

Management of post-cardiac arrest syndrome

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Post-cardiac arrest syndrome is a complex and critical issue in resuscitated patients undergone cardiac arrest. Ischemic-reperfusion injury occurs in multiple organs due to the return of spontaneous circulation. Bundle of management practices are required for post-cardiac arrest care. Early invasive coronary angiography should be considered to identify and treat coronary artery obstructive disease. Vasopressors such as norepinephrine and dobutamine are the first-line treatment for shock. Maintenance of oxyhemoglobin saturation greater than 94% but less than 100% is recommended to avoid fatality. Target temperature therapeutic hypothermia helps to resuscitated patients. Strict temperature control is required and is maintained with the help of cooling devices and monitoring the core temperature. Monitorings include electrocardiogram, oxymetry, capnography, and electroencephalography (EEG) along with blood pressure, temperature, and vital signs. Seizure should be treated if EEG shows evidence of seizure or epileptiform activity. Clinical neurologic examination and magnetic resonance imaging are considered to predict neurological outcome. Glycemic control and metabolic management are favorable for a good neurological outcome. Recovery from acute kidney injury is essential for survival and a good neurological outcome.

Key Words: cardiopulmonary resuscitation; induced hypothermia; out-of-hospital cardiac arrest

INTRODUCTION

Cardiac arrest is a critical event and causes over 30,000 fatalities per year in South Korea [1]. Although the survival rate was 3.0% with a good neurological recovery rate of 0.9% from 2006 to 2010 in South Korea, the Korean Cardiac Arrest Research Consortium reported a survival rate of 11.5% with a good neurologic recovery (cerebral performance category [CPC] 1-2) rate of 7.8% from 2014 to 2015 [1,2].

Nolan et al. [3] proposed the term post-cardiac arrest syndrome, which was associated with (1) post-cardiac arrest brain injury, (2) post-cardiac arrest myocardial dysfunction, (3) systemic ischemia/reperfusion response, and (4) persistent precipitating pathology. Post-cardiac arrest syndrome consists of five phases, which includes the immediate phase (20 minutes after the return of spontaneous circulation [ROSC]), early phase (from 20 minutes to 6-12 hours after ROSC), intermediate phase (from 6-12 to 72 hours after ROSC), recovery phase (3 days after ROSC), and rehabilitation phase.

During the post-cardiac arrest period, several systemic complications including acute respiratory distress syndrome, acute renal failure, refractory shock, and disseminated intravas-

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cular coagulation occur and are associated with mortality [4]. Although the Korean rapid response system has helped reduce the rate of hospital mortality and in-hospital cardiac arrest after it has been introduced as an essential part of the medical system [5], systematic and proper management of post-cardiac arrest patients is important. This paper summarizes post-cardiac arrest care, including the newest update after 2015 American Heart Association Guidelines.

PATHOPHYSIOLOGY AFTER RESUSCITATION

Post-cardiac arrest syndrome is a combination of pathophysiological processes, which include (1) post-cardiac arrest brain injury, (2) post-cardiac arrest myocardial dysfunction, and (3) systemic ischemia/reperfusion response [6]. Although prolonged whole-body ischemia initially causes global tissue and organ injury, additional damage occurs during and after reperfusion [7,8]. The mechanism of brain injury includes altered calcium homeostasis, free radical formation, mitochondrial dysfunction, protease activation, and inflammation [9].

Along with the brain, another organ that experiences ischemic insult is the heart. Myocardial dysfunction is a common cause of early mortality after cardiac arrest and transient global dysfunction, which becomes apparent approximately 7 hours after ROSC and recovery within 48–72 hours [10]. Ischemia/reperfusion causes generalized activation of immunologic and coagulation pathways, which increase the risk of multiple organ failure and infection [9]. Clinical manifestations of ischemic-reperfusion injury include the depletion of intravascular volume, impaired vasoregulation, impaired oxygen delivery, and increased infection.

HEMODYNAMIC AND CARDIAC MANAGEMENT

Coronary Angiography after Resuscitation

Acute myocardial infarction is a common cause of cardiac arrest. Coronary angiography performed within 24 hours of admission is associated with a 2.3-fold increase in good neurological outcome (CPC \leq 2) and survival at discharge [11,12]. Yao et al. [10] reported that 83 patients (44%) had myocardial dysfunction and total of 37 patients (45%) with myocardial dysfunction survived to discharge, 39% with intact neurologic status. Early myocardial dysfunction is not associated with neurologically intact survival. Chest pain complaint before arrest, ST segment elevation on ECG after ROSC, regional wall motion abnormality in echocardiography after resuscitation are more frequent in cardiac etiology group [13]. Patients suf-

KEY MESSAGES

- Management of post-cardiac arrest syndrome needs multimodality treatments of several systems.
- These include hemodynamic instability, myocardial dysfunction, coronary artery obstruction, airway and ventilator support, hypoxic-ischemic brain injury, targeted temperature therapeutic hypothermia, and prediction of neurologic outcome.

fering out-of-hospital cardiac arrest, those with old age, hypertension, positive cardiac enzyme, and initial shockable rhythm were associated with obstructive coronary artery disease. Early invasive coronary angiography should be considered in these patients [14].

Echocardiography

Echocardiography during resuscitation is suggested to be an important tool for the identification and treatment of reversible causes of death [13]. Post-resuscitation myocardial dysfunction occurs after ROSC. It is important to restore myocardial function to maintain blood pressure in the early post-cardiac arrest phase. Echocardiographic patterns of post-cardiac arrest left ventricle dysfunction include global hypokinesia, regional wall motion abnormalities, and Takotsubo pattern [15].

Hemodynamic Monitoring

Maintenance of systolic blood pressure greater than the fifth percentile for age is recommended with the use of parenteral fluid and/or inotropes or vasoactive drugs. Continuous arterial pressure monitoring is required to identify and treat hypotension.

Antiarrhythmic and Inotropic Drugs

There is insufficient evidence regarding the routine use of a β -blocker and lidocaine; however, the prophylactic use of lidocaine may be considered for recurrent ventricular fibrillation or ventricular tachycardia during transportation in the absence of contraindication. Avni et al. [16] recommended norepinephrine as the first-line vasopressor because norepinephrine was associated with decreased mortality, lower risk for major adverse events, and cardiac arrhythmias compared to dopamine. The combination norepinephrine-dobutamine is more effective and safer than epinephrine because epinephrine is associated with transient lactic acidosis, higher heart rate and arrhythmia, and inadequate gastric mucosa perfu-

sion [17].

Sodium nitroprusside can be used for poor myocardial function by reducing afterload and an inotrope to improve contractility. Sodium nitroprusside-enhanced cardiopulmonary resuscitation improved ROSC and 4-hour survival in a porcine model of prolonged ischemic, refractory ventricular fibrillation cardiac arrest [18].

AIRWAY AND VENTILATOR

Elevated levels of PO₂ contribute to oxidative stress that potentiates the post-cardiac arrest syndrome. Moreover, supranormal oxygen tension increases the risk of in-hospital mortality and decrease survival. However, there is some debate regarding hyperoxia. Temporary hyperoxia following hypoxic insult showed no difference in inflammatory reaction compared with hypoxia-normoxia. On the contrary, temporary hyperoxia may suppress or minimize inflammation by the attenuation of Toll-like receptor 4. Therefore, continuous hyperoxygenation after successful cardiac arrest harms patients, but temporary hyperoxygenation with 100% O₂ in a clinical situation may prove helpful [19].

A 100 mm Hg increase in partial pressure of oxygen (PaO₂) was associated with a 24% increase in mortality risk [20]. Mortality risk increased sharply with increasing hypoxia. Mortality risk was also associated with increasing hyperoxia although the association was not as significant as that with hypoxia [21]. Therefore, it is recommended to maintain an oxyhemoglobin saturation level of 94%–100%. To achieve normoxemia, hypoxemia should be avoided by titrating oxygen appropriately.

Lee et al. [22] reported mean PaO₂ had no independent association with in-hospital mortality, whereas hypocarbia was independently associated with in-hospital mortality. Del Castillo et al. [23] reported hypercapnia (odds ratio [OR], 3.27; 95% confidence interval [CI], 1.62 to 6.61; P=0.001) and hypocapnia (OR, 2.71; 95% CI, 1.04 to 7.05; P=0.04) after ROSC were associated with high mortality. It is recommended to avoid severe hypercapnia or hypocapnia and monitor end-tidal CO₂.

Pneumonia is the common cause of infection associated with post-cardiac arrest syndrome. However, prophylactic antibiotic therapy during hypothermia treatment in post-cardiac arrest patients cannot reduce the incidence of early-onset pneumonia [24]. Additionally, it does not affect the duration of mechanical ventilation, the length of ICU stay, in-hospital mortality, and poor neurological outcome [25].

NEUROLOGIC SYSTEM AND MANAGEMENT

Target Temperature Therapeutic Hypothermia

Targeted temperature management (TTM) is well known to benefit patients resuscitated from cardiac arrest. Kim et al. [26] found that TTM was related to a three-fold increase in neurologically favorable survival with TTM treatment in the initial non-shockable rhythm.

Time to target temperature was shorter and deviation from the maintenance temperature occurred less frequently using gel pad cooling device management. The gel pad cooling device is superior to the water blanket for strict temperature control during TTM [27]. The maximum target temperature should not exceed 36°C.

Monitoring

Intensive monitoring is needed for investigating organ dysfunction after ROSC. Monitoring includes elective cardiogram, pulse oximetry, capnography, blood pressure, temperature, and urine output. An arterial catheter should be placed for the identification and treatment of hypotension and a central venous catheter is useful for monitoring central venous oxygen saturation and fluid and medication administration. A bladder temperature catheter or esophageal probe will be used for monitoring the core body temperature.

Early electroencephalography (EEG) can predict neurological outcome. A suppressed and featureless EEG background is associated with a poor neurological outcome and electrographic seizures are associated with a good neurological outcome [28]. S-100B protein levels peaked at ROSC (0 hour), decreased rapidly to 6 hours, and maintained a similar level thereafter; therefore, it is a useful marker for predicting poor neurological outcome in post-cardiac arrest syndrome. The optimal sampling times of S-100B protein were 24 and 36 hours after ROSC [29].

Cerebral blood flow is low after cardiac arrest, and postanoxic encephalopathy-contributed autoregulation, loss of normal vascular tone, and increased cerebral blood flow may contribute to secondary brain damage and lead to fatal brain injury [30]. The incidence of seizures after cardiac arrest is about 8%–23%, and the presence of epileptiform activity or interictal epileptiform discharges are associated with a poor neurological outcome or death [31,32]. Although prophylactic anticonvulsant use is not beneficial, seizures should be treated with benzodiazepines and anticonvulsant drugs. The electroencephalogram should be monitored in resuscitated patients with a comatose mentality. Continuous EEG monitor-

ing provides dynamic information and can be used to assess the evolution of EEG patterns and detect seizures [33].

Predicting Neurological Outcome

Cerebral ischemia after cardiac arrest provokes morbidity and mortality through ischemic-reperfusion injury and organ failure. There are several parameters which predict the good neurological outcome of resuscitated patients. Cerebral oximetry measures regional cerebral oxygen saturation in the frontal lobe using near infra-red spectroscopy. Brain magnetic resonance imaging shows hypoxic-ischemic encephalopathy and neurologic sequelae include memory disturbance, amnesia, insomnia, and visual deficit.

Pupillary light reflex at ≥ 72 hours and corneal reflex at 72 hours likely indicate a poor outcome in patients. Myoclonus, short-latency somatosensory evoked potentials, neuron-specific enolase, and S-100B are also predictors of neurological outcome. Diffusion-weighted magnetic resonance images are taken 2–5 days after ROSC, and hypoxic ischemic brain injury includes the occipital cortex, deep grey nuclei, hippocampus, and cerebellum [34].

METABOLIC MANAGEMENT

Ammonia and lactate levels were higher and pH levels were lower in the poor outcome group [28]. Shida et al. [35] reported that high serum potassium level was significantly and dose-dependently associated with poor neurological outcomes. The highest proportion of favorable neurological outcome was 44.8% in Q1 group ($K \leq 3.8$ mEq/L), and the proportion of favorable neurological outcomes decreased as the serum potassium level increased. Therefore, serum potassium on hospital arrival may be an effective prognostic indicator for out-of-hospital cardiac arrest achieving ROSC.

Hyperglycemia and hypoglycemia are associated with poor neurological outcome, but no target range of glucose management is indicated in resuscitated patients from cardiac arrest. Blood glucose values up to 8.0 mmol/L are acceptable for out-of-hospital cardiac arrest patients treated with therapeutic hypothermia because a more strict approach seems not to offer additional mortality reduction, but instead may expose patients to the detrimental effects of hypoglycemia [36].

Renal System

Acute kidney injury (AKI) is serious problem and occurs in almost half of all patients after cardiac arrest. AKI contributes to inflammatory injury in the hippocampus and altered blood-

brain barrier permeability; therefore, after cardiac arrest, patients with AKI had more severe hemodynamic impairment and needed aggressive ICU therapy. Age, epinephrine dose, cumulative fluid balance, and presence of shock were independent predictors of AKI development [37]. Recovery from AKI is a potent predictor of survival and good neurological outcome at discharge after out-of-hospital cardiac arrest [38].

Decreased urine output (< 1 ml/kg/hr in infants and children or < 30 ml/hr in adolescents) may be caused by prerenal conditions (e.g., dehydration, inadequate systemic perfusion), renal ischemic damage, or a combination of the aforementioned factors. Avoidance of nephrotoxic medications and adjustment of the dose of medications excreted by the kidneys are recommended until renal function has been checked.

CONCLUSIONS

Although basic life support has been widely practiced to increase recovery from cardiac arrest, management of post-cardiac arrest patients have also made great progress. Management of post-cardiac arrest syndrome patients includes complex and multidisciplinary interventions. Early and intensive management should be focused on hemodynamic stability and neurologic recovery.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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