

Hypothermic Resuscitation

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Universitätsklinik für Notfallmedizin

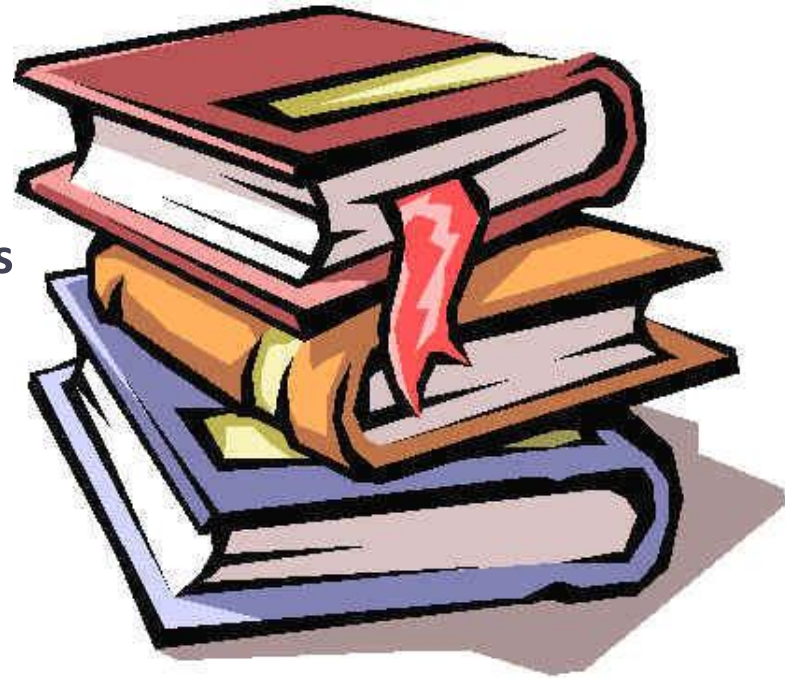
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Content

- Therapeutic hypothermia, current guidelines
- Optimal target temperature?
- The earlier/faster - the better?
- TH for patients with asystolie or PEA?
- Which method shall we use?
- What is the optimal sedation and shall we use muscle relaxants during hypothermia?

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Guidelines 2010

Resuscitation 81 (2010) 1305–1352



Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation



European Resuscitation Council Guidelines for Resuscitation 2010 Section 4. Adult advanced life support

Charles D. Deakin^{a,1}, Jerry P. Nolan^{b,*,1},
Gary B. Smith^f, Gavin D. Perkins^f

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION



**Part 9: Post–Cardiac Arrest Care : 2010 American Heart Association Guidelines for
Cardiopulmonary Resuscitation and Emergency Cardiovascular Care**
Mary Ann Peberdy, Clifton W. Callaway, Robert W. Neumar, Romergryko G. Geocadin, Janice
L. Zimmerman, Michael Donnino, Andrea Gabrielli, Scott M. Silvers, Arno L. Zaritsky, Raina
Merchant, Terry L. Vanden Hoek and Steven L. Kronick

Circulation. 2010;122:S768-S786

Guidelines 2010

- Unconscious adult patients with spontaneous circulation after
- out-of-hospital cardiac arrest should be cooled
- to 32°C to 34°C
- for 12 to 24 hours
- when the initial rhythm was ventricular fibrillation (VF)
- patients with asystoly and PEA are also likely to benefit

Guidelines 2010

- **Cold fluids (saline or Hartmanns solution), 30ml/kg, ice packs, then continue with another cooling method**
- **PCI without delay (if ACS is suspected)**

Cochrane Review 2009 und 2011



- **Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation**
 - 5 papers, 479 patients, unconscious after resuscitation, any primary heart rhythm
 - Intervention: Therapeutic hypothermia, any method
 - Control: best care without Therapeutic hypothermia
 - Primary endpoint: good neurologic outcome
 - Secondary endpoints: survival, adverse events
 - Meta-analysis with „Individual Patients Analysis“ and 10 subgroups

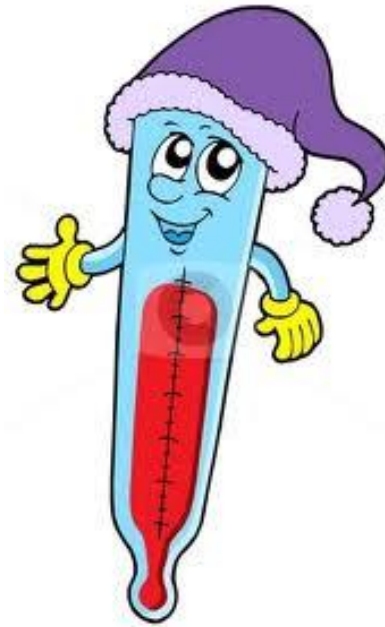
Cochrane Review 2009 und 2011



- **Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation**
 - **Results: Therapeutic hypothermia is beneficial**
 - **Conclusion: Confirmation of the 2010 guidelines**

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Optimal target temperature?

**Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest.
Nielsen et al. N Engl J Med. 2013; 369(23):2197-206**

- **Rational:** Patients in previous studies had fever which caused the unfavourable outcome in the control group
- **Methods:** 950 comatose patients after cardiac arrest
- **1st intervention** Therapeutic hypothermia with 36°C
- **2nd intervention:** Therapeutic hypothermia with 33°C
- **Result: No difference** in mortality and neurologic outcome
- **Result:** No difference in adverse events
- **But there are relevant limitations**



Optimal target temperature?

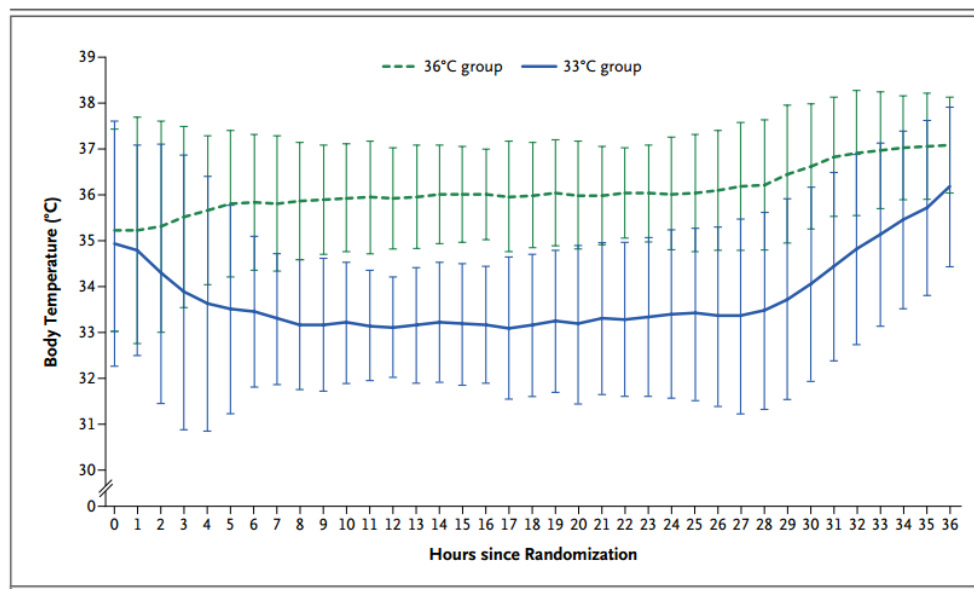
Difficult to compare to other Hypothermia trials

- **Study Design: RCT, equality study**
 - **Two cooling strategies were compared**
 - **No “Placebo Group”**
-
- **Assay sensitivity: can the study really show that there is truly no difference between the two interventions?**

Optimal target temperature?

- **Limitations – interventions**
 - **Mean time without circulation : 1 minute, in comparison to other studies very short time to resuscitation**
 - **Time to randomisation 4 hours**

Optimal target temperature?



- 9 hours before the temperature is different in the two groups
→ Both interventions too late to have an effect at all?
- No, placebo group – difficult to prove equality in this study

Optimal target temperature?

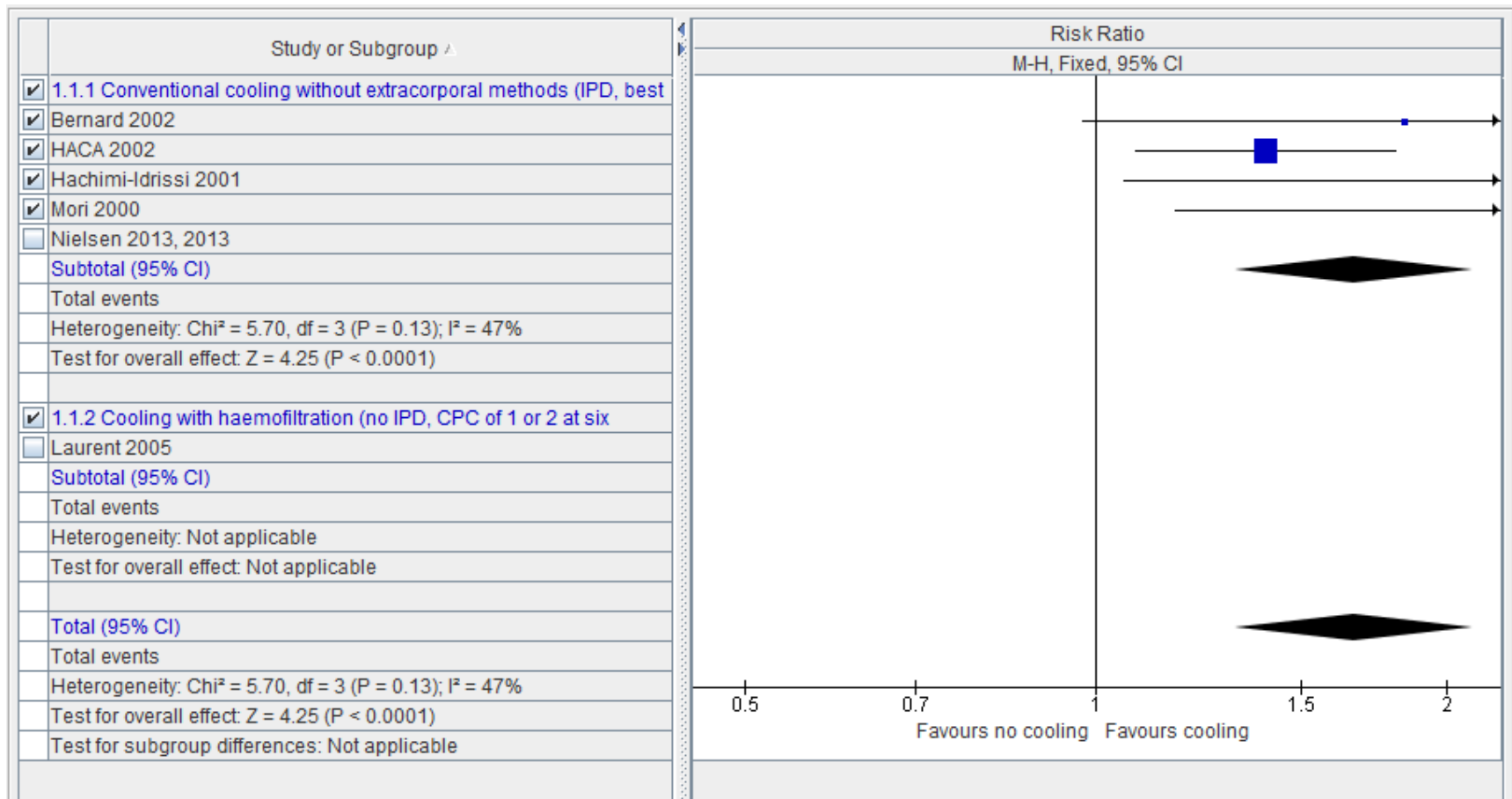
- **Relevant limitations -outcome**

- **Withdrawal of therapy**

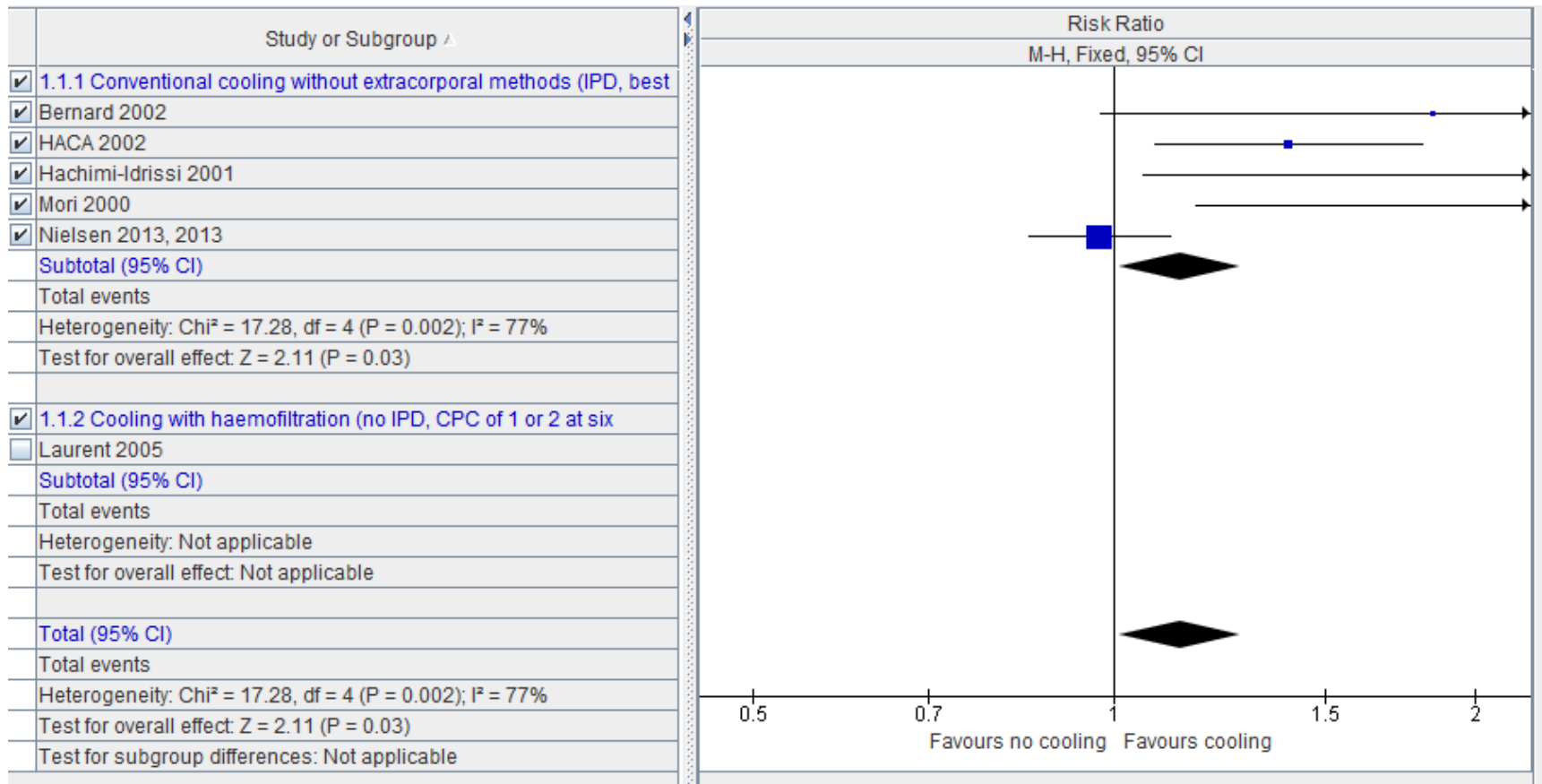
- 132 in 33°C group
 - 115 in 36°C group

→ Patients with 33°C more ill from the beginning on (selection bias?)

What happens if results of Nielsen et al. are added to previous studies?



What happens if results of Nielsen et al. are added to previous studies?



Lopez-de-Sa et al. Circulation 2012 126(24): 2826-2833

- **Randomised controlled trial**
- **Comparison 32°C versus 34°C for patients with prehospital cardiac arrest**
 - 36 patients
 - Hypothermia in the hospital with intravascular catheter and cold fluids
 - **Good neurologic outcome**
 - 32°C: 61%
 - 34°C : 15%

Optimal target temperature?

- Summarized data and guidelines (still) speak for a target temperature of 32-34°C.
- Also Nielsen et al. confirm that hypothermia is important, just question the degree of hypothermia
 - Limitations give many alternate explanations for the lack of a difference between 33°C and 36°C
- No patient after cardiac arrest should be treated without temperature management!

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The earlier the better?

Kim et al. JAMA. 2014 Jan 1;311(1):45-52

- Effect of prehospital cooling in comparison to hospital cooling for patients after cardiac arrest
 - **1359 patients after out-of hospital resuscitation**
 - **2 litres of 4°C cold saline in the prehospital setting versus cooling in-hospital**
 - **Results: no difference in mortality and neurologic outcome**
 - **Again relevant limitations**



The earlier the better?

Kim et al. JAMA. 2014 Jan 1;311(1):45-52

- **No presentations of the temperature curves**
- **50% of patients in preshospital group did not receive the full intervention**
- **25% of all patients in the prehospital group did not receive any cooling in the hospital**
- **→ interpret results with care!**

Other studies:

Study	Result
1. Wolff B_Int J Cardiology 2008 (n=49)	Green
2. Nielsen N_Acta Anesth Scand 2009 (n=975)	Yellow
3. Haugk M_Crit Care 2011 (n=588)	Red
4. Sendelbach S_Resuscitation 2012 (n=172)	Green
5. The Italian Cooling Experience Group_Resuscitation 2012 (n=122)	Red
6. Benz-Woerner JB_Resuscitation 2012 (n=177)	Yellow
8. Bernard et al. 2012 (n=163)	Red

1. Time to target, time to coldest
2. Time to initiation, time to target, depth, duration, rewarming
3. Time to target
4. Time to initiation, time to target
5. Time to initiation early versus late (<>2h)
6. Time to target, adjusted vs not adjusted for first temperature
7. RCT prehospital versus inhospital cooling
8. RCT prehospital versus inhospital cooling

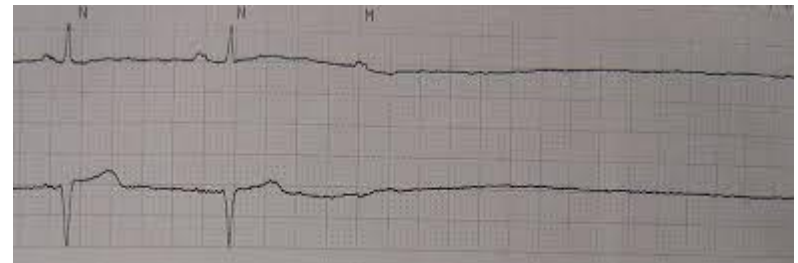
The earlier/faster the better?

We don't know

- **Animal data speak for fast cooling**
- **Retrospective data partly for partly against**
- **RCTs against beneficial effect of early/fast cooling but have significant limitations**
- **Our practice: we cool as soon as possible**

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Does therapeutic hypothermia benefit adult cardiac arrest patients presenting with non-shockable initial rhythms?: A systematic review and meta-analysis of randomized and non-randomized studies☆

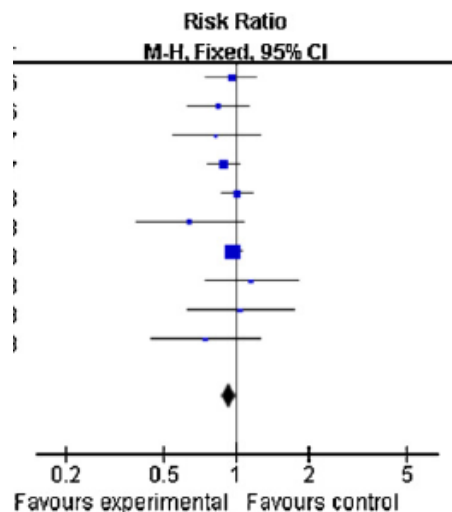
Young-Min Kim^a, Hyeon-Woo Yim^{b,c}, Seung-Hee Jeong^c, Mary Lou Klem^d, Clifton W. Callaway^{e,*}

^a Department of Emergency Medicine, School of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

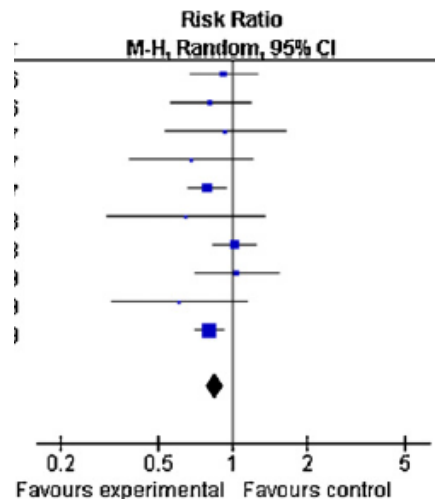
Resuscitation 83 (2012) 188– 196

2 randomised trials:

10 non-randomised trials:



Good neurologic outcome
(1286 patients): OR 1.07



Survival (1292 patients): OR 1.2

Mild therapeutic hypothermia is associated with favourable outcome in patients after cardiac arrest with non-shockable rhythms☆

Christoph Testori, Fritz Sterz *, Wilhelm Behringer, Moritz Haugk, Thomas Uray, Andrea Zeiner, Andreas Janata, Jasmin Arrich, Michael Holzer, Heidrun Losert

Department of Emergency Medicine, Medical University of Vienna, Austria

Resuscitation 82 (2011) 1162– 1167

□ **Retrospective analysis of a population based database:**

- **374 Patienten with PEA/Asystolie:**
- **Good neurologic outcome: OR 1,84**
- **Survival (1292 Patienten): OR 1,78**

TH for patients with asystolie or PEA?

- According to the guidelines and recent retrospective data: TH is most likely beneficial also for patients with asystoly and PEA
- Our daily practice: cool patient with all primary cardiac rhythms

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Invasive versus non-invasive cooling after in- and out-of-hospital cardiac arrest: a randomized trial

**Undine Pittl • Alexandra Schratter • Steffen Desch • Raluca Diosteanu •
Denise Lehmann • Katharina Demmin • Jacqueline Hörig • Gerhard Schuler •
Thorsten Klemm • Meinhard Mende • Holger Thiele**

- **Coolgard versus Arctic Sun**
- **80 patients**
- **Outcome: survival**
- **Coolgard 61% , Arctic Sun 54%, ns**
- **Better temperature control with Coolgard but more local bleeding complications**

What method shall we use

- **No answer because no data**
- **It depends on your own preferences and clinical environment**

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Thor W. Bjelland
Ola Dale
Kjell Kaisen
Bjørn O. Haugen
Stian Lydersen
Kristian Strand
Pål Klepstad

Propofol and remifentanil versus midazolam and fentanyl for sedation during therapeutic hypothermia after cardiac arrest: a randomised trial

- **RCT, 59 patients**
- **Propofol + remifentanyl versus midazolam +fentanyl**
- **No dosing fixed scheme**
- **Primary endpoint: time interval from end of sedation to extubation**
- **Secondary endpoint: haemodynamic, metabolics, adverse events
neurologic outcome**

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□ **Result:**

- Mean time from end of sedation to extubation
 - propofol : 13 hours
 - midazolam: 37 hours
- Need for vasopressors
 - propofol: 23%
 - midazolam: 12 %
 - Patients with midazolam needed 2 more hours to rewarm to $<34^{\circ}\text{C}$
- Other endpoints: no significant differences between the two groups

What is the optimal sedation?

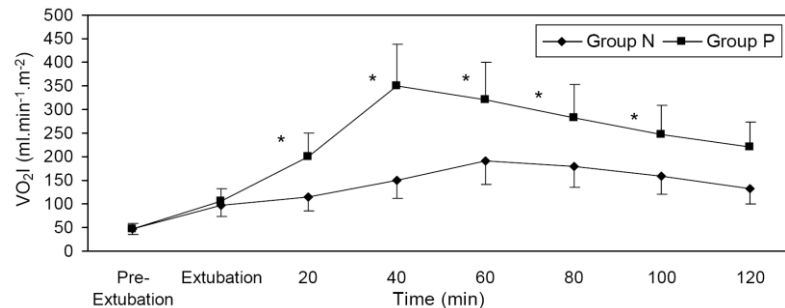
- **Not clear answer**
- **Patients with midazolam tend to need more time to extubation**
- **Patients sedated with propofol require norepinephrine more often**

Shall we use muscle relaxants during hypothermia?

- No interventional studies but one literature review of European ICUs
- **Chamorro et al. 2010 Anesth Analg. 2010 May 1;110(5):1328-35**
 - In European ICUs the following muscle relaxants are used:
 - Pancuronium
 - Cisatracurium
 - Vecuronium
 - Atracurium
 - Rocuronium
 - or no relaxants

Shall we use muscle relaxants during hypothermia?

- Muscle relaxants prevent shivering
- Shivering increases the oxygen demand in the body



- Bilotta et al. Anesthesia 2001;56:514

Shall we use muscle relaxants during hypothermia?

On the other side –

- muscle relaxants also may cover up a status epilepticus, which is reported to occur in around one third of patients after cardiac arrest
- – is that a problem?

Crepeau et al. Neurology 2013 Jan 22;80(4):339-44.

Observational study of 54 patients undergoing TH after cardiac arrest

- 18 patients had severe EEG changes (like SE)
- Of these 3 patients improved → 2 had a good neurologic outcome

Shall we use muscle relaxants during hypothermia?

- **We don't know**
- **Possible solutions:**
 - **Either use sedation/analgesia in a dosage that prevents status epilepticus**
 - **Use EEG and TOF watch**
 - **If you don't use muscle relaxants observe your patient very closely and treat shivering and status epilepticus when it occurs**

