and Support

The remainder of Part 9 focuses on organ-specific measures that should be included in the immediate post–cardiac arrest period.

Pulmonary System

Pulmonary dysfunction after cardiac arrest is common. Etiologies include hydrostatic pulmonary edema from left ventricular dysfunction; noncardiogenic edema from inflammatory, infective, or physical injuries; severe pulmonary atelectasis; or aspiration occurring during cardiac arrest or resuscitation. Patients often develop regional mismatch of ventilation and perfusion, contributing to decreased arterial oxygen content. The severity of pulmonary dysfunction often is measured in terms of the PaO_2/FIO_2 ratio. A PaO_2/FIO_2 ratio of ≤300 mm Hg usually defines acute lung injury. The acute onset of bilateral infiltrates on chest x-ray and a pulmonary artery pressure ≤18 mm Hg or no evidence of left atrial hypertension are common to both acute lung injury and acute respiratory distress syndrome (ARDS). A PaO_2/FIO_2 ratio <300 or <200 mm Hg separates acute lung injury from ARDS, respectively.[81] Positive end-expiratory pressure (PEEP), a lung-protective strategy for mechanical ventilation, and titrated FIO_2 are strategies that can improve pulmonary function and PaO_2 while the practitioner is determining the pathophysiology of the pulmonary dysfunction.

Essential diagnostic tests in intubated patients include a chest radiograph and arterial blood gas measurements. Other diagnostic tests may be added based on history, physical examination, and clinical circumstances. Evaluation of a chest radiograph should verify the correct position of the endotracheal tube and the distribution of pulmonary infiltrates or edema and identify complications from chest compressions (eg, rib fracture, pneumothorax, and pleural effusions) or pneumonia.

Providers should adjust mechanical ventilatory support based on the measured oxyhemoglobin saturation, blood gas values, minute ventilation (respiratory rate and tidal volume), and patient-ventilator synchrony. In addition, mechanical ventilatory support to reduce the work of breathing should be considered as long as the patient remains in shock. As spontaneous ventilation becomes more efficient and as concurrent medical conditions allow, the level of support may be gradually decreased.

The optimal FIO_2 during the immediate period after cardiac arrest is still debated. The beneficial effect of high FIO_2 on systemic oxygen delivery should be balanced with the deleterious effect of generating oxygen-derived free radicals during the reperfusion phase. Animal data suggests that ventilations with 100% oxygen (generating PaO_2 >350 mm Hg at 15 to 60 minutes after ROSC) increase brain lipid peroxidation, increase metabolic dysfunctions, increase neurological degeneration, and worsen short-term functional outcome when compared with ventilation with room air or an inspired oxygen fraction titrated to a pulse oximeter reading between 94% and 96%.[82–87] One randomized prospective clinical trial compared ventilation for the first 60 minutes after ROSC with 30% oxygen (resulting in $PaO_2=110\pm25$ mm Hg at 60 minutes) or 100% oxygen (resulting in $PaO_2=345\pm174$ mm Hg at 60 minutes).[88] This small trial detected no difference in serial markers of acute brain injury, survival to hospital discharge, or percentage of patients with good neurological outcome at hospital discharge but was inadequately powered to detect important differences in survival or neurological outcome.

Once the circulation is restored, monitor systemic arterial oxyhemoglobin saturation. It may be reasonable, when the appropriate equipment is available, to titrate oxygen administration to maintain the arterial oxyhemoglobin saturation ≥94%. Provided appropriate equipment is available, once ROSC is achieved, adjust the FIO_2 to the minimum concentration needed to achieve arterial oxyhemoglobin saturation ≥94%, with the goal of avoiding hyperoxia while ensuring adequate oxygen delivery. Since an arterial oxyhemoglobin saturation of 100% may correspond to a PaO_2 anywhere between ~80 and 500 mm Hg, in general it is appropriate to wean FIO_2 when saturation is 100%, provided the oxyhemoglobin saturation can be maintained ≥94% (Class I, LOE C).

Because patients may have significant metabolic acidosis after cardiac arrest, there is a temptation to institute hyperventilation to normalize blood pH. However, metabolic acidosis is likely to be reversed once adequate perfusion is restored, and there are several physiological reasons why hyperventilation may be detrimental. Minute ventilation alters the partial pressure of carbon dioxide ($PaCO_2$), which in turn can affect cerebral blood flow. In a normal brain a 1-mm Hg decrease in $PaCO_2$ results in a decrease in cerebral blood flow of approximately 2.5% to 4%; cerebral blood flow remains CO_2-reactive after cardiac arrest,[89,90] although the magnitude of the CO_2 reactivity (magnitude of change in cerebral blood flow per millimeters of mercury [mm Hg] change in PCO_2) may be diminished or suppressed for 1 to 3 hours after reperfusion,[91,92] especially after prolonged ischemia (≥15 minutes).[93,94] After ROSC there is an initial hyperemic blood flow response that lasts 10 to 30 minutes, followed by a more prolonged period of low blood flow.[95,96] During this latter period of late hypoperfusion, a mismatch between blood flow (as a component of oxygen delivery) and oxygen requirement may occur. Hyperventilation at this stage may lower $PaCO_2$, cause cerebral vasoconstriction, and exacerbate cerebral ischemic injury.

Physiological data in humans suggests that hyperventilation could cause additional cerebral ischemia in the post–cardiac arrest patient because sustained hypocapnia (low PCO_2) may reduce cerebral blood flow.[97,98] Transcranial Doppler measurements of the middle cerebral artery and jugular bulb oxygen saturation measurements in 10 comatose subjects after cardiac arrest revealed that hyperventilation with hypocapnia did not affect median flow velocity but did decrease jugular bulb oxygen saturation below the ischemic threshold (55%). Conversely, hypoventilation with hypercapnia produced the opposite effect.[99] In one study, controlled ventilation with specific goals to keep $PaCO_2$ 37.6 to 45.1 mm Hg (5 to 6 kPa) and SaO_2 95% to 98% as part of a bundle with multiple other goals (including hypothermia and blood pressure goals) increased survival from 26% to 56%.[11] In that study it was impossible to ascertain an independent effect of controlled ventilation separate from all other components of the bundle.

Hyperventilation also may compromise systemic blood flow because of occult or auto-PEEP and is deleterious in all low-flow states, including cardiopulmonary resuscitation (CPR)[100,101] and hypovolemia.[102,103] Auto-PEEP, also known as *intrinsic PEEP* or *gas trapping*, occurs preferentially in patients with obstructive lung disease and is aggravated by hyperventilation that does not allow sufficient time for complete exhalation. A gradual increase in end-expiratory volume and pressure in the lung (hyperinflation) is transmitted to the great veins in the thorax and depresses both venous return and cardiac output.[104,105] Similar effects may occur after cardiac arrest, suggesting that hyperventilation should be avoided, especially in hypotensive patients.

Other ventilatory parameters may affect the outcome of patients on mechanical ventilation after cardiac arrest, particularly when acute lung injury or ARDS develops. Over the last decade attention has focused on low-volume/high-rate ventilation. In a comparison of high- and low-tidal-volume ventilation, the death rate of patients with ARDS was reduced from 40% to 31% in the group with reduced tidal volume (V_T).[106] This and subsequent studies recommend ventilating patients to maintain V_T of 6 to 8 mL/kg predicted body weight and inspiratory plateau pressure ≤30 cm H_2O to reduce ventilator-associated lung injury.[107] Because low V_T ventilation (6 mL/kg) is associated with an increased incidence of atelectasis, PEEP and other lung "recruitment maneuver" procedures may be warranted.[108] However, one study reported no difference in the rate of discharge or survival between ARDS patients receiving high- or low-PEEP regimens.[109] Furthermore, a recent historical comparison of ventilation practice after cardiac arrest reported no differences in pneumonia, oxygenation, lung compliance, and ventilator days when a low V_T strategy versus a more liberal "old practice" V_T was applied.[110]

In conclusion, post–cardiac arrest patients are at risk of acute lung injury and ARDS, but refractory hypoxemia is not a frequent mode of death after cardiac arrest. There is no reason to recommend hyperventilation and "permissive hypercapnia" (hypoventilation) for these patients, and normocapnia should be considered the standard. There is also no data to recommend unique ventilation strategies in this population different from usual care of other mechanically ventilated patients at risk for acute lung injury and ARDS.

Routine hyperventilation with hypocapnia should be avoided after ROSC because it may worsen global brain ischemia by excessive cerebral vasoconstriction (Class III, LOE C). Hyperventilation or excessive tidal volumes resulting in increased intrathoracic pressure may also contribute to hemodynamic instability in certain patients. Ventilation rate and volume may be titrated to maintain high-normal $PaCO_2$ (40 to 45 mm Hg) or $PETCO_2$ (35 to 40 mm Hg) while avoiding hemodynamic compromise (Class IIb, LOE C).

Treatment of Pulmonary Embolism After CPR

Fibrinolytic use may benefit patients with massive pulmonary emboli who have not had CPR,[111] and use of fibrinolytics to treat pulmonary embolism after CPR has been reported.[112] The use of fibrinolytics during CPR has been studied, and CPR itself does not appear to pose an unacceptable risk of bleeding.[113–121] Alternatively, surgical embolectomy has also been used successfully in some patients after PE-induced cardiac arrest.[117,122–125] Mechanical thrombectomy was employed in a small case series and only one of seven patients died and pulmonary perfusion was restored in the majority (85.7%).[115] In post–cardiac arrest patients with arrest due to presumed or known pulmonary embolism, fibrinolytics may be considered (Class IIb, LOE C).

Sedation After Cardiac Arrest

Patients with coma or respiratory dysfunction after ROSC are routinely intubated and maintained on mechanical ventilation for a period of time, which results in discomfort, pain, and anxiety. Intermittent or continuous sedation and/or analgesia can be used to achieve specific goals. Patients with post–cardiac arrest cognitive dysfunction may display agitation or frank delirium with purposeless movement and are at risk of self-injury. Opioids, anxiolytics, and sedative-hypnotic agents can be used in various combinations to improve patient-ventilator interaction and blunt the stress-related surge of endogenous catecholamines. Other agents with sedative and antipsychotic-tranquilizer properties, such as α_2-adrenergic agonists,[126] and butyrophenones[127] are also used based on individual clinical circumstances.

If patient agitation is life-threatening, neuromuscular blocking agents can be used for short intervals with adequate sedation. Caution should be used in patients at high risk of seizures unless continuous electroencephalographic (EEG) monitoring is available. In general sedative agents should be administered cautiously with daily interruptions and titrated to the desired effect. A number of sedation scales[128–133] and motor activity scales[134] were developed to titrate these pharmacological interventions to a clinical goal.

Shorter-acting medications that can be used as a single bolus or continuous infusion are usually preferred. There is little evidence to guide sedation/analgesia therapy immediately after ROSC. One observational study[135] found an association between use of sedation and development of pneumonia in intubated patients during the first 48 hours of therapy. However, the study was not designed to investigate sedation as a risk factor for either pneumonia or death in patients with cardiac arrest.

Although minimizing sedation allows a better clinical estimate of neurological status, sedation, analgesia, and occasionally neuromuscular relaxation are routinely used to facilitate induced hypothermia and to control shivering. The duration of neuromuscular blocker use should be minimized and the depth of neuromuscular blockade should be monitored with a nerve twitch stimulator.

It is reasonable to consider the titrated use of sedation and analgesia in critically ill patients who require mechanical ventilation or shivering suppression during induced hypothermia after cardiac arrest (Class IIb, LOE C). Duration of neuromuscular blocking agents should be kept to a minimum or avoided altogether.

Cardiovascular System

ACS is a common cause of cardiac arrest.[14,16,34,35,134–147] The clinician should evaluate the patient's 12-lead ECG and cardiac markers after ROSC. A 12-lead ECG should be obtained as soon as possible after ROSC to determine whether acute ST elevation is present (Class I, LOE B). Because it is impossible to determine the final neurological status of comatose patients in the first hours after ROSC, aggressive treatment of ST-elevation myocardial infarction (STEMI) should begin as in non–cardiac arrest patients, regardless of coma or induced hypothermia. Because of the high incidence of acute coronary ischemia, consideration of emergent coronary angiography may be reasonable even in the absence of STEMI.[14,16] Notably, PCI, alone or as part of a bundle of care, is associated with improved myocardial function[14] and neurological outcomes.[11,16] Therapeutic hypothermia can be safely combined with primary PCI after cardiac arrest caused by AMI.[11,31,33–35] Other details of ACS treatment are discussed in Part 10.

Patients with cardiac arrest may receive antiarrhythmic drugs such as lidocaine or amiodarone during initial resuscitation. There is no evidence to support or refute continued or prophylactic administration of these medications.[7,148–152]

Vasoactive Drugs for Use in Post–Cardiac Arrest Patients

Vasopressors

Vasoactive drugs may be administered after ROSC to support cardiac output, especially blood flow to the heart and brain. Drugs may be selected to improve heart rate (chronotropic effects), myocardial contractility (inotropic effects), or arterial pressure (vasoconstrictive effects), or to reduce afterload (vasodilator effects). Unfortunately many adrenergic drugs are not selective and may increase or decrease heart rate and afterload, increase cardiac arrhythmias, and increase myocardial ischemia by creating a mismatch between myocardial oxygen demand and delivery. Myocardial ischemia, in turn, may further decrease heart function. Some agents may also have metabolic effects that increase blood glucose, lactate, and metabolic rate. There is a paucity of data about which vasoactive drug to select first, although providers should become familiar with the differing adverse effects associated with these drugs, which might make a particular agent more or less appropriate for a specific patient.[153]

Specific drug infusion rates cannot be recommended because of variations in pharmacokinetics (relation between drug dose and concentration) and pharmacodynamics (relation between drug concentration and effect) in critically ill patients,[154,155] so commonly used initial dose ranges are listed in Table 2. Vasoactive drugs must be titrated at the bedside to secure the intended effect while limiting side effects. Providers must also be aware of the concentrations delivered and compatibilities with previously and concurrently administered drugs.

In general, adrenergic drugs should not be mixed with sodium bicarbonate or other alkaline solutions in the IV line because there is evidence that adrenergic agents are inactivated in alkaline solutions.[156,157] Norepinephrine (levarterenol) and other catecholamines that activate α-adrenergic receptors may produce tissue necrosis if extravasation occurs. Therefore, administration through a central line is preferred whenever possible. If extravasation develops, infiltrate 5 to 10 mg of phentolamine diluted in 10 to 15 mL of saline into the site of extravasation as soon as possible to prevent tissue death and sloughing.

Table 2. Common Vasoactive Drugs

Drug	Typical Starting Dose (Then Titrate to Effect)
Epinephrine	0.1–0.5 mcg/kg/min (In 70-kg adult, 7–35 mcg/min) • Useful for symptomatic bradycardia if atropine and transcutaneous pacing fail or if pacing is not available • Used to treat severe hypotension (eg, systolic blood pressure <70 mm Hg) • Useful for anaphylaxis associated with hemodynamic instability or respiratory distress[158]
Norepinephrine	0.1–0.5 mcg/kg/min (In 70-kg adult, 7–35 mcg/min) • Used to treat severe hypotension (eg, systolic blood pressure <70 mm Hg) and a low total peripheral resistance • Relatively contraindicated in patients with hypovolemia. It may increase myocardial oxygen requirements, mandating cautious use in patients with ischemic heart disease • Usually induces renal and mesenteric vasoconstriction; in sepsis, however, norepinephrine improves renal blood flow and urine output[159,160]
Phenylephrine	0.5–2.0 mcg/kg/min (In 70-kg adult, 35–140 mcg/min) • Used to treat severe hypotension (eg, systolic blood pressure <70 mm Hg) and a low total peripheral resistance
Dopamine	5–10 mcg/kg/min • Used to treat hypotension, especially if it is associated with symptomatic bradycardia • Although low-dose dopamine infusion has frequently been recommended to maintain renal blood flow or improve renal function, more recent data have failed to show a beneficial effect from such therapy[161,162]
Dobutamine	5–10 mcg/kg/min • The (+) isomer is a potent beta-adrenergic agonist, whereas the (–) isomer is a potent alpha-1-agonist[163] • The vasodilating $beta_2$-adrenergic effects of the (+) isomer counterbalance the vasoconstricting alpha-adrenergic effects, often leading to little change or a reduction in systemic vascular resistance
Milrinone	Load 50 mcg/kg over 10 minutes then infuse at 0.375 mcg/kg/min • Used to treat low cardiac output • May cause less tachycardia than dobutamine

Use of Vasoactive Drugs After Cardiac Arrest

Hemodynamic instability is common after cardiac arrest.[6] Death due to multiorgan failure is associated with a persistently low cardiac index during the first 24 hours after resuscitation.[6,164] Vasodilation may occur from loss of sympathetic tone and from metabolic acidosis. In addition, the ischemia/reperfusion of cardiac arrest and electric defibrillation both can cause transient myocardial stunning and dysfunction[165] that can last many hours but may improve with use of vasoactive drugs.[158] Echocardiographic evaluation within the first 24 hours after arrest is a useful way to assess myocardial function in order to guide ongoing management.[14,17]

There is no proven benefit or harm associated with administration of routine IV fluids or vasoactive drugs (pressor and inotropic agents) to patients experiencing myocardial dysfunction after ROSC. Although some studies found improved outcome associated with these therapies, the outcome could not be solely ascribed to these specific interventions because they were only one component of standardized treatment protocols (eg, PCI and therapeutic hypothermia).[6,11,12,166] Invasive monitoring may be necessary to measure hemodynamic parameters accurately and to determine the most appropriate combination of medications to optimize perfusion.

Fluid administration as well as vasoactive (eg, norepinephrine), inotropic (eg, dobutamine), and inodilator (eg, milrinone) agents should be titrated as needed to optimize blood pressure, cardiac output, and systemic perfusion (Class I , LOE B). Although human studies have not established ideal targets for blood pressure or blood oxygenation,[11,12] a mean arterial pressure ≥65 mm Hg and an $ScvO_2$ ≥70% are generally considered reasonable goals.

Although mechanical circulatory support improves hemodynamics in patients not experiencing cardiac arrest,[167–171] it has not been associated with improved clinical outcome and routine use of mechanical circulatory support after cardiac arrest is not recommended.

Modifying Outcomes From Critical Illness

Cardiac arrest is thought to involve multiorgan ischemic injury and microcirculatory dysfunction.[68,69,172] Implementing a protocol for goal-directed therapy using fluid and vasoactive drug administration along with monitoring of central venous oxygen saturation may improve survival from sepsis,[173] suggesting that a similar approach may benefit post–cardiac arrest patients. By analogy, studies have explored several other interventions believed to be beneficial in sepsis or other critical illness.

Glucose Control

The post–cardiac arrest patient is likely to develop metabolic abnormalities such as hyperglycemia that may be detrimental. Evidence from several retrospective studies[7,73,174–176] suggests an association of higher glucose levels with increased mortality or worse neurological outcomes. Variable ranges for optimum glucose values were suggested, and the studies do not provide evidence that an interventional strategy to manage glucose levels will alter outcomes. Only one study examined patients with induced hypothermia.[175]

The optimum blood glucose concentration and interventional strategy to manage blood glucose in the post–cardiac arrest period is unknown. A consistent finding in clinical trials of glucose control[177–185] is that intensive therapy leads to more frequent episodes of severe hypoglycemia (usually defined as blood glucose level ≤40 mg/dL [2.2 mmol/L]). Hypoglycemia may be associated with worse outcomes in critically ill patients.[186,187]

Strategies to target moderate glycemic control (144 to 180 mg/dL [8 to 10 mmol/L]) may be considered in adult patients with ROSC after cardiac arrest (Class IIb, LOE B). Attempts to control glucose concentration within a lower range (80 to 110 mg/dL [4.4 to 6.1 mmol/L]) should not be implemented after cardiac arrest due to the increased risk of hypoglycemia (Class III, LOE B).

Steroids

Corticosteroids have an essential role in the physiological response to severe stress, including maintenance of vascular tone and capillary permeability. In the post–cardiac arrest phase, several authors report a relative adrenal insufficiency compared with the metabolic demands of the body.[188,189] Relative adrenal insufficiency in the post–cardiac arrest phase was associated with higher rates of mortality.[188–190]

At present there are no human randomized trials investigating corticosteroid use after ROSC. One investigation combined steroid therapy with use of vasopressin, which made interpretation of results specific to steroids impossible.[191] The post–cardiac arrest syndrome has similarities to septic shock, but the efficacy of corticosteroids remains controversial in patients with sepsis as well.[68,192–194] Whether the provision of corticosteroids in the post–cardiac arrest phase improves outcome remains unknown and the value of the routine use of corticosteroids for patients with ROSC following cardiac arrest is uncertain.

Hemofiltration

Hemofiltration has been proposed as a method to modify the humoral response to the ischemic-reperfusion injury that occurs after cardiac arrest. In a single randomized controlled trial there was no significant difference in 6-month survival among the groups.[195] Future investigations are required to determine whether hemofiltration will improve outcome in post–cardiac arrest patients.

Central Nervous System

Brain injury is a common cause of morbidity and mortality in post–cardiac arrest patients. Brain injury is the cause of death in 68% of patients after out-of-hospital cardiac arrest and in 23% after in-hospital cardiac arrest.[13] The pathophysiology of post–cardiac arrest brain injury involves a complex cascade of molecular events that are triggered by ischemia and reperfusion and then executed over hours to days after ROSC. Events and conditions in the post–cardiac arrest period have the potential to exacerbate or attenuate these injury pathways and impact ultimate outcomes. Clinical manifestations of post–cardiac arrest brain injury include coma, seizures, myoclonus, various degrees of neurocognitive dysfunction (ranging from memory deficits to persistent vegetative state), and brain death.[3]

Seizure Management

Whether there is any disease-specific management of seizures after cardiac arrest remains unknown and the true incidence of post–cardiac arrest electrographic seizures may be higher as the clinical diagnosis of seizures may not be readily apparent. It is accepted in other settings that prolonged, untreated seizures are detrimental to the brain, and seizures are common after ROSC, occurring in 5% to 20% of comatose cardiac arrest survivors with or without therapeutic hypothermia.[11,196,197]

An EEG for the diagnosis of seizure should be performed with prompt interpretation as soon as possible and should be monitored frequently or continuously in comatose patients after ROSC (Class I , LOE C). More clinical data are needed to define the diagnosis and management of seizures after cardiac arrest. Neuroprotective agents with anticonvulsant properties such as thiopental[196] and single-dose diazepam or magnesium or both[198] given after ROSC have not improved neurological outcome in survivors. No studies have addressed whether anticonvulsant therapy improves outcome after cardiac arrest, and several studies demonstrated that post–cardiac arrest seizures were refractory to traditional anticonvulsant agents.[199–201] The same anticonvulsant regimens for the treatment of seizures used for status epilepticus caused by other etiologies may be considered after cardiac arrest. (Class IIb, LOE C).

Neuroprotective Drugs

The molecular events that cause neurodegeneration after cardiac arrest occur over hours to days after ROSC. This time course suggests a potentially broad therapeutic window for neuroprotective drug therapy. However, the number of clinical trials performed to date is limited and has failed to demonstrate improved neurological outcome with potential neuroprotective drugs given after cardiac arrest.

Few neuroprotective drugs have been tested in clinical trials, and only one published randomized trial[202] was performed in which a neuroprotective drug was combined with therapeutic hypothermia. No neuroprotection benefit was observed when patients (without hypothermia) were treated with thiopental, glucocorticoids, nimodipine, lidoflazine, diazepam, and magnesium sulfate. One trial using coenzyme Q10 in patients receiving hypothermia failed to show improved survival with good neurological outcome.[202] The routine use of coenzyme Q10 in patients treated with hypothermia is uncertain (Class IIb, LOE B).

Prognostication of Neurological Outcome in Comatose Cardiac Arrest Survivors

The goal of post–cardiac arrest management is to return patients to their prearrest functional level. However, many patients will die, remain permanently unresponsive, or remain permanently unable to perform independent activities. Early prognostication of neurological outcome is an essential component of post–cardiac arrest care. Most importantly, when decisions to limit or withdraw life-sustaining care are being considered, tools used to prognosticate poor outcome must be accurate and reliable with a false-positive rate (FPR) approaching 0%. Poor outcome is defined as death, persistent unresponsiveness, or the inability to undertake independent activities after 6 months.[203] No prearrest or intra-arrest parameters (including arrest duration, bystander CPR, or presenting rhythm) alone or in combination accurately predict outcome in individual patients who achieve ROSC.

A thorough neurological evaluation is needed to obtain accurate prognostic findings. No postarrest physical examination finding or diagnostic study has as yet predicted poor outcome of comatose cardiac arrest survivors during the first 24 hours after ROSC. After 24 hours somatosensory evoked potentials (SSEPs) and select physical examination findings at specific time points after ROSC in the absence of confounders (such as hypotension, seizures, sedatives, or neuromuscular blockers) are the most reliable early predictors of poor outcome in patients not undergoing therapeutic hypothermia. However, the decision to limit care should never be made on the basis of a single prognostic parameter, and expert consultation may be needed.

Neurological Assessment

The neurological examination is the most widely studied parameter to predict outcome in comatose post–cardiac arrest patients. Prognostication of functional outcome has not been established in noncomatose patients. Neurological examination for this purpose can be reliably undertaken only in the absence of confounding factors (hypotension, seizures, sedatives, or neuromuscular blockers). On the basis of existing studies, no clinical neurological signs reliably predict poor outcome <24 hours after cardiac arrest.[204,205] Among adult patients who are comatose and have *not* been treated with hypothermia, the absence of both pupillary light and corneal reflexes at ≥72 hours after cardiac arrest predicted poor outcome with high reliability.[204] The absence of vestibulo-ocular reflexes at ≥24 hours (FPR 0%, 95% CI 0% to 14%)[205,206] or Glasgow Coma Scale (GCS) score <5 at ≥72 hours (FPR 0%, 95% CI 0% to 6%)[204,207,208] are less reliable for predicting poor outcome or were studied only in limited numbers of patients. Other clinical signs, including myoclonus,[209–213] are not recommended for predicting poor outcome (Class III, LOE C).

EEG

No electrophysiological study reliably predicts outcome in comatose patients during the first 24 hours after ROSC. In *normothermic* patients without significant confounders (sedatives, hypotension, hypothermia, neuromuscular blockade, or hypoxemia), an EEG pattern showing generalized suppression to <20 μV, burst-suppression pattern associated with generalized epileptic activity, or diffuse periodic complexes on a flat background is associated with a poor outcome (FPR 3%, 95% CI 0.9% to 11%).[203] One week after the initial arrest event, specific EEG findings may be useful for predicting poor outcomes in comatose cardiac arrest survivors,[161,203,204,206,214–221] The prognostic accuracy of malignant EEG patterns appears to be less reliable in patients treated with hypothermia. Status epilepticus in post-ROSC patients treated with hypothermia has an FPR of 7% (95% CI 1% to 25%) to 11.5% (95% CI 3% to 31%) for predicting poor outcome.[218,222]

In the absence of confounding factors such as sedatives, hypotension, hypothermia, neuromuscular blockade, seizures, or hypoxemia, it may be helpful to use an unprocessed EEG interpretation observed ≥24 hours after ROSC to assist with the prediction of a poor outcome in comatose survivors of cardiac arrest not treated with hypothermia (Class IIb, LOE B).

Evoked Potentials

Abnormalities in evoked potentials are associated with poor outcomes. Bilateral absence of the N20 cortical response to median nerve SSEPs predicts poor outcome (FPR 0%, 95% CI 0% to 3%).[161,203] Although other evoked potential measurements (for example, Brain stem Auditory Evoked Potentials) have been associated with poor outcomes in comatose cardiac arrest survivors, they are either less reliable predictors of poor outcome than SSEPs or have not been studied in enough patients to establish their reliability. Bilateral absence of the N20 cortical response to median nerve stimulation after 24 hours predicts poor outcome in comatose cardiac arrest survivors not treated with therapeutic hypothermia (Class IIa, LOE A).

The impact of therapeutic hypothermia on the prognostic accuracy of SSEPs has not been adequately studied.

Neuroimaging

The most studied neuroimaging modalities are magnetic resonance imaging (MRI) and computed tomography (CT) of the brain. Extensive cortical and subcortical lesions on MRI are associated with poor neurological outcome.[223–253] These studies varied widely in the MRI parameters used, sample size, and interval after arrest when testing occurred.

CT imaging to detect brain injury and predict functional outcome is supported by several studies.[233,244,245,247,248,254–267] The timing of CT in these studies varied widely. CT parameters associated with poor outcome were varied and included quantitative measure of gray matter:white matter Hounsfield unit ratio and qualitative description of brain structures. A nonenhanced CT scan can also provide information about structural lesions, stroke, or intracranial hemorrhage that may have contributed to cardiac arrest.[268,269]

Other less utilized and investigated neuroimaging modalities have included single-photon emission computed tomography,[253,267,270] cerebral angiography[244] and transcranial Doppler[240] A nuclear imaging study observed that abnormal tracer uptake in the cerebral cortices was associated with poor outcome in one case report.[248]

Despite tremendous potential, neuroimaging has yet to be proved as an independently accurate modality for prediction of outcome in individual comatose survivors of cardiac arrest and specific neuroimaging modalities cannot be recommended for predicting poor outcome after cardiac arrest.

Blood and Cerebrospinal Fluid Biomarkers

There has been extensive clinical research exploring biomarkers in the blood (plasma or serum) and cerebrospinal fluid (CSF) as early predictors of poor outcome in comatose cardiac arrest survivors. Biomarkers that are predictive of neurological outcome are typically released from dying neurons or glial cells in the brain (eg, neuron-specific enolase [NSE], S100B, GFAP, CK-BB) and can be measured in the blood or CSF. The primary advantage of biomarkers is that levels are unlikely to be confounded by sedation or neuromuscular blockade, which are commonly used in the first few days after cardiac arrest. However, for most biomarkers, only an association with outcome has been reported. When using a cutoff value that results in an FPR of 0% for predicting poor outcome, the 95% CI is unacceptably high due to the small number of patients studied.

The most promising and extensively studied biomarker is serum NSE, which has been reported to have a 0% FPR (95% CI 0% to 3%) for predicting poor outcome when measured between 24 and 72 hours after cardiac arrest.[203,204] Other guidelines have recommended the use of serum NSE to predict poor outcome in patients after ROSC.[203] However, the primary limitation of serum NSE is the variability among studies in both the assays used and the cutoff value that results in an FPR of 0% for predicting poor outcome.[271–282] Furthermore, interventions such as therapeutic hypothermia appear to variably alter the NSE cutoff value that is predictive of poor outcome.[283–285] Finally a number of clinical disorders, such as abdominal organ injury, have been associated with elevated NSE levels independent of cardiac arrest.[286]

The routine use of any serum or CSF biomarker as a sole predictor of poor outcome in comatose patients after cardiac arrest is not recommended (Class III, LOE B).

Changes in Prognostication With Hypothermia

There is a paucity of data about the utility of physical examination, EEG, and evoked potentials in patients who have been treated with induced hypothermia. Physical examination (motor response, pupillary light and corneal reflexes), EEG, SSEP, and imaging studies are less reliable for predicting poor outcome in patients treated with hypothermia. Durations of observation greater than 72 hours after ROSC should be considered before predicting poor outcome in patients treated with hypothermia (Class I, Level C).

Organ Donation After Cardiac Arrest

Despite maximal support and adequate observation, some patients will be brain-dead after cardiac arrest. Studies suggest that there is no difference in functional outcomes of organs transplanted from patients who are brain-dead as a consequence of cardiac arrest when compared with donors who are brain-dead due to other causes.[287–290] Adult patients who progress to brain death after resuscitation from cardiac arrest should be considered for organ donation (Class I, LOE B).

Summary

The goal of immediate post–cardiac arrest care is to optimize systemic perfusion, restore metabolic homeostasis, and support organ system function to increase the likelihood of intact neurological survival. The post–cardiac arrest period is often marked by hemodynamic instability as well as metabolic abnormalities. Support and treatment of acute myocardial dysfunction and acute myocardial ischemia can increase the probability of survival. Interventions to reduce secondary brain injury, such as therapeutic hypothermia, can improve survival and neurological recovery. Every organ system is at risk during this period, and patients are at risk of developing multiorgan dysfunction.

The comprehensive treatment of diverse problems after cardiac arrest involves multidisciplinary aspects of critical care, cardiology, and neurology. For this reason, it is important to admit patients to appropriate critical-care units with a prospective plan of care to anticipate, monitor, and treat each of these diverse problems. It is also important to appreciate the relative strengths and weaknesses of different tools for estimating the prognosis of patients after cardiac arrest.

Disclosures

Guidelines Part 9: Post–Cardiac Arrest Care: Writing Group Disclosures

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Clifton W. Callaway	University of Pittsburgh School of Medicine–Associate Professor; UPMC Health System–Physician	†Grants to University of Pittsburgh: NHLBI-Resuscitation Outcomes Consortium HRSA-Development and Dissemination of Program Tools for Uncontrolled Donation After Cardiac Death (UDCD)	*Loan of an Arctic Sun cooling device (without disposables) to human physiology laboratory for experiments on hypothermia by Medivance, Inc.	None	†Co-inventor on patent about ventricular fibrillation waveform analysis, licensed by University of Pittsburgh to Medtronic ERS, Inc.	None	None
Robert W. Neumar	University of Pennsylvania–Associate Professor of Emergency Medicine	†Funding Source: NIH/NINDS Grant Number: R21 NS054654 Funding Period 06/01/07 to 06/31/2010 Role on Project: Principal Investigator Title: Optimizing Therapeutic Hypothermia After Cardiac Arrest Description: The goal of this project is to evaluate how the onset and duration of therapeutic hypothermia after cardiac arrest impacts survival and neuroprotection	None	None	None	None	None
Romergryko G. Geocadin	Johns Hopkins University School of Medicine–Associate Professor of Neurology, Anesthesiology-Critical Care Medicine and Neurosurgery	†NIH RO1 Grant: "Consequence of Cardiac Arrest: Brain Injury" *NIH R44 Grant: "Cortical Injury Monitor Phase IIB"	None	*Academic Grand Rounds American Academy of Neurology	None	None	*Guest Editor: Neurology Clinics, Emergency Medicine Clinics, and Seminars in Neurology
Janice L. Zimmerman	The Methodist Hospital Physician Organization–Head, Critical Care Division and Director, MICU	None	None	*Society of Critical Care Medicine American College of Chest Physicians Center for Biomedical Communications	None	None	*Callaway and Associates Andrews and Kurth
Michael Donnino	Harvard Medical Faculty Physicians–Physician	†Corticosteroids in Post-cardiac Arrest Patients [Scientist Development Grant, American Heart Association] Thiamine as a Metabolic Resuscitator in Septic Shock [Pending] *Thiamine Deficiency in Septic Shock [completed, NIH through Harvard Medical School] Statin Therapy in Sepsis [Eleanor Shores Grant-nonindustry]	None	None	None	None	None

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Raina Merchant	University of Pennsylvania–Research fellow	None	None	None	None	None	None
Terry L. Vanden Hoek	University of Chicago–Associate Professor	*Principal Investigator 09/06/04–04/30/10 DOD/Office of Naval Research $885,639 Proteomic Development of Molecular Vital Signs: Mapping a Mitochondrial Injury Severity Score to Triage and Guide Resuscitation of Hemorrhagic Shock. This research grant is awarded to the University of Chicago	None	None	*Hypothermia Induction Patents (3 approved, 3 pending) no income	None	None
Steven L. Kronick	University of Michigan Health System Healthcare institution Assistant Professor	None	None	None	None	None	*Expert Witness: Reviewed a single case for an attorney. Less than 4 hours work total

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

*Modest.

†Significant.

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