Post-resuscitation care

The brain

Intensive Care Training Program
Radboud University Medical Centre Nijmegen
Death after ICU admission

Laver S. Intensive Care Med 2004;30:2126-2128
Hypothermia lowers mortality

- 5317 patients admitted to the ICU after cardiac arrest with GCS ≤ 8 (10 y period)
- 1547 before and 3770 after implementation of MTH

van der Wal G. Crit Care Med 2011;39:84-88
Brain damage after CPR

- Multiple cellular processes resulting in cell death
- Disturbed microcirculation (thrombosis)
- Global hypoperfusion with disturbed autoregulation / brain edema
- Fever and hyperglycemia
Hypothermia

- Decrease CMRO$_2$
  - $8\%/\degree C$

- Improve glucose metabolism

- Inhibit apoptosis

- Decrease O$_2$ radicals

- Decrease neuro excitotoxicity

- Maintain integrity BBB

- Decrease inflammation

- ?????
MTH and hemodynamics

During hypothermia

- Heart rate 80 → 65
- CI van 2.64 ± 0.87 → 2.45 ± 0.59
- 92% norepinephrine - increase during maintenance/rewarming

Only 13 patients with PA catheter

CBF and MTH

Time after admission to the ICU (hrs)

MFV\textsubscript{MCA} (cm/sec)

Bisschops LLA. Crit Care Med 2010;38:1542-1547
Jugular bulb saturation

Time after admission to the ICU (hrs)

SjbO2 (%)
3.6 ± 2.9% / mmHg PaCO$_2$

\[ y = 0.9654x + 2.7569 \]
\[ R^2 = 0.4126 \]
Pigs (N = 21)
VF (7 min) - BLS (2 min) - ACLS
38 °C - 33 °C - 33 °C + SV

Brain biopsy

Meyboom P. Crit Care 2010;14:R21
Increase in inflammation with rewarming?

Measure inflammatory parameters after 0 - 3 - 6 - 12 - 24 en 48 uur
Pro-inflammatory cytokines

IL-6

Time in hours

Bisschops LLA. Crit Care Med 2012;40:000-000
Prolonged hypothermia

$N = 10$
Hemodynamic effects of MTH for 72 hrs

Bisschops LLA. Crit Care Med 2012 - accepted
Prolonged hypothermia
Prolonged hypothermia
Prolonged hypothermia
Hyperoxia dangerous?
<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 after MTH

N = 103

A. M score favourable outcome

B. M score unfavourable outcome

Bisschops LLA. Resuscitation 201182:696-701
<table>
<thead>
<tr>
<th></th>
<th>Favourable N = 36</th>
<th>Unfavourable N = 67</th>
<th>P-value</th>
<th>PPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3 M1-2 or no PR or no CR</td>
<td>4/36 (11.1%)</td>
<td>54/67 (80.6%)</td>
<td>&lt; 0.001</td>
<td>0.93 (0.82-0.98)</td>
</tr>
<tr>
<td>Day 3 M1-2 and no PR and no CR</td>
<td>0/36 (0%)</td>
<td>10/67 (14.9%)</td>
<td>0.013</td>
<td>1.00 (0.66-1.00)</td>
</tr>
<tr>
<td>Spontaneous myoclonus</td>
<td>2/36 (5.6%)</td>
<td>24/67 (35.8%)</td>
<td>0.001</td>
<td>0.92 (0.73-0.99)</td>
</tr>
<tr>
<td>Stimulus sensitive myoclonus</td>
<td>1/36 (2.8%)</td>
<td>5/67 (7.5%)</td>
<td>0.027</td>
<td>0.83 (0.36-0.99)</td>
</tr>
<tr>
<td>Both types of myoclonus</td>
<td>1/36 (2.8%)</td>
<td>7/67 (10.4%)</td>
<td>0.166</td>
<td>0.89 (0.47-0.99)</td>
</tr>
</tbody>
</table>

**PPV** absent cortical response SSEP 1.00 (0.78 - 1.00)

Recorded encephalograms in 27 patients.

<table>
<thead>
<tr>
<th></th>
<th>Favourable(N = 4)</th>
<th>Unfavourable(N= 23)</th>
<th>p Value</th>
<th>PPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive theta</td>
<td>1/4 (25.0%)</td>
<td>3/23 (13.0%)</td>
<td>0.534</td>
<td>0.75 (0.22-0.99)</td>
</tr>
<tr>
<td>Predominant delta</td>
<td>0/4 (0.0%)</td>
<td>2/23 (8.7%)</td>
<td>0.540</td>
<td>1.00 (0.20-1.00)</td>
</tr>
<tr>
<td>Triphasic waves</td>
<td>1/4 (25.0%)</td>
<td>3/23 (13.0%)</td>
<td>0.534</td>
<td>0.75 (0.22-0.99)</td>
</tr>
<tr>
<td>Suppression</td>
<td>1/4 (25.0%)</td>
<td>9/23 (39.1%)</td>
<td>0.589</td>
<td>0.90 (0.54-0.99)</td>
</tr>
<tr>
<td>Burst suppression</td>
<td>0/4 (0.0%)</td>
<td>2/23 (8.7%)</td>
<td>0.540</td>
<td>1.00 (0.20-1.00)</td>
</tr>
<tr>
<td>PLEDs</td>
<td>3/4 (75%)</td>
<td>14/23 (60.9%)</td>
<td>0.589</td>
<td>0.82 (0.56-0.95)</td>
</tr>
<tr>
<td>Unreactive</td>
<td>0/4 (0.0%)</td>
<td>15/23 (65.2%)</td>
<td>0.015</td>
<td>1.00 (0.75-1.00)</td>
</tr>
</tbody>
</table>
Bilateral absence CR after 72 hrs
Bilateral absence PR after 72 hrs

TPR  STUDY  FPR

10/55  1  0/35
10/38  2  0/27
21/115  3  1/80
5/29  4  0/2
13/39  5  0/71
8/31  9  0/21
4/16  10  0/7
Summary measures of sensitivity and false positive rate

<table>
<thead>
<tr>
<th>Tests</th>
<th>Sensitivity (95% CI)</th>
<th>FPR (95% CI)</th>
</tr>
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<tr>
<td>Bilaterally absent SSEP 72 hrs</td>
<td>49.6 (42.4 to 56.8)</td>
<td>0.7 (0.1 to 4.7)</td>
</tr>
<tr>
<td>GCS motor score 1-2 72 hrs</td>
<td>80.2 (62.8 to 90.6)</td>
<td>20.6 (8.2 to 42.8)</td>
</tr>
<tr>
<td>Bilaterally absent corneal reflexes 72 hrs</td>
<td>32.4 (26.7 to 38.6)</td>
<td>1.8 (0.2 to 13)</td>
</tr>
<tr>
<td>Bilaterally absent pupillary reflexes 72 hrs</td>
<td>22 (17.7 to 26.9)</td>
<td>0.4 (0.1 to 3)</td>
</tr>
</tbody>
</table>

FPR: false positive rate
MRI after cardiac arrest

N = 20, median 123 hrs after CA

Majority in “watershed areas”

Järnum H. Resuscitation 2009;80:425-430
DWI-MRI after cardiac arrest - example

Fatal outcome after CA with lesions in basal ganglia and occipital cortex
Conclusion

• Hypothermia established treatment for brain protection after CA
• Initial strong decrease in CBF but in most cases preserved metabolic coupling
• Carbon dioxide responsivity preserved
• Possible inflammatory upsurge after MTH
• Increasing prognostic uncertainty