Hypothermic Resuscitation

Beyond “Therapeutic:” Intraarrest Hypothermia to Mitigate Reperfusion Injury after Cardiac Arrest

1st International Critical Care and Emergency Medicine Congress

Istanbul, 11/6-8/2013
HYPOTHERMIC RESUSCITATION
(non-official) definitions

Protective Hypothermia:
- Hypothermia induced before cardiac arrest (CA)
- Not feasible for sudden CA

Preservative Hypothermia:
- Hypothermia induced during cardiac arrest before reperfusion

Resuscitative or therapeutic Hypothermia:
- Hypothermia after restoration of spontaneous circulation

Nov. 8, 9:00, Room A
HYPOTHERMIC RESUSCITATION

timeline of reperfusion injury

hypothesis: the initial phase of reperfusion is crucial

eye mechanisms of reperfusion injury:

- calcium overload
- excitotoxicity amino acids
- ROS

Dirnagl U et al. TINS 2003
COOLING TECHNIQUES
how to induce hypothermia in a no flow state

surface cooling
- circulation needed
- cold capillary blood from skin cools the core
- ineffective during cardiac arrest

cooling during circulation and arrest
- 90 kg human sized swine
- cooling with -40°C cold gas
- brain temperatures

Bayegan et al. Resuscitation 2004 (abstract)
SURFACE COOLING
beating heart vs. cardiac arrest

cold gas:
beating heart
cardiac arrest

Bayegan et al. Resuscitation 2004 (abstract)
INVASIVE COOLING
aortic flush, extracorporeal circulation

cardiac arrest:
aortic flush, cold saline 100 ml/kg

ECMO with heat exchanger

Outcome after resuscitation using controlled rapid extracorporeal cooling,

Janata a et al Crit Care Med. 2006
HYPOTHERMERIC RESUSCITATION
ice cold iv. saline during resuscitation

- 33 patients
- 2L 4°C cold saline 0.9% over 30 min during ACLS
- ΔTesophagus -2.1°C
- median time to reach <34°C after ROSC: 16 minutes
- 1 patient developed pulmonary edema
- survival to discharge: 4/33 (12%)

Conclusion:
- 2L cold saline during ACLS is feasible, effective and safe
HYPOTHERMIC RESUSCITATION

ice cold iv. saline during resuscitation

--- LAD occlusion for 120 minutes --- balloon deflated ---

Control. no therapy.

External HTM with cooling blankets and ice.

5ml/kg/min 28°C intra-CPR NS infusion. No other therapy.

VF induction

DC cardioversion

ROSC time

reperfusion

5ml/kg/min 4°C NS infusion, intra-CPR HTM + post ROSC External HTM.

Volume-sparing ETHS device for intra-CPR + post ROSC HTM
HYPOTHERMIC RESUSCITATION

Ice cold iv. saline during resuscitation

46 pigs, LAD-occlusion cardiac arrest model

CoPP = coronary perfusion pressure (diastolic aortic pressure minus diastolic right atrial pressure during CPR)

SBP = systolic blood pressure

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>intervention</td>
<td>Surface cooling post ROSC</td>
<td>25 ml/kg 28°C iv saline intra-arrest</td>
<td>25 ml/kg 4°C iv saline intra-arrest</td>
<td>Cooling catheter intra-arrest</td>
</tr>
<tr>
<td>ROSC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>56%</td>
<td></td>
<td>13%</td>
<td>55%</td>
<td>100%</td>
</tr>
<tr>
<td>CoPP</td>
<td>100</td>
<td></td>
<td>102</td>
<td>11</td>
<td>113</td>
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</tbody>
</table>

**HYPOTHERMIC RESUSCITATION**

Ice cold intra-arterial saline during resuscitation

24 pigs, electrical VF-cardiac arrest model

15 min cardiac arrest

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<thead>
<tr>
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<th>A</th>
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<th>C</th>
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</thead>
<tbody>
<tr>
<td>ACLS</td>
<td>ACLS, no intervention</td>
<td>30 ml/kg 38°C iv saline intra-arrest</td>
<td>30 ml/kg 4°C iv saline intra-arrest</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional</th>
<th>Hypothermic Flush</th>
<th>Normothermic Flush</th>
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<tbody>
<tr>
<td>OPC 1</td>
<td></td>
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<tr>
<td>OPC 2</td>
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<tr>
<td>OPC 3</td>
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<tr>
<td>OPC 4</td>
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<td></td>
<td></td>
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<tr>
<td>OPC 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Rosc</td>
<td>●●●●●●●●●●●●</td>
<td>•●●●●●●●●●●●</td>
<td>•●●●●●●●●●●●</td>
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<thead>
<tr>
<th></th>
<th>OPC 1</th>
<th>OPC 2</th>
<th>OPC 3</th>
<th>OPC 4</th>
<th>OPC 5</th>
<th>No Rosc</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROSC</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival to 9 days</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NDS (%)</td>
<td>-</td>
<td>0,6,13</td>
<td>0,49</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HYPOTHERMIC RESUSCITATION

ice cold intra-arterial saline during resuscitation

Rapid induction of hypothermia with a small volume aortic flush during cardiac arrest in pigs
Hypothesis: a coolant into the nasal cavity will cool adjacent tissues – including the brain

- 16 pigs weighing 40±3kg
- 15 min VF
- 5-15 min of ACLS

randomization to nasal cooling vs. normothermia prior to shock

Results:
- no difference in brain temperature
- ROSC cooling group: 7/8 control group: 2/8 (p=0.04)

Conclusion: Nasal Cooling During CPR Facilitates ROSC


LOCAL SURFACE COOLING
nasopharyngeal cooling
LOCAL SURFACE COOLING

nasopharyngeal cooling with rhinochill

- 93 patients during arrest, cooled with transnasal cooling, compared to 101 control patients

- $\Delta T$ tympanic ROSC-admission: 1.3°C

- Safe, some local side effects

- Reliability of T tympanic?

- Good outcome (CPC1-2):
  - cooling group 11/93 (12%)
  - control group: 9/101 (9%)

Extracorporeal CPR (E-CPR) cooling with cardiopulmonary bypass during CA

Probability of ROSC decreases over time

Overall Hypothesis:

- support the heart for prolonged time periods
- achieve critical organ perfusion more reliably than chest compressions
- resuscitate the patients after prolonged periods of CA
- induce hypothermia rapidly
E-CPR
brain perfusion with E-CPR after 10 min cardiac arrest in rats

Cerebral blood flow with spin label MRI:
Hemispheric CBF by E-CPR is 76% of baseline

Baseline – 10 min Cardiac Arrest – CPB 50 ml/min
HYPOTHERMIA AND E-CPR
for refractory cardiac arrest – perfusion and cooling

1-year experience of Erasme Hospital, Brussels

Inclusion criteria:

(a) **witnessed** cardiac arrest with immediate CPR (<5 min from call to chest compression)

(b) refractory CA, as defined by the absence of ROSC after 10 min of Advanced Life Support (ALS)

(c) age less than 65 years and no major co-morbidity

(d) the ability to initiate ECMO within 1 h from arrest

Extracorporeal life support associated with hypothermia and normoxemia in refractory cardiac arrest. Fagnoul et al, Resuscitation 2013
E-CPR
for refractory cardiac arrest

Methods:

- mechanical CPR with Lucas
- 30 ml ice cold saline/kg during CPR
- veno-arterial ECMO
- heat exchanger to maintain 33°C for 24 h
- PCI after ECMO implantation

Extracorporeal life support associated with hypothermia and normoxemia in refractory cardiac arrest. Fagnoul et al, Resuscitation 2013
E-CPR for refractory cardiac arrest

General characteristics of the patients (n = 24) and cardiac arrest data.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: years</td>
<td>48 [38–55]</td>
</tr>
<tr>
<td>Male: n</td>
<td>14</td>
</tr>
<tr>
<td>Location of cardiac arrest</td>
<td></td>
</tr>
<tr>
<td>In hospital: n</td>
<td>10</td>
</tr>
<tr>
<td>Out hospital: n</td>
<td>14</td>
</tr>
<tr>
<td>By-stander CPR: n</td>
<td>22</td>
</tr>
<tr>
<td>Cardiac arrest to ALS time (min)</td>
<td>10 [5–15]</td>
</tr>
<tr>
<td>Initial recorded rhythm: n</td>
<td></td>
</tr>
<tr>
<td>VF/VT</td>
<td>10</td>
</tr>
<tr>
<td>PEA/asystole</td>
<td>14</td>
</tr>
<tr>
<td>Mechanical chest compression: n</td>
<td>22</td>
</tr>
<tr>
<td>Cooling (IV fluids/intranasal cooling): n</td>
<td>16</td>
</tr>
<tr>
<td>Temperature at ECMO initiation: (°C)</td>
<td>32.3 ± 2.9</td>
</tr>
<tr>
<td>Time from CA to ECMO (min)</td>
<td>58 [45–70]</td>
</tr>
<tr>
<td>ROSC: n</td>
<td>18</td>
</tr>
<tr>
<td>Duration of ECMO (Hours)</td>
<td>48 [2–66]</td>
</tr>
<tr>
<td>Survivors</td>
<td>96 [54–172]</td>
</tr>
<tr>
<td>Non-survivors</td>
<td>3.5 [2–48]</td>
</tr>
<tr>
<td>Weaning from ECMO; n (%)</td>
<td>7 (29%)</td>
</tr>
<tr>
<td>Survival to ICU discharge n (%)</td>
<td>6 (25%)</td>
</tr>
</tbody>
</table>

OHCA n=14
IHCA n=10

Refractory cardiac arrest N= 24

Survivors n=6
Non survivors n=18

Organ donation possible n=4
Organ donation not possible n=14

Organ donation accepted n=2
Organ donation refused n=2

Uncontrolled massive bleeding n=8

multiple organ dysfunction n=12
EPR
EMERGENCY PRESERVATION AND RESUSCITATION

Definition

„Torpor“ (lat. Erstarrung)
Reduced metabolic rate to protect the organism during adversity (harsh climate, low availability of food – or ischemia)

EPR, SA
A hibernation-like state, induced in animals that normally do not hibernate to protect the organism during adversity (shock, ischemia)
“preservation of viability of the organism for transport and repair during circulatory arrest of 2 h or longer, followed by delayed resuscitation to survival without brain damage”

Safar and Bellamy 1984
EPR

induction by hypothermia

- Metabolism is reduced by 5% to 8% /°C temperature reduction

  Rosomoff et al, Am J Physiol 1954
  Lanier et al, J Neurosurg Anesthesiol 1995
Swine after 10 min of VF-CA

Aortic flush (100 ml/kg) via balloon catheter

EPR
in vfib-cardiac arrest

![Graph showing Tbr, art pressure, and ven pressure over time.](Image)
EPR flush technique

Saline + Vasopressin 1.2 IU/kg

Cooling rate 4.8°C/min

Cooling effect 6.0°C/L flush

Which temperature buys how much time?

Groups with predominantly favourable outcome after ExCA.

- TTy - volume to 8°C (dogs) + O2 + Glucose
- TTy - volume to 10°C (dogs) – mixed outcome at 120 min
- TTy - volume to 10°C (dogs)
- TTy - volume to 15°C (dogs) (mixed outcome at 20°C)
- TTy 28°C (dogs, 100 ml/kg 4°C)
- TTy 34°C (dogs, 500 ml 4°C)


*Anesthesiology* 93:1491-1499 2000

*Acad Emerg Med* 7:1341-1348 2000
Antioxidant Tempol improves neurologic recovery vs. saline water-soluble, inexpensive, commercially available, penetrates the blood-brain-barrier

Tempol vs. saline

Adenosine

Fructose-1,6-bisphosphate, MK-801

Tiopental, Phenytoin

EPR flush cocktails – additions to improve protection

Wu et al. JCBFM 28:302-311 2008

Tempol vs. saline

Blehringer et al. JCBFM 22:105-117 2002


Behringer et al. Resuscitation 50:205-16 2001


Minutes

0  5  10  15  20  25  30

Hours

1  2  3
EPR after prolonged VF in pigs

15 min VF

No flush/CPR n=8

200 ml/kg 4°C NaCl/Epi/Vaso

Flush/no CPR

CPB

Controlled ventilation and mild hypothermia 20 h

Survival for 9 days

EPR after prolonged VF in pigs

15 min VF

No flush/CPR n=8

200 ml/kg 4°C NaCl/Epi/Vaso

Flush/CPR

Flush/no CPR

Controlled ventilation and mild hypothermia 20 h

Survival for 9 days

**EPR**

after prolonged vf in pigs

Brain temperature

HYPOTHERMIC RESUSCITATION

Need for more data

Venous volume load and CoPP?

Feasible for vf ca?

Combination with invasive resuscitation methods.

EPR+E-CPR?
HYPOTHERMIC RESUSCITATION

Thank You.