American Journal of Emergency Medicine 93 (2025) 26–36

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Emergency medicine updates: Managing the patient with return of spontaneous circulation

Brit Long, MD [a,*], Michael Gottlieb, MD [b]

[a] Department of Emergency Medicine, University of Virginia Medical School, Charlottesville, VA, USA
[b] Department of Emergency Medicine, Rush University Medical Center, Chicago, IL, USA

ARTICLE INFO

Article history:
Received 27 January 2025
Received in revised form 16 March 2025
Accepted 18 March 2025

Keywords:
Cardiac arrest
Return of spontaneous circulation
Resuscitation
Post-cardiac arrest syndrome
ROSC
Vasopressor
Angiography
TTM
Targeted temperature management

ABSTRACT

Introduction: Patients with return of spontaneous circulation (ROSC) following cardiac arrest are a critically important population requiring close monitoring and targeted interventions in the emergency department (ED). Therefore, it is important for emergency clinicians to be aware of the current evidence regarding the management of this condition.
Objective: This paper provides evidence-based updates concerning the management of the post-ROSC patient.
Discussion: The patient with ROSC following cardiac arrest is critically ill, including a post-cardiac arrest syndrome which may include hypoxic brain injury, myocardial dysfunction, systemic ischemia and reperfusion injury, and persistent precipitating pathophysiology. Initial priorities in the ED setting in the post-ROSC patient include supporting cardiopulmonary function, addressing and managing the underlying cause of arrest, minimizing secondary cerebral injury, and correcting physiologic derangements. Testing including laboratory assessment, electrocardiogram (ECG), and imaging are necessary, aiming to evaluate for the precipitating cause and assess end-organ injury. Computed tomography head-to-pelvis may be helpful in the post-ROSC patient, particularly when the etiology of arrest is unclear. There are several important components of management, including targeting a mean arterial pressure of at least 65 mmHg, preferably >80 mmHg, to improve end-organ and cerebral perfusion pressure. An oxygenation target of 92–98 % is recommended using ARDSnet protocol, along with carbon dioxide partial pressure values of 35–55 mmHg. Antibiotics should be reserved for those with evidence of infection but may be considered if the patient is comatose, intubated, and undergoing hypothermic targeted temperature management (TTM). Corticosteroids should not be routinely administered. While the majority of cardiac arrests in adults are associated with cardiovascular disease, not all post-ROSC patients require emergent coronary angiography. However, if the patient has ST-segment elevation on ECG following ROSC, emergent angiography and catheterization is recommended. This should also be considered if the patient had an initial history concerning for acute coronary syndrome or a presenting arrhythmia of ventricular fibrillation or pulseless ventricular tachycardia. TTM at 32-34° C does not appear to demonstrate improved outcomes compared with targeted normothermia, but fever should be avoided.
Conclusions: An understanding of literature updates can improve the ED care of patients post-ROSC.
Published by Elsevier Inc.

1. Introduction

Over 600,000 people per year experience cardiac arrest in North America, with a global incidence of 30–97 individuals per 100,000 [1-3]. There are a variety of causes of cardiac arrest based on population and age, but up to 70 % are associated with cardiac disease (e.g., occlusive myocardial infarction, congestive heart disease, cardiomyopathy) [4]. Other etiologies include arrhythmias (10 %), though 15–25 % of cases are associated with a non-cardiac etiology (e.g., intracranial hemorrhage [ICH], pulmonary embolism [PE], respiratory arrest, toxic ingestion, hypothermia, sepsis, and trauma) [1-7].

Keys to optimizing cardiac arrest management and improving the likelihood of achieving return of spontaneous circulation (ROSC) include rapid recognition of cardiac arrest, early high-quality cardiopulmonary resuscitation (CPR) with chest compressions, and defibrillation of shockable rhythms (i.e., pulseless ventricular tachycardia [VT] and ventricular fibrillation [VF]) [5]. The majority of patients with cardiac arrest lasting over several minutes are comatose at the time of admission and will not wake for hours or days, but a small number will awake rapidly [8]. The morbidity and mortality associated with

* Corresponding author.
E-mail address: Brit.long@yahoo.com (B. Long).

https://doi.org/10.1016/j.ajem.2025.03.039
0735-6757/Published by Elsevier Inc.

out-of-hospital cardiac arrest (OHCA) is significant, with approximately 90 % of patients with OHCA not surviving to discharge [1,3,7]. For those who obtain ROSC and are admitted following OHCA, the survival rate to discharge is 50–60 %, with a subset of these patients having favorable neurologic outcomes [6,7]. Following successful resuscitation from cardiac arrest, withdrawal of life-sustaining therapy accounts for approximately two-thirds of deaths, though shock and recurrent arrest also account for a significant proportion [6,9].

Following ROSC, there can be severe cerebral and cardiac dysfunction due to hypoperfusion of all organ systems, termed the post-cardiac arrest syndrome [10-18]. This is characterized by hypoxic brain injury, myocardial dysfunction, systemic ischemia and reperfusion injury, and persistent precipitating pathology (Table 1) [11,14-18]. The magnitude of effect of each of these components depends on the patient comorbidities, duration of the ischemia, underlying etiology of cardiac arrest, and interventions performed during the cardiac arrest. This post-cardiac arrest syndrome informs the emergency department (ED) and intensive care unit (ICU) management following ROSC [11,14-18].

Several systemic complications may also occur in the initial post-ROSC period and are associated with increased morbidity and mortality, including acute renal failure (12–50 %), acute respiratory distress syndrome (ARDS) (50–70 %), disseminated intravascular coagulation (DIC) (< 8 %), and refractory shock [3,5,10,15,17,19]. Importantly, the majority of patients with ROSC will experience hypotension, and approximately 40 % of patients with ROSC will experience at least one episode of rearrest, for which emergency clinicians should be prepared to intervene immediately. These are both associated with increased morality [5,20-24].

Importantly, there have been several recent advances in the evaluation and management of the post-ROSC patient. The following questions will highlight several key updates in the management of the post-ROSC patient and post-cardiac arrest syndrome; however, this paper is not intended to serve as a review of the condition in its entirety.

Table 1
Post-Cardiac Arrest Syndrome [14-18].

Hypoxic brain injury	• Characterized by cerebral ischemia, cerebral edema/increased ICP, impaired cerebrovascular autoregulation, post-ischemic neurodegeneration • Frequent cause of subsequent death and disability following ROSC • Primary injury occurs due to global ischemia and reperfusion injury, as the brain has reduced tolerance to ischemia • Secondary injury occurs following reperfusion due to impaired oxygen delivery associated with hypotension, hypoxemia, impaired vascular autoregulation, cerebral edema, increased ICP, hyper−/hypoglycemia, seizure, pyrexia • Cortex, cerebellum, corpus striatum, hippocampus, and thalamus are vulnerable areas most susceptible to ischemia • Global cerebral ischemia results in microcirculatory intravascular thrombosis, inhibiting microvascular perfusion despite restoration of macrocirculation
Myocardial dysfunction	• Characterized by reduced ejection fraction, increased LV end-diastolic pressure, decreased cardiac output • Ranges from mild to severe but is usually transient and responsive to management • Common cause of mortality after cardiac arrest • Occurs within the first 7 h after ROSC; recovery time course is 24–72 h • Labile hemodynamics following ROSC due to endogenous and exogenous circulating catecholamines • Global stunning of the myocardium may be worsened with regional ischemia from acute coronary syndrome, may contribute to dysrhythmias and cardiogenic shock
Systemic ischemia and reperfusion injury	• Characterized by vasoplegia, intravascular volume depletion, impaired oxygen delivery/utilization, immunosuppression, multiorgan failure • Follows cardiac arrest with complete cessation of oxygen delivery and metabolite removal • Relative adrenal insufficiency may be present • Impaired oxygen delivery with increased tissue oxygen extraction during CPR reduces central venous oxygen saturation; following ROSC, oxygen debt results in endothelial injury, activation of coagulation pathway, impaired vasoregulation, and systemic inflammation
Persistent precipitating pathophysiology	• Characterized by effects from underlying cause of the cardiac arrest • Acute coronary syndrome (myocardial dysfunction, dysrhythmia), cardiomyopathy, pulmonary embolism (hypoxemia, hemodynamic compromise), sepsis (hypotension, inflammation), stroke (cerebral ischemia) • Multiorgan failure common

Abbreviations: ICP - intracranial pressure; ROSC - return of spontaneous circulation; CPR - cardiopulmonary resuscitation; LV - left ventricle.

2. Discussion

2.1. What are primary management priorities in the post-ROSC patient?

The goals of assessment and management in the initial post-ROSC period in the ED setting include completing a focused history and physical examination, supporting cardiopulmonary function, addressing and managing the underlying cause of arrest, minimizing secondary cerebral injury, and correcting physiologic derangements (Table 2). Estimating neurologic prognosis should generally be reserved for the intensive care unit (ICU) setting and is not recommended in the ED setting, except for cases of obviously non-survivable causes of arrest [5,11,14,18].

If not obtained during the resuscitation, information concerning the circumstances around the cardiac arrest should be obtained, including the setting, events leading up to the arrest, any signs or symptoms, whether the event was witnessed and if bystander CPR was performed, initial cardiac rhythm, time from CPR initiation to ROSC, and prehospital interventions (e.g., access, defibrillation attempts, medication administered). If possible, patient comorbidities (e.g., coronary artery disease, thromboembolic risk factors), medications (e.g., anticoagulation, antiplatelet agents, antiarrhythmics), and advanced directives should also be obtained. The examination should focus on assessing for the etiology of the arrest. If ROSC is obtained, the examination should also include the severity of shock, hemodynamic status (e.g., blood pressure, heart rate, capillary refill, skin color and temperature), and neurologic status (e.g., mental status, pupils, motor, posturing). A neurologic examination should be conducted, including mental status with Glasgow coma scale (GCS), motor examination for the presence of lateralizing or localizing signs (suggestive of intracranial pathology), rhythmic or periodic facial

Table 2
Primary management strategies in the post-ROSC setting.

- Primary management for the post-ROSC patient are to stabilize cardiopulmonary function, address/treat underlying etiology of arrest, minimize secondary organ injury, and correct any physiologic derangements.
- Assess for underlying cause of arrest with history, examination (hemodynamics, cardiovascular, neurologic), ultrasound, and ECG following ROSC.
- Utilize POCUS: cardiac (contractility, ventricular dilation/dysfunction, aorta outflow tract, effusion), lungs (pneumothorax, effusion, endotracheal tube confirmation), abdomen (aortic aneurysm, free fluid).
- Utilize "Circulation-Airway-Breathing" approach for treatment during resuscitation in the peri-arrest and post-ROSC periods.
- Optimize MAP using vasopressors and IV fluids.
- Prophylactic antiarrhythmics are not routinely recommended, except for patients with recurrent or ongoing unstable ventricular arrhythmias.

ROSC – return of spontaneous circulation; ECG – electrocardiogram; MAP – mean arterial pressure; IV - intravenous.

or body movements to suggest seizure, pupil size and reactivity, and brainstem reflexes (e.g., corneal, gag/cough, spontaneous respirations).

Point-of-care ultrasound (POCUS) can be valuable for determining the etiology (e.g., focal myocardial dysfunction, tamponade, pneumothorax) [25]. Cardiac assessment includes evaluating for pericardial effusion, left ventricular function, right ventricular enlargement, and the aorta outflow tract [25-27]. Assessment of volume tolerance includes evaluation of the inferior vena cava (IVC) diameter and distensibility. Lung ultrasound can evaluate for pneumothorax, and POCUS can also be used to evaluate for location and depth of the endotracheal tube [28]. The RUSH examination has been primarily evaluated for those with undifferentiated shock, with limited data for post-ROSC patients, though it may be reasonable when the etiology remains unclear [26,29-31]. This may be used to assess for free intra-abdominal fluid and abdominal aortic aneurysm. A comprehensive transthoracic echocardiogram should be obtained to assess post-ROSC myocardial dysfunction, which may include global cardiac dysfunction, regional wall motion abnormalities, left ventricular outflow tract obstruction, valvular abnormalities, or cardiomyopathy [32].

Rather than following an "A-B-C" approach, we recommend utilizing "C-A-B", with focus on circulation in the peri-arrest and post-ROSC periods. Vascular access should be obtained if not already done so during the arrest. An intraosseous (IO) catheter can be removed if there is adequate intravenous (IV) access. As will be discussed in following sections, the mean arterial pressure (MAP) should be optimized using a vasopressor and IV fluids if needed. IV isotonic crystalloids are recommended if the patient is hypovolemic and fluid responsive. Amiodarone, lidocaine, and beta blockers may be used in patients with refractory VF or pulseless VT. However, the prophylactic use of these antiarrhythmics is controversial, with limited data demonstrating mixed results and no high-quality evidence concerning the routine use of antiarrhythmics in the post-ROSC patient [33-36]. At the time of this publication, antiarrhythmics are not routinely recommended for patients following ROSC, except for those with recurrent or ongoing unstable arrhythmias (e.g., VF or VT) [5]. This is based on the lack of strong evidence supporting the use of routine or prophylactic administration of antiarrhythmics following ROSC.

2.2. What are secondary management priorities in the post-ROSC patient?

Table 3. Secondary management strategies in the post-ROSC setting.

Following initial management priorities, there are several interventions to reduce end-organ injury, particularly cerebral injury. This includes targeted temperature management (TTM; see section 2.10); head-of-bed elevation; clearing the cervical collar (if present) as soon as possible; sedation; optimizing MAP (section 2.5), oxygenation, and ventilation (section 2.6); managing glucose levels; seizure control; and assessing for and treating increased intracranial pressure (ICP) (Table 3) [5,11,14,18].

Table 3
Secondary management strategies in the post-ROSC setting.

- Secondary management focuses on hemodynamic support, optimizing cerebral perfusion, and preventing other organ injury.
- Elevate head of bed to 30–45 degrees to reduce risk of VAP and lower ICP.
- Sedation is recommended to reduce metabolic demand, improve patient comfort, and reduce recall; may utilize propofol or ketamine.
- Maintain serum glucose between 80 and 180 mg/dL.
- Manage active seizures with benzodiazepines, but avoid routine seizure prophylaxis.
- Assess for increased ICP: evaluate for abnormal neurologic findings (e.g., focal neurologic deficit, loss of pupillary reflex, unilateral pupil abnormality) and consider POCUS for ONSD.
- If ICP elevated, reduce ICP: ensure adequate analgesia and sedation, raise the head of the bed, ensure head and neck are midline, administer hypertonic saline, and optimize MAP.

MAP – mean arterial pressure; ICP – intracranial pressure; VAP - ventilator associated pneumonia; POCUS - Point-of-care ultrasound; ONSD - optic nerve sheath.

The head of the bed should be elevated to 30–45 degrees, which may reduce ventilator associated pneumonia (VAP) and lower ICP while maintaining cerebral perfusion pressure (CPP) and improving lung recruitment [37,38]. A meta-analysis including studies of intubated and mechanically ventilated patients found the semirecumbent position compared with the supine position reduced the risk of VAP, hospital length of stay, and length of mechanical ventilation [39]. Another analysis found placing patients in the semirecumbent position at 45 degrees compared to 30 degrees was associated with reduced risk of VAP and gastric reflux, though there was increased risk of skin sores [40]. Head of bed elevation is also supported by the Neurocritical Care Society for patients with cerebral edema and the Agency for Healthcare Research and Quality and American Thoracic Society for mechanically ventilated patients [41-43].

Sedation is necessary in the post-ROSC period to reduce metabolic demand, improve patient comfort, and reduce recall [5]. The American Heart Association (AHA) and Neurocritical Care Society (NCS) recommend short-acting sedative and analgesic agents to reduce time to reawakening and duration of mechanical ventilation, as well as decreasing the confounding of delaying prognostication [5] Options for sedation include propofol (up to 3 mg/kg/h IV), dexmedetomidine (1.4 μg/kg/h IV), ketamine (1–2 mg/kg/h IV), or midazolam (2–10 mg/h IV). Propofol is the preferred sedative if possible, as it has rapid onset and offset, is an antiepileptic, is neuroprotective, and does not result in withdrawal. However, it can result in vasodilation and reduced cardiac contractility [44]. Dexmedetomidine does not cause respiratory depression but is typically only utilized in those requiring light sedation. Ketamine demonstrates a potential attenuation in neurologic injury following cardiac arrest and has dissociative, analgesic, and sedative properties [45]. While midazolam may reduce preload and afterload without significantly affecting contractility, benzodiazepine infusions can complicate the neurologic examination and have a longer half-life. Analgesics such as remifentanil and fentanyl infusion are recommended over morphine infusions by the AHA and NCS [5].

Both hypo- and hyperglycemia are associated with worse outcomes following cardiac arrest [46-49]. While tight glucose control (defined as 70–108 mg/dL) compared to more liberal glucose control (108–144 mg/dL) was not associated with benefit, higher rates of hypoglycemia may lead to cerebral injury [48,49]. Thus, glucose should be maintained between 81 and 180 mg/dL, and hypoglycemia should be avoided [5,10,11].

Following cardiac arrest, tonic-clonic or myoclonic seizure-like activity is common, occurring in up to 45 % of patients [50,51]. Continuous seizure activity (convulsive or non-convulsive) is associated with increased temperature, worse prognosis, and increased mortality [50]. Myoclonus in the post-ROSC period is suggestive of more severe brain injury, but over 20 % of patients with myoclonus fully recover [52-56]. In patients who are comatose following cardiac arrest, electroencephalogram (EEG) monitoring is recommended by the AHA and NCS to assess for post-anoxic myoclonus and seizures [5,10]. Patients who actively seize should receive benzodiazepines or other antiepileptics (e.g., propofol, levetiracetam, valproic acid) [5]; however, routine antiseizure medications for seizure prophylaxis are controversial. A 2022 randomized controlled trial (RCT) including 172 patients after cardiac arrest with rhythmic or periodic EEG patterns compared antiseizure medications for at least 48 h versus standard care. Authors found no difference in survival with favorable neurologic outcomes at 3 months [57]. Thus, at this time, routine seizure prophylaxis is not recommended.

Assessment for elevated ICP is recommended in the post-ROSC patient due to the risk of cerebral edema and hypoxic brain injury [5,10,11,58-61]. This may include imaging to assess for findings such as diffuse cerebral edema, examination for abnormal neurologic findings (e.g., focal neurologic deficit, loss of pupillary reflex, unilateral pupil abnormality), and indirect or noninvasive measurements (optic nerve sheath diameter [ONSD] on ultrasound, transcranial Doppler)

[5,10,59-64]. ONSD on POCUS has a sensitivity approximating 90 % and specificity over 85 % for detecting elevated ICP, though there can be inter-rater variability [62,63]. Thus, clinicians should incorporate imaging (e.g., non-contrast head computed tomography [CT], POCUS) and examination findings (e.g., unilateral pupil abnormalities, focal motor/tone abnormalities, posturing) in assessing for elevated ICP. If ICP is suspected to be elevated, the clinician should take measures to reduce ICP (e.g., ensure adequate analgesia and sedation, raise the head of the bed, ensure head and neck are midline, administer hypertonic saline) and optimize MAP (section 2.5) [5].

2.3. Following ROSC, what laboratory and imaging testing is recommended?

Dedicated testing following ROSC with laboratory assessment, ECG, and imaging is necessary to determine the etiology of arrest and to evaluate for end-organ injury (Table 4). Laboratory testing includes complete blood count, electrolytes, renal and liver function, troponin, serum lactate, and venous blood gas. Arterial blood gas is recommended in comatose patients, mechanically ventilated patients, and those with respiratory insufficiency to optimize oxygenation and ventilation. Respiratory and metabolic acidemia with elevated lactate is common following ROSC [5,11]. However, this should improve with resuscitation in the post-ROSC phase. If the lactate does not improve, other etiologies should be considered. Leukocytosis is common following ROSC and is typically associated with white blood cell demargination and systemic inflammation. Electrolyte changes often include hypo- or hyperkalemia, both potential causes of arrest, and should be corrected. Impaired renal and liver function is also common following cardiac arrest due to global hypoperfusion and reperfusion injury [5,10,11]. Electrocardiogram (ECG) should be obtained following ROSC to evaluate for arrhythmias, ST-segment elevation and depression, T wave changes, and interval abnormalities (e.g., QTc interval prolongation) [5,10,11].

Imaging can assist in determining the underlying etiology and assessing for complications following resuscitation. Observational studies evaluating patients with ROSC following cardiac arrest suggest a wide range in yield on different imaging tests, including CT of the head (10–45 %), chest CT (14–54 %), abdominal/pelvic CT (8–41 %), magnetic resonance imaging (6–27 %), and echocardiography (2–31 %) [65]. Common findings include ICH, PE, pericardial effusion, cardiomyopathy, regional wall abnormalities, and hemoperitoneum. Iatrogenic injuries include rib fractures (70–85 %) and sternal fractures (8–30 %) [66]. As discussed, due to its ease of use and accuracy, POCUS can rapidly diagnose a potential etiology and complication following ROSC with evaluation of the heart, lungs, and abdomen [25]. Echocardiography is recommended as soon as possible following ROSC to assess left and right ventricular function, cardiac output, and IVC size and distensibility [5]. Serial echocardiography can also be beneficial in guiding hemodynamic management [5].

2.4. What is the role of CT in the post-ROSC patient?

CT can play an important role in the post-ROSC patient in diagnosing a cause of arrest and assessing for end-organ injury and complications from resuscitation (Table 5). However, there is current controversy regarding CT in the post-ROSC patient. Non–contrast head CT may diagnose an underlying etiology of the cardiac arrest (e.g., ICH) and detect cerebral edema. Literature suggests 2–6 % of patients of cardiac arrest have ICH as the underlying cause, which alters further management such as avoiding anticoagulation and considering reversal of any specific antithrombotic agents, as well as altering prognosis [65,67-69]. Fall from standing or other traumatic mechanisms at the time of cardiac arrest may result in cervical spine fracture and injury, which may lead to respiratory failure and cardiac arrest. As the majority of patients following ROSC are comatose and unable to provide history, cervical spine CT should be obtained if trauma cannot be excluded. CT of the chest with IV contrast (angiogram with arterial phase) may be helpful by identifying causes of arrest (e.g., PE, aortic dissection) and injuries from resuscitation such as rib fractures, aspiration, and pneumothorax [65,70-72]. CT of the abdomen/pelvis with IV contrast may also detect an intra-abdominal cause of cardiac arrest such as aneurysm, dissection, and mesenteric ischemia, as well as detect liver or splenic injury in the context of trauma or from the resuscitation [70,71].

Based on this rationale, several studies have evaluated the use of head-to-pelvis CT following OHCA. A 2021 observational study included 104 patients and found that head-to-pelvis CT diagnosed the underlying etiology in 39 % and found urgent complications in 16 % (most commonly pneumothorax and solid organ injury) [70]. An observational study published in 2022 with 104 patients found head-to-pelvis CT diagnosed 81 % of resuscitation complications, but only 14 % of time-critical injuries [20]. Imaging found rib fractures in 74 % and sternal fractures in 18 %. A third observational study published in 2023 included 597 patients following cardiac arrest, with 491 undergoing cross-sectional imaging [73]. Authors found cerebral edema in 34 %, ICH in 8 %, rib or sternal fractures in 55 %, aspiration or pneumonia in 19 %, pneumothorax in 8 %, PE in 4 %, hemothorax in 2 %, liver or splenic laceration in 2 %, and cervical spine fracture in 1 % [73]. A 2023 observational study evaluated the diagnostic yield of head-to-pelvis CT with a before and after protocol implementation study within 6 h of cardiac arrest in post-ROSC patients [74]. They utilized non-contrast head CT, retrospective ECG-gated thoracic CT angiogram, and spiral abdomen/pelvic CT venous phase compared to standard care. Of note, 84 % of patients in the standard care group underwent at least one CT, most commonly non-contrast head CT [74]. The cause of cardiac arrest was found in 92 % of patients in the head-to-pelvis CT, versus 75 % in the standard care group. Time to diagnosis was 78 % faster (3.1 h versus 14.1 h) with head-to-pelvis CT, but survival to hospital discharge, acute kidney injury, identification of time-critical diagnosis, and delayed ascertainment of time critical diagnosis were not statistically different between the groups [74]. There was also no discussion of what diagnoses could have been made clinically, and there was no discussion of cost.

While the literature suggests no improvement in patient-oriented outcomes with head-to-pelvis CT, this imaging may assist in determining the etiology of arrest if unknown and assessing for any resuscitation complications, but there are several important considerations. If

Table 4
Recommended laboratory and imaging testing in the post-ROSC setting.

- Obtain laboratory assessment, ECG, and imaging to evaluation for end organ injury and arrest etiology
- Laboratory testing: complete blood count, electrolytes, renal and liver function, troponin, serum lactate, and venous blood gas.
- ECG: arrhythmias, ST-segment elevation and depression, T wave changes, and interval abnormalities.
- Imaging: POCUS (see Table 3, section 2.1 and 2.3) and CT (Table 5, section 2.4) play integral roles in assessing for the etiology of arrest and end organ injury

ECG – electrocardiogram; POCUS - Point-of-care ultrasound; CT – computed tomography.

Table 5
CT in the post-ROSC setting.

- Head-to-pelvis CT may assist in determining the etiology of arrest if unknown and evaluating for any resuscitation complications. However, literature suggests no improvement in patient-oriented outcomes with this imaging strategy.
- If obtained, head-to-pelvis CT may be most beneficial in the first six hours after cardiac arrest prior to ICU transfer for admission in patients with unknown cause of arrest despite clinical evaluation (e.g., examination, POCUS, x-ray).
- Timing of this modality must consider patient clinical stability, potential delay in other procedures such as catheterization, impact on other patients in the ED, and available CT technology.

ICU – intensive care unit, ED – emergency department; POCUS - Point-of-care ultrasound; CT – computed tomography.

obtaining head-to-pelvis CT, this is likely most beneficial within the first six hours after cardiac arrest prior to ICU transfer for admission in patients with unknown cause of arrest despite clinical evaluation (e.g., examination, POCUS, x-ray) [74]. However, the optimal timing depends on clinical stability (e.g., risk of rearrest, hypotension, hypoxemia during transport to CT and the scan) and consideration of the potential delay of other vital procedures (e.g., angiography for ST elevation myocardial infarction [STEMI]) and impact on imaging for other patients in the ED. This imaging strategy also depends on the type of CT technology available, and it may not be helpful in single coverage or stand-alone EDs, where stabilization and transfer to a higher level of care is typically recommended [5].

2.5. What is the recommended mean arterial pressure target, and what is the first-line vasopressor?

Following cardiac arrest and ROSC, clinicians must optimize end-organ perfusion and oxygenation while avoiding the furthering of other injuries, and thus, studies have sought to provide optimal MAP targets to balance these issues (Table 6) [5,10,11]. Of note, there is loss of normal cerebral perfusion autoregulation following cardiac arrest, and the MAP range in which cerebral blood flow is constant can be affected, moving the cerebrovascular autoregulation curve to the right [5,75]. As discussed previously, ICP may also be elevated due to cerebral edema and hypoxic brain injury, which will lower the CPP (CPP = MAP - ICP). In those with increased ICP and cerebral edema, a CPP of at least 60 mmHg is often recommended. This is another rationale for targeting MAP values greater than 65 mmHg in order to maintain adequate CPP in the setting of elevated ICP [5,58,59,75,76].

Literature suggests that lower MAP targets are associated with worse outcomes, while several observational studies suggest that MAP >65 mmHg is associated with improved neurologic outcomes [77-81]. Several recent RCTs have evaluated higher MAP targets. One multicenter RCT randomized patients to MAP targets of 65–75 mmHg versus 80–100 mmHg, finding these higher targets were feasible with no reduction in safety outcomes, though this study was not powered to evaluate survival or neurological outcomes [82]. A pooled analysis of these two prior RCTs found that MAP 80–100 mmHg was associated with reduced cardiac biomarkers and no increase in rearrest, but there was no difference in favorable functional outcome at 6 months [83]. Another RCT evaluated MAP >65 mmHg versus 85–100 mmHg, finding no evidence of harm with higher MAP targets, though higher MAP targets did not improve the extent of anoxic brain injury or neurologic outcomes [84]. An RCT comparing MAP of 77 mmHg versus 63 mmHg in post-ROSC patients following OHCA found no difference in the primary outcome of all-cause mortality or hospital discharge with a 90-day Cerebral Performance Category (CPC) of 3 or 4, as well as no difference in adverse events [85]. However, this study included predominantly (>80 %) patients with witnessed shockable rhythms and bystander CPR, interventions to achieve MAP targets were not started until the ICU, and there was a relatively small difference in blood pressures (10.7 mmHg) [85].

Based on the available evidence, in comatose patients following cardiac arrest, MAP should be maintained >65 mmHg but preferably >80 mmHg to ensure adequate CPP if advanced cerebral monitoring is not in routine use and if there are no clinical concerns or evidence of adverse effects (as recommended by the AHA and NCS) [5]. These targets can be obtained by incorporating IV fluid resuscitation, vasopressors, inotropes, and mechanical circulatory support.

Fluid resuscitation is recommended in those with a history or evidence of volume loss and should preferably be replaced with balanced crystalloids in those without cerebral edema (e.g., Lactated Ringers or Plasmalyte), which reduce the risk of hyperchloremic metabolic acidemia [86]. However, if there is cerebral edema, normal saline is recommended [5]. Boluses of 250–500 mL may be utilized, followed by reassessment of fluid status. Hypotonic fluids are not recommended due to the association of cerebral edema with hypoxic brain injury [5].

Vasopressors are often necessary within the first 48 h following ROSC to address vasoplegia [5,87,88]. One large cohort study found that 47 % of patients required some form of vasopressor support, and 25 % of those receiving vasopressors required norepinephrine doses between 0.05 and 0.1 μg/kg/min with 10 % requiring over 0.1 μg/kg/min [89]. Dopamine is not recommended due to the greater risk of arrhythmia and mortality [90]. Norepinephrine is a common first-line vasopressor, as it improves vasomotor tone and has inotropic effects. In those requiring additional inotropic support due to ongoing shock despite improved MAP, epinephrine (0.01–1 μg/kg/min), dobutamine (0.5–15 μg/kg/min), or milrinone (loading dose 50 μg/kg/min over 10 min, then 0.375–0.75 μg/kg/min) may be added. However, both dobutamine and milrinone may result in hypotension, and dobutamine may result in arrhythmias [5]. If dobutamine or milrinone are used, they should be combined with norepinephrine due to their risk of vasoplegia. Epinephrine has greater inotropy compared to norepinephrine, but it may worsen lactic acidemia and is associated with increased rates of refractory cardiogenic shock, cardiovascular-related mortality, and all-cause mortality [90-92]. Based on the degree of cardiac dysfunction, mechanical circulatory support may be necessary including intra-aortic balloon pump, left ventricular assist device, and veno-arterial extracorporeal membrane oxygenation [87].

2.6. What is the target for oxygen saturation and $PaCO_2$ in the post-ROSC patient?

Invasive mechanical ventilation is necessary in the majority of post-ROSC patients, with recent updates concerning oxygen saturation and $PaCO_2$ targets (Table 7). Lung-protective ventilation is recommended for mechanically ventilated patients, as these patients are at high risk of developing ARDS (48–71 %) [5,93,94]. In the ED, this includes utilizing a tidal volume of 4–8 mL/kg ideal body weight, titrating positive end-expiratory pressure to ensure appropriate alveolar filling and prevent collapse, and titrating the fraction of inspired oxygen (F_iO_2) to target an oxygen saturation that is adequate but not excessive. Importantly, both hypoxia and hyperoxia are harmful in the post-ROSC patient

Table 6
Recommended MAP target and vasopressors in the post-ROSC setting.

- In the post-ROSC patient, clinicians must optimize end-organ perfusion and oxygenation while avoiding worsening other injuries.
- MAP targets include >65 mmHg but preferably >80 mmHg for adequate CPP if advanced cerebral monitoring is not in routine use and if there are no clinical concerns or evidence of adverse effects.
- MAP targets may be obtained by IV fluids, vasopressors, inotropes, or mechanical circulatory support.
- Fluid resuscitation is recommended in those with volume loss with balanced crystalloids in those without cerebral edema; if cerebral edema present, use normal saline.
- Vasopressors improve vasomotor tone and are typically necessary in the first 48 h post-ROSC. Norepinephrine is first-line.
- In those requiring additional inotropic support due to ongoing shock despite improved MAP, epinephrine, dobutamine, or milrinone may be added.

ROSC – return of spontaneous circulation; MAP – mean arterial pressure; CPP – cerebral perfusion pressure; IV – intravenous.

Table 7
Recommended oxygen saturation and $PaCO_2$ targets in the post-ROSC setting.

- In the intubated post-ROSC patient, utilize lung-protective strategy with TV 4–8 mL/kg ideal body weight. Titrate PEEP for appropriate alveolar filling.
- Titrate F_iO_2 to achieve an oxygen saturation 92–98 %; avoid hypoxia and hyperoxia.
- Target $PaCO_2$ levels 35–55 mmHg; avoid hypocapnia. Moderate hypercapnia may be used for lung-protective settings or if the patient has suspected chronic hypercapnia as long as the pH can be maintained >7.2.

ROSC – return of spontaneous circulation; TV – tidal volume; PEEP - positive end-expiratory pressure; F_iO_2 - fraction of inspired oxygen.

[5,10,95,96]. A systematic review of 14 studies found $PaO_2 > 300$ mmHg was associated with increased mortality in patients after ROSC (odds ratio [OR] 1.4; 95 % confidence interval [CI] 1.02 to 1.93) [97]. An RCT including 425 prehospital and ED patients compared oxygen saturation targets of 90–94 % versus 98–100 % and found patients in the lower saturation target group had lower survival to hospital discharge (38 % versus 48 %, difference − 10 %, 95 % CI -19 % to −0.2 %) and more episodes of hypoxia before ICU admission (31 % versus 16 %, difference 15 %, 95 % CI 7 % to 23 %), but the study was stopped early due to COVID [98]. The BOX RCT compared PaO_2 of 68–75 mmHg versus 98–105 mmHg and found no difference in the composite outcome of all-cause mortality or CPC of 3–4 within 90 days, as well as no difference in adverse events [99].

Carbon dioxide (CO_2) also affects the cerebral vasculature, with hypocapnia resulting in vasoconstriction and hypercapnia leading to vasodilation. Hypocapnia due to hyperventilation can result in cerebral ischemia through arterial vasoconstriction and worsen injury [100,101]. Of note, end-tidal CO_2 values will be lower than $PaCO_2$. Observational studies suggest $PaCO_2$ levels of 35–55 mmHg may be associated with better outcomes compared to lower $PaCO_2$ values, but significant hypercarbia can worsen acidemia and be harmful in patients with elevated ICP. Observational studies also suggested either harm or no benefit with hypocapnia [95,102-104]. The TAME trial included 1700 patients and compared $PaCO_2$ targets of 50–55 mmHg versus 35–45 mmHg [105]. Authors found no difference in neurologically favorable survival, adverse events, or secondary outcomes [105]. There is likely a complex interplay among $PaCO_2$, ICP, and CPP, particularly in the setting of decreased or absent cerebral autoregulation that occurs in cardiac arrest. There is also no clear guidance on $PaCO_2$ targets in patients with chronic hypercapnia (e.g., chronic obstructive pulmonary disease), and this may not be known in the initial care of the post-ROSC patient. Thus, these considerations complicate recommending a specific $PaCO_2$ target [5].

Based on available data, using a lung-protective ventilation strategy with a tidal volume of 4–8 mL/kg ideal body weight is recommended, which is also supported by the AHA/NCS scientific statement [5]. Both hyperoxia and hypoxia can be harmful. Therefore, we recommend titrating the F_iO_2 to target an oxygen saturation of 92–98 % [5]. Targeting $PaCO_2$ levels of 35–55 mmHg is likely beneficial, and hypocapnia should be avoided [5,105]. Moderate hypercapnia may be utilized for lung-protective settings or if the patient has suspected chronic hypercapnia as long as the pH can be maintained >7.2 per the AHA/NCS scientific statement [5].

2.7. Should antibiotics be administered in the post-ROSC patient?

Post-ROSC patients are at significant risk of aspiration-associated pneumonia and VAP, as well as sepsis and bacteremia due to bacterial translocation across the intestinal mucosa during global hypoperfusion [5,11,106,107]. However, there is controversy in the literature concerning antibiotics in post-ROSC patients (Table 8). In the TTM1 trial, pneumonia occurred in 53 % and sepsis in 10 % of patients randomized to hypothermia [51]. A meta-analysis published in 2019 based on 3 RCTs and 8 observational studies found prophylactic or early antibiotic administration in patients with OHCA was not associated with increased survival (OR 1.16, 95 % CI 0.97 to 1.40), survival with good neurological outcome (OR 2.25, 95 % CI 0.93 to 5.45), critical care length of stay (mean difference − 0.6, 95 % CI -3.6 to 2.4), or pneumonia (OR 0.58, 95 % CI 0.23 to 1.46) [108]. Following this meta-analysis, a double-blind RCT including 198 intubated patients with OHCA from pulseless VT/VF treated with TTM found empiric administration of amoxicillin-clavulanate was associated with lower risk of VAP (hazard ratio 0.53; 95 % CI 0.31 to 0.92), with no difference in ventilator-free days, ICU length of stay, adverse events, and 28-day mortality [109]. Based on the available data, antibiotics should not be routinely administered in those without evidence of infection; however, they may be considered in intubated cardiac arrest patients receiving therapeutic hypothermia [5].

Table 8
Antibiotics in the post-ROSC setting.

- Post-ROSC patients are at risk of aspiration-associated pneumonia, VAP, and sepsis.
- However, literature is controversial concerning antibiotics in post-ROSC patients.
- Based on available data, antibiotics should not be routinely administered in those without evidence of infection. They may be considered in intubated cardiac arrest patients receiving hypothermic TTM.

ROSC – return of spontaneous circulation; VAP - ventilator associated pneumonia; TTM – targeted temperature management.

2.8. Is there a role for corticosteroids in the post-ROSC patient?

Corticosteroids may reduce the severe systemic inflammatory state after cardiac arrest, and there is an association with lower cortisol levels following cardiac arrest and the severity of shock and mortality within 48 h [110,111]. Thus, corticosteroids have been evaluated as a potential therapy in patients with cardiac arrest (Table 9).

Much of the literature evaluating corticosteroids in cardiac arrest has been published prior to the use of TTM. Several observational studies found no difference in mortality or regaining consciousness with corticosteroid treatment in patients after cardiac arrest, while others found improved rates in survival to discharge [112-116]. Two subsequent RCTs compared vasopressin, epinephrine, and corticosteroid administered for 7 days versus epinephrine and no corticosteroids in patients with in-hospital cardiac arrest [117,118]. These RCTs found the corticosteroid group had more frequent ROSC and improved survival to discharge [117,118]. A post-hoc analysis found benefit with steroids in those with septic shock [119]. Several other RCTs evaluating steroids (methylprednisolone and/or hydrocortisone) have found no clear difference in survival to discharge, survival with favorable neurologic outcome, shock reversal, length of stay, MAP, and time to shock reversal [120,121]. A 2024 meta-analysis of 11 studies with 2273 patients found corticosteroid administration during cardiac arrest was associated with increased rate of ROSC (OR 2.05, 95 % CI 1.24 to 3.37), but there was no benefit in favorable neurologic outcome or survival rate at hospital discharge [122]. On subgroup analysis, authors found increased survival rate and ROSC if a dose of methylprednisolone over 100 mg was utilized [122]. At this time with the current evidence, corticosteroids should not be routinely administered in patients with ROSC except in the setting of suspected or proven adrenal insufficiency or decompensated hypothyroidism [5].

2.9. Which post-ROSC patients should undergo coronary catheterization?

Coronary artery disease is a common cause of cardiac arrest, and an ECG should be obtained in all post-ROSC patients (Table 10). The 2024 AHA/NCS scientific statement on the management of patients after cardiac arrest states that there is reasonable consensus that early angiography, defined as within 6 h, is safe and may be beneficial for the post-ROSC patient [5]. This statement was based on non-randomized literature suggesting catheterization is associated with improved survival and neurologic recovery in post-ROSC patients with ST-segment elevation on ECG [5,123-126]. ST-segment elevation following ROSC of

Table 9
Corticosteroids in the post-ROSC setting.

- Corticosteroids should not be routinely administered in post-ROSC patients.
- Corticosteroids should be administered in the setting of suspected or proven adrenal insufficiency or decompensated hypothyroidism.

ROSC – return of spontaneous circulation.

Table 10
Coronary catheterization in the post-ROSC setting.

- Obtain an ECG in the post-ROSC period. If the initial ECG is concerning for acute coronary occlusion, emergent cardiology consultation is recommended.
- Catheterization is recommended in those with focal wall motion abnormalities on echocardiography, ongoing cardiogenic shock or electrical instability (recurrent VF or pulseless VT), or if repeat ECG obtained after ROSC demonstrates clear STEMI.
- Catheterization should be considered in those with an initial history concerning for ACS or if the presenting arrhythmia was VF or pulseless VT.
- In other post-ROSC patients, emergent catheterization is not associated with improved patient-oriented outcomes.

ECG – electrocardiogram; ROSC – return of spontaneous circulation; ACS – acute coronary syndrome; VF – ventricular fibrillation; VT – ventricular tachycardia; STEMI – ST elevation myocardial infarction.

the patient with an associated arrhythmia (e.g., VF or pulseless VT) is associated with a significant likelihood of coronary artery disease in 70–95 % of patients with ROSC, and 60–65 % of these patients have acute coronary occlusion [123,127]. Thus, ECG is important to identify STEMI, and patients with obvious STEMI following cardiac arrest should receive cardiac catheterization.

However, other literature has suggested that ST-segment elevation on ECG obtained immediately post-ROSC in the general population of patients with cardiac arrest has more limited predictive ability for acute coronary occlusion requiring revascularization [128]. The false positive rate of ECG for the diagnosis of STEMI is highest in the first seven minutes following ROSC, likely due to transient myocardial ischemia associated with global hypoperfusion and administration of epinephrine [129]. ST-segment elevation on initial ECG is 70 % sensitive (95 % CI 54 % to 82 %) and 85 % specific (95 % CI 78 % to 90 %) for acute coronary lesion, and it is 53 % (95 % CI 47 % to 58 %) sensitive and 86 % (95 % CI 80 % to 91 %) specific for need for revascularization [128]. Thus, while an ECG should be obtained immediately following ROSC, equivocal cases should be discussed with a cardiologist and another ECG obtained within 5–10 min to evaluate for further ST-segment elevation [129]. If the repeat ECG demonstrates new or worsening ST-segment elevation, angiography is recommended, whereas if it fully resolves, this may suggest a more transient finding.

In patients without STEMI, emergent angiography with catheterization is controversial. In-post ROSC patients with VF or pulseless VT without ST-segment elevation on ECG, the rate of significant coronary artery disease is 25–50 %, and 25–35 % of these patients can have acute coronary occlusion [123,127]. A meta-analysis of primarily retrospective studies found 30 % of post-ROSC patients without ST-segment elevation on ECG had an acute coronary artery occlusion, regardless of the presenting rhythm [130]. While the majority of the evidence suggests that early angiography is safe, literature suggests that immediate angiography is not associated with significant benefit when compared to delayed (>24–48 h) angiography. The COACT trial included 552 patients after OHCA who had an initial shockable rhythm and no ST-segment elevation on ECG and randomized them to immediate (median 2.3 h) versus delayed (median 121.9 h) angiography, with coronary intervention performed if necessary [131]. Authors found approximately 65 % had coronary disease, but they did not find an improvement in 90-day survival with early angiography [131]. The TOMAHAWK study included 554 patients experiencing OHCA without ST-segment elevation randomized to immediate or delayed selective angiography, irrespective of the initial rhythm [132]. Authors found no improvement in survival but a small increase in death and severe neurologic deficit in patients undergoing angiography emergently [132]. The DISCO trial randomized 79 patients without ST-segment elevation to immediate angiography versus standard care, while the PEARL trial evaluated 99 patients [133,134]. Both studies found no difference in survival or neurologic outcomes, though the DISCO trial found 37 % of patients had a culprit lesion and PEARL identified 47 % [133,134]. Of note, these studies excluded those with hemodynamic or electrical instability. The EMERGE trial randomized 279 patients to emergent versus delayed angiography and found no difference in survival with CPC 1 or 2 at 180 days [135]. While these studies did not find a difference in mortality or neurologic outcome, a significant number of patients in these studies had acute culprit lesions, and it is unclear if there may be other benefits in cardiac function or risk of subsequent heart failure [5].

When deciding on cardiac catheterization, it is valuable to also consider resuscitation features that may predict a lower likelihood to benefit from coronary intervention. These include unwitnessed arrest, non-VF initial rhythm, no bystander CPR, > 30 min to ROSC, ongoing CPR, pH < 7.2, lactate >7, age > 85 years, end-stage renal disease, and noncardiac cause of arrest [136]. These can help inform the discussion with the cardiologist regarding whether to pursue post-ROSC cardiac catheterization.

Based on the available data, if the first ECG is concerning for acute coronary occlusion, emergent cardiology consultation is recommended [5]. Importantly, patients with VF or pulseless VT have a high incidence of coronary artery disease [128,137]. If the patient had an initial history concerning for ACS or if the presenting arrhythmia was VF or pulseless VT, catheterization can be considered [5]. Catheterization is also recommended in those with focal wall motion abnormalities on echocardiography, those with ongoing cardiogenic shock or electrical instability (recurrent VF or pulseless VT), or if a repeat ECG obtained after ROSC meets STEMI criteria. The AHA/NCS scientific statement delineates that early coronary angiography in those without ST-segment elevation may be beneficial by salvaging myocardium and potentially reducing LV dysfunction [5]. Ultimately, the decision for coronary angiography and intervention in those without ST-segment elevation should be based on local resources and clinical circumstances in collaboration with the interventional cardiologist.

2.10. What is the current evidence regarding targeted temperature management?

Core body TTM, originally referred to as therapeutic hypothermia, is an integral intervention in post-ROSC comatose patients, as neurologic injury is one of the most common causes of death following cardiac arrest (Table 11) [5,10,11,138]. TTM has been shown to reduce secondary brain injury following cardiac arrest, as hyperthermia can worsen neurologic injury [51,58,59,138-151]. All patients who are comatose or not following commands after cardiac arrest should undergo temperature control, including pregnant patients, those undergoing angiography and catheterization, and hemodynamically unstable patients [139,146-150]. There are three phases of TTM: initiation, maintenance, and rewarming.

Table 11
TTM in the post-ROSC setting.

- TTM seeks to reduce secondary brain injury following cardiac arrest, as hyperthermia may result in further neurologic injury.
- Post-ROSC patients who are comatose or not following commands should undergo temperature control.
- Based on available data, target normothermia and avoid fever as soon as possible, following ROSC. There is no difference in survival or neurologic outcome when compared to hypothermia, but issues with hypothermic TTM include increased risk of arrhythmia, coagulopathy, cold diuresis, hypokalemia, hyperglycemia, and infection.
- Continuous monitoring of core body temperature is recommended with central venous, esophageal, bladder, or rectal temperature probes. Esophageal probes may be most accurate.
- After continuous temperature monitor placement, administer acetaminophen (1 g every 6–8 h) to avoid fever. If the patient is febrile despite acetaminophen, utilize a cooling device targeting a temperature < 37.5° C.
- Cooling devices include water or air circulating blankets and water-circulating gel-coated pads, an intravascular cooling catheter, or rapid infusion of cold saline or ice packs if other devices are not available.

ROSC – return of spontaneous circulation; TTM – targeted temperature management.

Initiation of TTM should begin in the ED immediately following ROSC. The exact temperature targets have evolved since the initial adoption of TTM. RCTs in the early 2000s suggested a target of 32-34° C, though these RCTs were proof of concept studies, single center, and unblinded [140,142]. The TTM1 trial published in 2013 with 939 patients did not find a benefit with 33° C versus 36° C [51]. Multiple other RCTs published after 2013 compared TTM targeting 32-34° C versus normothermia, including the TTM2 trial with 1850 patients published in 2021 [51,143,144]. The TTM2 trial found no difference in death at 6 months but higher risk of arrhythmias in the hypothermia group [144]. Several meta-analyses have evaluated hypothermic TTM versus normal temperature TTM (36.5–38° C). One meta-analysis of five trials found no difference in survival or favorable neurologic outcome at 90–180 days [145]. A second meta-analysis of 5 trials published in 2023 found no improvement with hypothermic TTM in survival or favorable neurologic outcome, but there was higher risk of arrhythmias [151]. Based on the available evidence, clinicians should target normothermia with avoidance of fever as soon as possible following ROSC. While there is no difference in survival or neurologic outcome when compared to hypothermia, there are other issues with hypothermic TTM including increased risk of arrhythmia, coagulopathy, cold diuresis, hypokalemia, hyperglycemia, and infection [144,147,152-159]. Inducing and maintaining hypothermic TTM is also more difficult and resource intensive.

Continuous monitoring of core body temperature is recommended. Axillary and tympanic membrane temperature measurements are not recommended, as they do not assess core temperature [5,11]. There is no clear gold standard for core temperature measurement, but potential options include central venous, esophageal, bladder, and rectal temperature probes [5,11,160,161]. Esophageal temperature monitoring may be the most accurate, as bladder monitoring is inconsistent due to fluctuating urinary output, and rectal temperatures can lag behind the core temperature [5,11,160,161].

Following placement of a continuous temperature monitor, acetaminophen (1 g every 6–8 h) should be administered to avoid fever. If the patient is febrile despite acetaminophen, a cooling device is recommended if available with a goal temperature < 37.5° C [5]. This may include surface methods with water or air circulating blankets and water-circulating gel-coated pads (most common), intravascular methods including an intravascular cooling catheter, and rapid infusion of cold saline or ice packs if other devices are not available [5,11,162-164]. There is no evidence demonstrating a clear benefit of one particular device, though surface cooling devices are available in most centers and able to achieve a desired temperature rapidly and effectively [162-164]. This may be combined with infusion of 1 L of cold isotonic crystalloids, as 1 L of 4° C crystalloid infused over 15 min has been shown to reduce the core temperature by 1° C [165-167]. However, caution is recommended in the initial resuscitation period following ROSC in the ED, due to reduced myocardial function and limited physiologic reserve. A cold crystalloid bolus is not recommended in those with heart failure, end-stage renal disease, or evidence of pulmonary edema [168,169].

Shivering can increase the core body temperature, ICP, and serum lactate; result in rhabdomyolysis; and impair monitoring such as pulse oximetry [5,10,11]. If shivering occurs, the clinician should utilize a multimodal approach. Magnesium should be repleted to >2 mg/dL, and buspirone 30 mg can be administered every 8 h. The temperature target can be increased to 37.5° C. Other therapies include infusion of dexmedetomidine, propofol, or ketamine. If shivering continues, administration of fentanyl boluses and a non-depolarizing paralytic (rocuronium 1 mg/kg IV bolus or cisatracurium bolus 0.15–0.2 mg/kg followed by 1–3 microgram/kg/min infusion) is recommended.

The specific duration of TTM with normothermia is controversial, though guidelines recommend avoiding fever for at least 72 h for comatose patients [5,10,14]. One RCT including 789 patients compared TTM 36° C for 24 h followed by 37° C for 12 h versus 37° C for 48 h. Authors found no difference in death or severe neurologic disability/coma at 90 days [170]. Another trial with 355 patients evaluated TTM for 48 h versus 24 h and found no difference in survival or neurologic outcome at 6 months [171].

3. Conclusions

The post-cardiac arrest syndrome includes hypoxic brain injury, myocardial dysfunction, systemic ischemia and reperfusion injury, and persistent precipitating pathophysiology. ED priorities for the post-ROSC patient include supporting cardiopulmonary function, addressing and managing the underlying etiology of arrest, minimizing secondary cerebral injury, and correcting any physiologic derangements. Targeted testing should aim to determine the etiology of arrest and assess for organ injury. CT head-to-pelvis may be considered in the post-ROSC patient in the setting of trauma or unclear etiology. A MAP target of least 65 mmHg is recommended, but preferably >80 mmHg, which may improve cerebral perfusion. An oxygenation saturation of 92–98 % is recommended, with ARDSnet protocol in mechanically ventilated patients. Routine antibiotics are not recommended unless the patient is intubated and receiving hypothermic TTM. The routine administration of corticosteroids is not recommended in all patients. Patients with ST-segment elevation on ECG following ROSC should undergo emergent angiography and catheterization. TTM aiming for normothermia is recommended following ROSC.

CRediT authorship contribution statement

Brit Long: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Conceptualization. **Michael Gottlieb:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Conceptualization.

Declaration of competing interest

None.
No AI program was used in the construction of this manuscript.

Acknowledgements

BL and MG conceived the idea for this manuscript and contributed substantially to the writing and editing of the review. This manuscript did not utilize any grants, and it has not been presented in abstract form. This clinical review has not been published, it is not under consideration for publication elsewhere, its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. This review does not reflect the views or opinions of the U.S. government, Department of Defense, Defense Health Agency, U.S. Army, U.S. Air Force, or SAUSHEC EM Residency Program.

References

[1] Virani SS, Alonso A, Benjamin EJ, American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. Circulation. 2020;141(9):e139–596.
[2] Kiguchi T, Okubo M, Nishiyama C, et al. Out-of-hospital cardiac arrest across the world: first report from the International Liaison Committee on Resuscitation (ILCOR). Resuscitation. 2020;152:39–49.
[3] Tsao CW, Aday AW, Almarzooq ZI, on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee, et al. Heart disease and stroke statistics—2022 update: a report from the American Heart Association [published correction appears in Circulation. 2022;146:e141]. Circulation. 2022;145:e153–639.
[4] Hayashi M, Shimizu W, Albert CM. The spectrum of epidemiology underlying sudden cardiac death. Circ Res. 2015;116(12):1887–906.

[5] Hirsch KG, Abella BS, Amorim E, American Heart Association, Neurocritical Care Society, et al. Critical care management of patients after cardiac arrest: a scientific statement from the American Heart Association and Neurocritical care society. Neurocrit Care. 2024 Feb;40(1):1–37.
[6] Lemiale V, Dumas F, Mongardon N, et al. Intensive care unit mortality after cardiac arrest: the relative contribution of shock and brain injury in a large cohort. Intensive Care Med. 2013;39(11):1972–80.
[7] Yan S, Gan Y, Jiang N, et al. The global survival rate among adult out-of-hospital cardiac arrest patients who received cardiopulmonary resuscitation: a systematic review and meta-analysis. Crit Care. 2020;24(1):61.
[8] Deakin CD, Fothergill R, Moore F, et al. Level of consciousness on admission to a heart attack centre is a predictor of survival from out-of-hospital cardiac arrest. Resuscitation. 2014;85(7):905–9.
[9] Elmer J, Torres C, Aufderheide TP, et al. Association of early withdrawal of life-sustaining therapy for perceived neurological prognosis with mortality after cardiac arrest. Resuscitation. 2016;102:127–35.
[10] Nolan JP, Sandroni C, Böttiger BW, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med. 2021 Apr;47(4):369–421.
[11] Singh A, Jefferson J. Post-cardiac arrest care. Emerg Med Clin North Am. 2023 Aug;41(3):617–32.
[12] Callaway CW, Donnino MW, Fink EL, et al. Part 8: post-cardiac arrest care: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132:S465.
[13] Merchant RM, Topjian AA, Panchal AR, et al. Part 1: executive summary: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2020;142:S337.
[14] Nolan JP, Neumar RW, Adrie C, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A scientific statement from the international liaison committee on resuscitation; the American Heart Association emergency cardiovascular care committee; the council on cardiovascular surgery and anesthesia; the council on cardiopulmonary, perioperative, and critical care; the council on clinical cardiology; the council on stroke. Resuscitation. 2008;79:350–79.
[15] Stub D, Bernard S, Duffy SJ, Kaye DM. Post cardiac arrest syndrome: a review of therapeutic strategies. Circulation. 2011 Apr 5;123(13):1428–35.
[16] Peberdy MA, Callaway CW, Neumar RW, et al. Part 9: post-cardiac arrest care: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2010;122:S768–86.
[17] Kang Y. Management of post-cardiac arrest syndrome. Acute Crit Care. 2019 Aug;34(3):173–8.
[18] Neumar RW, Nolan JP, Adrie C, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication: a consensus statement from the international liaison committee on resuscitation (American Heart Association, Australian and New Zealand council on resuscitation, European resuscitation council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, resuscitation Council of Asia, and the resuscitation Council of Southern Africa); the American Heart Association emergency cardiovascular care committee; the council on cardiovascular surgery and anesthesia; the council on cardiopulmonary, perioperative, and critical care; the council on clinical cardiology; and the stroke council. Circulation. 2008;118:2452–83.
[19] Kim JH, Oh YM, So BH, et al. Systemic complications of comatose survivors following cardiopulmonary resuscitation. J Korean Soc Emerg Med. 2008;19:88–93.
[20] Karatasakis A, Sarikaya B, Liu L, et al. Prevalence and patterns of resuscitation- associated injury detected by head-to-pelvis computed tomography after successful out-of-hospital cardiac arrest resuscitation. J Am Heart Assoc. 2022;11:e023949.
[21] Trzeciak S, Jones AE, Kilgannon JH, et al. Significance of arterial hypotension after resuscitation from cardiac arrest. Crit Care Med. 2009;37:2895.
[22] Bray JE, Bernard S, Cantwell K, et al. The association between systolic blood pressure on arrival at hospital and outcome in adults surviving from out-of-hospital cardiac arrests of presumed cardiac aetiology. Resuscitation. 2014;85:509.
[23] Kilgannon JH, Roberts BW, Reihl LR, et al. Early arterial hypotension is common in the post-cardiac arrest syndrome and associated with increased in-hospital mortality. Resuscitation. 2008;79:410.
[24] Gaieski DF, Band RA, Abella BS, et al. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. Resuscitation. 2009;80:418.
[25] Gottlieb M, Alerhand S. Managing cardiac arrest using ultrasound. Ann Emerg Med. 2022:1120–9. S0196-S0644(22).
[26] Seif D, Perera P, Mailhot T, et al. Bedside ultrasound in resuscitation and the rapid ultrasound in shock protocol. Crit Care Res Prac. 2012;2012:503254.
[27] Perera P, Mailhot T, Riley D, et al. The RUSH exam: rapid ultrasound in SHock in the evaluation of the critically lll. Emerg Med Clin North Am. 2010;28(1):29–56.
[28] Gottlieb M, O'Brien JR, Ferrigno N, Sundaram T. Point-of-care ultrasound for airway management in the emergency and critical care setting. Clin Exp Emerg Med. 2024 Mar;11(1):22–32.
[29] Keikha M, Salehi-Marzijarani M, Soldoozi Nejat R, et al. Diagnostic accuracy of rapid ultrasound in shock (RUSH) exam; a systematic review and meta-analysis. Bull Emerg Trauma. 2018;6(4):271–8.
[30] Stickles SP, Carpenter CR, Gekle R, et al. The diagnostic accuracy of a point-ofcare ultrasound protocol for shock etiology: a systematic review and meta-analysis. CJEM. 2019;21(3):406–17.
[31] Yanagawa Y, Ohsaka H, Nagasawa H, et al. An analysis using modified rapid ultrasound for shock and hypotension for patients with endogenous cardiac arrest. J Emerg Trauma Shock. 2019;12(2):135–40.
[32] Cha KC, Kim HI, Kim OH, et al. Echocardiographic patterns of postresuscitation myocardial dysfunction. Resuscitation. 2018;124:90–5.
[33] Bellut H, Guillemet L, Bougouin W, et al. Early recurrent arrhythmias after out-of-hospital cardiac arrest associated with obstructive coronary artery disease: analysis of the PROCAT registry. Resuscitation. 2019;141:81–7.
[34] Lee BK, Youn CS, Kim YJ, et al. Effect of prophylactic amiodarone infusion on the recurrence of ventricular arrhythmias in out-of-hospital cardiac arrest survivors: a propensity-matched analysis. J Clin Med. 2019;8(2):244.
[35] Freire-Tellado M, Navarro-Paton R, Mateos-Lorenzo J, et al. Prophylactic amiodarone administration on ROSC after a successful first defibrillation. Resuscitation. 2022;173:59–60.
[36] Kudenchuk PJ, Newell C, White L, et al. Prophylactic lidocaine for post resuscitation care of patients with out-of-hospital ventricular fibrillation cardiac arrest. Resuscitation. 2013;84(11):1512–8.
[37] Wang L, Li X, Yang Z, et al. Semi-recumbent position versus supine position for the prevention of ventilator-associated pneumonia in adults requiring mechanical ventilation. Cochrane Database Syst Rev. 2016;2016(1):CD009946.
[38] Schulz-Stubner S, Thiex R. Raising the head-of-bed by 30 degrees reduces ICP and improves CPP without compromising cardiac output in euvolemic patients with traumatic brain injury and subarachnoid haemorrhage: a practice audit. Eur J Anaesthesiol. 2006;23(2):177–80.
[39] Pozuelo-Carrascosa DP, Cobo-Cuenca AI, Carmona-Torres JM, et al. Body position for preventing ventilator-associated pneumonia for critically ill patients: a systematic review and network meta-analysis. J Intensive Care. 2022;10(1):9.
[40] Zhuo X, Pan L, Zeng X. The effects of the 45 semi-recumbent position on the clinical outcomes of mechanically ventilated patients: a systematic review and meta-analysis study. Ann Palliat Med. 2021;10(10):10643–51.
[41] Agency for Healthcare Research and Quality. https://www.ahrq.gov/hai/tools/mvp/modules/technical/head-bed-elevation-litreview.html.
[42] American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med. 2005;171(4):388–416.
[43] Cook AM, Morgan Jones G, Hawryluk GWJ, et al. Guidelines for the acute treatment of cerebral edema in neurocritical care patients. Neurocrit Care. 2020;32(3):647–66.
[44] Paul M, Bougouin W, Dumas F, et al. Comparison of two sedation regimens during targeted temperature management after cardiac arrest [published correction appears in Resuscitation. 2018 Oct;131:135]. Resuscitation. 2018;128:204–10.
[45] Ornowska M, Wormsbecker A, Andolfatto G, et al. The use of ketamine as a neuroprotective agent following cardiac arrest: a scoping review of current literature. CNS Neurosci Ther. 2023;29(1):104–10.
[46] Longstreth Jr WT, Diehr P, Cobb LA, et al. Neurologic outcome and blood glucose levels during out-of-hospital cardiopulmonary resuscitation. Neurology. 1986;36:1186.
[47] Skrifvars MB, Pettilä V, Rosenberg PH, Castrén M. A multiple logistic regression analysis of in-hospital factors related to survival at six months in patients resuscitated from out-of-hospital ventricular fibrillation. Resuscitation. 2003;59:319.
[48] Oksanen T, Skrifvars MB, Varpula T, et al. Strict versus moderate glucose control after resuscitation from ventricular fibrillation. Intensive Care Med. 2007;33:2093.
[49] NICE-SUGAR Study Investigators, Finfer S, Chittock DR, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360:1283.
[50] Berg KM, Soar J, Andersen LW, et al, Adult Advanced Life Support Collaborators. Adult advanced life support: 2020 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Circulation. 2020.;142(16_suppl_1) S92–139.
[51] Nielsen N, Wetterslev J, Cronberg T, TTM Trial Investigators, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013;369(23):2197–206.
[52] Elmer J, Rittenberger JC, Faro J, et al. Clinically distinct electroencephalographic phenotypes of early myoclonus after cardiac arrest. Ann Neurol. 2016;80:175.
[53] Seder DB, Sunde K, Rubertsson S, et al. Neurologic outcomes and postresuscitation care of patients with myoclonus following cardiac arrest. Crit Care Med. 2015;43:965.
[54] Dhakar MB, Sivaraju A, Maciel CB, et al. Electro-clinical characteristics and prognostic significance of post anoxic myoclonus. Resuscitation. 2018;131:114.
[55] Beuchat I, Sivaraju A, Amorim E, et al. MRI-EEG correlation for outcome prediction in postanoxic myoclonus: a multicenter study. Neurology. 2020;95:e335.
[56] Kongpolprom N, Cholkraisuwat J. Neurological prognostications for the therapeutic hypothermia among comatose survivors of cardiac arrest. Indian J Crit Care Med. 2018;22:509.
[57] Ruijter BJ, Keijzer HM, Tjepkema-Cloostermans MC, TELSTAR Investigators, et al. Treating rhythmic and periodic EEG patterns in comatose survivors of cardiac arrest. N Engl J Med. 2022 Feb 24;386(8):724–34.
[58] Sekhon MS, Gooderham P, Menon DK, et al. The burden of brain hypoxia and optimal mean arterial pressure in patients with hypoxic ischemic brain injury after cardiac arrest. Crit Care Med. 2019;47:960–9.
[59] Sekhon MS, Ainslie PN, Griesdale DE. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model. Crit Care. 2017;21:90.
[60] Gueugniaud PY, Garcia-Darennes F, Gaussorgues P, et al. Prognostic significance of early intracranial and cerebral perfusion pressures in post-cardiac arrest anoxic coma. Intensive Care Med. 1991;17:392–8.
[61] Naito H, Isotani E, Callaway CW, et al. Intracranial pressure increases during rewarming period after mild therapeutic hypothermia in postcardiac arrest patients. Ther Hypothermia Temp Manag. 2016;6:189–93.

[62] Aletreby W, Alharthy A, Brindley PG, et al. Optic nerve sheath diameter ultrasound for raised intracranial pressure: a literature review and meta-analysis of its diagnostic accuracy. J Ultrasound Med. 2022 Mar;41(3):585–95.
[63] Berhanu D, Ferreira JC, Abegão Pinto L, et al. The role of optic nerve sheath ultrasonography in increased intracranial pressure: a systematic review and meta analysis. J Neurol Sci. 2023 Nov 15;454:120853.
[64] Sakabe T, Tateishi A, Miyauchi Y, et al. Intracranial pressure following cardiopulmonary resuscitation. Intensive Care Med. 1987;13:256–9.
[65] Petek BJ, Erley CL, Kudenchuk PJ, et al. Diagnostic yield of non-invasive imaging in patients following non-traumatic out-of-hospital sudden cardiac arrest: a systematic review. Resuscitation. 2019;135:183–90.
[66] Kashiwagi Y, Sasakawa T, Tampo A, et al. Computed tomography findings of complications resulting from cardiopulmonary resuscitation. Resuscitation. 2015;88:86–91.
[67] Chen N, Callaway CW, Guyette FX, et al. Arrest etiology among patients resuscitated from cardiac arrest. Resuscitation. 2018;130:33.
[68] Metter RB, Rittenberger JC, Guyette FX, Callaway CW. Association between a quantitative CT scan measure of brain edema and outcome after cardiac arrest. Resuscitation. 2011;82:1180.
[69] Lee KY, So WZ, Ho JSY, et al. Prevalence of intracranial hemorrhage amongst patients presenting with out-of-hospital cardiac arrest: a systematic review and meta-analysis. Resuscitation. 2022;176:136.
[70] Branch KRH, Strote J, Gunn M, et al. Early head-to-pelvis computed tomography in out-of-hospital circulatory arrest without obvious etiology. Acad Emerg Med. 2021;28:394.
[71] Viniol S, Thomas RP, König AM, et al. Early whole-body CT for treatment guidance in patients with return of spontaneous circulation after cardiac arrest. Emerg Radiol. 2020;27:23.
[72] Jang SJ, Cha YK, Kim JS, et al. Computed tomographic findings of chest injuries following cardiopulmonary resuscitation: more complications for prolonged chest compressions? Medicine (Baltimore). 2020;99:e21685.
[73] Tam J, Soufleris C, Ratay C, et al. Diagnostic yield of computed tomography after nontraumatic out-of-hospital cardiac arrest. Resuscitation. 2023;189:109898.
[74] Branch KRH, Gatewood MO, Kudenchuk PJ, et al. Diagnostic yield, safety, and outcomes of head-to-pelvis sudden death CT imaging in post arrest care: the CT FIRST cohort study. Resuscitation. 2023 Jul;188:109785.
[75] Sundgreen C, Larsen FS, Herzog TM, et al. Autoregulation of cerebral blood flow in patients resuscitated from cardiac arrest. Stroke. 2001;32:128–32.
[76] Depreitere B, Citerio G, Smith M, et al. Cerebrovascular autoregulation monitoring in the management of adult severe traumatic brain injury: a Delphi consensus of clinicians. Neurocrit Care. 2021;34:731–73.
[77] Kilgannon JH, Roberts BW, Jones AE, et al. Arterial blood pressure and neurologic outcome after resuscitation from cardiac arrest. Crit Care Med. 2014;42:2083–91.
[78] Ameloot K, Meex I, Genbrugge C, et al. Hemodynamic targets during therapeutic hypothermia after cardiac arrest: a prospective observational study. Resuscitation. 2015;91:56–62.
[79] Laurikkala J, Wilkman E, Pettilä V, FINNRESUSCI Study Group, et al. Mean arterial pressure and vasopressor load after out-ofhospital cardiac arrest: associations with one-year neurologic outcome. Resuscitation. 2016;105:116–22.
[80] Russo JJ, Di Santo P, Simard T, CAPITAL Study Group, et al. Optimal mean arterial pressure in comatose survivors of out-of-hospital cardiac arrest: an analysis of area below blood pressure thresholds. Resuscitation. 2018;128:175–80.
[81] Roberts BW, Kilgannon JH, Hunter BR, et al. Association between elevated mean arterial blood pressure and neurologic outcome after resuscitation from cardiac arrest: results from a multicenter prospective cohort study. Crit Care Med. 2019;47:93–100.
[82] Jakkula P, Pettilä V, Skrifvars MB, COMACARE Study Group, et al. Targeting low-normal or high-normal mean arterial pressure after cardiac arrest and resuscitation: a randomised pilot trial. Intensive Care Med. 2018;44:2091–101.
[83] Ameloot K, Jakkula P, Hästbacka J, et al. Optimum blood pressure in patients with shock after acute myocardial infarction and cardiac arrest. J Am Coll Cardiol. 2020;76:812–24.
[84] Ameloot K, De Deyne C, Eertmans W, et al. Early goal-directed haemodynamic optimization of cerebral oxygenation in comatose survivors after cardiac arrest: the Neuroprotect post–cardiac arrest trial. Eur Heart J. 2019;40:1804–14.
[85] Kjaergaard J, Møller JE, Schmidt H, et al. Blood-pressure targets in comatose survivors of cardiac arrest. N Engl J Med. 2022;387:1456–66.
[86] Semler MW, Kellum JA. Balanced crystalloid solutions. Am J Respir Crit Care Med. 2019;199(8):952–60.
[87] Laurent I, Monchi M, Chiche JD, et al. Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest. J Am Coll Cardiol. 2002;40(12):2110–6.
[88] Ruiz-Bailén M, Aguayo de Hoyos E, Ruiz-Navarro S, et al. Reversible myocardial dysfunction after cardiopulmonary resuscitation. Resuscitation. 2005;66:175.
[89] Huynh N, Kloke J, Gu C, et al. The effect of hypothermia "dose" on vasopressor requirements and outcome after cardiac arrest. Resuscitation. 2013;84:189.
[90] Bougouin W, Slimani K, Renaudier M, et al. Epinephrine versus norepinephrine in cardiac arrest patients with post-resuscitation shock. Intensive Care Med. 2022;48:300.
[91] Normand S, Matthews C, Brown CS, et al. Risk of arrhythmia in post-resuscitative shock after out-of-hospital cardiac arrest with epinephrine versus norepinephrine. Am J Emerg Med. 2024 Mar;77:72–6.
[92] Levy B, Clere-Jehl R, Legras A, et al. Epinephrine versus norepinephrine for cardiogenic shock after acute myocardial infarction. J Am Coll Cardiol. 2018;72(2):173–82.
[93] Shih JA, Robertson HK, Issa MS, et al. Acute respiratory distress syndrome after in-hospital cardiac arrest. Resuscitation. 2022;177:78–84.
[94] Johnson NJ, Caldwell E, Carlbom DJ, et al. The acute respiratory distress syndrome after out-of-hospital cardiac arrest: incidence, risk factors, and outcomes. Resuscitation. 2019;135:37–44.
[95] Wang HE, Prince DK, Drennan IR, et al. Resuscitation outcomes consortium (ROC) investigators. Post-resuscitation arterial oxygen and carbon dioxide and outcomes after out-of-hospital cardiac arrest. Resuscitation. 2017;120:113–8.
[96] Elmer J, Scutella M, Pullalarevu R, et al. The association between hyperoxia and patient outcomes after cardiac arrest: analysis of a high-resolution database. Intensive Care Med. 2015;41:49.
[97] Wang CH, Chang WT, Huang CH, et al. The effect of hyperoxia on survival following adult cardiac arrest: a systematic review and meta-analysis of observational studies. Resuscitation. 2014;85:1142.
[98] Bernard SA, Bray JE, Smith K, EXACT Investigators, et al. Effect of lower vs higher oxygen saturation targets on survival to hospital discharge among patients resuscitated after out-of-hospital cardiac arrest: the EXACT randomized clinical trial. JAMA. 2022 Nov 8;328(18):1818–26.
[99] Schmidt H, Kjaergaard J, Hassager C, et al. Oxygen targets in comatose survivors of cardiac arrest. N Engl J Med. 2022;387:1467–76.
[100] Bouzat P, Suys T, Sala N, Oddo M. Effect of moderate hyperventilation and induced hypertension on cerebral tissue oxygenation after cardiac arrest and therapeutic hypothermia. Resuscitation. 2013;84:1540–5.
[101] Buunk G, van der Hoeven JG, Meinders AE. Cerebrovascular reactivity in comatose patients resuscitated from a cardiac arrest. Stroke. 1997;28:1569–73.
[102] Vaahersalo J, Bendel S, Reinikainen M, FINNRESUSCI Study Group, et al. Arterial blood gas tensions after resuscitation from out-of-hospital cardiac arrest: associations with long-term neurologic outcome. Crit Care Med. 2014;42:1463–70.
[103] Ebner F, Harmon MBA, Aneman A, et al. Carbon dioxide dynamics in relation to neurological outcome in resuscitated out-of-hospital cardiac arrest patients: an exploratory target temperature management trial substudy. Crit Care. 2018;22:196.
[104] Roberts BW, Kilgannon JH, Chansky ME, et al. Association between postresuscitation partial pressure of arterial carbon dioxide and neurological outcome in patients with postcardiac arrest syndrome. Circulation. 2013;127:2107–13.
[105] Eastwood G, Nichol AD, Hodgson C, et al. Mild hypercapnia or normocapnia after out-of-hospital cardiac arrest. N Engl J Med. 2023;389:45.
[106] Kakavas S, Mongardon N, Cariou A, et al. Early-onset pneumonia after out-of-hospital cardiac arrest. J Infect. 2015;70(6):553–62.
[107] Carr GE, Yuen TC, McConville JF, American Heart Association's Get With the Guidelines-Resuscitation (National Registry of CPR) Investigators, et al. Early cardiac arrest in patients hospitalized with pneumonia: a report from the American Heart Association's Get With The Guidelines-Resuscitation Program. Chest. 2012;141(6):1528–36.
[108] Couper K, Laloo R, Field R, et al. Prophylactic antibiotic use following cardiac arrest: a systematic review and meta-analysis. Resuscitation. 2019 Aug;141:166–73.
[109] François B, Cariou A, Clere-Jehl R, CRICS-TRIGGERSEP Network and the ANTHARTIC Study Group, et al. Prevention of early ventilator-associated pneumonia after cardiac arrest. N Engl J Med. 2019 Nov 7;381(19):1831–42.
[110] Ito T, Saitoh D, Takasu A, et al. Serum cortisol as a predictive marker of the outcome in patients resuscitated after cardiopulmonary arrest. Resuscitation. 2004;62:55–60.
[111] Kim JJ, Lim YS, Shin JH, et al. Relative adrenal insufficiency after cardiac arrest: impact on postresuscitation disease outcome. Am J Emerg Med. 2006;24:684–8.
[112] Grafton ST, Longstreth Jr WT. Steroids after cardiac arrest: a retrospective study with concurrent, nonrandomized controls. Neurology. 1988;38:1315–6.
[113] Jastremski M, Sutton-Tyrrell K, Vaagenes P, et al. Glucocorticoid treatment does not improve neurological recovery following cardiac arrest: brain resuscitation clinical trial I study group. JAMA. 1989;262:3427–30.
[114] Niimura T, Zamami Y, Koyama T, et al. Hydrocortisone administration was associated with improved survival in Japanese patients with cardiac arrest. Sci Rep. 2017;7:17919.
[115] Tsai MS, Chuang PY, Huang CH, et al. Postarrest steroid use may improve outcomes of cardiac arrest survivors. Crit Care Med. 2019;47:167–75.
[116] Tsai MS, Huang CH, Chang WT, et al. The effect of hydrocortisone on the outcome of out-of-hospital cardiac arrest patients: a pilot study. Am J Emerg Med. 2007;25:318–25.
[117] Mentzelopoulos SD, Malachias S, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. JAMA. 2013;310:270–9.
[118] Mentzelopoulos SD, Zakynthinos SG, Tzoufi M, et al. Vasopressin, epinephrine, and corticosteroids for in-hospital cardiac arrest. Arch Intern Med. 2009;169:15–24.
[119] Mentzelopoulos SD, Koliantzaki I, Karvouniaris M, et al. Exposure to stress-dose steroids and lethal septic shock after in-hospital cardiac arrest: individual patient data reanalysis of two prior randomized clinical trials that evaluated the vasopressin-steroids-epinephrine combination versus epinephrine alone. Cardiovasc Drugs Ther. 2018;32:339–51.
[120] Donnino MW, Andersen LW, Berg KM, et al, Collaborating authors from the Beth Israel Deaconess Medical Center's Center for Resuscitation Science Research Group. Corticosteroid therapy in refractory shock following cardiac arrest: a randomized, double-blind, placebo-controlled, trial. Crit Care. 2016;20:82.
[121] Granfeldt A, Sindberg B, Isbye D, et al. Effect of vasopressin and methylprednisolone vs. placebo on long-term outcomes in patients with in-hospital cardiac arrest a randomized clinical trial. Resuscitation. 2022;175:67–71.
[122] Zhou FW, Liu C, Li DZ, Zhang Y, Zhou FC. Efficacy and safety of corticosteroid therapy in patients with cardiac arrest: a meta-analysis of randomized controlled trials. Am J Emerg Med. 2024 Jan;75:111–8.

[123] Dumas F, Cariou A, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. Circ Cardiovasc Interv. 2010;3(3):200–7.
[124] Mooney MR, Unger BT, Boland LL, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest: evaluation of a regional system to increase access to cooling. Circulation. 2011;124:206–14.
[125] Cronier P, Vignon P, Bouferrache K, et al. Impact of routine percutaneous coronary intervention after out-of-hospital cardiac arrest due to ventricular fibrillation. Crit Care. 2011;15:R122.
[126] Aurore A, Jabre P, Liot P, et al. Predictive factors for positive coronary angiography in out-of-hospital cardiac arrest patients. Eur J Emerg Med. 2011;18:73–6.
[127] Yannopoulos D, Bartos JA, Aufderheide TP, American Heart Association Emergency Cardiovascular Care Committee, et al. The evolving role of the cardiac catheterization laboratory in the management of patients with out-of-hospital cardiac arrest: a scientific statement from the American Heart Association. Circulation. 2019;139(12):e530–52.
[128] McFadden P, Reynolds JC, Madder RD, Brown M. Diagnostic test accuracy of the initial electrocardiogram after resuscitation from cardiac arrest to indicate invasive coronary angiographic findings and attempted revascularization: a systematic review and meta-analysis. Resuscitation. 2021;160:20–36.
[129] Baldi E, Schnaubelt S, Caputo ML, et al. Association of timing of electrocardiogram acquisition after return of spontaneous circulation with coronary angiography findings in patients with out-of-hospital cardiac arrest. JAMA Netw Open. 2021;4(1):e2032875.
[130] Millin MG, Comer AC, Nable JV, et al. Patients without ST elevation after return of spontaneous circulation may benefit from emergent percutaneous intervention: a systematic review and meta-analysis. Resuscitation. 2016;108:54.
[131] Lemkes JS, Janssens GN, van der Hoeven NW, et al. Coronary angiography after cardiac arrest without ST-segment elevation. N Engl J Med. 2019;380(15):1397–407.
[132] Desch S, Freund A, Akin I, TOMAHAWK Investigators, et al. Angiography after out-of-hospital cardiac arrest without ST-segment elevation. N Engl J Med. 2021 Dec 30;385(27):2544–53.
[133] Elfwén L, Lagedal R, Nordberg P, et al. Direct or subacute coronary angiography in out-of-hospital cardiac arrest (DISCO)-an initial pilot-study of a randomized clinical trial. Resuscitation. 2019;139:253–61.
[134] Kern KB, Radsel P, Jentzer JC, et al. Randomized pilot clinical trial of early coronary angiography versus no early coronary angiography after cardiac arrest without ST-segment elevation: the PEARL study [published correction appears in circulation. 2020 Nov 24;142(21):e374]. Circulation. 2020;142(21):2002–12.
[135] Hauw-Berlemont C, Lamhaut L, Diehl JL, et al. EMERGE investigators. Emergency vs delayed coronary angiogram in survivors of out-of-hospital cardiac arrest: results of the randomized, multicentric EMERGE trial. JAMA Cardiol. 2022;7:700–7.
[136] Rab T, Kern KB, Tamis-Holland JE, et al. Cardiac arrest: a treatment algorithm for emergent invasive cardiac procedures in the resuscitated comatose patient. J Am Coll Cardiol. 2015;66(1):62–73.
[137] Spaulding CM, Joly LM, Rosenberg A, et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. N Engl J Med. 1997;336:1629.
[138] Laver S, Farrow C, Turner D, Nolan J. Mode of death after admission to an intensive care unit following cardiac arrest. Intensive Care Med. 2004;30:2126.
[139] Hovdenes J, Laake JH, Aaberge L, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest: experiences with patients treated with percutaneous coronary intervention and cardiogenic shock. Acta Anaesthesiol Scand. 2007;51:137.
[140] Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med. 2002;346(8):549–56.
[141] Eastwood GM, Schneider AG, Suzuki S, et al. Targeted therapeutic mild hypercapnia after cardiac arrest: a phase II multi-Centre randomised controlled trial (the CCC trial). Resuscitation. 2016 Jul;104:83–90.
[142] Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med. 2002 Feb 21;346(8):557–63.
[143] Lascarrou JB, Merdji H, Le Gouge A, CRICS-TRIGGERSEP Group, et al. Targeted temperature management for cardiac arrest with nonshockable rhythm. N Engl J Med. 2019 Dec 12;381(24):2327–37.
[144] Dankiewicz J, Cronberg T, Lilja G, TTM2 Trial Investigators, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. N Engl J Med. 2021;384(24):2283–94.
[145] Granfeldt A, Holmberg MJ, Nolan JP, International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support Task Force, et al. Targeted temperature management in adult cardiac arrest: systematic review and meta-analysis. Resuscitation. 2021 Oct;167:160–72.
[146] Reynolds JC, Callaway CW, El Khoudary SR, et al. Coronary angiography predicts improved outcome following cardiac arrest: propensity-adjusted analysis. J Intensive Care Med. 2009;24:179.
[147] Nielsen N, Hovdenes J, Nilsson F, et al. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. Acta Anaesthesiol Scand. 2009;53:926.
[148] Skulec R, Kovarnik T, Dostalova G, et al. Induction of mild hypothermia in cardiac arrest survivors presenting with cardiogenic shock syndrome. Acta Anaesthesiol Scand. 2008;52:188.
[149] Rittenberger JC, Kelly E, Jang D, et al. Successful outcome utilizing hypothermia after cardiac arrest in pregnancy: a case report. Crit Care Med. 2008;36:1354.
[150] Chauhan A, Musunuru H, Donnino M, et al. The use of therapeutic hypothermia after cardiac arrest in a pregnant patient. Ann Emerg Med. 2012;60:786.
[151] Maclaren R, Torian S, Kiser T, et al. Therapeutic hypothermia following cardiopulmonary arrest: a systematic review and meta-analysis with trial sequential analysis. JCCM. 2023;9(2):64–7.
[152] Michelson AD, MacGregor H, Barnard MR, et al. Reversible inhibition of human platelet activation by hypothermia in vivo and in vitro. Thromb Haemost. 1994;71:633.
[153] Reed 2nd RL, Bracey Jr AW, Hudson JD, et al. Hypothermia and blood coagulation: dissociation between enzyme activity and clotting factor levels. Circ Shock. 1990;32:141.
[154] Valeri CR, Feingold H, Cassidy G, et al. Hypothermia-induced reversible platelet dysfunction. Ann Surg. 1987;205:175.
[155] Jeppesen AN, Hvas AM, Duez CHV, et al. Prolonged targeted temperature management compromises thrombin generation: a randomised clinical trial. Resuscitation. 2017;118:126.
[156] Jarrah S, Dziodzio J, Lord C, et al. Surface cooling after cardiac arrest: effectiveness, skin safety, and adverse events in routine clinical practice. Neurocrit Care. 2011;14:382.
[157] Cueni-Villoz N, Devigili A, Delodder F, et al. Increased blood glucose variability during therapeutic hypothermia and outcome after cardiac arrest. Crit Care Med. 2011;39:2225.
[158] Polderman KH, Peerdeman SM, Girbes AR. Hypophosphatemia and hypomagnesemia induced by cooling in patients with severe head injury. J Neurosurg. 2001;94:697.
[159] Polderman KH, Herold I. Therapeutic hypothermia and controlled normothermia in the intensive care unit: practical considerations, side effects, and cooling methods. Crit Care Med. 2009;37:1101.
[160] Robinson J, Charlton J, Seal R, et al. Oesophageal, rectal, axillary, tympanic and pulmonary artery temperatures during cardiac surgery. Can J Anaesth. 1998;45:317.
[161] Erickson RS, Kirklin SK. Comparison of ear-based, bladder, oral, and axillary methods for core temperature measurement. Crit Care Med. 1993;21:1528.
[162] Lopez J, Cohn B. Does intravascular temperature management improve outcomes compared with surface cooling in comatose adults after cardiac arrest? Ann Emerg Med. 2021;77:589.
[163] Keum KT, Kim YH, Lee JH, et al. Comparison of hydrogel pad and water-circulating blanket cooling methods for targeted temperature management: a propensity score-matched analysis from a prospective multicentre registry. Resuscitation. 2021;169:78.
[164] Ramadanov N, Arrich J, Klein R, et al. Intravascular versus surface cooling in patients resuscitated from cardiac arrest: a systematic review and network meta-analysis with focus on temperature feedback. Crit Care Med. 2022;50:999.
[165] Bernard SA, Smith K, Cameron P, et al. Induction of therapeutic hypothermia by paramedics after resuscitation from out-of-hospital ventricular fibrillation cardiac arrest: a randomized controlled trial. Circulation. 2010;122:737.
[166] Kim F, Olsufka M, Longstreth Jr WT, et al. Pilot randomized clinical trial of prehospital induction of mild hypothermia in out-of-hospital cardiac arrest patients with a rapid infusion of 4 degrees C normal saline. Circulation. 2007;115:3064.
[167] Kliegel A, Losert H, Sterz F, et al. Cold simple intravenous infusions preceding special endovascular cooling for faster induction of mild hypothermia after cardiac arrest—a feasibility study. Resuscitation. 2005;64:347.
[168] Al-Senani FM, Graffagnino C, Grotta JC, et al. A prospective, multicenter pilot study to evaluate the feasibility and safety of using the CoolGard system and icy catheter following cardiac arrest. Resuscitation. 2004;62:143.
[169] Kim F, Nichol G, Maynard C, et al. Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest: a randomized clinical trial. JAMA. 2014;311:45.
[170] Hassager C, Schmidt H, Møller JE, et al. Duration of device-based fever prevention after cardiac arrest. N Engl J Med. 2023;388:888.
[171] Kirkegaard H, Søreide E, de Haas I, et al. Targeted temperature management for 48 vs 24 hours and neurologic outcome after out-of-hospital cardiac arrest: a randomized clinical trial. JAMA. 2017;318(4):341–50.