Therapeutic hypothermia for out-of-hospital cardiac arrest – an update for prehospital personnel

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Focus on Out-of-Hospital Therapeutic Hypothermia

The problem of out-of-hospital cardiac arrest

Coronary heart disease can result in out-of-hospital cardiac arrest (OHCA) and remains the commonest cause of premature death in the United Kingdom. OHCA is common and occurs in 40-60/100,000 population annually, approximately 275,000 patients with OHCA in Europe every year. Mortality from OHCA is high, with survival to discharge rates typically <10%.

Survival from OHCA is initially almost entirely dependent on pre-hospital events - the actions of lay bystanders, to initiate bystander cardiopulmonary resuscitation (CPR), and the emergency medical services to achieve return-of-spontaneous circulation (ROSC). Post-OHCA patients who arrive in the Emergency Department (ED) without spontaneous cardiac output rarely survive and transporting patients with ongoing resuscitation should be reserved for special circumstances (eg paediatric patients, hypothermic cardiac arrest). The focus of pre-hospital resuscitation must focus of good quality CPR and prompt defibrillation. Together with therapeutic hypothermia, these are the only three treatments shown in human trials to improve outcome from OHCA, as shown in Figure 1.

Patients who achieve ROSC following OHCA have a high incidence of neurological impairment and cardiac failure. Post-ROSC strategies to improve survival from OHCA need to focus on limiting neurological and cardiac dysfunction. Despite advances in critical care medicine, in-hospital mortality for patients who achieve ROSC following OHCA remains high, with an in-hospital mortality of 71% in the UK. Following ROSC, the only intervention shown in improving human survival and neurological outcome is mild therapeutic hypothermia (MTH).

The high mortality rate after OHCA results from multi-organ dysfunction, in particular post-arrest brain injury. This is the result of total body ischaemia and ischaemia-reperfusion injury in addition to pathologies such as acute coronary artery occlusion that have often precipitated the initial cardiac arrest. The key elements of post-resuscitation care include intensive care with multi-organ support, therapeutic hypothermia to reduce secondary injury, and coronary reperfusion therapy where appropriate to address the underlying precipitant. Care of OHCA is time sensitive and involves multiple specialties. It is becoming increasingly clear that this group of patients must be cared for by pre-hospital and hospital teams in a timely, collaborative manner in order to achieve optimal patient outcomes.

Ambulance personnel should, therefore, consider transporting patients who achieve ROSC in the field following OHCA to centres who regularly receive OHCA patients and can offer immediate PCI and therapeutic hypothermia in an ICU-setting.

The History of Mild Therapeutic Hypothermia

Descriptions of hypothermia being used to treat patients have been documented for over 200 years. There are documented cases of Hippocrates and several Greek physicians experimenting with its use. A Russian method of resuscitation in 1803
described OH-CA patients being covered in snow, in the hope this would achieve ROSC. Despite the possibility of therapeutic hypothermia showing promise in improving the poor survival rates from OHCA, it was largely abandoned until the 1990s, mainly due to is significant clinical side effects.

The concept of preserving the brain in the field, protecting it from hypoxia until the patient could be transported to hospital for spontaneous circulation to be restored or placed on cardiopulmonary bypass was first suggested by Peter Safar in 1984. In 2002, two randomised trials demonstrated the benefit of cooling survivors of witnessed OHCA who had ventricular fibrillation (VF) as the presenting rhythm. Both of these trials used surface cooling and in the larger (European) trial, cooling was only commenced several hours after hospital admission. This lead to the International Liaison Committee on Resuscitation, the American Heart Association and the European Resuscitation Council recommending therapeutic hypothermia in the management of unconscious patients following OHCA. Despite these recommendations, the use of MTH is not yet routine. Since 2002, multiple further trials have explored the use of therapeutic hypothermia for non-VF OHCA, traumatic cardiac arrests and in paediatric patients.

Therapeutic hypothermia in the pre-hospital setting

To date, there have been no published studies of therapeutic hypothermia initiated in the pre-hospital setting improving clinical outcome, despite some relatively large pre-hospital clinical trials being undertaken. This is due to the complexity of cooling patients in the field and the challenges of maintaining core body temperature. Intra-nasal cooling may be particularly effective for cooling patients post-OHCA due to a rapid reduction in core body temperature. Animal research shows cooling during this period confers the greatest survival benefit and brain protection. Current clinical trials are exploring this concept. The Rhinocill device is shown in Figure 1.

There is strong evidence to support the use of therapeutic hypothermia in comatose patients after OHCA whose initial cardiac rhythm was VF. Cooling in other rhythms is likely to be beneficial as well. Despite animal studies demonstrating the benefit of these findings, therapeutic hypothermia should be initiated as early as possible for patients with STEMI, and certainly not delayed until after primary percutaneous coronary intervention (PCI). Cooling is likely to be delayed if not commenced in the Emergency Department. Traditionally, therapeutic cooling has been accomplished by two methods: external cooling, by the use of cold packs and cooling blankets, and internal cooling, using cold intravenous infusions and, more recently, indwelling catheters. These methods are relatively slow to achieve target temperature. The different cooling modalities are shown in Table 1.

Table 1.3 Methods of inducing/maintaining therapeutic hypothermia

<table>
<thead>
<tr>
<th>Invasive techniques</th>
<th>Non-invasive techniques</th>
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<tbody>
<tr>
<td>Cold intravenous fluid infusion</td>
<td>Ice packs</td>
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<tr>
<td>Extracorporeal cooling blood circuit</td>
<td>Cooling blankets (water / air filled)</td>
</tr>
<tr>
<td>Cardiopulmonary bypass</td>
<td>Cooling helmets (water / air filled)</td>
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<tr>
<td>Femoral-carotid Lavage</td>
<td>Cold water immersion</td>
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<tr>
<td>Nasal / nasogastric immersion</td>
<td>Self adhesive cooling pads</td>
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<tr>
<td>Rectal / peritoneal Ice slush</td>
<td>Nasal, evaporative cooling</td>
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Cooling during resuscitation

A novel approach to hypothermia induction is the use of a nasopharyngeal device (Rhinochill; BeneChill Inc.) that facilitates brain and core-body cooling. This cooling technique involves delivering a coolant in spray form using an oxygen flow rate of 40 L/min, resulting in a coolant delivery rate of 32 mL/min. It is safe, and effective in cooling patients post-OHCA with a rapid reduction in core body temperature. Intra-nasal cooling may be especially beneficial when used during CPR. Animal research shows cooling during this period confers the greatest survival benefit and brain protection. Current clinical trials are exploring this concept. The Rhinochill device is shown in Figure 1.
Immediate cooling, either during CPR or immediately post ROSC, is mandatory in the resuscitation of OHCA patients. Patients suffering an OHCA who fail to have circulation restored by emergency medical services using conventional resuscitation techniques almost invariably die. Many of these patients have an acute coronary artery occlusion as a potentially reversible cause of cardiac arrest and death. Pilot studies have demonstrated the feasibility of placing OHCA patients who fail to achieve ROSC at scene on continuous CPR, usually a mechanical device (e.g., AutoPulse or LUCAS), initiate therapeutic hypothermia and use an extra-corporeal membrane oxygenation circuit (ECMO) and an intra-aortic balloon pump to maintain cerebral oxygenation and perfusion. The patient can then be transported for immediate coronary intervention, where resuscitation may result in ROSC. This approach has been effectively demonstrated in animals, with neurologically intact survival possible with periods of cardiac arrest of over an hour. Performing coronary intervention on patients whilst being treated with ECMO is feasible and although this technique is still very novel, it promises to improve survival.

Application of CPR is paramount in any resuscitation attempt. All OHCA patients with a presumed cardiac origin, regardless of initial cardiac rhythm, should be cooled. There is no current evidence to support pre-hospital cooling when transport-to-hospital times are short. OHCA patients who achieve ROSC should be transported to centres capable of performing immediate PCI and commencing cooling simultaneously. OHCA patients who achieve ROSC should be cooled for at least 24-hours. Further research is warranted to establish the value of novel cooling techniques, eg intra-nasal cooling and intra-arrest cooling.

**Key Messages**

- Quality of CPR is paramount in any resuscitation attempt.
- All OHCA patients with a presumed cardiac origin, regardless of initial cardiac rhythm, should be cooled.
- There is no current evidence to support pre-hospital cooling when transport-to-hospital times are short.
- OHCA patients who achieve ROSC should be transported to centres capable of performing immediate PCI and commencing cooling simultaneously.
- OHCA patients who achieve ROSC should be cooled for at least 24-hours.

Further research is warranted to establish the value of novel cooling techniques, eg intra-nasal cooling and intra-arrest cooling.

**Reference List**

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Reference List Continued