Part 7.5: Postresuscitation Support

Few randomized controlled clinical trials deal specifically with supportive care following cardio-pulmonary-cerebral resuscitation (CPCR) from cardiac arrest. Nevertheless, postresuscitation care has significant potential to improve early mortality caused by hemodynamic instability and multi-organ failure and later mortality/morbidity resulting from brain injury.[1] This section summarizes our evolving understanding of the hemodynamic, neurologic, and metabolic abnormalities encountered in patients who are resuscitated from cardiac arrest.

Initial objectives of postresuscitation care are to

- Optimize cardiopulmonary function and systemic perfusion, especially perfusion to the brain
- Transport the victim of out-of-hospital cardiac arrest to the hospital emergency department (ED) and continue care in an appropriately equipped critical care unit
- Try to identify the precipitating causes of the arrest
- Institute measures to prevent recurrence
- Institute measures that may improve long-term, neurologically intact survival

Improving Postresuscitation Outcomes

Postresuscitation care is a critical component of advanced life support. Patient mortality remains high after return of spontaneous circulation (ROSC) and initial stabilization. Ultimate prognosis in the first 72 hours may be difficult to determine,[2] yet survivors of cardiac arrest have the potential to lead normal lives.[3–5] During postresuscitation care providers should (1) optimize hemodynamic, respiratory, and neurologic support; (2) identify and treat reversible causes of arrest; and (3) monitor temperature and consider treatment for disturbances of temperature regulation and metabolism. The first sections below discuss initial stabilization and temperature/metabolic factors that may be relevant to improving postresuscitation outcome, particularly in the critically ill survivor. Subsequent sections highlight organ-specific evaluation and support.

Return of Spontaneous Circulation

The principal objective of postresuscitation care is the reestablishment of effective perfusion of organs and tissue. After ROSC in the out-of-hospital or in-hospital setting, the provider must consider and treat the cause of the arrest and the consequences of any hypoxemic/ischemic/reperfusion injury. In most cases the acidemia associated with cardiac arrest improves spontaneously when adequate ventilation and perfusion are restored. But restoration of blood pressure and improvement in gas exchange do not ensure survival and functional recovery. Significant myocardial stunning and hemodynamic instability can develop, requiring vasopressor support. Most postresuscitation deaths occur during the first 24 hours.[6,7]

Ideally the patient will be awake, responsive, and breathing spontaneously. Alternatively the patient may initially be comatose but have the potential for full recovery after postresuscitation care.[3] Indeed, up to 20% of initially comatose survivors of cardiac arrest have been reported to have good 1-year neurologic outcome.[8] The pathway to the best hospital postresuscitation care of all initial survivors is not completely known, but there is increasing interest in identifying and optimizing practices that can improve outcome.[9] Regardless of the patient's initial status, the provider should support adequate airway and breathing, administer supplementary oxygen, monitor the patient's vital signs, establish or verify existing intravenous access, and verify the function of any catheters in place.

The clinician should assess the patient frequently and treat abnormalities of vital signs or cardiac arrhythmias and request studies that will further aid in the evaluation of the patient. It is important to identify and treat any cardiac, electrolyte, toxicologic, pulmonary, and neurologic 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), hyper-/hypokalemia, hypoglycemia, hypothermia; toxins, tamponade (cardiac), tension pneumothorax, thrombosis of the coronary or pulmonary vasculature, and trauma. For further information see Part 10: "Special Resuscitation Situations."

After initial assessment and stabilization of airway, ventilation, and circulation, transfer the patient to a special care unit for observation, continuous monitoring, and further therapy. Personnel with appropriate training and resuscitation equipment must accompany the patient during transport to the special care unit.

Temperature Regulation

Induced Hypothermia

Both permissive hypothermia (allowing a mild degree of hypothermia >33°C [91.5°F] that often develops spontaneously after arrest) and active induction of hypothermia may play a role in postresuscitation care. In 2 randomized clinical trials (LOE 1[3]; LOE 2[4]) induced hypothermia (cooling within minutes to hours after ROSC) resulted in improved outcome in adults who remained comatose after initial resuscitation from out-of-hospital ventricular fibrillation (VF) cardiac arrest. Patients in the study were cooled to 33°C (91.5°F)[3] or to the range of 32°C to 34°C (89.6°F to 93.2°F)[4] for 12 to 24 hours. The Hypothermia After Cardiac Arrest (HACA) study[3] included a small subset of patients with in-hospital cardiac arrest.

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A third study (LOE 2)[10] documented improvement in metabolic end points (lactate and O_2 extraction) when comatose adult patients were cooled after ROSC from out-of-hospital cardiac arrest in which the initial rhythm was pulseless electrical activity (PEA)/asystole.

In the HACA[3] and Bernard[4] studies, only about 8% of patients with cardiac arrest were selected for induced hypothermia (ie, patients were hemodynamically stable but comatose after a witnessed arrest of presumed cardiac etiology). This highlights the importance of identifying the subset of patients who may most benefit. Although the number of patients who may benefit from hypothermia induction is limited at present, it is possible that with more rapid and controlled cooling and better insights into optimal target temperature, timing, duration, and mechanism of action, such cooling may prove more widely beneficial in the future.[11] A recent multicenter study in asphyxiated neonates showed that hypothermia can be beneficial in another select population.[12]

Complications associated with cooling can include coagulopathy and arrhythmias, particularly with an unintentional drop below target temperature. Although not significantly higher, cases of pneumonia and sepsis increased in the hypothermia-induction group.[3,4] Cooling may also increase hyperglycemia.[4]

Most clinical studies of cooling have used external cooling techniques (eg, cooling blankets and frequent applications of ice bags) that may require a number of hours to attain target temperature. More recent studies[13] suggest that internal cooling techniques (eg, cold saline, endovascular cooling catheter) can also be used to induce hypothermia. Providers should continuously monitor the patient's temperature during cooling.[3,4]

In summary, providers should not actively rewarm hemodynamically stable patients who spontaneously develop a mild degree of hypothermia (>33°C [91.5°F]) after resuscitation from cardiac arrest. Mild hypothermia may be beneficial to neurologic outcome and is likely to be well tolerated without significant risk of complications. In a select subset of patients who were initially comatose but hemodynamically stable after a witnessed VF arrest of presumed cardiac etiology, active induction of hypothermia was beneficial.[3,4,13] Thus, unconscious adult patients with ROSC after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours when the initial rhythm was VF (Class IIa). Similar therapy may be beneficial for patients with non-VF arrest out of hospital or for in-hospital arrest (Class IIb).

Hyperthermia

After resuscitation, temperature elevation above normal can create a significant imbalance between oxygen supply and demand that can impair brain recovery. Few studies (with either frequent use of antipyretics or "controlled normothermia" with cooling techniques) have directly examined the effect of temperature control immediately after resuscitation. Because fever may be a symptom of brain injury, it may be difficult to control it with conventional antipyretics. Many studies of brain injury in animal models, however, show exacerbation of injury if body/brain temperature is increased during or after resuscitation from cardiac arrest.[14–17] Moreover, several studies have documented worse neurologic outcome in humans with fever after cardiac arrest (LOE 3)[18] and ischemic brain injury (LOE 7 extrapolated from stroke victims[18]). Thus, the provider should monitor the patient's temperature after resuscitation and avoid hyperthermia.

Glucose Control

The postresuscitation patient is likely to develop electrolyte abnormalities that may be detrimental to recovery. Although many studies have documented a strong association between high blood glucose after resuscitation from cardiac arrest and poor neurologic outcomes (LOE 4[21,22]; LOE 5[9,22–26]; LOE 6[27]), they did not show that control of serum glucose level alters outcome.

A prospective randomized study by van den Berghe (LOE 1)[28] did show that tight control of blood glucose using insulin reduced hospital mortality rates in critically ill patients who required mechanical ventilation. The study did not specifically focus on postresuscitation patients, but the effect of blood glucose control on outcome is compelling. The study documented not only improved survival but decreased mortality from infectious complications, a common problem in the postresuscitation setting.

In comatose patients, signs of hypoglycemia are less apparent, so clinicians must monitor serum glucose closely to avoid hypoglycemia when treating hyperglycemia. On the basis of findings of improved outcomes in critically ill patients when glucose levels are maintained in the normal range, it is reasonable for providers to maintain strict glucose control during the postresuscitation period. Additional study is needed, however, to identify the precise blood glucose concentration that requires insulin therapy, the target range of blood glucose concentration, and the effect of tight glucose control on outcomes of patients after cardiac arrest.

Organ-Specific Evaluation and Support

After ROSC patients may remain comatose or have decreased responsiveness for a variable period of time. If spontaneous breathing is absent or inadequate, mechanical ventilation via an endotracheal tube or other advanced airway device may be required. Hemodynamic status may be unstable with abnormalities of cardiac rate, rhythm, systemic blood pressure, and organ perfusion.

Clinicians must prevent, detect, and treat hypoxemia and hypotension because these conditions can exacerbate brain injury. Clinicians should determine the baseline postarrest status of each organ system and support organ function as needed.

The remainder of this chapter focuses on organ-specific measures that should be provided in the immediate postresuscitation period.

Respiratory System

After ROSC patients may exhibit respiratory dysfunction. Some patients will remain dependent on mechanical ventilation and will need an increased inspired concentration of oxygen. Providers should perform a full physical examination and evaluate the chest radiograph to verify appropriate

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endotracheal tube depth of insertion and identify cardiopulmonary complications of resuscitation. Providers should adjust mechanical ventilatory support based on the patient's blood gas values, respiratory rate, and work of breathing. As the patient's spontaneous ventilation becomes more efficient, the level of respiratory support may be decreased until spontaneous respiration returns. If the patient continues to require high inspired oxygen concentrations, providers should determine if the cause is pulmonary or cardiac and direct care accordingly.

Debate exists as to the length of time patients who require ventilatory support should remain sedated. To date there is little evidence to guide therapy. One observational study (LOE 3)[29] found an association between use of sedation and development of pneumonia in intubated patients during the first 48 hours of therapy. The study, however, was not designed to investigate sedation as a risk factor for either pneumonia or death in patients with cardiac arrest. At this time there is inadequate data to recommend for or against the use of a defined period of sedation or neuromuscular blockade after cardiac arrest (Class Indeterminate). Use of neuromuscular blocking agents should be kept to a minimum because these agents preclude thorough neurologic assessments during the first 12 to 72 hours after ROSC.[2]

Sedation may be necessary to control shivering during hypothermia. If shivering continues despite optimal sedation, neuromuscular blockade may be required in addition to deep sedation.

Ventilatory Parameters

Sustained hypocapnea (low P_{CO_2}) may reduce cerebral blood flow.[30–31] After cardiac arrest, restoration of blood flow results in an initial hyperemic blood flow response that lasts 10 to 30 minutes, followed by a more prolonged period of low blood flow.[32,33] During this latter period of late hypoperfusion, a mismatch between blood flow (oxygen delivery) and oxygen requirement may occur. If the patient is hyperventilated at this stage, cerebral vasoconstriction may further decrease cerebral blood flow and increase cerebral ischemia and ischemic injury.

There is no evidence that hyperventilation protects the brain or other vital organs from further ischemic damage after cardiac arrest. In fact, Safar et al[34] provided evidence that hyperventilation may worsen neurologic outcome. Hyperventilation may also generate increased airway pressures and augment intrinsic positive end-expiratory pressure (so-called "auto PEEP"), leading to an increase in cerebral venous and intracranial pressures.[35,36] Increases in cerebral venous pressure can decrease cerebral blood flow and increase brain ischemia.

In summary, no data supports targeting a specific arterial P_{aCO_2} level after resuscitation from cardiac arrest. But data extrapolated from patients with brain injury supports ventilation to normocarbic levels as appropriate. Routine hyperventilation is detrimental (Class III).

Cardiovascular System

Both the ischemia/reperfusion of cardiac arrest and electrical defibrillation can cause transient myocardial stunning and dysfunction[37] that can last many hours but may improve with vasopressors.[38] Cardiac biomarker levels may be increased in association with global ischemia caused by absent or decreased coronary blood flow during cardiac arrest and CPR. Increased cardiac biomarkers may also indicate acute myocardial infarction as the cause of cardiac arrest.

Hemodynamic instability is common after cardiac arrest, and early death due to multi-organ failure is associated with a persistently low cardiac index during the first 24 hours after resuscitation (LOE 5).[6,39] Thus, after resuscitation clinicians should evaluate the patient's electrocardiogram, radiographs, and laboratory analyses of serum electrolytes and cardiac biomarkers. Echocardiographic evaluation within the first 24 hours after arrest is useful to guide ongoing management.[5,40]

One large case series (LOE 5)[6] of patients resuscitated following out-of-hospital cardiac arrest documented significant early but reversible myocardial dysfunction and low cardiac output, followed by later vasodilation. The hemodynamic instability responded to fluid administration and vasoactive support.[6] Invasive monitoring may be necessary to measure blood pressure accurately and to determine the most appropriate combination of medications to optimize blood flow and distribution. The provider should titrate volume administration and vasoactive (eg, norepinephrine), inotropic (eg, dobutamine), and inodilator (eg, milrinone) drugs as needed to support blood pressure, cardiac index, and systemic perfusion. The ideal target blood pressure or hemodynamic parameters associated with optimal survival have not been established.

Both cardiac arrest and sepsis are thought to involve multi-organ ischemic injury and microcirculatory dysfunction. Goal-directed therapy with volume and vasoactive drug administration has been effective in improving survival from sepsis.[41] The greatest survival benefit is due to a decreased incidence of acute hemodynamic collapse, a challenge also seen in the postresuscitation setting. Data extrapolated from a study of goal-directed therapy for sepsis (LOE 1[41] for sepsis; LOE 7 [extrapolated] for cardiac arrest) suggests that providers should try to normalize oxygen content and oxygen transport.

Relative adrenal insufficiency may develop following the stress of cardiac arrest, but the use of early corticosteroid supplementation in such patients to improve either hemodynamics or outcome is unproven and requires further evaluation.[42]

Although sudden cardiac arrest may be precipitated by cardiac arrhythmia, it is unclear if antiarrhythmics are beneficial or detrimental in the postresuscitation period. Thus, there is insufficient evidence to recommend for or against prophylactic administration of antiarrhythmic drugs to patients who have survived cardiac arrest from any cause. It may be reasonable, however, to continue an infusion of an antiarrhythmic drug that was associated with ROSC (Class Indeterminate). Also, given the cardioprotective effects of β-blockers in the context of ischemic heart disease, the use of β-blockers in the postresuscitation setting seems prudent if there are no contraindications.[9]

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Central Nervous System

A healthy brain and a functional patient are the primary goals of cardio-pulmonary-cerebral resuscitation. Following ROSC, after a brief initial period of hyperemia cerebral blood flow is reduced (the "no-reflow phenomenon") as a result of microvascular dysfunction. This reduction occurs even when cerebral perfusion pressure is normal.[43,44]

Neurologic support for the unresponsive patient should include measures to optimize cerebral perfusion pressure by maintaining a normal or slightly elevated mean arterial pressure and reducing intracranial pressure if it is elevated. Because hyperthermia and seizures increase the oxygen requirements of the brain, providers should treat hyperthermia and consider therapeutic hypothermia. Witnessed seizures should be promptly controlled and maintenance anticonvulsant therapy initiated (Class IIa). Because of a paucity of data, routine seizure prophylaxis is a Class Indeterminate recommendation at present.

Prognostic Factors

The period after resuscitation is often stressful to medical staff and family members as questions arise about the patient's ultimate prognosis. Ideally a clinical assessment, laboratory test, or biochemical marker would reliably predict outcome during or immediately after cardiac arrest. Unfortunately no such predictors are available. Determination of prognosis based on initial physical examination findings can be difficult, and coma scores may be less predictive than individual motor and brainstem reflexes found in the first 12 to 72 hours after arrest.[2]

In a meta-analysis (LOE 1)[44] bilateral absence of cortical response to median nerve somatosensory-evoked potentials predicted poor outcome in normothermic patients who were comatose for at least 72 hours after hypoxic-ischemic insult. A case report[46] also documents the usefulness of this evaluation. Therefore, median nerve somatosensory-evoked potentials measured 72 hours after cardiac arrest can be used to predict neurologic outcome in patients with hypoxic-anoxic coma.

A recent meta-analysis (LOE 1) of 11 studies involving 1914 patients[2] documented 5 clinical signs that were found to strongly predict death or poor neurologic outcome, with 4 of the 5 predictors detectable at 24 hours after resuscitation:

- Absent corneal reflex at 24 hours
- Absent pupillary response at 24 hours
- Absent withdrawal response to pain at 24 hours
- No motor response at 24 hours
- No motor response at 72 hours

An electroencephalogram performed >24 to 48 hours after resuscitation has also been shown to provide useful predictive information (LOE 5[47–50]) and can help define prognosis.

Other Complications

Sepsis is a potentially fatal postresuscitation complication.[51] Patients with sepsis will benefit from goal-directed therapy. Renal failure[52] and pancreatitis, while often transient, should be diagnosed and evaluated.[3,53]

Summary

The postresuscitation period is often marked by hemodynamic instability as well as laboratory abnormalities. This is also a period for which promising technological interventions such as controlled therapeutic hypothermia are being evaluated. Every organ system is at risk during this time, and patients may ultimately develop multi-organ dysfunction. A complete discussion of this topic is beyond the scope of this chapter. The goal of the postresuscitation period is to manage the patient's vital signs and laboratory abnormalities and support organ system function to increase the likelihood of intact neurologic survival.

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