THE PRINCESS TRIAL
PREHOSPITAL RESUSCITATION INTRA-ARREST COOLING EFFECTIVENESS SURVIVAL STUDY

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Cooling device provided without cost, BrainCool AB
THE FACTS

- Hypothermia in cardiac arrest protects the brain
- Animal data shows that "the earlier, the better"
- Most studies are based on hospital cooling
- Prehospital cooling with cold fluids is not hemodynamically safe
THE METHOD
TRANSNASAL EVAPORATIVE COOLING

• Primarily brain cooling
• Easy to use, early initiation
• Non-invasive
• Continuous cooling
• No volume load
THE AIM

- To study the effect of intra-arrest, trans-nasal evaporative cooling on neurologic intact survival in out-of-hospital cardiac arrest patients.

- Primary outcome was survival with CPC 1-2 at 90 days
THE DESIGN

OUT-OF-HOSPITAL CARDIAC ARRESTS

- PREHOSP COOLING
  - COOLING AT ICU

- STANDARD CARE
  - COOLING AT ICU

EUROPEAN MULTICENTER RANDOMIZED CONTROLLED TRIAL IN 7 COUNTRIES

11 EMS SYSTEMS, 17 RECEIVING HOSPITALS
Study period 2010-2018
THE PATIENTS

Inclusion criteria
Bystander witnessed cardiac arrest
Age ≥18 years

Predefined subgroup:
Ventricular fibrillation

Exclusion criteria
Age ≥80 years
Obvious non-cardiac cause
A barrier to place intra nasal catheters
DNAR orders
Achieve ROSC prior to randomization
Response time of EMS > 15 minutes
RESULTS

343 intervention (intra-arrest cooling) 6 were excluded
337 were included in the modified ITT

677 patients were randomized

334 control (cooling at hospital)
334 were included in the modified ITT
THE STUDY POPULATION AND EVENT TIMES

- **75%** Male
- **60%** Bystander CPR
- **40%** Had Ventricular Fibrillation

**Median Age**: 65 Years

**Event Times**:
- EMS Initiated CPR: 9 Minutes
- Airway Established: 14 Minutes
- Time to Randomization: 17 Minutes
- Cooling Started: 19 Minutes
COOLING EFFICACY

Temperature Comparison:
- AT ROSC: 35.7°C vs 36.0°C
- AT HOSPITAL ARRIVAL: 34.6°C vs 35.8°C

Time to Target (<34GR):
- 101 MIN vs 182 MIN
- P<0.001
# Safety

<table>
<thead>
<tr>
<th>Device-related Events</th>
<th>Intervention, N=324</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged nose bleed</td>
<td>1 %</td>
</tr>
<tr>
<td>Minor nosebleed</td>
<td>14 %</td>
</tr>
<tr>
<td>White nose tip</td>
<td>6 %</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications within 7 days</th>
<th>Intervention, N=143</th>
<th>Control, N=141</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular fibrillation</td>
<td>2 %</td>
<td>4 %</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>22 %</td>
<td>24 %</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>5 %</td>
<td>13 %</td>
</tr>
<tr>
<td>Vasopressor required</td>
<td>76 %</td>
<td>70 %</td>
</tr>
</tbody>
</table>
PRIMARY OUTCOME

SURVIVAL WITH CPC 1–2 AT 90 DAYS

INTERVENTION

ALL PATIENTS

16.6% (N=56/337) VS. 13.5% (N=45/334)

Absolute difference 3.1%, relative difference 23%

CONTROL

PATIENTS WITH VENTRICULAR FIBRILLATION

34.8% (N=48/138) VS. 25.9% (N=35/135)

Absolute difference 8.9%, relative difference 25%

P=0.26

P=0.11
COMPLETE NEUROLOGIC RECOVERY, CPC 1

ALL PATIENTS WITH VF

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Control</th>
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<tbody>
<tr>
<td>32.6%</td>
<td>20%</td>
</tr>
<tr>
<td>(45/138)</td>
<td>(27/135)</td>
</tr>
<tr>
<td>14.8%</td>
<td>10.5%</td>
</tr>
<tr>
<td>(50/337)</td>
<td>(35/334)</td>
</tr>
</tbody>
</table>

P = 0.02

P = 0.09
NEUROLOGIC OUTCOMES, CPC 1-4

NUMBER OF PATIENTS ALIVE AT 90 DAYS

INTERVENTION
n=60

CPC 1
n=50

CONTROL
n=52

CPC 1
n=35
TIME TO COOLING AND NEUROLOGIC OUTCOME

ALL PATIENTS / PATIENTS WITH VF

MEDIAN TIME TO COOLING 19 MINUTES
CONCLUSIONS

TRANS Nasal EVAPORATIVE COOLING IN OUT-OF-HOSPITAL CARDIAC ARREST

- HEMODYNAMICALLY SAFE
- SIGNIFICANTLY SHORTENED TIME TO TARGET TEMPERATURE
- THE DIFFERENCE IN PRIMARY OUTCOME (CPC 1-2) WAS NOT STATISTICALLY SIGNIFICANT
- TREND TOWARDS IMPROVED NEUROLOGIC OUTCOME IN PATIENTS WITH VENTRICULAR FIBRILLATION
- SIGNIFICANTLY IMPROVED COMPLETE RECOVERY (CPC 1) IN PATIENTS WITH VENTRICULAR FIBRILLATION
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