MEDIZINISCHE UNIVERSITÄT WIEN

hanusch krankenhaus

1st INTERNATIONAL CRITICAL CARE AND EMERGENCY MEDICINE CONGRESS
NOVEMBER 6-8, 2013
THE GREEN PARK PENDİK HOTEL - İSTANBUL

EMCOOLS | EASY EFFICIENT PATIENT COOLING

Hypothermia in Post Resuscitation Care

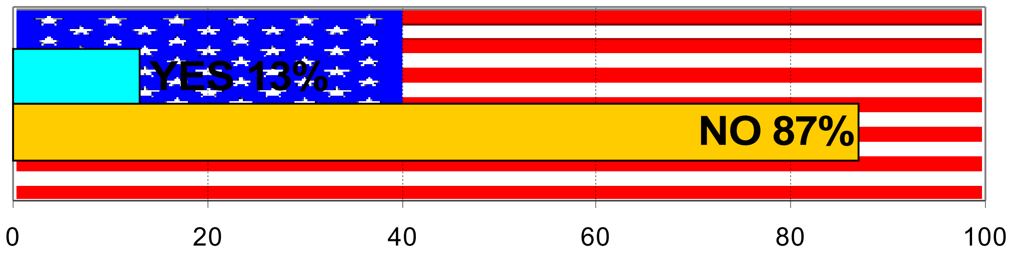
Ass. Prof. Dr. Andreas Janata

DO YOU COOL?

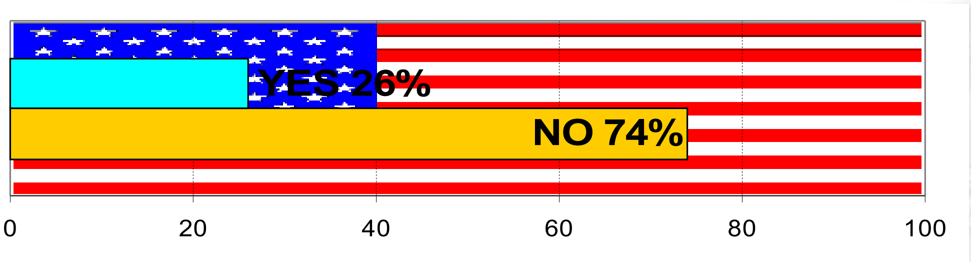
EMCOOLS EASY EFFICIENT PATIENT COOLING

DO YOU COOL?

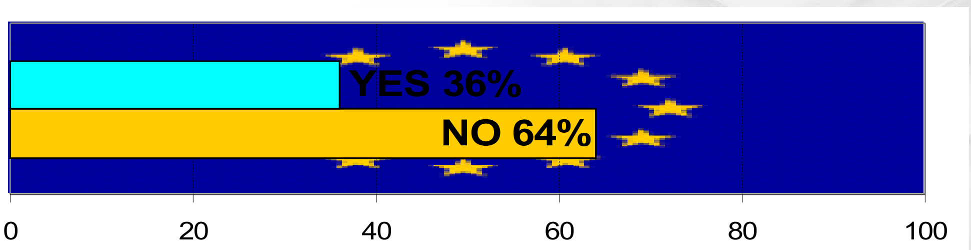
Internet based survey in UK, US, Finland and Australia (2248 of 13272 email surveys completed), emergency and critical care physicians and cardiologists



2003

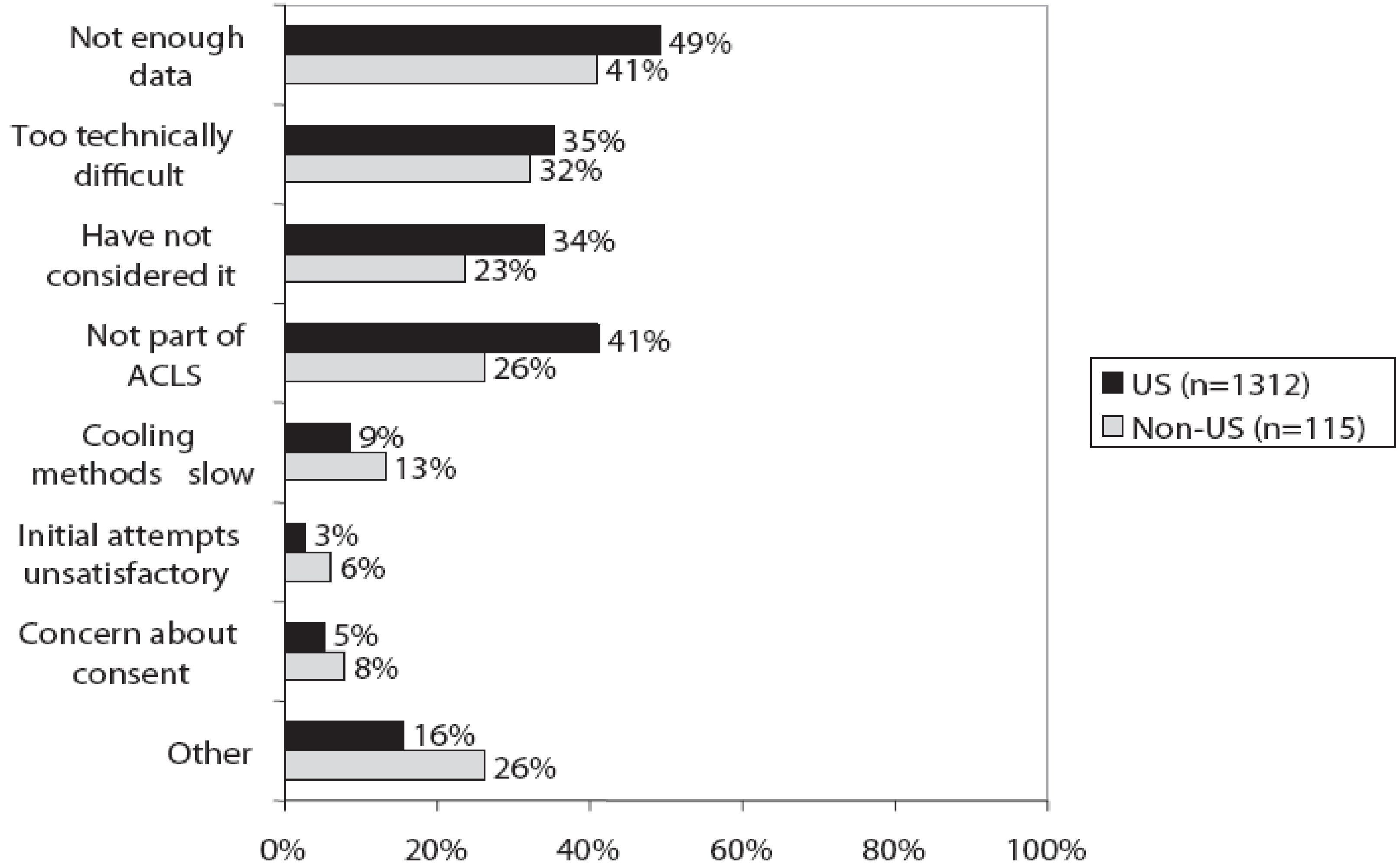


2005



Merchant *Crit Care Med* 2006;34:7

WHY BEING UN-COOL?



Merchant *Crit Care Med* 2006;34:7

START OF A HYPOTHERMIA PROGRAM

- Pre-hospital treatment?
- How to cool?
- Side effects?
- Infection management?
- Sedoanalgesia regime?
- Time to recovery?

CARDIAC ARREST IN VIENNA

- Patient data*

  - 7.030 patients without signs of circulation (206/100,000/year)
  - 1.448 resuscitation atten
  - Vienna Ambulance Servi

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

CASE REPORT

INITIAL SITUATION – OUT-OF-HOSPITAL CARDIAC ARREST

- PRE-HOSPITAL TREATMENT (9/20/2013)
  - 58 year old male, found unconscious in the street (unwitnessed CA)
  - 11:20 Emergency Call & Telephone-supported Basic Life Support (BLS)
  - 11:25 Arrival of Vienna Ambulance Service & Advanced Cardiac Life Support

CARDIAC ARREST IN VIENNA

- OUTCOME – PEA AND UNWITNESSED ARREST
  - ROSC 17.8%
  - Survival 4.0%
  - CPC 1 or 2 2.7%

	All			Bystander witnessed and cardiac aetiology		
	First monitored rhythm			First monitored rhythm		
	All	Shockable	Non-shockable	All	Shockable	Non-shockable
N	1448	446	778	546	287	259
Any ROSC[a]	433 (29.9%)	209 (46.9%)	157 (20.2%)	207 (37.9%)	142 (49.5%)	65 (25.1%)
Survival to discharge	164 (11.3%)	110 (24.7%)	35 (4.5%)	97 (17.8%)	83 (28.9%)	14 (5.4%)
CPC[b] 1 or 2	126 (8.7%)	91 (20.4%)	22 (2.8%)	80 (14.7%)	72 (25.1%)	8 (3.1%)

[a] **ROSC**: return of spontaneous circulation.
[b] **CPC**: cerebral performance categories.

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

PRE-HOSPITAL COOLING

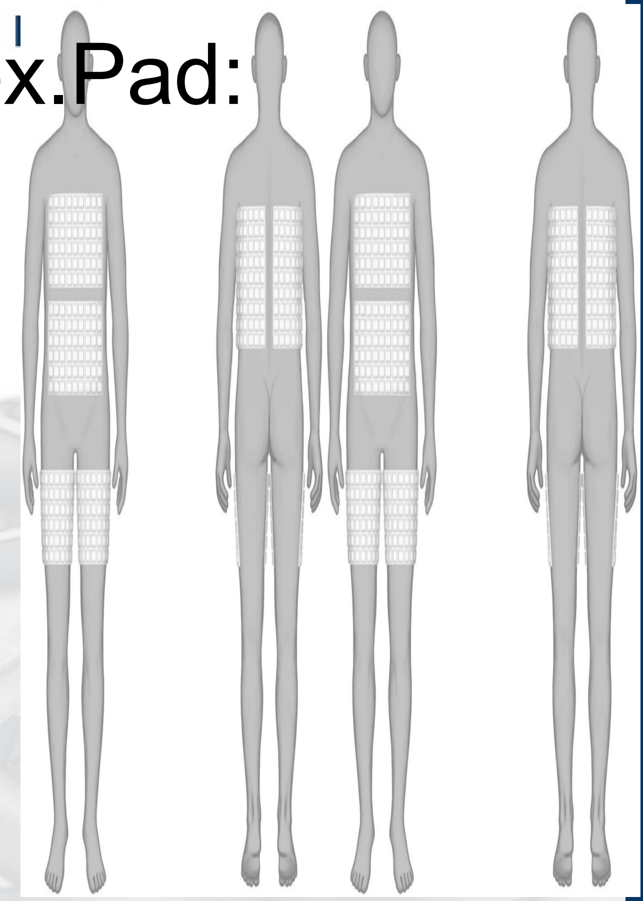
WHO IS COOLED

- Witnessed/unwitnessed
- >18 years old
- Comatose after ROSC, unresponsive to external stimuli
- Patients under sedation who received chest compressions
- Esophageal temperature >34°C

PRE-HOSPITAL COOLING

ON-SITE INDUCTION OF HYPOTHERMIA WITH COOLING PADS

- Application of EMCOOLS Flex.Pad:
  - 1 pad on the chest
  - 1 pad on the back
  - 1 pad on the abdomen
  - 1 pad per tigh



PRE-HOSPITAL COOLING

CLINICAL DATA

15 patients after cardiac arrest

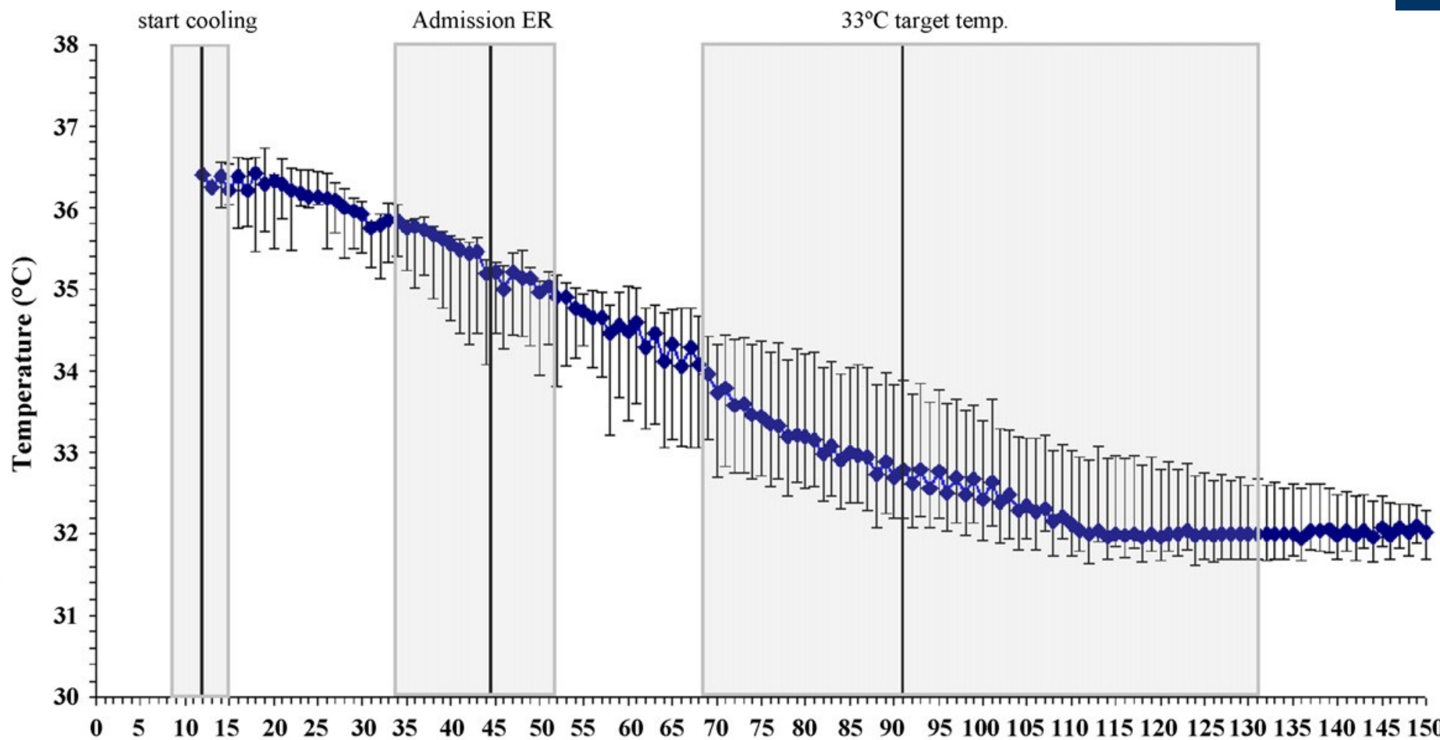
Time to start of cooling: **12 min**

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.

PRE-HOSPITAL COOLING

COLD FLUIDS

- 63 Patients randomized to pre-hospital cooling with iv. saline, 125 control patients
- ΔTesophagus ROSC-admission: 1.24°C
- Out-of-hospital cooling is possible and safe
- Limited by fluid overload (upper

Pilot Randomized Clinical Trial of Prehospital Induction of Mild Hypothermia.
Kim et al. Circulation 2007.

CASE REPORT

IN-HOSPITAL TREATMENT – CATH LAB

- CATH LAB (9/20/2013)

- 11:58 Arrival at Cath Lab (Cardiology, Hanusch Hospital)
- 12:10 Start cooling during coronary angiography
- Monitoring of esophageal temperature

PRE-HOSPITAL HYPOTHERMIA

Temperatures during immersion in 2°C cold water

TEMPERATURE MEASUREMENT

Site of measurement	Temperature °C
Rectal temperature: **normothermia**	37.5±0.05
Esophageal temperature	34.5±1.2
Tympanic	35.9±1.0

Cooling hyperthermic subjects (healthy volunteers) with 2°C cold ice water to a Trec of 37.5°C causes a hypothermic esophageal temperature.

Safe cooling limits from exercise-induced hyperthermia.
Proulx et al. Eur J Appl Physiol 2006.

Proulx CI et al. Eur J Appl Physiol 2006

COOLING IS SIMPLE.

IV SALINE/LACTATED RINGERS

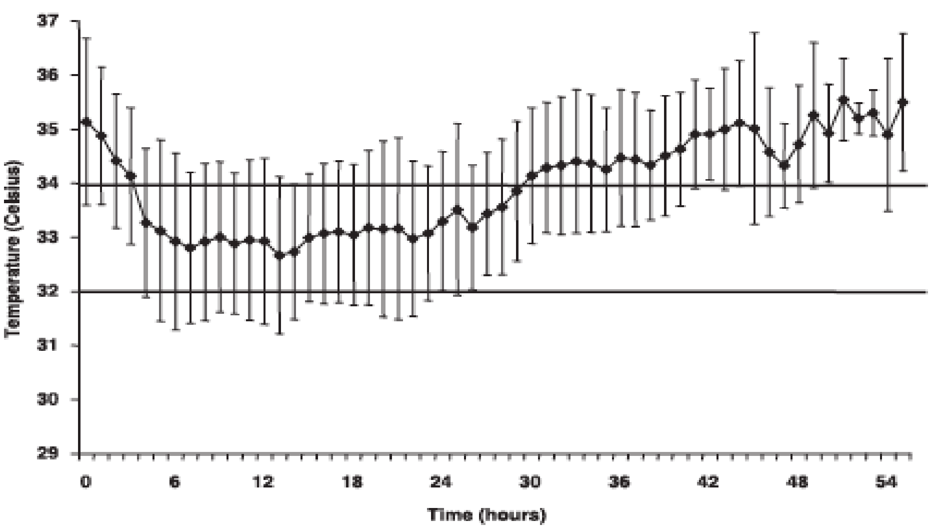
+	-
Rapid initiation	Limit: 30 ml/kg
Fast cooling rate (3.2°/h)	(1.6° over 30 min)
Cheap	No maintenance
Out-of-hospital possible	

Ideal adjunct to other cooling methods (e.g. surface cooling, intravascular catheters) to enhance cooling rate

SURFACE COOLING

COOLING PACKS, ICE

+	-
Rapid initiation	Rather ineffective
Cheap	Manpower necessary
Out-of-hospital possible	Risk of failure to achieve targe
	Risk of overcooling:



32 patients after cardiac arrest, Overcooling >1 hr:

- 63% <32°C
- 28% <31°C
- 13% <30°C

Merchant et al. CCM 2006

SURFACE COOLING

EMCOOLSpad

- Latex, destilled water, graphite, glue
- Adaptable to body surface

MOBILE COOLING UNIT

SURFACE COOLING

EMCOOLSpad

+	-
Rapid initiation	No feedback control
High cooling rates	Some manpower necessary
Energy independance	
Out-of-hospital possible	
Cooling during angiography	

SURFACE COOLING / FEEDBACK CONTROL

E.G. ARCTIC SUN, ALLON THERMOWRAP, INNERCOOL STX

Examples:

Arctic Sun®, Medivance

pads transfer energy by direct conduction from water to skin

Allon Thermowrap®, MTRE

pads transfer energy by direct conduction from water to skin

Innercool STX, Philips

SURFACE COOLING / FEEDBACK CONTROL

E.G. ARCTIC SUN, ALLON THERMOWRAP, INNERCOOL STX

+	-
Tight Temperature Control	Energy dependance
Non-invasive	
Established methods	

INTRAVASCULAR CATHETERS

COOLGARD, RADIANT MEDICAL, INNERCOOL

Examples:

Coolgard 3000® , Zoll

intravenous catheter circulating cooled saline

Radiant Medical

Innercool RTX, Philips

high cooling rate (4,7°C/h)

INTRAVASCULAR CATHETERS

COOLGARD, RADIANT MEDICAL, INNERCOOL

+

Tight temperature control

Easy to handle

Established methods

-

Invasive procedure

Energy dependent

COOLING METHODS

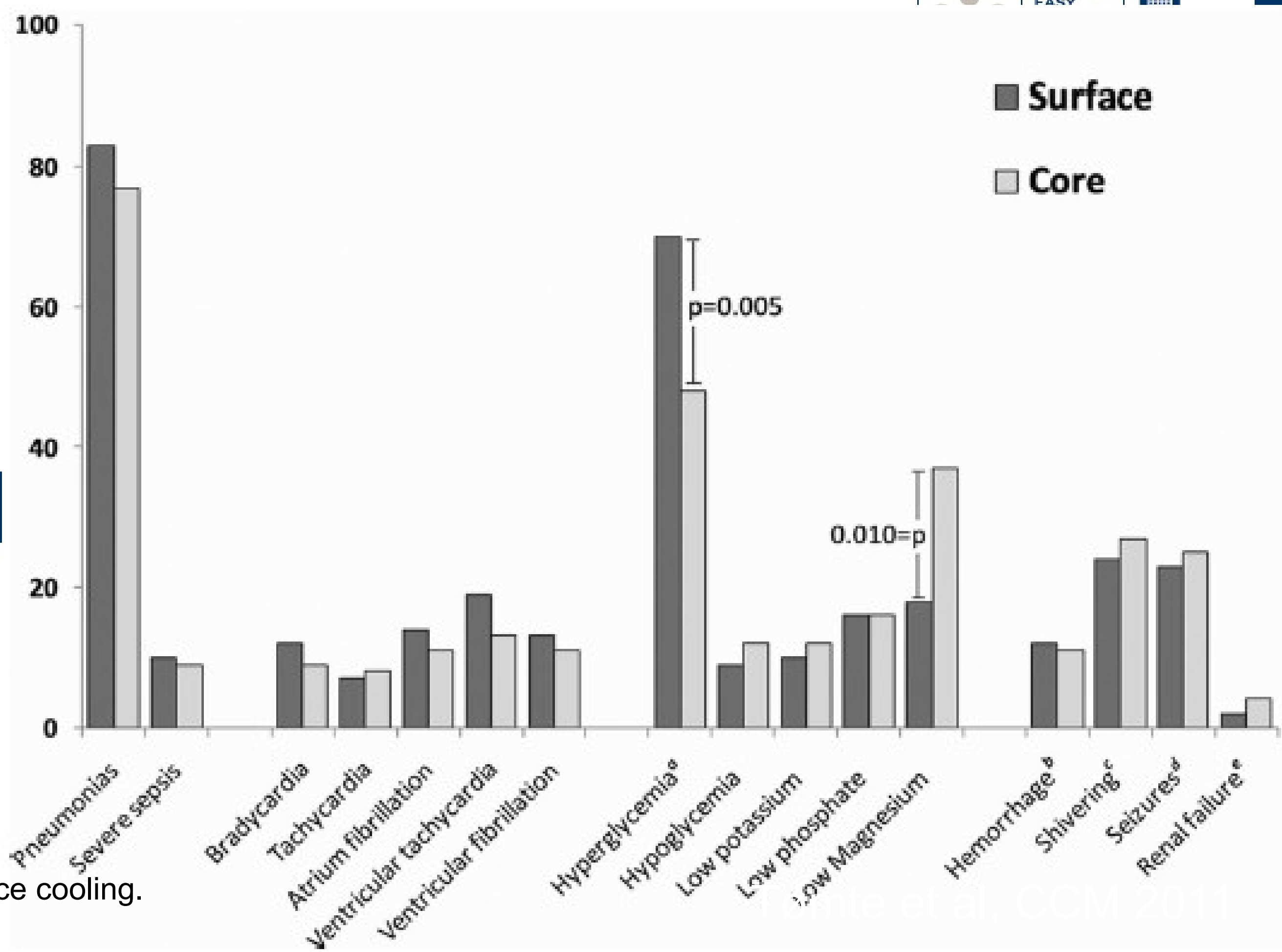
SIDE EFFECTS INTRAVASCULAR VS. SURFACE COOLING

167 patients after CA
Arctic Sun vs. Coolgard

surface cooling :
↑ episodes of hyperglycemia

Intravascular cooling:
↑ hypomagnesaemia

same outcome



A comparison of intravascular and surface cooling.
Tømte et al. CCM 2011.

COOLING METHODS

CONSIDERATIONS

Price

Energy independence

Ease of use

Manpower needed?

Automated feedback control

Invasiveness

Prehospital use?

CASE REPORT

IN-HOSPITAL TREATMENT

- 9/21/2013: increase of inflammatory parameters ✳ Decision for antibiotic therapy (aspiration pneumonia?)

Creatinine

Leucocytes

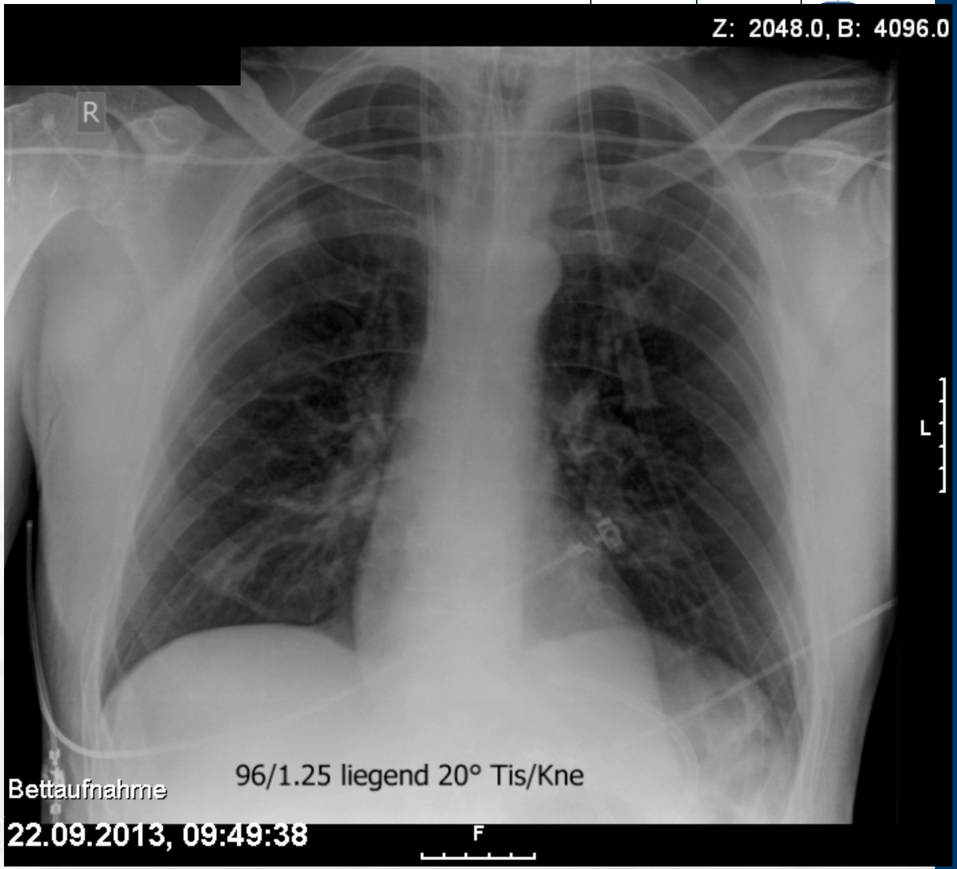
Troponine

CRP

CASE REPORT

IN-HOSPITAL TREATMENT

- chest x-ray was unremarkable



THERAPEUTIC HYPOTHERMIA

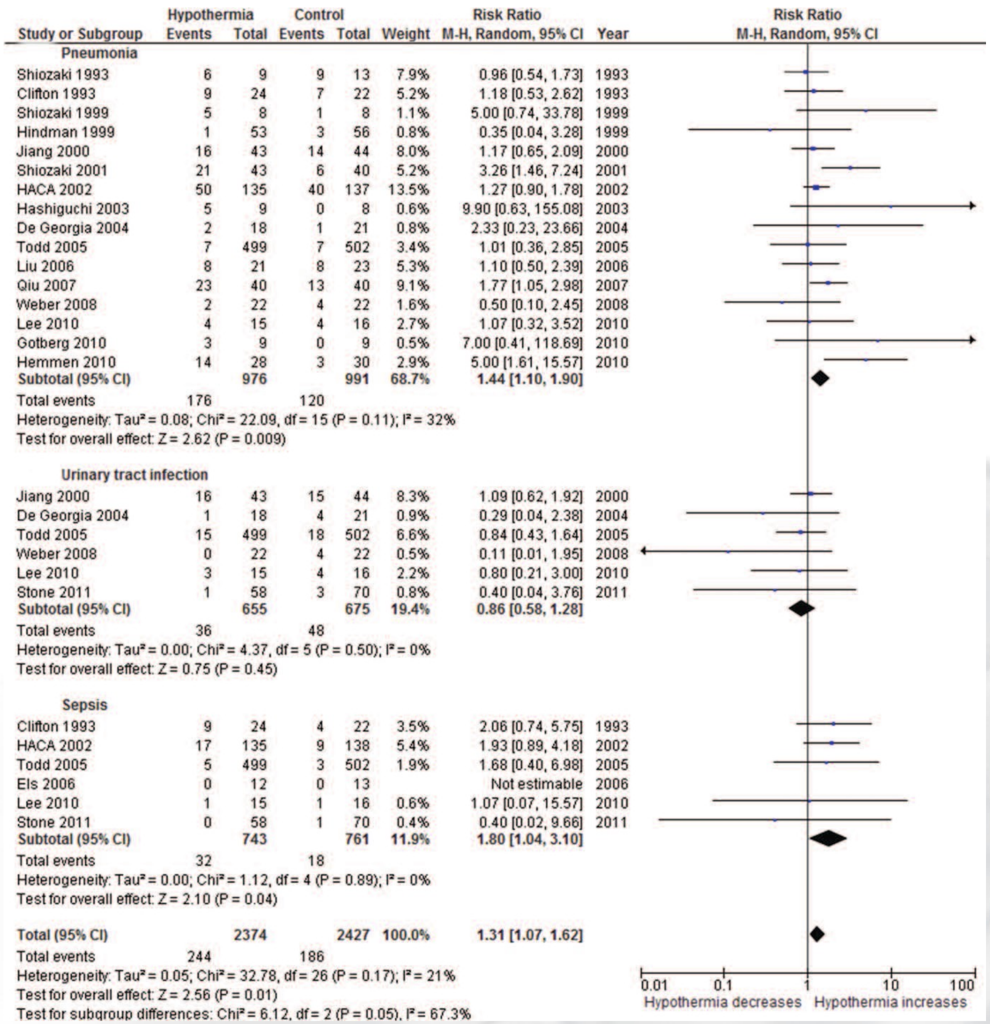
SIDE EFFECTS - RISK OF INFECTION

- 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

THERAPEUTIC HYPOTHERMIA

SIDE EFFECTS - RISK OF INFECTION

- **Findings**
- All infections: no increased risk
- Risk of pneumonia ↑ (risk ratio 1.44 [95% CI, 1.10–1.90]



Study or Subgroup	Hypothermia Events	Hypothermia Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Pneumonia							
Shiozaki 1993	6	9	9	13	7.9%	0.96 [0.54, 1.73]	1993
Clifton 1993	9	24	7	22	5.2%	1.18 [0.53, 2.62]	1993
Shiozaki 1999	5	8	1	8	1.1%	5.00 [0.74, 33.78]	1999
Hindman 1999	1	53	3	56	0.8%	0.35 [0.04, 3.28]	1999
Jiang 2000	16	43	14	44	8.0%	1.17 [0.65, 2.09]	2000
Shiozaki 2001	21	43	6	40	5.2%	3.26 [1.46, 7.24]	2001
HACA 2002	50	135	40	137	13.5%	1.27 [0.90, 1.78]	2002
Hashiguchi 2003	5	9	0	8	0.6%	9.90 [0.63, 155.08]	2003
De Georgia 2004	2	18	1	21	0.8%	2.33 [0.23, 23.66]	2004
Todd 2005	7	499	7	502	3.4%	1.01 [0.36, 2.85]	2005
Liu 2006	8	21	8	23	5.3%	1.10 [0.50, 2.39]	2006
Qiu 2007	23	40	13	40	9.1%	1.77 [1.05, 2.98]	2007
Weber 2008	2	22	4	22	1.6%	0.50 [0.10, 2.45]	2008
Lee 2010	4	15	4	16	2.7%	1.07 [0.32, 3.52]	2010
Gotberg 2010	3	9	0	9	0.5%	7.00 [0.41, 118.69]	2010
Hemmen 2010	14	28	3	30	2.9%	5.00 [1.61, 15.57]	2010
Subtotal (95% CI)		**976**		**991**	**68.7%**	**1.44 [1.10, 1.90]**	
Total events	176		120				
Heterogeneity: Tau² = 0.08; Chi² = 22.09, df = 15 (P = 0.11); I² = 32%							
Test for overall effect: Z = 2.62 (P = 0.009)							
Urinary tract infection							
Jiang 2000	16	43	15	44	8.3%	1.09 [0.62, 1.92]	2000
De Georgia 2004	1	18	4	21	0.9%	0.29 [0.04, 2.38]	2004
Todd 2005	15	499	18	502	6.6%	0.84 [0.43, 1.64]	2005
Weber 2008	0	22	4	22	0.5%	0.11 [0.01, 1.95]	2008
Lee 2010	3	15	4	16	2.2%	0.80 [0.21, 3.00]	2010
Stone 2011	1	58	3	70	0.8%	0.40 [0.04, 3.76]	2011
Subtotal (95% CI)		**655**		**675**	**19.4%**	**0.86 [0.58, 1.28]**	
Total events	36		48				
Heterogeneity: Tau² = 0.00; Chi² = 4.37, df = 5 (P = 0.50); I² = 0%							
Test for overall effect: Z = 0.75 (P = 0.45)							
Sepsis							
Clifton 1993	9	24	4	22	3.5%	2.06 [0.74, 5.75]	1993
HACA 2002	17	135	9	138	5.4%	1.93 [0.89, 4.18]	2002
Todd 2005	5	499	3	502	1.9%	1.68 [0.40, 6.98]	2005
Els 2006	0	12	0	13		Not estimable	2006
Lee 2010	1	15	1	16	0.6%	1.07 [0.07, 15.57]	2010
Stone 2011	0	58	1	70	0.4%	0.40 [0.02, 9.66]	2011
Subtotal (95% CI)		**743**		**761**	**11.9%**	**1.80 [1.04, 3.10]**	
Total events	32		18				
Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 4 (P = 0.89); I² = 0%							
Test for overall effect: Z = 2.10 (P = 0.04)							
Total (95% CI)		**2374**		**2427**	**100.0%**	**1.31 [1.07, 1.62]**	
Total events	244		186				
Heterogeneity: Tau² = 0.05; Chi² = 32.78, df = 26 (P = 0.17); I² = 21%							
Test for overall effect: Z = 2.56 (P = 0.01)							
Test for subgroup differences: Chi² = 6.12, df = 2 (P = 0.05), I² = 67.3%							

THERAPEUTIC HYPOTHERMIA
SIDE EFFECTS - RISK OF INFECTION

- **Conclusion**
- - lack of definition of infections
- - assessment of infections not blinded
- - only one cardiac arrest study included

THERAPEUTIC HYPOTHERMIA

SEDATION

- **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

THERAPEUTIC HYPOTHERMIA

SEDATION

EMCOOLS EASY EFFICIENT PATIENT COOLING

- **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

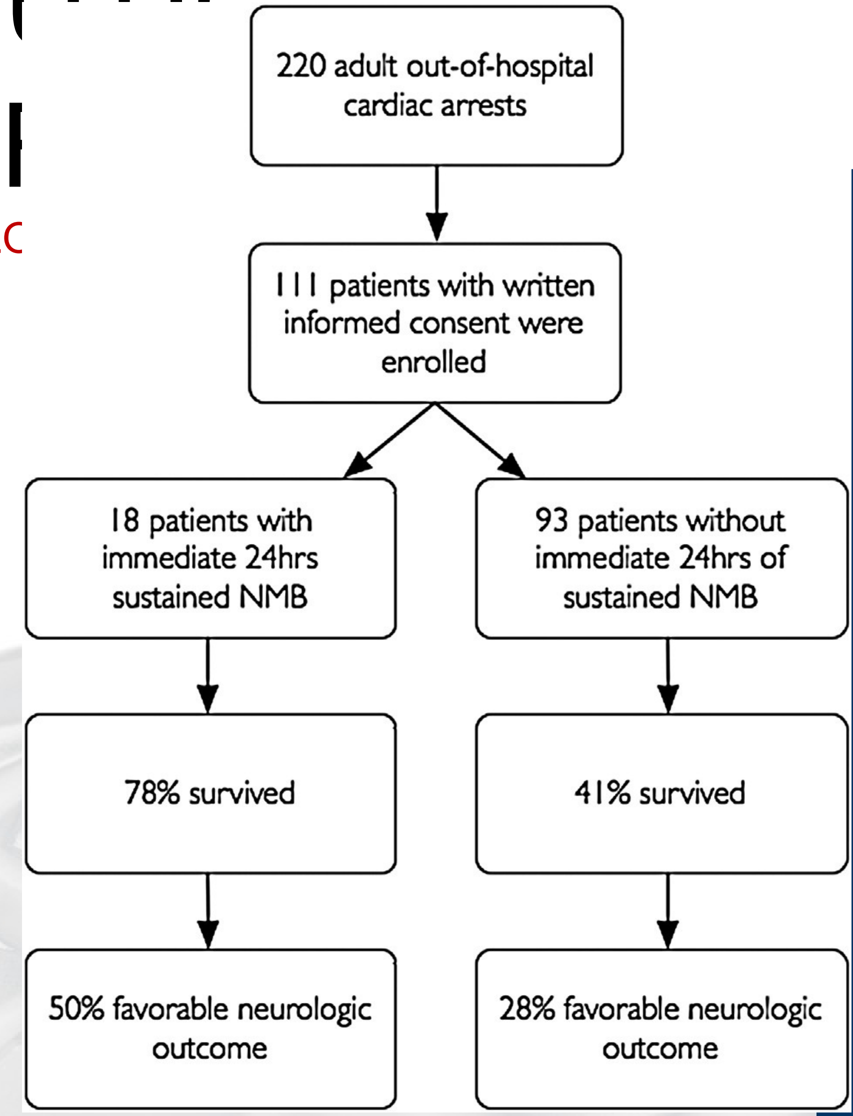
Propofol and remifentanil versus midazolam and fentanyl for sedation during therapeutic hypothermia after cardiac arrest. Intensive Care Med 2012

THERAPE HYPOTHE

NEUROMUSCULAR BL

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

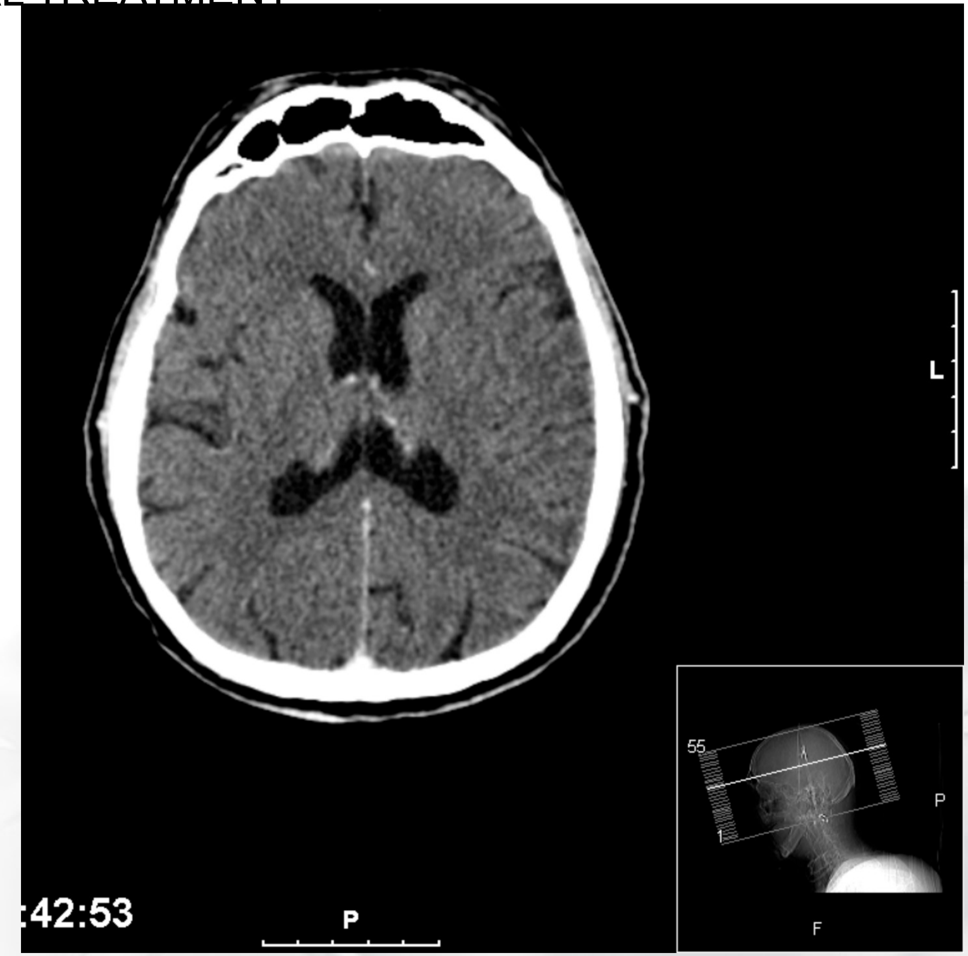


Continuous neuromuscular blockade is associated with decreased mortality in post-cardiac arrest patients. Resuscitation, in press.

CASE REPORT

IN-HOSPITAL TREATMENT

- 9/24/2013 1st Epileptic seizure during weaning from sedation



CASE REPORT

IN-HOSPITAL TREATMENT

- EEG: Generalized repetitive spike waves as in status epilepticus

- Start with Levetiracetam

CASE REPORT

IN-HOSPITAL TREATMENT

- Patients regained consciousness after 5 days
- Gait insecure – falls nearly daily
- Reduced short term memory

EFFECT OF HYPOTHERMIA ON WAKING UP

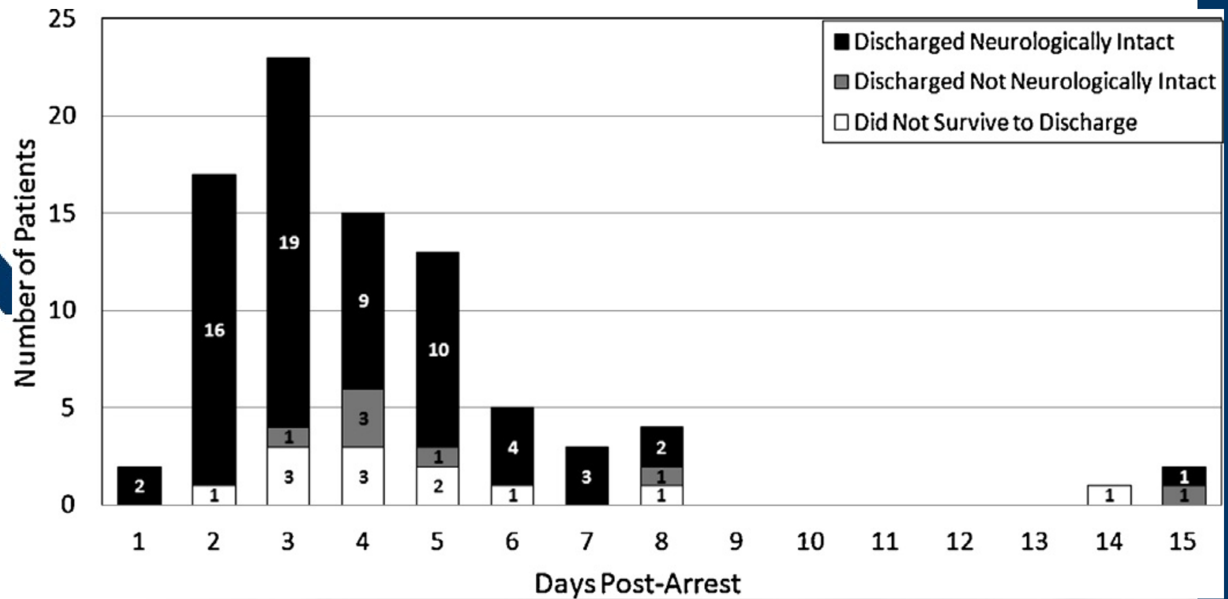
- retrospective chart review of 194 consecutive TH-treated CA patients 2005-2011
- survival to discharge 44%
  - good outcome 78%
- 85 patients woke up

Time to awakening and neurologic outcome in therapeutic hypothermia-treated cardiac arrest patients. Grossestreuer, Resuscitation in press.

EFFECT OF HYPOTHERMIA ON WAKING UP

- median time to awakening was **3.2 days** (IQR 2.2, 4.5)
  - 2.8 days (IQR 2.0, 4.5) for good outcome
  - 4.0 days (IQR 3.5, 7.6) for unfavourable outcome

- 10 patients awakened
- >6 days after arrest
- antiepileptics
- sepsis
- recurrent arrest



Time to awakening and neurologic outcome in therapeutic hypothermia-treated cardiac arrest patients. Grossestreuer, Resuscitation in press.

FEVER FOLLOWING HYPOTHERMIA

REBOUND HYPERTHERMIA

141 patients, mean age 60 years, 2005-2010

„rebound hyperthermia": core temperature of ≥38.5°C within 24h after TH

rebound hyperthermia was observed in 30% of patients and was associated with

- increased hospital mortality (64% vs. 40%)
- worse neurologic outcome

	Modified Rankin score						
	0	1	2	3	4	5	6
No rebound hyperthermia ($n = 99$)	6 (6.06%)	6 (6.06%)	10 (10.1%)	8 (8.08%)	19 (19.2%)	10 (10.1%)	40 (40.4%)
Rebound hyperthermia ($n = 42$)	1 (2.38%)	2 (4.76%)	2 (4.76%)	1 (2.38%)	5 (11.9%)	4 (9.52%)	27 (64.3%)

Assessment of risk factors for post-rewarming "rebound hyperthermia" in cardiac arrest patients undergoing therapeutic hypothermia. Winters et al, Resuscitation 2013.

FEVER FOLLOWING HYPOTHERMIA

REBOUND HYPERTHERMIA

236 patients, mean age 58 years, 2005-2011

„rebound hyperthermia": core temperature of ≥38.0°C within 24h after TH

rebound hyperthermia was observed in 41% of patients and was associated with

- no difference in hospital mortality (46% vs. 48%)
- no difference in neurologic outcome

pyrexia ≥38.7°C: lower proportion of CPC 1–2 survivors (58% v 80%)

Pyrexia and neurologic outcomes after therapeutic hypothermia for cardiac arrest. Leary et al, Resuscitation 2013.

REBOUND HYPERTHERMIA

DESERVES TREATMENT

- conclusion: vigorous maintenance of normothermia for up to 72h after CA

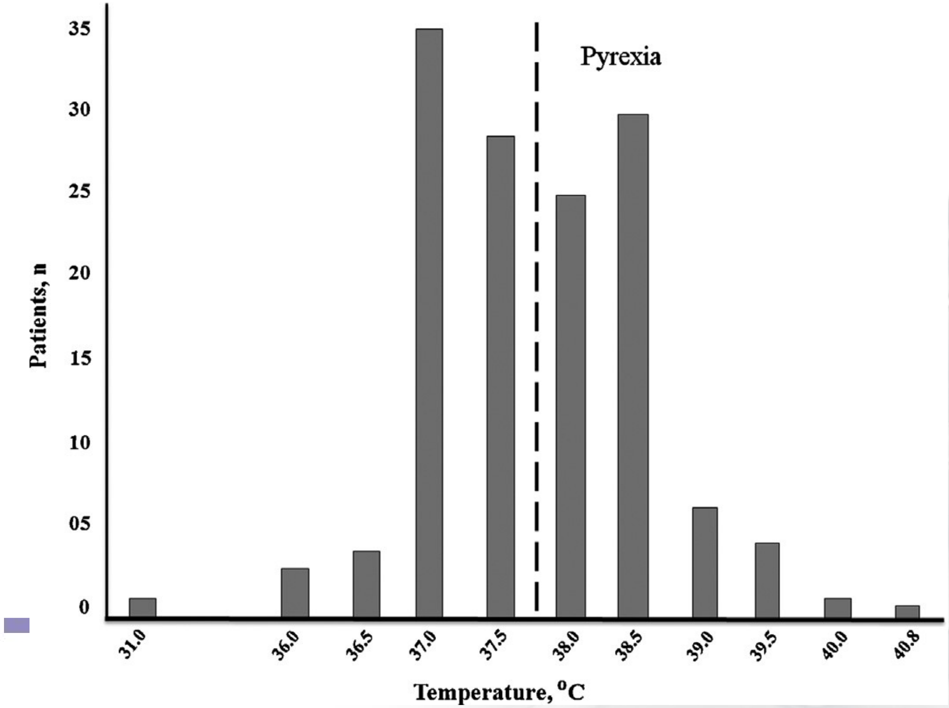
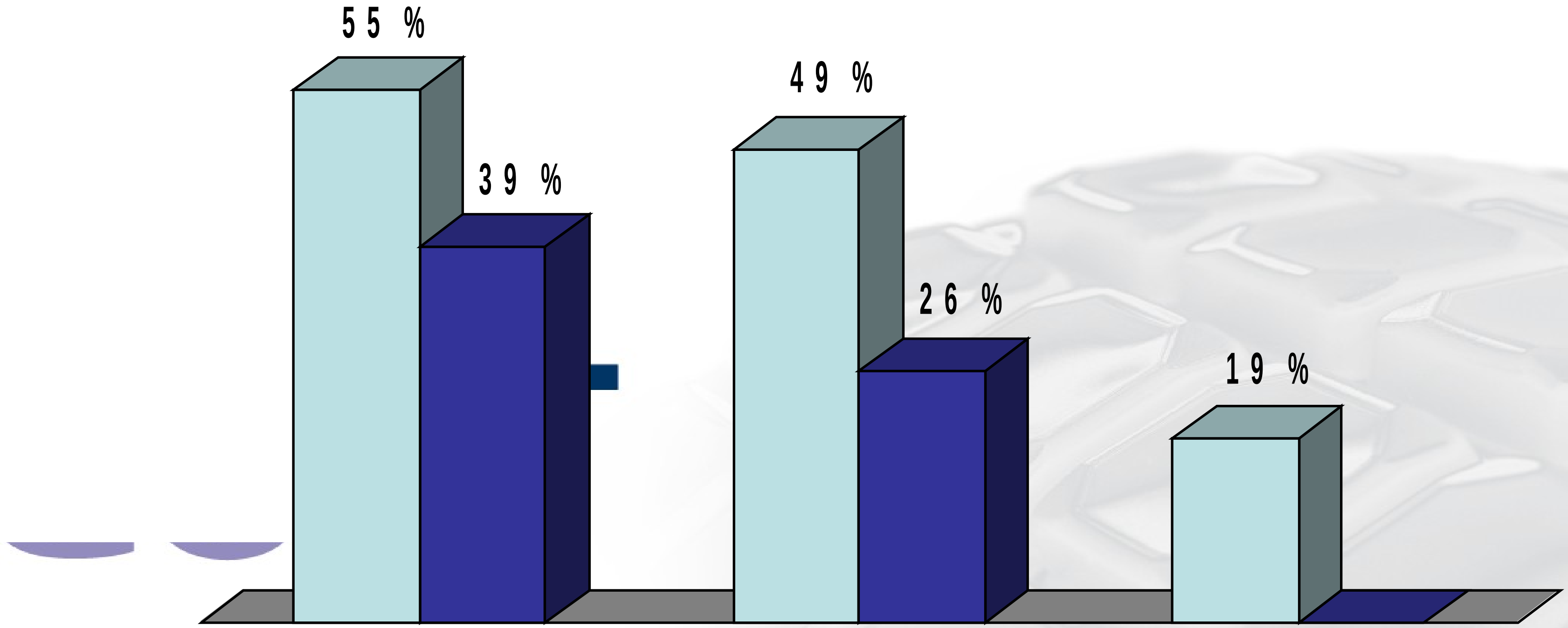


Fig. 2. Frequency histogram of maximum temperatures during the 24 h period following post-arrest TTM rewarming. The dashed line represents the cut-off defining pyrexia in this investigation.

THERAPEUTIC HYPOTHERMIA

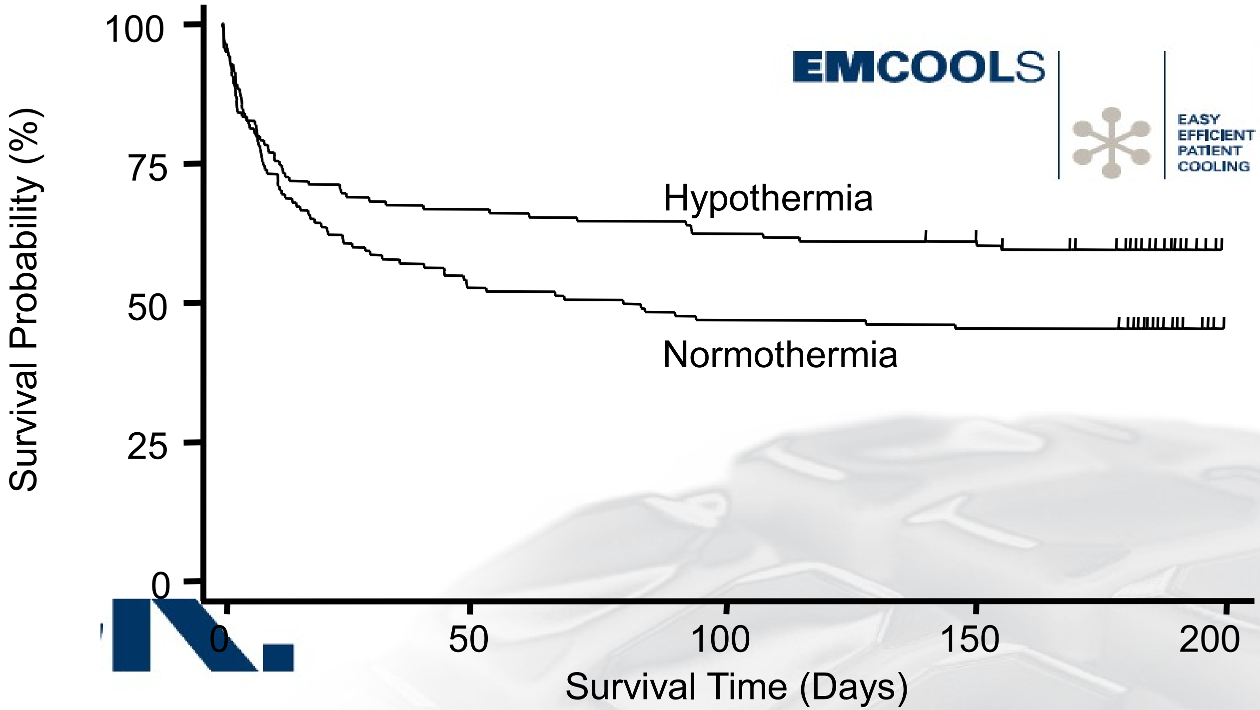
First randomized trials (2002).

EFFECT ON OUTCOME – VF PATIENTS, HACA-STUDY



THERAPEUTIC HYPOTHERMIA

EFFECT ON OUTCOME – LONG TERM SURVIVAL



No. at Risk					
Hypothermia	138	93	87	84	11
Normothermia	137	73	65	63	9

Risk Ratio 0.74 (CI 0.58 – 0.95) p = 0.02

RANDOMIZED CLINICAL TRIALS

INDIVIDUAL DATA META-ANALYSIS

N = 384

Short term effects of hypothermia

- survive until discharge -> risk ratio 1.36 (95% CI 1.11 to 1.59)
- good neurological -> risk ratio 1.53 (95% CI 1.24 to 1.99)
- **6** patients needed to be treated -> 6 (95% CI 4 to 17)

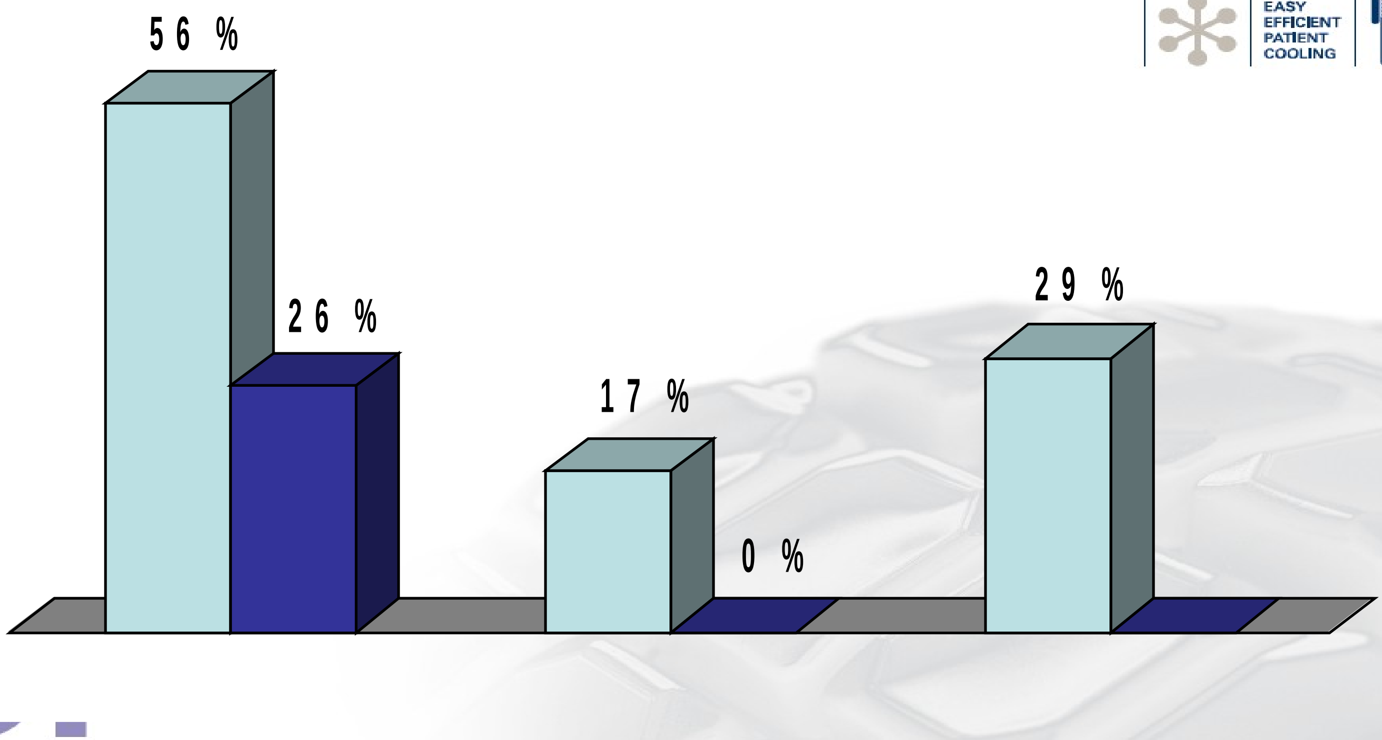
***Long term effects of hypothermia** (6 months)*

- good neurological within -> risk ratio 1.40 (95% CI 1.10 to 1.69)
- alive & good at -> risk ratio 1.47 (95% CI 1.13 to 1.80)
- **6** patients needed to be treated (95% CI 4 to 21)

From evidence to clinical practice

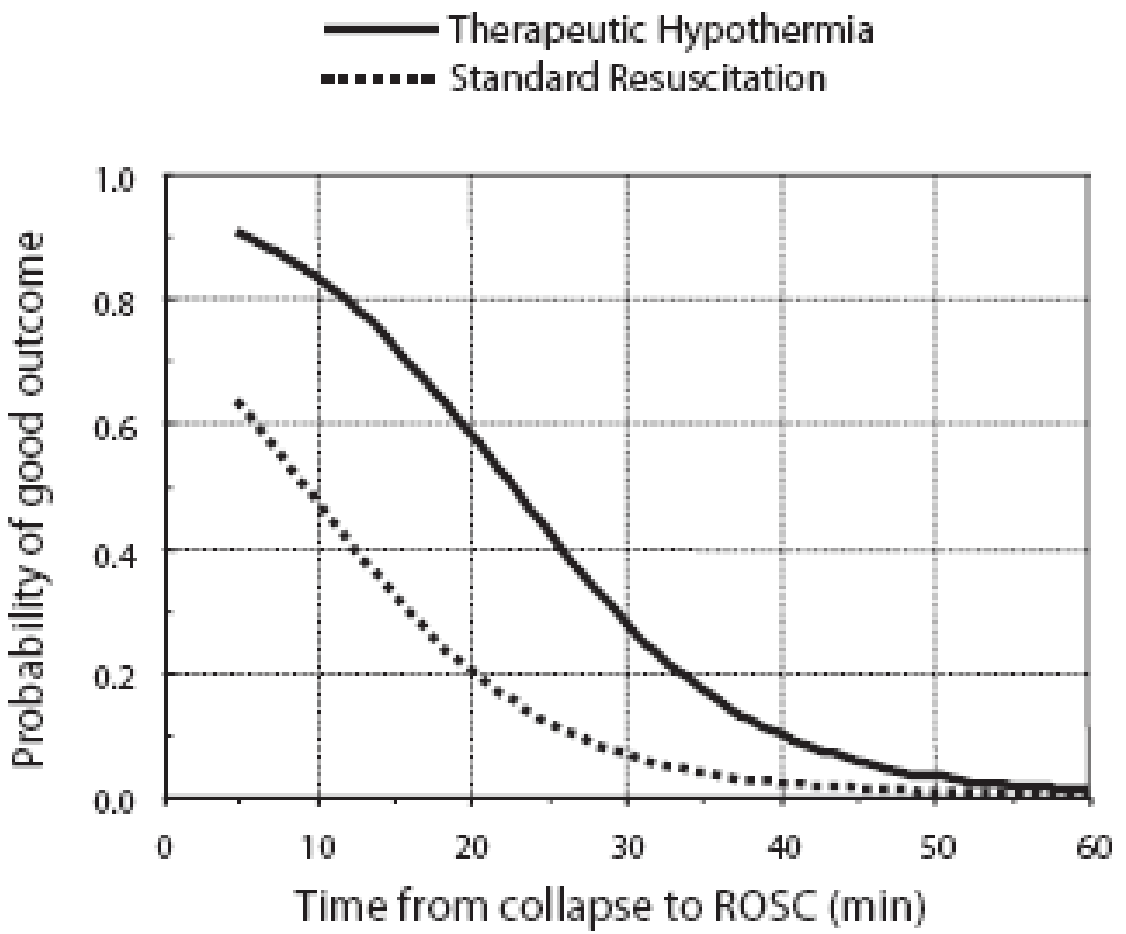
EFFECTIVE IMPLEMENTATION OF A HYPOTHERMIA PROGRAM

EMCOOLS EASY EFFICIENT PATIENT COOLING



*p=.004
**NS
***P=.027

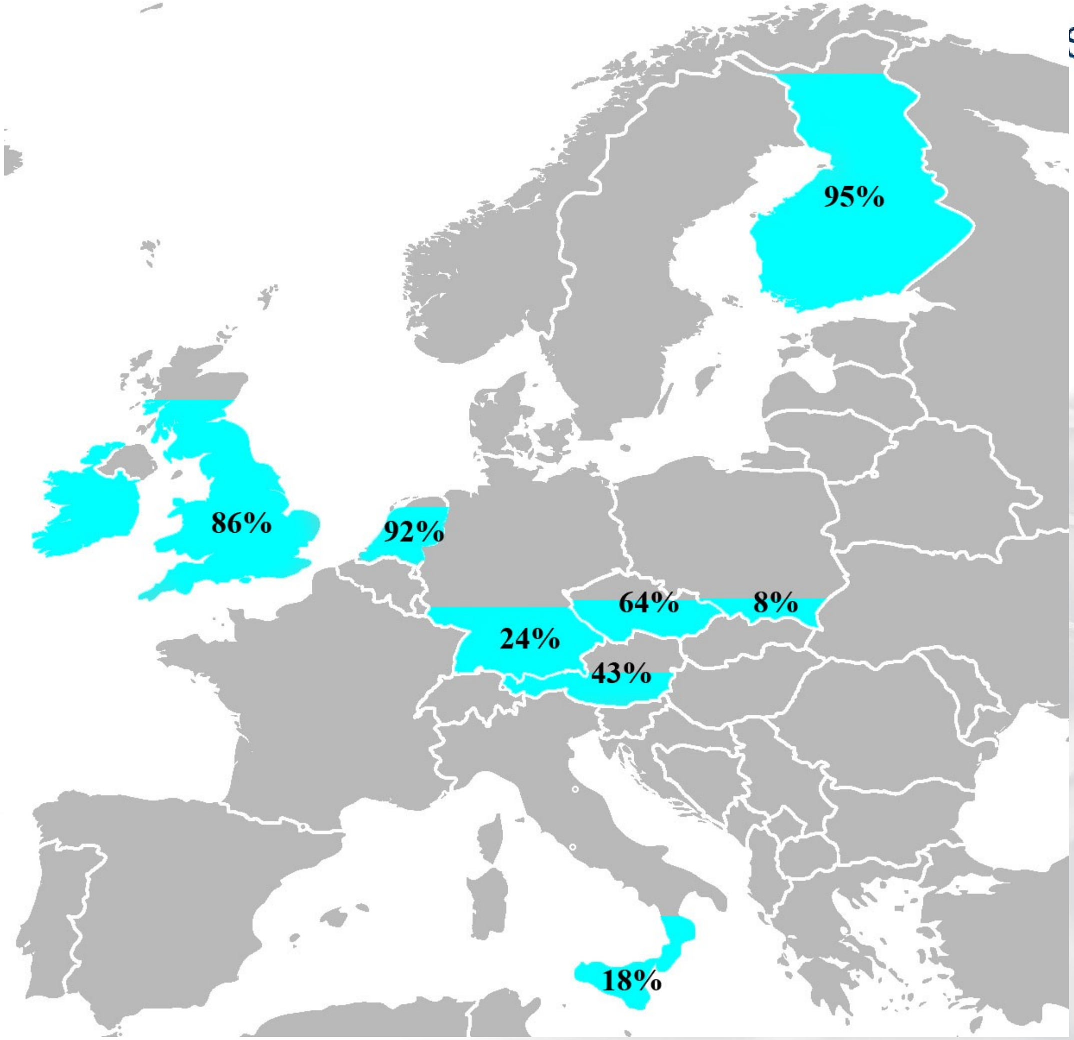
Oddo et al. CCM 2006;34:1865



Oddo et al. CCM 2006;34:1865

HYPOTHERMIA AFTER CA

IMPLEMENTATION IN EUROPE



ERC/AHA GUIDELINES 2010

EMCOOLS EASY EFFICIENT PATIENT COOLING

- Adult patients who are comatose with spontaneous circulation after out-of-hospital VF cardiac arrest should be cooled to 32–34◦C for 12–24h.
- Induced hypothermia might also benefit comatose adult patients with spontaneous circulation after OHCA from a nonshockable rhythm or in-hospital cardiac arrest.
- **AHA recommendation: Class I, Level of evidence B**

Deakin et al. Resuscitation 2010.
Nolan et al. Circulation 2010

HYPOTHERMIA AFTER CA

EMCOOLS
EASY EFFICIENT PATIENT COOLING

Thank You.