Available online **www.ijpras.com**

International Journal of Pharmaceutical Research & Allied Sciences, 2023, 12(3):78-87
https://doi.org/10.51847/g6LylgeiXe

Review Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

Management of Post-Resuscitative Era in Patients with Cardiac Arrest: Post-Cardiac Arrest Syndrome

Sedat Ozbay[1], Canan Akman[2], Neslihan Ergun Suzer[3], Ilknur Simsik[4], Mustafa Ayan[1], Orhan Ozsoy[1], Ozgur Karcioglu[5*]

[1]Department of Emergency Medicine, Sivas Numune Education and Research Hospital, Sivas, Turkey.
[2]Department of Emergency Medicine, Canakkale Onsekiz Mart University, Canakkale, Turkey.
[3]Department of Emergency Medicine, Darica Farabi Education and Research Hospital, Kocaeli, Turkey.
[4]Department of Emergency Medicine, Niğde Omer Halisdemir Education and Research Hospital, University of Health Sciences, Nigde, Turkey.
[5]Department of Emergency Medicine, Taksim Education and Research Hospital, University of Health Sciences, Istanbul, Turkey.

***Email:** okarcioglu@gmail.com*

ABSTRACT

Cardiac arrest (CA) resulting from sudden cardiac death and acute coronary syndromes affects many people every day all over the world. Post-cardiac arrest syndrome (PCAS) encompasses post-CA brain injury, myocardial dysfunction, reperfusion injury, and the continuation of the causative event, as a complex and critical issue that requires multidisciplinary intervention. Successful intervention in these cases can only be achieved with advanced cardiac life support (ACLS) management to provide the return of spontaneous circulation (ROSC). Favorable neurological outcome targets have been established in recent decades and some progress has been made despite many uncertainties still exist. Optimization of oxygenation and hemodynamics, early coronary interventions, ACLS, and early and intensive management of targeted temperature management (TTM) has been reported to positively affect survival with fewer neurological sequelae in patients with ROSC. Institution of extracorporeal cardiopulmonary resuscitation (eCPR) initiated within 50 min of collapse, and combination of TTM with eCPR were advocated as predictors of favorable prognosis. In this study, efforts to provide the best outcomes after CA and related advances are described.

Key words: *Return of spontaneous circulation, Sudden cardiac death, Cardiac arrest, Post-cardiac arrest syndrome, Targeted temperature management*

INTRODUCTION

Sudden cardiac death affects many people every day all over the world. However, the optimal hospital care, when and how it is performed in cases with "Return of Spontaneous Circulation" (ROSC) as a result of cardiopulmonary resuscitation (CPR) is not fully elucidated.

The care of the cases in this period prompts simultaneous support of the organ systems. The term "Post-cardiac arrest syndrome" (PCAS), encompasses the continuation of the event that caused cardiac arrest (CA), myocardial dysfunction, systemic reperfusion injury, and brain damage with the provision of ROSC, and the end of this picture with high mortality is determined by the procedures performed in the Post Resuscitative Period (PRD) [1]. PRD management aims to keep neurological damage to a minimum and to ensure that victims of CA are discharged from the hospital at a normal or near-normal level of independent activities of daily life. The main goals of PRD management are optimization of hemodynamics and oxygenation, early percutaneous coronary

intervention (PCI) to coronary arteries in selected cases, therapeutic hypothermia, and recognition and treatment of seizures and infections after the initial stabilization of patients with ROSC.

Where to care for the patients with OHCA?

At present there is considerable variability in in-hospital mortality following cardiac arrest among different hospitals in the US [2]. Therefore, ERC recommends non-traumatic patients resuscitated successfully after OHCA be admitted into CA centers when compared to non-cardiac arrest centers with very low certainty of evidence [3].

Stabilization of airway and breathing

Endotracheal intubation and mechanical ventilation are standards of care in CA cases that have not fully alert or gained a sufficient level of consciousness for airway patency and adequate oxygenation after ROSC is provided. On the other hand, respiratory support may not be necessary for patients who recover rapidly, can maintain airway patency safely, and have no respiratory distress for oxygenation. It should be kept in mind that not only hypoxemia but also hyperoxemia may be associated with poor outcomes in PRD, that hypocarbia will increase cerebral vasoconstriction and ischemia, and hypercarbia will increase vasogenic edema by vasodilation and consequently adversely affect the neurological outcome [4-6]. It has been reported that Acute Respiratory Distress Syndrome (ARDS) develops in around 50% of survivors of CA (at least 48 hrs) and this situation is related to poor outcome [7]. In light of all this information, SaO2 levels should be kept in the range of 94-98% and end-tidal carbon dioxide levels should be kept in the range of 35-45 mmHg in patients with ROSC. In addition, considering the risk of developing ARDS, low tidal volume ventilation and prone positioning should be considered if there is no other specific indication.

Management of hemodynamics and cardiac functions

The blood pressures tend to be low in those with ROSC after CA. Hemodynamic instability following ROSC stems from myocardial dysfunction, volume depletion, and disordered vasoregulation, which can be apparent with dysrhythmias, hypotension, and low cardiac index [8]. Therefore, an optimal BP is a must for organ perfusion, and the objective should be to ensure adequate perfusion of vital organs, especially the heart and brain in patients with ROSC. Studies have reported that hypotension is associated with increased mortality rates, whereas those with better neurological outcomes have higher blood pressure [9]. Therefore, in these cases, fluid replacement should be performed to ensure hemodynamic stability, and positive inotropic, positive chronotropic, and vasopressor agents should be used when necessary. However, it should be kept in mind that the agent to be used may adversely affect the balance between oxygen delivery to the heart and its consumption.

Another prognostic factor can be substantial changes in hemoglobin levels. These alterations are shown to reflect the degree of vascular permeability and are thus associated with neurological function after CA. Some authors pointed out that for every g/dl increase in hemoglobin from presentation to 12 h, the odds of poor neurological status increased by 26% (crude OR 1.26, 1.07-1.49, $p = 0.006$) [10].

In addition to all these, 5H – 5T approach encompasses factors that may have caused arrest in CA victims with ROSC: hypoxia, hypovolemia, hydrogen (acidosis), hyper/hypokalemia, and hypothermia (5H), cardiac thrombosis (ACS), pulmonary thromboembolism, toxins (poisoning), tamponade, tension pneumothorax (5T) that should be sought for and therapeutic interventions should be initiated accordingly for them.

Coronary artery disease is known to be the most common cause in cases with out-of-hospital CA (OHCA) without any obvious disease. For this reason, ECG should be taken as soon as possible in those with ROSC. Cardiac enzymes including troponins do not appear to be of much help in this situation, as CPR and other procedures may interfere with the levels of these enzymes. The combination of neuron-specific enolase (NSE) with cardiac troponin-T (cTnT), measured at the 48th hour, elevated the AUC to 0.98 (95% CI 0.95-1, LR test p-value 0.07) [11]. Copeptin is also among the markers thought to indicate severity of the PCAS. In a multicenter randomized trial, copeptin measured at 24 h was demonstrated to predict short-term survival accurately, HR 1.17, $p = 0.001$; cardiovascular cause of death, OR 1.03, $p = 0.001$; and cardiovascular deterioration composite, OR of 1.05, $p < 0.001$ [12].

Immediate defibrillation cannot be overemphasized in patients with OHCA, as the main dysrhythmia is VF-triggering CA. In a retrospective study, Felder *et al*. reported that routine application of defibrillation pads to patients with prehospital ST-elevation myocardial infarction (STEMI) diminishes the time to the first defibrillation in OHCA [13].

Angiography and PCI

It has been shown that the absence of ST-segment elevation on ECGs does not completely rule out the presence of a new coronary occlusion in patients with OHCA and ROSC [14]. Previous medical history, warning symptoms, initial cardiac rhythm, ECG following ROSC, and echocardiographic findings are of vital importance. In addition, patients with hemodynamic and/or electrical instability should be treated with a similar approach to patients with STEMI if the probability of acute coronary occlusion is predicted to be high [15]. Intra-aortic balloon pump, left ventricular assist device, or arterio-venous extracorporeal membrane oxygenation (ECMO) need to be evaluated in patients with hemodynamic instability (e.g., those with ventricular tachycardia or ventricular fibrillation episodes despite optimal therapy).

CAG should be planned for patients who do not have an obvious non-cardiac disease that may have caused CA (such as ICH), if a definite cause could not be revealed as a result of these investigations, or even if the patient's ECG does not have ST elevation. Many observational studies are reporting a significant relationship between early PCI and survival and positive neurological outcomes in patients with ST-elevation myocardial infarction (STEMI) on ECGs in patients with OHCA. Therefore, ROSC cases with STEMI findings in the ECGs should be evaluated for emergency cardiac catheterization and PCI should be performed if necessary [16]. Early PCI is demonstrated to be associated with a lower death rate, reinfarction, congestive heart failure, and cardiogenic shock than in those receiving conventional modes of treatment [17, 18].

Recent ESC guidelines state that delayed angiography should be considered in hemodynamically stable patients without ST-segment elevation with ROSC following an OHCA [19]. Likewise, a recent meta-analysis did not advocate the routine performance of emergent (early) CAG, since it was not associated with any improvement in survival and neurological outcomes among patients with OHCA without ST elevations in ECGs [20]. Various factors are expected to affect clinical courses and outcomes from OHCA. Patient-related factors and CPR-related circumstances are among these **(Table 1)** [21].

Table 1. Patient-related and CPR factors affecting outcome from OHCA (Adapted from Kandala 2017).

Patient-related factors	Age
	Gender
	Comorbid diseases • Cardiac functions • Respiratory status • Renal functions • Injuries
	Other/Special situations
Cardiopulmonary resuscitation	Location (private vs. public)
	Performance of bystander CPR
	Witnessed vs. unwitnessed CA
	Type of bystander CPR (compression only vs. standard CPR)
	First recorded rhythm after CA
	Use of automated external defibrillation (AED)
	Time to ROSC

In 2021, most researchers agreed that emergent PCI should be available for those without ST-elevation on the ECG after OHCA, should there be a high probability of an acute coronary event (e.g., haemodynamic and/or electrical instability). Some authors cited that 90-day survival was similar following OHCA due to VF in patients without ST-elevation either with immediate coronary angiography versus delayed angiography [22].

Neurological system and its management

The most common cause of death after CA is neurological damage. Targeted temperature management (TTM) is developed to alleviate the death toll and improve neurological prognosis in those who do not gain ROSC after CA. Hypoxic-ischemic brain injury is the major cause of grave outcomes following CA [23]. In addition,

myoclonic status epilepticus also appears to be a predictor of poor outcomes which can be overlooked by most clinicians [24, 25].

TTM may be used as a brain-protective therapy for patients with ROSC. This procedure is considered to mitigate hypoxic-ischemic brain injury by decreasing the cerebral rate of metabolism, which alleviate reperfusion injury, and inhibits pathways that cause neuronal death [26]. The consensus papers for post-resuscitation care from the ERC and the AHA advocate TTM for comatose adults following ROSC [27].

Institution of extracorporeal cardiopulmonary resuscitation (eCPR) initiated within 50 min of collapse, and combination of TTM (cooling to 33°C expediently) with eCPR were advocated as predictors of favorable prognosis [28, 29]. Likewise, in a swine model, Bergan *et al*. showed that two-hour TTM performed simultaneously with eCPR resulted in a similar success rate of resuscitation, but does not preserve the post-arrest cardiac function, compared to normothermic eCPR [30].

Prediction of neurological outcome

Tools used to evaluate the neurological consequences of hypoxic brain injury include diffusion-weighted magnetic resonance imaging (2 to 5 days after ROSC) pupillary light reflex and corneal reflex (at 72 hours), myoclonus, somatosensory evoked potentials, neuron-specific enolase, and S-100B [31].

Normal S100B and NSE have foreseen favorable prognoses with NPV 76–82%, while normal NSE predicted only one-third of patients with good outcomes among those recorded as "indeterminate outcomes" by guidelines [32]. Normal readings of brain injury markers in blood accompany a favorable neurological course following CA. Briefly, incorporating biomarkers into prognostic estimates may be adjuncts to beware of premature withdrawal of advanced life support measures.

Imaging principles in patients with ROSC after CA

Bedside USG/echocardiography provides evidence of the etiology of CA. Pericardial tamponade, massive pulmonary embolism, and cardiogenic shock are among the most easily recognized entities. In hypovolemic shock cases, inferior vena cava dimensions, and collapsibility status can help establish the diagnosis. Likewise, cardiac motion detected by USG during CA resuscitation is correlated with ROSC [33]. On the other hand, non-contrast computed tomography (CT) of the brain will reveal catastrophic events such as massive intracranial hemorrhage that may have caused CA.

Echocardiography is advocated to be used by experienced physicians soon **i**n patients with CA or hemodynamic instability of presumed CVS origin. It is used to assess regional and global LV function and to rule in or rule out differential diagnoses. In patients with no recurrence of chest pain, normal ECG findings, and normal readings of high-sensitivity cardiac troponins, but with suspicion of coronary lesions, a noninvasive stress test to detect induced ischemia or coronary CT-angiography (CCTA) is the diagnostic modality of choice before deciding on PCI [19].

Targeted temperature management (TTM) / Therapeutic hypothermia

TTM can be used to prevent fever, maintain normothermia, or induce hypothermia in eligible patients. TTM is sometimes referred to as therapeutic hypothermia, especially when a target temperature below 36°C is used. Targeted normothermia is core temperature ≤37.7°C instead of cooling to a specific target temperature (eg 36°C) after CA [34].

ERC and AHA guidelines recommend TTM in both OHCA and in-hospital CA cases to ensure optimal neurologic recovery after arrest. They recommended maintenance of a constant body temperature between 32°C and 36 °C for at least 24 hours, absence of fever above 37.7 °C for at least 72 hours in comatose patients after ROSC, and not using prehospital IV cold fluids to induce hypothermia [35, 36].

Hypothermia reduces cerebral oxygen consumption by 5-7% for each degree decrease in core temperature (blood, bladder, esophageal temperature measurements). This reduces the release of excitatory amino acids and the production of free radicals and suppresses various inflammatory processes that occur following global ischemia and reperfusion. However, there was no difference in the inflammatory cytokine response of adult patients in the 33 to 36 °C temperature range [36].

TTM should not be applied in active, bleeding patients in whom compressions cannot be performed, and in hemodynamically unstable patients. Before starting TTM, the patient must be hemodynamically stable and have a safe airway. All hemodynamic variables should be closely monitored throughout the procedure. Effective use

of TTM requires the cooperation of health professionals (emergency medical technicians, ED physicians, nurses, and intensive care unit teams) working in a coordinated and efficient manner [37].

The TTM process takes place in three stages: induction, maintenance, and reheating. The aim is to achieve a core temperature of 33 to 37.5 °C expediently, keep this temperature for 12 to 24 hrs and then reheat at a controlled rate of 0.2 to 0.5 °C per hour. Cooling can be done superficially with cooling blankets or gel-coated pads with water circulation, or centrally with endovascular cooling catheters. Rapid cold saline infusion and ice packs can be used in an emergency when automatic cooling devices are not available or when the patient needs to be transferred to a TTM-capable facility.

There is insufficient evidence to favor one cooling method over another. The gold standard for measuring central temperature (which is very close to brain temperature) is to measure the temperature of the blood using a pulmonary artery catheter, as an invasive method. Therefore, the most common and ideal measurement site is the esophagus. Although there is no universal optimal TTM rule, the target range of 33-37.5 °C can be determined by considering patient-specific conditions [37, 38]. Slow rewarming prevents rapid changes in metabolic rates and plasma electrolyte concentrations, thus avoiding hyperkalemia, seizures, and cerebral edema. In addition, fever should be avoided during the rewarming phase and for 48 hours thereafter to reduce the risk of detrimental neurological effects due to hyperthermia.

For a successful TTM application, it is necessary to be aware of the physiological and pathophysiological changes. For example, induced hypothermia causes decreased cardiac stroke volume, moderate acidosis, and increased amylase and lactate levels. These are physiological changes and do not require treatment.

The main untoward effects associated with TTM are chills and coagulopathy. When the body temperature drops below 36.5 °C, shivering begins and raises the body temperature. To get the maximum benefit from hypothermia, shivering should be avoided. Therefore, paralyzing agents such as vecuronium and rocuronium are used in addition to sedative drugs such as propofol, fentanyl, and midazolam [34, 37]. However, paralyzing agents may disguise seizures in a significant percentage of patients (33%) after CA. This may cause the cases not to wake up and to progress the existing brain damage. Therefore, continuous EEG monitoring is recommended to determine nonconvulsive status epilepticus. Epilepsy prophylaxis is not recommended. The risk of infection increases with prolonged hypothermia. Therefore, necessary precautions should be taken for the prevention and early detection of infections in patients with therapeutic hypothermia. The use of prophylactic antibiotics has no place [34, 37]. Complications and adverse effects associated with TTM or hypothermia are summarized in **Table 2** below.

Table 2. Adverse effects and/or complications attributed to therapeutic hypothermia

Affected system	Adverse effects/ Complications
Cardiovascular	Arrhythmias (tachycardia, bradycardia, long PR, QT, QRS intervals, ventricular dysrhythmias) Coronary vasoconstriction Reduced cardiac index Increased blood pressure and peripheral vascular resistance
Metabolic and endocrine	Metabolic acidosis Reduced O2 consumption and CO2 production Hyperglycemia Decreased insulin secretion, increased insulin resistance Increased levels of cortisol, adrenaline, noradrenaline Reduced clearance of drugs
Neurological	Confusion, lethargy, coma Seizures EEG abnormalities
Infection	Compromised immunity Aspiration pneumonia, ventilator-associated pneumonia Catheter site infection Skin infection, pressure ulcers
Renal	Cold diuresis (results in hypovolemia, hypokalemia, hypomagnesemia, and hypophosphatemia) Decreased GFR, impaired tubular functions, acute renal failure
Hematological	Thrombocytopenia

	Prolonged PT, and aPTT Impaired coagulation cascade
Respiratory	Neurologic pulmonary edema Acute respiratory distress syndrome (ARDS)
Gastrointestinal	Prolonged gastric emptying Ileus- bowel obstruction Increased levels of liver enzymes, amylase, lactate

The application of TTM was first advocated nearly 20 years ago to prevent severe brain damage and improve neurological outcomes in unresponsive patients after CA. However, the first studies ended with unsatisfactory results due to a lack of blindness and a small sample size. The first TTM study was in 2013, in which 939 unresponsive patients after OHCA were randomized to hypothermia (33 °C) and normothermia (36 °C) groups [38]. At the end of the study, the number of patients who died or had poor neurological outcomes at six months was similar in both groups (54% in the hypothermia group, 52% in the normothermia group, RR 1.02; 95% CI, 0.88-1.16). In a recently published multinational, multicenter study with a robust sample group, Dankiewicz *et al*. randomized 1850 unresponsive patients following CA into two groups: TTM with gradual rewarming at 33 °C (hypothermia) for 28 hours, or temperature at 37.5 °C or to maintain a lower level (normothermia) [39]. Mortality rates were similar at 6 months in the normothermia and hypothermia groups (50% in those with hypothermia vs. 48% in those with normothermia, RR 1.04; 95% CI; 0.9-1.1). The percentage of patients with poor neurological outcomes (54%, RR 1.0; 95% CI; 0.91-1.08) also did not differ between the groups.

In a network meta-analysis, Amagasa *et al*. compared four intervention groups (normothermia, TTM for 24 h (TTM 24h), TTM for 48 h (TTM 48h), and TTM for 72 h (TTM 72h)) [40]. In the ranking analysis, the hierarchies for efficacy for survival and favorable neurological outcome were TTM 72h > TTM 48h > TTM 24h > normothermia. The evidence to support prolonged TTM this result is only weak to very weak in children with ROSC after CA. There is no conclusive evidence regarding the effectiveness and length of TTM and high-quality RCRs comparing long-length TTM to short-length hypothermia and normothermia are needed.

In brief, a clear benefit of hypothermia has not been demonstrated by the findings of recent studies. However, it is well known that hyperthermia causes poor neurological outcomes. We may not need to aggressively cool the patient to 33 °C after CA, but we should closely monitor the patient's body temperature (via probes in the bladder, nasopharynx, or esophagus), and more importantly, we should keep the patient's temperature below 37.8 °C following CA.

Blood pressure (BP)

2021 ERC and ESICM Guidelines affirmed that clinicians should avoid reduced BP readings (MAP <65 mmHg). Target MAP to have a urine output greater than 0.5 mL /kg per hour and normal or decreasing levels of lactate as a marker of anaerobic glycolysis [27]. Hypotension (<65 mmHg) is usually accompanied by grave outcomes. Optimal targets of MAP should be based on individual characteristics to avoid over- and undertreatment.

Use of drugs and blood products in PCAS

standard vasopressor treatment of dobutamine, dopamine, and norepinephrine can be used to improve the patient's hemodynamic profile. Noradrenaline is the agent of choice to maintain adequate blood pressure and urine output [41]. vasopressin alone or vasopressin combined with epinephrine or vasopressin, steroids, and epinephrine (VSE) versus epinephrine combined with placebo as the control group. A recent meta-analytic study compared vasopressin alone or vasopressin combined with epinephrine or vasopressin, steroids, and epinephrine (VSE) versus epinephrine combined with placebo as the control group [42]. The study could not demonstrate a significant benefit from vasopressin with or without epinephrine compared with standard care. On the other hand, vasopressin as a part of VSE accompanied an increased ROSC rate in those with in-hospital CA. In a recent systematic review, authors have concluded that glucocorticoid infusion during and after CPR appears to produce favorable results concerning death rates, and an improved rate of ROSC, especially in patients with unstable hemodynamic status and previous cardiac illnesses [43].

Oxygenation management

After ROSC, it is recommended that patients maintain normoxaemia with a SpO2 of 94–98% or PaO2 of 75 to 100 mm Hg [27]. Early administration of oxygen in the context of emergency care has not been proven to

accompany survival improvement and thus needs to be avoided [41]. The findings do not support the use of a SpO2 target of 90% to 94% after resuscitation from OHCA cardiac arrest [44]. After the patient is hospitalized, the oxygen fraction can be reduced as necessary.

In a different study, investigating how different oxygenation strategies in adults with OHCA and ROSC admitted to the ICU can have an impact, Schmidt *et al*. conducted a randomized controlled trial (RCT) [45]. The patients were randomized to receive either a restrictive (68 to 75 mm Hg) or liberal (98 to 105 mm Hg) oxygenation strategy for 5 days, where no differences between both groups were found. Of note, low tidal volume (6 ml/kg) ventilation is preferred over high volumes to prevent barotrauma in the lungs.

Impact of new technologies on PCAS

CPR and other measures in the context of emergency care delivered early and appropriately have a major impact on PCAS and the successful management of the patient. The main areas of interest are applications to locate AEDs, smartphones and smartwatches to be used by the first responder and healthcare providers to reach the patients. These advanced technological tools defined the potential effects of drones and machine learning on survival rates [46].

CONCLUSION

Cerebral ischemia and hypoxia following CA cause morbidity and mortality through ischemic reperfusion injury and organ failures. Close monitoring of the neurological outcomes of resuscitated patients is of vital importance. Optimization of oxygenation and hemodynamics, early coronary interventions, ACLS, and early and intensive management of TTM has been reported to increase survival with fewer neurological sequelae in patients with ROSC. Appropriate use of drones and other technological advances hold a lot of promise for improving healthcare, especially in the transportation of AEDs to patients with OHCA to save lives. New well-designed, population-based controlled interventional studies are necessary to enlighten the details of the optimal management of patients resuscitated after CA.

ACKNOWLEDGMENTS : None

CONFLICT OF INTEREST : None

FINANCIAL SUPPORT : None

ETHICS STATEMENT : None

REFERENCES

1. Neumar RW, Nolan JP, Adrie C, Aibiki M, Berg RA, Böttiger BW, et al. Post-cardiac arrest syndrome. Circulation. 2008;118(23):2452-83.
2. Andersen LW, Holmberg MJ, Berg KM, Donnino MW, Granfeldt A. In-Hospital Cardiac Arrest: A Review. JAMA. 2019;321(12):1200-10. doi:10.1001/jama.2019.1696
3. Soar J, Böttiger BW, Carli P, Couper K, Deakin CD, Djärv T, et al. European Resuscitation Council Guidelines 2021: Adult advanced life support. Resuscitation. 2021;161:115-51. doi:10.1016/j.resuscitation.2021.02.010. Erratum in: Resuscitation. 2021;167:105-106.
4. Patel JK, Kataya A, Parikh PB. Association between intra- and post-arrest hyperoxia on mortality in adults with cardiac arrest: A systematic review and meta-analysis. Resuscitation. 2018;127:83-8.
5. Meng L, Gelb AW. Regulation of cerebral autoregulation by carbon dioxide. Anesthesiology. 2015;122(1):196-205.
6. Wang HE, Prince DK, Drennan IR, Grunau B, Carlbom DJ, Johnson N, et al. Post-resuscitation arterial oxygen and carbon dioxide and outcomes after out-of-hospital cardiac arrest. Resuscitation. 2017;120:113-8.
7. Johnson NJ, Caldwell E, Carlbom DJ, Gaieski DF, Prekker ME, Rea TD, et al. The acute respiratory distress syndrome after out-of-hospital cardiac arrest: Incidence, risk factors, and outcomes. Resuscitation. 2019;135:37-44.

8. Laurent I, Monchi M, Chiche JD, Joly LM, Spaulding C, Bourgeois B, et al. Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest. J Am Coll Cardiol. 2002;40:2110-6.
9. Bhate TD, McDonald B, Sekhon MS, Griesdale DE. Association between blood pressure and outcomes in patients after cardiac arrest: A systematic review. Resuscitation. 2015;97:1-6.
10. Schriefl C, Schoergenhofer C, Ettl F, Poppe M, Clodi C, Mueller M, et al. Change of Hemoglobin Levels in the Early Post-cardiac Arrest Phase Is Associated With Outcome. Front Med (Lausanne). 2021;8:639803. doi:10.3389/fmed.2021.639803
11. Annborn M, Nilsson F, Dankiewicz J, Rundgren M, Hertel S, Struck J, et al. The Combination of Biomarkers for Prognostication of Long-Term Outcome in Patients Treated with Mild Hypothermia After Out-of-Hospital Cardiac Arrest-A Pilot Study. Ther Hypothermia Temp Manag. 2016;6(2):85-90. doi:10.1089/ther.2015.0033
12. Düring J, Annborn M, Cronberg T, Dankiewicz J, Devaux Y, Hassager C, et al. Copeptin as a marker of outcome after cardiac arrest: a sub-study of the TTM trial. Crit Care. 2020;24(1):185. doi:10.1186/s13054-020-02904-8
13. Felder S, Vanaarsen K, Davis M. Decreasing time to first shock: routine application of defibrillation pads in prehospital STEMI. Can J Emerg Med. 2019;22(1):82-5. doi:10.1017/cem.2019.408
14. Elfwén L, Lagedal R, James S, Jonsson M, Jensen U, Ringh M. Coronary angiography in out-of-hospital cardiac arrest without ST elevation on ECG—Short-and long-term survival. Am Heart J. 2018;200:90-5.
15. Dumas F, Bougouin W, Geri G, Lamhaut L, Rosencher J, Pène F, et al. Emergency percutaneous coronary intervention in post–cardiac arrest patients without ST-segment elevation pattern: insights from the PROCAT II registry. JACC Cardiovasc Interv. 2016;9(10):1011-8.
16. Callaway CW, Donnino MW, Fink EL, Geocadin RG, Golan E, Kern KB, et al. Part 8: Post-Cardiac Arrest Care: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132(18 Suppl 2):S465-82.
17. Garot P, Lefevre T, Eltchaninoff H, Morice MC, Tamion F, Abry B, et al. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. Circulation. 2007;115(11):1354-62.
18. Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med. 2009;360(26):2705-18.
19. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, et al. ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42(14):1289-367. doi:10.1093/eurheartj/ehaa575. Erratum in: Eur Heart J. 2021;42(19):1908. Erratum in: Eur Heart J. 2021;42(19):1925.
20. Goel V, Bloom JE, Dawson L, Shirwaiker A, Bernard S, Nehme Z, et al. Early versus deferred coronary angiography following cardiac arrest. A systematic review and meta-analysis. Resusc Plus. 2023;14:100381. doi:10.1016/j.resplu.2023.100381
21. Kandala J, Oommen C, Kern KB. Sudden cardiac death. Br Med Bull. 2017;122(1):5-15. doi:10.1093/bmb/ldx011
22. Lemkes JS, Janssens GN, van der Hoeven NW, Jewbali LSD, Dubois EA, Meuwissen M, et al. Coronary Angiography after Cardiac Arrest without ST-Segment Elevation. N Engl J Med. 2019;380(15):1397-407. doi:10.1056/NEJMoa1816897
23. Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Bottiger BW, 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 (Part II). Int Emerg Nurs. 2010;18:8-28.
24. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006;67(2):203-10.
25. English WA, Giffin NJ, Nolan JP. Myoclonus after cardiac arrest: pitfalls in diagnosis and prognosis. Anaesthesia 2009;64(8):908-11.

26. Scholefield BR, Perkins GD, Duncan HP, Gao F, Morris KP. Should children who have a cardiac arrest be treated with therapeutic hypothermia? BMJ. 2014;348.
27. Nolan JP, Sandroni C, Böttiger BW, Cariou A, Cronberg T, Friberg H, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care. Resuscitation. 2021;161:220-69. doi:10.1016/j.resuscitation.2021.02.012. Erratum in: Resuscitation. 2021;167:109-110.
28. Azman KJ, Gorup V, Noc M. Rescue percutaneous coronary intervention during cardiopulmonary resuscitation. Resuscitation. 2004;61(2):23-6.
29. Morimura N, Sakamoto T, Nagao K, Asai Y, Yokota H, Tahara Y, et al. Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: a review of the Japanese literature. Resuscitation. 2011;82:10-4.
30. Bergan HA, Halvorsen PS, Skulstad H, Fosse E, Bugge JF. Does therapeutic hypothermia during extracorporeal cardiopulmonary resuscitation preserve cardiac function? J Transl Med. 2016;14(1):345. doi:10.1186/s12967-016-1099-y
31. Kang Y. Management of post-cardiac arrest syndrome. Acute Crit Care. 2019;34(3):173-8.
32. Moseby-Knappe M, Mattsson-Carlgren N, Stammet P, Backman S, Blennow K, Dankiewicz J, et al. Serum markers of brain injury can predict good neurological outcomes after out-of-hospital cardiac arrest. Intensive Care Med. 2021;47(9):984-94. doi:10.1007/s00134-021-06481-4
33. Kedan I, Ciozda W, Palatinus JA, Palatinus HN, Kimchi A. Prognostic value of point-of-care ultrasound during cardiac arrest: a systematic review. Cardiovasc Ultrasound. 2020;18:1. doi:10.1186/s12947-020-0185-8
34. Elmer J, Rittenberger J. Initial assessment and management of the adult post-cardiac arrest patient. Available from: https://www.uptodate.com/contents/initial-assessment-and-management-of-the-adult-post-cardiac-arrest-patient? This topic last updated: Feb 07, 2022. Accessed: May 20, 2023.
35. Panchal AR, Bartos JA, Cabañas JG, Donnino MW, Drennan IR, Hirsch KG, et al. Part 3: Adult Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142:366-468.
36. Nolan JP, Sandroni C, Böttiger BW, Cariou A, Cronberg T, Friberg H, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med. 2021;47:369-421.
37. Omairi AM, Pandey S. Targeted Hypothermia Temperature Management. [Updated 2021 Dec 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK556124/. Accessed May 07, 2023.
38. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013;369(23):2197-206.
39. Dankiewicz J, Cronberg T, Lilja G, Jakobsen JC, Levin H, Ullén S, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. N Engl J Med. 2021;384(24):2283-94.
40. Amagasa S, Yasuda H, Oishi T, Kodama S, Kashiura M, Moriya T. Target Temperature Management Following Pediatric Cardiac Arrest: A Systematic Review and Network Meta-Analysis to Compare the Effectiveness of the Length of Therapeutic Hypothermia. Cureus. 2022;14(11):e31636. doi:10.7759/cureus.31636
41. Katzenschlager S, Popp E, Wnent J, Weigand MA, Gräsner JT. Developments in Post-Resuscitation Care for Out-of-Hospital Cardiac Arrests in Adults-A Narrative Review. J Clin Med. 2023;12(8):3009. doi:10.3390/jcm12083009
42. Yan W, Dong W, Song X, Zhou W, Chen Z. Therapeutic effects of vasopressin on cardiac arrest: a systematic review and meta-analysis. BMJ Open. 2023;13(4):e065061. doi:10.1136/bmjopen-2022-065061
43. Sahebnasagh A, Najmeddin F, Najafi A, Saghafi F, Salehi-Abargouei A, Ahmadi A, et al. Efficacy of Glucocorticoid Administration in Patients with Cardiac Arrest: A Systematic Review of Clinical Studies. Curr Med Chem. 2022;29(1):136-51. doi:10.2174/0929867328666210531145617
44. Bernard SA, Bray JE, Smith K, Stephenson M, Finn J, Grantham H, 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;328(18):1818-26.
45. Schmidt H, Kjaergaard J, Hassager C, Mølstrøm S, Grand J, Borregaard B, et al. Oxygen Targets in Comatose Survivors of Cardiac Arrest. N Engl J Med. 2022;387(16):1467-76. doi:10.1056/NEJMoa2208686

46. Olasveengen TM, Semeraro F, Ristagno G, Castren M, Handley A, Kuzovlev A, et al. European Resuscitation Council Guidelines 2021: Basic Life Support. Resuscitation. 2021;161:98-114. doi:10.1016/j.resuscitation.2021.02.009