Clinical paper

Esophageal temperature after out-of-hospital cardiac arrest: An observational study

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A B S T R A C T

Introduction: Out-of-hospital cardiac arrest (OHCA) is a significant cause of death and severe neurological disability. The only post-return of spontaneous circulation (ROSC) therapy shown to increase survival is mild therapeutic hypothermia (MTH). The relationship between esophageal temperature post OHCA and outcome is still poorly defined.

Methods: Prospective observational study of all OHCA patients admitted to a single centre for a 14-month period (1/08/2008 to 31/09/2009). Esophageal temperature was measured in the Emergency Department and Intensive Care Unit (ICU). Selected patients had pre-hospital temperature monitoring. Time taken to reach target temperature after ROSC was recorded, together with time to admission to the Emergency Department and ICU.

Results: 164 OHCA patients were included in the study. 105 (64.0%) were pronounced dead in the Emergency Department. 59 (36.0%) were admitted to ICU for cooling; 40 (24.4%) died in ICU and 19 (11.6%) survived to hospital discharge. Patients who achieved ROSC and had esophageal temperature measured pre-hospital (n = 29) had a mean pre-hospital temperature of 33.9 °C (95% CI 33.2–34.5). All patients arriving in the ED post OHCA had a relatively low esophageal temperature (34.3 °C, 95% CI 34.1–34.6). Patients surviving to hospital discharge were warmer on admission to ICU than patients who died in hospital (35.7 °C vs 34.3 °C, p < 0.05). Patients surviving to hospital discharge also took longer to reach $T_{\text{target}}$ than non-survivors (2 h 48 min vs 1 h 32 min, p < 0.05).

Conclusions: Following OHCA all patients have esophageal temperatures below normal in the pre-hospital phase and on arrival in the Emergency Department. Patients who achieve ROSC following OHCA and survive to hospital discharge are warmer on arrival in ICU and take longer to reach target MTH temperatures compared to patients who die in hospital. The mechanisms of action underlying esophageal temperature and survival from OHCA remain unclear and further research is warranted to clarify this relationship.

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1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a significant cause of death and severe neurological disability across Europe. Resuscitation is attempted in 66 per 100,000 population annually.\textsuperscript{1} Despite efforts to optimise early access to advanced cardiac life support, survival rates from OHCA remain low, with survival to hospital discharge rates varying from less than 5% to over 10%.\textsuperscript{2,3} Good quality cardiopulmonary resuscitation and prompt defibrillation are key interventions to achieve return of spontaneous circulation (ROSC) and neurologically intact survival. Following ROSC the aim is to limit further brain injury and minimise subsequent morbidity and mortality. The only post-ROSC therapy shown to increase survival and improve neurological outcome following OHCA is mild therapeutic hypothermia (MTH).

In 2002 two prospective randomised trials found that inducing MTH (32–34 °C) after OHCA could increase survival and reduce neurological morbidity.\textsuperscript{4,5} Both trials had similar recruitment criteria and included patients with ROSC who remained intubated and ventilated after OHCA due to ventricular fibrillation (VF) of presumed cardiac aetiology. Despite the uniformity of study groups, the implementation of MTH differed significantly between the two trials.

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In 2003, the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation (ILCOR) published an advisory statement indicating that further research was required to establish the optimum target temperature, optimal duration of hypothermia, rates of cooling and re-warming and an understanding of the mechanism of MTH.6 This call for further research was reiterated by ILCOR in 2007.7 To generate explanatory hypotheses answering some of these important clinical questions baseline observational data is required. Establishing the pattern of change of body temperature after OHCA will inform decisions about the most effective time to commence cooling and may enhance understanding of the mechanisms of MTH.

This prospective study aims to describe the natural progression of esophageal temperature following OHCA from the pre-hospital phase until arrival on the Intensive Care Unit (ICU) and observe any relationship between esophageal temperature, outcome and time to reach target temperature.

2. Methods

We prospectively collected data on OHCA in the Edinburgh area (population approximately 500,000) over a 14-month period (1st of August 2008 to 31st September 2009). OHCA patients transported to the Emergency Department (ED) of a single university teaching hospital (Royal Infirmary of Edinburgh) were enrolled in the study. Inclusion criteria were adult cardiac arrest of non-traumatic cause, unwitnessed by ambulance personnel and who remained comatose after ROSC. The study was approved by the Scottish national medical research ethics committee.

The Scottish Ambulance Service routinely collect Utstein template data on all OHCA patients. Time of emergency call, ambulance dispatch and on-scene times are recorded automatically by the ambulance service computer system with the aid of real-time satellite positioning. Ambulance records were matched with the ED and ICU patient notes. Patients were followed up to the point of discharge from the admitting hospital or death. Cerebral Performance Category8 was noted at the point of hospital discharge.

For a proportion of the OHCA episodes studied, a research doctor (RL) attended the scene with an ambulance crew. For these patients esophageal temperature ($T_{es}$) measurement was commenced in the field. All other OHCA patients had esophageal temperature measuring commenced on arrival in the ED. Esophageal temperature monitoring is the most practical means of accurately measuring core body temperature during the pre-hospital phase of patient care. An esophageal temperature probe was marked at 15 cm from the tip and inserted as soon as practical during the resuscitation. The thermometer tip was therefore 15 cm from the nostril and the position confirmed by laryngoscopy. The probe was linked to a digital recording thermometer (DataTherm II) with esophageal temperature recorded every 10 min to 0.1 °C accuracy. Esophageal temperature recording continued for a 24-h period.

We recorded the pattern of change in esophageal temperature from either the pre-hospital or ED phase of the OHCA patient’s journey until target temperature ($T_{targ} < 34$ °C) was reached in the ICU. Time taken to reach $T_{targ}$ after ROSC was recorded, together with time to admission to the ED and ICU and the time active cooling was commenced.

The study was approved by the Scottish National Research Ethics Committee. Consent from the next-of-kin was sought until the patient was able to give informed consent. If the patient did not survive, permission was granted from the Ethics Committee to use the research data.

In the receiving hospital, cooling is routinely initiated after admission to the ICU. Body surface cooling (Arctic Sun, Medivance Ltd) is used with automatic temperature feedback control. In a small proportion of cases cooling is commenced in the ED by placing ice packs on the patient. Patients who had active cooling initiated in the ED were excluded from the time point at which cooling was commenced. Data were entered into a database (Microsoft Access 2007) and analysed using statistical analysis software (Microsoft Excel 2007).
Table 1
Out-of-hospital cardiac arrest (OHCA) patient demographics. CPR: cardiopulmonary resuscitation; VF: ventricular fibrillation; PEA: pulseless electrical activity; NS: not significant; ROSC: return of spontaneous circulation; and Tₐ: target interquartile range.

<table>
<thead>
<tr>
<th>Number</th>
<th>Died in hospital (%)</th>
<th>Survived to hospital discharge (%)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>23 (57.5)</td>
<td>14 (73.7)</td>
<td>–</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>61.7</td>
<td>59.4</td>
<td>NS</td>
</tr>
<tr>
<td>Witnessed OHCA</td>
<td>23 (57.5)</td>
<td>12 (63.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Bystander CPR performed</td>
<td>19 (47.5)</td>
<td>9 (47.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2
Esophageal temperature of OHCA patients arriving in the Emergency Department (ED). Tₑ: esophageal temperature and ICU: Intensive Care Unit.

<table>
<thead>
<tr>
<th></th>
<th>Mean Tₑ on arrival ED</th>
<th>Standard deviation</th>
<th>95% CI of mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>34.3</td>
<td>1.59</td>
<td>34.1–34.6</td>
</tr>
<tr>
<td>Died in ED</td>
<td>34.1</td>
<td>1.70</td>
<td>33.8–34.5</td>
</tr>
<tr>
<td>Survived to ICU admission</td>
<td>34.4</td>
<td>1.37</td>
<td>34.0–34.9</td>
</tr>
<tr>
<td>Survived to hospital discharge</td>
<td>34.8</td>
<td>1.42</td>
<td>34.2–35.6</td>
</tr>
</tbody>
</table>

Excel 2009, SPSS 16.0). Values in the survivor and non-survivor groups were compared at two time points (arrival in the ED and arrival on the ICU) using an unpaired t-test. Statistical significance was taken at the 95% level.

3. Results

During the study period 183 OHCA patients were transported to the ED. Of these, 29 patients had pre-hospital esophageal temperature measurements performed. Four patients had cooling commenced in the ED, either ice packs or cold IV fluid and were excluded after cooling commenced as they could not be compared to the rest of the study cohort. Two patients were excluded as they were not comatose on arrival. ED temperature data was not available for 12 patients, all of whom subsequently died in the ED. Temperature data was available to all patients admitted to ICU. One patient refused consent after discharge from ICU. Patient enrolment into the study is shown in Fig. 1. A total of 164 patients were enrolled into the study and all were followed up until hospital discharge. On arrival in the ED, one patient was noted to have the temperature probe situated next to the cuff of the endotracheal tube on direct laryngoscopy and the probe was re-sited. Otherwise, no complications from temperature monitoring were observed.

105 (64.0%) patients were pronounced dead in the ED, 59 (35.6%) patients enrolled in the ED survived to admission to ICU and were eligible for inclusion. 19 (11.7%) enrolled patients survived to hospital discharge. 40 (25.0%) patients admitted to ICU subsequently died in hospital. Patient demographics and resuscitation details of survivors and non-survivors are shown in Table 1.

Patients who achieved ROSC and had esophageal temperature measured pre-hospital (n = 29) had a mean esophageal temperature of 33.9 °C (95% CI 33.2–34.5). All eligible patients arriving in the ED post OHCA (n = 164) also had a relatively low esophageal temperature (Table 2) but there was no significant difference in ED esophageal temperature between patients who died in hospital (n = 40) and patients surviving to hospital discharge (n = 19).

The majority of survivors had a favourable Cerebral Performance Score (CPC) at hospital discharge (CPC 1: n = 8, CPC 2: n = 8). Three survivors had poor neurological outcome at hospital discharge (CPC 3: n = 2, CPC 4: n = 1). 16 non-survivors who were admitted to ICU had severe, isolated, ischaemic brain injury (including three with brain stem death). All of these patients arrived in the ED cool (mean Tₑ 34.5 °C; 95% CI 33.7–35.3) and did not appear to re-warm prior to ICU admission (mean ICU admission Tₑ 34.2 °C; 95% CI 33.6–34.8).

Patients surviving to hospital discharge were warmer on admission to ICU than patients who survived to ICU admission but subsequently died in hospital. There was no significant difference from the time of ROSC to ICU admission in survivors and non-survivors (3 h 18 min vs 3 h 38 min, p = 0.71). Patients surviving to hospital discharge also took longer to reach Tₑ targ (<34 °C) once cooling was commenced (Table 3). The progression of Tₑ post-ROSC is shown in Fig. 2.

4. Discussion

In this single centre observational study, we found that esophageal temperature follows a predictable pattern in the first few minutes and hours after OHCA. Patients in our study cooled quickly in the pre-hospital phase and remained cool in transit to the ED. Thereafter, patients destined to survive to discharge appeared to re-warm faster before cooling was commenced and took longer to reach target temperature, a finding not yet described in the literature. Esophageal temperature on arrival in the ED was 34.4 °C (range 30.5–36.6 °C) – comparable to the target temperature reached in a recent pre-hospital pilot study of the feasibility of cooling post OHCA and also previously published studies. Patients in our study maintained esophageal temperature close to the target range for MTH throughout the pre-hospital phase without specific intervention to lower temperature. Despite the paucity of clinical evidence demonstrating benefit, some ambulance services have adopted methods of initiating hypothermia in the pre-hospital phase. Cooling at the scene or during transport requires additional equipment, resources and monitoring and may distract from the basic practice of maintaining a patent airway, ventilation

Table 3
Esophageal temperature on admission to the Intensive Care Unit (ICU) and time to reach target temperature. Tₑ: esophageal temperature; ROSC: return of spontaneous circulation; and Tₑ targ: target therapeutic hypothermia of <34 °C.

<table>
<thead>
<tr>
<th></th>
<th>Died in hospital</th>
<th>Survived to hospital discharge</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Tₑ on arrival ICU</td>
<td>34.3 (95% CI 33.9–34.8)</td>
<td>35.7 (95% CI 35.2–36.3)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Mean time from ROSC to arrival ICU</td>
<td>159 min (95% CI 137–183)</td>
<td>169 min (95% CI 140–198)</td>
<td>0.60</td>
</tr>
<tr>
<td>Mean time from ROSC to Tₑ targ (&lt;34 °C)</td>
<td>219 min (95% CI 165–271)</td>
<td>320 min (95% CI 266–374)</td>
<td>0.019</td>
</tr>
<tr>
<td>Mean time from arrival ICU to Tₑ targ</td>
<td>96 min (95% CI 56–136)</td>
<td>168 min (95% CI 118–217)</td>
<td>0.028</td>
</tr>
</tbody>
</table>
and adequate circulation. Further research is currently underway to establish whether pre-hospital cooling really confers additional benefit. A North American study of outcome from cardiac arrest when cold IV fluids are infused in the pre-hospital setting is currently recruiting (http://www.ClinicalTrials.gov/identifier NCT00391469).

Several studies have previously noted episodes of hyperthermia occurring in patients following cardiac arrest but our study reports a correlation between early changes in esophageal temperature within the normothermic range and patient survival. The reason for this observation remains uncertain. We noted a significant difference in the time between collapse and ROSC between survivors non-survivors. Longer collapse-ROSC times are likely to be associated with greater neurological injury and impairment of central mechanisms of body temperature control.

Patients who survive to hospital discharge may have better cardiac function following ROSC and less hypothalamic damage, leading to a higher esophageal temperature as a function of greater cardiac output and intact thermoregulation. Several (n = 16) non-survivors had severe neurological injury as their eventual cause of death and all remained hypothermic after ROSC.

Body temperature lability – episodes of both hyperpyrexia and spontaneous hypothermia – have recently been shown to be adversely linked to outcome in patients following in-hospital cardiac arrest. The mechanism for this is unknown though there are similarities to the temperature dysregulation found in severe sepsis. In sepsis, development of spontaneous hypothermia is associated with greater neurological injury although animal work suggests that controlled MTH may improve outcomes.

The optimal timing for initiating MTH after OHCA is unclear. There is limited animal evidence suggesting that early initiation of cooling is beneficial. There is no direct clinical evidence to support the immediate initiation of cooling, although retrospective analysis has indicated a possible benefit to patients cooled shortly after ROSC. Several studies have examined the possibility of pre-hospital cooling but prospective randomised clinical trials have, so far, failed to demonstrate any survival benefit. A temperature rise >38°C is often seen in patients following OHCA but it is unclear whether this bears any causal relationship to survival or neurological outcome, and the reason for this pyrexia is unknown.

In our study, cooling was initiated approximately 2 h after ROSC, on arrival on the ICU. If MTH is not commenced in patients following OHCA, many patients develop a mild pyrexia commencing around 8 h after ROSC. Hyperthermia following OHCA has previously been associated with poor outcome. Episodes of pyrexia are correlated with poorer neurological outcome in focal ischaemic brain injury, and measures are taken to actively keep these patients normothermic. Pyrexia after OHCA may reflect a pro-inflammatory cytokine-mediated response to the whole body ischaemia-reperfusion insult during resuscitation. It is postulated that this inflammatory response may cause multi-organ injury and, that in particular, exacerbate neurological injury. Because the mechanism of the benefit accrued from MTH is uncertain it is difficult to build a physiological rationale for the optimum target temperature for therapeutic hypothermia. It is unclear whether it is tissue cooling per se (with reduction in oxygen demand and modulation of tissue injury pathways) that improves outcome, or whether the attenuation of specific elements in the inflammatory response to OHCA is also crucially important. It is possible that maintenance of normothermia with immune-modulation and other strategies for neuroprotection post-ROSC could provide similar benefits to whole body cooling. Further research is warranted to determine the mechanism by which MTH confers neurological protection and the optimum modality, timing and duration of cooling.

Our study should be interpreted in the context of certain limitations. Whilst we observed several statistically significant results, our data was collected from a relatively small number of patients in a single centre. We did, however, achieve a high degree of data capture on all patients enrolled in the study. Body temperature was recorded using esophageal probes with instructions given to insert the probe to 15 cm from the nostril. Placing these probes in the field or in the ED may have resulted in probes not being inserted to adequate length and sitting in the posterior nasopharynx. This may have altered temperature recordings slightly, however there was strong pre-hospital agreement in temperature in all patients. The esophagus is an accurate site to measure body temperature, second only to the pulmonary artery, and is more robust than other techniques commonly used in our setting (e.g. tympanic membrane temperature using an infrared probe). Esophageal temperature monitoring is also the most practical means of accurately measuring body temperature during the pre-hospital phase of patient care.

5. Conclusion

Following OHCA all patients have esophageal temperatures below normal in the pre-hospital phase and on arrival in the ED. Patients who achieve ROSC following OHCA and survive to hospital discharge are warmer on arrival in ICU and take longer to reach target MTH temperatures compared to patients who die in hospital. The mechanisms of action underlying esophageal temperature and survival from OHCA remain unclear and further research is warranted to clarify this relationship.

Conflict of interest statement

The authors have no relationships with organisations that could inappropriately influence their work. The manuscript, data, tables and figures have not been submitted for publications elsewhere. Dr Lyon is supported by a Clinical Research Fellowship from Chest, Heart and Stroke Scotland. Dr Clegg is supported by a Fellowship from the Chief Scientist Office, Scotland. Dr Lyon had full access to the generated data and takes full responsibility for the integrity of data and accuracy of data analysis.
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