Post-Arrest Care: Beyond Hypothermia

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Sunnybrook Health Sciences Centre
Disclosures

- CIHR
- Physicians’ Services Incorporated
WHY
ARE
YOU
STILL
HERE?
Main Discussion Topics

- Post-cardiac arrest syndrome
- Hypothermia
- Hemodynamic and Ventilation Goals
- Neuroprognostication
1. The Post-Cardiac Arrest Syndrome
Cardiac arrest can be a devastating event

- 213 out of hospital arrests / 100,000 adults
- Overall survival about 8%

Aufderheide T et al. NEJM 2011;365:798-806
# Local OHCA survival rates

<table>
<thead>
<tr>
<th></th>
<th>all</th>
<th>VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamilton</td>
<td>6.3%</td>
<td>15.1%</td>
</tr>
<tr>
<td>Peel</td>
<td>7.5%</td>
<td>21.5%</td>
</tr>
<tr>
<td>Toronto</td>
<td>6.1%</td>
<td>21%</td>
</tr>
<tr>
<td>Durham</td>
<td>6.2%</td>
<td>16%</td>
</tr>
<tr>
<td>Simcoe</td>
<td>3.8%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Muskoka</td>
<td>8.0%</td>
<td>18.2%</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>6.1%</strong></td>
<td><strong>19%</strong></td>
</tr>
<tr>
<td><strong>Pre 2005</strong></td>
<td><strong>2.6%</strong></td>
<td><strong>8%</strong></td>
</tr>
</tbody>
</table>
About 50 to 70% of cardiac arrest patients that survive to hospital admission die in-hospital.

13,263 Patients Health-Person Oriented Information Database

Redpath Am Heart J 2010

62% Mortality

In-hospital survival rates in patients admitted after OHCA stratified by year ($P = .30$).
But about two thirds of survivors have minimal disability

13,263 Patients Health-Person Oriented Information Database

Redpath Am Heart J 2010

62% Mortality

Aufderheide T et al. NEJM 2011;365:798-806
The Chain of Survival

- Early recognition and call for help
  - to prevent cardiac arrest
  - to buy time

- Early CPR

- Early Defibrillation
  - to restart the heart

- Post resuscitation care
  - to restore quality of life
Post-Cardiac Arrest Syndrome: 4 key components

- Post-cardiac arrest brain injury
- Post-cardiac arrest myocardial dysfunction
- Systemic ischemia-reperfusion response
- Persistent precipitating pathology

Circulation 2008; 118(23):2452-83
2. Hypothermia
Metabolic Chain of Events in Cardiac Arrest

Cardiac Arrest

No Blood Flow → Ischemia → Cell Damage

Free Radicals → O₂ Reperfusion → Cell Death and Cerebral Injury

CPR / Pulse
Mild therapeutic hypothermia for Cardiac Arrest Survivors

- Theory is based on its ability to prevent the cascade of events following a cardiac arrest which inhibit neurologic functioning.
Hypothermia improved survival with good neurological outcome

OR for survival with good outcome: 5.25 (95% CI 1.47-18.76; P=.011)

[1] Holzer et al, NEJM 2002; 0.3C/hr cooling with cold air and ice packs
[2] Bernard et al, NEJM 2002; 0.9C/hr cooling with ice packs
Which patients should be cooled?

- Non-traumatic cardiac arrest without full neurological recovery
  - Especially if due to VF or pulseless VT

- ALS 2010:
  - “might also benefit comatose adult patients with ROSC after OHCA, nonshockable rhythm, or cardiac arrest in hospital”
Does the Evidence Base Justify Cooling All Patients?

Review

The role of hypothermia in post-cardiac arrest patients with return of spontaneous circulation: A systematic review

James H. Walters a,*, Peter T. Morley b, Jerry P. Nolan c

a Intensive Care Medicine, Royal United Hospital, Bath BA1 3NG, UK
b Director of Medical Education, Royal Melbourne Hospital, University of Melbourne, Australia
c Anaesthesia and Intensive Care Medicine, Royal United Hospital, Bath BA1 2NG, UK
Review

The role of hypothermia in post-cardiac arrest patients with return of spontaneous circulation: A systematic review∗

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- 7 randomized trials (LOE 1)
  - note overlapping patient sets
- 9 non-randomized, concurrent controls (LOE 2)
- 15 studies with retrospective controls (LOE 3)
- 40 studies with no controls (LOE 4)
Evidence SUPPORTING Therapeutic Hypothermia Post-Arrest

**Table 3**
Evidence supporting therapeutic hypothermia following OHCA.

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Arrich, CD9,16</th>
<th>Arrich, CD67</th>
<th>Arrich, CD97</th>
<th>Hovdenes, CD71</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>HACA study group, CDb18</td>
<td>Tiainen, Eb19</td>
<td>Nielsen, D17</td>
<td>Wolff, DE59</td>
</tr>
<tr>
<td></td>
<td>Holzer, CDa14</td>
<td>Holzer, CD25</td>
<td>Kagawa, D32</td>
<td>Oksanen, C84</td>
</tr>
<tr>
<td>Fair</td>
<td>Bernard, D25</td>
<td>Knafelj, CD33</td>
<td>Busch, C34</td>
<td>Sagalyn, C85</td>
</tr>
<tr>
<td></td>
<td>Belliard, CD35</td>
<td>Oddo, D36</td>
<td>Sunde, CD37</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>Hachimi-Idrissi, E20</td>
<td>Storrm, CDE38</td>
<td>Don, CD39</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cheung, CD4,15</td>
<td>Bro-Jeppesen, D40</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arich, CD97</td>
<td>Castrejon, D91</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Williams, D86</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evidence OPPOSING Therapeutic Hypothermia Post-Arrest

Table 5
Evidence opposing hypothermia following OHCA.

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Fries, E31</th>
<th>Yanagawa, E7</th>
<th>Nielsen, CE73</th>
<th>Simosa, E74</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Review

The role of hypothermia in post-cardiac arrest patients with return of spontaneous circulation: A systematic review

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Who to cool?

- Most compelling evidence for patients with VT/VF
- 6 studies with historical controls showing benefit from cooling after OHCA from all rhythms
- 2 studies with concurrent controls showing benefit from cooling after in- and out-of-hospital cardiac arrest, all rhythms
Niklas Nielsen et al.

- RCT, OHCA, All rhythms
- Arms: Target 33 degrees versus Target 36 degrees
  - Cooling for 24 hours, rewarming for 12 hours
  - Observation for at least 72 hours (total 108 hours)
- Outcome: Mortality
- Sample Size: 850
Other treatments and Hypothermia

- **Vasopressors during 24 first 24 hours:**
  - 59% (vs 49%) of pts in Bernard trial (mean 2.2 mg epi)
  - 55% (vs 49%) in HACA trial (median 3 mg epi)

- **Thrombolytics during cooling:**
  - 20% of patients in HACA trial

- **PCI during cooling:**
  - Infrequent in both trials
  - ALS 2010: “5 studies indicated that the combination of therapeutic hypothermia and PCI is feasible and safe after cardiac arrest” (3 studies LOE 3, 2 studies LOE 4)
Approach to cooling

• Basic approach:
  – Surface cooling (ice packs, blankets)
  – Sedation (benzo + analgesic)
  – **Cold IV bolus** (i.e. 2 litres 4° C normal saline)

• Other methods:
  – Water immersion
  – Cooling catheters
  – Intranasal cooling
  – Cooling helmets
  – Etc.
36 hospitals, 2-years
The Intervention: Passive then Active QI

- **Passive Intervention:**
  - educational presentation, generic hypothermia protocol and order set

- **Active Intervention:**
  - audit-feedback, local detailing by nurse educator, email notifications of OHCA patients
Rates of Cooling to Target (primary outcome)

Unadjusted Results

- Baseline: 9.4% (30/320)
- Passive: 24.3% (96/395)
  - vs baseline: OR 2.24 (95% CI 1.54-3.26)
- Active: 24.7% (86/348)
  - vs baseline: OR 0.94 (95% CI 0.70-1.28)
Are more powerful strategies required?

Harnessing the Power of Default Options to Improve Health Care

Scott D. Halpern, M.D., Ph.D., Peter A. Ubel, M.D., and David A. Asch, M.D., M.B.A.
Initiation of Cooling by Emergency medical services to Promote the Adoption of in-hospital therapeutic hypothermia in Cardiac arrest Survivors

The ICE-PACS trial
• Hypothesis: Pre-hospital cooling will act as a default option (or a ‘forced reminder’) to facilitate cooling
Interventions: Cold Saline and Frozen Saline

• 2 litres of cold saline IV initiated by EMS

• Saline kept cold by frozen saline bags, which will be applied to neck and groin
Interventions:
Wrist and ankle bands
ICE-PACs

- Anticipated sample size ~ 1,000 patients over 2 years
- EMS in **Toronto, Peel, Halton**
- Possibly EMS in York, Durham, Simcoe
3.
Hemodynamic and Ventilation Goals
(Proposed) goal-directed strategies

- Normal oxygenation (O2)
- Normal ventilation (CO2)
- Hemodynamic optimization (BP)
- Coronary Reperfusion

Aufderheide T et al. NEJM 2011;365:798-806
(Proposed) goal-directed strategies
Oxygenation Goals

**Oxygenation Goals**

**PaO2 > 300**

**60 < PaO2 < 300**

**N=6326**

**Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality**

J Hope Kilgannon, MD
Alan E. Jones, MD
Nathan L. Shapiro, MD, MPH
Mark C. Angloc, MD
Barry Milbrand, PhD
Krystal Hunter, MBI
Joseph E. Parrillo, MD, MPH
for the Emergency Medicine Shock Research Network (EMShock/Net)

**Objective** To test the hypothesis that postresuscitation hyperoxia is associated with increased mortality.

**Design, Setting, and Patients** Multicenter cohort study using the Project IMPACT critical care database of intensive care units (ICUs) at 120 US hospitals between 2001 and 2005. Patients inclusion criteria were age older than 17 years, nontraumatic cardiac arrest and resuscitation within 24 hours prior to ICU arrival, and arterial blood gas analysis performed within 24 hours following ICU arrival. Patients were divided into 3 groups defined a priori based on PaO2 on the first arterial blood gas values obtained in the ICU. Hyperoxia was defined as PaO2 of 300 mm Hg or greater; hypoxia, PaO2 of less than 60 mm Hg (or ratio of PaO2 to fraction of inspired oxygen <300); and normoxia, not classified as hyperoxia or hypoxia.

**Main Outcome Measure** In-hospital mortality.

**Results** Of 6326 patients, 1171 had hyperoxia (18%), 3999 had hypoxia (62%), and 1171 had normoxia (19%). The hyperoxia group had significantly higher in-hospital mortality (732/1171 [69%] vs 641/3999 [16%]) compared with the normoxia group (512/1171 [44%] vs 1140/3999 [29%]), proportion difference, 18% (95% CI, 14%-22%). The hyperoxia group (229/732 [31%]) and the hypoxia group (227/641 [35%]) had higher mortality than the normoxia group (229/1140 [21%]), proportion difference, 13% (95% CI, 2%-25%). In a model controlling for potential confounders (age, preadmission functional status, comorbid conditions, vital signs, and other physiological measures), hyperoxia exposure had an odds ratio for death of 1.8 (95% CI, 1.5-2.2).

**Conclusion** Among patients admitted to the ICU following resuscitation from cardiac arrest, arterial hyperoxia was independently associated with increased in-hospital mortality compared with either hypoxia or normoxia.

For editorial comment see p 2590.

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**Figure. In-Hospital Death Between Hyperoxia and Normoxia N=6326**

**Survival Proportion**

**PaO2 > 300**

**Log-rank P<.001**

**Days**

**No. at risk**

Normoxia 1171 514 236 129 83

Hyperoxia 1156 406 211 115 70

For editorial comment see p 2590.
Oxygenation Goals

Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality

J. Hope Kilgannon, MD
Alan E. Jones, MD
Nathan I. Shapiro, MD, MPH
Mark C. Angeles, MD

Limitations:
- used only first set of arterial blood gases in the ICU to assess oxygenation
- excluded nearly 1/3 of patients because of lack of arterial blood gas data
- did not adjust for standard illness severity scores
Oxygenation Goals

Abstract

Interruption of hypoxaemia has been reported as an independent risk factor for mortality in patients resuscitated from cardiac arrest. We examined the independent relationship between hypoxaemia and outcomes in such patients.

Methods: We followed patients resuscitated from nontraumatic cardiac arrest from 13 intensive care units (ICUs) into three groups according to mean PAO2 (end-tidal alveolar oxygen pressure) in the first 24 hours after admission. We defined hypoxaemia as PAO2 < 60 mm Hg or an arterial saturation of <90% at the time of the first arterial blood gas sample. The outcome of interest was in-hospital mortality.

Results: Of 13,135 total patients, 7,580 (58.0%) had hypoxaemia (PAO2 < 60 mm Hg), and 5,555 (42.3%) had hypoxaemia within 24 hours of arrest. The patients with hypoxaemia had a significantly higher mortality rate (17.6%) than those without hypoxaemia (14.6%) (P < .001). In a multivariable analysis, adjusting for potential confounders, including baseline characteristics, hypoxaemia was an independent predictor of hospital mortality (odds ratio [OR], 1.06; 95% confidence interval, 1.04 to 1.08; P < .001).

Conclusions: In order to identify patients at risk of adverse outcomes after cardiac arrest, it is important to assess the timing of hypoxaemia and to evaluate the impact of interventions that may prevent or delay the development of hypoxaemia.

Introduction

The majority of patients who experience cardiac arrest die at the scene or in the hospital, and their outcomes are influenced by the time from cardiac arrest to resuscitation efforts and the severity of neurologic injury. In a study of 13,135 patients with cardiac arrest, the mortality rate was significantly higher among those with hypoxaemia (PAO2 < 60 mm Hg) than among those without hypoxaemia. These findings suggest that hypoxaemia may be an important factor in the outcomes of patients with cardiac arrest. Therefore, interventions aimed at reducing the incidence of hypoxaemia may improve patient outcomes.
Insufficient evidence for recommendations.

Once ROSC is achieved, reasonable to adjust the FiO2 to the minimum concentration needed to achieve O2 saturation > 94%
Ventilation Goals

Fig. 2. Jugular bulb oxygen saturation (%) according to intervention phase. Lines depict median, bars interquartile range and error bars range. Asterisk denotes $p<0.05$. 

*  

**  

***  

****  

- Baseline
- Hypocapnia
- Normocapnia
- Hypercapnia
- Routine hyperventilation with hypocapnia should be avoided
Hemodynamic Targets

Autoregulation of Cerebral Blood Flow
Hemodynamic Targets

Autoregulation of Cerebral Blood Flow

Blood flow (ml/100g/min) vs. MAP (mmHg)
Hemodynamic Targets

Significance of arterial hypotension after resuscitation from cardiac arrest

Stephen Trzeciak, MD, MPH; Alan E. Jones, MD; J. Hope Kilgannon, MD; Barry Mackersie, PhD; Krytal Hanler, MBA; Nathan I. Shapiro, MD, MPH; Steven M. Hollenberg, MD; R. Phillip Dellinger, MD; Joseph E. Parrillo, MD

LEARNING OBJECTIVES
After participating in this educational activity, the participant will be able to:
1. Define post-resuscitation hypotension.
2. Reap the impact of post-returns of spontaneous circulation.
3. Use this information in a clinical setting.

Table 4. Outcomes

| Metric | All Subjects (n = 8736) | Hypotension Present (n = 4092) | Hypotension Absent (n = 4644) | p
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality, n (%)</td>
<td>4375 (50)</td>
<td>2672 (65)</td>
<td>1703 (37)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Survivors, n</td>
<td>4361</td>
<td>1420</td>
<td>2843</td>
<td></td>
</tr>
<tr>
<td>Functional status of survivors at hospital discharge, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>1840 (42)</td>
<td>460 (32)</td>
<td>1380 (47)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Partially dependent</td>
<td>1652 (38)</td>
<td>616 (44)</td>
<td>1036 (35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fully dependent</td>
<td>869 (20)</td>
<td>344 (24)</td>
<td>525 (18)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Decline in functional status on discharge compared with preadmission, n (%)</td>
<td>1653 (42)</td>
<td>627 (49)</td>
<td>1026 (38)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Hemodynamic Targets

Hypotension = SBP < 90 within 1 hour post ROSC

Table 6. Subgroup analysis of outcomes for subjects without vasopressor-dependent shock (defined as not requiring vasopressors at any time)

<table>
<thead>
<tr>
<th></th>
<th>All Subjects (n = 4200)</th>
<th>Hypotension Present (n = 1062)</th>
<th>Hypotension Absent (n = 3138)</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality, n (%)</td>
<td>1287 (31)</td>
<td>487 (46)</td>
<td>800 (25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total survivors, n</td>
<td>2913</td>
<td>575</td>
<td>2388</td>
<td></td>
</tr>
<tr>
<td>Decline in functional status on discharge compared with preadmission, n (%)</td>
<td>976 (36)</td>
<td>227 (43)</td>
<td>749 (35)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Hemodynamic Targets

- Bernard trial: target MAP 90 to 100 mmHg
- HACA trial: not specified

- ALS 2010: “Despite limited clinical data, the known pathophysiology of post–cardiac arrest syndrome provides a rationale for titrating hemodynamics to optimize organ perfusion”
Recommendations

- Avoid hyperventilation after cardiac arrest
- Avoid hypoxemia after cardiac arrest
  - Titrate down FiO2 after ROSC to avoid hyperoxemia
- Avoid hypotension after cardiac arrest
  - Target MAP > ~ 65, possibly higher
4. Neuroprognostication in the cooling era
Competing goals after cardiac arrest

Avoid prematurely terminating life support in patients who will survive.

Avoid continuing life support in patients who will have poor neurological outcomes.
The problem is…
we’re not very good at it!

- Clinicians are generally poor at subjectively predicting survival, functional outcome and quality after critical illness
- Physicians tend to over-estimate poor outcomes and under-estimate good outcomes
- Physicians tend to be more optimistic than nurses (and vice versa)

Copeland-Fields et al. Am J Crit Care 2001; 10:313
• No clinical signs reliably predict poor outcome at 24 hrs

In absence of hypothermia:
• Reliable:
  – Absence of both pupillary light and corneal reflex at 72 hrs

• Less reliable:
  – Absence of vestibuloocular reflexes at 24 hrs
  – GCS motor score ≤ 2 at 72 hrs

• Not recommended: Other clinical signs, including myoclonus
Electrophysiology

- Bilateral absence of the N20 cortical response (24hrs) to median nerve stimulation predicts poor outcome in comatose cardiac arrest survivors NOT TREATED with hypothermia.
Hypothermia may change accuracy of predictors used for neuroprognostication

- Confounding due to sedating/paralyzing medications used to induce and maintain hypothermia
- *May change accuracy of predictors used for neuroprognostication* by attenuating degree of brain injury
37 cardiac arrest patients treated with hypothermia

No recovery
- 6/6 absent pupils day 3
- 6/6 absent corneal reflexes day 3
- 8/8 with myoclonus status epilepticus

Recovery:
- 2/14 with motor responses no better than extension at day 3

Conclusions: Poor motor exam on day 3 was unreliable
Prognostication after Cardiac Arrest and Hypothermia
A Prospective Study

Andrea O. Rossetti, MD,¹ Mauro Oddo, MD,²
Giancarlo Logroscino, MD, PhD,³ and Peter W. Kaplan, MBBS, FRCP¹,⁴

• 111 cardiac arrests treated with hypothermia
• Neurological examination 36-72 HOURS
• EEG
• SSEP
• All measurements during normothermia and off sedation
• CPC assessed at 3 to 6 months
<table>
<thead>
<tr>
<th>Variable</th>
<th>FPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-VF CA (asystole or PEA)</td>
<td>0.15 (0.06–0.29)</td>
</tr>
<tr>
<td>ROSC &gt;25 minutes</td>
<td>0.24 (0.13–0.40)</td>
</tr>
<tr>
<td>≥1 brainstem reflexes absent&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.04 (0.01–0.15)</td>
</tr>
<tr>
<td>Motor response worse than flexion</td>
<td>0.24 (0.13–0.40)</td>
</tr>
<tr>
<td>Early myoclonus</td>
<td>0.03 (0.00–0.11)</td>
</tr>
<tr>
<td>Epileptiform activity on first EEG</td>
<td>0.09 (0.02–0.21)</td>
</tr>
<tr>
<td>Unreactive EEG background</td>
<td>0.07 (0.01–0.18)</td>
</tr>
<tr>
<td>Bilaterally absent N20 on SSEP</td>
<td>0.00 (0.00–0.08)</td>
</tr>
</tbody>
</table>
Prognosis of Coma After Therapeutic Hypothermia: A Prospective Cohort Study

Aline Bouwes, MD,¹,² Jan M. Binnekade, PhD,¹ Michael A. Kuiper, MD, PhD,¹,³ Frank H. Bosch, MD, PhD,⁴ Durk F. Zandstra, MD, PhD,⁵ Arnoud C. Toornvliet, MD, PhD,⁶ Hazra S. Biemond, MD, PhD,⁷ Bas M. Kors, MD,⁸ Johannes H.T.M. Koelman, MD, PhD,⁹ Marcel M. Verbeek, PhD,¹⁰ Henry C. Weinstein, MD, PhD,¹¹,¹² Albert Hijdra, MD, PhD,¹² and Janneke Horn, MD, PhD¹

• 391 OHCA patients admitted to 10 hospitals
  – All treated with hypothermia
  – 76.5% VF or VT
• Systematic assessments:
• Clinical exams, SSEPs, NSE
• “In the Netherlands… absent SSEP cortical responses are a reason to withdraw treatment”
Hypothermia likely increases false positive rate of clinical predictors

<table>
<thead>
<tr>
<th></th>
<th>Patients tested, n</th>
<th>Positive test result, n (%)</th>
<th>Patients with positive test result and good outcome, n</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>FPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>72-hr Motor score 1 or 2</td>
<td>284</td>
<td>112 (39)</td>
<td>16</td>
<td>74 (66–81)</td>
<td>90 (84–94)</td>
<td>10 (6–16)</td>
</tr>
<tr>
<td>72-hr Absent pupillary light responses</td>
<td>196</td>
<td>22 (11)</td>
<td>1</td>
<td>18 (12–26)</td>
<td>99 (93–100)</td>
<td>1 (0–7)</td>
</tr>
<tr>
<td>72-hr Absent corneal reflexes</td>
<td>130</td>
<td>23 (18)</td>
<td>2</td>
<td>26 (18–37)</td>
<td>96 (87–99)</td>
<td>4 (1–13)</td>
</tr>
<tr>
<td>Absent N20s SEP hypothermia</td>
<td>263</td>
<td>43 (16)</td>
<td>3</td>
<td>28 (21–36)</td>
<td>98 (93–99)</td>
<td>3 (1–7)</td>
</tr>
<tr>
<td>Absent N20s SEP normothermia</td>
<td>128</td>
<td>42 (33)</td>
<td>0</td>
<td>38 (30–48)</td>
<td>100 (82–100)</td>
<td>0 (0–18)</td>
</tr>
</tbody>
</table>

*79% withdrawal after absent SSEP
Reversible brain death after cardiopulmonary arrest and induced hypothermia*

“A 55-yr-old man presented with cardiac arrest... spontaneous perfusion restored, and therapeutic hypothermia provided”

“Death was pronounced and the family consented to organ donation.”
Reversible brain death after cardiopulmonary arrest and induced hypothermia*

“24 hrs after brain death, on arrival to the operating room for organ procurement, the patient was found to have regained corneal reflexes, cough reflex, and spontaneous respirations.”

Webb and Samuels, CCM 2011.
Coma

Exclude major confounders

No brain stem reflexes at any time (pupil, cornea, oculocephalic, cough)

Or

Day 1
Myoclonus Status Epilepticus

Or

Day 1-3 SEP absent N1b responses*

Or

Day 1-3
Serum NSE >33 μg/L*

Or

Day 3
Absent pupil or corneal reflexes; extensor or absent motor response

Yes

Brain death testing

FPR 0% (0-8.8)

Poor outcome

FPR 0% (0-3.7)

FPR 0% (0-3)

Poor outcome

Poor outcome

Indeterminate outcome

FPR 0% (0-3)
Recommendations

• Once hypothermia has been initiated
  • Do not attempt neuroprognostication until sedatives, paralytics have worn off, hypotension is treated
  • Do not base WDLS decisions on determinations of neurological prognosis within first 72 hours
Recommendations

- Once hypothermia has been initiated
  - Bilateral absence of N20 peak on SSEP > 72 hrs
    - studies may be biased by “self-fulfilling prophesies”
  - If SSEPs unavailable, avoid recommendations based on only 1 predictor

- Beware false positives for motor exam
Do we stop too early?

Feature Articles

Timing of neuroprognostication in postcardiac arrest therapeutic hypothermia

Sarah M. Perman, MD, MS; James N. Kirkpatrick, MD; Angelique M. Reitsma, MD; David F. Galeski, MD; Bonnie Lau, MD; Thomas M. Smith, RN; Marion Leary, RN; Barry D. Fuchs, MD; Joshua M. Levine, MD; Benjamin S. Abella, MD; MPhil; Lance B. Becker, MD; Raina M. Merchant, MD, MS

Objective: Early assessment of neurologic recovery in patients following cardiopulmonary arrest is challenging for healthcare providers, particularly in patients who received therapeutic hypothermia. We sought to evaluate the use of a novel technique to predict neurologic recovery in consecutive cardiac arrest survivors who received therapeutic hypothermia.

Design: A retrospective chart review of consecutive postcardiac arrest patients receiving therapeutic hypothermia. Twenty-four-hour neurological monitoring was performed using a novel technique and was followed by documentation of "poor" or "good" neurologic recovery.

Setting: Two academic urban emergency departments.

Population: A total of 16 consecutive patients who received therapeutic hypothermia were reviewed between September 2005 and April 2006.

Intervention: None.

Results: Of our cohort of consecutive postcardiac arrest patients (96 of 48) were male, and the mean age was 52 ± 10 years. Approximately 300,000 out-of-hospital cardiac arrests occur annually in the United States (1), and nearly 20% of these arrests occur in hospital cardiac arrests (3). Currently, the median survival 6 h of hospital survival is 65% for in-hospital cardiac arrest (3). The median duration of therapy is 7 days; however, this duration is variable and may range from 1 to 30 days.

Conclusion: Documentation of "poor" or "good" outcomes occurred early during the initial phase of cooling, rewarming, or within 15 h of rewarming. In this cohort, no patient who had documented "poor" outcomes survived to discharge, whereas 100% of patients with "good" outcomes survived to discharge with favorable neurologic outcome. The final 10 h from rewarming of patients with "poor" outcomes occurred early during the initial phase of cooling, rewarming, or within 15 h of rewarming. In this cohort, no patient who had documented "poor" outcomes survived to discharge, whereas 100% of patients with "good" outcomes survived to discharge with favorable neurologic outcome.
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- 2 academic hospitals (Philadelphia)
  - 49 consecutive patients receiving hypothermia
    - all rhythms
  - 57% (28) documentation of “grave” prognosis during cooling or rewarming
    - Of these, 25% had life support stopped earlier than 72 hours
    - 21% went on to have favourable neurological recovery
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Do we stop too early?
• All OHCA patients during 2009
  – 293 admitted to hospital
  – 209 (70% died)
  – Of these deaths, 122 (60%) died due to WDLS
  • 70% (86/122) of WDLS occurred earlier than 72 hours
  • 41% of these early deaths had received hypothermia
Preventing Premature Termination Of Resuscitation in Patients with Anoxic Brain Injury

The PremaTOR study
Summary

- Therapeutic hypothermia improves survival AND neurological outcomes
- Avoid secondary brain insults – especially hypoxemia (and possibly hyperoxemia), hypocapnia, and hypotension
- Beware higher false positive rate of some clinical predictors of neurological prognosis after treatment with hypothermia
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