

Temperature management in ventilated adults admitted to Australian and New Zealand ICUs following out of hospital cardiac arrest: study protocol

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BACKGROUND

Out-of-hospital cardiac arrest (OHCA) carries a high risk for major neurological morbidity and mortality[1]. Among comatose patients admitted to intensive care units (ICUs) following resuscitation from cardiac arrest, targeted temperature management appears to improve in neurological outcome[2, 3] and survival[3] compared to strategies employing no temperature management. Prior to 2013 the standard of care involved cooling patients to 32-34°C for 12-24 hours[4, 5]. In 2013 the *Targeted Temperature Management at 33°C versus 36°C After Cardiac Arrest trial (the TTM trial)* revealed no difference in survival or major neurological disability between patients allocated to targeted temperature management at 33°C compared to those receiving temperature management at 36°C[6]. However, the confidence intervals around survival estimates in the TTM trial (hazard ratio with a temperature of 33°C, 1.06; 95% confidence interval [CI], 0.89 to 1.28; P=0.51)[6] did not preclude the possibility of clinically important benefit or harm with either temperature strategy. Moreover, recent data raise the possibility that implementation of a policy of targeted temperature management (TTM) at 36°C may reduce complications compared to TTM at 33°C[7, 8].

Data from the UK, USA, Finland and Netherlands have demonstrated that risk-adjusted mortality following OHCA is reducing over time[9-12]. Similar data have not been published from Australia and New Zealand (ANZ), and, of particular interest, the changes in temperature management that have occurred in ANZ ICUs following the publication of the TTM trial are unknown.

HYPOTHESES

Our primary hypothesis is that there has been widespread adoption of TTM at 36°C in ANZ ICUs since the publication of the TTM trial. We further hypothesise that the mortality of OHCA patients in ANZ ICUs has been decreasing with time and that this temporal trend towards decreasing mortality has accelerated in association with the increased adoption of TTM at 36°C.

METHODS

Study design

Retrospective cohort study using data from the Australian and New Zealand Intensive Care Centre for Outcome and Resource Evaluation Adult Patient Database (ANZICS-CORE APD).

Eligibility

Patients will be eligible for inclusion if they fulfil all of the following inclusion criteria:

1. Mechanically ventilated adults (aged 18 years or older)
2. Admitted to ICU from an emergency department within 24 hours of hospital admission
3. An admission APACHE diagnostic code of cardiac arrest (diagnostic code 102) OR documented cardiac arrest within 24 hours prior to ICU admission

Patients will be excluded if they are admitted to ICU for palliative care or with limitations of treatment in place.

Exposures of interest

The primary exposure of interest is the admission before vs. after publication of the TTM trial results in December 2013.

Outcome variables

The primary outcome variable of interest to evaluate the adoption of TTM in ANZ ICUs is the lowest temperature in the 1st 24 hours in ICU before and after the publication of the TTM trial (in December 2013).

The primary clinical outcome variable of interest is in-hospital mortality.

Other clinical outcome variables of interest are:

1. the proportion of patients with a body temperature of 38°C or more in the first 24 hours in ICU
2. the ICU length of stay overall and for survivors and non-survivors separately
3. the hospital length of stay overall and for survivors and non-survivors separately
4. the proportion of patients discharged home
5. the proportion of survivors discharged home
6. the proportion of survivors discharged to a rehabilitation facility

Baseline variables of interest, effect modifiers, and confounders

Age, gender, chronic comorbidities, smoking status, location of ICU (Australia vs. New Zealand) and type of ICU (tertiary vs. non-tertiary) will be reported as baseline variables. The ANZ risk of death (ROD) score, which is based on co-morbidities and physiological data from the first 24 hours in ICU will be reported[13, 14].

Because use of therapeutic hypothermia will directly alter the temperature in the first 24 hours in ICU, the ANZ ROD score will also be reported with contribution to the score from the temperature component removed.

In addition, because arterial blood gas measurements of partial pressure of oxygen (PaO₂) and blood pH may be affected by blood temperature[15] and

cooling to 33°C would be expected to directly alter heart rate, urine output, and respiratory rate without necessarily altering illness severity an ANZ ROD score with temperature, PaO₂, pH, heart rate, urine output, and respiratory rate components removed will be reported.

Subgroups

Pre-specified subgroups of interest are:

1. Patients admitted to tertiary ICUs vs. not
2. Patients admitted to NZ ICUs vs. Australian ICUs
3. Patients less than the median age vs. patients of the median age or older

Statistical analyses

The statistical analysis plan will be outlined in a separate statistical analysis plan document. Analyses will be reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (Strobe) Checklist[16].

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