**Clinical question.**

In adult patients (prehospital or in-hospital) who are comatose after cardiac arrest (P) does treatment of pyrexia (I) compared to no temperature intervention (C) improve outcome (eg. survival).

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** Intervention-

**State if this is a proposed new topic or revision of existing worksheet:** Revision

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? **No conflict of interest**

**Search strategy (including electronic databases searched).**

- PubMed "pyrexia" AND "cardiac arrest"
- Embase "pyrexia" AND "cardiac arrest"
- Cochrane database "pyrexia" AND "cardiac arrest"
- PubMed search using "cardiopulmonary resuscitation" [Mesh] and pyrexia
- PubMed search using "heart arrest" [Mesh] and pyrexia
- PubMed search using: body temperature, stroke, mortality.

Twenty one Articles found were in pediatric population, animal studies, review articles, commentaries and studies concerned adult population in comatose state after cardiac arrest. Other studies found investigated the role of hyperthermia in short and long term mortality in patients with cerebrovascular event. Eleven articles included based on inclusion and exclusion criteria.

**State inclusion and exclusion criteria**

**Inclusion Criteria:**
1. Original studies with comatose patients after cardiac arrest and outcome (e.g. survival) related to pyrexia
2. Original studies with comatose patients after cerebrovascular event and outcome (e.g. survival) related to pyrexia.

**Exclusion Criteria:**
1. Animal studies
2. Review articles
3. Commentaries
4. Meta analysis

**Number of articles/sources meeting criteria for further review:**
Eleven studies met the criteria for further review. Five were LOE 4 and six studies were LOE 5.
## Summary of evidence

### Evidence Supporting Clinical Question

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<th>Level of evidence</th>
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<td>Italics = Animal studies</td>
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- A = Return of spontaneous circulation
- B = Survival of event
- C = Survival to hospital discharge
- D = Intact neurological survival
- E = Other endpoint

Italics = Animal studies
### Evidence Neutral to Clinical question

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#### Level of evidence

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italics = Animal studies*

### Evidence Opposing Clinical Question

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#### Level of evidence

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italics = Animal studies*
It is known that the pathophysiology of hyperthermia after cardiac arrest is attributed to mechanisms such as the endogenous release of catecholamines and heat production and also the thermodynamicsregulation of the central nervous system. Moreover, decreased heat loss or altered distribution of body heat due to vasoconstriction may also add to the yet not clearly defined mechanism of post resuscitation hyperthermia. From the literature review, in observational and retrospective studies is shown that patients with pyrexia post cardiac arrest were associated with worse outcome. It seems that the degree and rate of development of hyperthermia is greater in groups with poorer outcome (Kammersgaard. 2003, 5), (Hanchaiphiboolkul.S 2005, 28), (Zeiner A. 2001, 161). Nevertheless, there is no strong evidence to prove that the treatment of pyrexia versus no treatment improves outcome, in comatose patients after cardiac arrest. The main reason is that no randomized trials were found in the literature, for this, we don't know whether this is simply attributed to the presence of pyrexia or other factors such as delay to start CPR. It seems that it is not possible to determine whether temperature control influence survival and or neurologic outcome. The studies of (Takino 1991, 419), (Takasu 2001, 273), (Zeiner A. et al 2001, 2007) show an association between fever and worsened neurologic outcome after cardiac arrest. Additionally, in other studies than those included for this question we found that comatose patients after cerebrovascular event which develop pyrexia were also associated with worsened neurologic outcome such as increase In mortality (Diringer 2004, 2170), (Yang, et al 2000, 204). There is only one randomized prospective trial pertaining to fever in neurological patients in which No cardiac arrest patients are enrolled. (Diringer 2004, 559)

If fever can exacerbate brain injury, either in patients after stroke or cardiac arrest, then this is a serious clinical problem that should be managed expectantly (Hickey 2000, 118).

Acknowledgements:
Nil

Citation List


Elevated temperature worsens outcome in experimental models of cerebral ischemia and brain trauma; this is associated with increased levels of excitotoxins and oxygen radicals, destabilization of cell membranes, and increased number of abnormal electrical depolarizations (1-5). Even an increase in temperature of 0.5°C results in a greater zone of injury and neuronal loss (5-8). Fever is common in critically ill neurologic and neurological patients, and its causes include not only infections but also the release of endogenous pyrogens due to neuronal injury or the presence of blood in the cerebral parenchymal, ventricles, and subarachnoid space.

Fever is an independent predictor of poor outcome in patients with ischemic stroke, intracerebral hemorrhage and subarachnoid hemorrhage (9-14). The impact of fever control on clinical outcome, however, has not yet been tested, in large part due to the lack of an effective means to control fever. Despite this, taking measures to reduce fever is recommended by guidelines for the management of ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and traumatic brain injury (15-18). The most commonly used antipyretic is acetaminophen, although aspirin, ibuprofen, or indomethacin are used when the risk of bleeding is considered low. Acetaminophen is not very effective at preventing or reducing fever. When high-dose acetaminophen was given prospectively to ischemic stroke patients, the average temperature during the first 24 hrs after admission was 0.4°C lower than placebo-treated patients and no different after 5 days (19). In a prospective, randomized study of 220 febrile neurologic intensive care unit (ICU) patients, half were treated with acetaminophen and half with acetaminophen plus air-cooled blanket therapy. In the acetaminophen group about one third of patients remained febrile, and the air-cooled blanket did not improve fever control (20).

Physical means used to lower temperature include surface cooling with water or air-filled cooling blankets, ice packs, nasogastric or rectal lavage, and alcohol baths. These methods may have limited efficiency due to skin vasoconstriction and shivering. In one study, (20) 12% of patients refused or were unable to tolerate the air-cooled blanket therapy. External cooling with rotary fans, cooling blankets, and alcohol sponge baths are also time consuming and challenging for the nursing staff (21). The goal of this study was to test the hypothesis that in neurologic ICU patients, an intravascular catheter-based cooling system was more effective in controlling fever than conventional means.

Level 5 study neutral — Quality assessment: poor

   Level 5 study neutral – Quality assessment: poor


   Level 5 study neutral – Quality assessment: good


   Level 4 study neutral – Quality assessment: poor.


   Level 5 study neutral – Quality assessment: good


   Level 4 study neutral - Quality assessment: poor.


   Level 5 study neutral – Quality assessment: poor


   Level 4 study neutral - Quality assessment: poor.


   Level 4 study neutral - Quality assessment: Good.


   Level 5 study neutral – Quality assessment: good


   Level 4 study neutral - Quality assessment: Good.