Review of Hypothermia Protocol and Timing of the Echocardiogram

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Abstract: Targeted temperature management, also known as therapeutic hypothermia (TH), is recommended for out-of-hospital cardiac arrest (OHCA). Both internal or external methods of cooling can be applied. Individuals resuscitated from OHCA frequently develop postarrest myocardial dysfunction resulting in decreased cardiac output and left ventricular systolic function. This dysfunction is usually transient and improves with spontaneous recovery over time. Echocardiogram (ECHO) can be a vital tool for the assessment and management of these patients. This manuscript reviewed methods available for TH after OHCA and reviews role of ECHO in the diagnosis and prognosis in this setting. (Curr Probl Cardiol 2021;46:100786.)

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Introduction

More than half a million patients experience an out-of-hospital cardiac arrest (OHCA) in the United States every year, and survival ranges between 6.7% and 8.4%.[1] Most patients die during the postresuscitation period due to critical neurologic damage secondary to cerebral ischemia during cardiac arrest.[2] The use of therapeutic hypothermia (TH) is associated with better survival outcomes and is associated with neuroprotection in OHCA.[3] Hypothermia results in a decreased metabolic need in the brain due to lower ATP, oxygen, and glucose consumption. There are various methods used: surface cooling with ice packs, cold saline infusion, cooling blankets or pads, and cooling catheters.[2] In certain conditions, TH application is contraindicated; these include active bleeding, clotting disorders, sepsis, pregnancy, and patients with do-not-resuscitate code status. Some adverse effects of TH include seizures, cardiac arrhythmias, and electrolyte imbalances. One other area that is not clearly understood is the optimal timing for initiation of TH. Some studies have shown that early induction of TH is associated with favorable neurological outcomes while some studies have shown that prehospital initiation of TH with a rapid infusion of ice-cold fluids, even though it leads to decreased core temperature at arrival, has not shown to affect the survival or neurological outcomes in patient.[2,4] Kang and colleagues showed that even delayed and slow induction of TH up to 8 hours after the return of spontaneous circulation (ROSC) resulted in improved survival rates and better neurologic outcomes. Experimental studies' of TH in acute myocardial infarction when initiated before reperfusion have reduced infarct size.[5] The optimal temperature for TH is still a topic of uncertainty. Clinical guidelines have recommended a target temperature ranging from 32˚C to 34˚C. In a recent update from the International Liaison Committee on Resuscitation, the advised temperature range is between 32˚C and 36˚C.[3,6]

Echocardiogram (ECHO) is an inexpensive, widely available, noninvasive, and safe clinical tool. Performing an ECHO early on may be beneficial in assessing the cardiac functioning and intravascular volume status.[7] Studies have shown that patients with risk factors for postarrest myocardial dysfunction might benefit from earlier screening and prompt treatment.[8] The current American Heart Association (AHA) guideline for postcardiac arrest care recommends ECHO within 24 hours of presentation to guide management. In up to two-thirds of patients after cardiac arrest and ROSC, postarrest myocardial dysfunction (PAMD) is present. It usually manifests as reduced left ventricular ejection fraction (LVEF),

low cardiac index (CI), left ventricular systolic dysfunction, left ventricular diastolic dysfunction, or right ventricular dysfunction.[9] In this manuscript, we will review the TH guidelines emphasizing the role and timing of ECHO in OHCA.

Temperature and timing

TH in individuals presenting with OHCA involves cooling the body, for 12-24 hours, from their current body temp to anywhere from 32˚C to 36˚C. This can be achieved via noninvasive methods, such as ice packs or cooling pads, or invasive methods such as cooling catheters.[1] Current ways to induce TH fall under two categories: external or surface cooling (ice packs, cold towels, cooling vests, cool air ventilation, water, or air-cooled circulating mattress) and internal endovascular (ice-cold perfusion, endovascular catheter, extracorporeal membrane oxygenation).[10] Among these methods, endovascular cooling (eg, intravenous cold saline) and gel-adhesive pads (external) are the more effective for providing rapid induction and maintenance of hypothermia than cooling blankets.[10] Since many patients with ROSC are often mildly hypothermic, minimally invasive cooling techniques can often achieve the desired temperature, and in such cases, endovascular cooling is not superior to external cooling.[11-13] During induction of cooling, shivering should be prevented since it can delay reaching the desired temperature. This is achieved by utilizing medications such as continuous propofol, fentanyl, and benzodiazepines.[14] Neuromuscular blocking agents can also achieve similar results.[15] Currently, there is no "best" temperature to target. Nielsen and colleagues did not find a reduction in all-cause mortality or neurological outcomes when they compared TH at 33˚C-36˚C.[16] Furthermore, studies have shown that any temperature in the range of 32˚-36˚C is not superior over the others, thus maintaining a temperature at 36˚C or lower for 24 hours is ideal.[17,18] For patients with the most severe postcardiac arrest illness, such as brain edema, TH at 33˚C is associated with better survival than at 36˚C.[19] Thus, choosing the right TH therapy for OHCA is crucial.

Hypothermia protocols

The 2015 update of the AHA guidelines recommend inducing the hypothermic protocol to a target temperature of 32˚C-36˚C as early as possible after achieving ROSC in patients with OHCA.[20] Targeted temperature management after OHCA is a class 1B recommendation for patients with an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia. The guidelines also mention a possible benefit for

in-hospital cardiac arrest patients and patients with OHSA with non-shockable rhythm.[17] The elapsed time between arrest and ROSC may predict survival and long-term outcomes. Mooney et al. (2011) found that extended time between collapse and ROSC was associated with worse outcomes. Every hour of delay in the initiation of TH was associated with a 20% increase in mortality. The same study found that only 36% of the patients were alive at hospital discharge if their downtime was more than 30 minutes.[21] However, a recent meta-analysis of 5 randomized controlled trials failed to show any significant difference in all-cause mortality among patients randomized to the hypothermia protocol compared to the control arm of normothermia. The same study also showed no difference in all-cause mortality among patients randomized to prehospital hypothermia versus in-hospital hypothermia.[22]

A delay to ROSC of more than 30 minutes in cardiac arrest patients is associated with a very poor clinical prognosis.[23,24] Duration of hypothermia protocol is also important. The 2003 Advanced Life Support Task Force of the International Liaison Committee on Resuscitation recommended that unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest due to ventricular fibrillation should be cooled to 32˚C-34˚C for 12-24 hours.[25] Subsequently, observational studies have supported this therapy in patients with nonventricular fibrillation cardiac arrest and postresuscitation circulatory shock. Clinical data has also suggested that fever should be avoided for at least 48 hours following cardiac arrest.[16,26] Additionally, the 2015 AHA guidelines provide an expert opinion of providing prolonged hyperthermia prevention in patients at higher risk of ischemic brain injury.[20] Thus rewarming rate and duration depend on the original inciting event, and the method of rewarming is dependent on each case. Nevertheless, the beneficial outcomes of the therapy have are demonstrated in various methods used.[16,27,28]

Role of echocardiogram

In OHCA, the constellation of abnormalities that follow is known as postcardiac arrest syndrome (PCAS). These include abnormalities such as neurological deficits, PAMD, and ischemic injuries. PAMD is caused by the physiologic and pathological interdependencies of prearrest etiologies and cardiac insults caused by the arrest. PAMD is reported in up to two-thirds of patients after cardiac arrest (CA), including those without prior cardiac diseases.[8,9] The mechanism of PAMD overlaps those insults that produce myocardial dysfunction during myocardial infarction, stress-induced cardiomyopathy, and sepsis, which can lead to

hemodynamic instability and shock.[29] PAMD manifests as reduced LVEF, cardiac index, right ventricular dysfunction (RVD), and left ventricular diastolic dysfunction (LVDD). Thus the need for assessment of cardiac function with ECHO within the first 24 hours of OHCA.

The dynamic changes in LVEF, peak systolic myocardial tissue Doppler velocity, and tricuspid annular plane systolic excursion is established, and it is shown that after the acute insult and rewarming, LVEF shows gradual recovery. The LVEF distribution does not correlate with higher or lower pressor requirements or temperature.[16] Bro-Jeppesen et al. (2014) reported an early reduction in mitral annular diastolic tissue Doppler velocity immediately after ROSC, which increased over the first 48 hours, suggesting transient myocardial diastolic dysfunction mirroring the systolic dysfunction reflected by reduced velocities.[30] TH at 33˚C leads to decreased heart rate, elevated lactate levels, and require more vasopressors.[31] Furthermore, in survivors treated with TH, hemodynamic changes reverse after reversal of TH, and it does not affect the need for vasopressor support.[31] Implementing TH in patients with ventricular fibrillation and ventricular tachycardia leads to better performance outcomes at the time of discharge.[32]

PAMD leads to impaired cardiac output requiring hemodynamic support associated with worse outcomes after a CA. It remains uncertain whether PAMD directly impairs survival and recovery after a CA or whether the development of PAMD merely reflects a greater degree of ischemic injury sustained during severe CA. Further research is needed to define the role of PAMD on cardiac arrest outcomes and identify therapeutic strategies, and ECHO will likely play a pivotal role in this process. After CA, hemodynamic stabilization involves restoration of preload, vasopressor support, and inotropic support to reverse the effects of myocardial dysfunction and improve systemic perfusion. Hypotension, shock, and the need for vasopressor support after ROSC consistently predict worse overall outcomes, and the mean arterial pressure (MAP) is inversely related to the level of neurologic insult.[7,33] Nordmark and colleagues demonstrated ECHO's crucial role in TH for volume assessment and demonstrated the potential reserve of cardiac function to recover. Serial ECHOs performed demonstrated that many of the patients were hypovolemic during TH despite a positive fluid balance. It also showed that despite the lower LVEF due to the acute insult, there was no evidence of harmful effects of volume loading in these patients. Central venous pressure assessment by ECHO failed to show marked changes during volume resuscitation.[7] Thus performing timely ECHO with repeat serial studies in patients can give vital information that could help in the acute management of OHCA.

Role of angiography

Coronary artery disease is the most common etiology and cause of OHCA. After ROSC, immediate coronary angiography (CA) has found a culprit lesion in up to 80% of the patients. In postmortem examination of sudden cardiac death (SCD) victims, a coronary thrombus is seen in up to 80% of the cases. CA is the gold standard in defining and characterizing coronary anatomy. If one more lesion is found and presumed to be responsible for the arrest, percutaneous coronary intervention (PCI) can be immediately performed.[34] Noc reports that in OHCA, due to ventricular fibrillation and ST-elevation myocardial infarction (STEMI), CA with primary PCI was attempted in 98% of the patients and coronary obstruction was seen in the majority this group. Long-term outcomes were significantly better in patients who had PCI after regaining consciousness.[35] The survival rate decreased dramatically when patients remain comatose.[36] Spaulding et al. demonstrated that ST-elevation and chest pain have low predictive value in coronary artery occlusion and can not be reliably used to predict the likelihood of occlusion in OHCA. In their study population, 11% of patients had neither findings of STEMI on ECG nor chest pain post-OHCA.[37] Valente et al. demonstrated that comatose survivors of OHCA present a high-risk subgroup for STEMI and CA with similar efficacy to conscious STEMI patients.[38] The question becomes whether TH will affect the outcomes for OHCA patients negatively. Safety in the use of TH in STEMI patients has been well documented.[39] Zimmermann et al. investigated whether long-term outcomes for STEMI would be affected if TH was combined with OHCA due to STEMI. They showed that TH does not affect 30-day survival in OHCA due to STEMI and their observation was in line with the previous studies.[32,40] Nonsurvivors had higher lactate levels at presentation and often presented with well-known predictors for mortality in STEMI such as renal insufficiency, longer duration to obtain ROSC, and higher pressor requirement. Patients treated with TH also had a favorable neurological status.[5,40] Additionally, during CA of STEMI patients, the utilization of a left ventriculogram can help assess cardiac function, adding another method for assessment of cardiac function. CA also provides the ability to rule out the most dangerous cause for death by assessing for occlusion and if no coronary lesion is present, other differential diagnoses can be pursued. Thus, the utilization of CA in OHCA is a pivotal point of management and should be underscored. Figure 1 demonstrates the investigations mentioned above and management for patients presenting with OHCA.

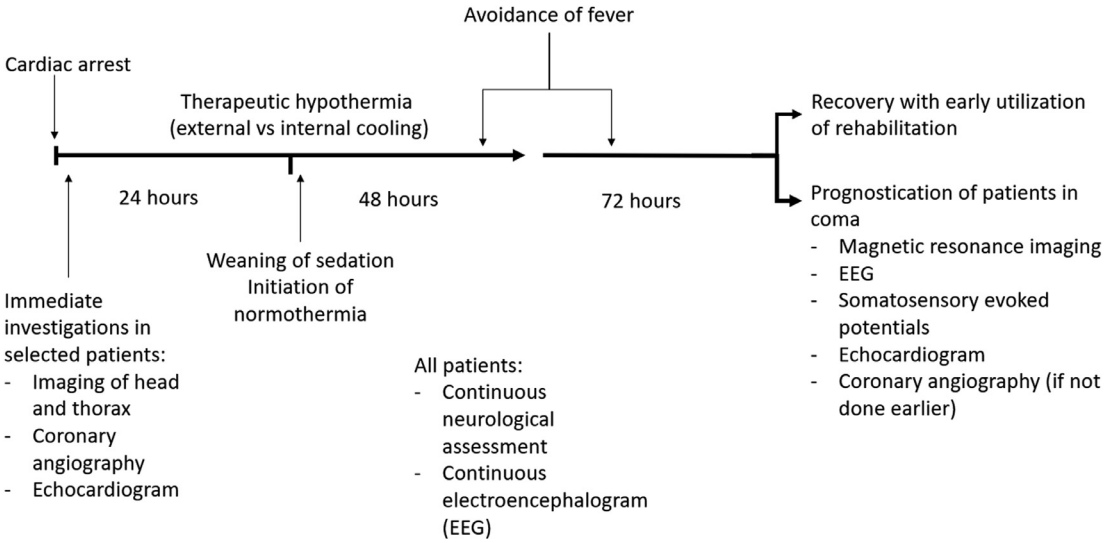

FIG 1. A working model for the management of patients requiring TH. Continuous electroencephalogram (EEG).

Conclusion

OHCA is associated with myocardial dysfunction. During TH, serial ECHOs can help guide patients' management by providing vital hemodynamic information and adjustment of vasopressor and ionotropic requirements. LVEF during TH undergoes dynamic changes and most patients have a recovery of cardiac function during the hospital course. ECHO can assist in determining which patients need further close monitoring at discharge. Currently, there are no long-term data available for serial cardiac function assessment for patients with OHCA. This data could demonstrate the relationship between the type of OHCA and its effect on long-term cardiac recovery. Until such data is available, the necessity of the application of ECHO to OHCA should be underscored.

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