Chlazení pacientů po CPR

- state of the art

OA Dr. Stibor B.

ICU, Landesklinikum Baden bei Wien, Austria

no conflict of interest

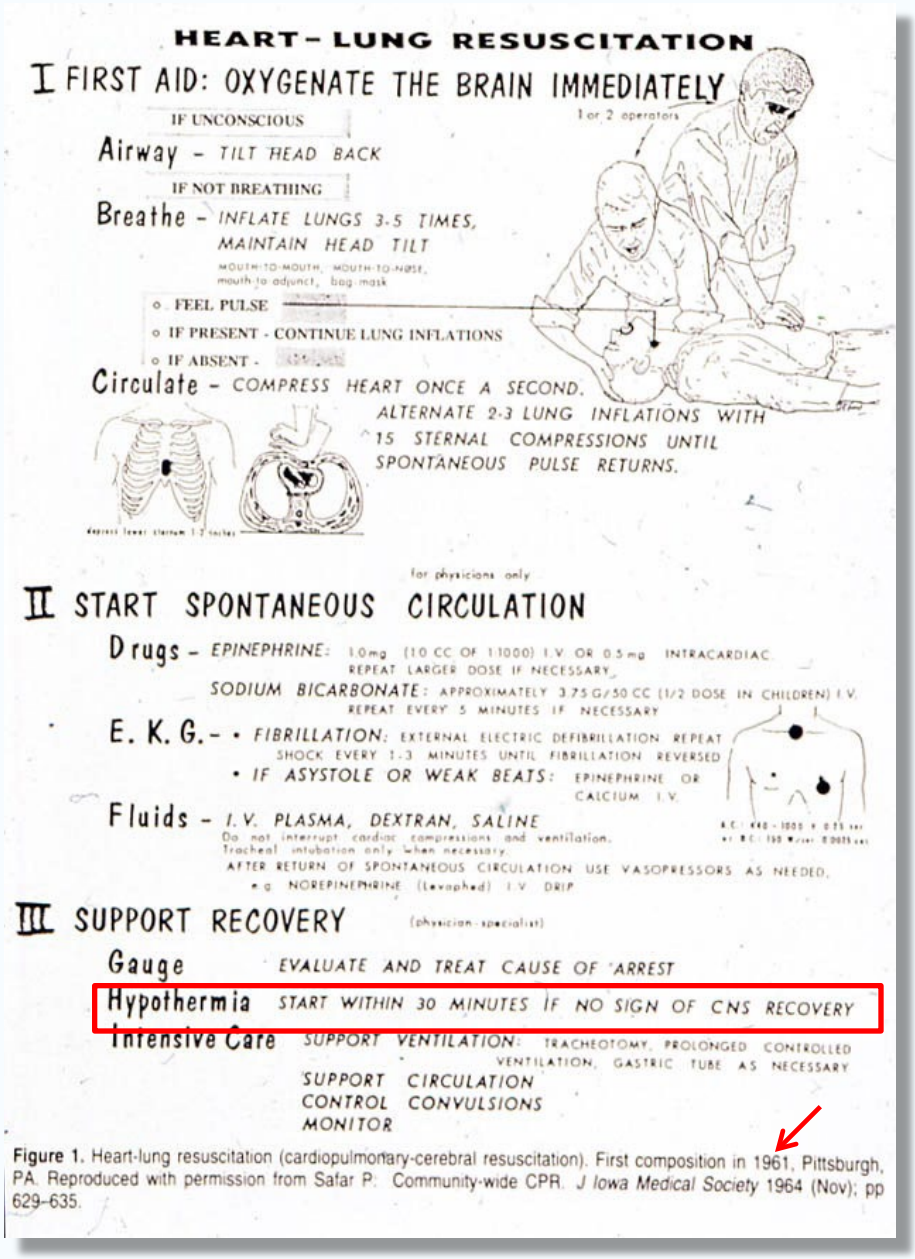
OA Dr. Stibor B.

ICU, Landesklinikum Baden bei Wien, Austria

přehled

1. proč hypotermie
2. fyzikální principy
3. postup chlazení
4. metody chlazení
5. studie TTM a TTM2
6. máme přestat chladit?
7. guidelines
8. realita
9. současná doporučení
10. *future?*

jak to začalo



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

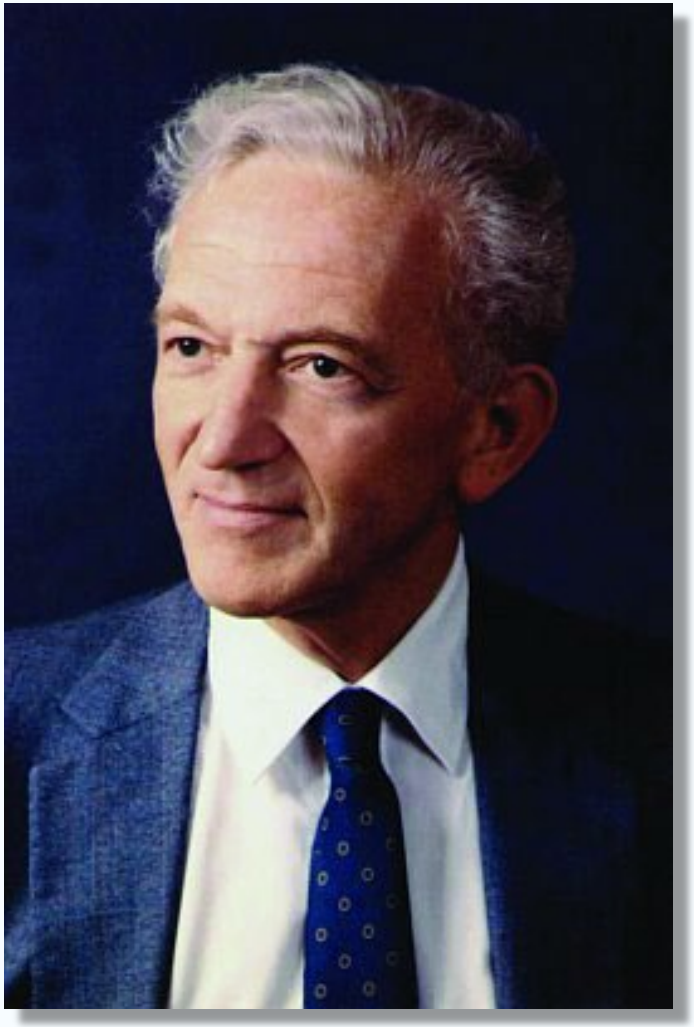
Intensive Care – SUPPORT VENTILATION: TRACHEOTOMY, PROLONGED CONTROLLED VENTILATION, GASTRIC TUBE AS NECESSARY

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.



†Dr. Peter Safar

HACA trial

The New England Journal of Medicine

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

Conclusions In patients who have been successfully resuscitated after cardiac arrest due to ventricular fibrillation, therapeutic mild hypothermia increased the rate of a favorable neurologic outcome and reduced mortality. (N Engl J Med 2002;346:549-56.)

Bernard trial

The New England Journal of Medicine

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

STEPHEN A. BERNARD, M.B., B.S., TIMOTHY W. GRAY, M.B., B.S., MICHAEL D. BUIST, M.B., B.S., BRUCE M. JONES, M.B., B.S., WILLIAM SILVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.SC.

Conclusions Our preliminary observations suggest that treatment with moderate hypothermia appears to improve outcomes in patients with coma after resuscitation from out-of-hospital cardiac arrest. (N Engl J Med 2002;346:557-63.)

- in **2002**, two landmark **RCTs** were published simultaneously in **NEJM**
- they have found that **therapeutic hypothermia** (TH) is effective in **reducing the risk** of neurological disability in patients with **OHCA** due to an initial **shockable rhythm** who were comatose post-arrest
- a rapid adoption of TH into clinical practice in post-arrest patients (**revolution in therapy** after cardiac arrest)
- TH received a **class I recommendation** in resuscitation **guidelines**
- TH has since **expanded** to include patients with non-shockable rhythms and patients with IHCA
- **standard procedure** in the postresuscitation care

všichni chladili……


17 10:32 AM

fyzikální principy

Radiation

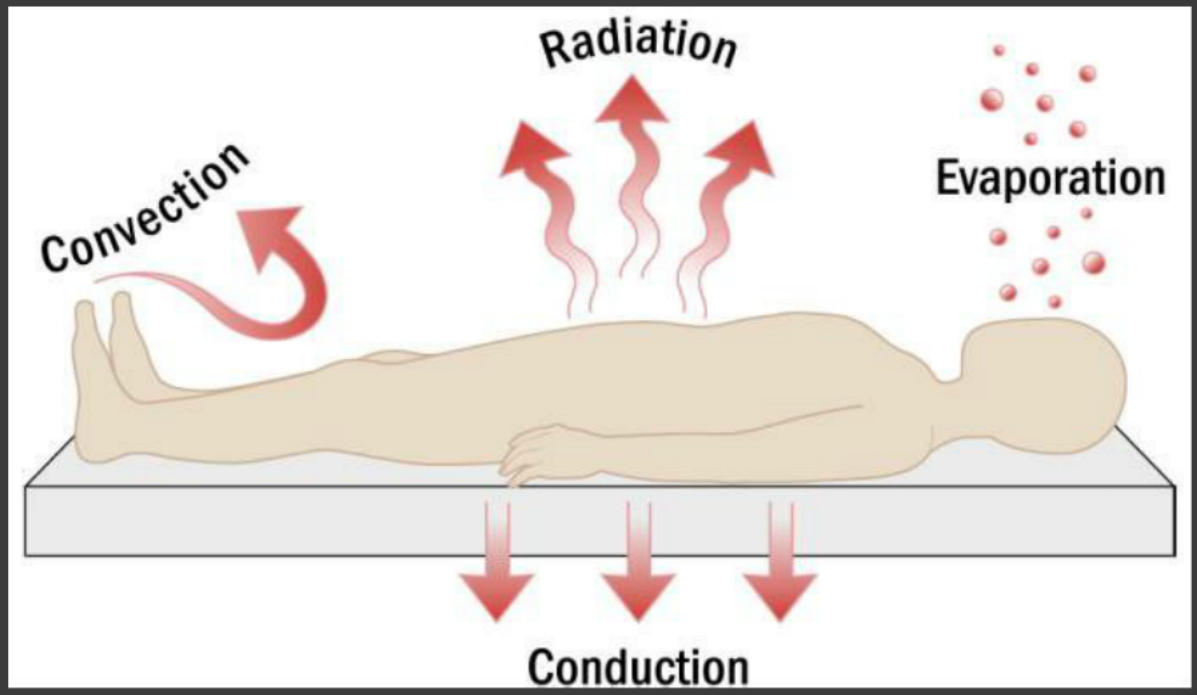
Transfer of heat between the separated surfaces of two objects via electromagnetic (infrared) radiation.

Accounts for 50–70% of heat loss in awake patients

Evaporation

Heat loss derived from the evaporation of water from skin & lungs

Accounts for ±15% of heat loss (5% from the skin, 10% from the lungs)



Convection

Transfer of heat from a surface to the surrounding air.

Accounts for 20–30% of heat loss

Conduction

Direct transfer of between surfaces

Amount of heat loss is closely related to contact surface

Increases in the sitting or lying position

postup chlazení

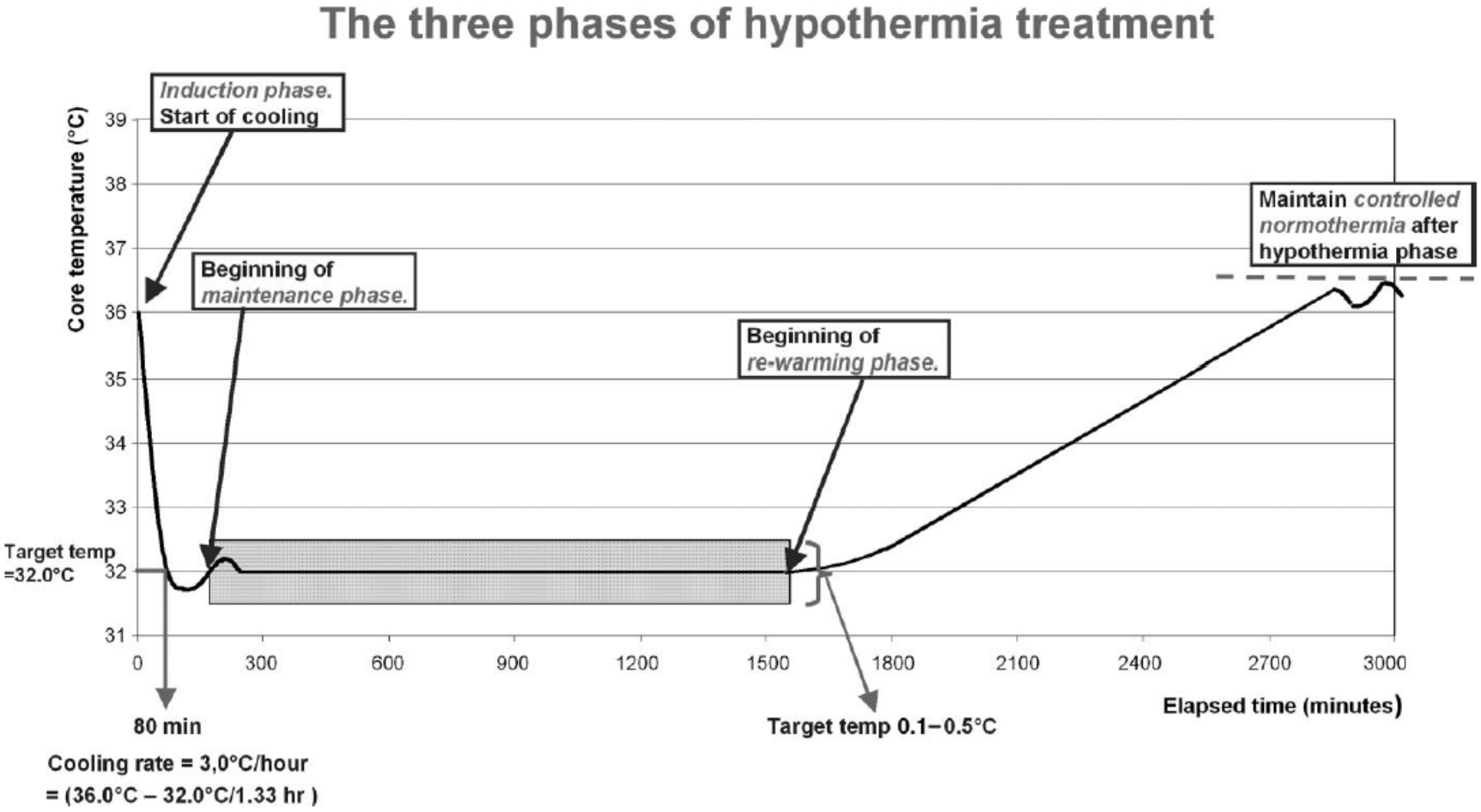


Figure 3. Graphic depiction of the three phases of hypothermia treatment. The induction phase should last between 30 and 120 mins; rapid cooling may lead to a small overshoot, which should be accepted provided it is no greater than 1°C. The maintenance phase usually lasts 24 hrs in cardiac arrest patients (may be longer for other indications) and should be characterized by no or minimal fluctuations in temperature. The rewarming phase should be slow and controlled, with rewarming rates of 0.2°C to 0.5°C in cardiac arrest patients and lower rewarming rates for other indications. Fever should be prevented after rewarming.

phases of hypothermia

1. induction phase

get to target temperature (34ºC?) as quickly as possible

(small overshoot acceptable provided temperature remains > 30 ºC)

2. maintenance phase

should be reliable, with no or minor fluctuations (max. 0,2-0,5 ºC)

3. re-warming phase

slow and controlled (max 0,2-0,5 ºC/h)

4. fever-control phase

maintain controlled normothermia

metody chlazení

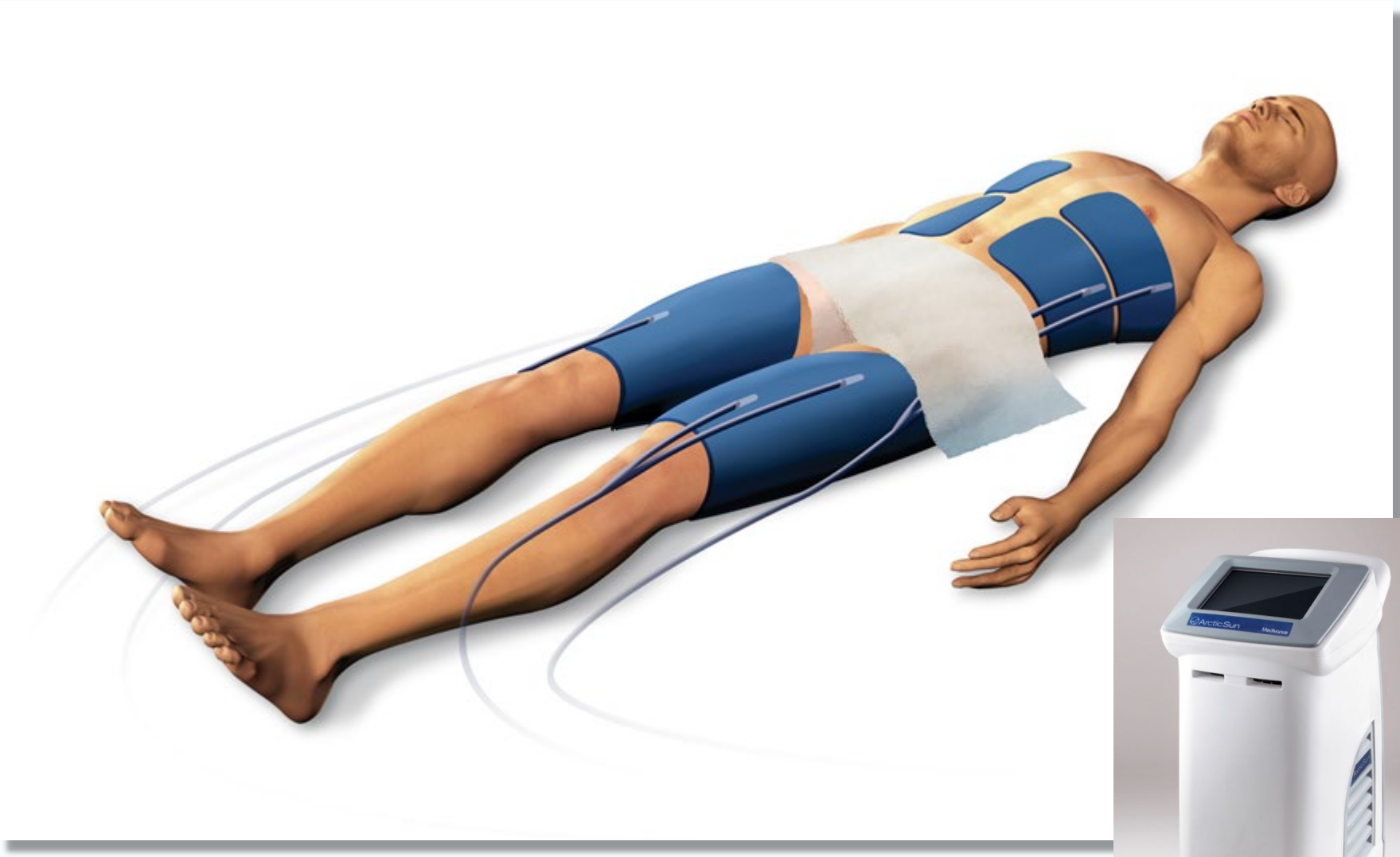
metody chlazení

- **povrchové chlazení**
  - ledové obklady, polévání vodou, alkoholem
  - systémy s cirkulující vodou
  - systémy s cirkulujícím vzduchem

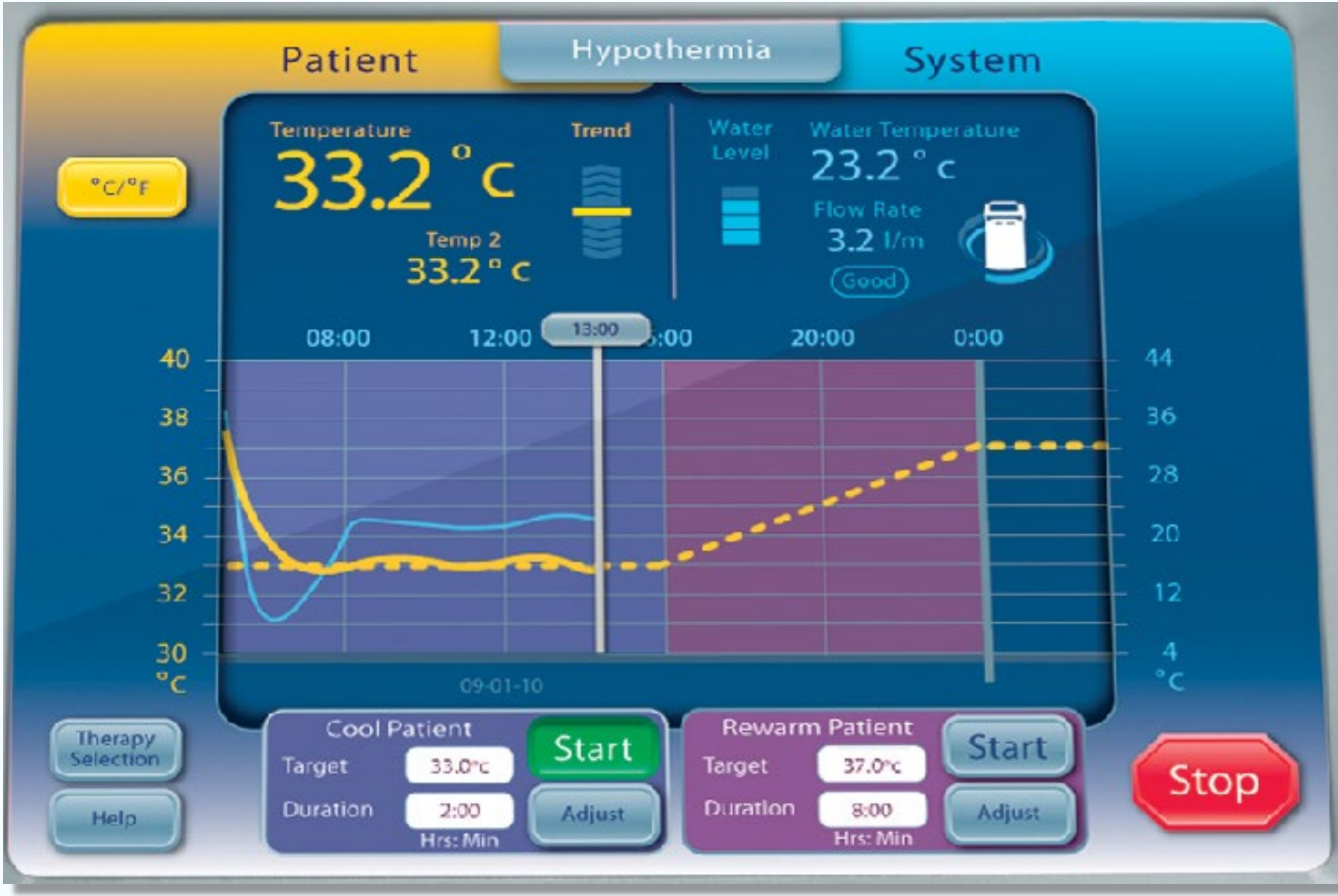
- **intravenózní roztoky**

- **intravaskulární chlazení**
- **selektivní ochlazování mozku** (RhinoChill)

povrchové chlazení



Arctic Sun® 5000, Colorado, USA


Patient
Hypothermia
System
°C/°F
Temperature
33.2 °C
Temp 2
33.2 °C
Trend
Water Level
Water Temperature
23.2 °C
Flow Rate
3.2 l/m
Good
08:00
12:00
13:00
20:00
0:00
40
38
36
34
32
30
°C
44
36
28
20
12
4
°C
09-01-10
Therapy Selection
Help
Cool Patient
Target
33.0°C
Duration
2:00
Hrs: Min
Start
Adjust
Rewarm Patient
Target
37.0°C
Duration
8:00
Hrs: Min
Start
Adjust
Stop


ARCTIC SUN
ARCTICGEL™ Pad
L


Auto Logic
arjo
with people in mind
Temperatur des Patienten
halten bei 35.5°c
35.4°c
Patiententemperatur
Trend
Wassertemperatur
34.1°c
Flussrate
Gut
ARCTIC SUN
TEMPERATURE MANAGEMENT SYSTEM
Medivance

Blanketrol III®, Cincinnati Sub-Zero, USA

intravenózní chlazení

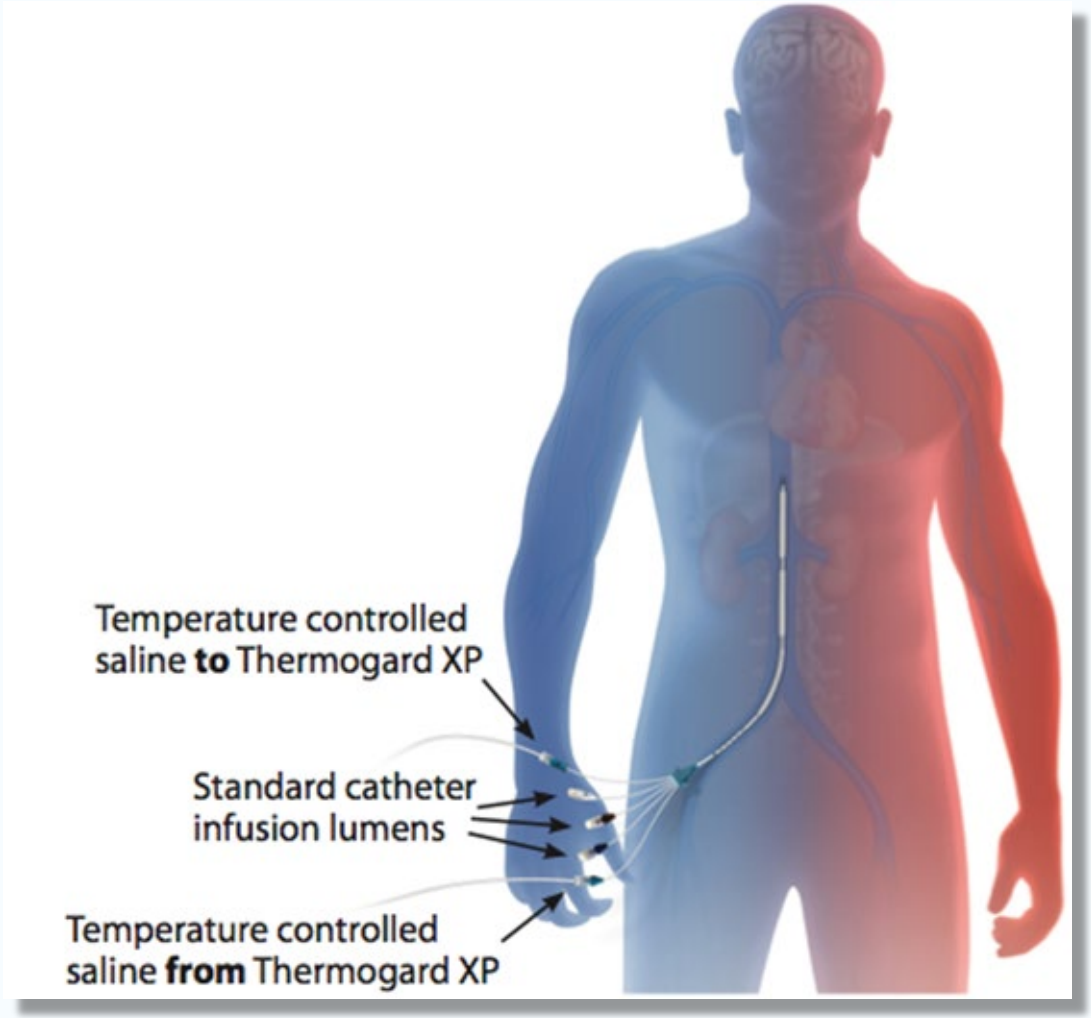
intravenózní chlazení

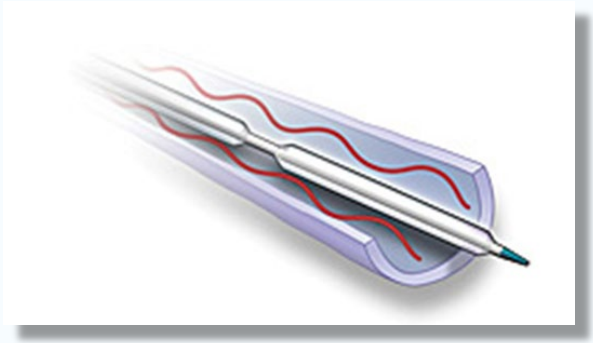
- **cold fluids** 4 ºC i.v. 30 ml/kg
- with pressure bag
- „as **rapidly** as possible“
- type of fluid: 0,9% NaCl, Ringer, Hartmann, Elo-Mel... (crystalloids)
- begin **prehospital**
- **cave:** overfluid, electrolytes!!!

intravaskulární chlazení

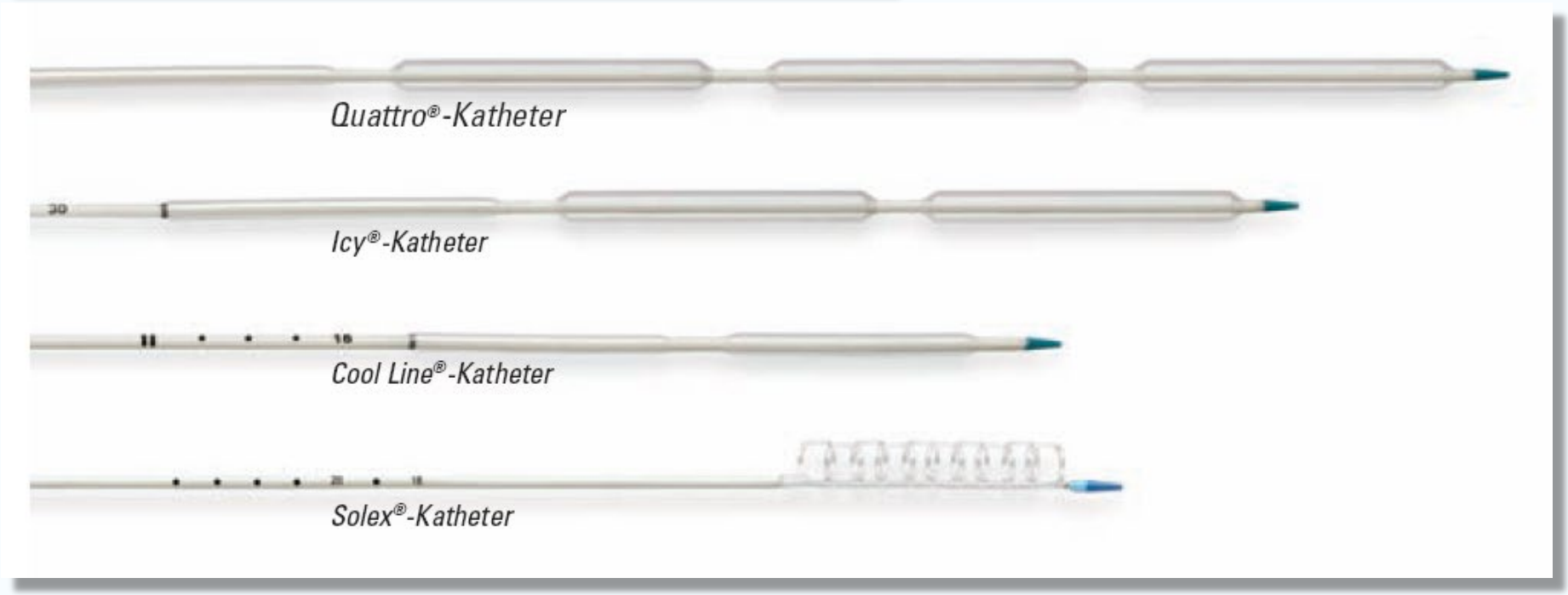
intravaskulární chlazení

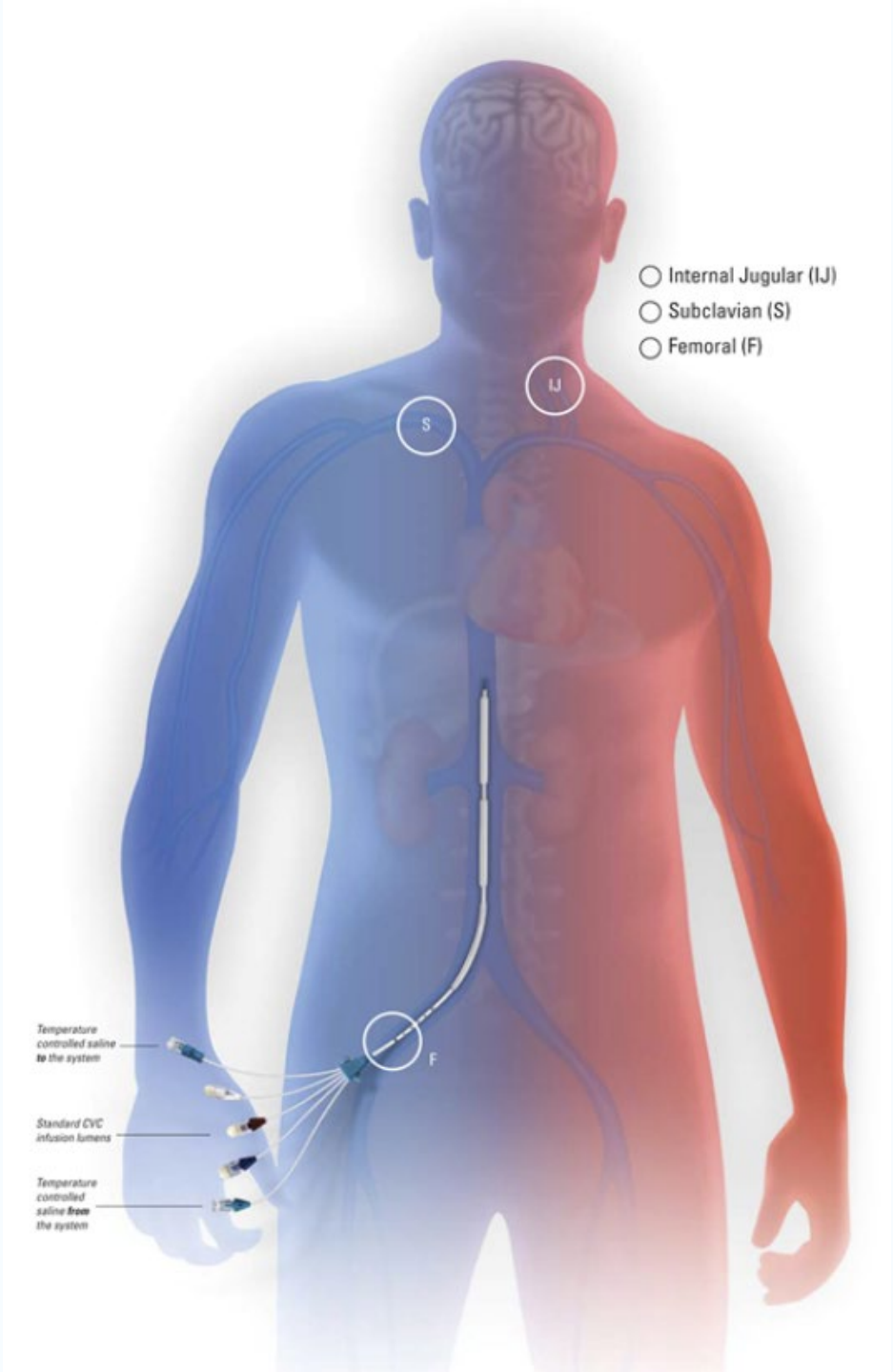
- **intravenózně** zavedený katetr (v. femoralis)
- cirkulující chladný roztok 0,9 % NaCl
- „**invazivní**“, proveditelná pouze nemocničně
- velmi rychlé dosažení cílové teploty
- **nejlépe se udržuje** nastavená teplota TTM („autopilot“)

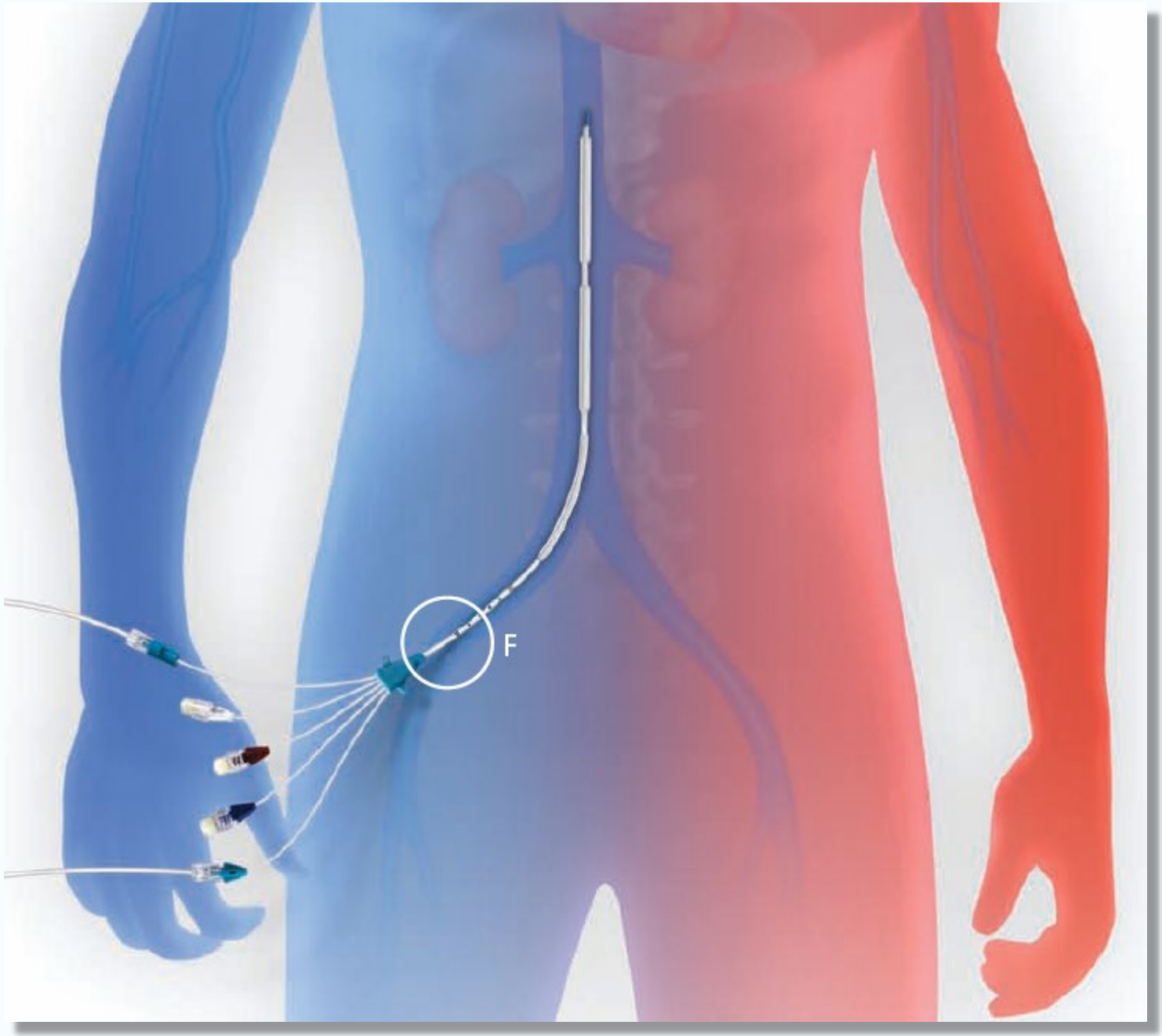


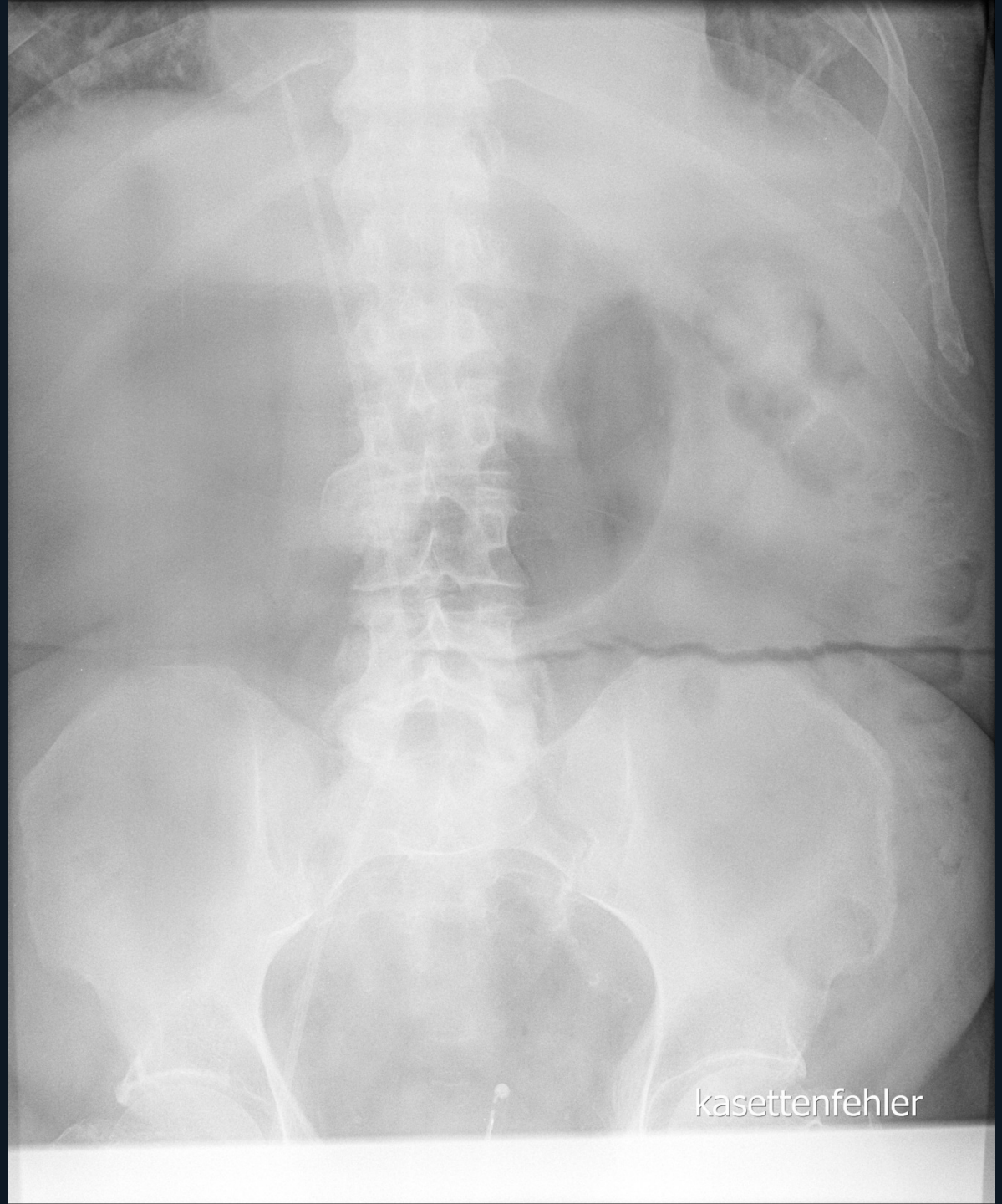


ThermoGard XP®, Alsius, USA

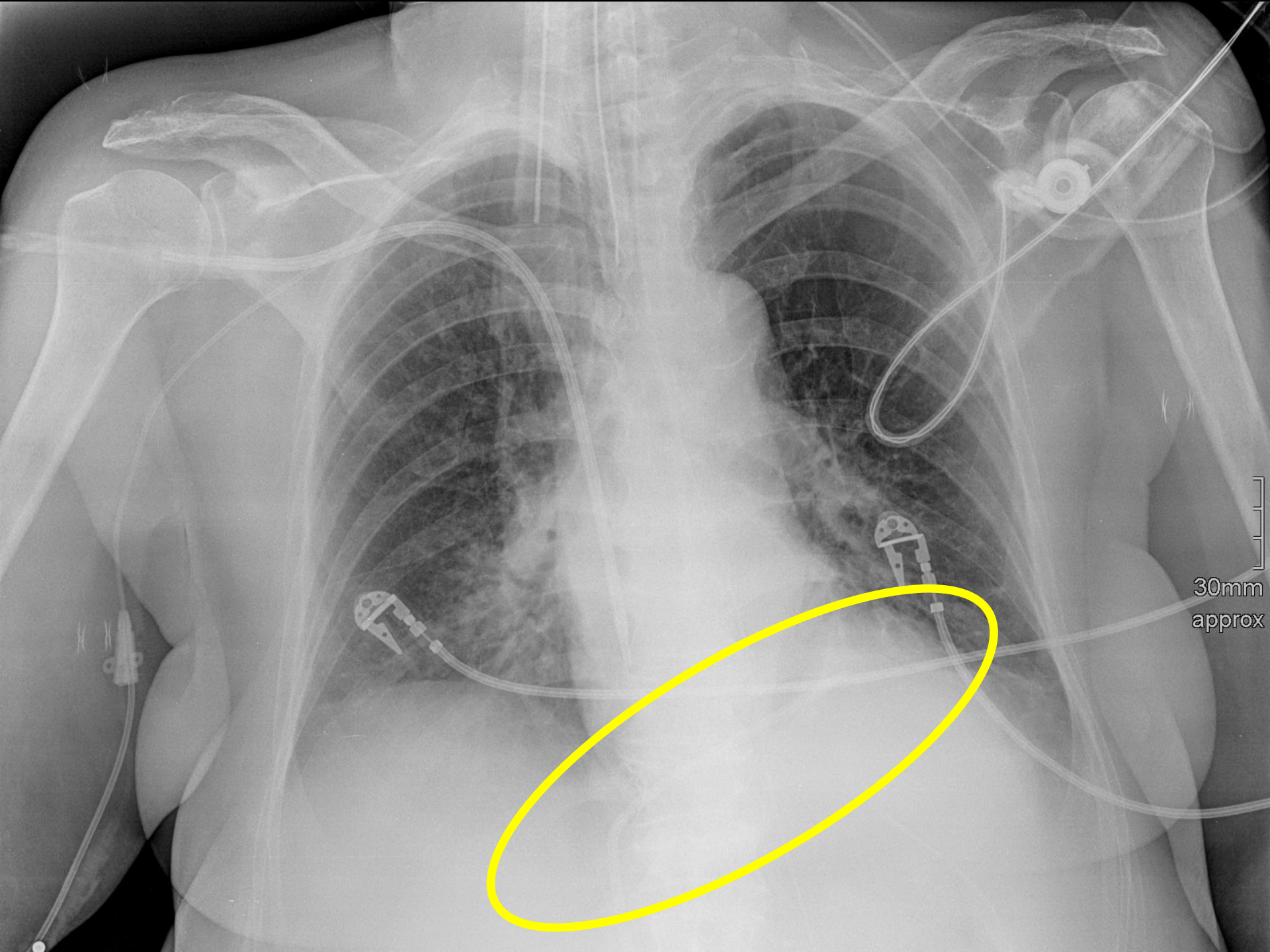

Quattro®-Katheter
Icy®-Katheter
Cool Line®-Katheter
Solex®-Katheter

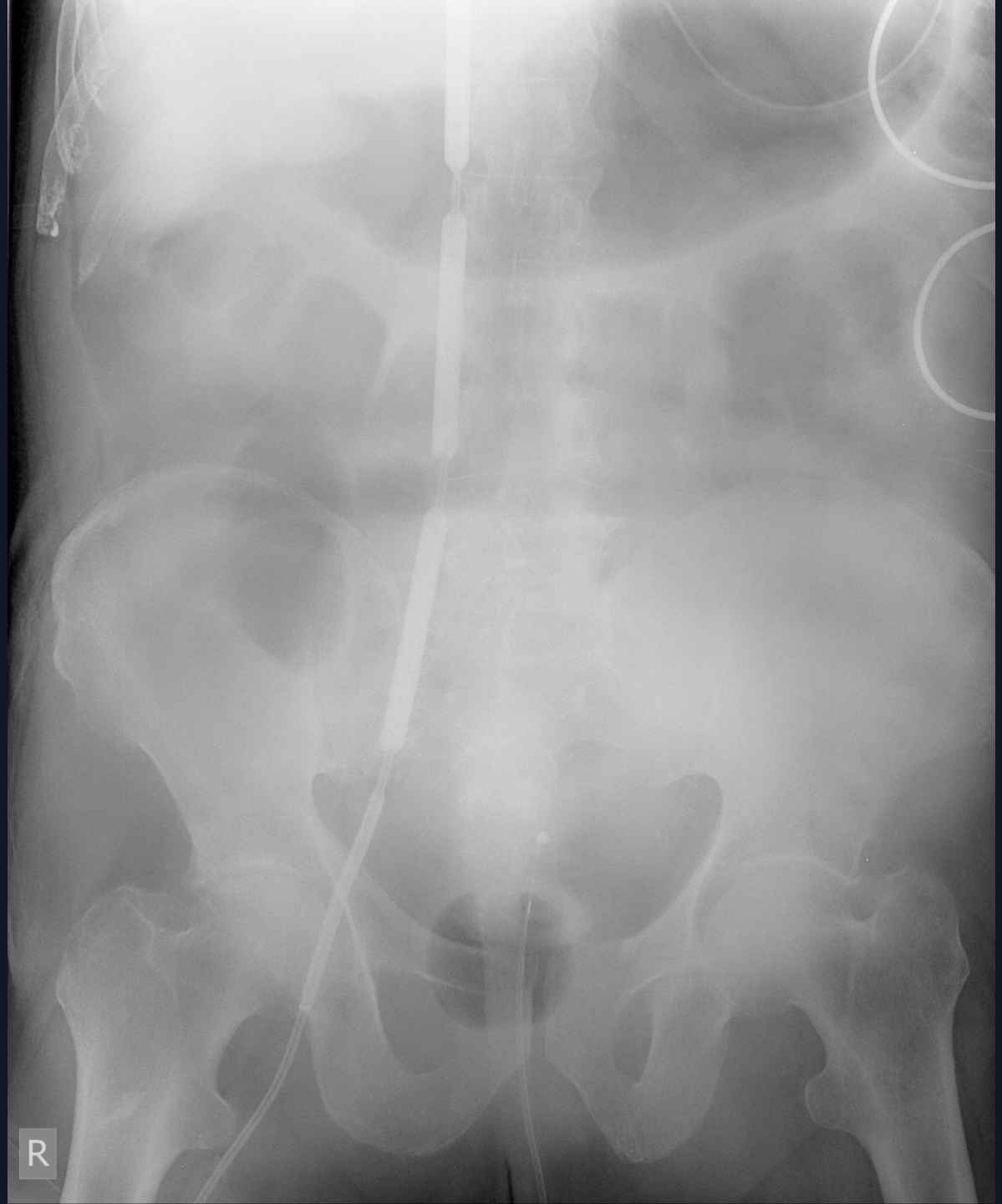

Internal Jugular (IJ)
Subclavian (S)
Femoral (F)
IJ
S
F
Temperature controlled saline to the system
Standard CVC infusion lumens
Temperature controlled saline from the system


F


kasettenfehler


30mm
approx
R
Bettaufnahme

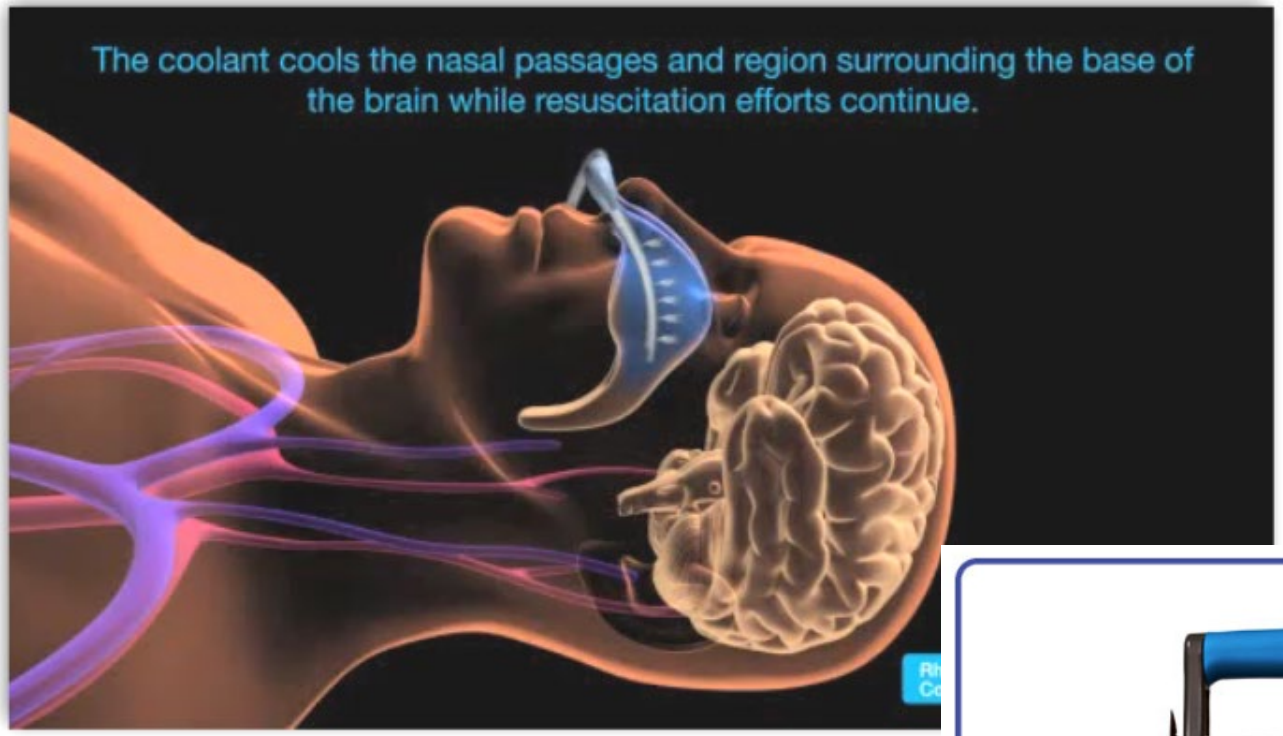

30mm
approx


R


kasettenfehler

RhinoChill

- perfluorohexan vstřikován do oblasti nazofaryngu
- rychlým odpařováním se ↓ teplota sliznice na 2-4°C
- mozek se ochlazuje kondukcí a perfúzí
- CAVE: perfluorohexan se sráží v nasofaryngu a zatéká do žaludku


The coolant cools the nasal passages and region surrounding the base of the brain while resuscitation efforts continue.


RhinoChill

srovnání metod

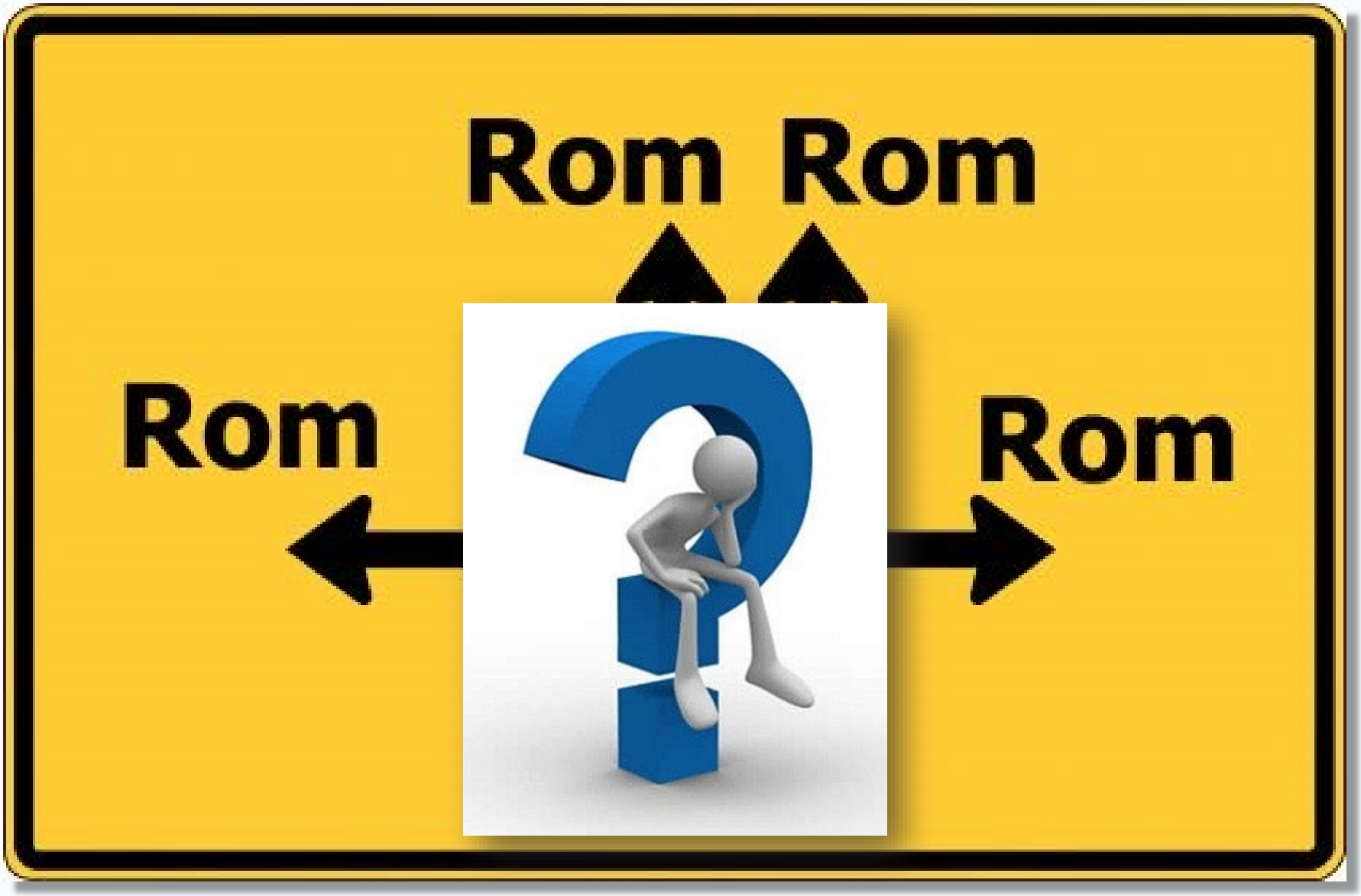

Rom Rom
Rom
Rom

Abb.3 Kühltechniken zur Indikation einer therapeutischen Hypothermie[16]

Kühltechnik	**Kühlrate °C/h**
Eispacks	0,9
Kaltluft	0,4-0,8
Kältematten	0,9
Infusion kalter Flüssigkeiten	3,2
Endovaskulärer Kühlkatheder	0,8-4,7
Venovenös (z.B. Hämofilter)	3,5
Extrakorporale Zirkulation	12

Research

Open Access

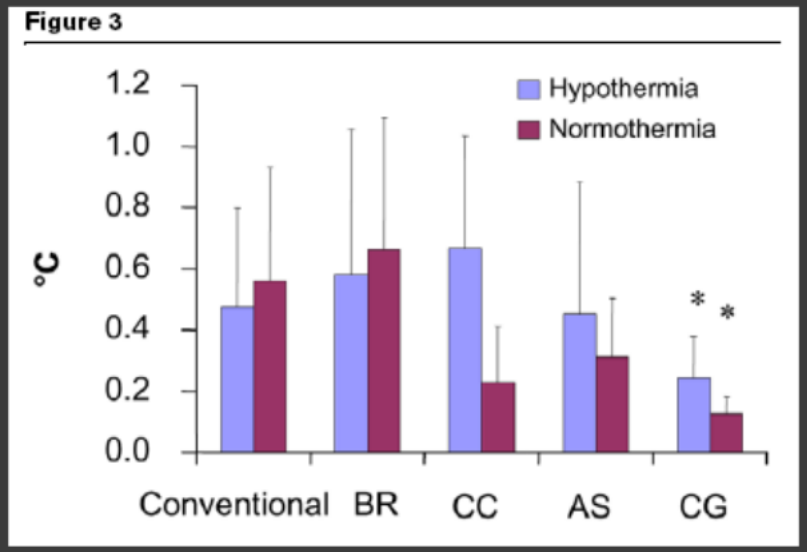
Comparison of cooling methods to induce and maintain normo- and hypothermia in intensive care unit patients: a prospective intervention study

Cornelia W Hoedemaekers, Mustapha Ezzahti, Aico Gerritsen and Johannes G van der Hoeven

- 50 patients
  - Indications for mild hypothermia or strict euthermia
  - Randomized to 5 groups
    - "Conventional" = 30cc/kg cold IVF + ice/cold packs
    - Water circulating blankets (Blanketrol II, Cincinnati Subzero)
    - Air circulating blankets
    - Arctic Sun
    - Intravascular balloon device
  - Endpoints: speed of cooling, % time above or below temperature range

Crit Care 2007;11:R91

Cooling efficacy



Mean temperature deviation from target temperature.

- Water-circulating blankets, gel-coated water circulating pads and intravascular cooling were equally efficient in inducing hypothermia and normothermia
- Intravascular cooling with heat-exchange balloons was the most effective way to maintain goal temperature

Crit Care 2007;11:R91

Resuscitation 124 (2018) 14–20

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Efficacy of different cooling technologies for therapeutic temperature management: A prospective intervention study☆

Petra Sonder[a], Gladys N. Janssens[a], Albertus Beishuizen[b,c], Connie L. Henry[d], Jon C. Rittenberger[e], Clifton W. Callaway[e], Cameron Dezfulian[e], Kees H. Polderman[a,*]

Results: 129 consecutive patients admitted after CA and treated with hypothermia were screened, and 120 were enrolled in the study. Two researchers dedicated fulltime to this study monitored TH treatment in all patients, including antishivering measures, additional cooling measures used (e.g. icepacks and cold fluid infusion), and all other issues related to temperature management. Baseline characteristics were similar for all groups. Cooling rates were 2.06 ± 1.12 °C/h for endovascular cooling, 1.49 ± 0.82 for Arctic sun, 0.61 ± 0.36 for Meditherm and 1.22 ± 1.12 for Blanketrol. Time within target range ±0.5 °C was $97.3 \pm 6.0\%$ for Thermogard, $81.8 \pm 25.2\%$ for Arctic Sun, $57.4 \pm 29.3\%$ for Meditherm, and $64.5 \pm 20.1\%$ for Blanketrol. The following differences were significant: Thermogard vs. Meditherm ($p < 0.01$), Thermogard vs. Blanketrol ($p < 0.01$), and Arctic Sun vs. Meditherm ($p < 0.02$). No major complications occurred with any device.

Conclusions: Endovascular cooling and gel-adhesive pads provide more rapid hypothermia induction and more effective temperature maintenance compared to water-circulating cooling blankets. This applied to induction speed, but (more importantly) also to time within target range during maintenance.

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- **standard procedure** in the postresuscitation care

všichni chladili……

… až do studie TTM

TTM1 trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D., David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sci., Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D., Jesper Kjaergaard, M.D., D.M.Sci., Michael Kuiper, M.D., Ph.D., Tommaso Pellis, M.D., Pascal Stammet, M.D., Michael Wanscher, M.D., Ph.D., Matt P. Wise, M.D., D.Phil., Anders Åneman, M.D., Ph.D., Nawaf Al-Subaie, M.D., Søren Boesgaard, M.D., D.M.Sci., John Bro-Jeppesen, M.D., Iole Brunetti, M.D., Jan Frederik Bugge, M.D., Ph.D., Christopher D. Hingston, M.D., Nicole P. Juffermans, M.D., Ph.D., Matty Koopmans, R.N., M.Sc., Lars Køber, M.D., D.M.Sci., Jørund Langørgen, M.D., Gisela Lilja, O.T., Jacob Eifer Møller, M.D., D.M.Sci., Malin Rundgren, M.D., Ph.D.,

N Engl J Med. 2013 Dec 5;369(23):2197-2206.

ORIGINAL ARTICLE

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

RESULTS

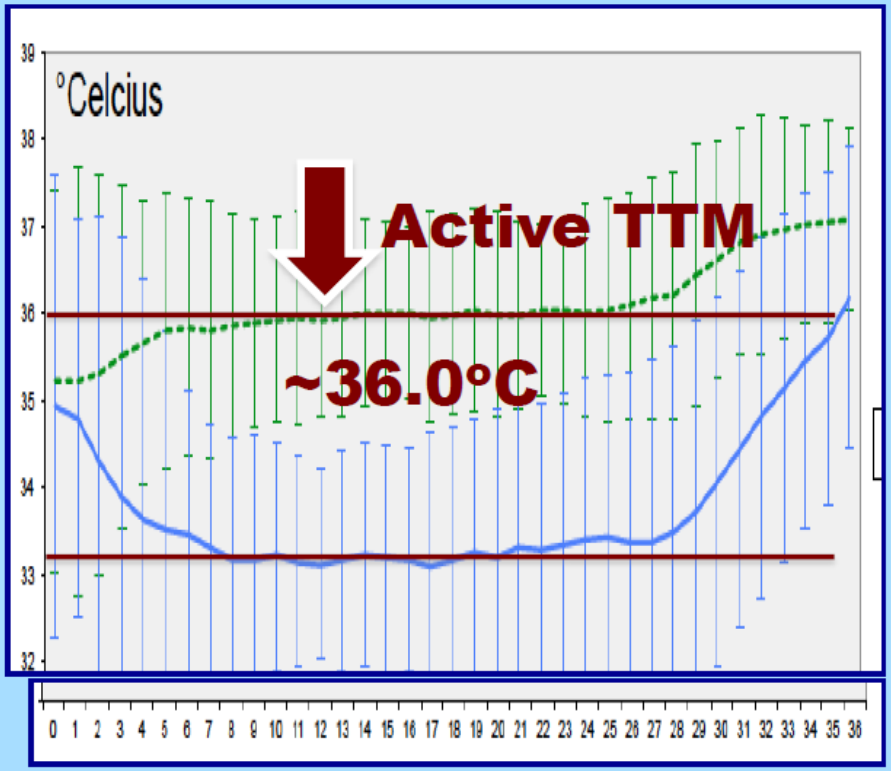
In total, 939 patients were included in the primary analysis. At the end of the trial, 50% of the patients in the 33°C group (235 of 473 patients) had died, as compared with 48% of the patients in the 36°C group (225 of 466 patients) (hazard ratio with a temperature of 33°C, 1.06; 95% confidence interval [CI], 0.89 to 1.28; P=0.51). At the 180-day follow-up, 54% of the patients in the 33°C group had died or had poor neurologic function according to the CPC, as compared with 52% of patients in the 36°C group (risk ratio, 1.02; 95% CI, 0.88 to 1.16; P=0.78). In the analysis using the modified Rankin scale, the comparable rate was 52% in both groups (risk ratio, 1.01; 95% CI, 0.89 to 1.14; P=0.87). The results of analyses adjusted for known prognostic factors were similar.

CONCLUSIONS

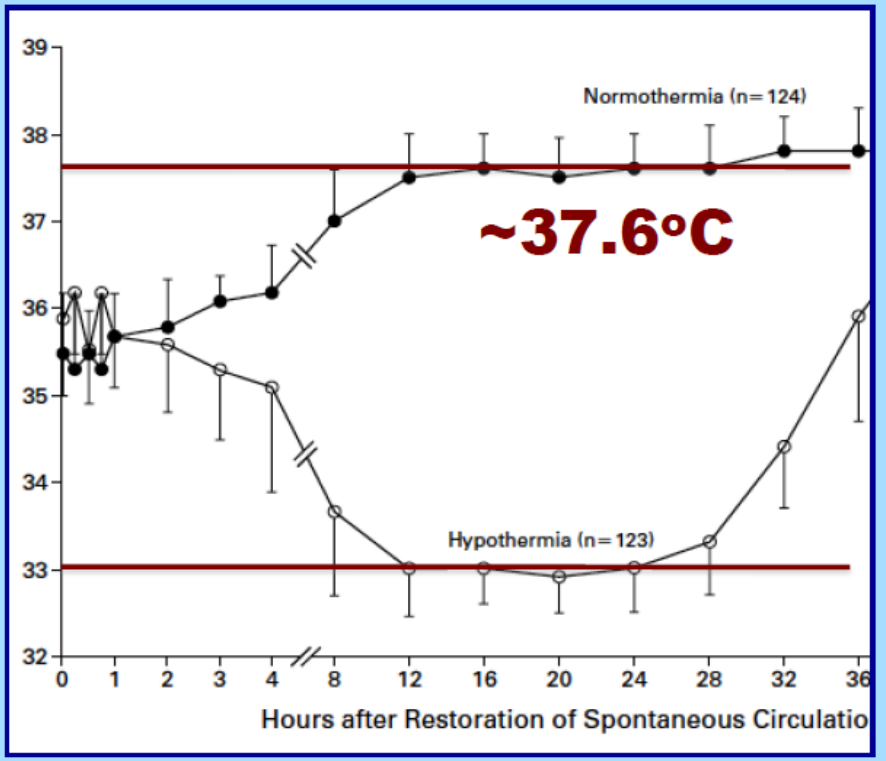
In unconscious survivors of out-of-hospital cardiac arrest of presumed cardiac cause, hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C. (Funded by the Swedish Heart–Lung Foundation and others; TTM ClinicalTrials.gov number, NCT01020916.)

Marked differences in “control” group

Nielsen et al



HACA study



Bernard et al: ~37.3°C

Large difference in maintenance temperatures

TTM2 trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

J. Dankiewicz, T. Cronberg, G. Lilja, J.C. Jakobsen, H. Levin, S. Ullén, C. Rylander, M.P. Wise, M. Oddo, A. Cariou, J. Bělohlávek, J. Hovdenes, M. Saxena, H. Kirkegaard, P.J. Young, P. Pelosi, C. Storm, F.S. Taccone, M. Joannidis, C. Callaway, G.M. Eastwood, M.P.G. Morgan, P. Nordberg, D. Erlinge, A.D. Nichol, M.S. Chew, J. Hollenberg, M. Thomas, J. Bewley, K. Sweet, A.M. Grejs, S. Christensen, M. Haenggi, A. Levis, A. Lundin, J. Düring, S. Schmidbauer, T.R. Keeble, G.V. Karamasis, C. Schrag, E. Faessler, O. Smid, M. Otáhal, M. Maggiorini, P.D. Wendel Garcia, P. Jaubert, J.M. Cole, M. Solar, O. Borgquist, C. Leithner, S. Abed-Maillard, L. Navarra, M. Annborn, J. Undén, I. Brunetti, A. Awad, P. McGuigan, R. Bjørkholt Olsen, T. Cassina, P. Vignon, H. Langeland, T. Lange, H. Friberg, and N. Nielsen, for the TTM2 Trial Investigators*

N Engl J Med. 2021 Jun 17;384(24):2283-2294.

TTM2 trial

Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

RESULTS

A total of 1850 patients were evaluated for the primary outcome. At 6 months, 465 of 925 patients (50%) in the hypothermia group had died, as compared with 446 of 925 (48%) in the normothermia group (relative risk with hypothermia, 1.04; 95% confidence interval [CI], 0.94 to 1.14; P=0.37). Of the 1747 patients in whom the functional outcome was assessed, 488 of 881 (55%) in the hypothermia group had moderately severe disability or worse (modified Rankin scale score ≥4), as compared with 479 of 866 (55%) in the normothermia group (relative risk with hypothermia, 1.00; 95% CI, 0.92 to 1.09). Outcomes were consistent in the prespecified subgroups. Arrhythmia resulting in hemodynamic compromise was more common in the hypothermia group than in the normothermia group (24% vs. 17%, P<0.001). The incidence of other adverse events did not differ significantly between the two groups.

CONCLUSIONS

In patients with coma after out-of-hospital cardiac arrest, targeted hypothermia did not lead to a lower incidence of death by 6 months than targeted normothermia.

guidelines?

RESUSCITATION 161 (2021) 220 –269

Available online at www.sciencedirect.com

Resuscitation

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

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care☆

Jerry P. Nolan[a,b,1,*], *Claudio Sandroni*[c,d,1], *Bernd W. Böttiger*[e], *Alain Cariou*[f], *Tobias Cronberg*[g], *Hans Friberg*[h], *Cornelia Genbrugge*[i,j], *Kirstie Haywood*[k], *Gisela Lilja*[l], *Véronique R.M. Moulaert*[m], *Nikolaos Nikolaou*[n], *Theresa Mariero Olasveengen*[o], *Markus B. Skrifvars*[p], *Fabio Taccone*[q], *Jasmeet Soar*[r]

POST RESUSCITATION CARE 2021
5 TOP MESSAGES

EUROPEAN RESUSCITATION COUNCIL

1. After ROSC use ABC approach

- Insert an advanced airway (tracheal intubation when skills available)
- Titrate inspired oxygen to an SpO_2 of 94-98% and ventilate lungs to achieve normocapnia
- Obtain reliable intravenous access, restore normovolaemia, avoid hypotension (aim for systolic BP > 100mmHg)

2. Emergent cardiac catheterisation +/- immediate PCI after cardiac arrest of suspected cardiac origin and ST-elevation on the ECG

3. Use targeted temperature management (TTM) for adults after either OHCA or IHCA (with any initial rhythm) who remain unresponsive after ROSC

4. Use multimodal neurological prognostication using clinical examination, electrophysiology, biomarkers, and imaging

5. Assess physical and non-physical impairments before and after discharge from the hospital and refer for rehabilitation if necessary

Table 1 – Summary of changes since the 2015 Guidelines on Post-resuscitation care.

2015 Guidelines	2021 Guidelines	Rationale for change
Temperature control • Maintain a constant, target temperature between 32 °C and 36 °C for those patients in whom temperature control is used (strong recommendation, moderate-quality evidence). • Whether certain subpopulations of cardiac arrest patients may benefit from lower (32–34 °C) or higher (36 °C) temperatures remains unknown, and further research may help elucidate this. • TTM is recommended for adults after OHCA with an initial shockable rhythm who remain unresponsive after ROSC (strong recommendation, low-quality evidence). • TTM is suggested for adults after OHCA with an initial non-shockable rhythm who remain unresponsive after ROSC (weak recommendation, very low-quality evidence). • TTM is suggested for adults after IHCA with any initial rhythm who remain unresponsive after ROSC (weak recommendation, very low-quality evidence). • If targeted temperature management is used, it is suggested that the duration is at least 24 h (weak recommendation, very low-quality evidence).	• We recommend TTM for adults after either OHCA or IHCA (with any initial rhythm) who remain unresponsive after ROSC. • Maintain a target temperature at a constant value between 32 °C and 36 °C for at least 24 h. • Avoid fever (>37.7 °C) for at least 72 h after ROSC in patients who remain in coma.	A recent randomised controlled trial of both IHCA and OHCA patients with initial non-shockable rhythms showed a higher percentage of patients survived with a favourable neurological outcome when treated with TTM at 33 °C versus 37 °C.[13] This has enabled the recommendation to be extended to all rhythms and locations. The definition of fever (>37.7 °C) is consistent with that used in the TTM2 trial.[14]

- We recommend TTM for adults after either OHCA or IHCA (with any initial rhythm) who remain unresponsive after ROSC.
- Maintain a target temperature at a constant value between 32 °C and 36 °C for at least 24 h.
- Avoid fever (>37.7 °C) for at least 72 h after ROSC in patients who remain in coma.

RESUSCITATION 172 (2022) 229–236

Available online at ScienceDirect

Resuscitation

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

ERC-ESICM guidelines on temperature control after cardiac arrest in adults ☆

Table 2 – ERC-ESICM Recommendations for temperature control after cardiac arrest in adults.

We recommend continuous monitoring of core temperature in patients who remain comatose after ROSC from cardiac arrest (good practice statement).
We recommend actively preventing fever (defined as a temperature > 37.7 °C) in post-cardiac arrest patients who remain comatose (weak recommendation, low-certainty evidence).
We recommend actively preventing fever for at least 72 hours in post-cardiac arrest patients who remain comatose (good practice statement).
Temperature control can be achieved by exposing the patient, using anti-pyretic drugs, or if this is insufficient, by using a cooling device with a target temperature of 37.5 °C (good practice statement).
There is currently insufficient evidence to recommend for or against temperature control at 32–36 °C in sub-populations of cardiac arrest patients or using early cooling, and future research may help elucidate this. We recommend not actively rewarming comatose patients with mild hypothermia after ROSC to achieve normothermia (good practice statement).
We recommend not using prehospital cooling with rapid infusion of large volumes of cold IV fluid immediately after ROSC (strong recommendation; moderate certainty evidence).

máme

přestat

chladit?

- výsledky **studií**

- **experimentální** modely

- klinické **zkušenosti**

- změna ***outcome*** po zavedení protokolu TTM1

- detaily studií **TTM1** a **TTM2**

what happened after TTM1?

after TTM1

- ↑mortality ↓neurol. outcome
  (Bray JE; Resuscitation 2017; 113:39)

- ↑mortality ↑tělesné teploty
  (Salter R; Crit Care Med 2018; 46:1722)

- ↑mortality ↓adherence k hypotermii
  (Garfield B; Ther Hypothermia Temp Manag 2020; e-pub; Nolan JP; Resuscitation 2021; 162:304)

- ↑mortality
  (Nishikimi M; Crit Care Med 2021; 49:e741)

- ↓mortality 25% vs 44% (HACORE dle TTM1)
  (Akin M; JACC Cardiovasc Interv 2018; 11:1811)

problémy studií

TTM2 trial

- study **protocol**: **90 min** from ROSC to 33°C

TTM2 trial

- study **protocol**: **90 min** from ROSC to 33°C
- time from **ROSC** to **randomisation**: **135 min**
- time from **randomisation** to **33°C**: **5 hours** (median)
- more than **50% of pts** needed **7 hours** from **ROSC** to **33°C**!
- only **few pts** with **intravascular** cooling (TTM1 24%, TTM 29%)
- **other studies** with more intravascular cooling had lower mortality (**25-35 %**)
- approximately **50%** of pts had **insufficient** control of **fever** at day 3
- 85% (88%) pts had propofol (0% in HACA, Bernard study)
- protocol for determination of the **neurologic prognosis** and withdrawal of life-supporting therapies

EJA European Journal of Anaesthesiology

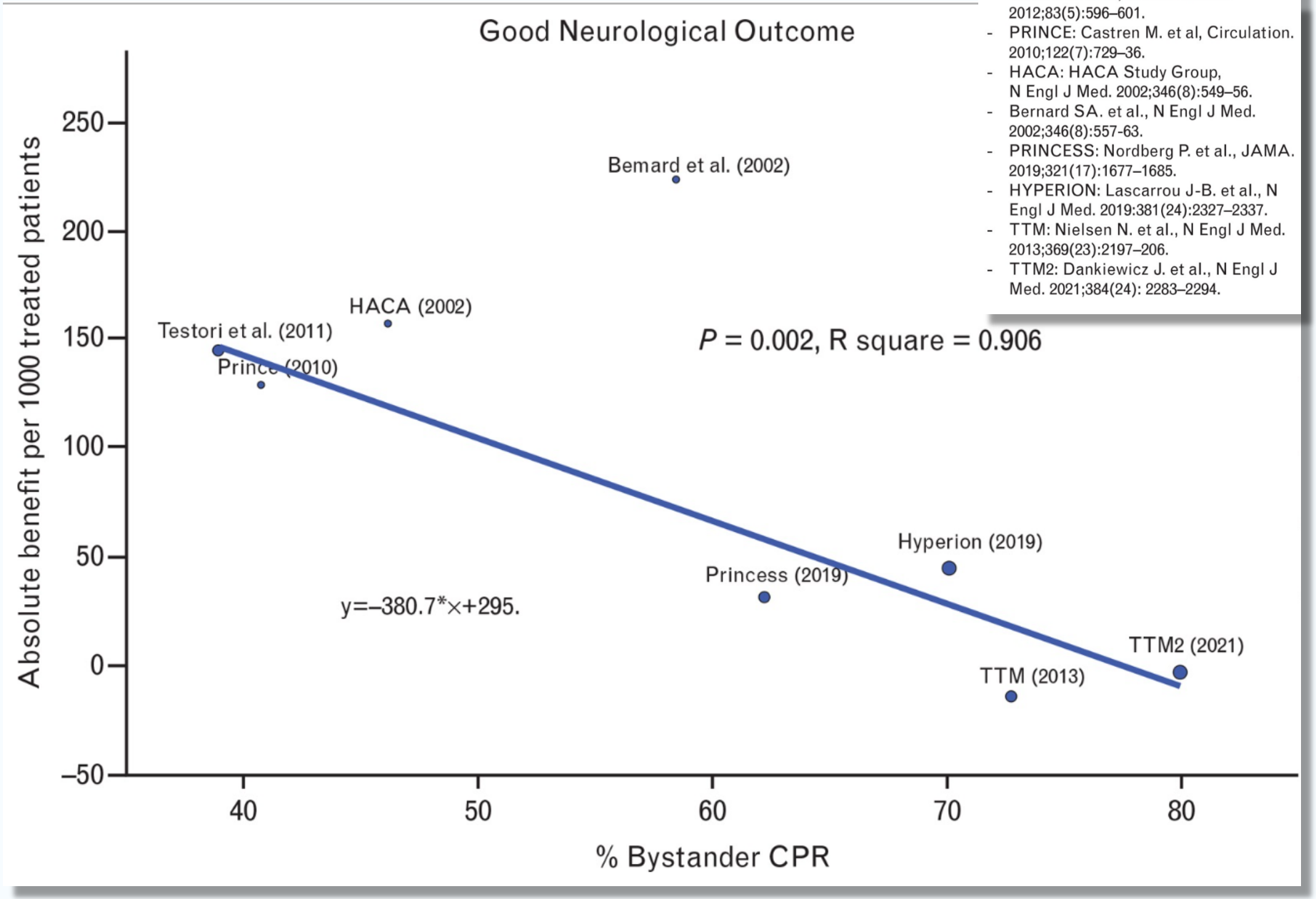
The effectiveness of targeted temperature management following cardiac arrest may depend on bystander cardiopulmonary resuscitation rates

Böttiger, Bernd W.; Hellmich, Martin; Wetsch, Wolfgang A.

Author Information

European Journal of Anaesthesiology 39(4):p 401-402, April 2022. | **DOI:** 10.1097/EJA.0000000000001663

40% 57%



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- TTM2: Dankiewicz J. et al., N Engl J Med. 2021;384(24): 2283–2294.

guidelines

vs.

reality

Roedl *et al. Critical Care* (2023) 27:35
https://doi.org/10.1186/s13054-023-04319-7

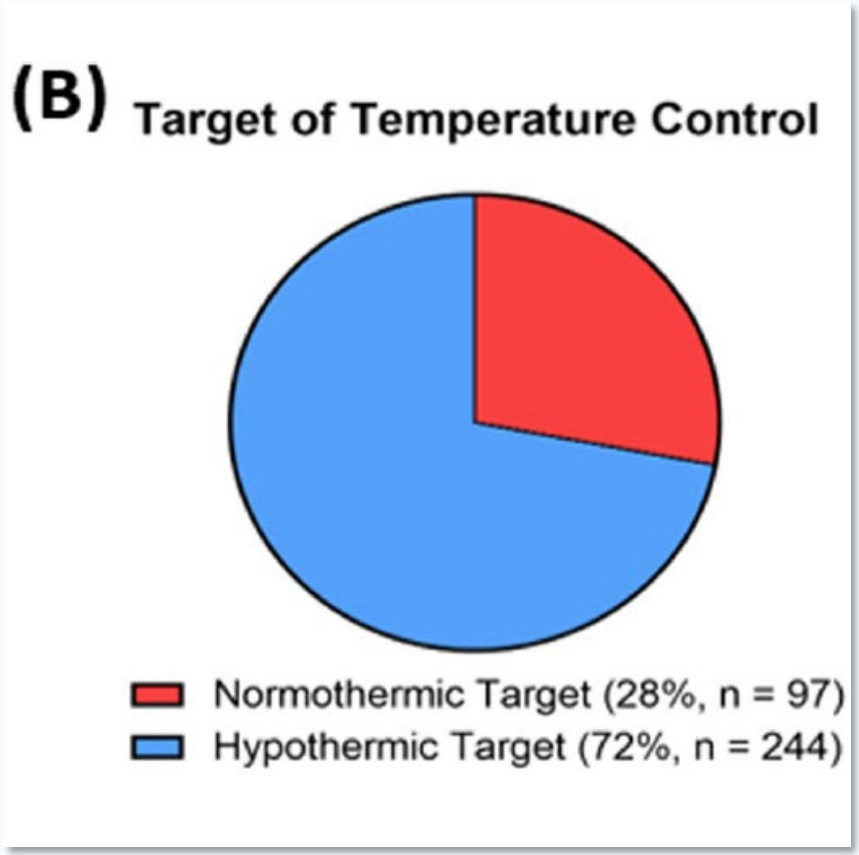
Critical Care

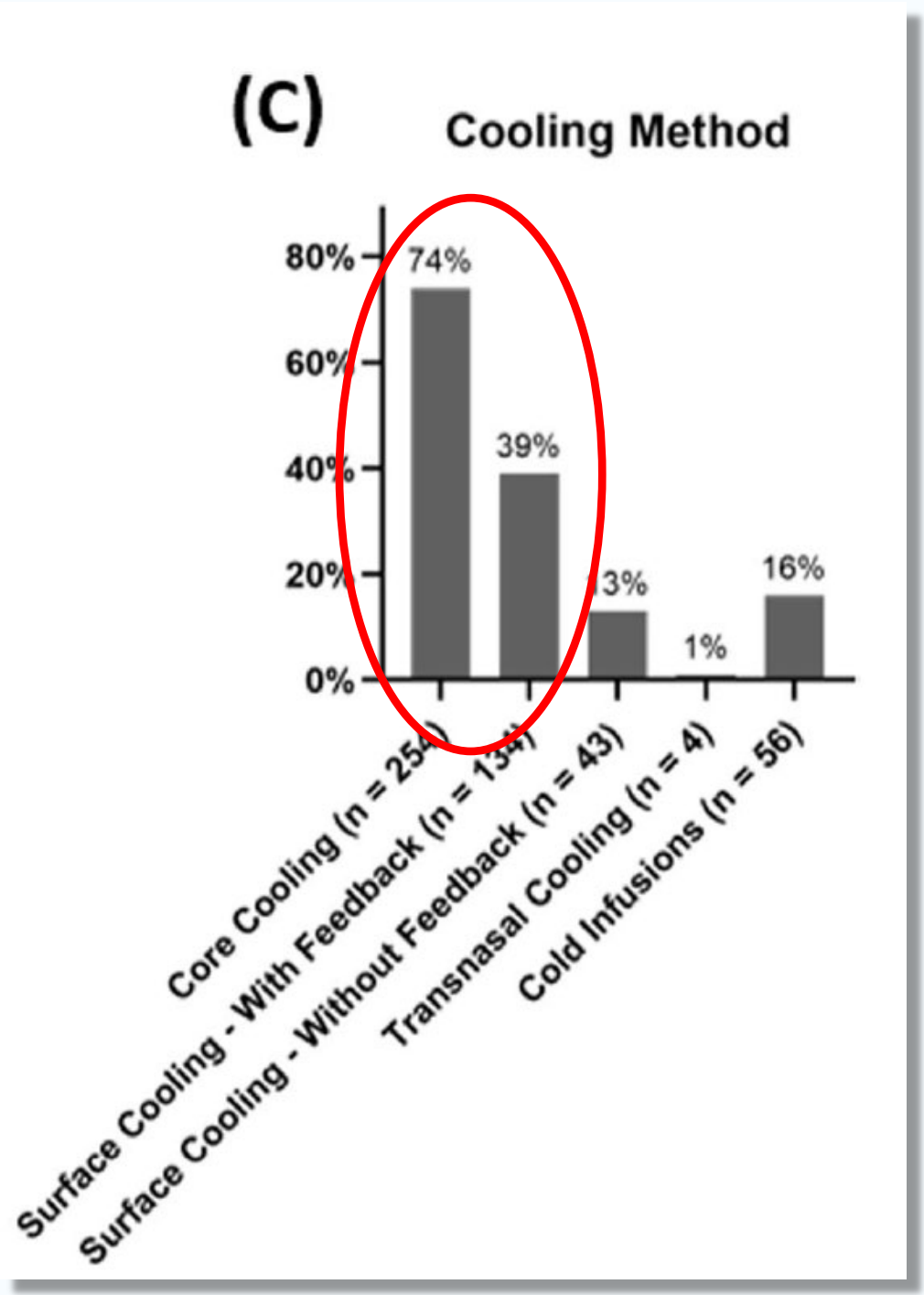
BRIEF REPORT Open Access

Temperature control in adults after cardiac arrest: a survey of current clinical practice in Germany

Kevin Roedl[1*], Sebastian Wolfrum[2], Guido Michels[3], Martin Pin[4], Gerold Söffker[1], Uwe Janssens[5] and Stefan Kluge[1]

Published online: 23 January 2023


(B)
Target of Temperature Control
Normothermic Target (28%, n = 97)
Hypothermic Target (72%, n = 244)


(C)
Cooling Method
80%
60%
40%
20%
0%
74%
39%
13%
1%
16%
Core Cooling (n = 254)
Surface Cooling - With Feedback (n = 134)
Surface Cooling - Without Feedback (n = 43)
Transnasal Cooling (n = 4)
Cold Infusions (n = 56)

Cochrane Library

Cochrane Database of Systematic Reviews

Publication status and date: published in Issue 6, 2023.

Hypothermia for neuroprotection in adults after cardiac arrest (Review)

Arrich J, Schütz N, Oppenauer J, Vendt J, Holzer M, Havel C, Herkner H

Data collection and analysis

We used standard Cochrane methods. Our primary outcome was 1. neurological recovery. Our secondary outcomes were 2. survival to hospital discharge, 3. quality of life, 4. cost-effectiveness and 5. adverse events. We used GRADE to assess certainty.

Main results

We found 12 studies with 3956 participants reporting the effects of therapeutic hypothermia on neurological outcome or survival. There were some concerns about the quality of all the studies, and two studies had high risk of bias overall. When we compared conventional cooling methods versus any type of standard treatment (including a body temperature of 36 °C), we found that participants in the therapeutic hypothermia group were more likely to reach a favourable neurological outcome (risk ratio (RR) 1.41, 95% confidence interval (CI) 1.12 to 1.76; 11 studies, 3914 participants). The certainty of the evidence was low.

When we compared therapeutic hypothermia with fever prevention or no cooling, we found that participants in the therapeutic hypothermia group were more likely to reach a favourable neurological outcome (RR 1.60, 95% CI 1.15 to 2.23; 8 studies, 2870 participants). The certainty of the evidence was low.

Authors' conclusions

Current evidence suggests that conventional cooling methods to induce therapeutic hypothermia may improve neurological outcomes after cardiac arrest. We obtained available evidence from studies in which the target temperature was 32 °C to 34 °C.

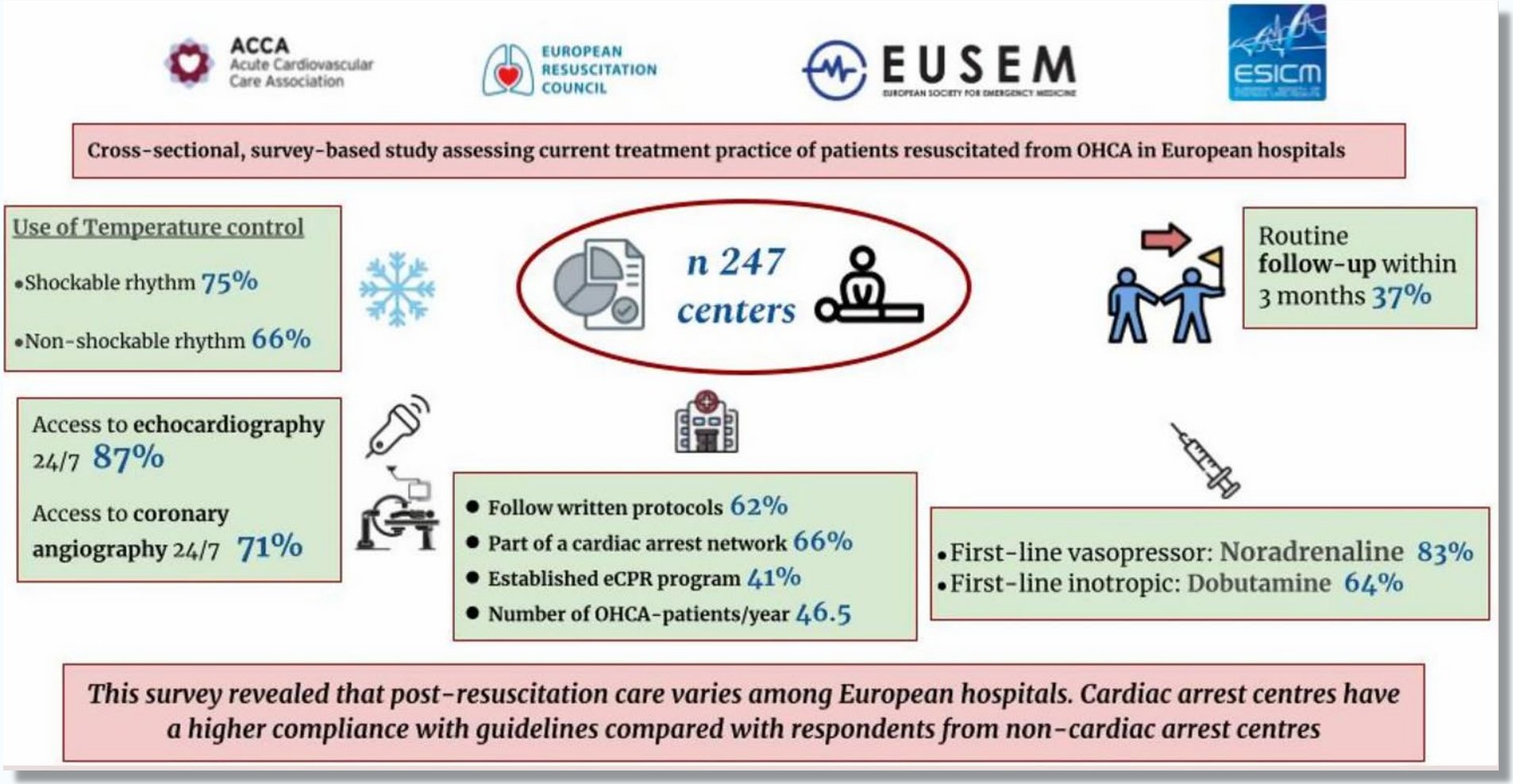
ESC European Society of Cardiology

European Heart Journal: Acute Cardiovascular Care (2023) **12**, 96–105
https://doi.org/10.1093/ehjacc/zuac153

ORIGINAL SCIENTIFIC PAPER

Management of comatose survivors of out-of-hospital cardiac arrest in Europe: current treatment practice and adherence to guidelines. A joint survey by the Association for Acute CardioVascular Care (ACVC) of the ESC, the European Resuscitation Council (ERC), the European Society for Emergency Medicine (EUSEM), and the European Society of Intensive Care Medicine (ESICM)

Received 26 June 2022; revised 15 October 2022; accepted 30 November 2022; online publish-ahead-of-print 2 December 2022



Received 26 June 2022; revised 15 October 2022; accepted 30 November 2022; online publish-ahead-of-print 2 December 2022

Table 3 General intensive care and targeted temperature management

	Overall $n = 237$	Cardiac arrest centre $n = 165$ (70%)	Not cardiac arrest centre $n = 72$ (30%)	*P*-value
Targeted temperature management				
routinely use of TTM for initial shockable rhythm	160 (75%)	123 (80%)	37 (60%)	0.006
routinely use of TTM for initial non-shockable rhythm	142 (66%)	108 (70%)	34 (57%)	0.06
Place of TTM induction				
ICU	141 (66%)	100 (65%)	41 (70%)	0.43
Emergency Department	32 (15%)	24 (15%)	8 (14%)	
Cath lab	10 (5%)	9 (6%)	1 (2%)	
Other	10 (4%)	9 (6%)	1 (2%)	
TTM-methods (more than one is possible)				
Antipyretic medication	104 (44%)	69 (42%)	35 (49%)	0.33
Cold fluids	99 (42%)	69 (42%)	30 (42%)	0.98
External cooling without feedback	109 (46%)	71 (43%)	38 (53%)	0.25
Invasive and external cooling with feedback	89 (38%)	72 (44%)	17 (24%)	0.0003

Level of target temperature	
< 32°C	1 (0.5%)
between 32–34°C	46 (21%)
Between 34–36°C	103 (52%)
< 37.5°C	35 (16%)
Duration of TTM including fever control after cooling	
24 h in total from start of TTM	28 (14%)
48 h in total from start of TTM	29 (14%)
72 h in total from start of TTM	64 (31%)
More than 72 h if patient has fever	25 (12%)
Other	60 (29%)

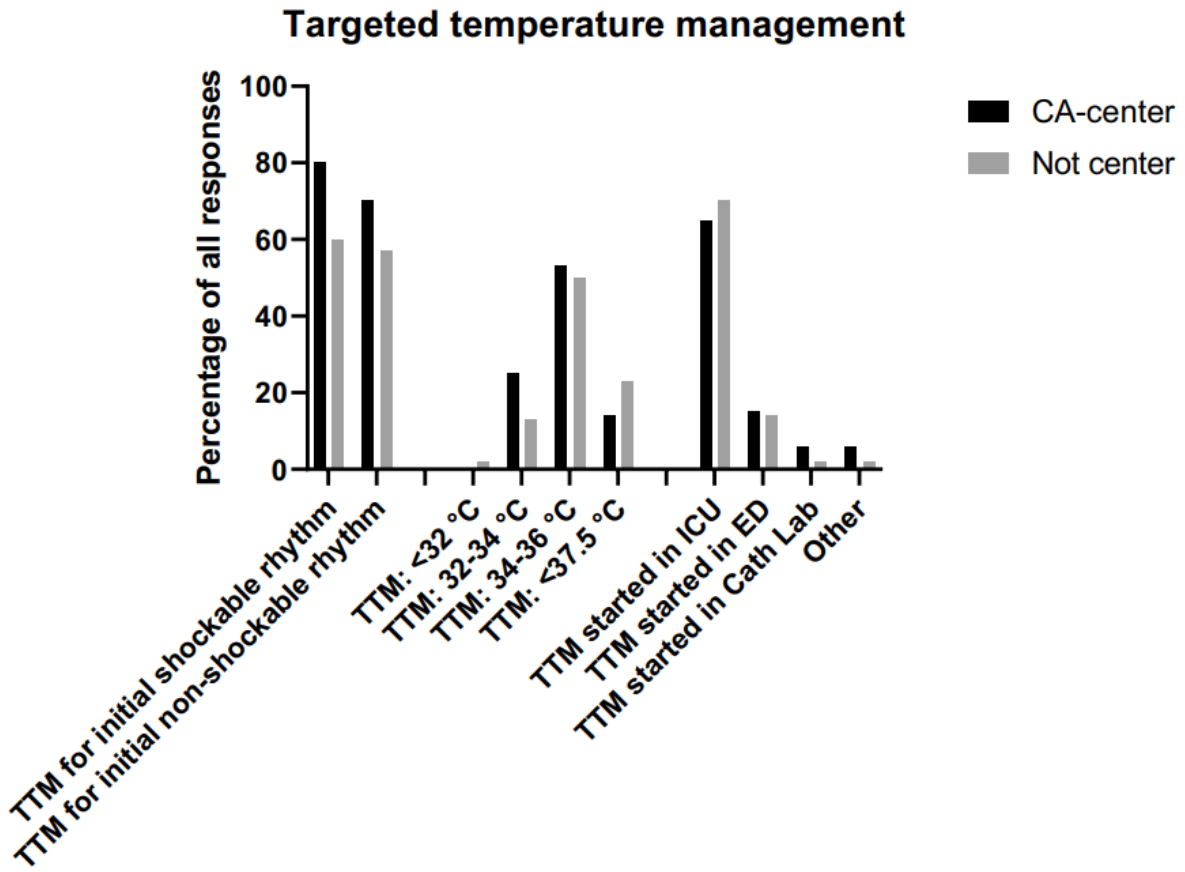


Figure 3 Temperature control practices following OHCA. TTM, targeted temperature management; ICU, intensive care unit; ED, Emergency Department; CA centre, cardiac arrest centre.

what

now?

Medizinische Klinik
Intensivmedizin und Notfallmedizin

Positionspapier

Med Klin Intensivmed Notfmed 2023 · 118 (Suppl 1):S59–S63
https://doi.org/10.1007/s00063-023-01092-x
Angenommen: 9. November 2023
Online publiziert: 5. Dezember 2023

Hypotherme Temperaturkontrolle nach erfolgreicher Wiederbelebung eines außerklinischen Herz-Kreislauf-Stillstands beim Erwachsenen

Statement der Arbeitsgruppen Reanimation und Post-Reanimationsbehandlung in der Deutschen Gesellschaft für Internistische Intensiv- und Notfallmedizin (DGIIN) und Deutschen Interdisziplinären Vereinigung für Intensiv- und Notfallmedizin (DIVI), der Deutschen Gesellschaft Interdisziplinäre Notfall- und Akutmedizin (DGINA) und der Österreichischen Gesellschaft für Notfallmedizin (AAEM)

Hans-Jörg Busch[1] · Wilhelm Behringer[2] · Paul Biever[3] · Bernd W. Böttiger[4] · Philip Eisenburger[5] · Katrin Fink[1] · Harald Herkner[2] · Uwe Kreimeier[6] · Martin Pin[7] · Sebastian Wolfrum[8]

Germany and Austria

- Germany 60.000 Austria 5.000 OHCA/year
  (Fischer M; 2022; Außerklinische Reanimation)
- pouze 10-15% pacientů bez neurologického deficitu
  (Gräsner JT; Resuscitation 2020; 148:218)

statement:

- Deutsche Gesellschaft für Internistische Intensiv- und Notfallmedizin **(DGIIN)**
- Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin **(DIVI)**
- Deutsche Gesellschaft Interdisziplinäre Notfall- und Akutmedizin **(DGINA)**
- Österreichische Gesellschaft für Notfallmedizin **(AAEM)**

TTM trials:

1) rate of **bystander CPR** in all groups was **73 to 82%,** which is **considerably higher** than the **average** rate in **Europe** of **58% (D 40%, A 57%)**

patients with a **short** cardiac arrest time, as it is in the case of **bystander CPR**, presumably have **less** brain damage and so might **not benefit** from hypothermia

2) both **TTM studies** allowed a **delay** of up to **3 to 4 h** between ROSC and **randomisation**, and the **targeted temperature** has taken up to **7 h after** cardiac arrest to achieve

reperfusion injury starts **immediately** following resuscitation from cardiac arrest, and all **pathophysiology shows** that **earlier cooling** is more **effective**

3) both TTM studies included **many centres** from various countries, with **each centre** enrolling only a **few patients**

this creates **potential** for considerable **heterogeneity** in all other aspects of **postresuscitation care**

guidelines ERC/ESICM:

1) are predominantly based on the **meta-analysis** by **Granfeld** *(Resuscitation 2021)*

- the selected studies were **separated** into **two** different analyses *(30ds vs 3-6ms)*
- both meta-analyses showed a risk ratio in **favour of hypothermia** at 32 to 34°C compared with normothermia; however, the 95% confidence interval crossed 1, and so the results of these two group analyses were **not statistically significant**
- why the data was split into these **underpowered groups** is **not clear**

2) new meta-analysis by **Granfeldt** *(Resuscitation 2023)*

- there were more, but still **not all available studies** are taken into account again **no statistically significant benefit** of therapeutic hypothermia at 32-34°C
- which is why there were **no subsequent changes** to the **recommendations** for post-resuscitation therapy by the ERC ESICM

Hypothermic temperature control after successful resuscitation of out-of-hospital cardiac arrest in adults. Statement from the resuscitation and postresuscitation treatment working groups of the German Society of Medical Intensive Care and Emergency Medicine (DGIIN) and the German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI), the German Society for Interdisciplinary Emergency and Acute Medicine (DGINA) and the Austrian Association of Emergency Medicine (AAEM)

Online publiziert: 5. Dezember 2023

Recommendation:

Based on current scientific evidence, it is **recommended** that comatose adult patients after out-of-hospital cardiac arrest and primarily successful **resuscitation** should be placed in **controlled hypothermia** with a **target temperature of 32 - 34 °C** for at least **24 hours as soon as possible**, unless there are contraindications

Med Klin Intensivmed Notfalmed. 2023;118:59-63

EJA

Eur J Anaesthesiol 2024; **41:**278–281

OPEN

STATEMENT

Temperature control after successful resuscitation from cardiac arrest in adults

A joint statement from the European Society for Emergency Medicine and the European Society of Anaesthesiology and Intensive Care

Wilhelm Behringer*†, Bernd W. Böttiger*‡, Daniele G. Biasucci‡, Athanasios Chalkias‡, Jim Connolly†, Christoph Dodt†, Abdo Khoury†, Said Laribi†, Robert Leach† and Giuseppe Ristagno‡

published 2024 Apr 1; e-published 2023 Dec 19

Summary of 2023 evidence

(1) Animal studies with cardiac arrest models show a remarkable benefit from hypothermia in the range of 32 to 34 °C on neuronal damage and neurological outcome when hypothermia is induced early after ROSC.

(2) Some RCT show a statistically significant benefit from hypothermia in the range of 32 to 34 °C compared with normothermia or no temperature control after cardiac arrest, though other randomised controlled trials do not confirm this beneficial effect. Which patients may benefit from lower (32 to 34 °C) or higher temperatures is still unknown.

(3) Earlier and more recent meta-analyses of RCT show a statistically nonsignificant effect in favour of hypothermia in the range of 32 to 34 °C compared to normothermia or no temperature control in patients after cardiac arrest. In the most recent and comprehensive Cochrane systematic review and meta-analyses including all RCT, the beneficial effect of hypothermia in the range of 32 to 34 °C compared with normothermia or no temperature control was statistically significant.

Summary of 2023 evidence

(1) Animal studies with cardiac arrest models show a remarkable benefit from hypothermia in the range of 32 to 34 °C on neuronal damage and neurological outcome when hypothermia is induced early after ROSC.

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Summary of 2023 evidence

(4) Several retrospective clinical studies indicate a beneficial effect of hypothermia in the range of 32 to 34 °C compared with normothermia, especially in subgroups with presumed moderate brain damage.

(5) There is no animal or human study showing that hypothermia in the range 32 to 34 °C results in worse neurological or overall outcome compared with normothermia or no temperature control.

Summary of 2023 evidence

(4) Several retrospective clinical studies indicate a beneficial effect of hypothermia in the range of 32 to 34 °C compared with normothermia, especially in subgroups with presumed moderate brain damage.

(5) There is no animal or human study showing that hypothermia in the range 32 to 34 °C results in worse neurological or overall outcome compared with normothermia or no temperature control.

Recommendation 2023

Some uncertainty exists as to whether hypothermia in the range of 32 to 34 °C compared with normothermia is beneficial in terms of improving neurological outcome in all patients after cardiac arrest. The current recommendations from the ERC and ESICM to merely prevent fever, in our view, neither take into account all current available evidence, nor consider the shortcomings of studies. Based on retrospective studies showing that a large proportion of patients with presumed moderate brain damage significantly benefit from hypothermia in the range of 32 to 34 °C, along with the most recent Cochrane systematic review and meta-analyses of RCT showing a statistically significant benefit of hypothermia in the range of 32 to 34 °C, and based on the fact that no study has shown a deleterious effect of hypothermia in the range of 32 to 34 °C on neurological or overall outcome, we suggest that international guidelines follow the current Cochrane analyses and in the interim period, clinicians should consider hypothermia in the range of 32 to 34 °C in all adults after cardiac arrest as soon as feasible, and to maintain this temperature range for at least 24 h. Active normothermia (36.5 to 37.7 °C) should be ensured after rewarming before and during neurological assessment, to avoid fever.

Recommendation 2023

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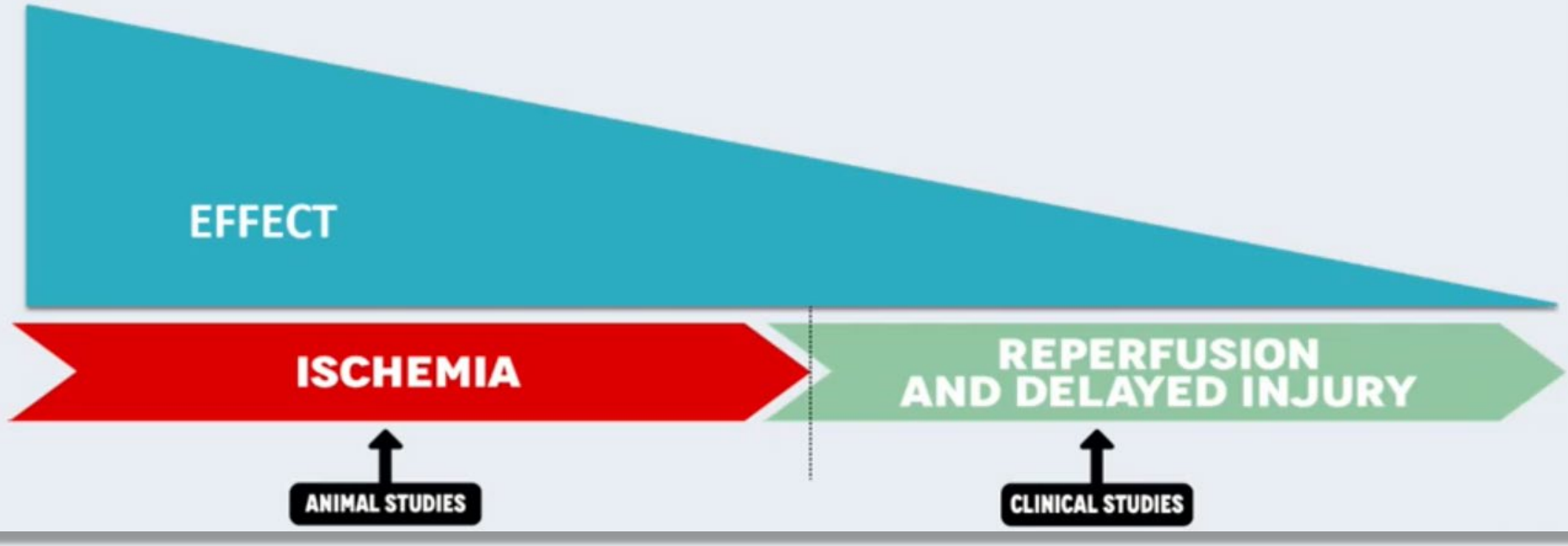
WHAT'S ONGOING AND WHAT'S UPCOMING?

- Dose of hypothermia and outcome - ICECAP
- Need for TTM device to control fever – STEPCARE
- Ultrafast cooling at the scene of the arrest– PRINCESS2

www.princess2.org

THE CONCEPT



INTERVENTION

ACLS and Cooling at the scene of the arrest.

Standardized post-resuscitation protocol

- Hypothermia to 33°C for 24 hours
- Fever control for 72 hours
- Standardized prognostication

CONTROL

ACLS at the scene of the arrest

Standardized post-resuscitation protocol

- Fever control for 72 hours
- Standardized prognostication

- Study start Q1 2024 in Sweden, Austria, Germany, Slovenia
- Expected full inclusion rate (20-25 sites) Q3-4 2024

...please keep cooling!

Antarctica 2024