EMCOOLS

EASY EFFICIENT PATIENT COOLING

PATIENT COOLING
PRE- & IN-HOSPITAL PRACTICAL INSIGHTS

March 2015

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CARDIAC ARREST IN VIENNA

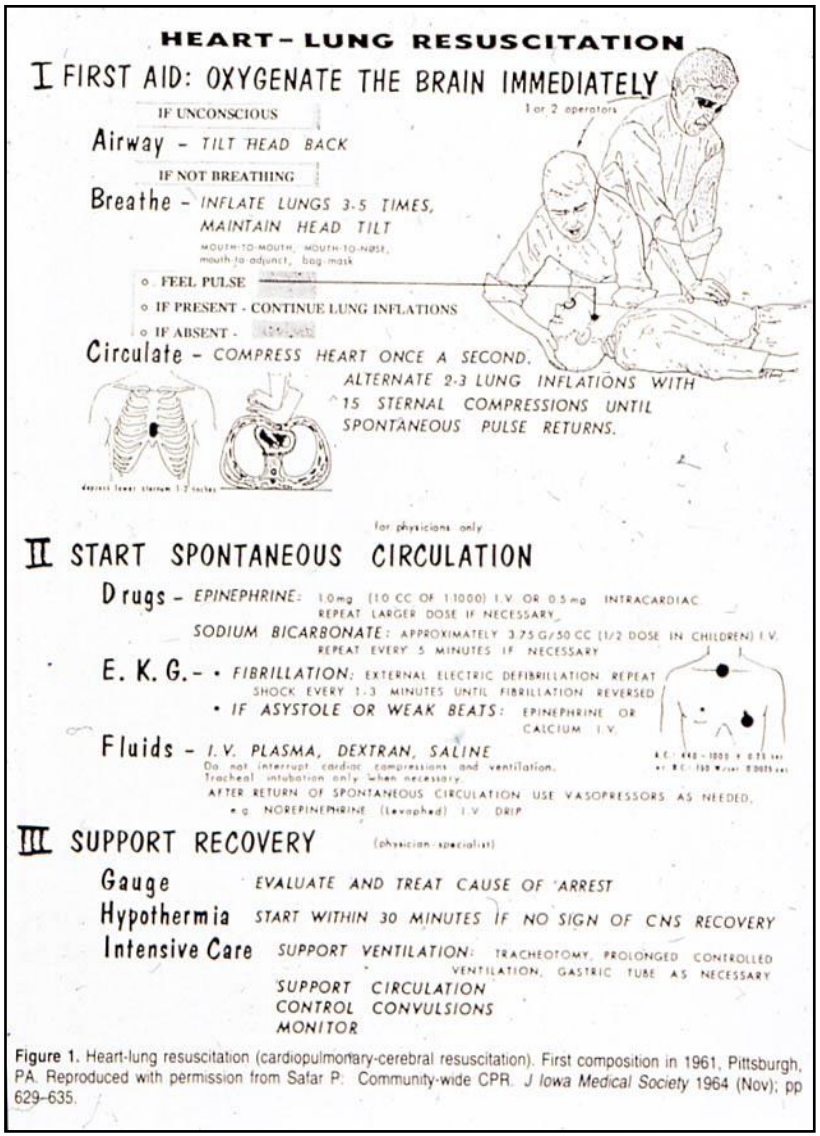
Patient data*

- 7.030 patients without signs of circulation (206/100,000/year)
- 1.448 resuscitation attempts by the Vienna Ambulance Service
- 361 patients with sustained ROSC (25%)
- 164 (11.3%) discharged
- 126 (8.7%) with good outcome / CPC 1-2

* * 2009-2010

Out of Hospital Cardiac Arrest in Vienna: Incidence and Outcome.
Nürnberger et al. Resuscitation 2013

VIENNA – A SHORT STORY OF COOLING



HEART–LUNG RESUSCITATION

I FIRST AID: OXYGENATE THE BRAIN IMMEDIATELY

IF UNCONSCIOUS

Airway – TILT HEAD BACK

IF NOT BREATHING

Breathe – INFLATE LUNGS 3-5 TIMES, MAINTAIN HEAD TILT

MOUTH-TO-MOUTH, MOUTH-TO-NOSE, mouth-to-adjunct, bag-mask

- FEEL PULSE
- IF PRESENT - CONTINUE LUNG INFLATIONS
- IF ABSENT -

Circulate – COMPRESS HEART ONCE A SECOND. ALTERNATE 2-3 LUNG INFLATIONS WITH 15 STERNAL COMPRESSIONS UNTIL SPONTANEOUS PULSE RETURNS.

1 or 2 operators

for physicians only

II START SPONTANEOUS CIRCULATION

Drugs – EPINEPHRINE: 1.0 mg (10 CC OF 1:1000) I.V. OR 0.5 mg INTRACARDIAC. REPEAT LARGER DOSE IF NECESSARY.

SODIUM BICARBONATE: APPROXIMATELY 3.75 G/50 CC (1/2 DOSE IN CHILDREN) I.V. REPEAT EVERY 5 MINUTES IF NECESSARY

E. K. G. – • FIBRILLATION: EXTERNAL ELECTRIC DEFIBRILLATION. REPEAT SHOCK EVERY 1-3 MINUTES UNTIL FIBRILLATION REVERSED

• IF ASYSTOLE OR WEAK BEATS: EPINEPHRINE OR CALCIUM I.V.

Fluids – I.V. PLASMA, DEXTRAN, SALINE

Do not interrupt cardiac compressions and ventilation. Tracheal intubation only when necessary.

AFTER RETURN OF SPONTANEOUS CIRCULATION USE VASOPRESSORS AS NEEDED.

e.g. NOREPINEPHRINE (Levophed) I.V. DRIP

III SUPPORT RECOVERY (physician-specialist)

Gauge – EVALUATE AND TREAT CAUSE OF ARREST

Hypothermia – START WITHIN 30 MINUTES IF NO SIGN OF CNS RECOVERY

Intensive Care – SUPPORT VENTILATION: TRACHEOTOMY, PROLONGED CONTROLLED VENTILATION, GASTRIC TUBE AS NECESSARY

SUPPORT CIRCULATION

CONTROL CONVULSIONS

MONITOR

Figure 1. Heart-lung resuscitation (cardiopulmonary-cerebral resuscitation). First composition in 1961, Pittsburgh, PA. Reproduced with permission from Safar P. Community-wide CPR. *J Iowa Medical Society* 1964 (Nov); pp 629–635.

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VIENNA RESUSCITATION APPROACH

MECHANICAL CHEST COMPRESSION DIVCE

PREHOSPITAL COOLING

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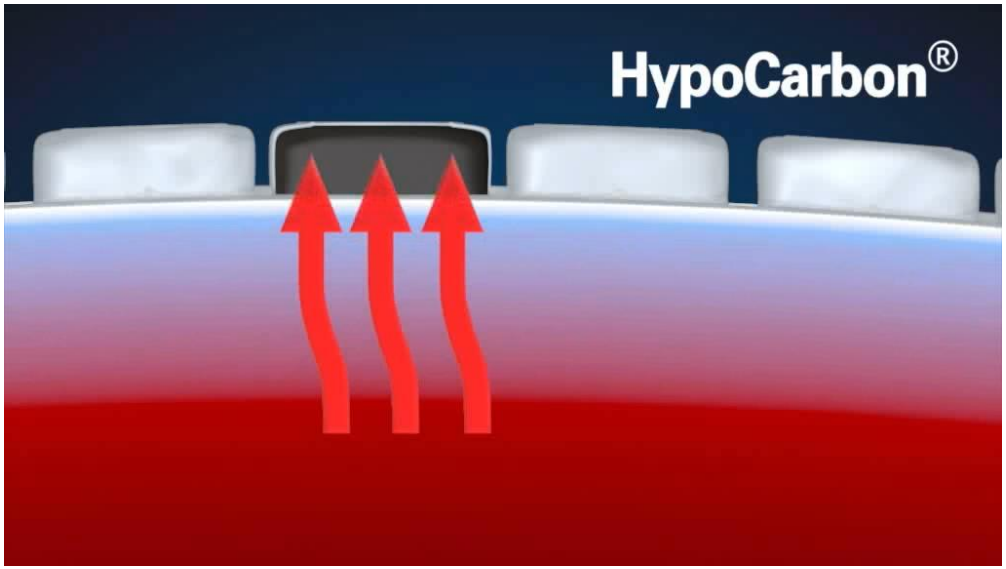
EMCOOLS FLEX.PAD

HYPOCARBON ®

EMCOOLS EASY EFFICIENT PATIENT COOLING

- Cooling rates of up to 3.3°C/h
- Biocompatible material (skin- and environmentally friendly, non-toxic)



Data on file at EMCOOLS,.

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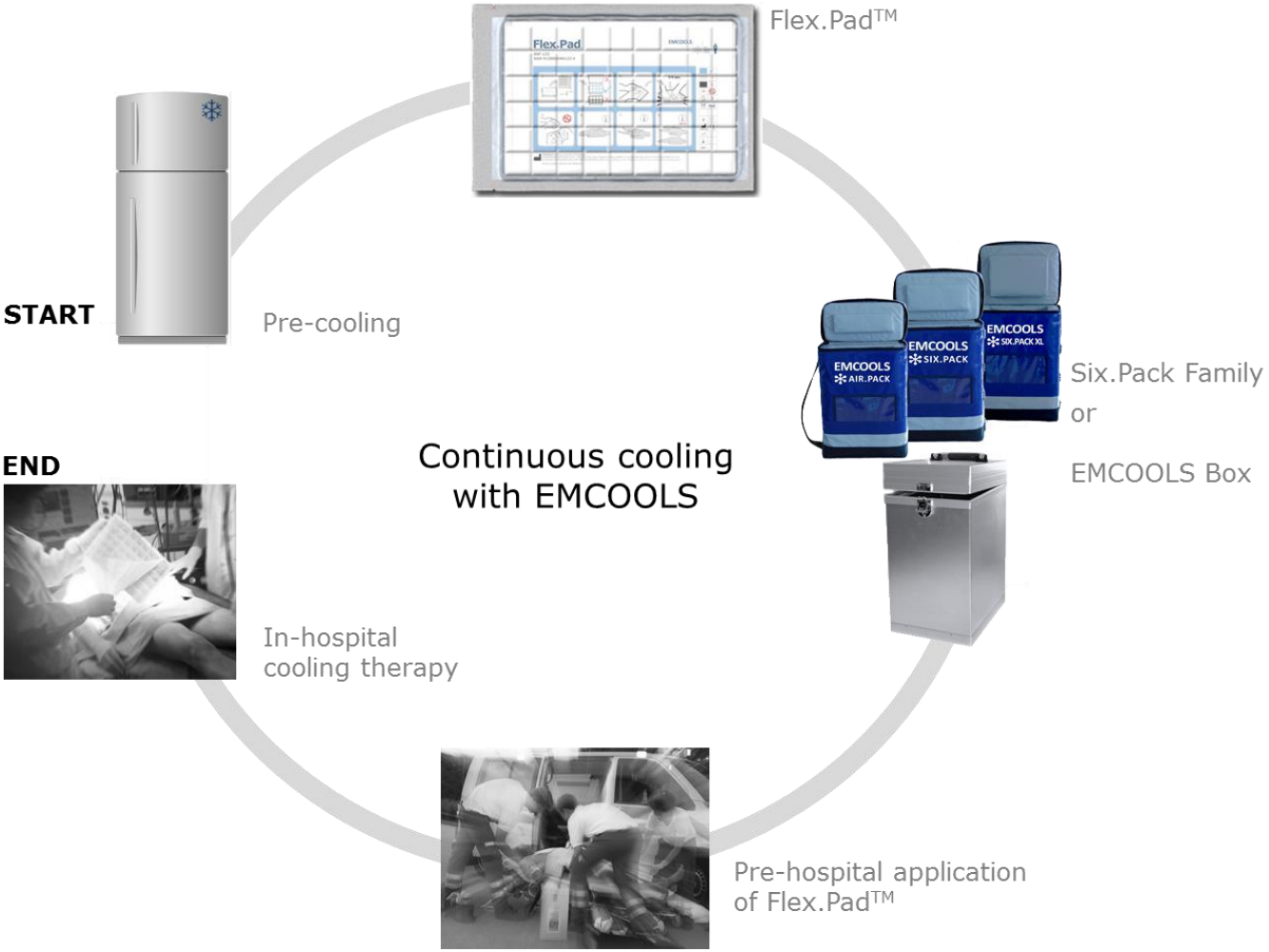
CONTINUOUS COOLING CHAIN



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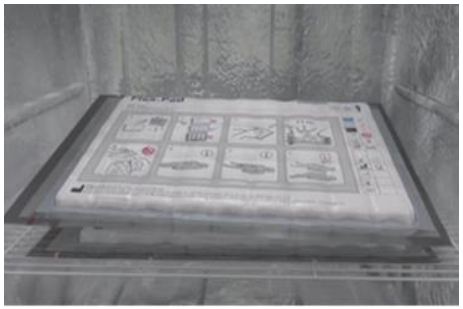
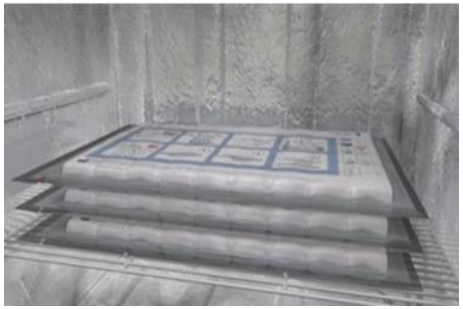
PREPARATION



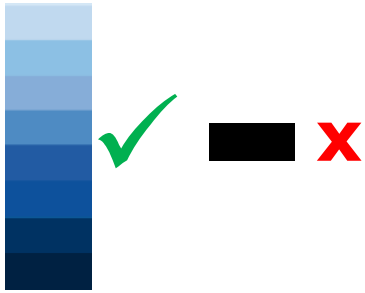
1 Preparation

- Remove transportation- and storage box
- Freeze Flex.Pad™ at -8 to -11°C horizontally
- **Note:** This temperature range reflects a pre-cooling phase of 48h (during first-time freezing)



2 Operational readiness

- Ready to use pads are indicated by a blue color indicator label
- If the pad is too cold the label turns black



3 Application

- Take out ready to use Flex.Pad™ (blue color indicator label)
- Open packaging, remove protective foil and apply immediately on **dry skin**
- **Note:** For activating the adhesive press down evenly for 3-5 seconds

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PRE-HOSPITAL START WITH FLEX.PAD

INITIAL SITUATION - OUT-OF-HOSPITAL CARDIAC ARREST

EMCOOLS EASY EFFICIENT PATIENT COOLING

PRE-HOSPITAL TREATMENT (1/30/2015)

- 16:25 69 year old male, loses consciousness in public bus
- 16:26 Emergency call & start bystander basic life support
- 16:33 Arrival of Vienna Ambulance Service & advanced cardiac life support
  - → Ventricular fibrillation as initial rhythm
  - → 6 mg epinephrine , 300 mg amiodarone
  - → 6 defibrillations
- 16:46 → ROSC
- Application of Flex.Pad at an initial temperature of 35.3°C

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PRE-HOSPITAL START WITH FLEX.PAD

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1. Sedation, analgesia and paralysis

- Midazolam 10 mg
- Fentanyl 0.1 mg
- Atracurium 25 mg
- Bolus administered every 30 min

2. Continuous temperature monitoring

Esophageal temperature probe (inserted by a tubus)

3. Can be used on top of defibrillator pads

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PRE-HOSPITAL START WITH FLEX.PAD

APPLICATION

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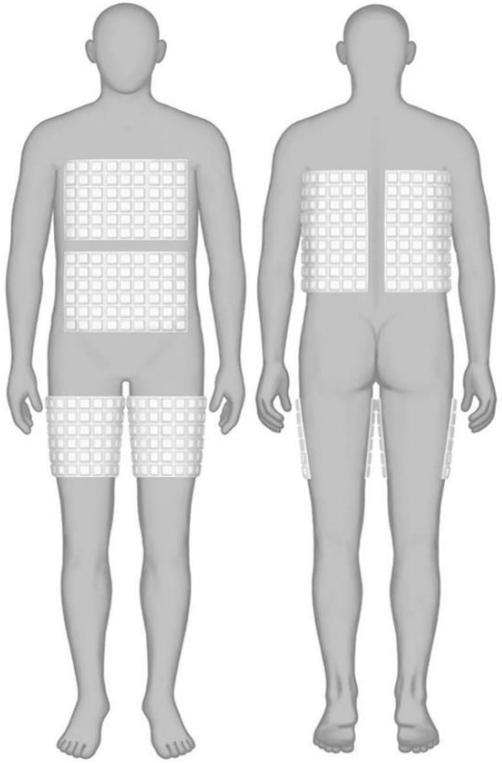
Flex.Pads are applied by the first responders

- 1 pad on the chest (not on female breast tissue)
- 2 pad on the back
- 1 pad on the abdomen
- 1 pad per tigh

→ The application procedure takes about 8 minutes



Rule-of-thumb

- 1 Flex.Pad per 10 kg body weight

Notes

- Don’t apply on face, toes, fingers, genital region, female breast tissue or pregnant
- Don‘t apply in case of skin diseases, inflammation, burns or any other skin injuries
- During treatment skin temperature does not drop below 4 to 8°C

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PRE-HOSPITAL COOLING

CLINICAL DATA

15 patients after cardiac arrest

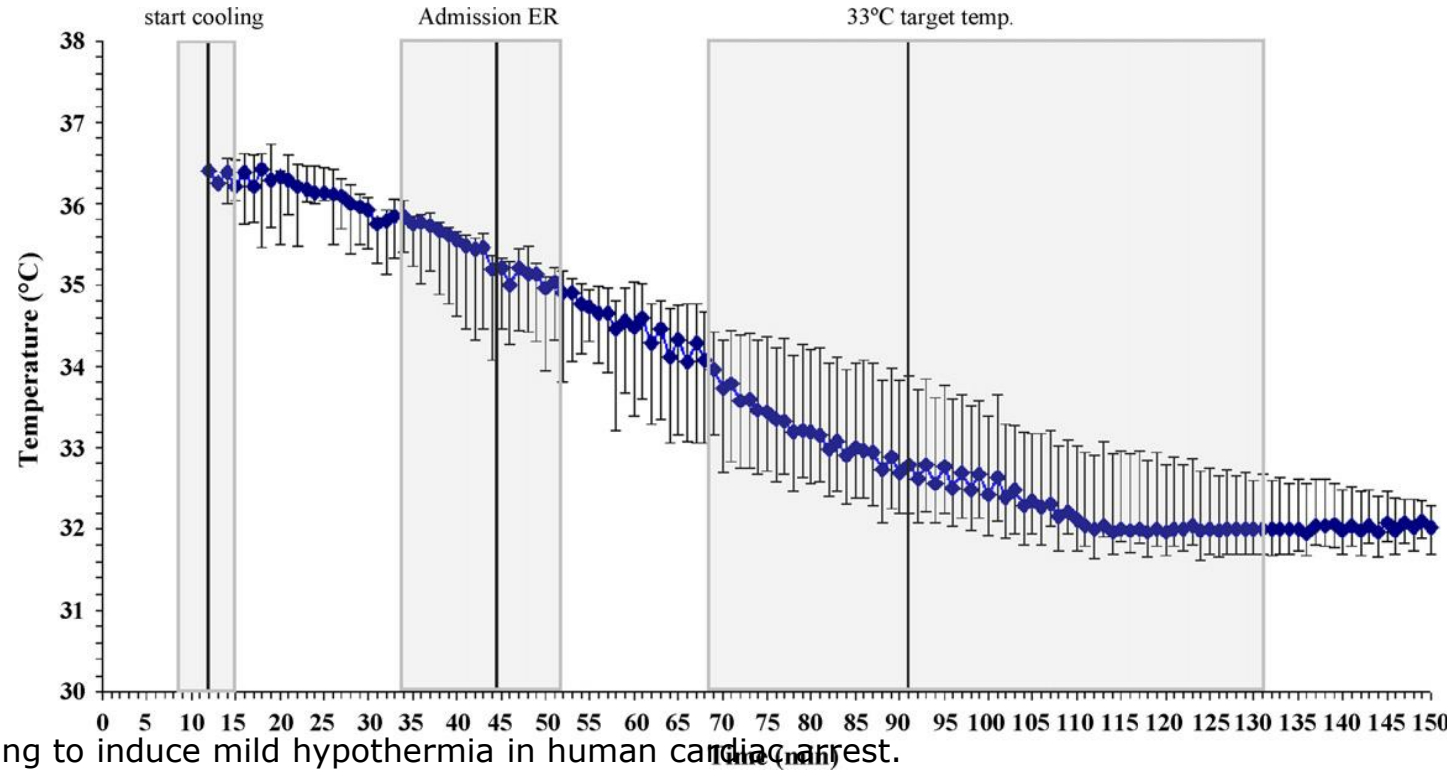
Time to start of cooling: **12 min**

Time to target temperature: **70 min**

ΔTesophagus ROSC-admission: **1.2˚ C**

Feasible and safe

No skin lesions



Out-of-hospital surface cooling to induce mild hypothermia in human cardiac arrest.
Uray et al. Resuscitation 2008.

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INITIAL SITUATION - OUT-OF-HOSPITAL CARDIAC ARREST

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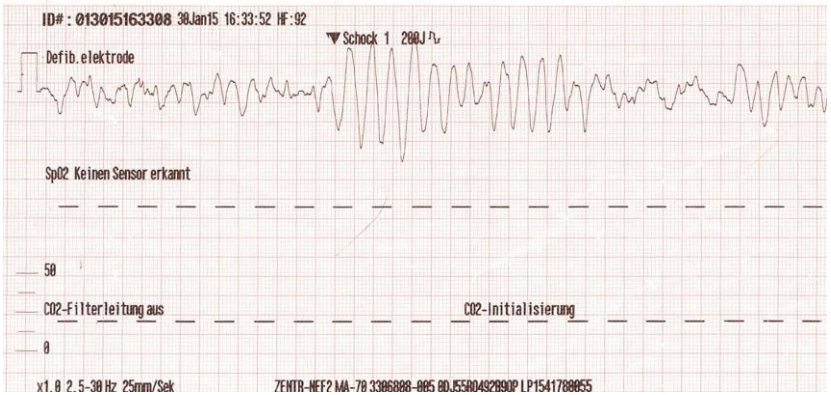

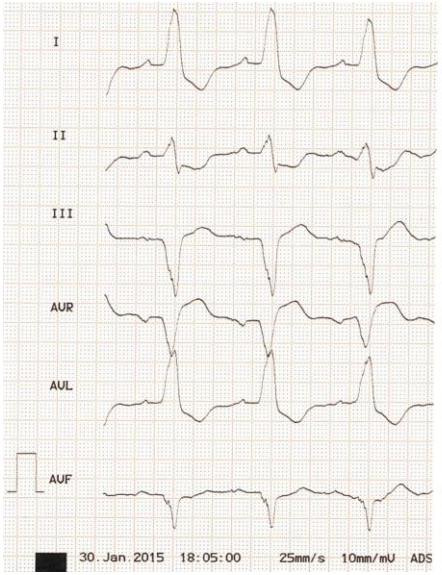

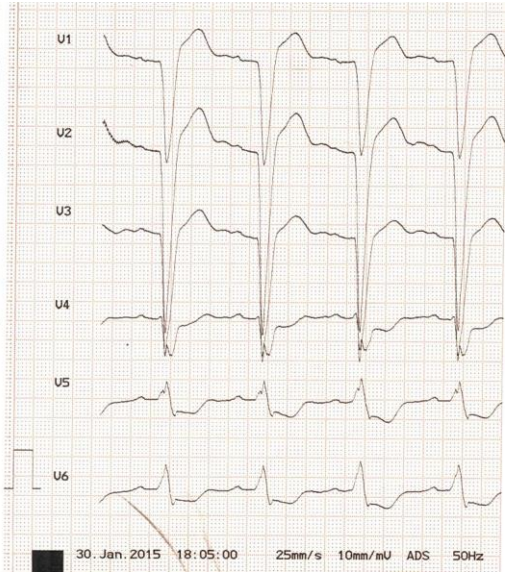

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IN-HOSPITAL CONTINUATION / CATH LAB

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CATH LAB (1/30/2015)

- 17:16 Arrival at Cath Lab (Cardiology, Hanusch Hospital)
- PTCA and two stents into circumflex artery

→ All Flex.Pads are to be removed at 34°C

→ Temperature on arrival: 33.8°C → Initial phase already completed

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IN-HOSPITAL START WITH FLEX.PAD

CATH LAB – ANGIOGRAPHY DURING COOLING

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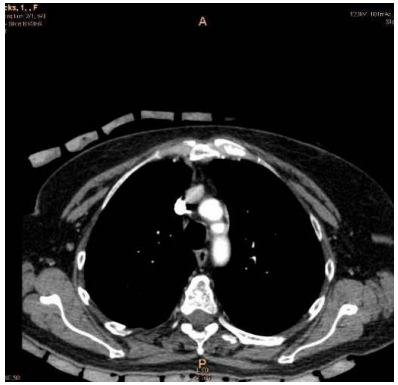
→ Pads are radiolucent

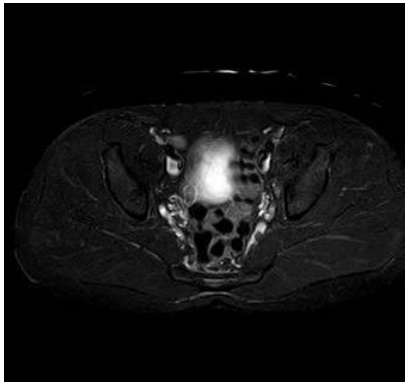
- Good data on safety and feasibity of cooling during angiography, X-Ray, CT, and MRI

1 **X-Ray**

2 **CT**



3 **MRI**



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IN-HOSPITAL CONTINUATION / CARDIAC CARE UNIT

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CARDIAC CARE UNIT (1/30/2015)

* 18:05 Arrival at the CCU

→ Maintenance and rewarming

Therapeutic Hypothermia at 33°±1°C for 24 hours (1/30/2015 – 1/31/2015)

* Continuous temperature monitoring by esophageal and bladder temperature probes (used simultaneously)
* Continuous administration of analgo-sedation and paralytics (standard medication)

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IN-HOSPITAL CONTINUATION / CARDIAC CARE UNIT

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Maintenance at 33-34°C

- 2 Flex.Pad reapplied twice to maintain the targeted temperature range

Passive Rewarming to 37°C

- Patient only covered by a regular blanket
- Target is rewarming to 37°C in about 8 hours, at a rewarming rate of 0.4°C/h
- At 37.0°C all medication is stopped

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IN-HOSPITAL CONTINUATION / CARDIAC CARE UNIT

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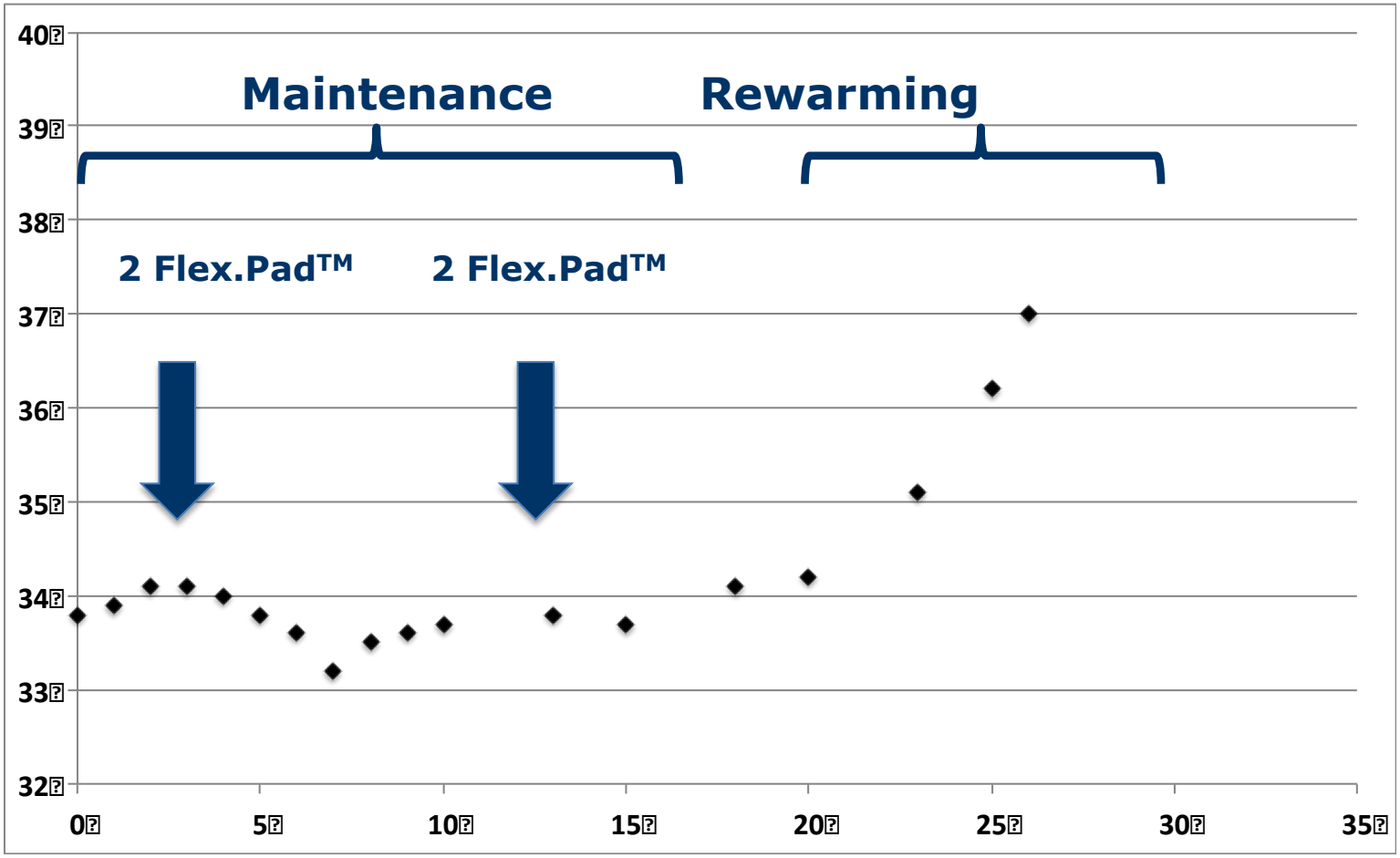
Maintenance and Rewarming (1/31/2015)



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IN-HOSPITAL CONTINUATION / CARDIAC CARE UNIT

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CCU (1/31/2015 – 2/02/2015)

Normothermia

- 37.0°C for day two and three (until 72 hours after cardiac arrest)

Fever control

- Paracetamol, Novalgin
- EMCOOLS Flex.Pad™ or other form of active temperature control

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IN-HOSPITAL CONTINUATION / CARDIAC CARE UNIT

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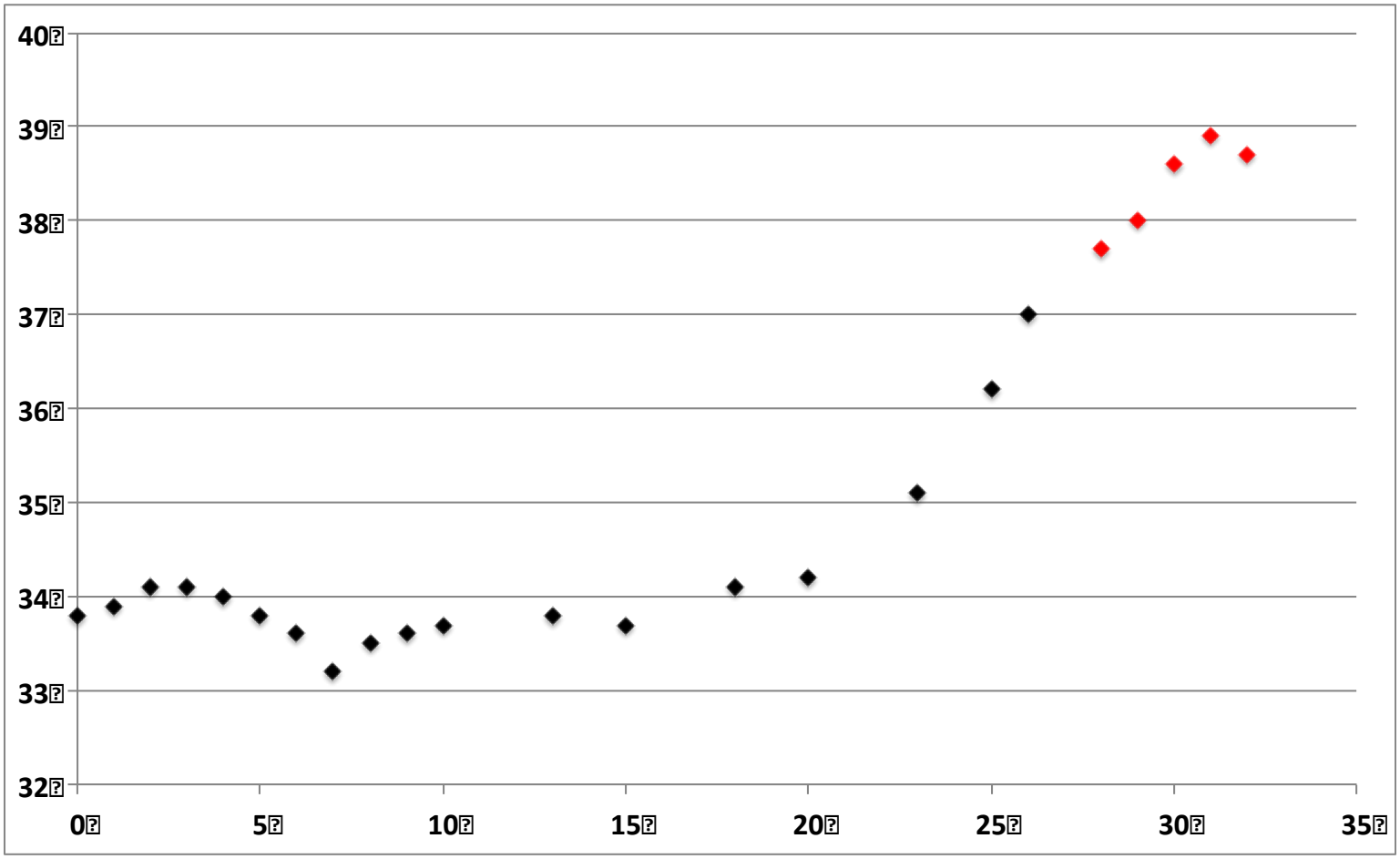

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EXAMINATIONS & FURTHER TREATMENT OF SEPSIS / PNEUMONIA

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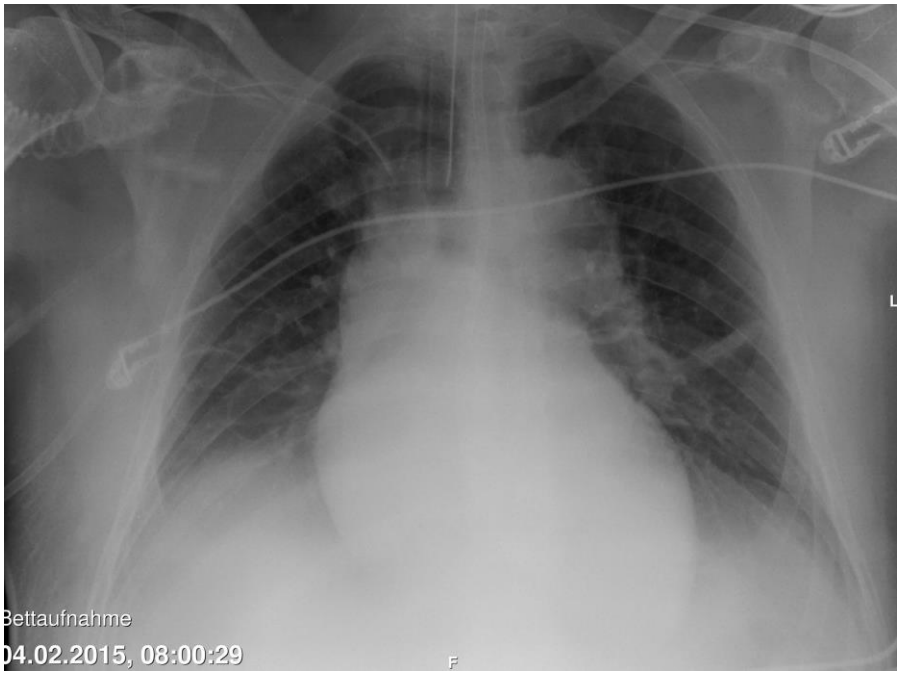
CCU 2/04/2015

Chest x-ray

- Unremarkable, but putrid secretions from suctioning
- Started Amoxi/Clav, changed to Moxifloxacillin, finally Merpoenem/Linezolid
- Tracheal secretions
- Pseudomonas aeruginosa,
- Citrobacter freundii

→ **Pneumonia and sepsis**



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THERAPEUTIC HYPOTHERMIA

SIDE EFFECTS - RISK OF INFECTION

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Therapeutic Hypothermia and the Risk of Infection:

* A Systematic Review and Meta-Analysis; Geurts et al, CCM 2013

Objectives

* Systematic review and meta-analysis of randomized trials to examine the risk of infections in patients treated with hypothermia

Results

* 23 studies, 2820 patients, 1396 cooled patients
* Cooling for several hours-days (prodecures, cardiac arrest, TBI, stroke)

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THERAPEUTIC HYPOTHERMIA

SIDE EFFECTS - RISK OF INFECTION

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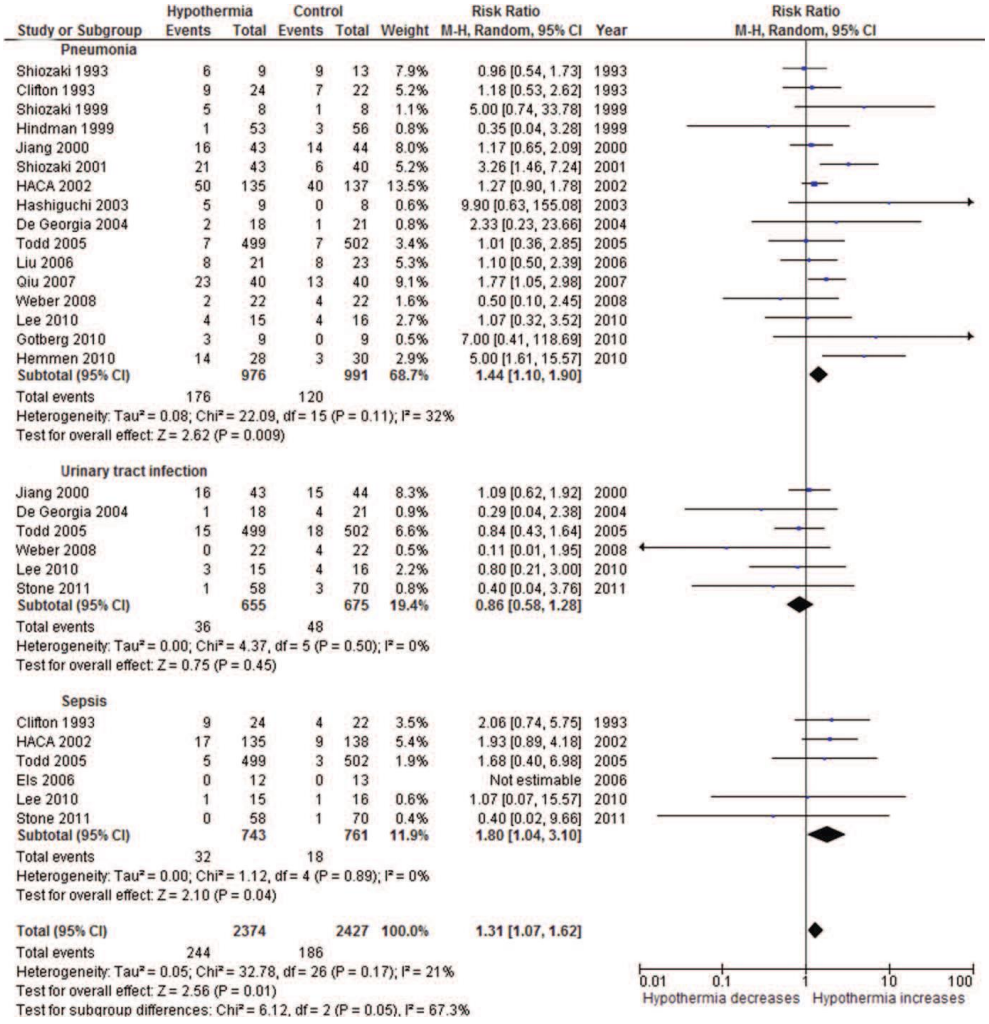
Findings

All infections: no increased risk

Risk of pneumonia ↑
(risk ratio 1.44 [95% CI, 1.10–1.90])

Risk of sepsis ↑
(risk ratio 1.80 [95% CI, 1.04–3.10])

Overall prevalence of sepsis was low.



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THERAPEUTIC HYPOTHERMIA

SIDE EFFECTS - RISK OF INFECTION

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Conclusio

- Lack of definition of infections
- Assessment of infections not blinded
- Only one cardiac arrest study included
- Take-home-message: high alertness towards signs of infection

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THERAPEUTIC HYPOTHERMIA

PROPHYLACTIC ANTIBIOTICS?

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Prophylactic antibiotics are associated with a lower incidence of pneumonia in cardiac arrest survivors treated with targeted temperature management☆

David J. Gagnon[a,e,*], Niklas Nielsen[b,e], Gilles L. Fraser[a,c,e], Richard R. Riker[c,d,e], John Dziodzio[c,e], Kjetil Sunde[e,f], Jan Hovdenes[e,g], Pascal Stammet[e,h], Hans Friberg[e,i], Sten Rubertsson[e,j], Michael Wanscher[e,k], David B. Seder[c,d,e]

Univariate analysis of outcomes related to prophylactic antibiotics.

Variable	All Patients (n = 1240)	PRO (n = 416)	No-PRO (n = 824)	p[a]
Serious infections, n (%)[b]	(n = 1206)	(n = 414)	(n = 792)	
Any serious infection	553 (45.9%)	67 (16.2%)	486 (61.4%)	<0.001
Pneumonia	487 (40.4%)	52 (12.6%)	435 (54.9%)	<0.001
Sepsis	50 (4.1%)	5 (1.2%)	45 (5.7%)	<0.001
Other	57 (4.7%)	13 (3.1%)	44 (5.6%)	0.06
None	653 (54.1%)	347 (83.8%)	306 (38.6%)	<0.001

Conclusio

Prophylactic antibiotics were associated with a reduced incidence of pneumonia
Functional outcome was similar

RESUSCITATION, IN PRESS

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NEUROLOGIC RECOVERY

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CCU (02/03/2015)

- Patient regained consciousness
- Patient is extubated on 02/06/2015

Time on CCU: 01/30-02/11/2015

Regular Ward: 02/11-02/20/2015

→ **No neurologic sequelae (OPC 1, CPC 1)**

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SEDATION

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Sedation Standard - Department for Emergency Medicine, Medical Univ. Vienna

- Midazolam 0,125 mg/kg/h
- Fentanyl 0,002 mg/kg/h
- Esmeron 0,25 mg/kg/h

Hypothermia and Drugs

- Affects drug metabolism
- Affects drug/receptor interaction
- During hypothermia: high blood levels, reduced effect
- During rewarming: toxicity develops

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SEDATION

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Comparison of midazolam/ fentanyl versus propofol/remifentanil

- Randomized clinical study comparing, 50 Patients

- Lower time to offset for propofol/remifentanil 13.2 (2.3–24) vs. 36.8 (28.5–45.1)
- Norepinephrine infusion needed twice as often
- Same outcome

- Free full text review:
- **Zhou and Poloyac**

  The effect of therapeutic hypothermia on drug metabolism and drug response: cellular mechanisms to organ function
- Expert Opin Drug Metab Toxicol. 2011 July ; 7(7): 803–816.

Propofol and remifentanil versus midazolam and fentanyl for sedation during therapeutic hypothermia after cardiac arrest. Intensive Care Med 2012.

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NEUROMUSCULAR BLOCKADE

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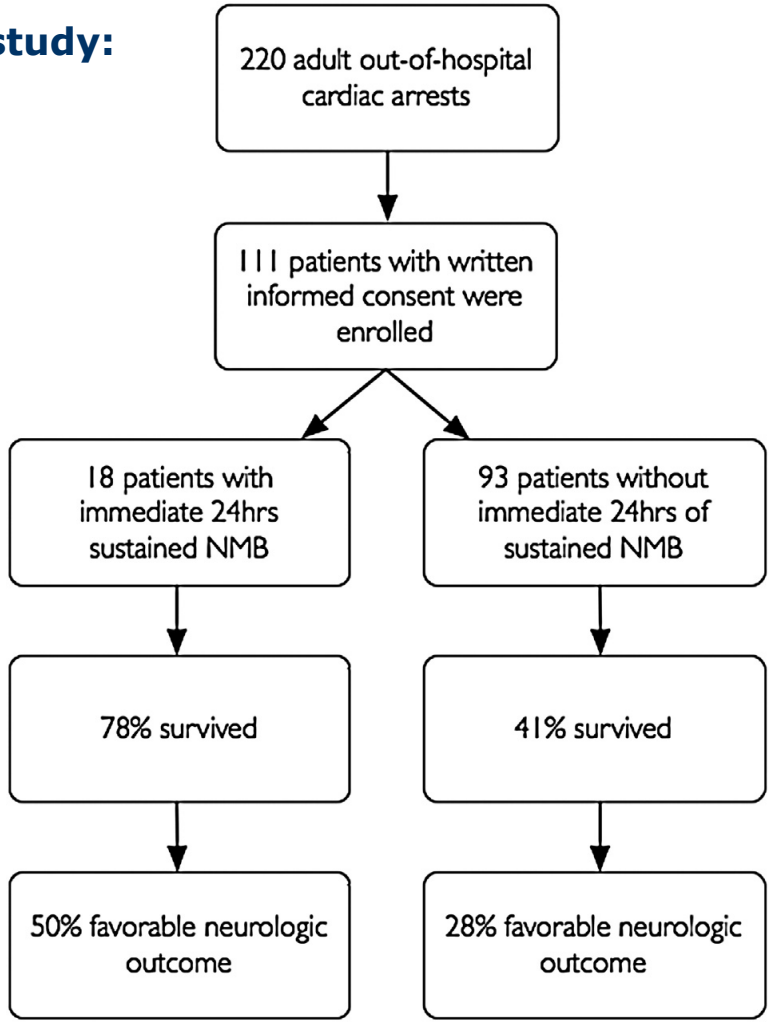
Post hoc analysis of a prospective observational study:

* Better survival
* improved lactate clearance

Some problems

* longer collapse to ROSC interval in the No-MB-group



Salciccioli et al. Continuous neuromuscular blockade is associated with decreased mortality in post-cardiac arrest patients. Resuscitation 2013.

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THERAPEUTIC HYPOTHERMIA

EFFECT ON OUTCOME – VF PATIENTS, HACA-STUDY

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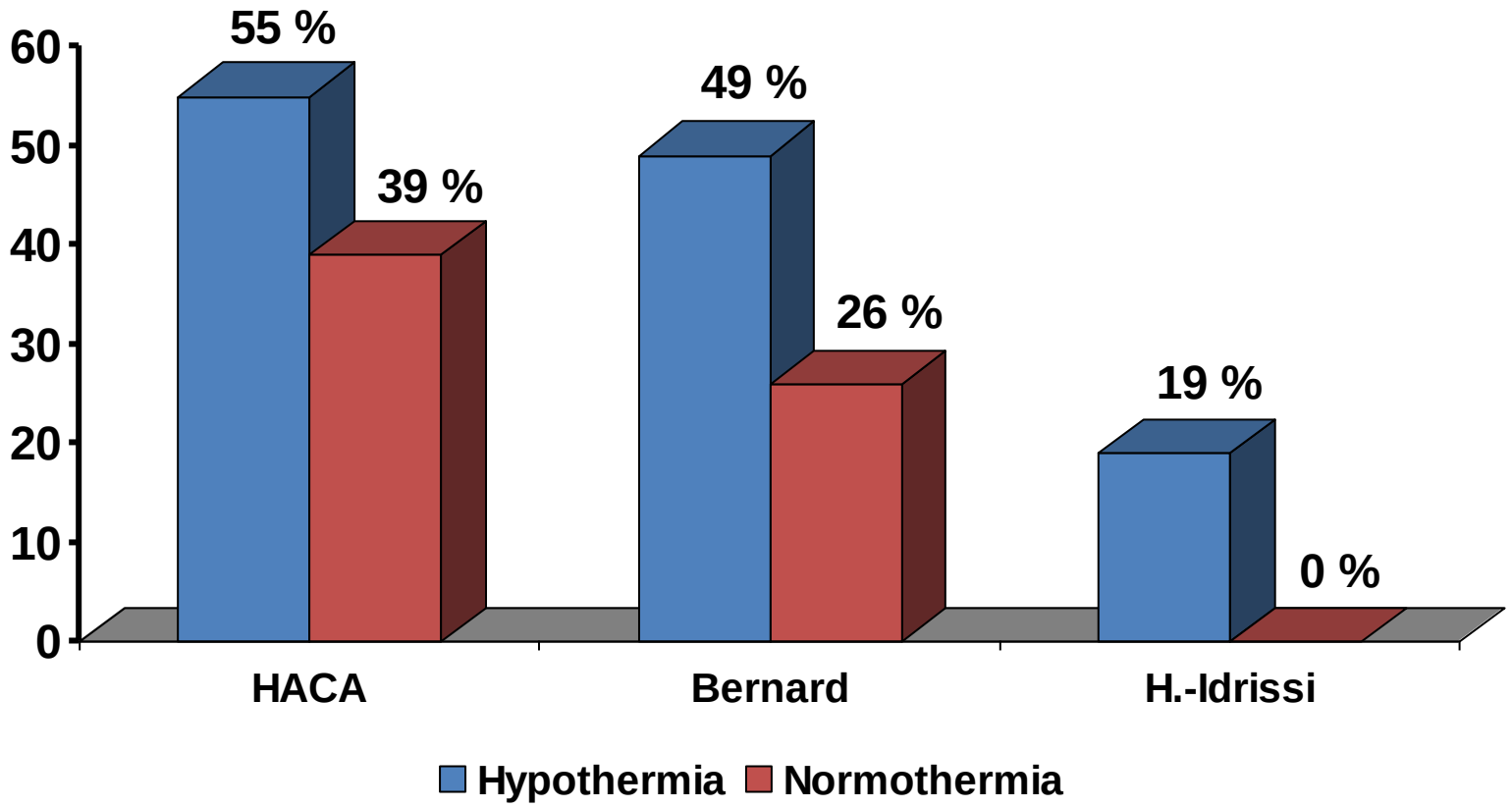
First randomized trials (2002)



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THERAPEUTIC HYPOTHERMIA

HACA-STUDY

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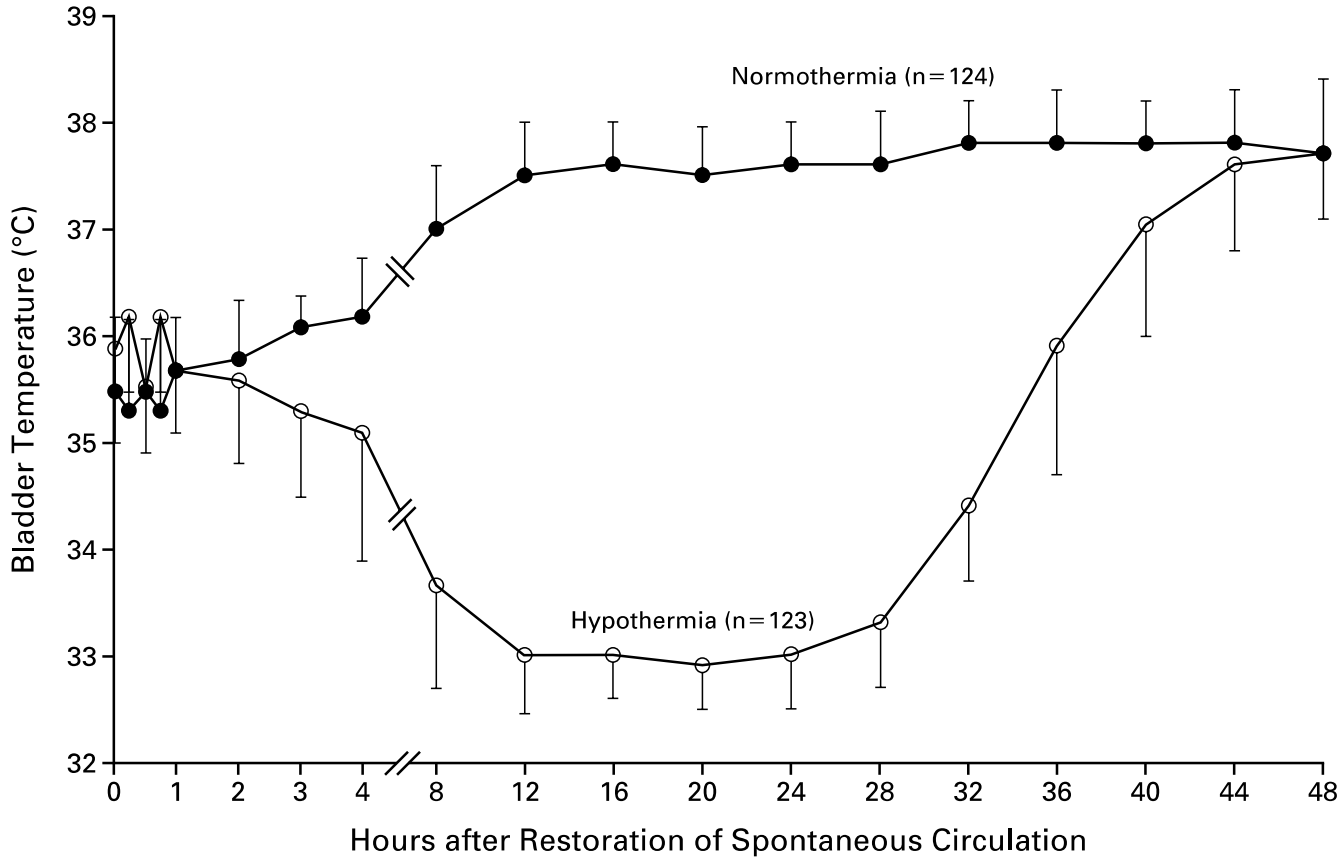

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33°C vs. 36°C

How cool is cool enough?

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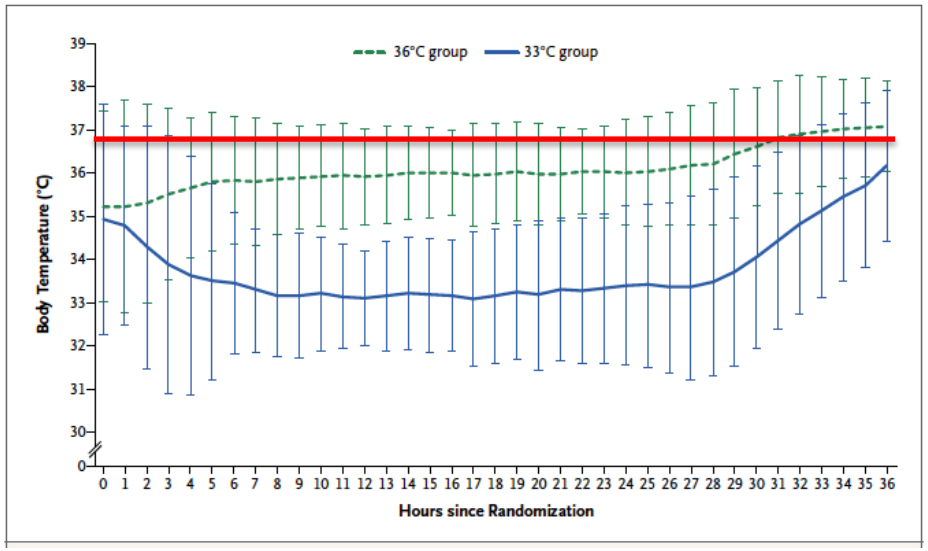
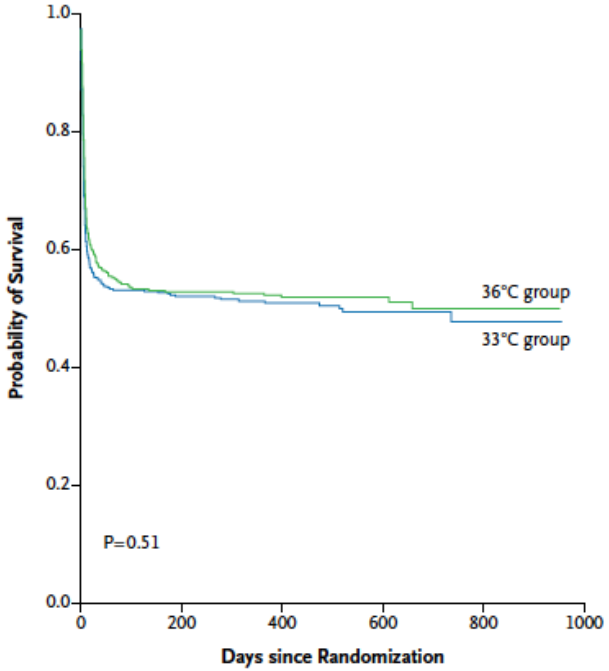


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest



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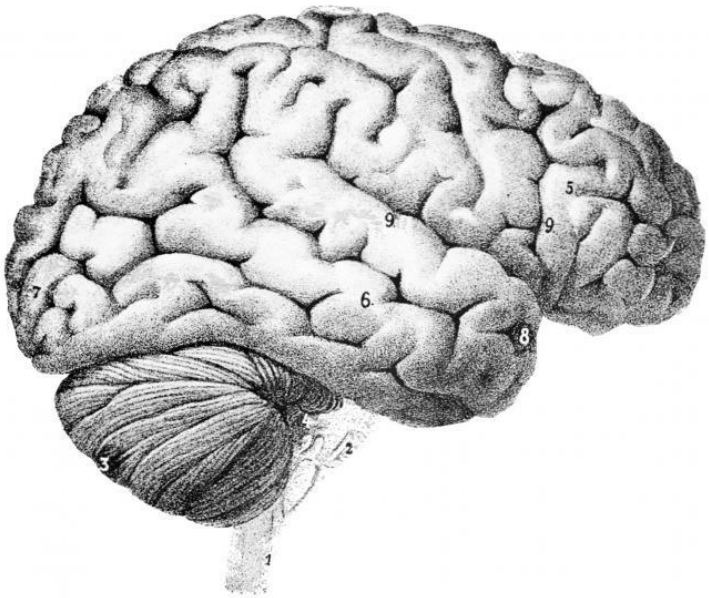
33°C vs. 36°C

How close do you want your brain to the heat?



33°C vs. 36°C

How close do you want your brain to be to the heat?

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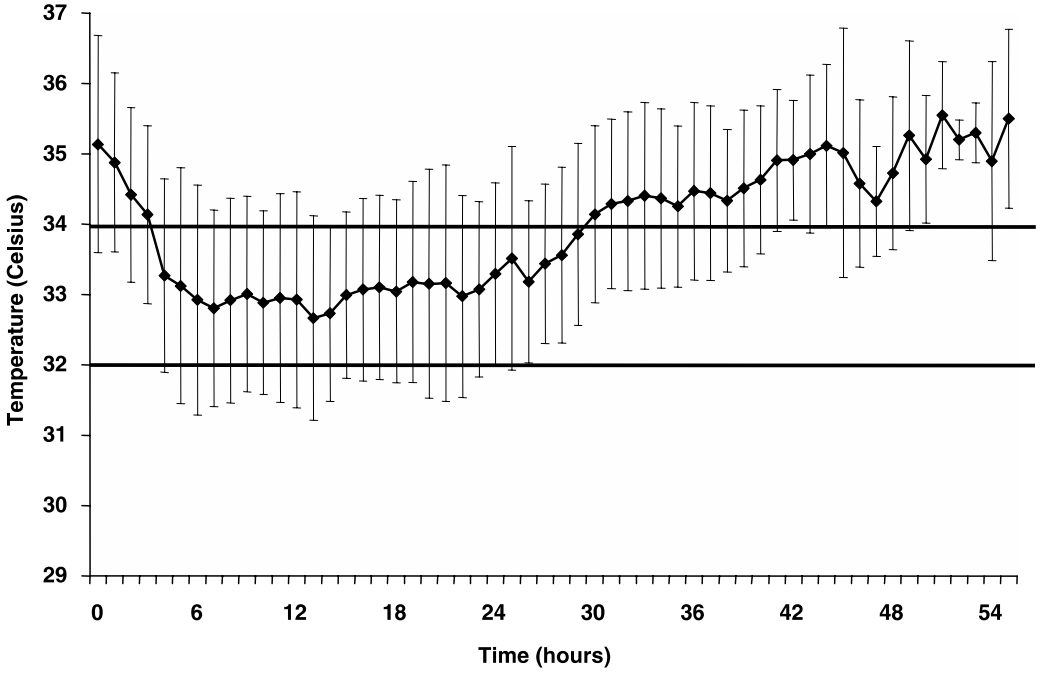

Figure 1. Mean temperature recordings for all patients. *Horizontal bars* mark the target temperature range of 32–34°C. Time 0 represents cooling initiation (n = 32).

Merchant et al, CCM 2006: Therapeutic hypothermia after cardiac arrest: Unintentional overcooling is common using ice packs and conventional cooling blankets

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EMERGING INDICATIONS

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ONGOING STUDIES IN:

- **Cooling during CPR**
- **Stroke**
- **MI**
- **Traumatic brain injury**
- **Spinal chord injury**
- **Hepatic encephalopathy**

Heat stroke

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Thank you!

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