Therapeutic hypothermia after cardiac arrest and in critical care

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Speaker disclosures

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Cardiac arrest: introduction

Cardiac arrest epidemiology

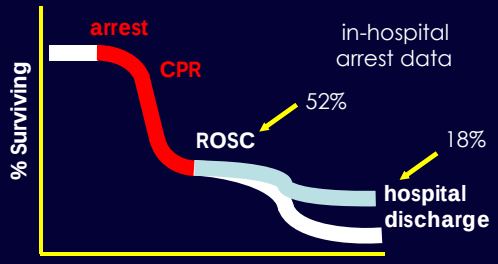
300,000 arrests / year in U.S.A.

3 / 4 Out-of-hospital	1 / 4 In-hospital
1-5%	10-20%

survival to hospital discharge

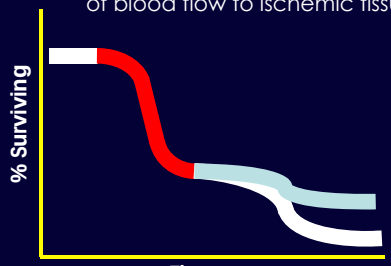
Becker et al, 1993
Peberdy et al, 2003

The post-arrest problem

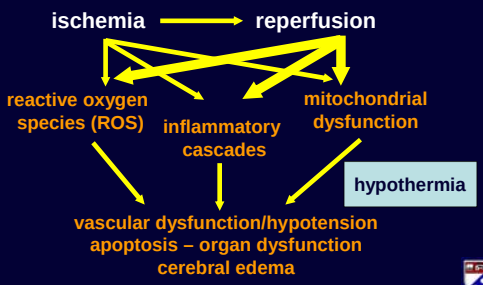


Reperfusion injury

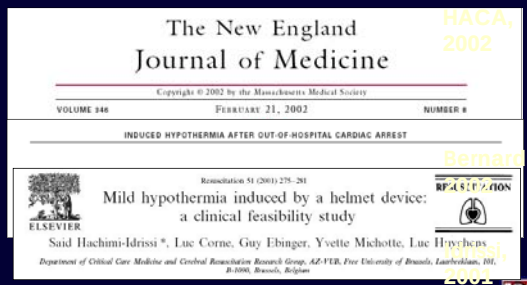
Damage observed after restoration of blood flow to ischemic tissues



Hypothermia mechanisms



Modern era of hypothermia use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INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

Resuscitation 51 (2001) 275–281

Mild hypothermia induced by a helmet device: a clinical feasibility study

Said Hachimi-Idrissi *, Luc Corne, Guy Ebinger, Yvette Michotte, Luc Huyghens

Department of Critical Care Medicine and Cerebral Resuscitation Research Group, AZ-VUB, Free University of Brussels, Laarbeeklaan, 101, B-1090, Brussels, Belgium

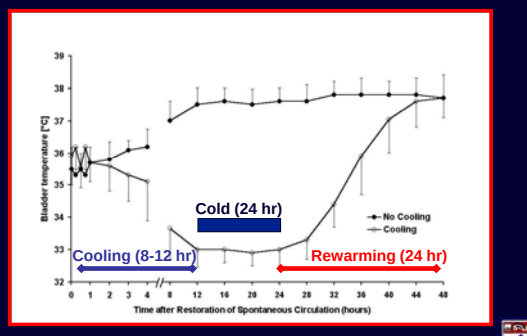
HACA, 2002

Bernard, 2002

Modern era of hypothermia use

	Age (years)	Female sex (%)	VF (#)	ROSC (min)	Target temp (°C)	Duration (hours)	Method
HACA	59 (51-68)	65 (24)	254 (92%)	22 (16-30)	33	24	Cool air
Bernard	68 (57-75)	25 (32)	77 (100%)	24 (17-32)	33	12	Ice packs
Idrissi	74 (66-79)	13 (39)	0 -	33 (27-37)	34	Up to 4	Helmet

Modern era of hypothermia use



HACA, 2002

Adverse events: HACA trial

	Normothermia n = 138	Hypothermia n = 137
Bleeding	19%	26%
Arrhythmia	32%	36%
Pneumonia	29%	37%
Sepsis	7%	13%
Pancreatitis	2%	1%
Renal failure	10%	10%
Pressure sores	0%	0%

Differences not statistically significant

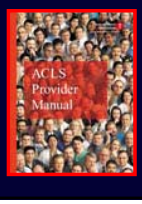
HACA, 2002

Hypothermia trials: outcomes

	Hypothermia (%)	Normothermia (%)	RR (95% CI)	P value
Alive at hospital discharge with favourable neurological recovery				
HACA	72/136 (53%)	50/137 (36%)	1.51 (1.14-1.89)	0.006
Bernard	21/43 (49%)	9/34 (26%)	1.75 (0.99-2.43)	0.052
Idrissi	4/16 (25%)	1/17 (6%)	4.25 (0.70-53.83)	0.16
Alive at 6 months with favourable neurological recovery				
HACA	71/136 (52%)	50/137 (36%)	1.44 (1.11-1.76)	0.009

Hypothermia in the guidelines

AHA Guidelines 2005 conference
Dallas, January 22-29, 2005
Several hundred cardiac arrest experts
Closed meeting, rigorous process



CPR/BLS/ACLS guidelines underwent revision

New guidelines released supporting hypothermia, published 11/2005

Hypothermia in the guidelines

Comatose out-of-hospital VF:
Class IIa recommendation

In-hospital arrest, other rhythms:
Class IIb recommendation

Post-resuscitation care module to be included in NRCPR registry: in-hospital data collection

Are we using hypothermia?

Two internet survey studies of U.S. physicians
Critical care, cardiology, emergency medicine

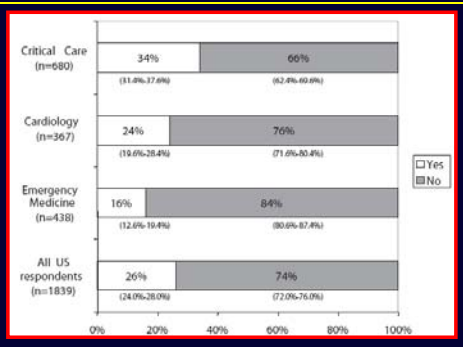
Abella BS et al, 2005

Ever used hypothermia: 13% (n=263)

Merchant RM et al, 2006

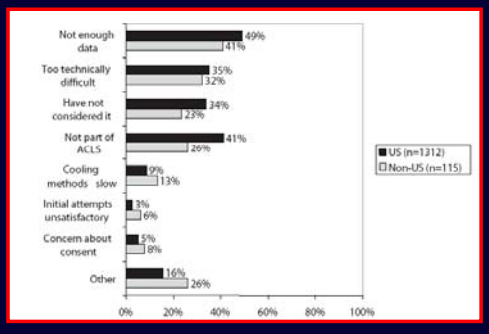
Ever used hypothermia: 26% (n=1839)

Are we using hypothermia?



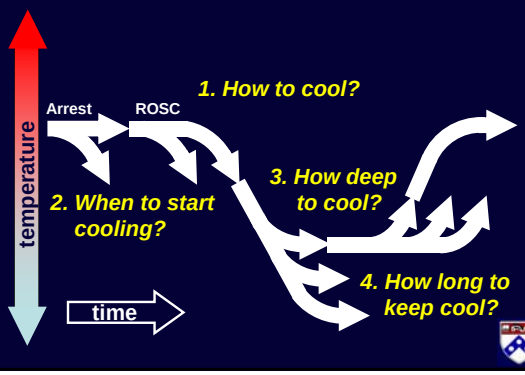
Merchant RM et al, 2006

Utilization of hypothermia



Merchant RM et al, 2006

Practical issues of cooling



How to cool?

Ice packs, cooling blankets, catheters…

How to cool?

University of Chicago Hospitals (UCH) initial experience (2003-4):

cooling blanket
and/or ice packing

Advantages: cheap, non-invasive, 'off the shelf'

Disadvantages: slow cooling, can be messy, lack of thermostatic control

Difficulties with ice bag cooling

Merchant RM et al, 2006

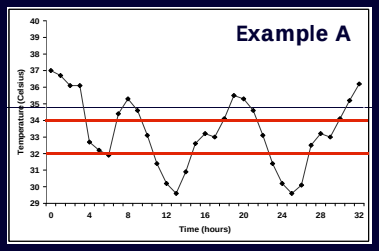
Retrospective chart review of cooling cases From three hospitals (2 in U.S., 1 in U.K.)

Found 20/32 cases (63%) were overcooled

Trends towards better outcome in non-overcooled pts

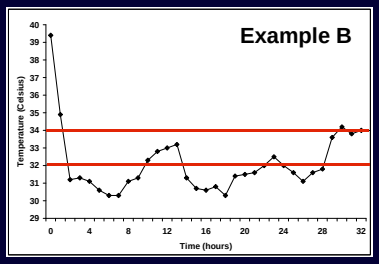
Suggests need for thermostatic feedback control

Surface cooling in the real world



Merchant RM et al, 2006

Surface cooling in the real world



Merchant RM et al, 2006

Simple cooling methods

Induced hypothermia using large volume, ice-cold intravenous fluid in comatose survivors of out-of-hospital cardiac arrest: a preliminary report

Stephen Bernard[a,b,*], Michael Buist[a], Orlando Monteiro[a], Karen Smith[b]

Bernard S et al, 2003

Study in 22 post-arrest patients
Infused 30 ml/kg ice cold saline
Average temperature drop of 1.5 °C

Remember: 1. No maintenance or rewarming
2. Large fluid load (safety unproven)

Is cold saline enough?

Cold infusions alone are effective for induction of therapeutic hypothermia but do not keep patients cool after cardiac arrest☆ *2007*

Andreas Kliegel[a], Andreas Janata[a], Cosima Wandaller[a], Thomas Uray[a], Alexander Spiel[b], Heidrun Losert[a], Matthias Kliegel[c], Michael Holzer[a], Moritz Haugk[a], Fritz Sterz[a,*], Anton N. Laggner[a]

Cooling was fast … But maintenance was hard

65% cooled to target within 60 minutes

77% failed to stay cool during course

Real world usage: Switzerland

From evidence to clinical practice: Effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest☆ *2006*

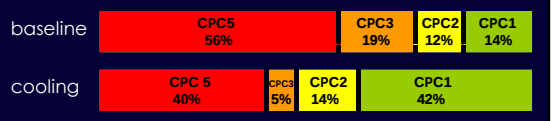
Mauro Oddo, MD; Marie-Denise Schaller, MD; François Feihl, MD; Vincent Ribordy, MD; Lucas Liaudet, MD

Oddo M et al, 2006

- Retrospective study at one hospital in Switzerland
- Cooling intervention with historical controls
- Survivors of out-of-hospital arrest (n=109)
- Cooling initially via ice bags, then cooling mattress
- Target temperature 33°C, maintained for 24 hrs
- All post-arrest ST elevations received cardiac cath

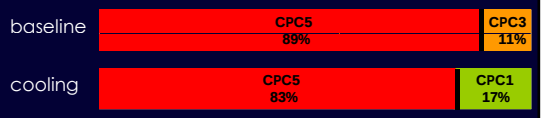
Real world usage: Switzerland

Outcome at discharge for out-of-hospital VF arrest



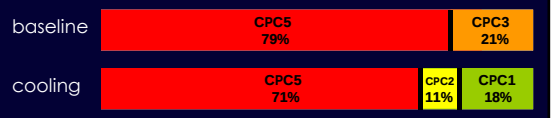
Real world usage: Switzerland

Outcome at discharge for out-of-hospital asystole arrest



Real world usage: Switzerland

Outcome at discharge for all rhythms with post-arrest hypotension and shock



Real world usage: Philadelphia

Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest☆,☆☆ *2009*

David F. Gaieski[a,b,*], Roger A. Band[a,b], Benjamin S. Abella[a,b], Robert W. Neumar[a,b], Barry D. Fuchs[c], Daniel M. Kolansky[d], Raina M. Merchant[a,b], Brendan G. Carr[a,b], Lance B. Becker[a,b], Cheryl Maguire[e], Amandeep Klair[a], Julie Hylton[a], Munish Goyal[a,b]

Gaieski et al, 2009

- Combined hypothermia and early goal-directed therapy
- Cooling intervention with historical controls
- Cooled any rhythm, both in and out of hospital arrest
- Target temperature 33°C, maintained for 24 hrs

CPC 1-2 survivors

Before protocol **22%** **44%** After protocol

Real world usage: Oklahoma

	survivors	non-survivors
Time to target temp (min)	194	188
Coronary intervention	7/19 (37%)	4/30 (13%)
Admission G.C.S.	4.2	3.2
Survival to discharge	19/49 (39%)	
Survival with G.C.S. 14-15	16/19 (84.2%)	

NRCPR registry survival to discharge: 18%

HACA registry data

Large multinational registry of post-arrest patients

Started by Alsius Corporation; now via European Resuscitation Council

Collects data from any cooling method

HACA registry data

Clinical application of mild therapeutic hypothermia after cardiac arrest* **2007**

Jasmin Arrich, MD; The European Resuscitation Council Hypothermia After Cardiac Arrest Registry Study Group

Arrich J et al, 2007

Hypothermia patients: n=462

endovascular device n=347

ice packs, fluids n=114

Most with witnessed O-O-H, most "cardiac cause"

HACA registry data

Arrich J et al, 2007

Technique

average cool duration:	24 hours
cooling rate:	1.1/1.3 °C per hr
rewarming time:	8-9 hours

Outcomes

CPC1,2 at discharge:	45% (32% b.l.)
Bleeding rate:	3%
Bleeding requiring Rx:	1.2%

A second hypothermia registry

(a) Adverse events: all 34 centres and (b) adverse events: 22 reporting centers.

	n = 986
(a)	
Bradycardia <40 beats/min	127 (13)
Tachycardia >130 beats/min	57 (6)
Atrial fibrillation	88 (9)
VT	89 (9)
VF	71 (7)
Any combination of arrhythmia	385 (39)
Pneumonia	407(41)
Sepsis	35 (4)
Other infection	41 (4)
Bleeding requiring transfusion	44 (4)
Intracerebral bleeding	2 (0.2)
Seizures	233 (24)

Nielsen et al, 2009

Infection and seizures are common

Bradycardia (13%)
Significant bleed (4%)

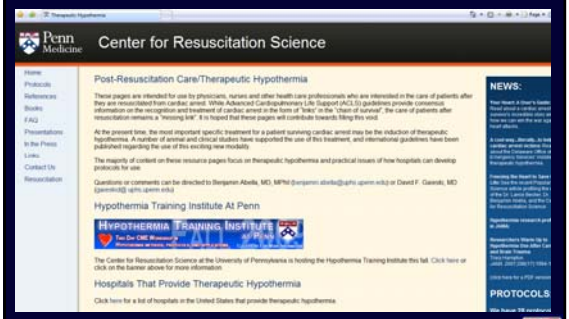
Cooling and PCI

Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to acute ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention*

Sebastian Wolfrum, MD; Christian Pierau; Peter W. Radke, MD; Heribert Schunkert, MD; Volkhard Kurowski, MD **2008**

Bottom line: cooling and immediate cardiac cath are safe and compatible

Hypothermia resource website



www.med.upenn.edu/resuscitation/Hypothermia.htm

Hypothermia in pediatrics

Post-resuscitation trials being initiated currently

external cooling (ice bags and cooling blanket)

Use of ECMO as cooling circuit?

VF more common in pediatrics than thought

Nadkarni V et al, 2004
Nadkarni V et al, 2006

Cooling and MI

COOL MI trial (2003):

Failed to show benefit
In human randomized trial
Using catheter-based cooling
-- however…

Rapid cooling preserves the ischaemic myocardium against mitochondrial damage and left ventricular dysfunction **2009**

Renaud Tissier[1,2,3†], Nicolas Couvreur[1,2,3†], Bijan Ghaleb[1,2,3], Patrick Bruneval[4], Fanny Lidouren[1,2,3], Didier Morin[1,2,3], Roland Zini[1,2,3], Alain Bize[1,2,3], Mourad Chenoune[1,2,3], Marie-France Belair[4], Chantal Mandet[4], Martine Douheret[4], Jean-Luc Dubois-Rande[1,2], James C. Parker[5], Michael V. Cohen[5,6], James M. Downey[5], and Alain Berdeaux[1,2,3*]

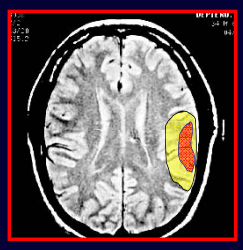
Other hypothermia applications

General concept:

cooling as "brain protection"

- traumatic brain injury
- subarachnoid hemorrhage
- cerebrovascular accident
- fever control in all of the above

Cerebrovascular accident

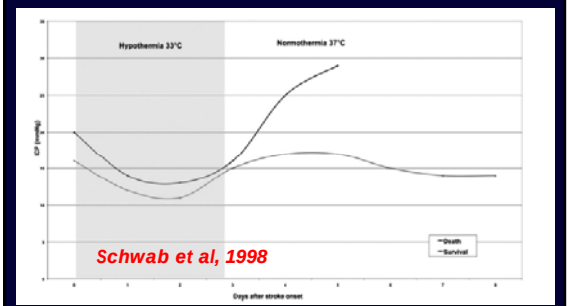


penumbra

ischemia

Plentiful animal data:
Cooling shrinks penumbra, lowers ICP

Clinical experience: CVA



Schwab et al, 1998

Cooling lowers ICP – and ICP matters!

Hypothermia in the news

July 23, 2007

Cover story on Hypothermia

Human angle: Profiled survivors

Hypothermia in the news

msnbc.com
A Fuller Spectrum of News

Buffalo Bills player Kevin Everett treated with hypothermia

"I was trying to pull out all the stops to help this young man," Cappuccino said Wednesday at a news conference. He had heard of the therapy, called moderate hypothermia, at a conference attended by doctors from the Miami Project to Cure Paralysis who have been experimenting with it for more than a decade.

September 14, 2007

Hypothermia in the news

Popular Science

January, 2009

"Freezing the Heart to Save the Life"

Good graphics showing effects of cooling

The future: regionalized care?

The feasibility of a regional cardiac arrest receiving system☆

Daniel P. Davis[a,*], Roger Fisher[b], Steven Aguilar[c], Marcelyn Metz[d], Ginger Ochs[b], Lana McCallum-Brown[a], Prasanthi Ramanujam[a], Colleen Buono[a], Gary M. Vilke[a,d], Theodore C. Chan[a], James V. Dunford[a,b]

2007

Hypothermia and post-arrest care – Not for everyone?

Idea being implemented:

- ***Minnesota***
- ***North Carolina***
- ***Arizona***

The future: cooling during arrest?

Mild hypothermia during advanced life support: a preliminary study in out-of-hospital cardiac arrest

Cédric Bruel[1], Jean-Jacques Parienti[2], William Mario[1], Xavier Arrot[3], Cédric Daubin[1], Damien Du Cheyron[1], Massimo Massetti[4] and Pierre Charbonneau[1]

2008

Supported by animal data

Problem: how to cool rapidly enough?

How to make it feasible?

Training for hypothermia

Hypothermia Training Institute at Penn

Philadelphia – Oct 29-30, 2009

Intensive two day CME course in hypothermia methods, protocols, and applications

Designed for critical care, cardiology or emergency medicine physicians and nurse managers – i.e., local champions

Will offer "hypothermia certification"

Workshop design – small course size – will hold quarterly

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