Guideline 11.8 – Targeted Temperature Management (TTM) after Cardiac Arrest

Summary

This guideline provides advice on targeted temperature management (TTM) during the post-arrest period which is a therapy associated with improved outcomes.

Who does this guideline apply to?

This guideline applies to adults who require advanced life support after cardiac arrest

Who is the audience for this guideline?

This guideline is for health professionals and those who provide healthcare in environments where equipment and drugs are available.

Recommendations

The Australian and New Zealand Committee on Resuscitation (ANZCOR) make the following recommendations:

1. ANZCOR recommends TTM as opposed to no TTM for adults with out-of-hospital cardiac arrest (OHCA) with an initial shockable rhythm who remain unresponsive after ROSC.
2. ANZCOR suggests TTM as opposed to no TTM for adults with OHCA with an initial non-shockable rhythm who remain unresponsive after ROSC.
3. ANZCOR suggests TTM as opposed to no TTM for adults with in-hospital cardiac arrest (IHCA) with any initial rhythm who remain unresponsive after ROSC.
4. ANZCOR recommends selecting and maintaining a constant target temperature between 32°C and 36°C for those patients in whom TTM is used.
5. No studies specifically address cardiac arrests due to non-cardiac causes, but it is reasonable to assume that these patients might also benefit from targeted temperature management.
6. Rapid infusion of ice-cold intravenous fluid, up to 30 ml kg-1 or ice packs are feasible, safe and simple methods for initially lowering core temperature up to 1.5 degrees. When intravenous fluids are used to induce hypothermia additional cooling strategies will be required to maintain hypothermia.
7. ANZCOR recommends against routine use of pre-hospital cooling with rapid infusion of

large volumes of cold intravenous fluid immediately after ROSC.
8. ANZCOR suggests that if TTM is used, duration should be at least 24 hours.
9. ANZCOR suggests that percutaneous coronary intervention during TTM is feasible and safe and may be associated with improved outcome.
10. ANZCOR suggests institutions or communities planning to implement complex guidelines, such as targeted temperature management should consider using a comprehensive, multifaceted approach, including: clinical champions; a consensus-building process; multidisciplinary involvement; written protocols; detailed process description; practical logistic support; multi-modality, multi-level education; and rapid cycle improvement methods.
11. ANZCOR suggests prevention and treatment of fever in persistently comatose adults after completion of TTM between 32°C and 36°C.

Guideline

Induced hypothermia has been successfully used during cardiac surgery to protect against global cerebral ischaemia. Its use has been described in other clinical settings since the 1950s, particularly following cardiac arrest. Several animal and human studies have demonstrated the potential for therapeutic hypothermia to improve survival and neurological outcome in victims of cardiac arrest. The term targeted temperature management (TTM) is preferred to therapeutic hypothermia.

1.0 | Who to cool and what temperature to cool to?

All studies of post-cardiac arrest therapeutic hypothermia have included only patients in coma. One trial defined coma as “not responding to verbal commands”. The other trials defined coma similarly, used GCS ≤8, or did not provide a clear definition.[1]

One randomised controlled trial[2] (RCT) and a quasi-randomised trial[3] demonstrated improved neurological outcome at hospital discharge or at 6 months after hospital discharge in comatose patients after out-of-hospital ventricular fibrillation cardiac arrest. Cooling was initiated within minutes to hours after return of spontaneous circulation and a temperature range of 32-34ºC was maintained for 12- 24 hours. Studies with historical control groups have shown improvement in neurological outcome after therapeutic hypothermia for comatose survivors of ventricular fibrillation cardiac arrest and a systematic review demonstrated that conventional cooling methods were more likely to reach a best cerebral performance category score of 1 or 2 (five point scale where one is good and five is brain death) with a relative risk of 1.55 995% CI 1.22-1.96) and more likely to survive to hospital discharge (relative risk of 1.35 95% CI 1.1 to 1.65) compared with standard post resuscitation care.[1, 4]

Cohort studies comparing mild induced hypothermia (32–34◦C) to no temperature management in OHCA found no difference in neurological outcome.[5-7] While a retrospective registry study of 1830 patients documented an increase in poor neurological out-come among those with non shockable OHCA and treated with mild hypothermia.[8] One retrospective cohort study of 8316 in-hospital cardiac arrest (IHCA) patients of any initial rhythm showed no difference in survival to

hospital discharge among those who were treated with mild induced hypothermia compared with no active temperature management.[9]

One large RCT (the TTM trial, 939 patients) compared cooling to 33°C compared with tight temperature control at 36°C in adult patients with OHCA of any initial rhythm except unwitnessed asystole, and found no benefit in outcome (survival or neurological).[10]

The vast majority of the patients studied with induced hypothermia were from cardiac arrests due to presumed cardiac causes.

Recommendations

ANZCOR recommends TTM as opposed to no TTM for adults with out-of-hospital cardiac arrest (OHCA) with an initial shockable rhythm who remain unresponsive after ROSC (CoSTR 2015, strong recommendation, low-quality evidence).[11]

ANZCOR suggests TTM as opposed to no TTM for adults with OHCA with an initial non-shockable rhythm who remain unresponsive after ROSC (CoSTR 2015, weak recommendation, very low-quality evidence).[11]

ANZCOR suggests TTM as opposed to no TTM for adults with in-hospital cardiac arrest (IHCA) with any initial rhythm who remain unresponsive after ROSC (CoSTR 2015, weak recommendation, very low-quality evidence).[11]

ANZCOR recommends selecting and maintaining a constant target temperature between 32°C and 36°C for those patients in whom TTM is used. (CoSTR 2015, strong recommendation, moderate-quality evidence). Whether certain subpopulations of cardiac arrest patients may benefit from lower (32-34°C) or higher (36°C) temperatures remains unknown.[11]

No studies specifically addressed cardiac arrests due to non-cardiac causes, but it is reasonable to assume that these patients might also benefit from targeted temperature management. [Class B; Expert consensus opinion]

Values and preferences

We place a higher value on the potential for increased survival with good neurologic outcome as compared with the possible risks (which appear to be minimal) and the cost of TTM. We emphasize that the mortality after cardiac arrest is high and the treatment options are limited. Although the evidence for TTM compared with no temperature management is of low quality, it is the only post-ROSC intervention that has been found to improve survival with good neurologic outcome.[11]

2.0 | How to cool?

Nineteen studies indicated that cooling could be initiated safely with intravenous ice-cold fluids (30 ml/kg of saline 0.9% or Ringer's lactate).[1] Six studies indicated that cooling with IV cold saline could be initiated in the prehospital phase.[1] Thirteen studies documented the use of an intravascular heat exchanger to induce and maintain hypothermia.[1] Twelve studies documented the use of ice packs and either water or air circulating blankets to induce and maintain

hypothermia.[1]

Seven studies documented the use of ice packs (sometimes combined with wet towels) alone to induce and maintain hypothermia. Four studies documented the use of ice packs alone to maintain hypothermia. Seven studies documented the use of cooling blankets or pads alone to induce and maintain hypothermia.[1] Eight studies documented the use of water circulating gel-coated pads to induce and maintain, or just maintain, hypothermia.[1]

One randomised controlled trial used a cold air tent and another used a cooling helmet to induce and maintain hypothermia. In one registry study, cooling was maintained with ice-packs (17%), air cooling (8%), circulating water blankets (63%), an intravascular cooling device (16%) and other methods (8%).[1] More recently transnasal evaporative cooling and cooling by extracorporeal circulation have also been studied.[12-14]

There are currently no data indicating that any specific cooling technique increases survival when compared with any other cooling technique.

Studies that documented improved outcome with therapeutic hypothermia after cardiac arrest used continuous temperature monitoring.[1] Shivering may necessitate sedation and intermittent or continuous neuromuscular blockade. Use of continuous neuromuscular blockade could mask seizure activity.[1]

Recommendation

Rapid infusion of ice-cold intravenous fluid, up to 30 ml kg-1 or ice packs are feasible, safe and simple methods for initially lowering core temperature up to 1.5 degrees. When intravenous fluids are used to induce hypothermia additional cooling strategies will be required to maintain hypothermia.[1] [Class B; LOE III-3, IV]

3.0 | When to cool?

One registry-based case series of 986 comatose post-cardiac arrest patients suggested that time to initiation cooling (median 90 min; interquartile range 60 -165 min) was not associated with improved neurological outcome post discharge.[15]

A case series of 49 consecutive comatose post-cardiac arrest patients who were intravascularly cooled after out-of-hospital cardiac arrest also documented that time to target temperature (median 6.8 hours [IQR 4.5 to 9.2 hours]) was not an independent predictor of neurologic outcome.[16]

5 trials (1,867 subjects) of OHCA showed no difference in neurologic outcomes after initiation of induced hypothermia in the pre-hospital environment compared with later initiation. Seven trials found no improvement in mortality for patients treated with pre-hospital cooling compared to those who did not receive pre-hospital cooling.[11]

Four RCTs showed an increased risk of re-arrest for those who received pre-hospital induced hypothermia. This result was driven by data from the largest trial (the TTM trial).[10]

Three trials reported no pulmonary oedema in any group. Two small pilot trials found no

difference between groups, and one trial showed an increase in pulmonary oedema in patients who received pre-hospital cooling.[11]

Recommendation

ANZCOR recommends against routine use of pre-hospital cooling with rapid infusion of large volumes of cold intravenous fluid immediately after ROSC (CoSTR 2015, strong recommendation, moderate-quality evidence).[11]

Values and Preferences

Pre-hospital cooling has not demonstrated benefit despite a large number of patients studied, and there has been the suggestion of increased risk of re-arrest with pre-hospital induction of mild hypothermia using rapid infusion of cold intravenous fluids.

However, it is acknowledged that cold intravenous fluid might still be used in patients who have been further evaluated or in other settings.[11]

4.0 | Duration of Cooling

No human trials have compared different durations of targeted temperature management after cardiac arrest. Published trials have treated patients with cooling for 12-28 hours and the TTM trial maintained strict normothermia (<37.5◦C) after hypothermia until 72 h after ROSC.[10] Two observational studies found no difference in outcome with 24 h compared with 72 h of hypothermia[17,18]

Recommendation

ANZCOR suggests that if TTM is used, duration should be at least 24 hours (CoSTR 2015, weak recommendation, very low-quality evidence).[11]

5.0 | Safety with Percutaneous Coronary Intervention?

Five studies indicate that the combination of therapeutic hypothermia and primary percutaneous intervention was feasible and safe after cardiac arrest caused by acute myocardial infarction.[1]

Recommendation

ANZCOR suggests that percutaneous coronary intervention during TTM is feasible and safe and may be associated with improved outcome.[1] [Class B; LOE III-3, IV]

ANZCOR suggests institutions or communities planning to implement complex guidelines, such as targeted temperature management should consider using a comprehensive, multifaceted approach, including: clinical champions; a consensus-building process; multidisciplinary

involvement; written protocols; detailed process description; practical logistic support; multi-modality, multi-level education; and rapid cycle improvement methods.[19] [Class B; Expert consensus opinion]

6.0 | Avoidance of Fever after ROSC

In the absence of the use of targeted temperature management, five observational studies have demonstrated poor outcome with fever after ROSC.

When targeted temperature management has been used, six observational studies have not shown an association between fever after TTM and outcome (survival or neurological). However, two observational studies have demonstrated poorer outcome (survival or neurological) with fever after TTM.[11]

Recommendation

ANZCOR suggests prevention and treatment of fever in persistently comatose adults after completion of TTM between 32°C and 36°C (CoSTR 2015, weak recommendation, very low quality evidence).[11]

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