Clinical question.
In post-cardiac arrest patients treated with hypothermia (P), can the same prognostication tools that are used in normothermic patients (I) reliably predict outcome (O)

Suggested changes: 1. Change “post-cardiac arrest patients” to “patients that remain comatose 24 hours after cardiac arrest who were”
2. Change “outcome” to “poor outcome”

Is this question addressing an intervention/therapy, prognosis or diagnosis? PROGNOSIS

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

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

Search strategy (including electronic databases searched).

Neumar
Cochrane Library: Title, Abstract, Keywords: “Heart Arrest” and “Prognosis” and “Hypothermia” (0 Cochrane reviews and 0 other reviews)
Embase: Search (heart arrest.mp or exp Heart Arrest/) or (cardiopulmonary arrest.mp or exp Cardiopulmonary Arrest/) or (cardiopulmonary resuscitation) and (prognosis.mp or exp PROGNOSIS/) and (hypothermia.mp. or exp HYPOTHERMIA/ or exp INDUCED HYPOTHERMIA/) (110 articles)
AHA Endnote Library: Key Word “Prognostication” 13 articles

Searches Repeated October 29th, 2009
Cochrane Library: 6 Articles
Pubmed: 203 articles
Embase: 225 articles

Friberg and Rundgren
PubMed - search 1:
"Heart Arrest" or "Cardiopulmonary Resuscitation" as MESH (headings) AND "Hypothermia, Induced". Clinical Queries - prognosis - narrow, specific search: this yielded 34 articles. After addition of Limits; human studies, English, adults, 16 articles remained.

PubMed - search 2:
"Heart Arrest" AND "Hypothermia Induced" AND "Prognosis"; this yielded 131 articles. After addition of Limits; humans, english, all adults 19+ years, clinical trial, meta-analysis, RCT, 20 articles remained.

Cochrane Library:
"Heart Arrest" AND "Hypothermia Induced" AND "Prognosis". 15 articles were identified.

AHA Endnote Database:
"Cardiac Arrest" AND "Hypothermia" AND "Prognosis", 22 articles were identified.

Searches Repeated October 29th, 2009
Pubmed 1: 26 articles
Pubmed 2: 57 articles
Cochrane Library: 8 articles

• State inclusion and exclusion criteria

Neumar
Inclusion: Human studies that included post-cardiac arrest patients treated with induced hypothermia and evaluated tools for early prognostication of poor outcome.

Exclusion: 1) Non-human studies, 2) studies of coma after non-cardiac arrest brain injury 3) studies that did not separately analyze post-cardiac arrest patients treated with induced hypothermia 4) isolated case studies, 5) review articles.

Friberg and Rundgren
PubMed search 1; 9 of 16 studies were excluded:
Review-articles (1), Irrelevant intervention studies (2), Implementation or outcome studies (5), case report (1).

PubMed search 2; 17 of 20 articles were excluded:
Review-articles (2), Irrelevant intervention studies (6). Implementation or outcome studies (9).

Cochrane Library: 13 of 15 articles were excluded; Irrelevant intervention studies (12), Implementation or outcome studies (1)

AHA Endnote Database: 20 of 22 were excluded; review articles (6), Irrelevant intervention studies (1), case reports (2), 11 articles prior to 2002 excluded

- Number of articles/sources meeting criteria for further review:

**Neumar**
13 Studies were reviewed

**Friberg and Rundgren**
A total of 7 separate articles were identified from the PubMed, Cochrane and AHA searches, listed below.

Another 6 articles were identified by ourselves through reference lists of relevant articles etc, listed below.

Hence, a total of 13 articles were reviewed, see below.
The reason why 14 references are listed is that the Zandbergen reference (Propac study) is just used in the discussion below.

## Summary of evidence

### Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th>Kaneko 2009E*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td>Oksanen 2009E*</td>
</tr>
<tr>
<td>Poor</td>
<td>Tiainen 2005 E*</td>
</tr>
<tr>
<td></td>
<td>Al Thenayan 2008 E*</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
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<td>3</td>
<td>4</td>
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<tr>
<td>5</td>
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</tr>
</tbody>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
* = Poor outcome (CPC 3-5)  
*Italic = Animal studies
### Evidence Neutral to Clinical question

<table>
<thead>
<tr>
<th>Good</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Fair</td>
<td>Stammert 2009 E*</td>
<td>Derwall 2009 E#</td>
<td>Rundgren 2006 E*</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>Hachimi-Idrissi 2005</td>
<td></td>
<td>Yannopoulus 2007 D</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
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<td>5</td>
</tr>
</tbody>
</table>

**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

* = Poor outcome (CPC 3-5)  
#= 14 day survival

### Evidence Opposing Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td>Rossetti 2009 E*</td>
<td>Rossetti 2007 E*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>Al Thenayan 2008 E*</td>
<td>Tiainen 2003 E*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**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

* = Poor outcome (CPC 3-5)
**REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:**

### A. Context

A recently published practice parameter based on structured evidence evaluation recommended that the following prognosticators of poor outcome in comatose post-cardiac arrest patients are accurate enough to justify withdrawal of care in the absence of major confounders. (Wijdicks, 2006, 203)

1. Brain death at any time post-arrest
2. Myoclonus status epilepticus on day 1 [False positive rate (FPR) 0% (0-8.8%)]
3. SSEP bilaterally absent N20 responses on day 1-3 [FPR 0.7% (0.3-7%)]
4. Serum NSE > 33 ug/L on day 1-3 [FPR 0% (0-3%)]
5. Absent pupil or corneal reflexes, extensor or absent motor response on day 3 [FPR 0% (0-3%)]

Major confounders include the use or prior use of sedatives or neuromuscular blocking agents, *induced hypothermia therapy*, presence of organ failure or shock.

### B. Evidence evaluation for post-cardiac arrest patients treated with therapeutic hypothermia

#### Neurologic Examination

On retrospective chart review (Thenayan, 2009, 1535, LOE P1) of 37 consecutive patients who were comatose after cardiac arrest and treated with hypothermia found that 6 of 6 patients with absence of corneal reflex and pupillary activity 3 days post ROSC did not regain consciousness [FPR 0% (95% CI: 0-48%]. However, two of 14 patients with Glasgow Coma Scale motor score of 3 or less on day 3 regained consciousness. [FPR 14% 95% CI:3-44%] One had a 3-month Glasgow Outcome Score of 4 (disabled but independent) and one died in hospital of non-neurologic causes.

#### Myoclonus status epilepticus

On retrospective chart review (Thenayan, 2009, 1535, LOE P1 E) of 37 consecutive patients who were comatose after cardiac arrest and treated with hypothermia found that 8 of 8 patients with myoclonus status did not regain consciousness. [FPR 0% (95% CI:0-40%)]

#### Somatosensory Evoked Potentials (SSEP)

One study using data collected in a single center as part of a prospective randomized controlled clinical trial [Tiainen, 2005, 1736, LOE P1 E] demonstrated that although hypothermia decreases the latency, the bilateral absence of N20 wave on median nerve SSEPs had a false positive rate of 0% for poor outcome (CPC 3-5) in both the hypothermia and normothermia control groups. However only 3 patients in the study treated with hypothermia had this finding. [FPR 0%, (95% CI; 0-60%)].

#### Serum Neuron Specific Enolase (NSE)

One study using data collected in single center as part of a prospective randomized controlled clinical trial [Tianinen, 2003, 2881 LOE P2 E] demonstrated that the 48 hour NSE and S100 value which achieves a 0-4% FPR for poor outcome is 2 to 3 times higher in patients treated with hypothermia compared to the normothermic control group. [NSE >25 vs. 8.8 ug/L; S-100B 0.23 vs 0.12 ug/L]. Data was not reported in a way that allowed calculate the FNR 95% CI. Two studies serially measured neurons specific enolase in cohorts of patients treated with post-cardiac arrest hypothermia and reported cutoff values for 0% FPR. Oksanen et al (Oksnaen, 2009, 165) reported that all patients with a 48 hour NSE value >33ug/L had a poor outcome (FPR 0%, 95% CI 0-23%). Rundgren et al (Rundgren, 2009, 784, LOE P2) reported that all patients with a 48 hour NSE > 28 ug/L had a poor outcome (FPR 0%, 95% CI 0-18). Variability in 0% FPR cutoff values from these derivation cohorts potentially results from variability among assays and performance sites.

#### Glial Fibrillary Acidic Protein (GFAP)

One single center retrospective study [Kaneko, 2009, 790 LOE 2P E] measured serum GFAP levels at 12, 24, and 48 hours after cardiac arrest in patients treated with normothermia or hypothermia. A GFAP level >1.0 ng/dL at any time point predicted poor outcome (defined as CPC 3-5 at 6 months) with a 0% FPR [95% CI 0-27%] for normothermia treated patients and a 0% FPR [95% CI 0-48%] for hypothermia treated patients.

#### EEG

One retrospective study compared outcome of post-cardiac arrest patients with an EEG diagnosis of status epilepticus with or without therapeutic hypothermia [Rossetti, 2007, 255, LOE P3 E]. 8/8 patients in the normothermic group with SE died [FPR 0% (95% CI 0-40%). 23/26 patients in the hypothermic group died. [FPR 11.5% (95% CI 4-29%). In follow-up study by the same group, 28 prospectively evaluated post-cardiac arrest patients treated with hypothermia were noted to have status epilepticus, and 2 had a CPC 1 or 2 at 6 months. (FPR 7%, 95% CI 0-20%)
One case series of comatose post-cardiac arrest patients treated with therapeutic hypothermia for 24 hours [Rundgren 2006, 836, LOE P4 E] demonstrated that a noncontinuous amplitude-integrated EEG (aEEG) signal at the time of rewarming (30-40 hours post-arrest) had a false positive rate of 0%. However only 14 patients in the study had this finding making the 95% CI approximately 0-27%. In this study non-continuous was defined as generalized status epilepticus, lateralized status epilepticus, suppression-burst, or flat.

**Bispectral Index Monitoring (BIS)**

One single center prospective study (Seder, 2009, 1, LOE P2) measured bispectral index and suppression ratio (SR) during the first 5-10 minutes after the first dose of neuromuscular blockade in post-cardiac arrest patients treated with therapeutic hypothermia. Poor outcome was defined as CPC 3-5. BIS <= 22 had a FPR of 6% [95% CI 0-28%]. SRI => 48 had a FPR for predicting poor outcome of 7% [95% CI 1-26%].

One single center prospective study [Stammet, 2009, 437] performed continuous BIS monitoring for the first 72 hours in post-cardiac arrest patients treated with hypothermia under neuromuscular blockade. Poor outcome was defined as CPC 3-5. A BIS level of 0 at any time predicted poor outcome with a FPR of 0% [95% CI 0-27%].
## Summary of Key Data

<table>
<thead>
<tr>
<th>Prognosticator</th>
<th>Treatment</th>
<th>Time after ROSC</th>
<th># with positive test</th>
<th>FPR</th>
<th>95% CI</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent corneal reflex</td>
<td>Hypothermia</td>
<td>3 days</td>
<td>6</td>
<td>0%</td>
<td>0-48%</td>
<td>Thenayan 2008</td>
</tr>
<tr>
<td>Absent pupillary reflex</td>
<td>Hypothermia</td>
<td>3 days</td>
<td>6</td>
<td>0%</td>
<td>0-48%</td>
<td>Thenayan 2008</td>
</tr>
<tr>
<td>Motor Score 3 or less</td>
<td>Hypothermia</td>
<td>3 days</td>
<td>14</td>
<td>14%</td>
<td>3-44%</td>
<td>Thenayan 2008</td>
</tr>
<tr>
<td>Myoclonus Status</td>
<td>Hypothermia</td>
<td>Not noted</td>
<td>8</td>
<td>0%</td>
<td>0-40%</td>
<td>Thenayan 2008</td>
</tr>
<tr>
<td>SSEP: Bilaterally absent N20 peak</td>
<td>Normothermia</td>
<td>24-28 hrs</td>
<td>8</td>
<td>0%</td>
<td>0-40%</td>
<td>Tiainen 2005</td>
</tr>
<tr>
<td>NSE &gt; 8.8 ug/L</td>
<td>Hypothermia</td>
<td>48 hrs</td>
<td>?</td>
<td>0%</td>
<td>?</td>
<td>Tiainen 2003</td>
</tr>
<tr>
<td>NSE &gt; 25 ug/L</td>
<td>Hypothermia</td>
<td>48 hrs</td>
<td>?</td>
<td>4%</td>
<td>?</td>
<td>Tiainen 2003</td>
</tr>
<tr>
<td>NSE &gt; 33 ug/L</td>
<td>Hypothermia</td>
<td>48 hrs</td>
<td>17</td>
<td>0%</td>
<td>0-23%</td>
<td>Oksanen 2009</td>
</tr>
<tr>
<td>Delta NSE &gt;6.4 ug/L</td>
<td>Hypothermia</td>
<td>48-24 hrs</td>
<td>18</td>
<td>0%</td>
<td>0-22%</td>
<td>Oksanen 2009</td>
</tr>
<tr>
<td>NSE &gt; 28 ug/L</td>
<td>Hypothermia</td>
<td>48 hrs</td>
<td>22</td>
<td>0%</td>
<td>0-18%</td>
<td>Rundgren 2009</td>
</tr>
<tr>
<td>S-100β&gt;0.12 ug/L</td>
<td>Normothermia</td>
<td>48 hrs</td>
<td>?</td>
<td>0%</td>
<td>?</td>
<td>Tiainen 2003</td>
</tr>
<tr>
<td>S-100β&gt;0.23 ug/L</td>
<td>Hypothermia</td>
<td>48 hrs</td>
<td>?</td>
<td>4%</td>
<td>?</td>
<td>Tiainen 2003</td>
</tr>
<tr>
<td>GFAP &gt; 1.0 ng/dL</td>
<td>Normothermia</td>
<td>12-48 hrs</td>
<td>14</td>
<td>0%</td>
<td>0-27%</td>
<td>Kaneko 2009</td>
</tr>
<tr>
<td>Status epilepticus EEG</td>
<td>Hypothermia</td>
<td>12-48 hrs</td>
<td>6</td>
<td>0%</td>
<td>0-48%</td>
<td>Kaneko 2009</td>
</tr>
<tr>
<td>Non-continuous aEEG</td>
<td>Hypothermia</td>
<td>30-40 hrs</td>
<td>14</td>
<td>0%</td>
<td>0-27%</td>
<td>Rundgren 2006</td>
</tr>
<tr>
<td>Bispectral Index &lt;=22</td>
<td>Hypothermia</td>
<td>3-6 hours</td>
<td>19</td>
<td>6%</td>
<td>0-28%</td>
<td>Seder 2006</td>
</tr>
<tr>
<td>Suppression Ratio (SR) =&gt;48</td>
<td>Hypothermia</td>
<td>3-6 hours</td>
<td>26</td>
<td>7%</td>
<td>1-26%</td>
<td>Seder 2009</td>
</tr>
</tbody>
</table>

## ILCOR ALS Task Force Knowledge Gaps and Needed Research

- **Knowledge Gaps**
  - What is the effect of therapeutic hypothermia on the accuracy post-cardiac arrest prognostication tools?
  - What is the effect of therapeutic hypothermia on the optimal timing of post cardiac arrest prognostication?

- **Specific research required**
  - Prospective derivation and validation of a clinical decision rule for early prediction of poor outcome in post-cardiac arrest patients treated with or without hypothermia

## Acknowledgements
Citation List

Al Thenayan E, Savard M, Sharpe M, Norton L, Young B.
Title: Predictors of poor neurologic outcome after induced mild hypothermia following cardiac arrest.

LOE P1
Quality Poor: Inadequate numbers, no information about withdrawal of care.
Supporting (corneal reflex at 3 days, pupillary reflex at 3 days, and myoclonus status)
Opposing: (Glasgow motor score 3 or less at 3 days)
Summary: Retrospective chart review of 37 consecutive patients who were comatose after cardiac arrest and treated with hypothermia. Tested accuracy of practice parameter proposed by American Academy of Neurology (Wijdicks, 2006, 2003)
Funding Source: None listed
Investigator COI: Authors report no conflicts

Derwall M, Stoppe C, Brücken D, Rossaint R, Fries M.
Title: Changes in S-100 protein serum levels in survivors of out-of-hospital cardiac arrest treated with mild therapeutic hypothermia: a prospective, observational study.

LOE P3
Quality: Fair
Neutral
This study measured serial S-100 levels in 68 patients with ROSC after cardiac arrest: 37 were treated with mild therapeutic hypothermia at physician discretion. S-100 levels on baseline were significantly lower in patients with a good neurological outcome at 14 days after the event in comparison to their peers with adverse outcome. Data is not present in a way that allows calculation of false positive rate for prognostication of poor outcome for normothermic or hypothermic post-cardiac arrest patients
False positive rate (FPR) data not available
Funding Source Laerdal Foundation for Acute Medicine, Stavanger, Norway. The sponsor had no involvement in the study design, or in the collection, analysis and interpretation of data, in the writing of the manuscript or in the decision to submit the manuscript for publication.
Investigator COI: No declared conflicts

Authors: Hachimi-Idrissi et al.

LOE 2P
Quality: Poor
Neutral
Summary: Prospective randomized trial (61 patients), four study arms, few patients in each. S-100B values lower in the hypothermia groups at 24h after admission which correlated to a better outcome. No individual values, no cut-off values for a poor outcome are presented for normothermia group or hypothermia group.


LOE P2
Quality: Good
Supporting
GFAP (>0.1 ng dL⁻¹) 12-48 hours post-ROSC was a specific predictor of poor neurological outcome at 6 months with or without TH treatment.
GFAP > 0.1 ng/dL
Normothermia FPR 0%, 95% CI (0-27%) 14 positives at 12-48 hours with poor outcome
Hypothermia FPR 0%, 95% CI (0-48%) 6 positives at 12-48 hrs with poor outcome
Funding Source: This clinical study was supported by a research project grant from the Japanese Ministry of Health, Labor, and Welfare (number 19791329).
Investigator COI: This study was conducted independently of funding bodies, except for a governmental grant. This grant did not influence the study design or its publication.

Oksanen T, Tiainen M, Skrifvars MB, Varpula T, Kuitunen A, Castrén M, Pettilä V.
Title: Predictive power of serum NSE and OHCA score regarding 6-month neurologic outcome after out-of-hospital ventricular fibrillation and therapeutic hypothermia.
Institution: Department of Anaesthesiology and Intensive Care Medicine, Helsinki University Hospital, Finland

LOE P1
Quality: Fair relative to question. No normothermic patients for comparison
Supportive for NSE at 48 hours after ROSC
Summary: Prospective cohort of 90 patients treated with therapeutic hypothermia after ventricular fibrillation cardiac arrest. 40 patients had poor outcome. NSE level >33 ug/L had a 0% FPR (95% CI 0-23%) with a reported sensitivity of 43% (calculated 17 patients with positive test). This cutoff value is the same as reported for American Academy of Neurology practice guideline based on studies of normothermic post-arrest patients. (Wijdicks, 2006, 203) Change in NSE between 24 and 48 hours of >6.4 had 0% FPR (95% CI 0-22%) with a reported sensitivity of 44 % (calculated 18 patients with positive test).

Rossetti AO, Logroscino G, Liaudet L, Ruffieux C, Ribordy V, Schaller MD, Despland PA, Oddo M.
Title: Status epilepticus: an independent outcome predictor after cerebral anoxia.

LOE P3
Quality: Fair
Opposing: False positive rate (FPR) high with hypothermia but inadequate power to detect potentially important difference in FPR between groups
107 comatose post-cardiac arrest patients had single EEG. The median latency 2 days. 67% of these died
Hypothermia 3 out of 26 pts with PSE survived FPR 11.5% [95% CI 4-29%]
Normothermia 0 out of  8 pts with PSE survived.  FPR 0% [95% CI 0-40%]
Funding Source Not reported
Investigator COI: No declared conflicts

Rossetti AO, Oddo M, Liaudet L, Kaplan PW.
Title: Predictors of awakening from postanoxic status epilepticus after therapeutic hypothermia.
Institution: Service de Neurologie, Centre Hospitalier Universitaire Vaudois, Lausanne

LOE 3
Quality: Fair
Opposing: FPR 7% for patients treated with hypothermia
Summary: Prospective cohort of post-cardiac arrest patients treated with therapeutic hypothermia. 28 patients had status epilepticus between 1 and 9 days after cardiac arrest. Awakening occurred in 1/24 (4%) patients with electroclinical myoclonic PSE, 2/4 (50%) with subclinical PSE, and 0/5 with myoclonus without ictal EEG changes. Overall 2 of the 28 patients had a good outcome defined as CPC 1 or 2 at 6 month. (FPR 7%; 95% CI 0-20%)

Rundgren M. Rosen I. Friberg H.
Title Amplitude-integrated EEG (aEEG) predicts outcome after cardiac arrest and induced hypothermia.

LOE P4
Quality: Fair
Neutral: No normothermic controls
Summary: This is case series of comatose post-cardiac arrest patients treated with therapeutic hypothermia for 24 hours demonstrated that a noncontinuous amplitude-integrated EEG (aEEG) signal at the time of rewarming (30-40 hours post-arrest) had a false positive rate of 0%. However only 14 patients in the study had this finding making the 95% CI approximately 0-27%. In this study non-continuous was defined as generalized status epilepticus, lateralized status epilepticus, suppression-burst, or flat.
Funding Source Swedish Research Council grant # 84.
Investigator COI: No declared conflicts
Title: Neuron specific enolase and S-100B as predictors of outcome after cardiac arrest and induced hypothermia.

LOE P2
Quality: Fair
Supporting
Summary: Prospective serial measurement of NSE and S100β in post-cardiac arrest patient treated with hypothermia.
Study design limited relative to question because no direct comparison with normothermic post-cardiac arrest patients. Study quality limited by missing samples and omission of one of the three original centers. Most accurate predictor of poor prognosis was NSE > 28 ug/L at 48 hours after ROSC. 22 of 22 patients with NSE > ug/L had a poor outcome (CPC <2 at 6 months) (FPR 0% 95% CI 0-18%). The cutoff of 28 ug/L is lower the 33 ug/L cutoff used in the American Academy of Neurology Paractice Guideline derived from mainly normothermic post-arrest patients (Wijdicks et al., 2006, 206)
Funding Source This study was supported by Skane county council’s research and development foundation and by the governmental funding of clinical research within the Swedish National Health Service. The funding sources had no influence in study design, data collection or interpretation, writing or decision to submit the manuscript.
Investigator COI: None

Seder D.B. Fraser G.L. Robbins T. Libby L. Riker R.R.
Title: The bispectral index and suppression ratio are very early predictors of neurological outcome during therapeutic hypothermia after cardiac arrest

LOE P2
Quality: Fair
Neutral
Measured BIS1 and SR1 as the sustained plateau values in the 5–10 min after the first dose of neuromuscular blockade. Only patients treated with hypothermia
BIS1 and SR1 were recorded 3-6 hours after ROSC on after initial neuromuscular blockade
BIS <= 22 FPR 6%, 95% CI (0-28%) 19 positives
SR1 => 48 FPR 7% 95% CI (1-26%) 26 positives
Funding Source: Aspect Medical Systems for equipment support and expertise, and the Maine Medical Center Neuroscience and Research Institutes for generous financial support
Investigators COI: Not reported


LOE P2
Quality Fair
Neutral
Continuous BIS monitoring for 72 hours post-ROSC with hypothermia and neuromuscular blockade.
BIS level of 0 at any time between 0-72 hours post ROSC. FPR 0% [95% CI 0-27%] 14 positives.

Tiainen M. Kovala T.T. Takkunen O.S. Roine R.O.
Title Somatosensory and brainstem auditory evoked potentials in cardiac arrest patients treated with hypothermia.

LOE P1
Quality: Poor-severely underpowered
Supporting: No statistical difference in FPR compared to normothermic controls
Funding Source Finnish Neurology Foundation, Clinical Research Institute of Helsinki University Central Hospital, Maire Taponen Foundation, Laerdal Foundation, Kinetic Concepts Inc, Wareham UK provided cooling device used in the study.
Investigator COI: No declared conflicts
Summary: This study use data collected in a single center as part of a prospective randomized controlled clinical trial. The demonstrated that although hypothermia decreases the latency, the bilateral absence of N20 wave on median nerve SSEPs had a false
positive rate of 0% for predicting poor outcome in both the hypothermia and normothermia control groups. However only 3 patients in the study treated with hypothermia had this finding making the 95% CI approximately 0-69%.

Tiainen M, Roine RO, Pettilä V, Takkunen O.
Title: Serum neuron-specific enolase and S-100B protein in cardiac arrest patients treated with hypothermia.

LOE P2
Quality: Underpowered and inadequate data to calculate 95% CI of FPR.
Opposing: Cutoff values for 0% FPR in predicting poor outcome different for normothermia and hypothermia
This study used data collected in a single center as part of a prospective randomized controlled clinical trial. The 48 hour NSE and the 48 hour S100 value which achieved a 0% FPR for poor outcome was 2 to 3 times higher in patients treated with hypothermia compared to the normothermic control group. [NSE >25 vs. 8.8 ug/L; S-100B 0.23 vs 0.12 ug/L]. Data was not reported in a way that allowed calculate the FNR 95% CI.
Funding Source Finnish Neurology Foundation, Laerdal Foundation, Maire Taponen Foundation, Helsinki University Central Hospital, European Union (Biomed 2, for the HACA study) , Kinetic Concepts Inc, Wareham UK provided cooling device used in the study.
Investigator COI: No declared conflicts

Yannopoulos D, Kotsifas K, Aufderheide TP, Lurie KG
Title: Cardiac arrest, mild therapeutic hypothermia and unanticipated cerebral recovery.
Source: Neurologist 2007;13(6):369-75

LOE 4
Quality: Poor
Neutral
Summary: Case study, 4 patients. Neurological evaluation performed during ongoing hypothermia treatment suggested a poor outcome in all patients but all recovered consciousness within 24h of rewarming.

Zandbergen EG, Hijdra A, Koelman JH, Hart AA, Vos PE, Verbeek MM, de Haan RJ; PROPAC Study Group
Title: Prediction of poor outcome within the first 3 days of postanoxic coma.