Hypothermie thérapeutique post-arrêt cardiaque

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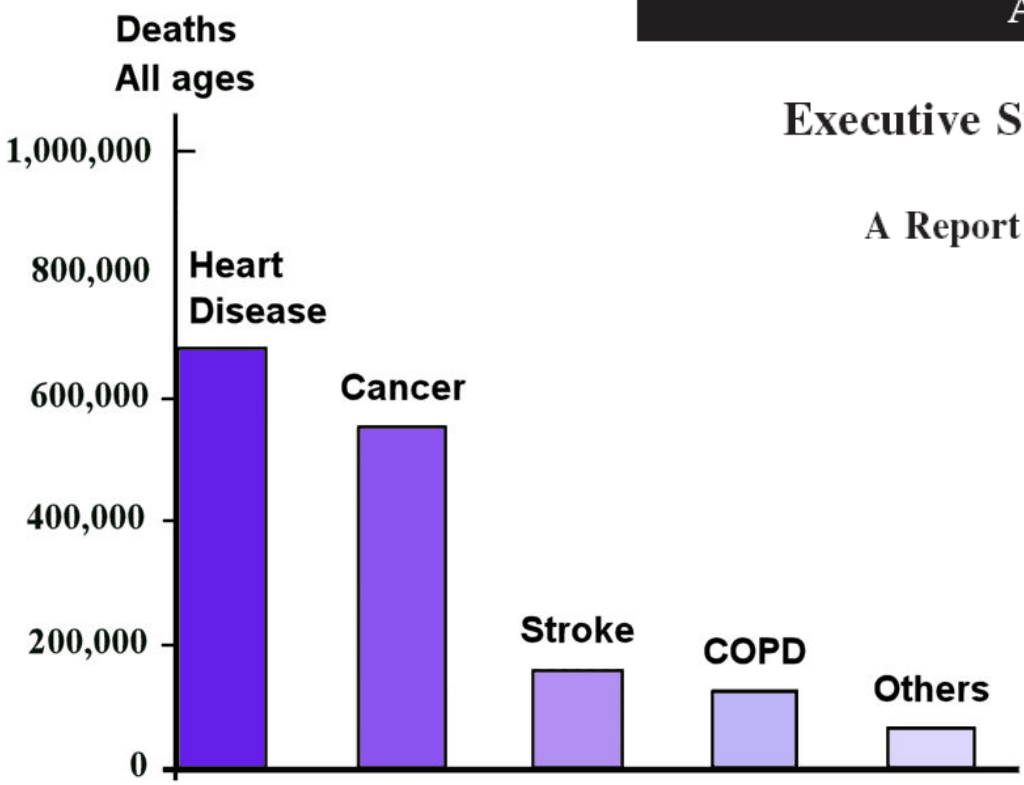
Equipe « physiopathologie et pharmacologie des insuffisances coronaires et cardiaques », Ecole Nationale Vétérinaire d'Alfort, Maisons-Alfort

GROUPE HOSPITALIER
HENRI MONDOR
ALBERT CHENEVIER - GEORGES CLEMENCEAU
JOFFRE-DUPUYTREN - EMILE ROUX

- **Déclaration de liens d'intérêt :**
- Mon intervention ne présente aucun potentiel conflit d'intérêt

L'enjeu



AHA Statistical Update

Executive Summary: Heart Disease and Stroke Statistics—2012 Update

A Report From the American Heart Association

Causes de décès en 2008 au Etats-Unis

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

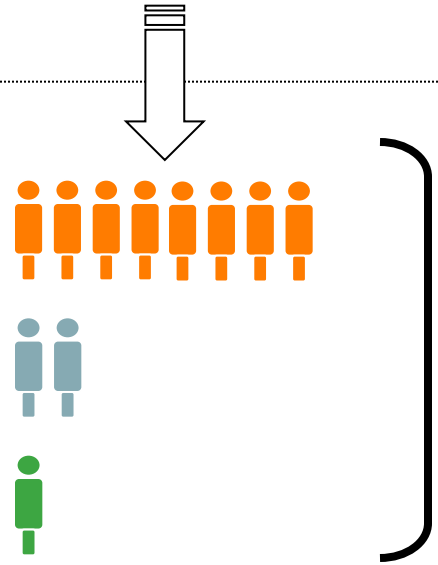
Arrêt cardiaque extra hospitalier à réanimer

30% ROSC…

20% admis à l'hôpital

5% survivant

1-3% sans séquelles sévères à 1 an

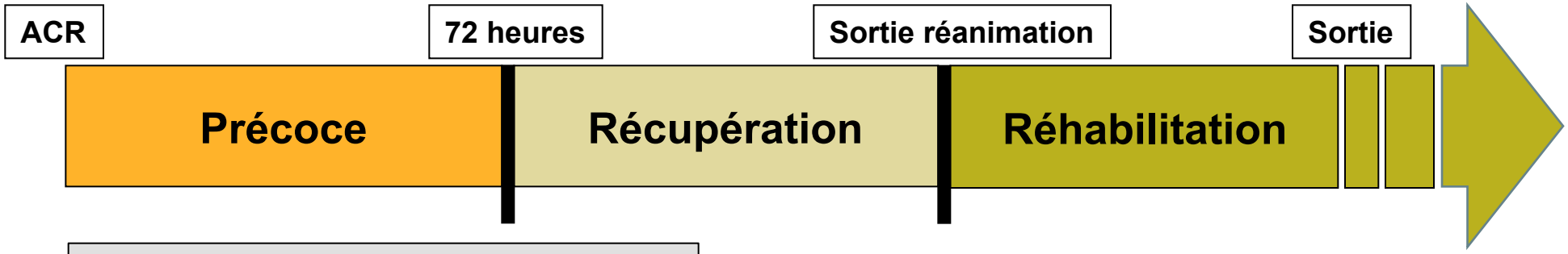


Période intra hospitalière

➔ **Syndrome post ACR / neuroprotection**

Gueugniaud PY, NEJM 2008

Prise en charge



Traiter les défaillances

Limiter la progression des lésions:
- **Mesures générales**
- **Traitements spécifiques : hypothermie**

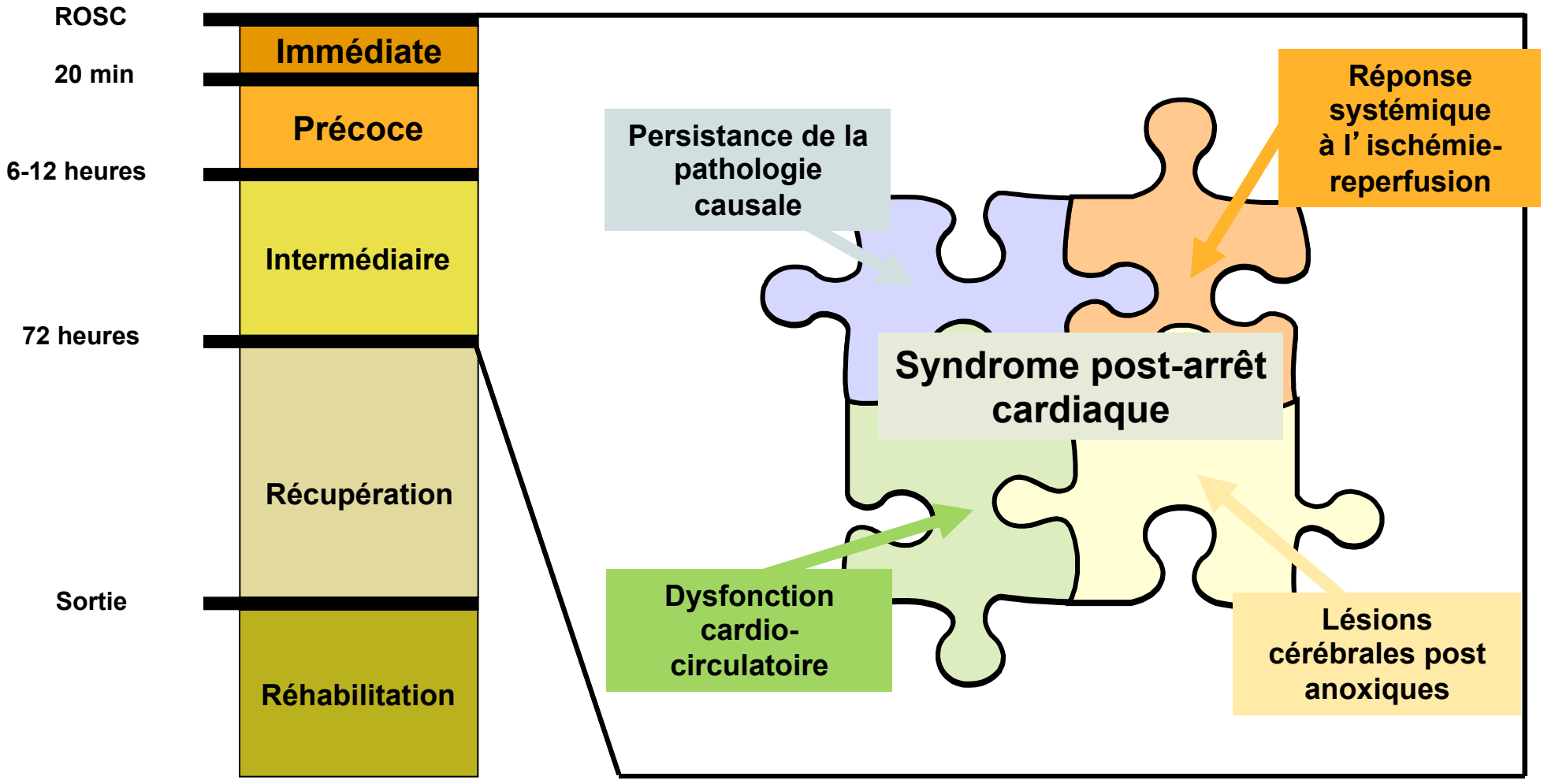
Autre thérapeutique neuroprotectrice???

Déterminer le pronostic

Traitements étiologiques: éviter les récidives, améliorer le pronostic

Réhabilitation

Physiopathologie



ILCOR, Circulation 2008

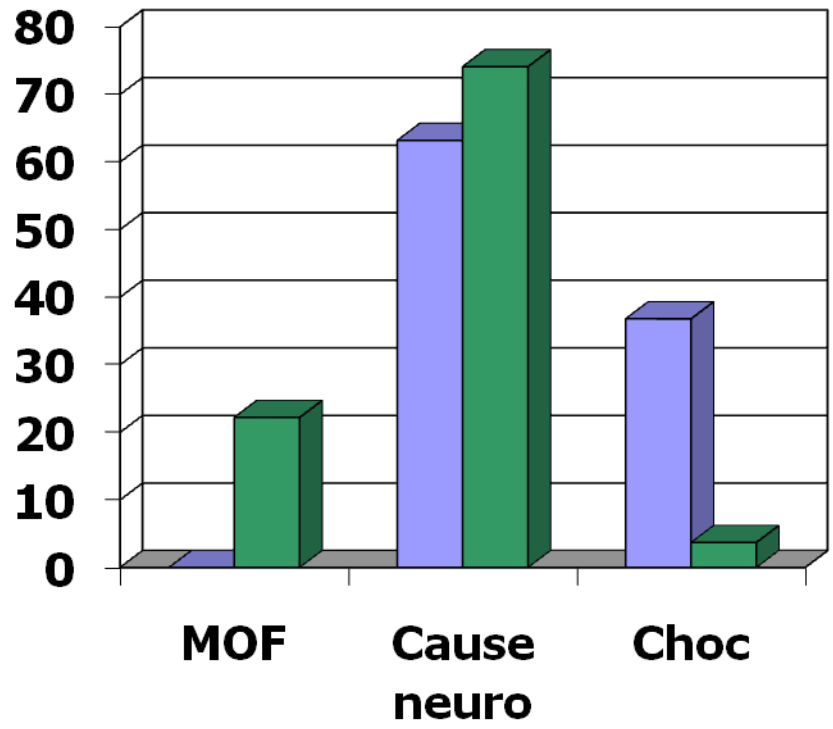
Intensive Care Med (2004) 30:2126–2128
DOI 10.1007/s00134-004-2425-z

BRIEF REPORT

Stephen Laver
Catherine Farrow
Duncan Turner
Jerry Nolan

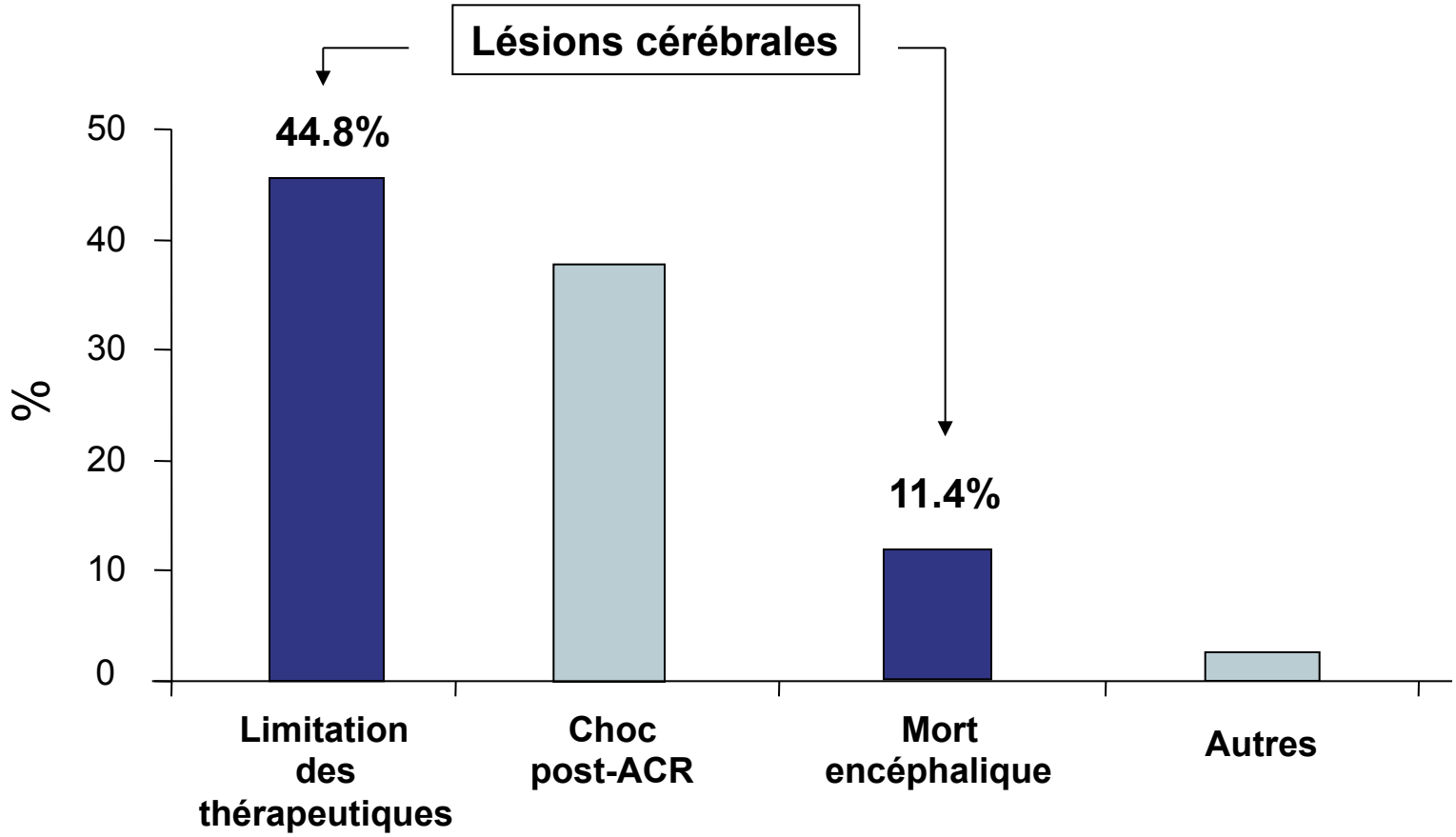
Mode of death after admission to an intensive care unit following cardiac arrest

	Number (%)	Deaths *n* (%)
All arrests	205 (100)	126 (61.5)
Out-of-hospital	113 (55.1)	65 (56.8)
VF/VT	83 (73.4)	38 (45.8)
PEA/asystole	30 (26.6)	27 (90.0)
In-hospital	92 (44.9)	61 (66.3)
VF/VT	32 (34.8)	17 (53.1)
PEA/Asystole	60 (65.2)	44 (73.3)



ICU mortality after cardiac arrest: the relative contribution of shock and brain injury in a large cohort

Lemiale V, Dumas F, Mongardon N, Giovanetti O, Charpentier J, Chiche JD, Carli P, Mira JP, Nolan J, Cariou A.



Soumis

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JOFFRE-DUPUYTREN - EMILE ROUX

Hypothermie thérapeutique post-arrêt cardiaque :

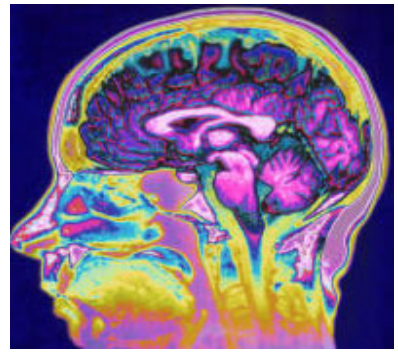
Pourquoi ?

Pour qui ?

Comment ?

Quels risques?

Quelles mesures associées?



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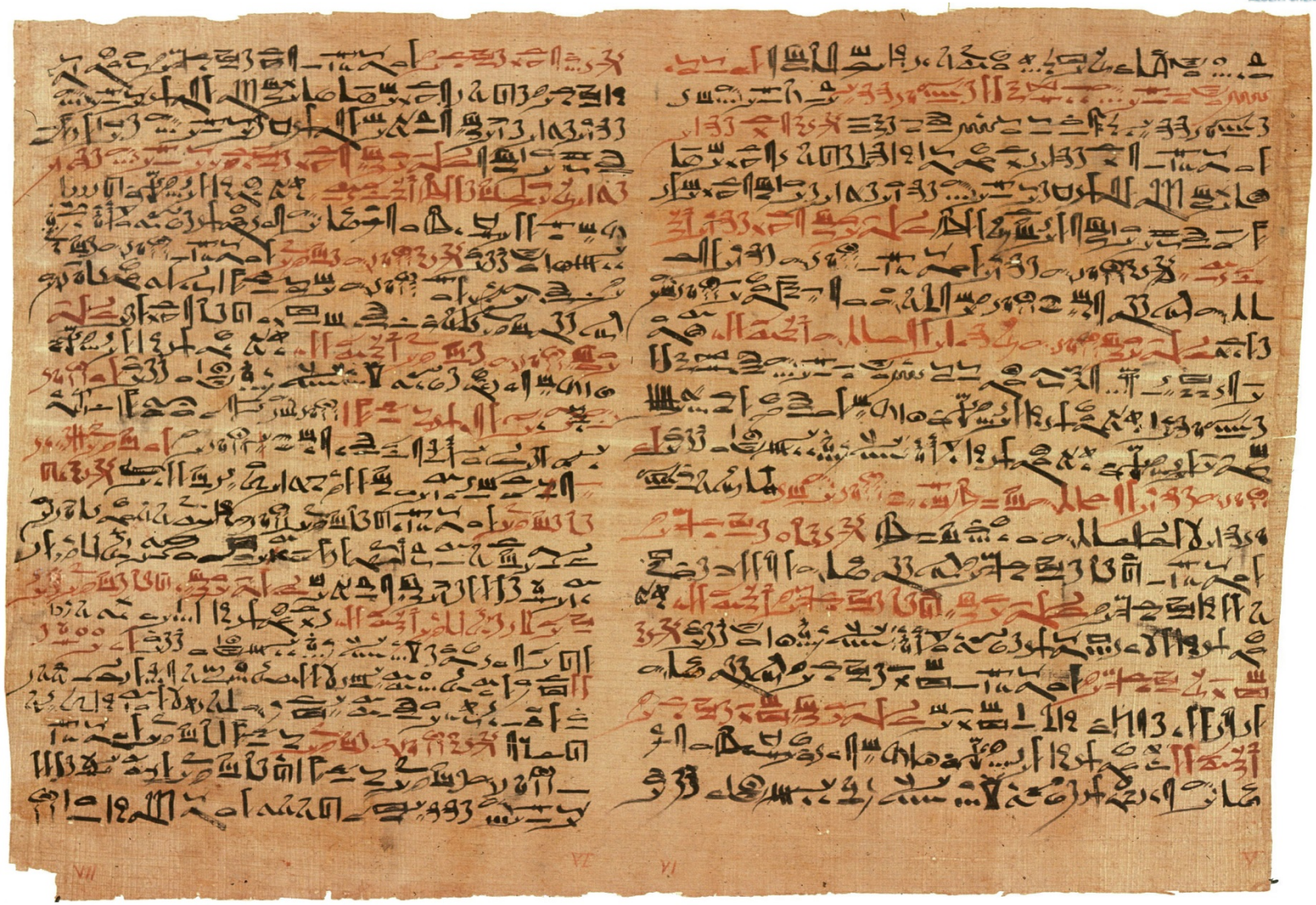
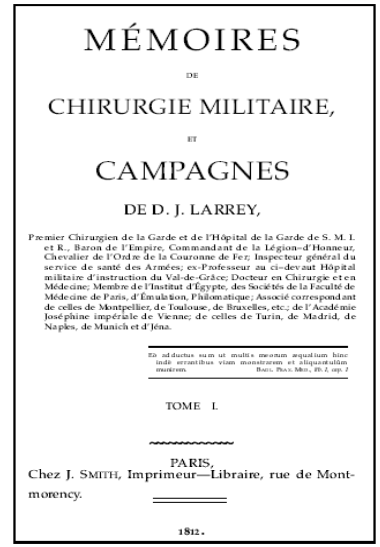
Hypothermie thérapeutique

Pourquoi?



Papyrus Edwin Smith ~ 17^{tème} siècle avant JC

Un bénéfice suggéré depuis longtemps



MÉMOIRES

DE

CHIRURGIE MILITAIRE,

ET

CAMPAGNES

DE D. J. LARREY,

Premier Chirurgien de la Garde et de l'Hôpital de la Garde de S. M. I. et R., Baron de l'Empire, Commandant de la Légion-d'Honneur, Chevalier de l'Ordre de la Couronne de Fer; Inspecteur général du service de santé des Armées; ex-Professeur au ci-devant Hôpital militaire d'instruction du Val-de-Grâce; Docteur en Chirurgie et en Médecine; Membre de l'Institut d'Égypte, des Sociétés de la Faculté de Médecine de Paris, d'Émulation, Philomatique; Associé correspondant de celles de Montpellier, de Toulouse, de Bruxelles, etc.; de l'Académie Joséphine impériale de Vienne; de celles de Turin, de Madrid, de Naples, de Munich et d'Iéna.

Ea adducta sum ut multis meorum aequalium hinc indè errantibus viam monstrarem et aliquantulùm iuuarem.

Boet. Phos. Mus., lib. I, cap. I

TOME I.

PARIS,
Chez J. SMITH, Imprimeur—Libraire, rue de Montmorency.

1812.

« Nous remarquons que les blessés qui sont très froids mais que l'on réchauffe près du feu meurent plus vite que ceux qui demeurent froids »

Baron Dominique-Jean Larrey
Mémoires de chirurgie militaire et campagnes (1812-1817)

General versus specific actions of mild-moderate hypothermia in attenuating cerebral ischemic damage

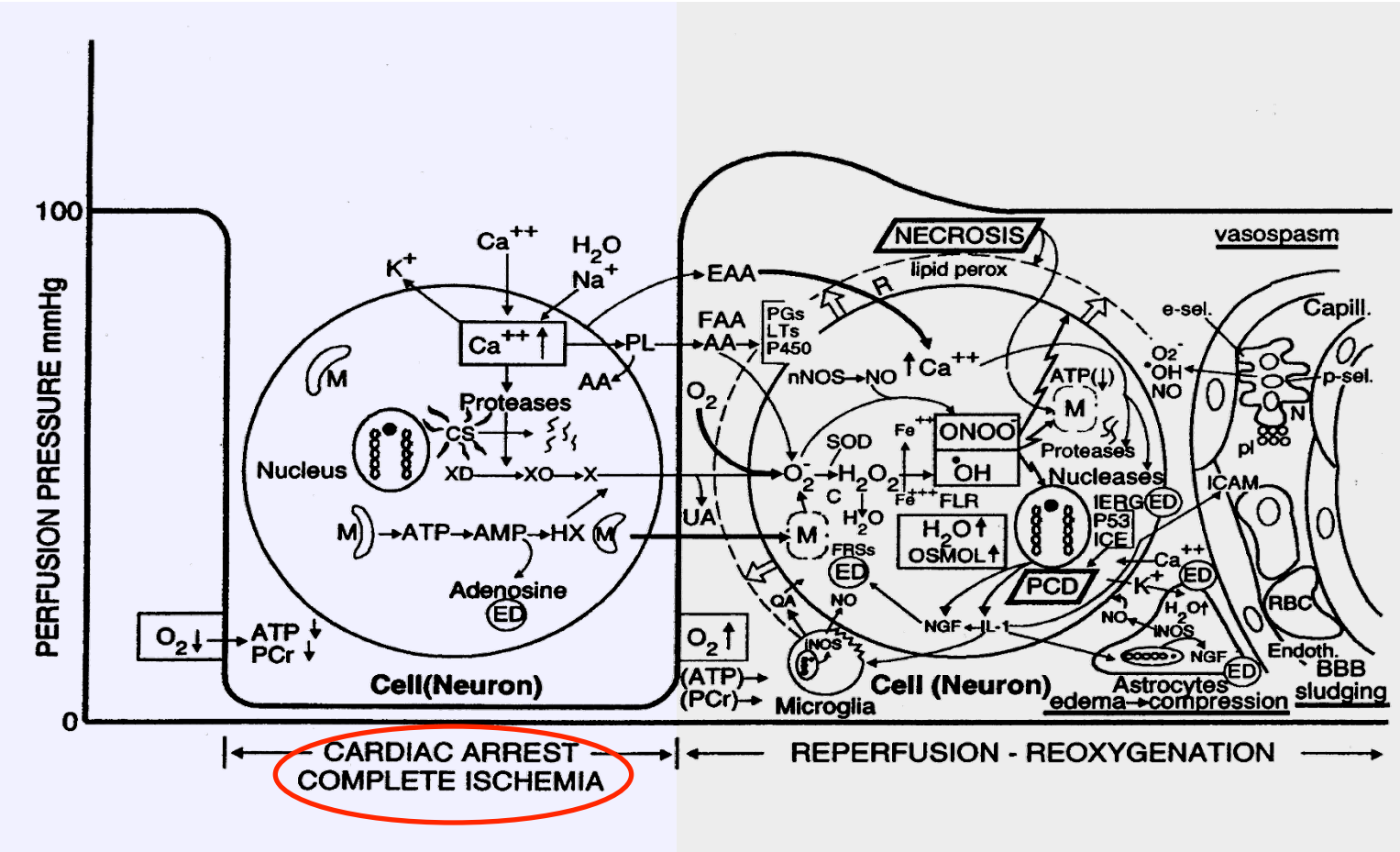
Journal of Cerebral Blood Flow & Metabolism (2007) 27, 1879–1894

Heng Zhao[1,2], Gary K Steinberg[1,2] and Robert M Sapolsky[1,2,3]

Reference	*Model*	*S*	*T (°C)*	*Factors*
Takeda *et al* (2003)	Global	G	31 and 34	Anoxic depolarization
Busto *et al* (1989*b*)	Global	R	30 and 33	Glutamate
Dietrich *et al* (1990)	Global	R	30 and 33	BBB
Kawanishi (2003)	Hemorrhage	R	35	Edema; BBB; PMNL
Kawai *et al* (2000)	Focal	R	33	ICAM-1 mRNA; PMNL
Wang *et al* (2002)	Focal	R	30	ICAM-1; neutrophil and monocyte; microglia
Hamann *et al* (2004)	Focal	R	32 and 34	MMP-2; MMP-9; μ-PA; t-PA
Maier *et al* (2002)	Focal	R	33	O^{2-}
Karibe *et al* (1994*a*)	Focal	R	33	Ascorbate; glutathione
Kader *et al* (1994)	Focal	R	33	NOS; nitrite
Toyoda *et al* (1996)	Focal	R	30	Neutrophil
Chopp *et al* (1992)	Global	R	30	HSP-70
Mancuso *et al* (2000)	Focal	R	33	HSP-70; C-fos
Tohyama *et al* (1998)	Focal	R	30	PKC
Shimohata *et al* (2007*a*)	Focal	R	30	εPKC
Shimohata *et al* (2007*b*)	Focal	R	30	δPKC
Harada *et al* (2002)	Global	R	32	CaM kinase II; PKC-α,β,γ synaptosome
Tsuchiya *et al* (2002)	Global	M	33	Zn^{2+}
Phanithi *et al* (2000)	Focal	R	33	Fas; caspase-3
Zhao *et al* (2007)	Focal	R	33	Cytochrome *c* and AIF
Karabiyikoglu *et al* (2003)	Focal	R	33 intra or post	iNOS; nNOS
Wagner *et al* (2003)	Focal	R	33 post	BBB; MMP-9
Inamasu *et al* (2000)	Focal	R	34.5 post	Neutrophil infiltration; microglia
Horstmann *et al* (2003)	Stroke	Hu	33 post	MMP-9
Horiguchi *et al* (2003)	Global	R	32 post	Hydroxyl radical
Han *et al* (2003)	Focal	R	33 post	NF-κB; iNOS; TNF-α
Van Hemelrijck *et al* (2005)	Focal	R	34 post	Caspase-3; nNOS
Inamasu *et al* (2000)	Focal	R	34.5 post	Bax
Friedman *et al* (2001)	Global	R	30 intra/post	GluR1A; GluR2B; GluR3C; NMDAR1
Ohta *et al* (2007)	Focal	R	35 post	Inflammatory genes: osteopontin, early growth response-1, and macrophage inflammatory protein-3α
Luo *et al* (2007)	Focal	R	33 post	Base-excision repair pathway
Preston and Webster (2004)	Global	R	32 post	BBB
Liebetrau *et al* (2004)	Focal	R	32 post	Calpain

Mécanismes d'action

Cascade biochimique des lésions d'ischémie / reperfusion



Bellamy R, Safar P, Tisherman S, Critical Care Medicine. 1996

Mécanismes d'action

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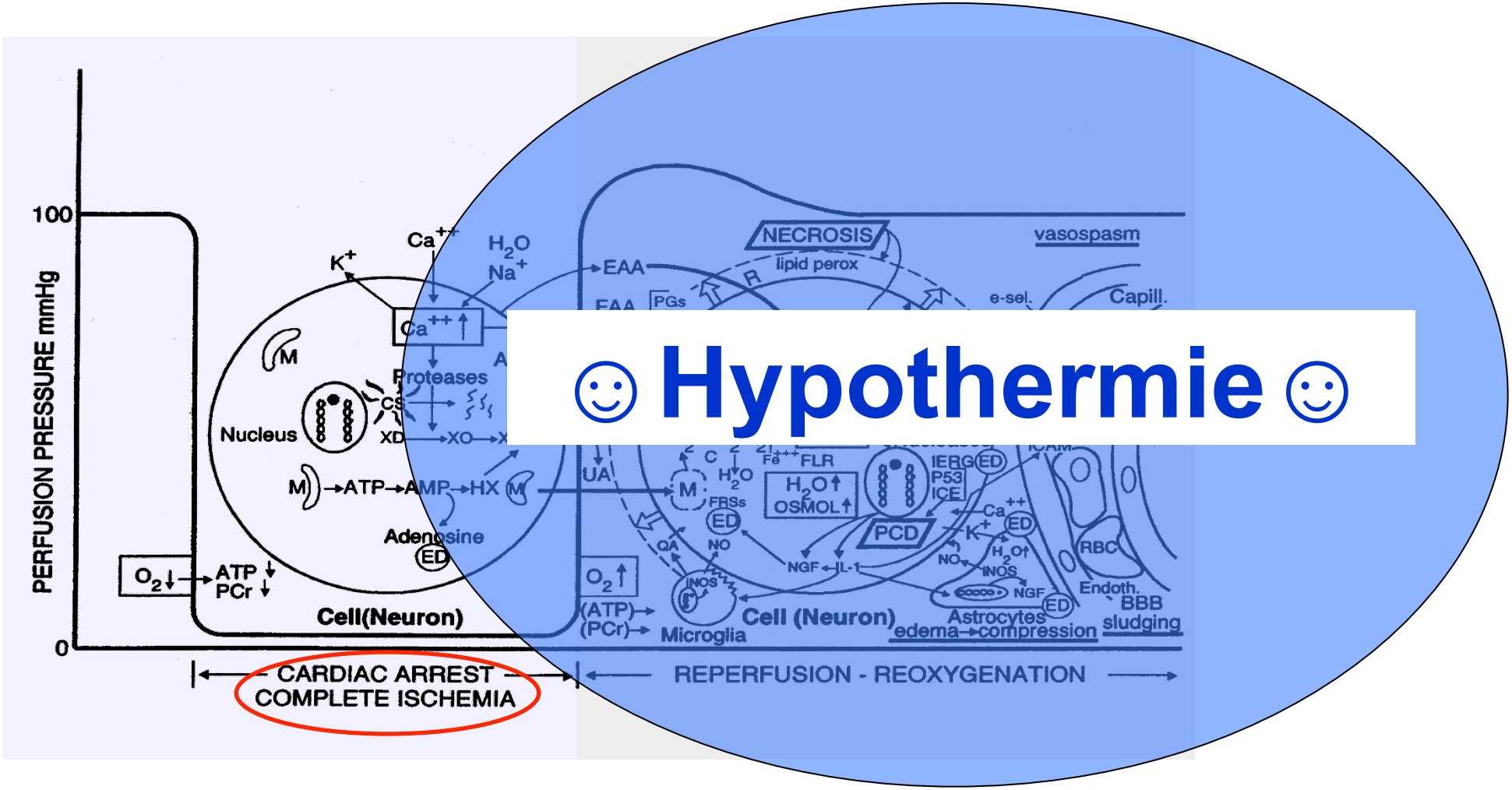
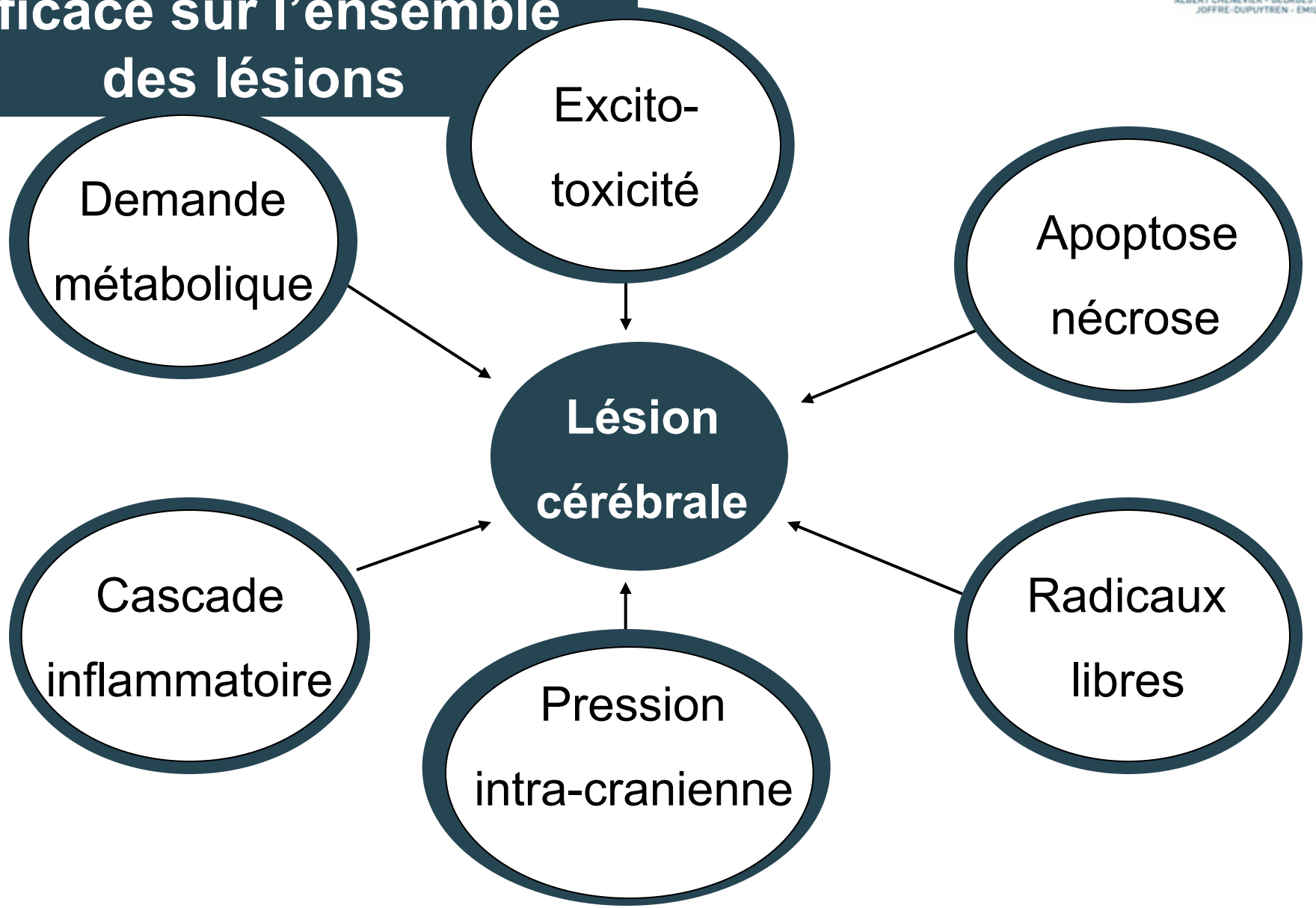
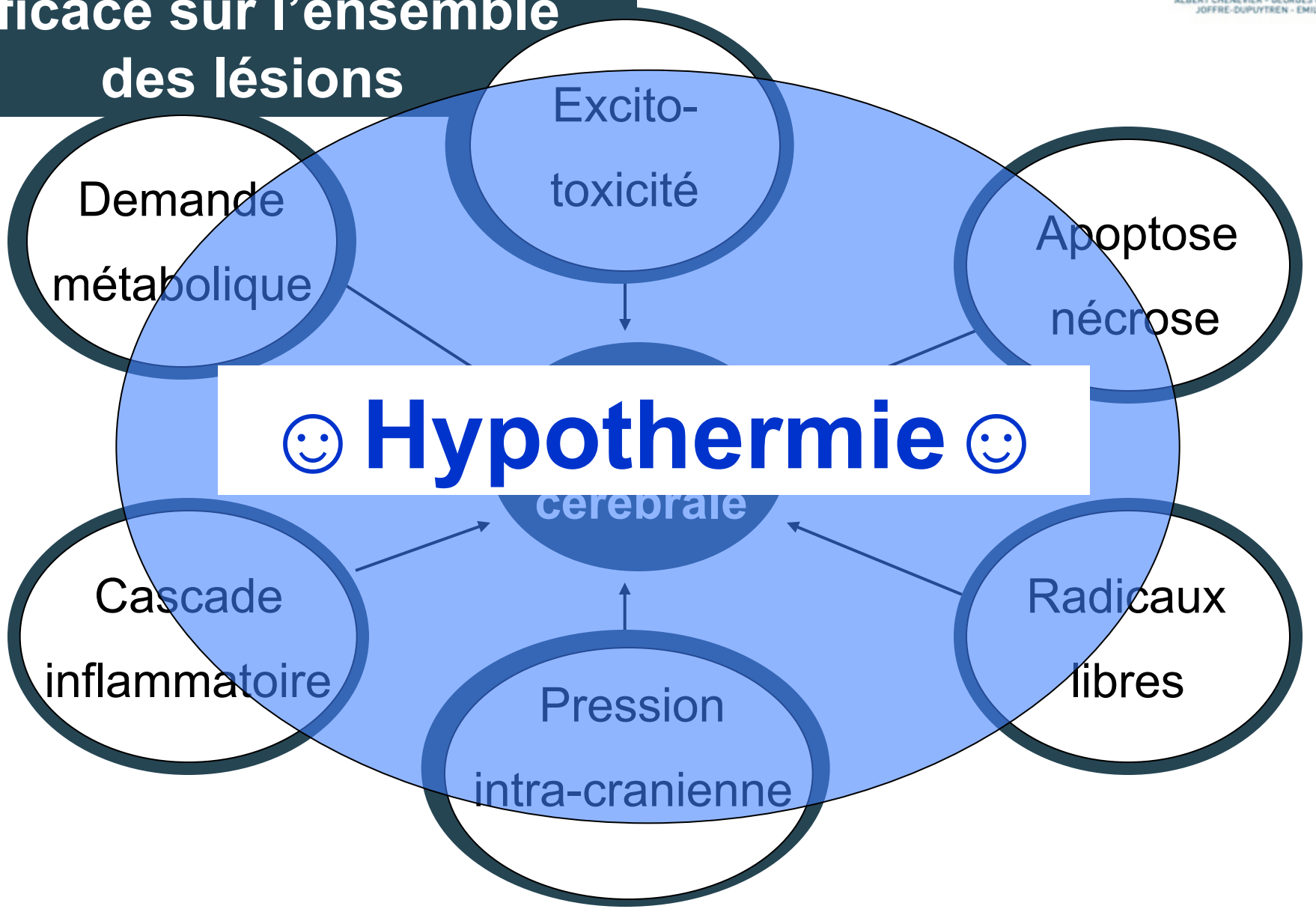


Bellamy R, Safar P, Tisherman S, Critical Care Medicine. 1996

Hypothermie efficace sur l'ensemble des lésions



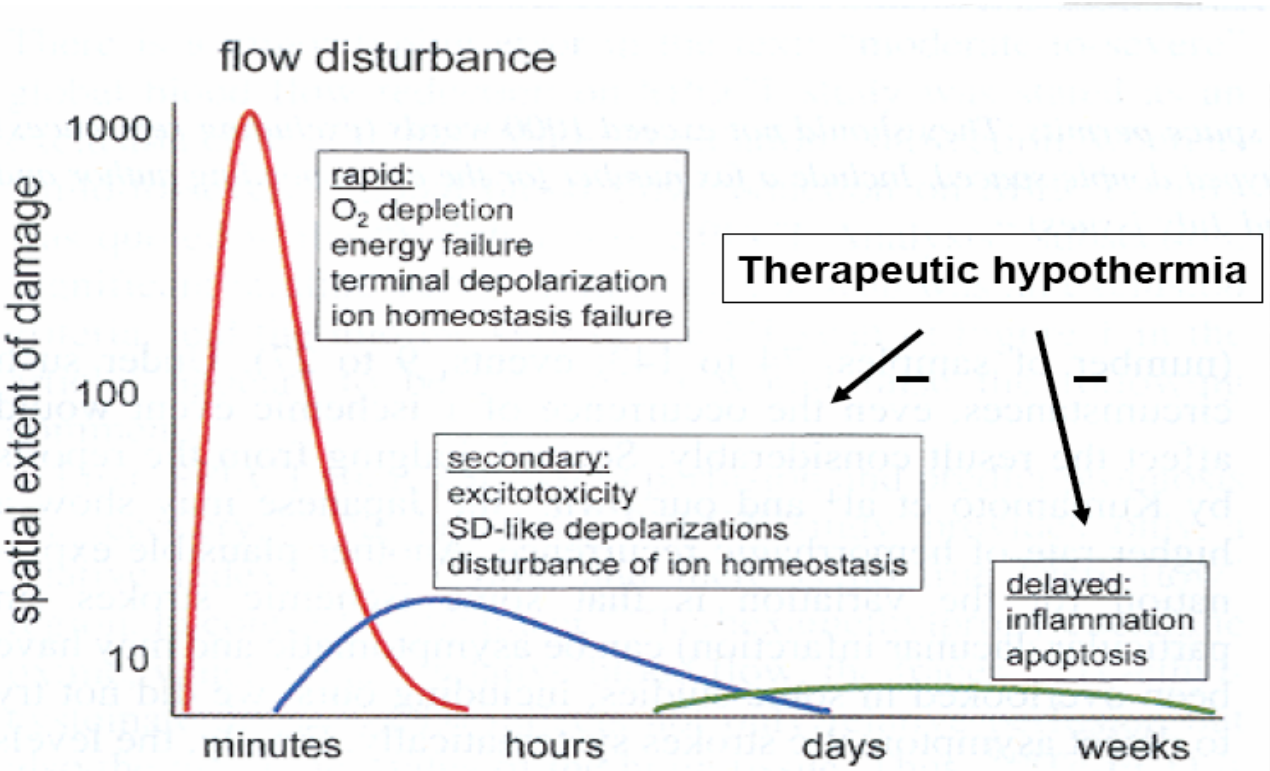
Hypothermie efficace sur l'ensemble des lésions



Mechanisms	Time frame after injury
Prevention of apoptosis*	Hours to many days or even weeks
Reduced mitochondrial dysfunction, improved energy homoeostasis†	Hours to days
Reduction of excessive free radical production†	Hours to days
Mitigation of reperfusion injury†	Hours to days
Reduced permeability of the blood–brain barrier and the vascular wall; reduced oedema formation*	Hours to days
Reduced permeability of cellular membranes (including membranes of the cell nucleus)†	Hours to days
Improved ion homoeostasis†	First minutes to 72 h
Reduction of metabolism*	Hours to days
Depression of the immune response and various potentially harmful proinflammatory reactions*	First hour to 5 days
Reduction in cerebral thermopooling*	Minutes to many days
Anticoagulant effects*	Minutes to days
Suppression of epileptic activity and seizures*	Hours to days

Kees H Polderman

Lancet 2008; 371: 1955–69



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Kees H Polderman

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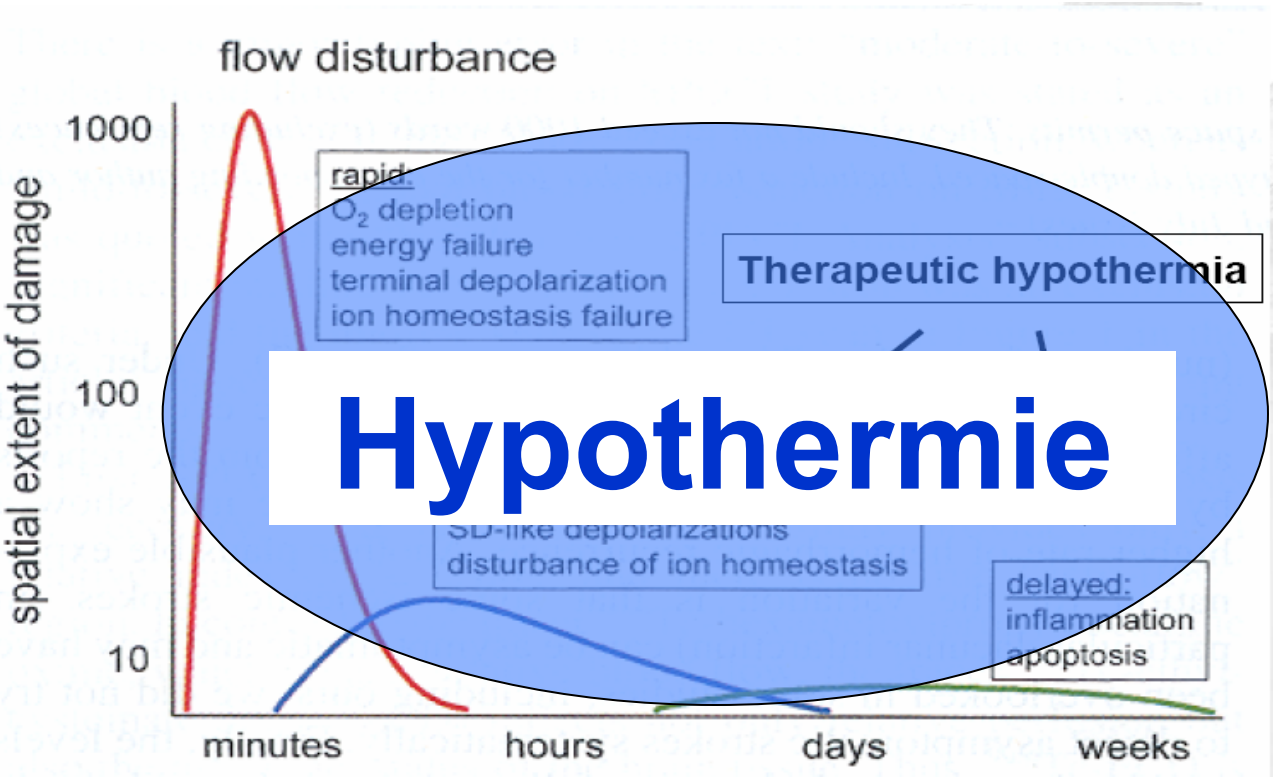

Etudes cliniques préliminaires

GROUPE HOSPITALIER HENRI MONDOR
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Benson DW, Williams GR, Spencer FC. The use of hypothermia after cardiac arrest. Anesth Analg. 1958; 38:423–4

Williams GR Jr, Spencer FC. Clinical use of hypothermia following cardiac arrest. Ann Surg. 1959; 148:462–468

Mild Resuscitative Hypothermia to Improve Neurological Outcome After Cardiac Arrest

A Clinical Feasibility Trial

Andrea Zeiner, MD; Michael Holzer, MD; Fritz Sterz, MD; Wilhelm Behringer, MD; Waltraud Schörkhuber, MD; Marcus Müllner, MD; Michael Frass, MD; Peter Siostrzonek, MD; Klaus Ratheiser, MD; Alfred Kaff, MD; Anton N. Laggner, MD; for the Hypothermia After Cardiac Arrest (HACA) Study Group*

Stroke 2000; 31:86-94

Hypothermia After Cardiac Arrest

Feasibility and Safety of an External Cooling Protocol

R.A. Felberg, MD; D.W. Krieger, MD; R. Chuang, MD; D.E. Persse, MD; W.S. Burgin, MD; S.L. Hickenbottom, MD; L.B. Morgenstern, MD; O. Rosales, MD; J.C. Grotta, MD

Circulation. 2001;104:1799-1804

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*

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.

Editorial

THERAPEUTIC HYPOTHERMIA AFTER CARDIAC ARREST

Designs respectifs

Etude européenne	Etude australienne
• ACR extra-hospitalier • Rythme initial = FV • Coma CGS < 7 • Origine cardiaque probable	• ACR extra-hospitalier • Rythme initial = FV • Coma • Origine cardiaque probable
• Température : 32-34°C • Durée 24 h • Curarisation	• Température : 33°C • Durée 12 h, dès le pré-hospitalier • Curarisation

Survie hospitalière et à 6 mois

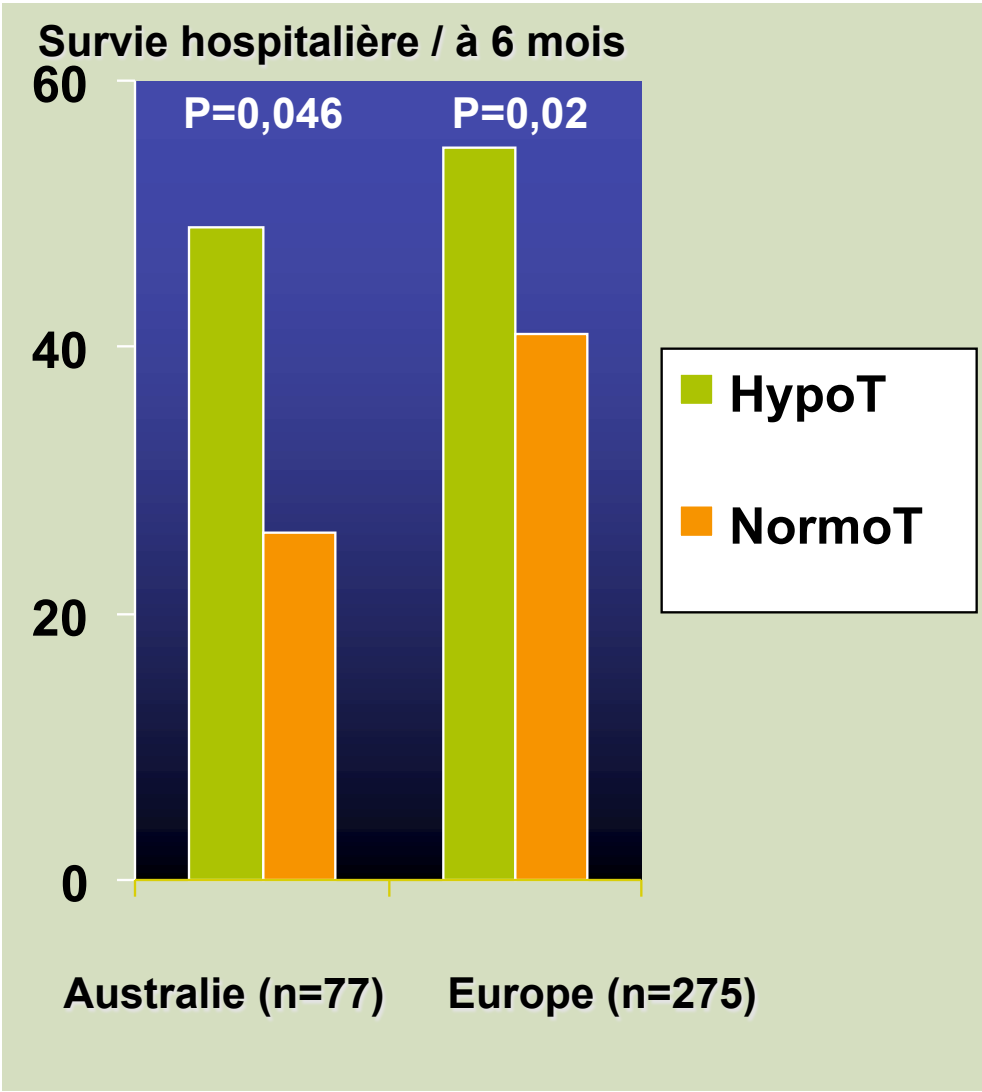
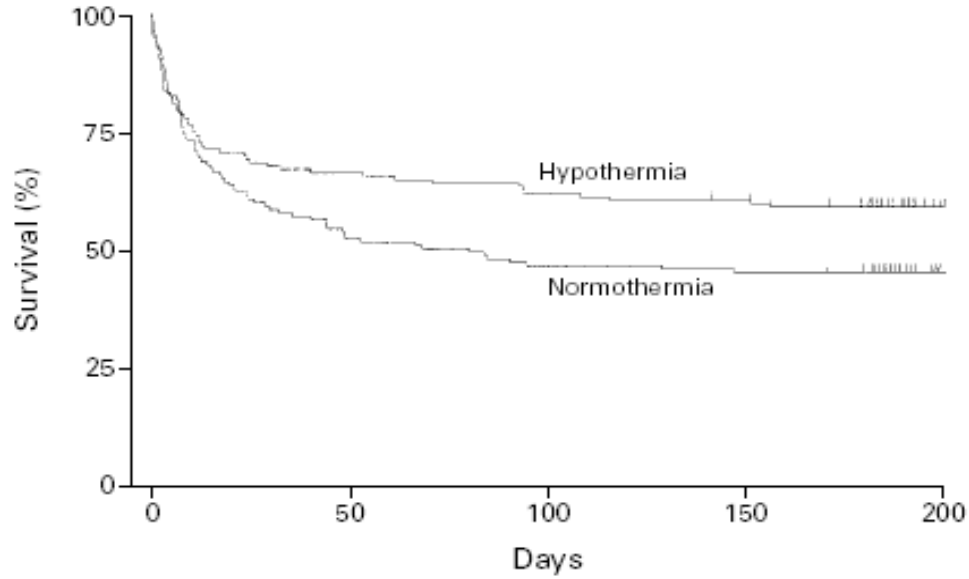
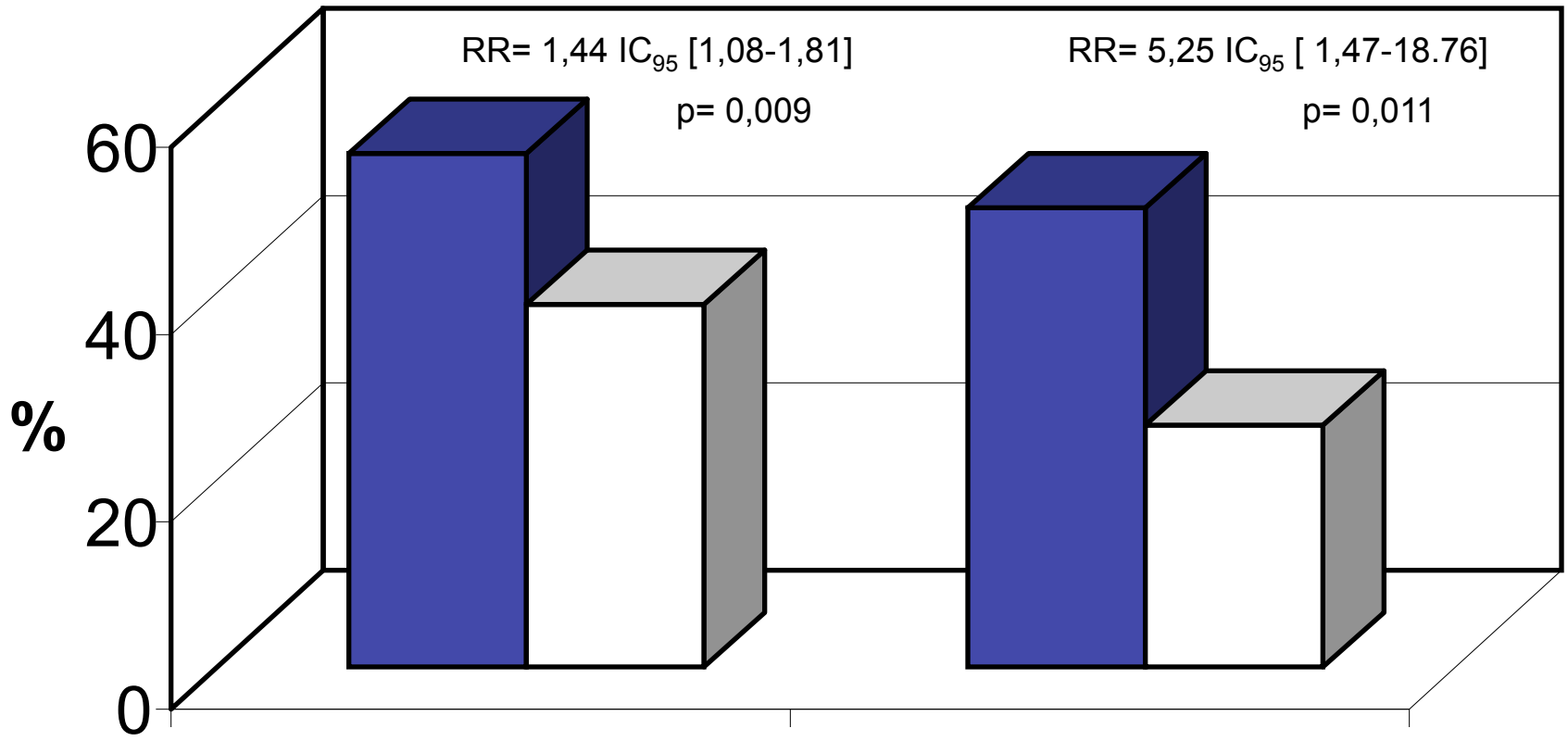


TABLE 2. NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02



Évolution neurologique favorable



N Engl J Med 2002

ILCOR Advisory Statement

GROUPE HOSPITALIER HENRI MONDOR
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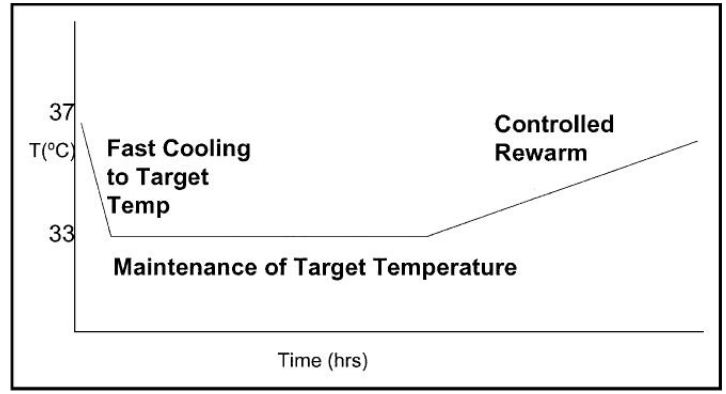
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®
Learn and Live℠

Therapeutic Hypothermia After Cardiac Arrest

An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation



« On the basis of the published evidence to date, the Advanced Life Support (ALS) Task Force of the International Liaison Committee on Resuscitation (ILCOR) made the following recommendations in October 2002 :

- **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)**
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest »

Circulation 2003

Therapeutic Hypothermia: The Safar Vision

JOURNAL OF NEUROTRAUMA 26:417–420 (March 2009)

DOI: 10.1089/neu.2008.0612

Patrick M. Kochanek,[1,2] Tomas Drabek,[1,3] and Samuel A. Tisherman[1,2,4]

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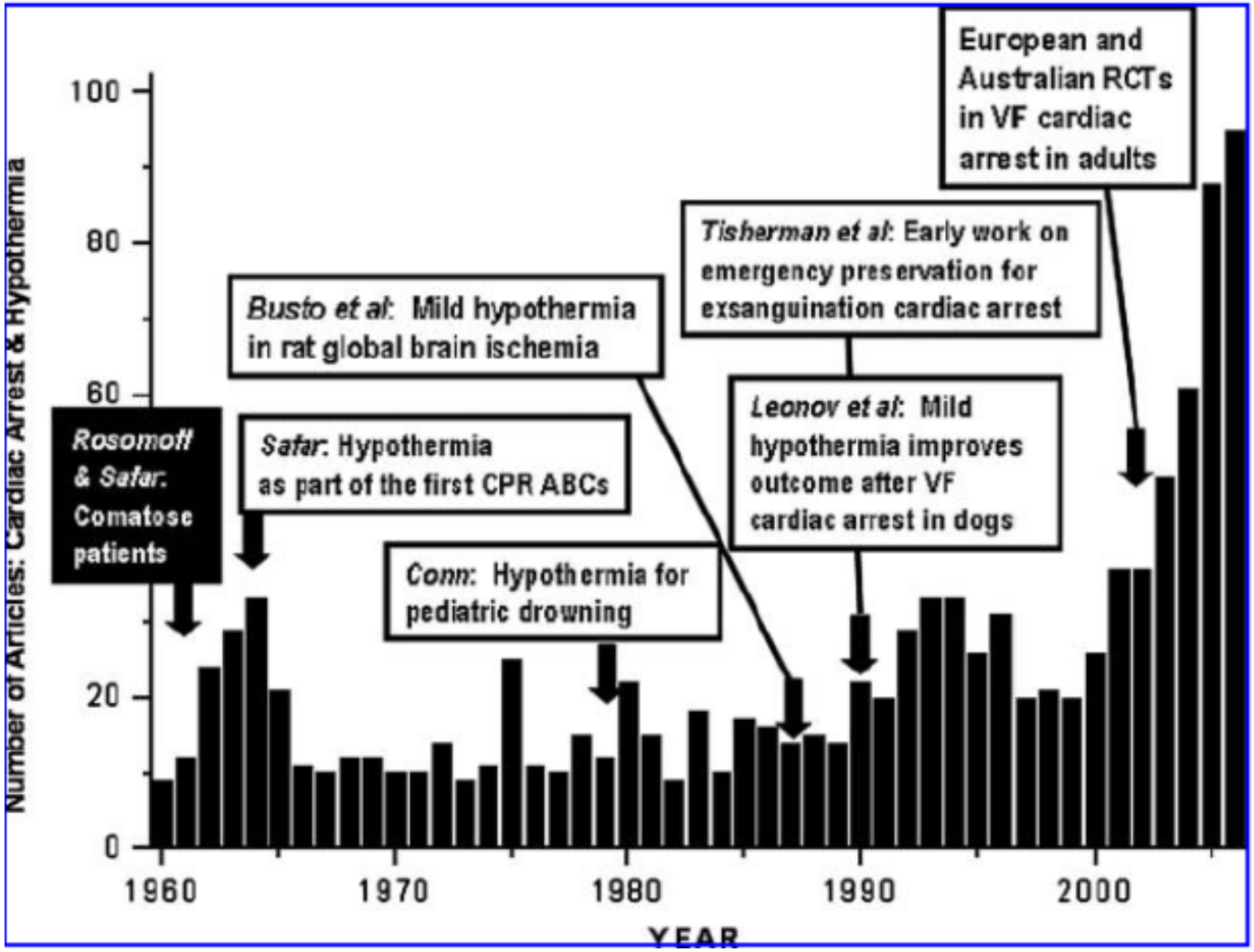

Hypothermie & ACR

Induced hypothermia and fever control for prevention and treatment of neurological injuries

GROUPE HOSPITALIER HENRI MONDOR
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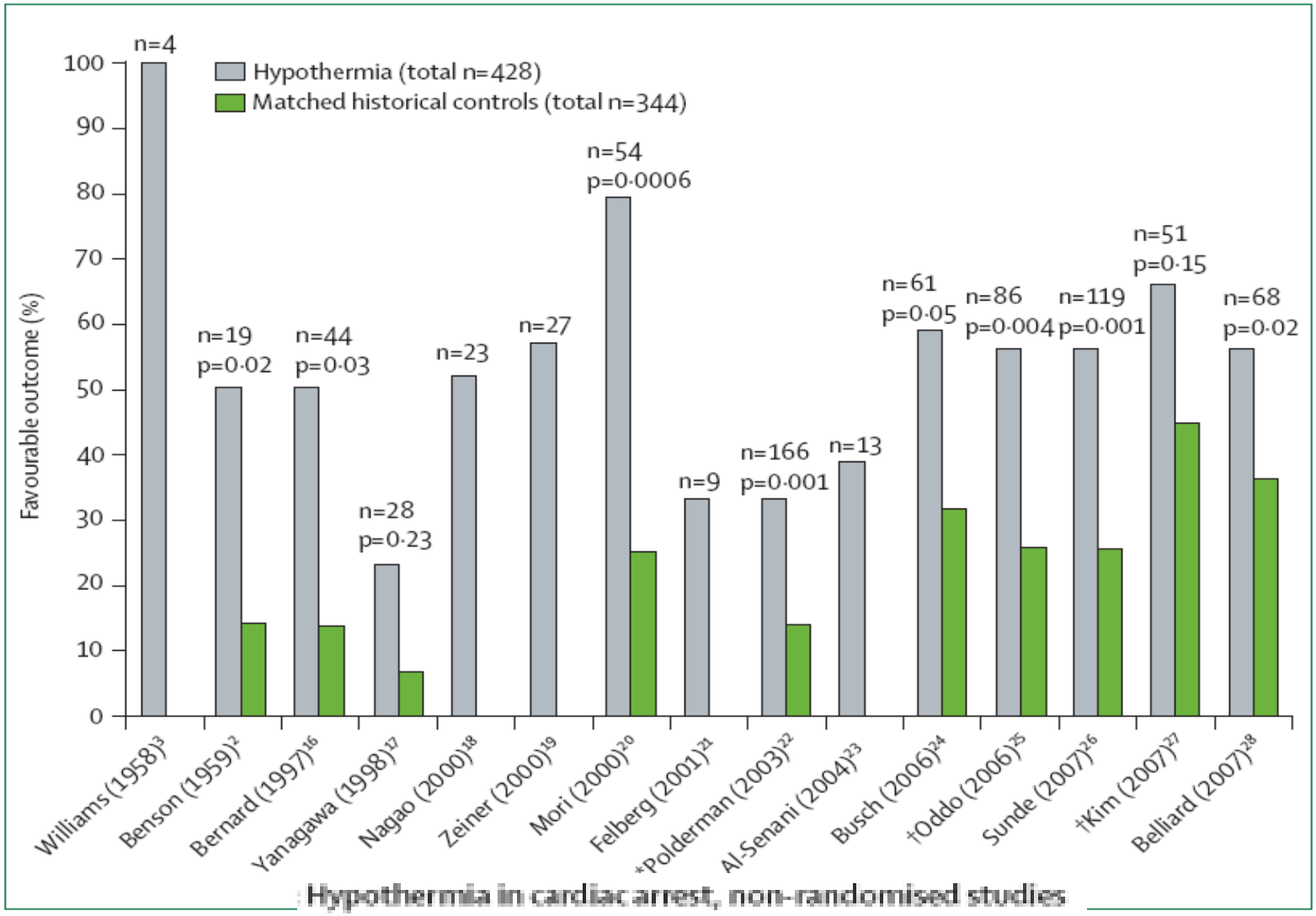
JOFFRE-DUPUYTREN - EMILE ROUX

Lancet 2008; 371: 1955–69

Kees H Polderman



Hypothermia in cardiac arrest, non-randomised studies

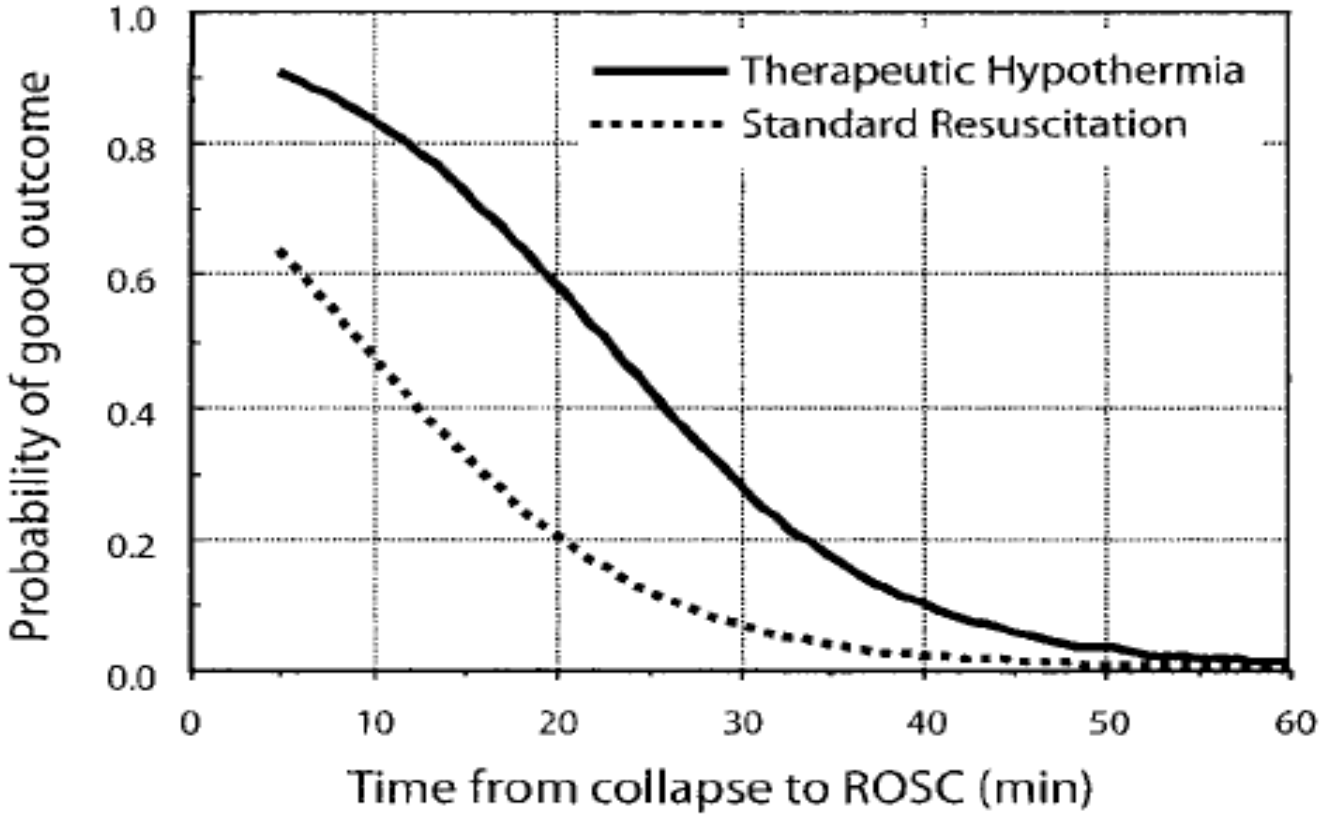
Should All Patients Be Treated With Hypothermia Following Cardiac Arrest?

Steven Deem MD and William E Hurford MD

Condition	Therapy	NNT
Cardiac Arrest	Hypothermia	6
ALI/ARDS	Lung-protective ventilation	11
Sepsis	Dotrecogin alpha	16
Stroke	Aspirin	33
Acute myocardial infarction	Thrombolytics	37–91*

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

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



55 patients avec HT
Vs 44 patients contrôles

(Crit Care Med 2006; 34:1865–1873)

Hypothermia For Neuroprotection In Adults After Cardiopulmonary Resuscitation

Jasmin Arrich, Michael Holzer, Harald Herkner, Marcus Müllner

April 2010 • Volume 110 • Number 4

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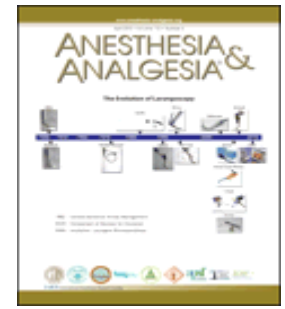
THE COCHRANE COLLABORATION®



Study or subgroup	Experimental n/N	Control n/N	Risk ratio M-H, fixed, 95% CI	Weight	Risk ratio M-H, fixed, 95% CI
1 Conventional cooling without extracorporal methods (IPD, best ever reached CPC of 1 or 2 during hospital stay)					
Bernard 2002	21/43	9.34		129%	1.84 [0.97, 3.49]
HACA 2002	75/136	54/137		69.1%	1.40 [1.08, 1.81]
Hachimi-Idrissi 2001	8/16	2/17		25%	4.25 [1.06, 17.08]
Subtotal (95% CI)	**195**	**188**		**84.5%**	**1.55 [1.22, 1.96]**
Total events 104 (experimental), 65 (control)					
Heterogeneity: $\chi^2 = 2.92$, df = 2 ($P = 0.23$); $I^2 = 32\%$					
Test for overall effect: $Z = 3.64$ ($P = 0.00027$)					
2 Cooling with haemofiltration (no IPD, CPC of 1 or 2 at six months)					
Laurent 2005	7/22	9/20		12.1%	0.71 [0.32, 1.54]
Subtotal (95% CI)	**22**	**20**		**12.1%**	**0.71 [0.32, 1.54]**
Total events 7 (experimental), 9 (control)					
Heterogeneity: not applicable					
Test for overall effect: $Z = 0.87$ ($P = 0.38$)					
3 Unknown method (no IPD, Glasgow outcome scale of 1-3 at one month)					
Mori 2000	18/36	2/18		3.4%	4.50 [1.17, 17.30]
Subtotal (95% CI)	**36**	**18**		**3.4%**	**4.50 [1.17, 17.30]**
Total events 18 (experimental), 2 (control)					
Total (95% CI)	**253**	**226**		**100.0%**	**1.55 [1.24, 1.94]**
Total events 129 (experimental), 76 (control)					
Heterogeneity: $\chi^2 = 9.21$, df = 4 ($P = 0.06$); $I^2 = 57\%$					
Test for overall effect: $Z = 3.84$ ($P = 0.00012$)					

0.01 0.1 1 10 100

Favours no cooling Favours cooling

En faveur d'un pronostic favorable
CPC 1-2

Influence of mild therapeutic hypothermia after cardiac arrest on hospital mortality

Greetje van der Wal, MD; Sylvia Brinkman, MSc; Laurens L. A. Bisschops, MD;
Cornelia W. Hoedemaekers, MD, PhD; Johannes G. van der Hoeven, MD, PhD; Dylan W. de Lange, MD, PhD;
Nicolette F. de Keizer, PhD; Peter Pickkers, MD, PhD

5317 patients, 1999-2009

Covariate	Odds Ratio	95% Confidence Interval	*p*
Simplified Acute Physiology Score II score	1.069	1.063–1.0750	<.001
Before mild therapeutic hypothermia	1.0	—	—
After mild therapeutic hypothermia	0.800	0.654–0.978	.029
Out-of-hospital cardiac arrest	1.0	—	—
In-hospital cardiac arrest	1.159	1.018–1.319	.026
Female	1.0	—	—
Male	0.754	0.659–0.861	<.001
Age	1.000	0.996–1.005	.965
Logit (propensity score)	0.945	0.911–0.982	.003

Crit Care Med 2011 Vol. 39, No. 1

Circulation
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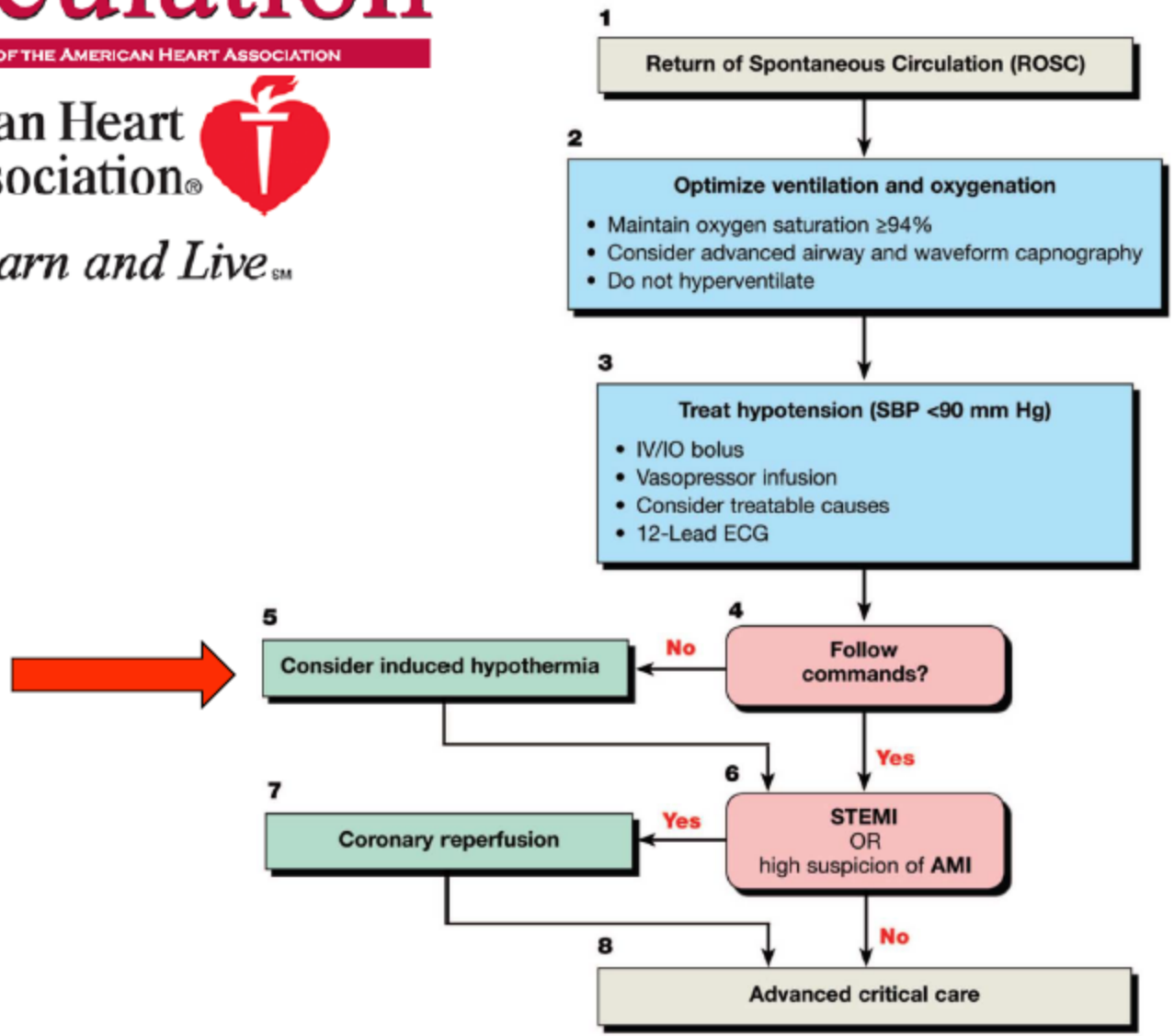
Adult Immediate Post–Cardiac Arrest Care



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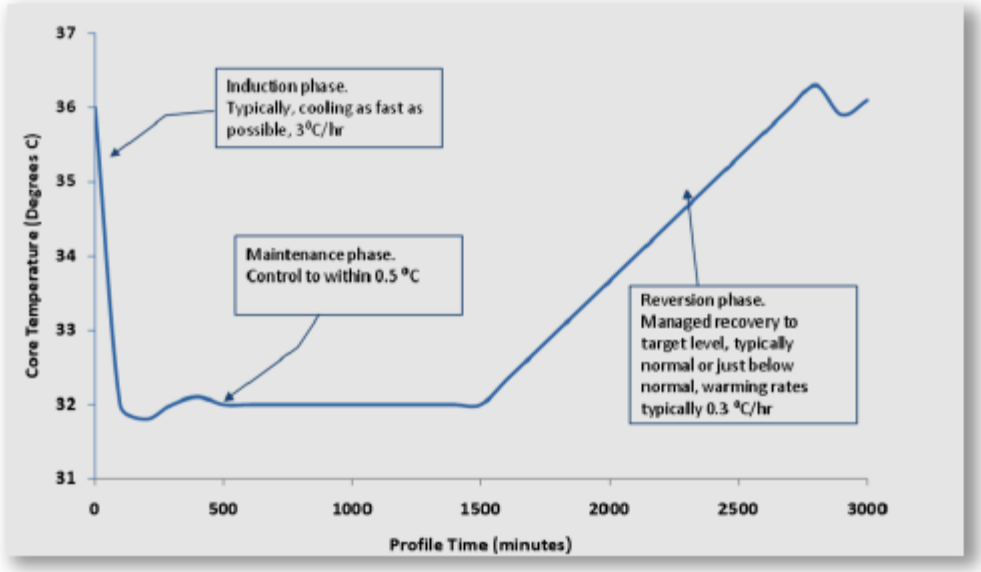
International Consensus Conference 2009

Sponsoring Societies:

ATS – American Thoracic Society – http://www.thoracic.org
ERS- European Respiratory Society – http://www.ersnet.org
ESICM- European Society of Intensive Care Medicine – http://www.esicm.org
SCCM- Society of Critical Care Medicine – http://www.sccm.org
SRLF – Société de Réanimation de Langue Française – http://www.srlf.org

Targeted Temperature Management in Critical Care:

. Report and Recommendations from Five Professional Societies



"The jury RECOMMENDS STRONGLY FOR TTM to a target of 32-34°cas preferred treatment (versus unstructured temperature management) of **out of hospital** adult cardiac arrest victims with a **first registered rhythm of VF or pulseless VT** and still unconscious after restoration of spontaneous circulation."

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2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Laurie J. Morrison, Co-Chair*; Charles D. Deakin, Co-Chair*; Peter T. Morley; Clifton W. Callaway; Richard E. Kerber; Steven L. Kronick; Eric J. Lavonas; Mark S. Link; Robert W. Neumar; Charles W. Otto; Michael Parr; Michael Shuster; Kjetil Sunde; Mary Ann Peberdy; Wanchun Tang; Terry L. Vanden Hoek; Bernd W. Böttiger; Saul Drajer; Swee Han Lim; Jerry P. Nolan; on behalf of the Advanced Life Support Chapter Collaborators

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Treatment recommendations related to post–cardiac hypothermia

- **Comatose adult patients with spontaneous circulation after out-of-hospital VF cardiac arrest** should be cooled to 32 to 34°C for 12 to 24 hours.
- **Induced hypothermia might also benefit** comatose adult patients with spontaneous circulation **in other settings**

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Hypothermie thérapeutique

Pour qui?

The Practice of Therapeutic Hypothermia after Cardiac Arrest in France: A National Survey

Jean-Christophe Orban[1,2]*, Florian Cattet[1], Jean-Yves Lefrant[3], Marc Leone[4], Samir Jaber[5], Jean-Michel Constantin[6], Bernard Allaouchiche[7], Carole Ichai[1,2] for the AzuRéa group

	ACR EXTRA HOSPITALIER		ACR INTRA HOSPITALIER
HT	**FV/TV**	**DEM/ASYS**	
Systématique	137 (87%)	109 (69%)	94 (60%)
Parfois	18 (11%)	40 (25%)	56 (36%)
Jamais	2 (2%)	8 (6%)	7 (4%)

PLOS ONE 2012:
Adhésion aux recommandations sur 132 services de réanimation français

2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Laurie J. Morrison, Co-Chair*; Charles D. Deakin, Co-Chair*; Peter T. Morley; Clifton W. Callaway; Richard E. Kerber; Steven L. Kronick; Eric J. Lavonas; Mark S. Link; Robert W. Neumar; Charles W. Otto; Michael Parr; Michael Shuster; Kjetil Sunde; Mary Ann Peberdy; Wanchun Tang; Terry L. Vanden Hoek; Bernd W. Böttiger; Saul Drajer; Swee Han Lim; Jerry P. Nolan; on behalf of the Advanced Life Support Chapter Collaborators

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Treatment recommendations related to post–cardiac hypothermia

- **Comatose adult patients with spontaneous circulation after out-of-hospital VF cardiac arrest** should be cooled to 32 to 34°C for 12 to 24 hours.
- **Induced hypothermia might also benefit** comatose adult patients with spontaneous circulation **in other settings**

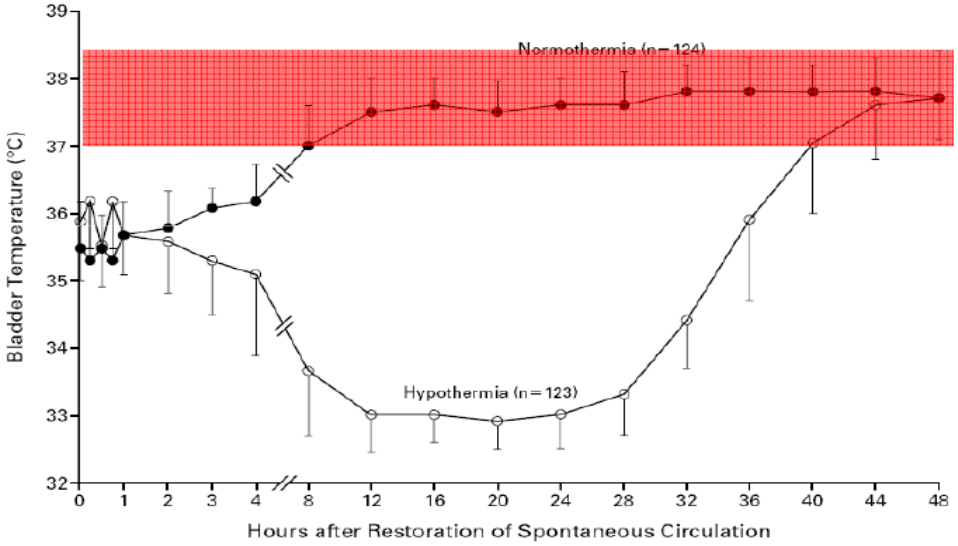
Critical knowledge gaps related to post–cardiac hypothermia treatment

- Further investigation is needed to determine the benefit of therapeutic hypothermia after **non shockable cardiac arrest and in-hospital cardiac arrest**.

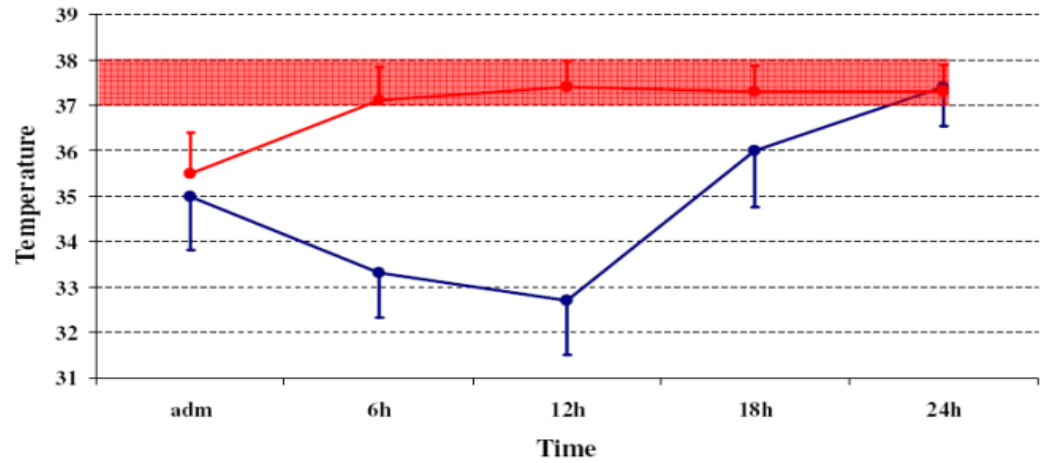
Limites des deux études princeps

* Population très ciblée (FV/TV)
    - Exemple de l'HACA: 18-75 ans, présence d'un témoin, rythme choquable, no-flow <15min, ROSC<60min, PAs<90 mmHg
* Patients du groupe contrôle légèrement hyperthermes (37-38°pendant les 48 premières heures)

Europe



Australie



QUI NE PAS REFROIDIR ?

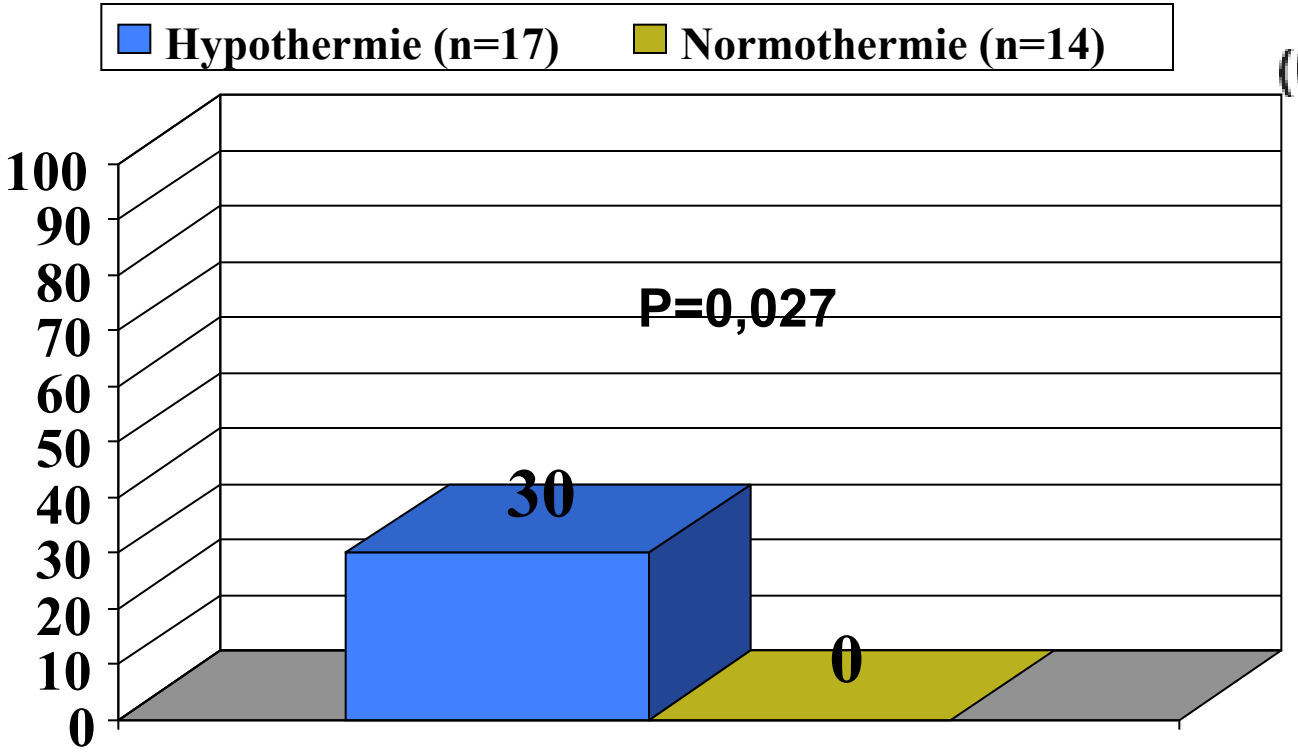
Hémorragie intra-cérébrale
Choc hémorragique
Température initiale < 30°C
Troubles de l'hémostase sévères
Maladie terminale

choc cardiogénique sévère ?
ACR intra-hospitalier ?
rythme non-choquable ?

Choc post-ACR et hypothermie

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

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



(Crit Care Med 2006; 34:1865–1873)

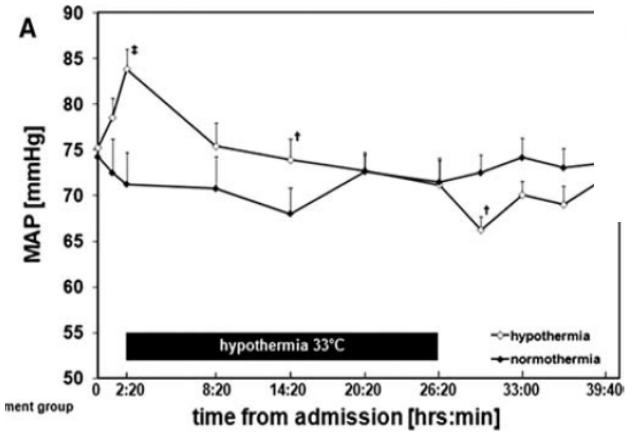
Sous-groupe de patients en choc post-ACR

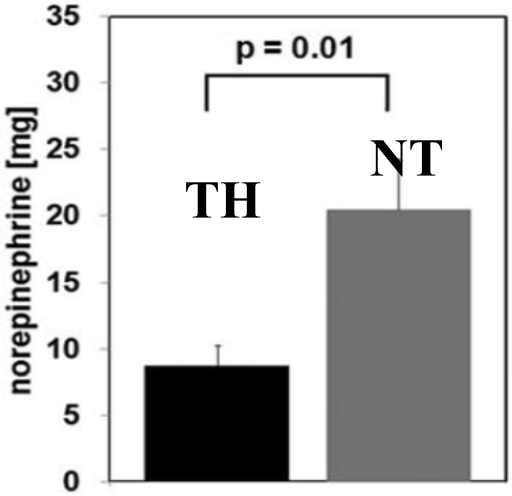
Mild therapeutic hypothermia in cardiogenic shock syndrome*

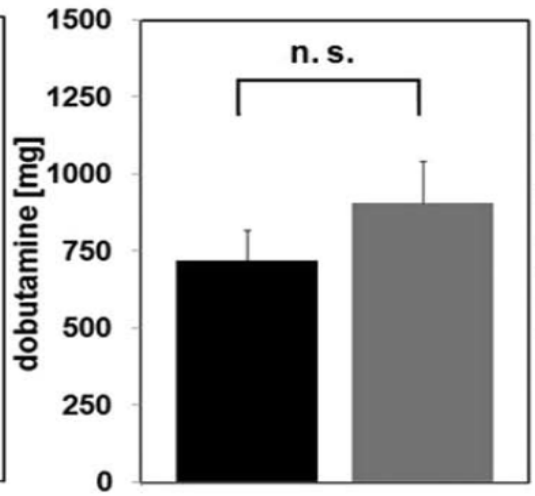
Carsten Zobel, MD; Christoph Adler, MS; Anna Kranz, MS; Catherine Seck, MD; Roman Pfister, MD; Martin Hellmich, MD; Matthias Kochanek, MD; Hannes Reuter, MD

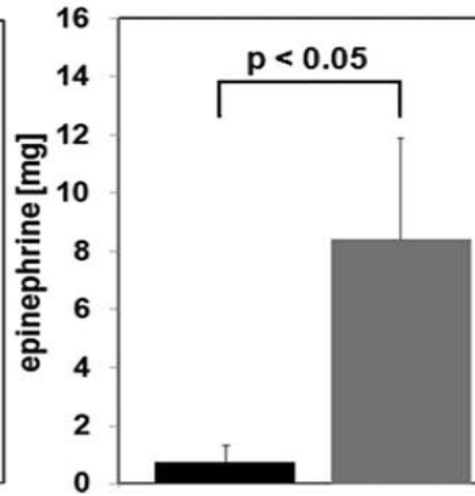
40 patients en choc post-ACR: 20 HT matchés avec 20 NT

Epargne en catécholamines (RVS ↑, DC préservé grâce au remplissage)









CCM 2012

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AHA Consensus Statement

Strategies for Improving Survival After In-Hospital Cardiac Arrest in the United States: 2013 Consensus Recommendations

A Consensus Statement From the American Heart Association

Induction of Goal-Directed Mild Therapeutic Hypothermia

Mild therapeutic hypothermia (32°C to 34°C) improves outcome of comatose survivors of witnessed OHCA when the initial rhythm is VF.[109,110] Similar studies have not been performed in patients who achieve ROSC after IHCA. The potential detrimental or beneficial effect of mild therapeutic hypothermia on active pathologies, comorbidities, and ongoing therapies must be considered. The role of therapeutic hypothermia in the management of IHCA and with initial rhythms other than VF in either the out-of-hospital or in-hospital setting is an important knowledge gap that needs to be addressed by future research. Despite this gap in research, the *2010 AHA Guidelines for CPR and ECC* recommend that induced hypothermia may be considered for comatose adult patients with ROSC after IHCA of any initial rhythm.[111]

Rythme non choquable

Mild hypothermia treatment in patients resuscitated from non-shockable cardiac arrest

EMJ 2011

Christian Storm,[1] Jens Nee,[1] Mattias Roser,[2] Achim Jörres,[1] Dietrich Hasper[1]

CPC 1-2 (sortie ICU): TH 28% (n=87), NT 18% (n=88)… NS (0.18)

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

Resus 2011

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

CPC 1-2 (6 mois): TH 35% (n=135), NT 23% (n=239)… p=0.02 (OR 1.84)

Therapeutic hypothermia is associated with improved neurologic outcome and survival in cardiac arrest survivors of non-shockable rhythms☆

Resus 2011

Justin B. Lundbye[a,b,*], Mridula Rai[a,b], Bhavadharini Ramu[a,b], Alireza Hosseini-Khalili[a], Dadong Li[a], Hanna B. Slim[a], Sanjeev P. Bhavnani[a,b], Sanjeev U. Nair[a], Jeffrey Kluger[a,b]

CPC 1-2 (sortie hôpital): TH 29% (n=52), NT 10% (n=43)… p=0.02

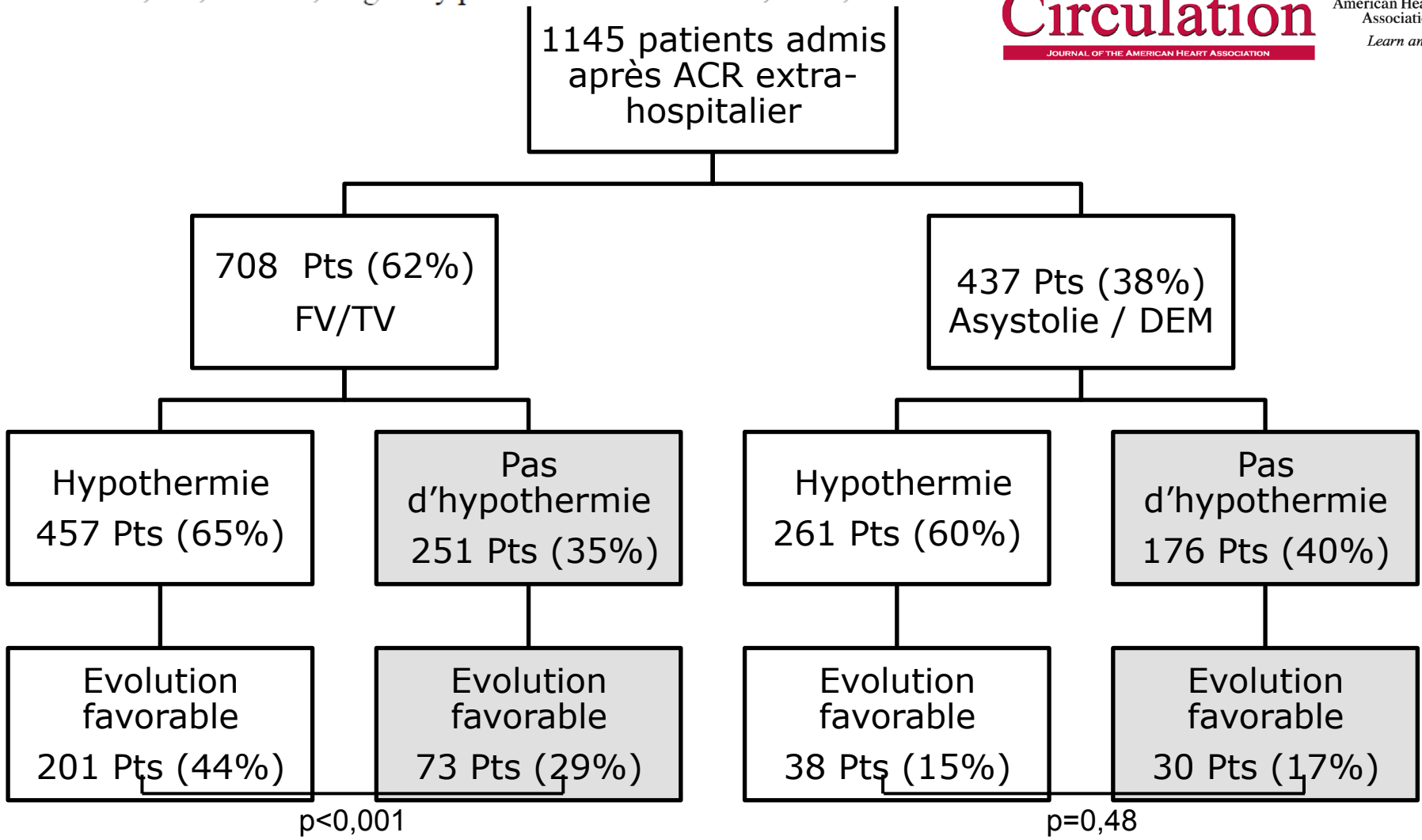
Méta-analyse (Kim Young Min, Resuscitation 2012)

« TH is associated with reduced in-hospital mortality for adults patients resuscitated from non-shockable CA. However, most of the studies had substantial risks of bias and quality of evidence was very low »

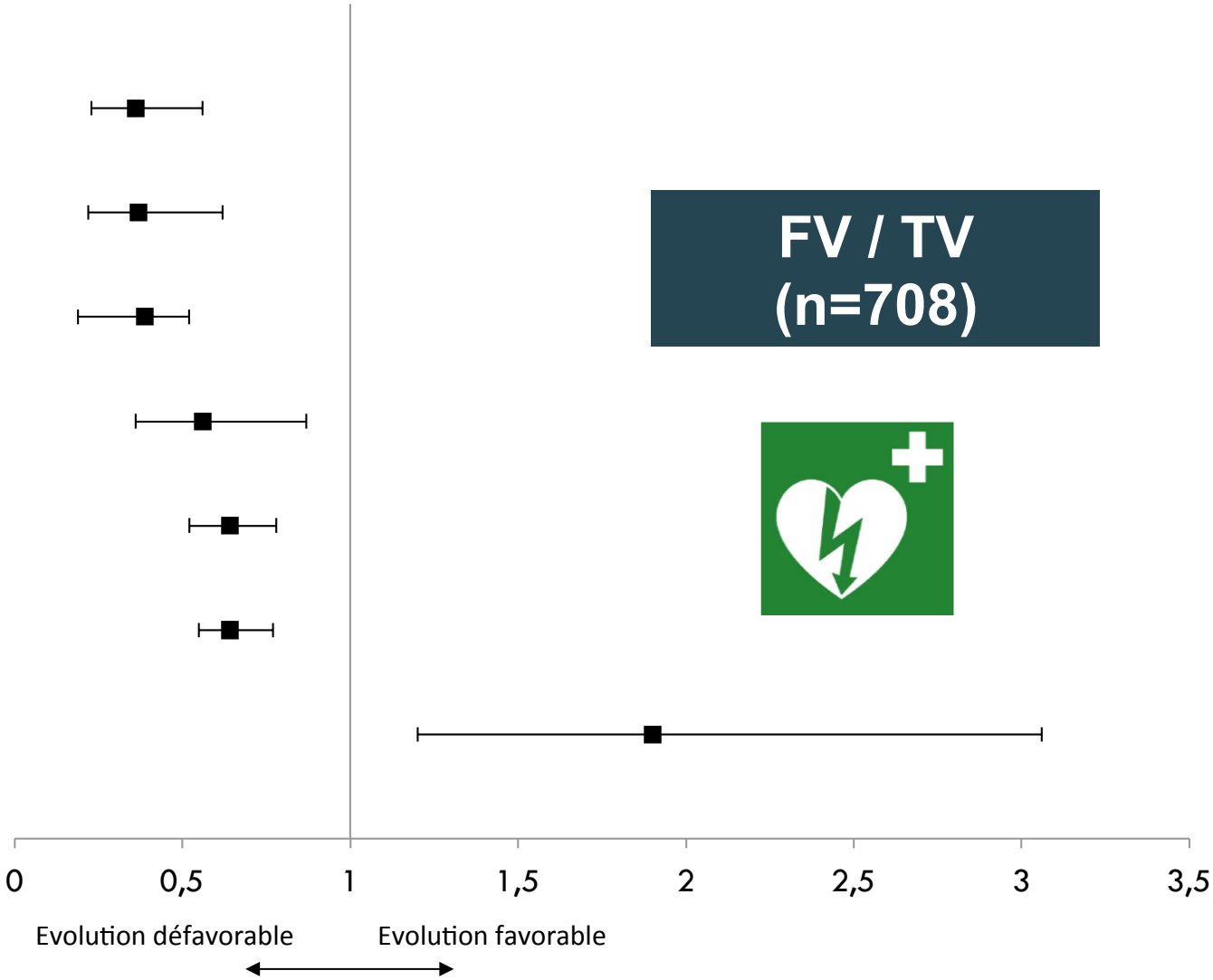
Is Hypothermia After Cardiac Arrest Effective in Both Shockable and Nonshockable Patients?: Insights From a Large Registry

Florence Dumas, David Grimaldi, Benjamin Zuber, Jérôme Fichet, Julien Charpentier, Frédéric Pène, Benoît Vivien, Olivier Varenne, Pierre Carli, Xavier Jouven, Jean-Philippe Empana and Alain Cariou

Circulation 2011;123;877-886; originally published online Feb 14, 2011;



Variables indépendantes associées au pronostic



*Low flow > 15 mn

*Adrénaline > 3 mg

*No flow ≥ 4 mn

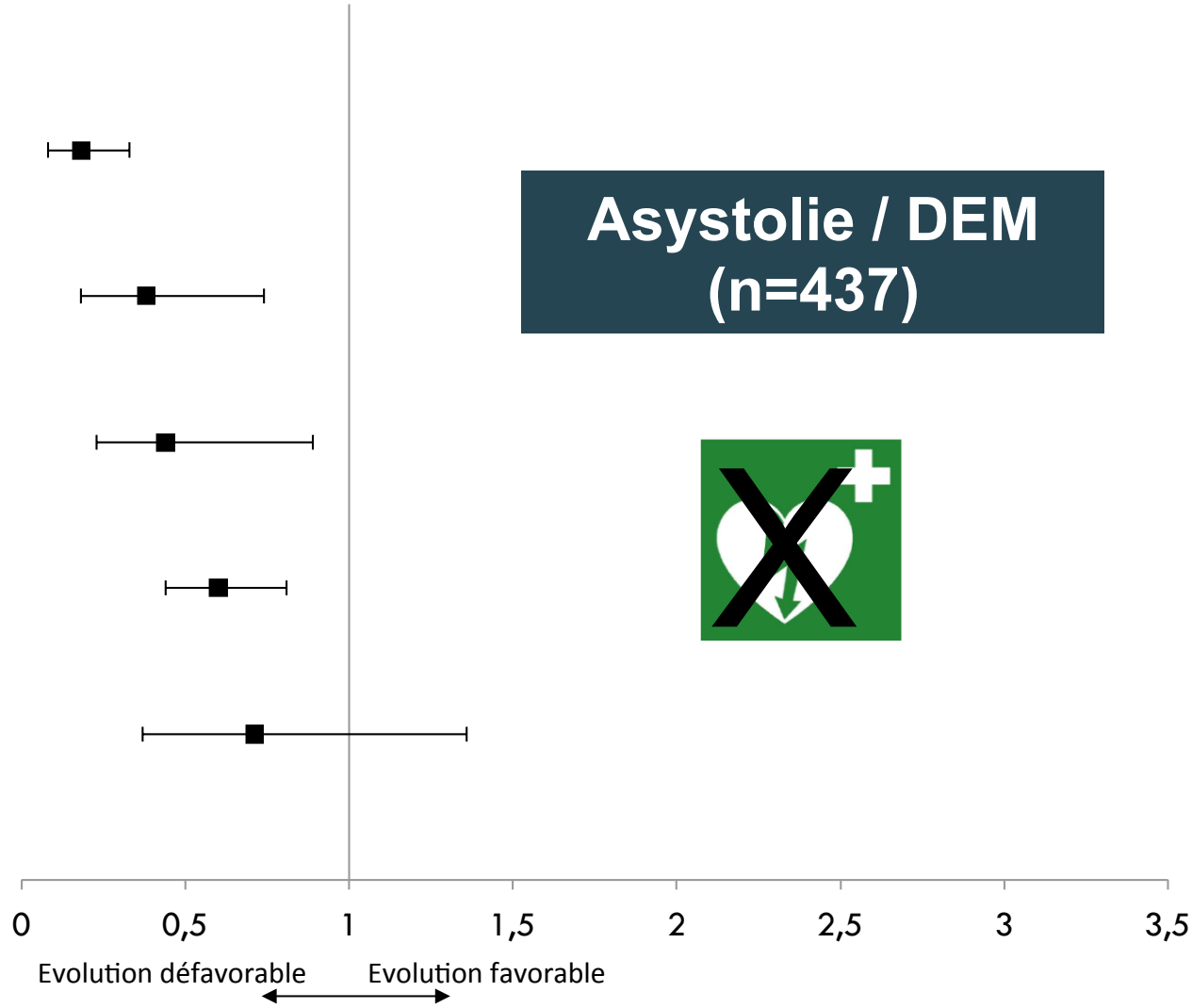
*Choc post-ACR

*Lactate (par quartile)

*Age (par quartile)

*Hypothermie thérapeutique

Variables indépendantes associées au pronostic



Asystolie / DEM (n=437)

***Low flow > 15 mn**

***Choc post-ACR**

***No flow ≥ 4 mn**

***Lactate (par quartile)**

***Hypothermie thérapeutique**

Faut-il refroidir tous les ACR ?

- Non discutable
  - ACR récupéré adulte comateux sur FV
- Option thérapeutique, recommandée pour l'instant
  - ACR récupéré adulte comateux non FV
  - ACR intra-hospitalier
- Situations à éclaircir (controversées)
  - Femme enceinte
  - Enfant
  - Coagulopathie sévère

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Hypothermie thérapeutique

Quels risques?

Surveillance des effets indésirables

Complications des études pilotes

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HACA

"Proportion of patients with any complication did not differ significantly“

The New England Journal of Medicine
Copyright © 2002 by the Massachusetts Medical Society
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*

- **Bleeding, pneumonia and sepsis** were more likely but not significantly different. In TH group, 22% more complications (not reaching significance), with a trend toward a higher incidence of sepsis in the hypothermia group (17 / 135 [13%] *vs* 9 / 138 [7%], p = 0.09).
- **Cases of pneumonia (number needed to harm 12), bleeding (NNH 14), and sepsis (NNH 16).**

INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

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.

Bernard

"Hypothermia ... is not associated with clinical significant adverse effects", but **lower CI, higher SVR, more hyperglycemia** in TH group

Hachimi-Idrissi

"No significant complications occurred... "

Resuscitation 51 (2001) 275–281
ELSEVIER
RESUSCITATION
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

Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation (Review)

THE COCHRANE COLLABORATION®

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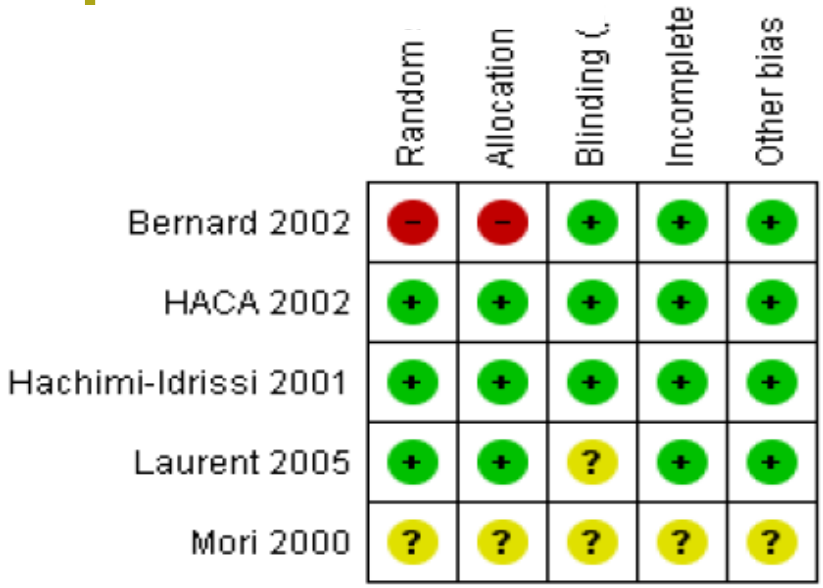
CD 2010-2012

Arrich J, Holzer M, Herkner H, Müllner M

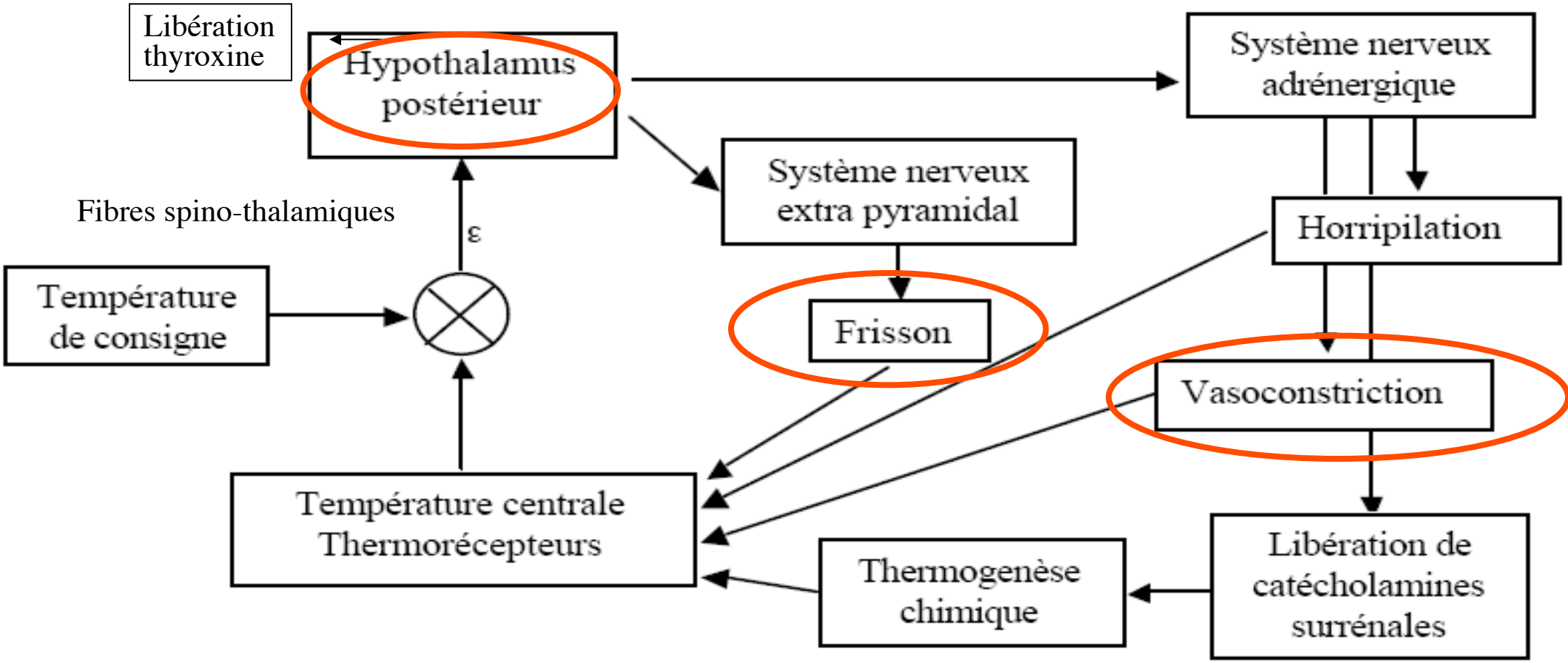
Pas de différence significative dans les effets indésirables reportés entre les patients HT et contrôle



Outcome or Subgroup	Studies	Participants	Risk Ratio (M-H, Fixed, 95%CI)
Bleeding of any severity	1	273	1.38 [0.88, 2.16]
Need for platelet transfusion	1	273	5.11 [0.25, 105.47]
Pneumonia	1	273	1.27 [0.90, 1.78]
Sepsis	1	273	1.93 [0.89, 1.78]
Pancreatitis	1	273	0.51 [0.05, 5.57]
Renal failure or oliguria	2	303	0.88 [0.48, 1.61]
Haemodialysis	2	350	1.11 [0.41, 3.01]
Pulmonary edema	1	273	1.76 [0.61, 5.12]
Seizures	1	273	0.89 [0.39, 2.02]
Lethal or long lasting arrhythmia	2	315	1.21 [0.88, 1.67]
Pressure sores	1	273	Not estimable
Significant haemorrhagic complications	1	77	Not estimable
Cardiac complications	1	77	0.16 [0.01, 3.21]
Hypokalaemia	1	42	0.91 [0.31, 2.68]
Hypophosphataemia	1	42	1.12 [0.65, 2.25]

- **Frissons, hyperactivité musculaire**
- **Infectieux** → Sepsis, immunosupppression
- **Pharmacocinétique** → ↘ activité cytochrome P450
- **Hémodynamiques** → Fc ↓, Qc ↓, hypovolémie
- **Coagulation**
  - → coagulopathie, hémorragie
  - → plaquettes, GB (PNN) ↓
- **Électrolytiques** → ↓ K, Ph, Mg, Ca → arythmies
- **Hyperdiurèse** → hypovolémie
- **Métaboliques** → hyperglycémie, cortisol ↑, ASAT ↑
  acidose (lactique) ↑, amylase ↑

Systèmes mis en jeu en réponse au froid



Frisson disparaît < 30 -32°C ou si lésions hypothalamiques

A Prospective, Observational Clinical Trial of Fever Reduction to Reduce Systemic Oxygen Consumption in the Setting of Acute Brain Injury

J. Steven Hata · Constance R. Shelsky · Bradley J. Hindman · Thomas C. Smith · Jonathan S. Simmons · Michael M. Todd

neurocritical care society Neurocrit Care
DOI 10.1007/s1
2007

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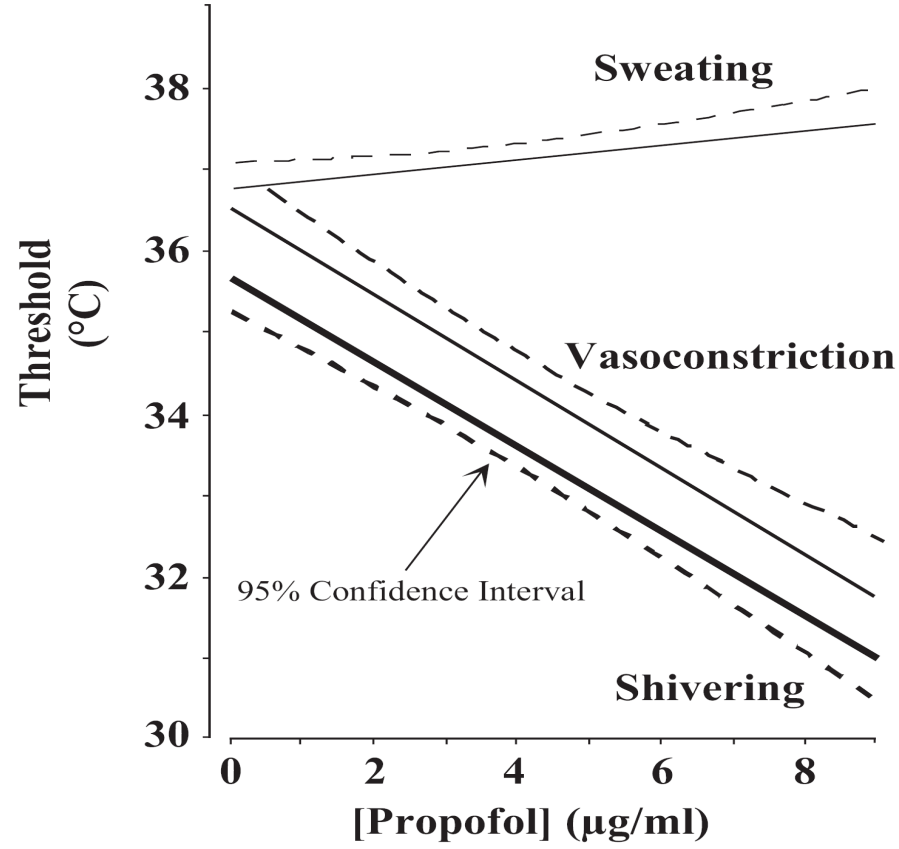
Parameters	All patients	Non-shivering	Shivering	*P*-Value
Patients	10	5	5	NS
Episodes of shivering	2 ± 3	0	5 ± 1	0.01
Temperature base (°C)	38.6 ± 0.9	39.0 ± 0.9	38.2 ± 0.7	0.16
Temperature target (°C)	36.3 ± 1.2	36.5 ± 1.6	36.2 ± 1.0	0.74
Temperature change (°C)	−2.3 ± 0.7	−2.5 ± 0.8	−2.0 ± 0.6	0.29
% Temperature change	−5.9 ± .9	−7.0 ± 2.4	−5.3 ± 1.6	0.34
VO2 baseline (ml/min)	378 ± 98	415 ± 123	341 ± 56	0.26
VO2 target (ml/min)	367 ± 152	308 ± 115	426 ± 173	0.24
VO2 change (ml/min)	−11 ± 162	−107 ± 71	84 ± 177	0.05
% VO2 change	0 ± 50	−27 ± 18	27 ± 58	0.04
VCO2 baseline (ml/min)	272 ± 44	292 ± 41	252 ± 40	0.15
VCO2 target (ml/min)	282 ± 120	221 ± 31	343 ± 149	0.06
VCO2 change (ml/min)	−10 ± 122	−72 ± 22	91 ± 128	0.01
% VCO2 change	5 ± 44	−24 ± 5	34 ± 48	0.03

Température, VO_2, VCO_2 et frissons = liés

Anesthésie et thermorégulation

- Halogénés
- Propofol
- Opioides
- Non opioides
  - Nefopam
  - Clonidine
  - Dexmedetomidine
  - Buspirone



Matsukawa T et al. *Anesthesiology* 1995

DYSFONCTION MYOCARDIQUE & HYPOTHERMIE

Dysfonction systolique mais pas de dysfonction diastolique (12 cochons jusqu'à 25°C) :

Baisse: DC, MAP, VES, indices de contractilité, VTDVG, VTSVG

Hausse: RVS, CaO_2 et CvO_2 (VO_2)

PTDVG constante

Après réchauffement:

VO_2 et Qc: retour à la normale normale

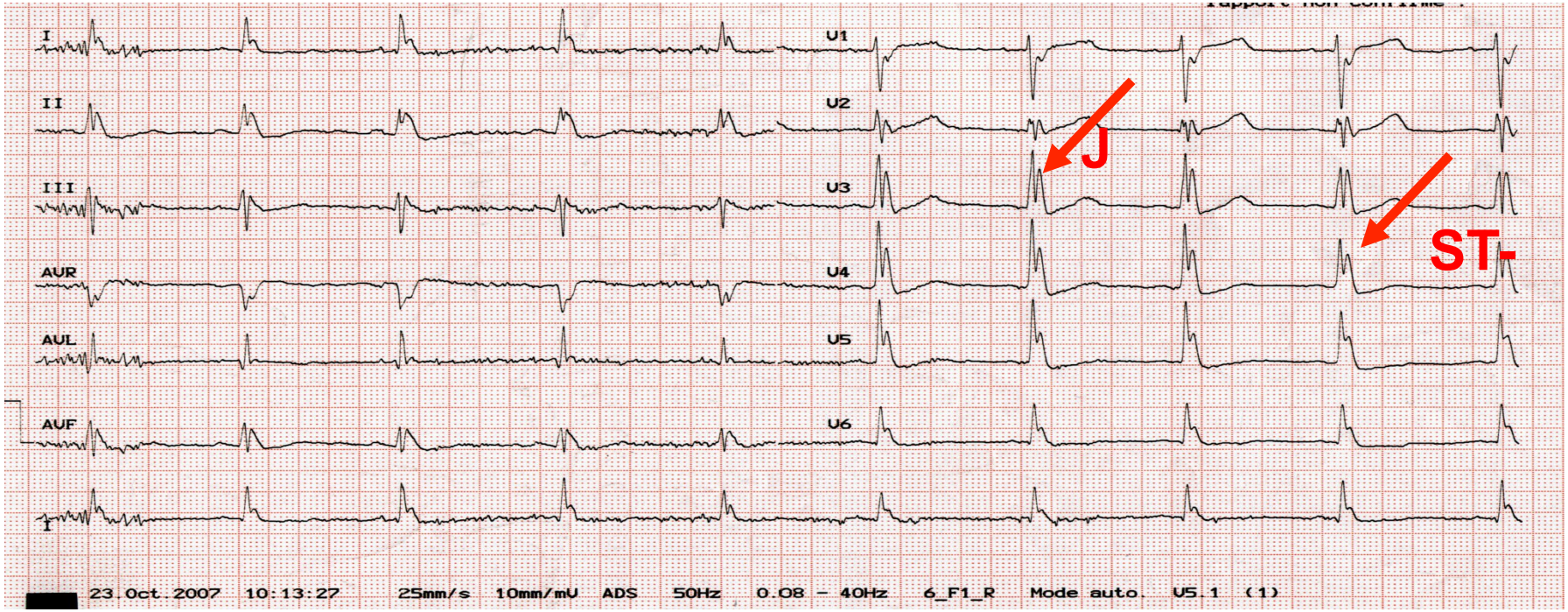
Tachycardie compensatrice

PAM, VES, RVS restent + bas qu'initialement

TnT augmente

CRITICAL CARE

Filseth 2010



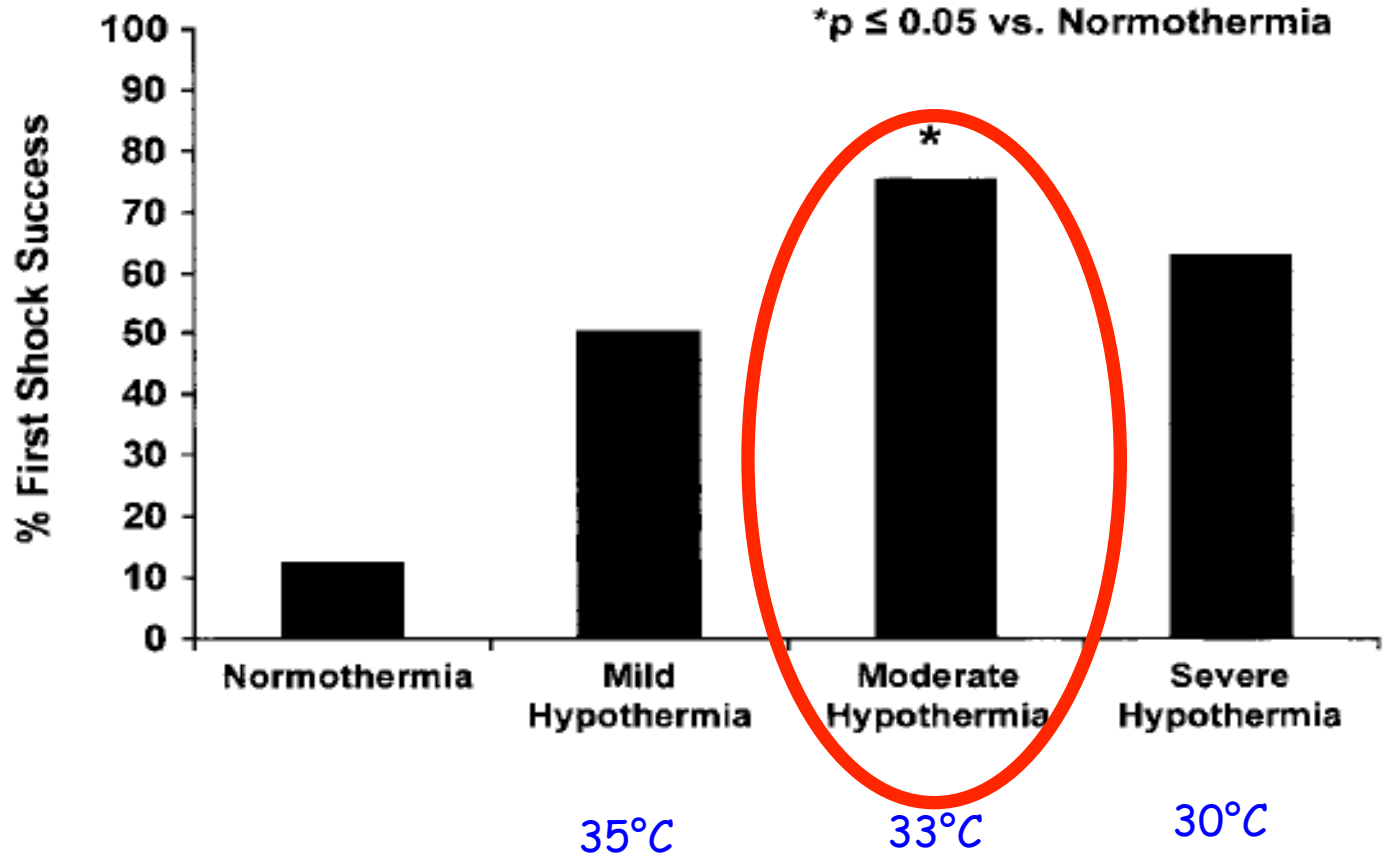
Onde en dos de chameau (Δ inversé) ou onde "J" d'Osborn : ressaut avec épaulement (crochetage) du bas de la portion descendante de R

Bradycardie sinusale, allongement de PR et QT. TDC. AC/FA lente, TDRV (si < 30°C)

Hypothermia Improves Defibrillation Success and Resuscitation Outcomes From Ventricular Fibrillation

Kimberly A. Boddicker, Yi Zhang, M. Bridget Zimmerman, Loyd R. Davies and Richard E. Kerber

Circulation 2005;111;3195-3201; originally published online Jun 13, 2005;
DOI: 10.1161/CIRCULATIONAHA.104.492108



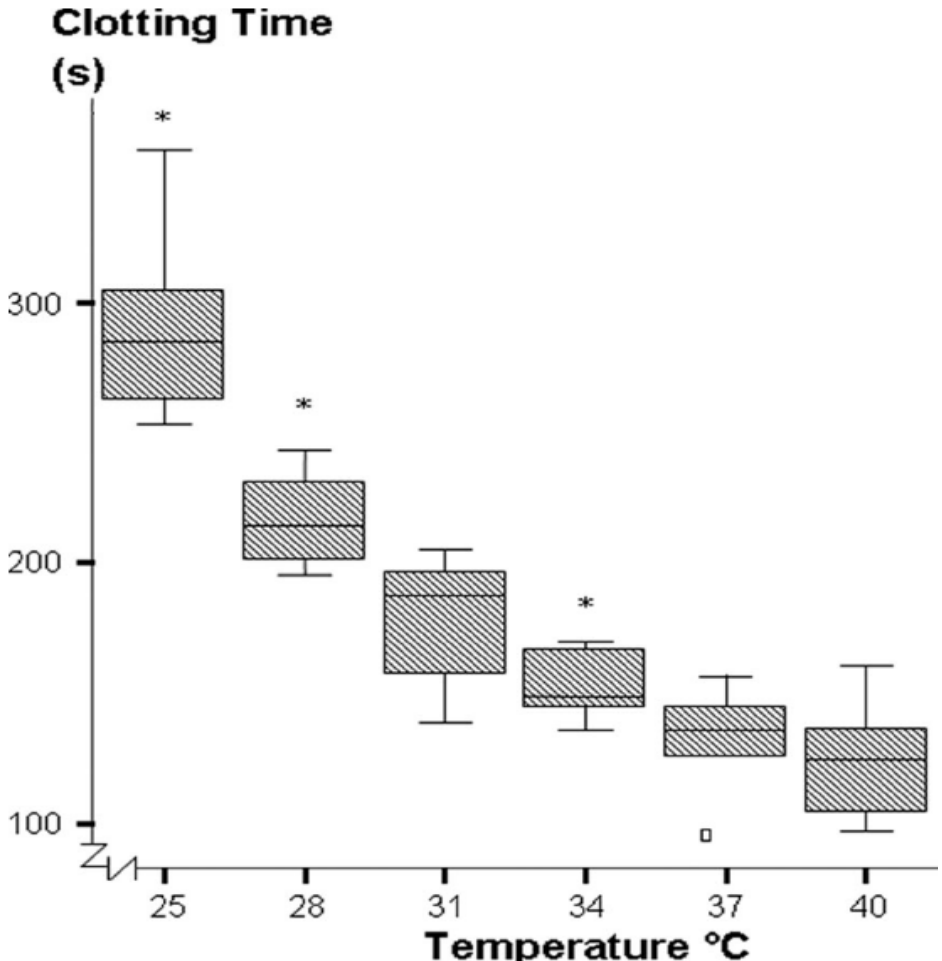
32 porcs
FV = 8 min sans CPR

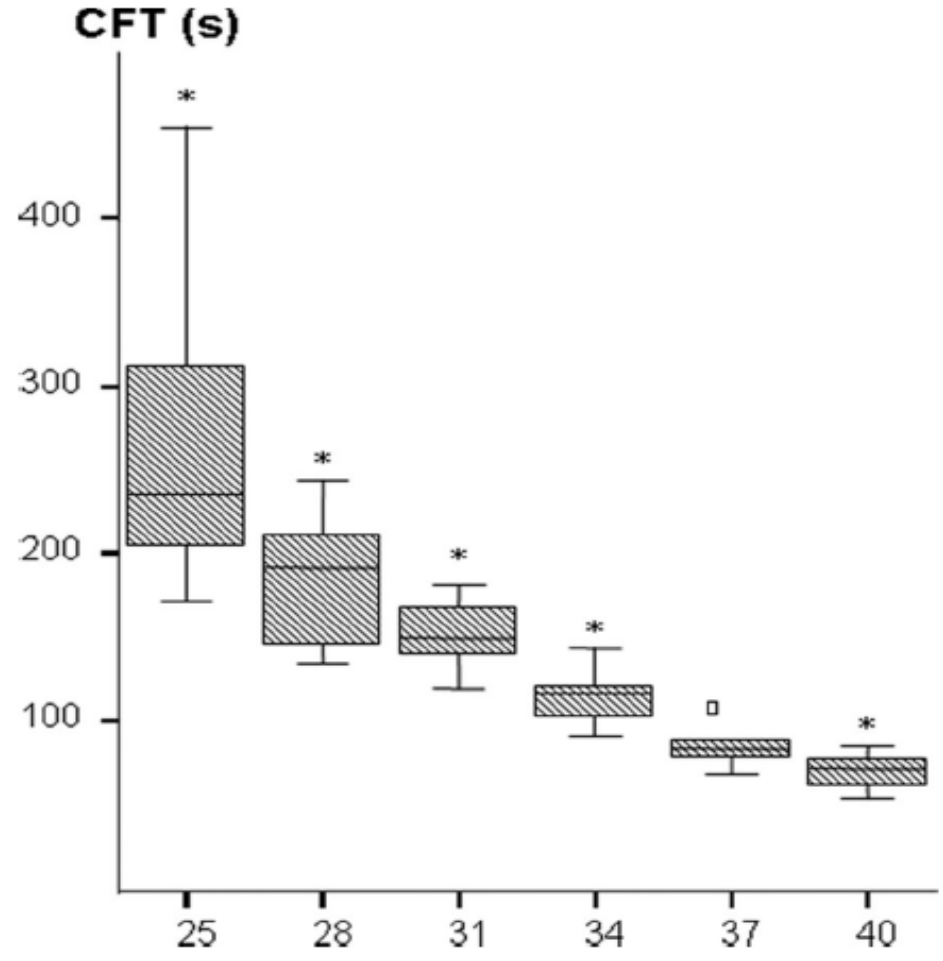
A Thromboelastometric Evaluation of the Effects of Hypothermia on the Coagulation System

Malin Rundgren, MD*

Martin Engström, MD, PhD†

(Anesth Analg 2008;107:1465–8)





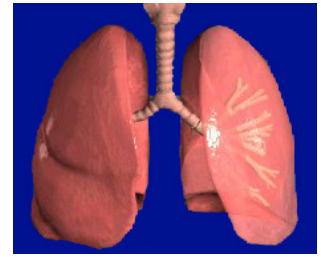
Hypothermie & poumon

Diminution de l'activité ciliaire de l'épithélium bronchique

Effondrement des capacités de résorbtion liquidienne de l'épithélium alvéolaire (Sakuma Appl Physiol 1996)

Modification de l'humidification des voies aériennes si VM (diminution si filtre humidificateur et majoration si humidificateur chauffant+++) (Lellouche ICM 2006)

Lésion inflammatoire de la barrière capillaro-alvéolaire pendant le réchauffement (Taniguchi ICM 2007)



HYPOTHERMIE : ↗ solubilité plasmatique O_2 et CO_2

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α-Stat respect de l'alcalose hypocapnique ; interprétation GDS = en normothermie

pH-Stat correction à la température réelle (en VM : on hypoventile)

Best evidence topic - Cardiopulmonary bypass

Is pH-stat or alpha-stat the best technique to follow in patients undergoing deep hypothermic circulatory arrest?

Khairul Anuar Abdul Aziz*, Ayo Meduoye

INTERACTIVE CARDIOVASCULAR AND THORACIC SURGERY

2010

16 études : pH-stat en pédiatrie et α-stat chez l'adulte

6 en faveur de α-stat, 3 pour pH-stat, 4 NS pour le métabolisme cérébral

3 en faveur de α-stat, 3 pour pH-stat, 3 NS pour le devenir neurologique

Briot et al. Réanimation 2010.

Tremey et Vigue B. AFAR. 2004.

Meilleure autorégulation cérébrale en α-stat et plus simple

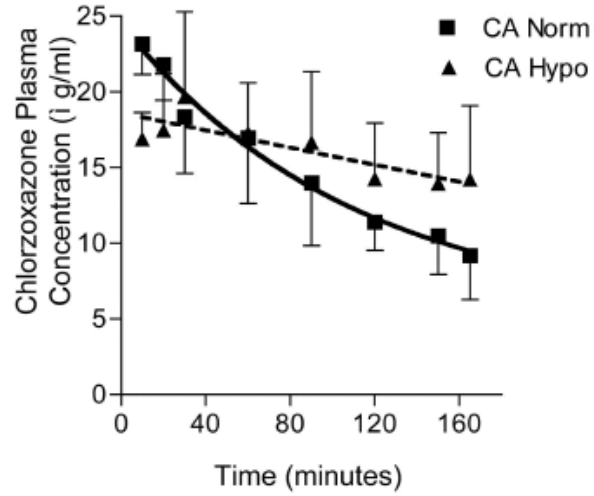
annales françaises d'ANESTHÉSIE et de RÉANIMATION

Therapeutic hypothermia-induced pharmacokinetic alterations on CYP2E1 chlorzoxazone-mediated metabolism in a cardiac arrest rat model

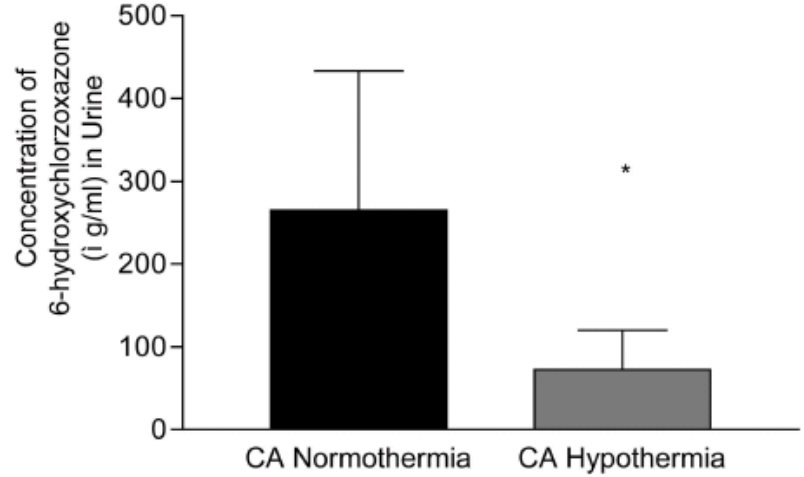
	37°	30°
V_{max}, nmol/mg/min	2.27 ± 0.22	2.64 ± 0.48
K_m, μM	255 ± 52	551 ± 150[a]
Cl_{int}, mL/min/mg protein	0.00890 ± 0.0017	0.00500 ± 0.00040[a]
Cl_s estimated, mL/min	2.10 ± 0.39	1.19 ± 0.21[a]

V_{max}, maximum velocity; K_m, Michaelis-Menten constant; Cl_{int}, intrinsic clearance; Cl_s, systematic clearance.

A



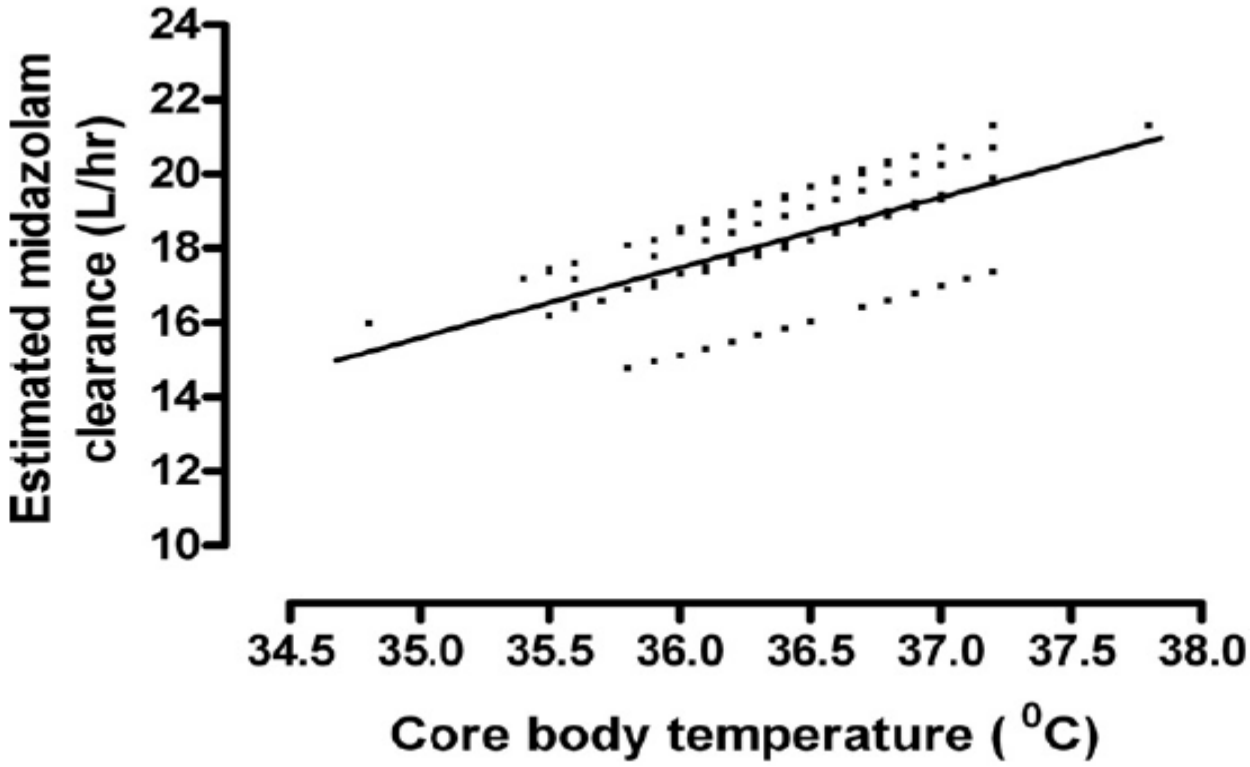
B

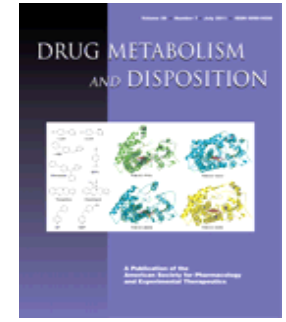


Tortorici, Crit Care Med 2006

Mild Hypothermia Alters Midazolam Pharmacokinetics in Normal Healthy Volunteers

David Hostler, Jiangquan Zhou, Michael A. Tortorici, Robert R. Bies, Jon C. Rittenberger, Philip E. Empey, Patrick M. Kochanek, Clifton W. Callaway, and Samuel M. Poloyac





Drug Metabolism and Disposition 2010

Adverse events and their relation to mortality in out-of-hospital cardiac arrest patients treated with therapeutic hypothermia*

Niklas Nielsen, MD, PhD; Kjetil Sunde, MD, PhD; Jan Hovdenes, MD, PhD; Richard R. Riker, MD; Sten Rubertsson, MD, PhD; Pascal Stammet, MD; Fredrik Nilsson, PhD; Hans Friberg, MD, PhD; the Hypothermia Network

Crit Care Med 2011 Vol. 39, No. 1

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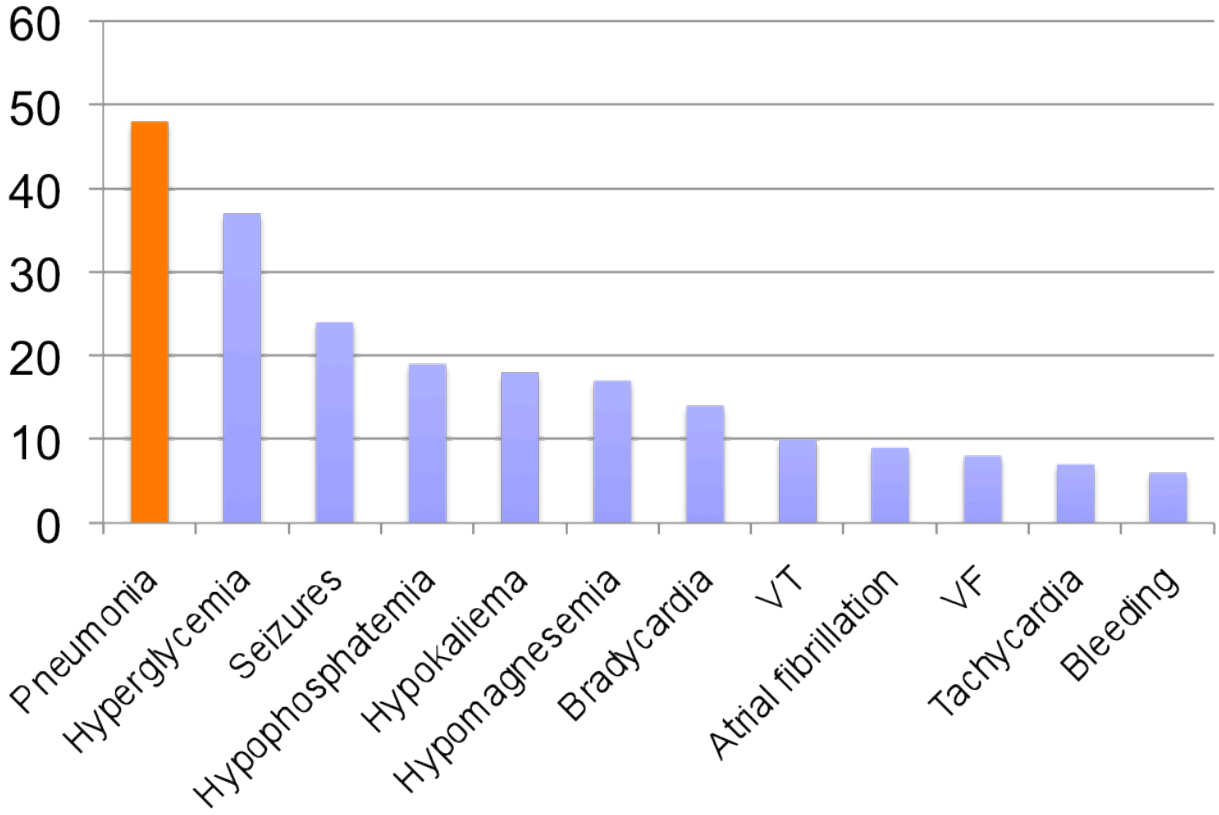
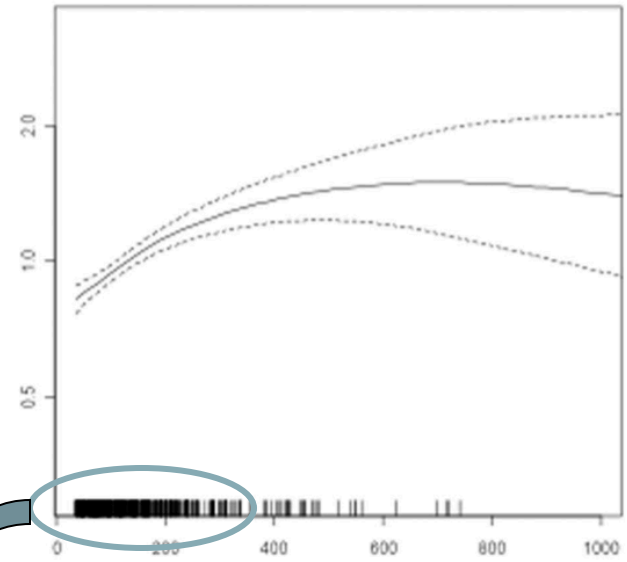
Fréquence des effets indésirables



Pneumonie

OR



Durée de séjour (h)

"Early onset pneumonia= Pneumonie précoce"

Complications infectieuses et hypothermie

Double aspect du potentiel rôle de l'hypothermie :

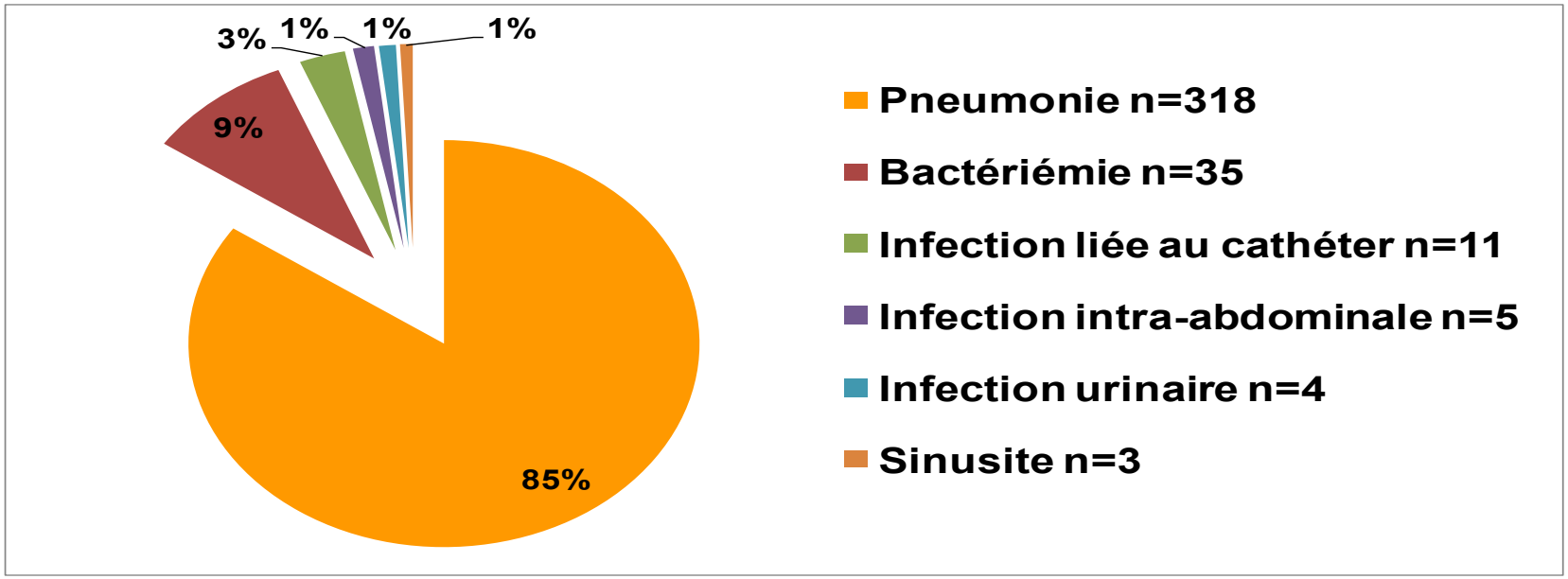
- ***Altère les défenses immunitaires***
  - **Inhibition de la sécrétion des cytokines pro-inflammatoires**
  - **Inhibition de la phagocytose et de la migration leucocytaire**
  - **Insulino-résistance et hyperglycémie** (Beiling Anesthesio 1998, Torossian CCM 2004, Xiao CCM 2005, Polderman Lancet 2008)

- ***Modifie les critères diagnostiques usuels***

Infectious complications in out-of-hospital cardiac arrest patients in the therapeutic hypothermia era*

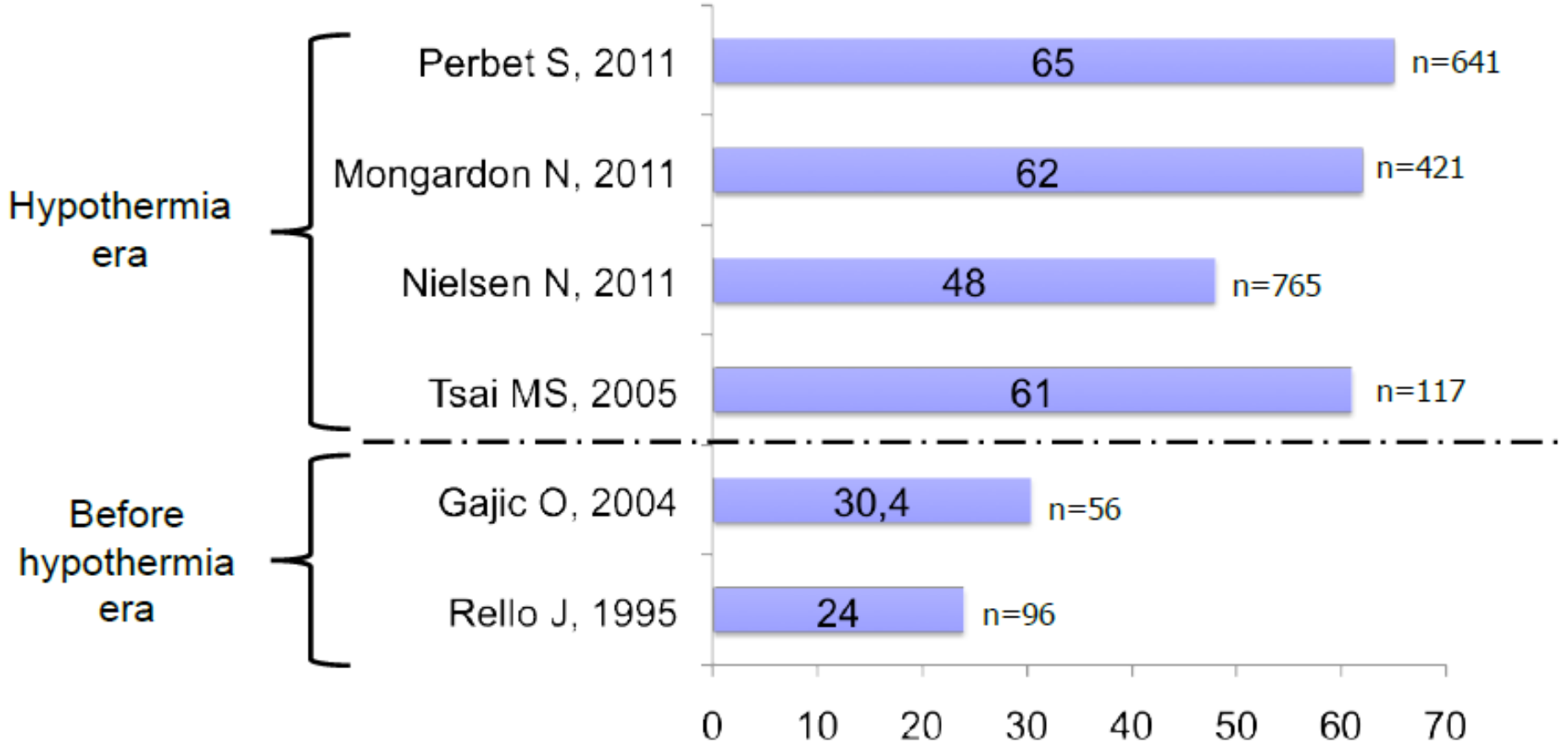
Nicolas Mongardon, MD; Sébastien Perbet, MD; Virginie Lemiale, MD; Florence Dumas, MD; Hélène Poupet, MD; Julien Charpentier, MD; Frédéric Péne, MD; Jean-Daniel Chiche, MD; Jean-Paul Mira, MD; Alain Cariou, MD

281/421 patients (67%) ont développé un total de 373 épisodes infectieux:



Crit Care Med 2011 Vol. 39, No. 6

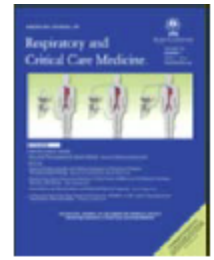
Incidence des pneumonies



Early-Onset Pneumonia after Cardiac Arrest

Characteristics, Risk Factors and Influence on Prognosis

Sébastien Perbet[1,2], Nicolas Mongardon[1,5], Florence Dumas[3,9], Cédric Bruel[2,8], Virginie Lemiale[1], Bruno Mourvillier[2], Pierre Carli[4,5], Olivier Varenne[5,6], Jean-Paul Mira[1,5,7], Michel Wolff[2,8], and Alain Cariou[1,5,9]



Am J Respir Crit Care Med Vol 184. pp 1048–1054, 2011

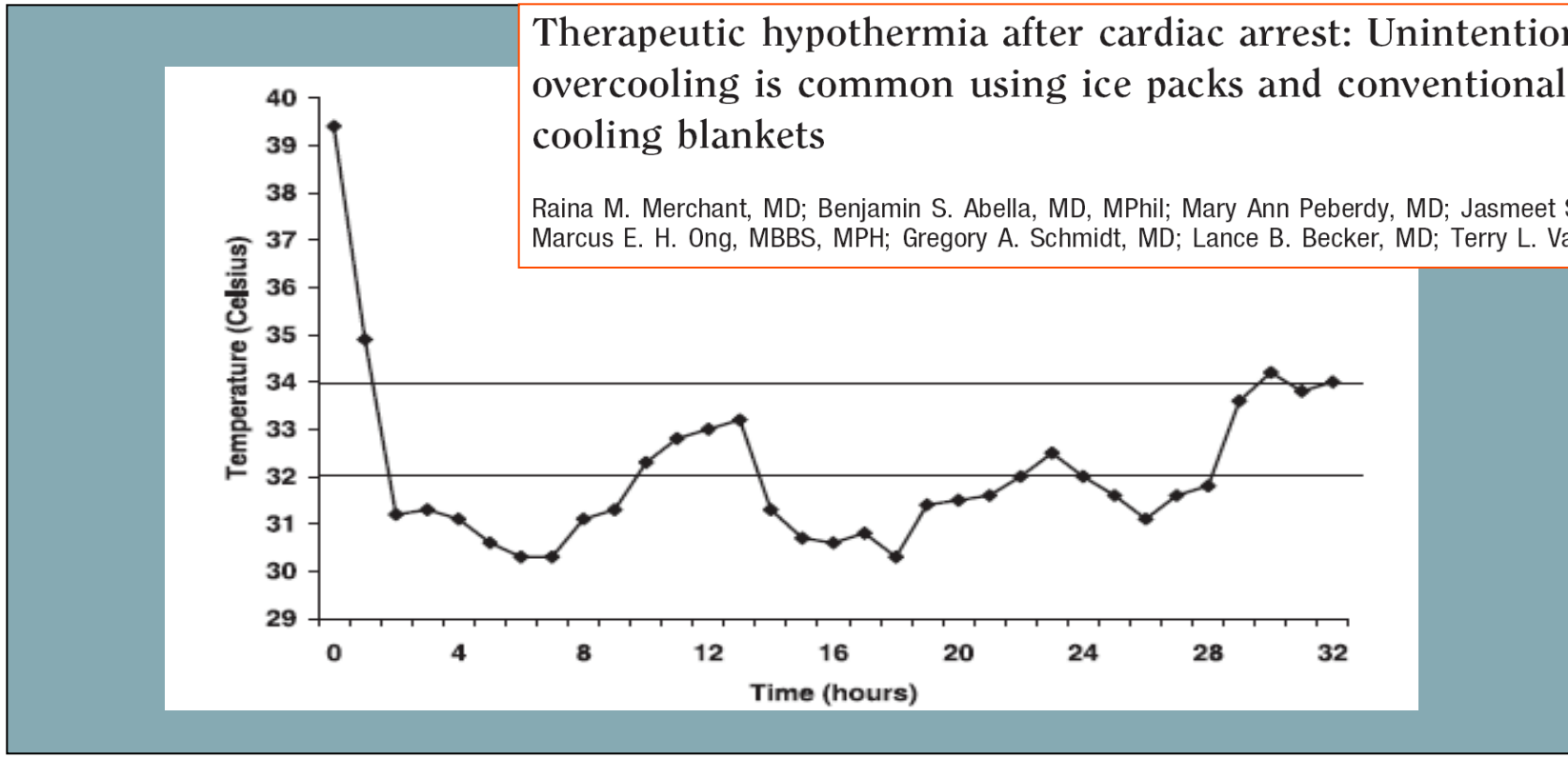
	Odds Ratio	Std. Err.	z	[95% Conf.Interval]	p value
Hypothermia	1.90	0.38	3.20	1.28-2.80	0.001

	Total ($n = 641$)	Pneumonia ($n = 419$)	No Pneumonia ($n = 222$)	*P* Value
LOS in ICU, d*	7.5	7.9 ± 7.2	6.7 ± 7.6	0.001
MV duration, d*	5.4	5.7 ± 5.9	4.7 ± 6.2	0.001
VAP, *n* (%)	91 (14)	64 (18)	27 (14)	0.25
Hospital survival, *n* (%)	253 (39)	172 (41)	81 (36)	0.26
CPC1/2, *n* (%)	238 (37)	161 (38)	77 (34)	0.35

La conséquence dans la vraie vie: objectifs dépassés

Therapeutic hypothermia after cardiac arrest: Unintentional overcooling is common using ice packs and conventional cooling blankets

Raina M. Merchant, MD; Benjamin S. Abella, MD, MPhil; Mary Ann Peberdy, MD; Jasmeet Soar, MD; Marcus E. H. Ong, MBBS, MPH; Gregory A. Schmidt, MD; Lance B. Becker, MD; Terry L. Vanden Hoek, MD



Critical Care Med 2006

➔ Fenêtre thérapeutique étroite?

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Hypothermie thérapeutique

Comment?

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JOFFRE-DUPUYTREN - EMILE ROUX

2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Laurie J. Morrison, Co-Chair*; Charles D. Deakin, Co-Chair*; Peter T. Morley; Clifton W. Callaway; Richard E. Kerber; Steven L. Kronick; Eric J. Lavonas; Mark S. Link; Robert W. Neumar; Charles W. Otto; Michael Parr; Michael Shuster; Kjetil Sunde; Mary Ann Peberdy; Wanchun Tang; Terry L. Vanden Hoek; Bernd W. Böttiger; Saul Drajer; Swee Han Lim; Jerry P. Nolan; on behalf of the Advanced Life Support Chapter Collaborators

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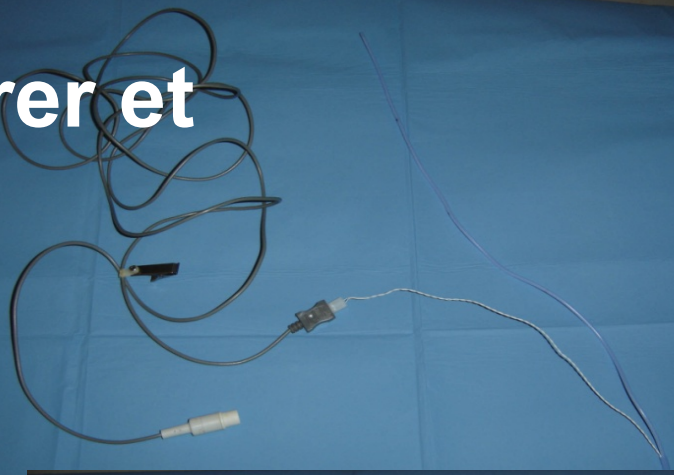
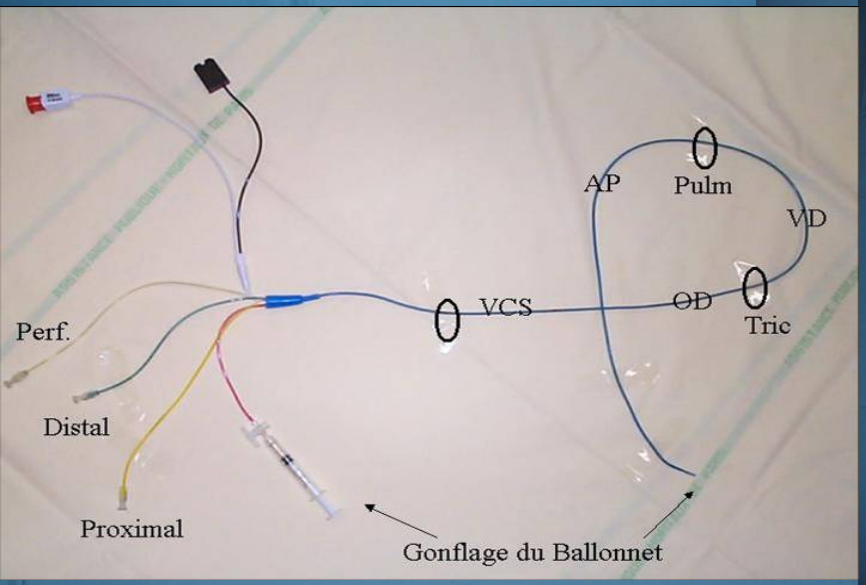
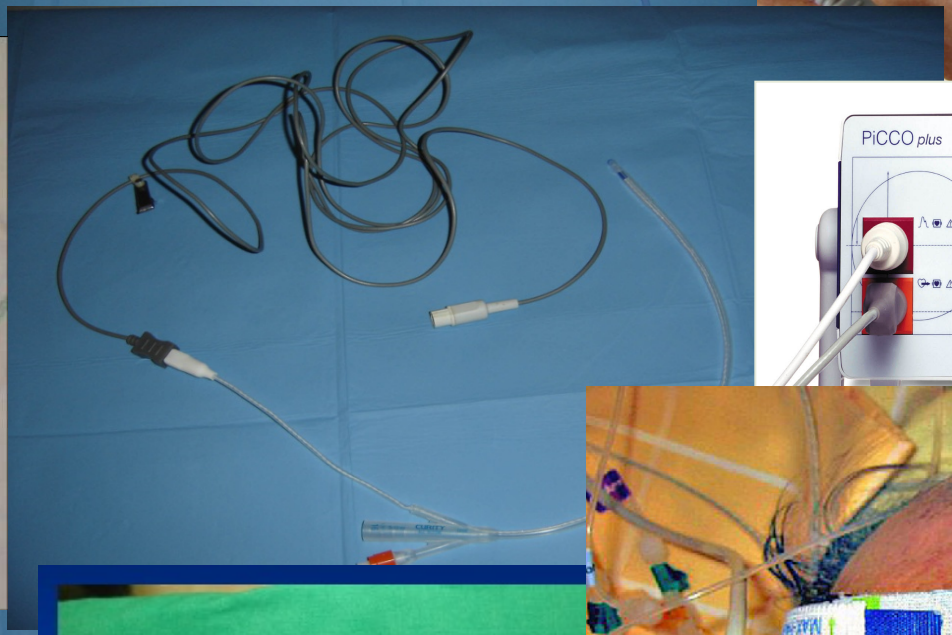
Critical Knowledge Gaps Related to Post–Cardiac Arrest Hypothermia Treatment

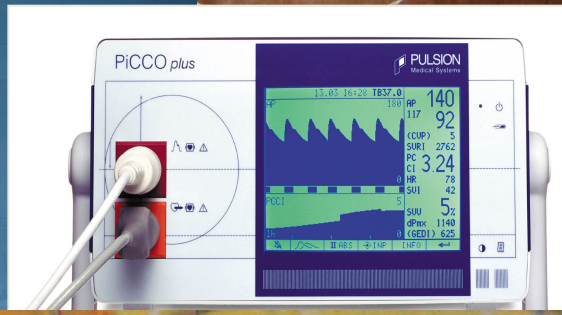
- The **optimal method, onset, duration and rewarming rate, and therapeutic window** remain unknown.
- **Clinical and cost comparisons** are required of the methods used for inducing and maintaining therapeutic hypothermia.

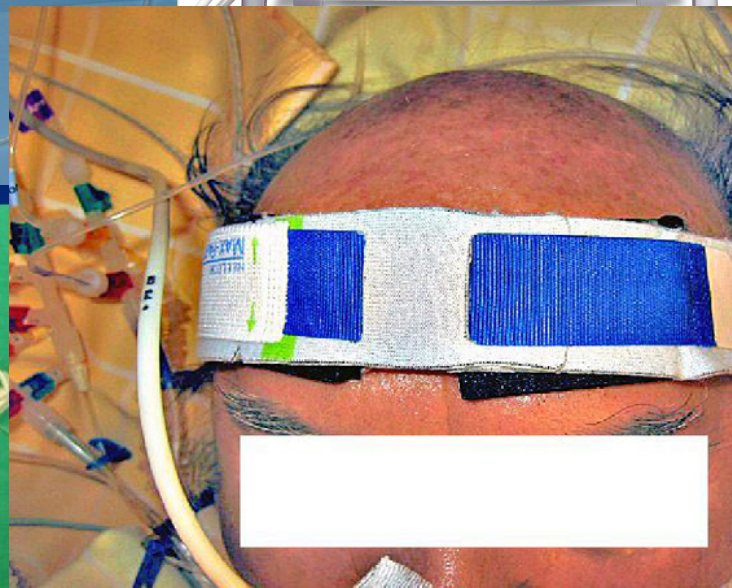
Comment monitorer et mesurer?



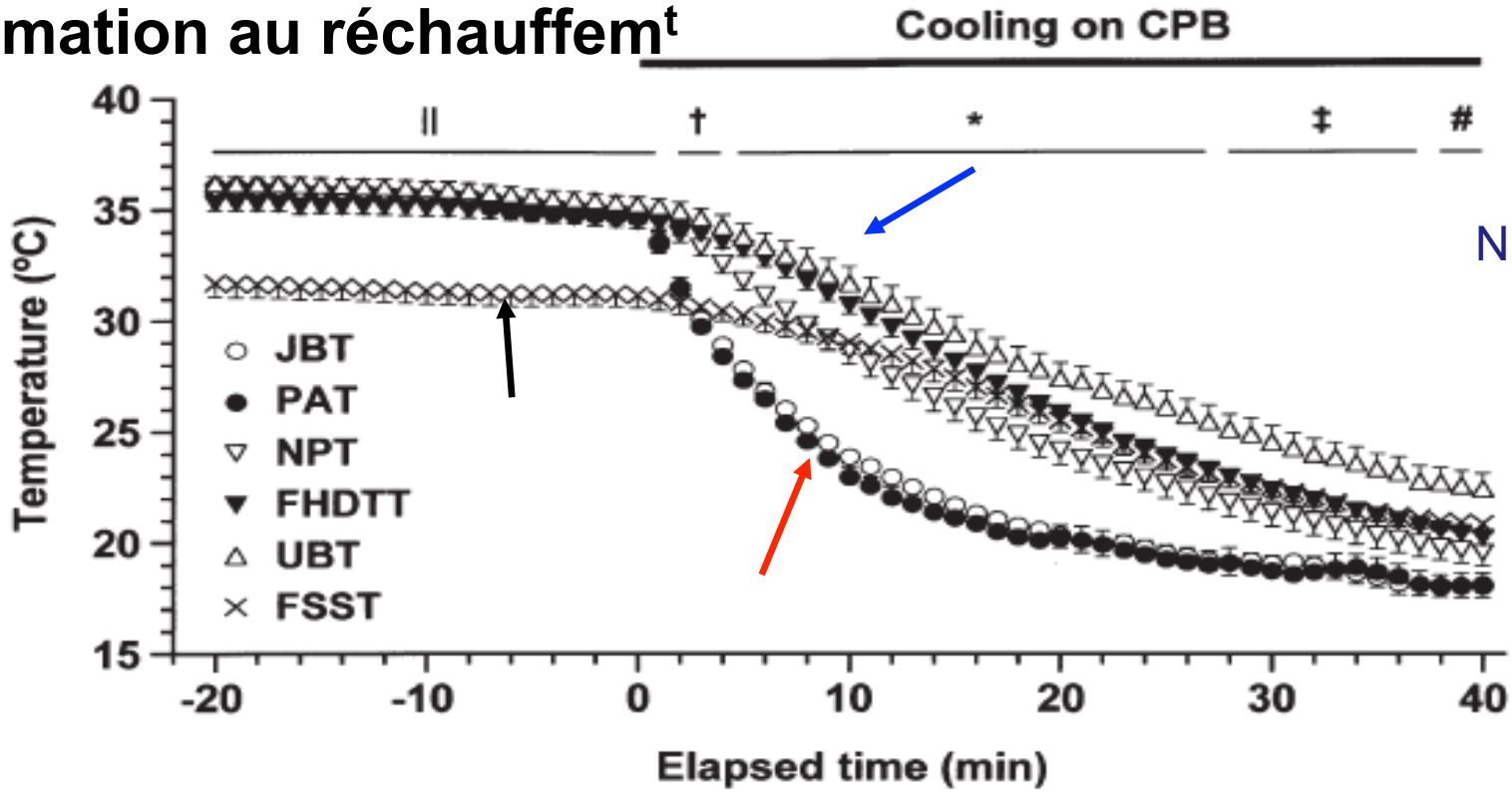








Sur estimation au refroidissemt ; sous estimation au réchauffemt



N=20

Akata et al. J Thorac Cardiovasc Surg. 2007

Nussmeier Anesth Analg 2006

Fiabilité mesure t°

Bulbe jugulaire : JBT > artère pulmonaire : PAT

Naso-pharyngienne : NPT ou ESO > vésicale : UBT

Tympanique (peu fiable : cerumen…)

Rectale (peu fiable : isolation par matière fécale)

Cutanée : FSST (pas fiable)

QUELLE TECHNIQUE UTILISER ?

Refroidissement “conventionnel” externe (tunnel, glace)?
Refroidissement externe (couverture à eau ou air)?
Refroidissement endovasculaire?
Perfusion de fluides glacés?
Circulation extra-corporelle?

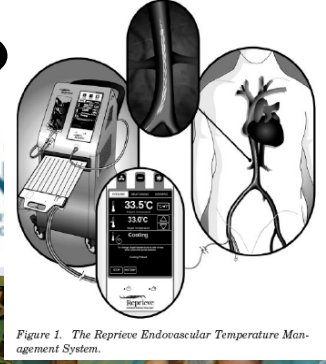
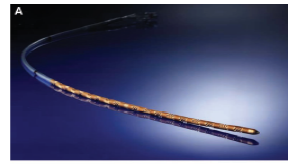
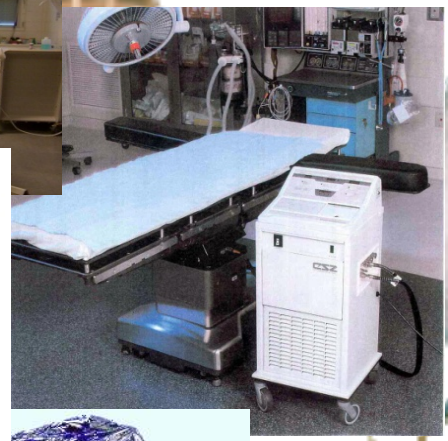
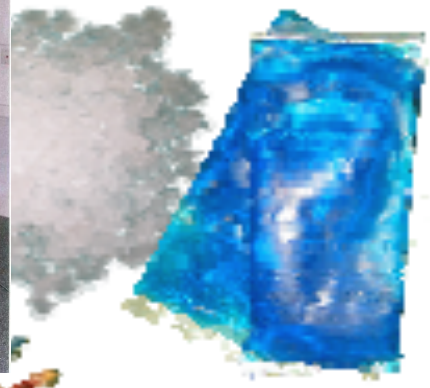


Figure 1. The Reprieve Endovascular Temperature Management System.

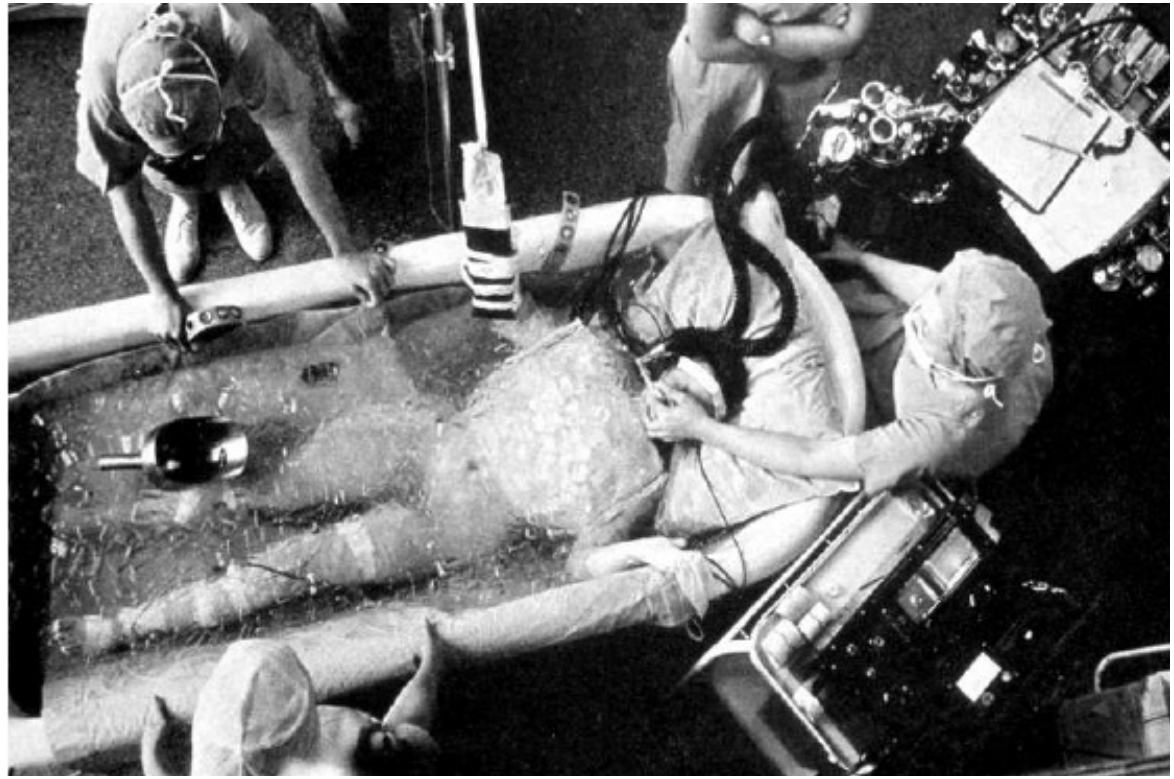






Première description après ACR

Benson DW, Williams GR, Spencer FC.
The use of hypothermia after cardiac arrest.
Anesthesia Analgesia. 1958; 38:423–4.



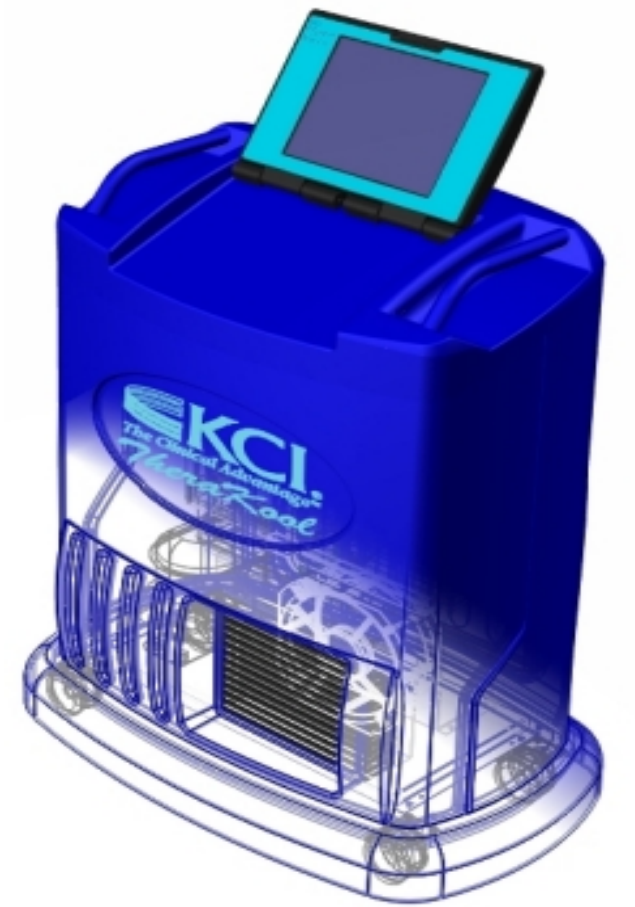
Méthodes de refroidissement

Méthodes	Vitesse (°C/h)	Maintien de l'hypothermie	Utilisable pour réchauffement	Coût
Couverture à air froid	Lent	+/-	+++	+
Packs de glace	Lent	++	0	0
Tunnel glacé	1.1	++	0	0
Casque réfrigérant	1.5	+	0	++
Lit liquide froid circul.	1,5-3	+++	+++	++
Bain froid	9,3	+++	0	?
Lit à air refroidissant	-	++	+++	?
Perfusion sérum froid	0,6-2,5	0	0	+
KT endovasculaire	2	+++	+++	+++
CEC	>4	+++	+++	+++

Lemiale V, Deye N, Cariou A. Traité de Réanimation Médicale 2009

Refroidissement externe

Cooling externe : de multiples systèmes…



Automated peritoneal lavage: an extremely rapid and safe way to induce hypothermia in post-resuscitation patients

Critical Care 2013, **17**:R31

Monique C de Waard[1*†], Hagen Biermann[1†], Stijn L Brinckman[2], Yolande E Appelman[2], Ronald H Driessen[1], Kees H Polderman[3], Armand RJ Girbes[1] and Albertus Beishuizen[1]

Table 2 Mild therapeutic hypothermia timing and temperature data

	Control group	PL group	*P*-value
First temperature measured (°C)	35.0 (34.0 to 35.6)	35.0 (34.9 to 35.7)	0.14
Induction:			
Start time (min)	74 (52 to 130)	169 (137 to 187)*	0.0001
Time to target temperature of 32.5°C (min)	150 (112 to 240)	30 (19 to 60)*	<0.0001
Cooling rate (°C/h)	0.9 (0.5 to 1.3)	4.1 (2.2 to 8.2)*	0.01
Maintenance:			
Mean temperature (°C)	32.4 (32.1 to 32.8)	32.4 (32.4 to 32.5)	0.28
Lowest temperature (°C)	31.2 (31.0 to 31.7)	32.2 (32.2 to 32.3)*	<0.0001
Temperature <31°C, n (%)	23 (23)	0 (0)	0.066
Temperature variability (°C)	0.45 (0.38 to 0.70)	2.20 (1.70 to 3.05)*	<0.0001
Re-warming:			
Duration to reach 36.5°C (h)	15.7 (11.0 to 23.0)	12.8 (10.0 to 14.8)*	0.005

Encore une autre méthode…

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Traitements associés

Sédation/analgésie

Ventilation mécanique

Maintien de l'homéostasie

Prévention du frisson

Sédation et analgésie

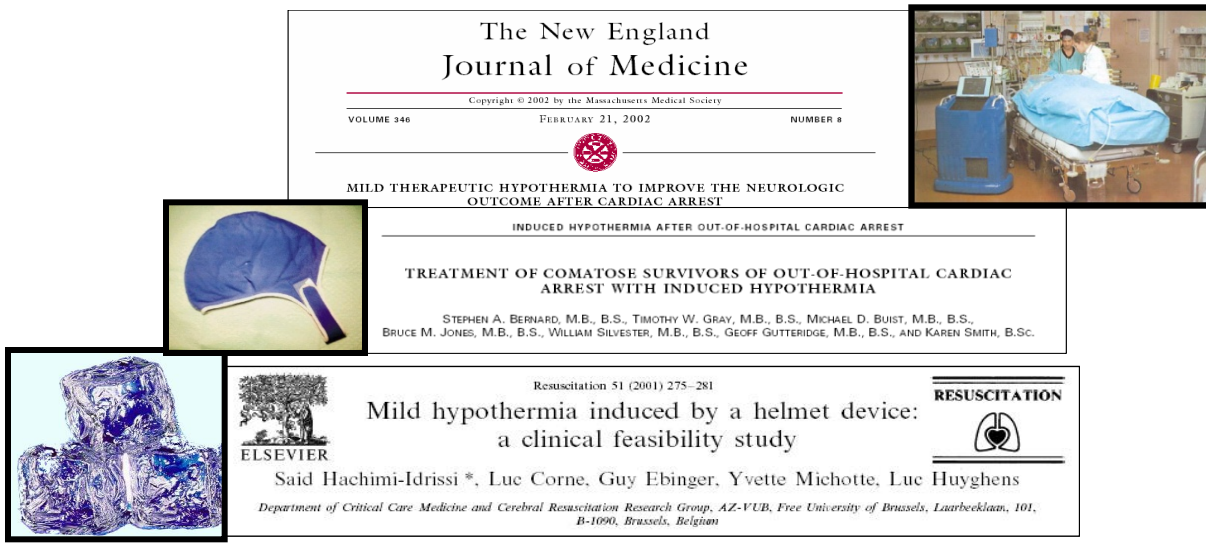
HACA et Hachimi-Idrissi

Midazolam 0.13 mg/kg/h

Fentanyl 2µg/kg/h

Bernard

Midazolam 2-5 mg



Relaxation

HACA et Hachimi-Idrissi

Pancuronium 0.1 mg/kg toutes les 2 h

Bernard

Vecuronium 8-12 mg

Practical protocol for treatment of patients

Sédation
Analgésie
Curarisation, au moins pour l'induction; alternative: Mg

Normoxie en ventilation mécanique (contrôlée)

Normocapnie

Contrôle de la PA (et du débit sanguin cérébral), euvolémie (PAS > 90 mmHg et PAM ≥ 65 mmHg)

Normonatrémie
Contrôle des désordres métaboliques (normo-K+, Mg, Ph)
Normoglycémie (protocole d'insuline)
Position demi-assise (30°)
Prévention des complications :
traitement thrombo-embolique, anti-arrhythmique

Sterz F, Behringer W, Holzer M. 2006. Global hypothermia for neuroprotection. Acute Carddiac Care.
Sunde K. Resuscitation. 2007. Implementation of a standardised protocol for post resuscitation care.
Deye N. Textbook "Acute heart failure syndromes" . 2007. Acute cardiac failure & neuroprotection.
Kupchnick NL. CCM. 2009. Suppl. Implementation of a TH protocol.
Seder DB, Van der Kloot TE. CCM. 2009. Suppl. Methods of cooling. Practical aspects.

GROUPE HOSPITALIER

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American Heart Association
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2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Laurie J. Morrison, Co-Chair*; Charles D. Deakin, Co-Chair*; Peter T. Morley; Clifton W. Callaway; Richard E. Kerber; Steven L. Kronick; Eric J. Lavonas; Mark S. Link; Robert W. Neumar; Charles W. Otto; Michael Parr; Michael Shuster; Kjetil Sunde; Mary Ann Peberdy; Wanchun Tang; Terry L. Vanden Hoek; Bernd W. Böttiger; Saul Drajer; Swee Han Lim; Jerry P. Nolan; on behalf of the Advanced Life Support Chapter Collaborators

Blood Glucose Control

Treatment Recommendation

- Strategies to treat hyperglycemia > 180 mg/dL (10 mmol/L) should be considered in adult patients with sustained ROSC after cardiac arrest. Hypoglycemia should be avoided.

Knowledge Gaps

- Adequately powered intervention trials of moderate ranges of glucose control in patients who survive cardiac arrest are required.

CARING FOR THE CRITICALLY ILL PATIENT

Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality

GROUPE HOSPITALIER HENRI MONDOR
ALBERT CHENEVIER - GEORGES CLEMENCEAU
JOFFRE-DUPUYTREN - EMILE ROUX

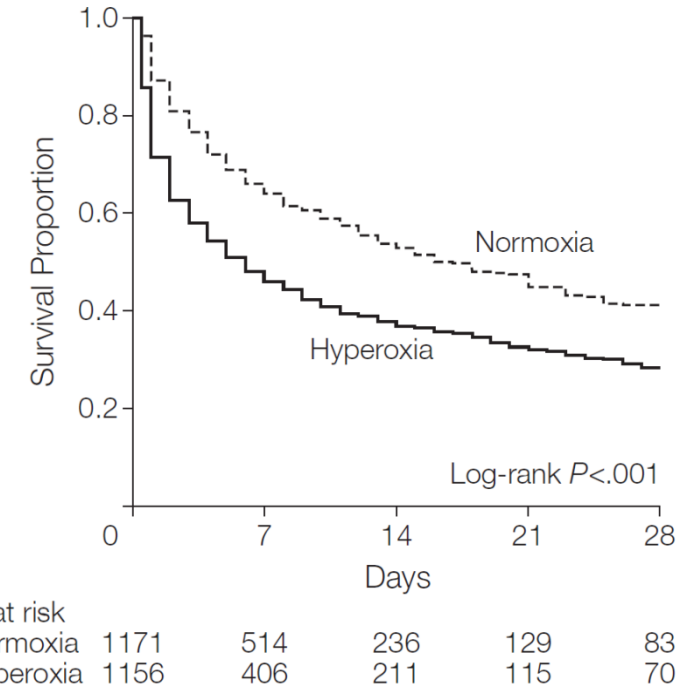
Kilgannon JH et al. JAMA. 2010

Large US database
n=6326 post-CA pts

Exposed to **Hypoxia**	*Exposed to* **Normoxia**	*Exposed to* **Hyperoxia**
<60 mmHg	60-300 mmHg	>300 mmHg
n=3999	n=1171	n=1156

Independant predictors of in-hospital mortality

Variable	OR (95% CI)	*P* Value
Age decile	1.1 (1.1-1.2)	<.001
Emergency department origin	1.5 (1.3-1.7)	<.001
Nonindependent functional status at admission	1.3 (1.1-1.4)	<.001
Chronic renal failure	1.6 (1.3-1.9)	<.001
Active chemotherapy	2.8 (1.8-4.6)	<.001
High heart rate in ICU[b]	1.9 (1.7-2.1)	<.001
Hypotension at ICU arrival[c]	2.1 (1.9-2.3)	<.001
Hypoxia exposure	1.3 (1.1-1.5)	.009
Hyperoxia exposure	1.8 (1.5-2.2)	<.001



CRITICAL CARE

GROUPE HOSPITALIER HENRI MONDOR
ALBERT CHENEVIER - GEORGES CLEMENCEAU JOFFRE-DUPUYTREN - EMILE ROUX

Arterial hyperoxia and in-hospital mortality after resuscitation from cardiac arrest

Critical Care 2011, **15**:R90 doi:10.1186/cc10090

Rinaldo Bellomo (rinaldo.bellomo@austin.org.au)

Table 6: Multiple Regression Models for In-Hospital Mortality and Survival Time using an APACHE Based Marker of Severity

Variable	Hospital Mortality OR (95%CI)	P-value	Time to Death HR (95%CI)	P- Value
AP3no-ox [a]	1.5 (1.5-1.6)	<0.0001	1.2 (1.2-1.2)	<0.0001
Treatment Limitation [b]	5.3 (3.8-7.2)	<0.0001	1.7 (1.5-1.8)	<0.0001
Year of admission	0.9 (0.9-0.9)	<0.0001	0.97 (0.96-0.98)	<0.0001
Lowest Glucose in the first 24 hours	1.1 (1.1-1.1)	<0.0001	1.02 (1.02-1.03)	<0.0001
Hospital admission from home	1.3 (1.1-1.4)	0.0002	1.1 (1.0-1.1)	0.02
Hypoxia/poor O_2 exchange vs. Normoxia	1.2 (1.1-1.4)	0.002	1.1 (1.0-1.2)	0.01
Hyperoxia vs. Normoxia	1.2 (1.0-1.5)	0.04	1.1 (1.0-1.2)	0.20

2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Laurie J. Morrison, Co-Chair*; Charles D. Deakin, Co-Chair*; Peter T. Morley; Clifton W. Callaway; Richard E. Kerber; Steven L. Kronick; Eric J. Lavonas; Mark S. Link; Robert W. Neumar; Charles W. Otto; Michael Parr; Michael Shuster; Kjetil Sunde; Mary Ann Peberdy; Wanchun Tang; Terry L. Vanden Hoek; Bernd W. Böttiger; Saul Drajer; Swee Han Lim; Jerry P. Nolan; on behalf of the Advanced Life Support Chapter Collaborators

GROUPE HOSPITALIER HENRI MONDOR
ALBERT CHENEVIER - GEORGES CLEMENCEAU
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In adult patients with ROSC after cardiac arrest, does the use of a controlled oxygenation strategy (including specific oxygenation goal), as opposed to standard care, improve outcome (eg, survival)?

Treatment Recommendations

- There is insufficient clinical evidence to support or refute the use of inspired oxygen concentration titrated to arterial blood oxygen saturation in the early care of cardiac arrest patients following sustained ROSC.

Knowledge Gaps

- Prospective randomized controlled clinical trials are needed to compare ventilation with 100% oxygen versus ventilation with inspired oxygen titrated to an arterial blood oxygen saturation goal (possibly 94% to 96%) for the first hour after sustained ROSC.

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Hypothermie thérapeutique

Perspectives?

Critical Time Window for Intra-Arrest Cooling With Cold Saline Flush in a Dog Model of Cardiopulmonary Resuscitation

Ala Nozari, Peter Safar, S. William Stezoski, Xianren Wu, Scott Kostelnik, Ann Radovsky, Samuel Tisherman and Patrick M. Kochanek

Circulation
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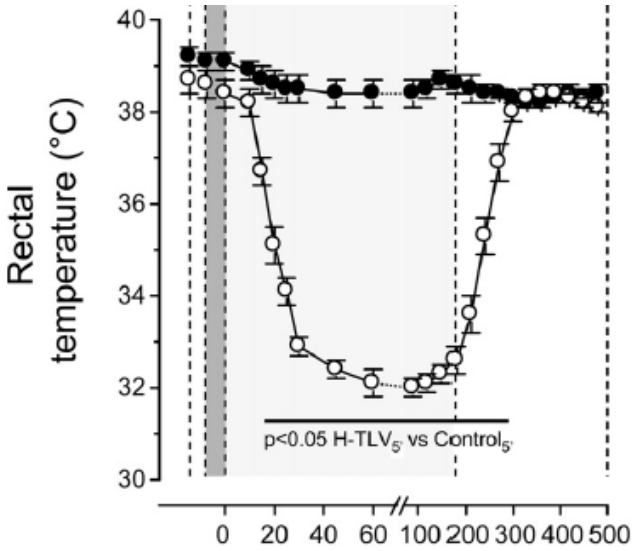
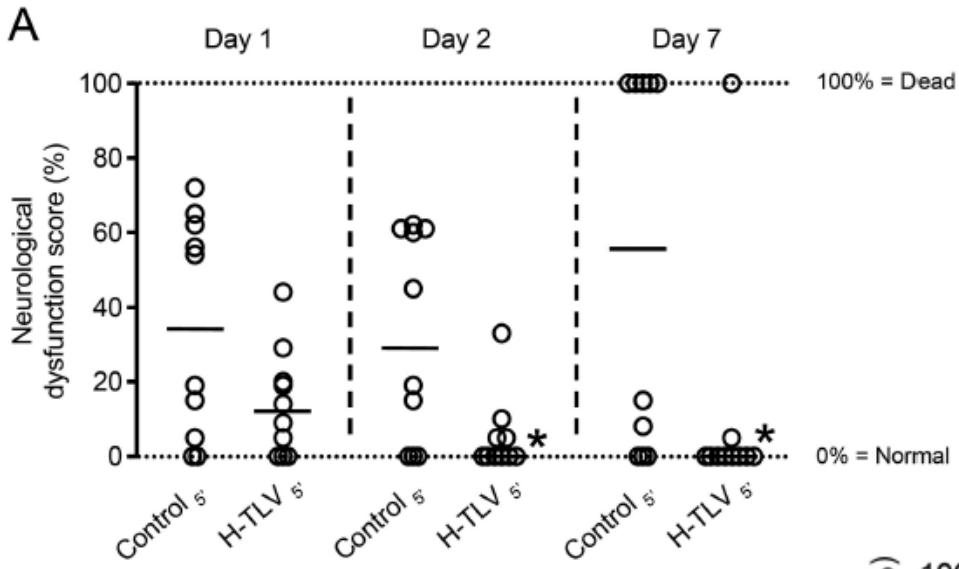
	Delayed hypothermia	Early hypothermia
OPC 5 or death	ooooooo	o
OPC 4		o
OPC 3		o
OPC 2		o
OPC 1	o	oooo
NDS (%)	[0]	5.5 (0-57)
HDS	[32, 38, 45]	0 (0-98)
MDS (%)	68.5 (47-93)	58.5 (43-93)

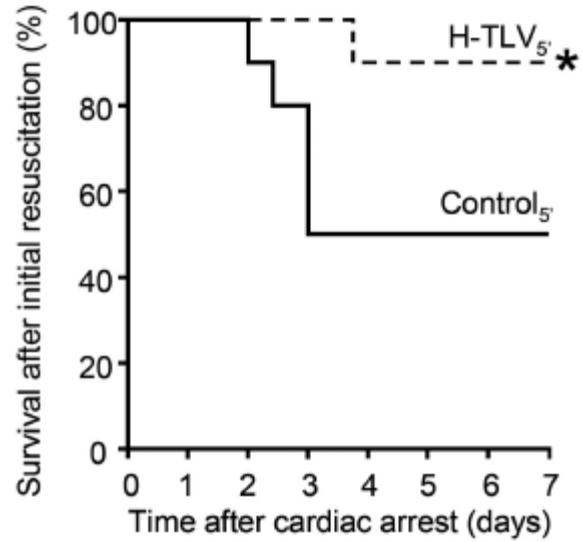
Circulation. 2006;113:2690-2696.

Ultrafast and Whole-Body Cooling With Total Liquid Ventilation Induces Favorable Neurological and Cardiac Outcomes After Cardiac Arrest in Rabbits

M. Chenoune, F. Lidouren, C. Adam, S. Pons, L. Darbera, P. Bruneval, B. Ghaleh, R. Zini, J.-L. Dubois-Randé, P. Carli, B. Vivien, J.-D. Ricard, A. Berdeaux and R. Tissier







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Circulation 2011, 124:901-911

Critical Care 2008, **12**:R31

CRITICAL CARE

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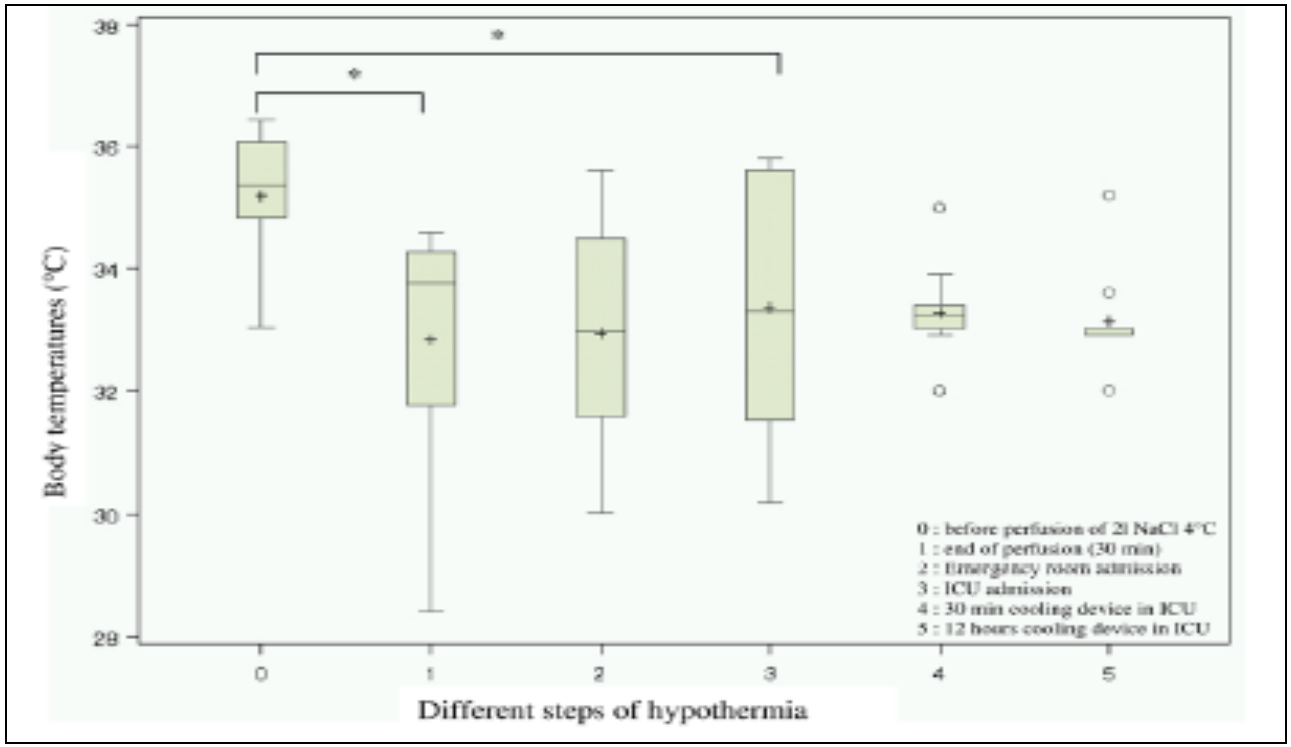
Mild hypothermia during advanced life support: a preliminary study in out-of-hospital cardiac arrest

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



Induction: 2000 ml NaCl 0,9% à 4°C (1 OAP)

Maintien: Coolgard 3000™, 33°C pendant 24h

Induction (N = 33)

↓

ROSC
et admission en réa
(N = 20)

↓

Maintien (N = 11)

↓

Réchauffement (N = 11)

↓

Survie à 6 mois
CPC 1-2
(N = 4)

Pilot Randomized Clinical Trial of Prehospital Induction of Mild Hypothermia in Out-of-Hospital Cardiac Arrest Patients With a Rapid Infusion of 4°C Normal Saline

Francis Kim, MD; Michele Olsufka, RN; W.T. Longstreth, Jr, MD; Charles Maynard, PhD; David Carlbom, MD; Steven Deem, MD; Peter Kudenchuk, MD; Michael K. Copass, MD; Leonard A. Cobb, MD

TABLE 3. Outcomes in 125 Patients Resuscitated From Out-of-Hospital Cardiac Arrest and Randomized to Standard Care With or Without Field Cooling

	Cooling (n=63), n (%)		No Cooling (n=62), n (%)	
	VF (n=29)	No VF (n=34)	VF (n=22)	No VF (n=40)
Deaths before hospital admission	3 (10)	11 (32)	3 (14)	11 (27)
In-hospital deaths	7 (24)	21 (62)	9 (41)	21 (52)
Discharged alive*	19 (66)	2 (6)	10 (45)	8 (20)

Circulation JOURNAL OF THE AMERICAN HEART ASSOCIATION 2007;115:3064-3070

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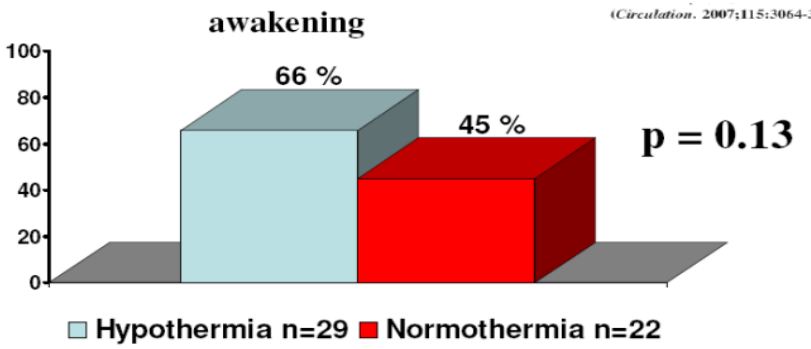
In-hospital deaths	7 (24)	21 (62)	9 (41)	21 (52)
awakening	19 (66)	2 (6)	10 (45)	8 (20)

(*Circulation*. 2007;115:3064-3070.)



Risk ration 1.44 (95% CI 0.85-2.45)

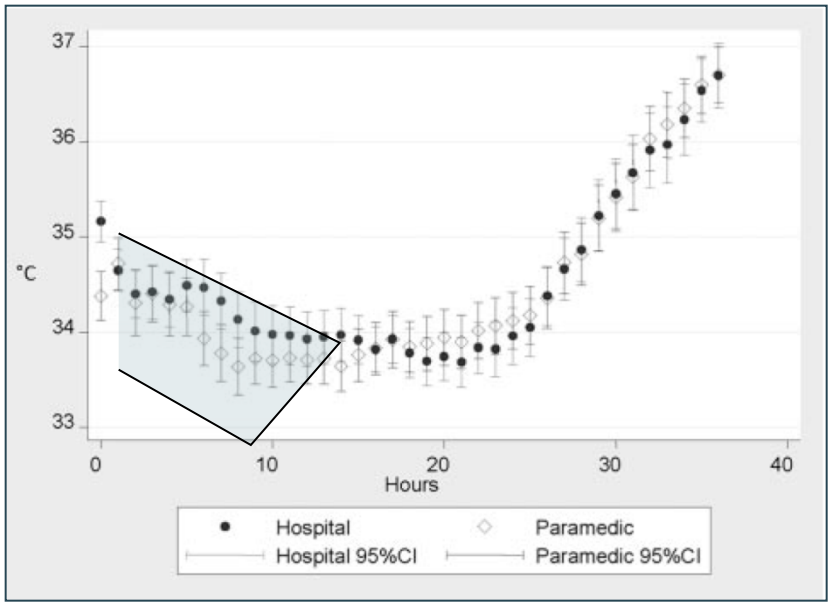
Circulation 2007;115:3064-3070

Induction of Therapeutic Hypothermia by Paramedics After Resuscitation From Out-of-Hospital Ventricular Fibrillation Cardiac Arrest

A Randomized Controlled Trial

Stephen A. Bernard, MD; Karen Smith, BSc, PhD; Peter Cameron, MD; Kevin Masci; David M. Taylor, MD; D. James Cooper, MD; Anne-Maree Kelly, MD; William Silvester, MB, BS; for the Rapid Infusion of Cold Hartmanns (RICH) Investigators*

Circulation 2010;122;737-742;



118 cooling par les paramedics
(1.9 L de RingerLacate froid; IQ 1-2 L)
vs 116 cooling intra-hospitalier

	Paramedic Cooling (n=118)	Hospital Cooling (n=116)	*P**
Favorable outcome, n (%; 95% CI)	56 (47.5; 38.2–56.9)	61 (52.6; 43.1–61.9)	0.433
Discharge to home, n (%; 95% CI)	24 (20.3; 13.5–28.7)	34 (29.3; 21.2–38.5)	…
Discharge to rehabilitation, n (%; 95% CI)	32 (27.1; 19.3–36.1)	27 (23.3; 15.9–32.0)	…
Discharge to nursing home awake, n	0	0	…
Discharge to nursing home comatose, n (%; 95% CI)	0	1 (0.9; 0.02–4.7)	…
Dead, n (%; 95% CI)	62 (52.5; 43.1–61.8)	54 (46.6; 27.2–56.0)	…

"In summary, we found that paramedics were able to effect a modest reduction in patient temperature during transport to hospital using a rapid infusion of LVICF; however, this decrease in core temperature was transient, and there was no measurable effect on patient outcomes compared with patients treated without active cooling."

Resuscitation Science

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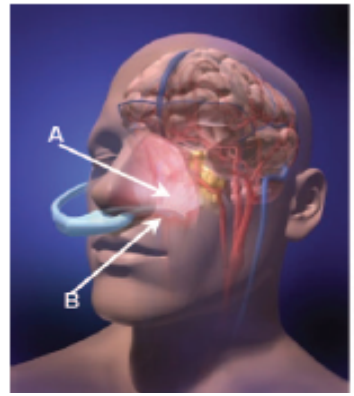
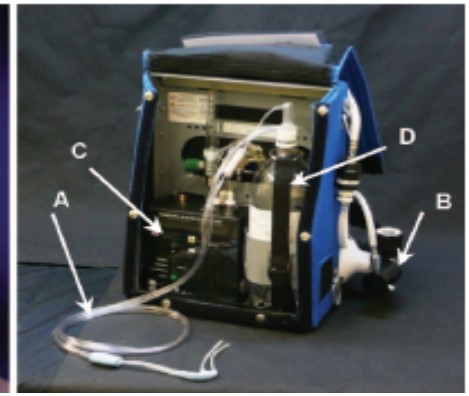
Intra-Arrest Transnasal Evaporative Cooling

A Randomized, Prehospital, Multicenter Study (PRINCE: Pre-ROSC IntraNasal Cooling Effectiveness)

Maaret Castrén, MD, PhD*; Per Nordberg, MD*; Leif Svensson, MD, PhD; Fabio Taccone, MD; Jean-Louise Vincent, MD, PhD; Didier Desruelles, MD; Frank Eichwede, MD; Pierre Mols, MD, PhD; Tilmann Schwab, MD; Michel Vergnion, MD; Christian Storm, MD; Antonio Pesenti, MD, PhD; Jan Pachl, MD, PhD; Fabien Guérisse, MD; Thomas Elste, MD; Markus Roessler, MD, DEAA; Harald Fritz, MD; Pieterjan Durnez, MD; Hans-Jörg Busch, MD; Becky Inderbitzen, MSE; Denise Barbut, MD





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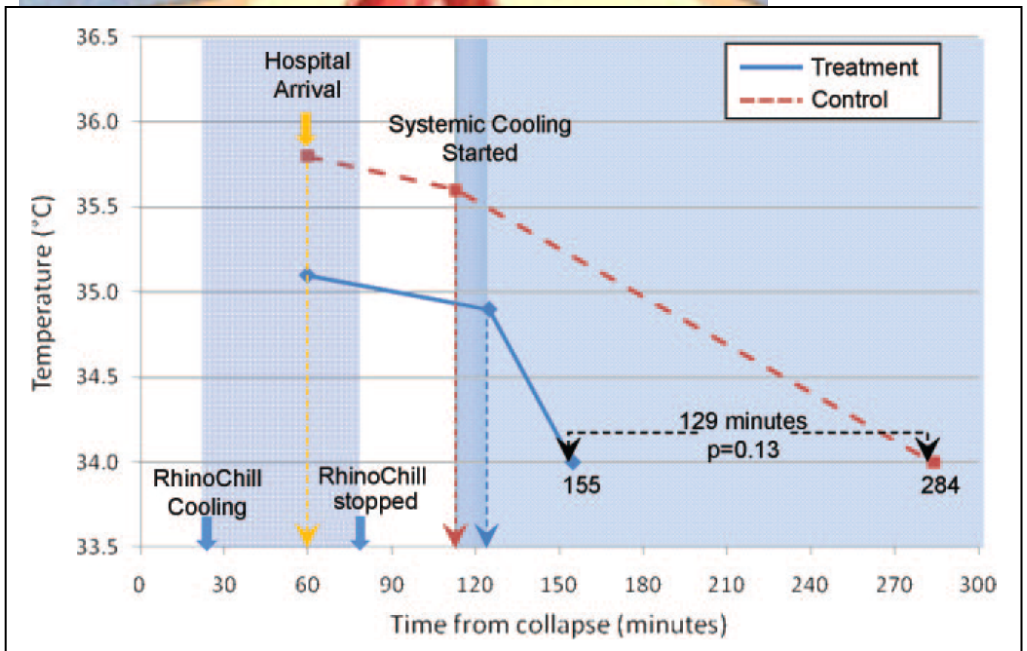
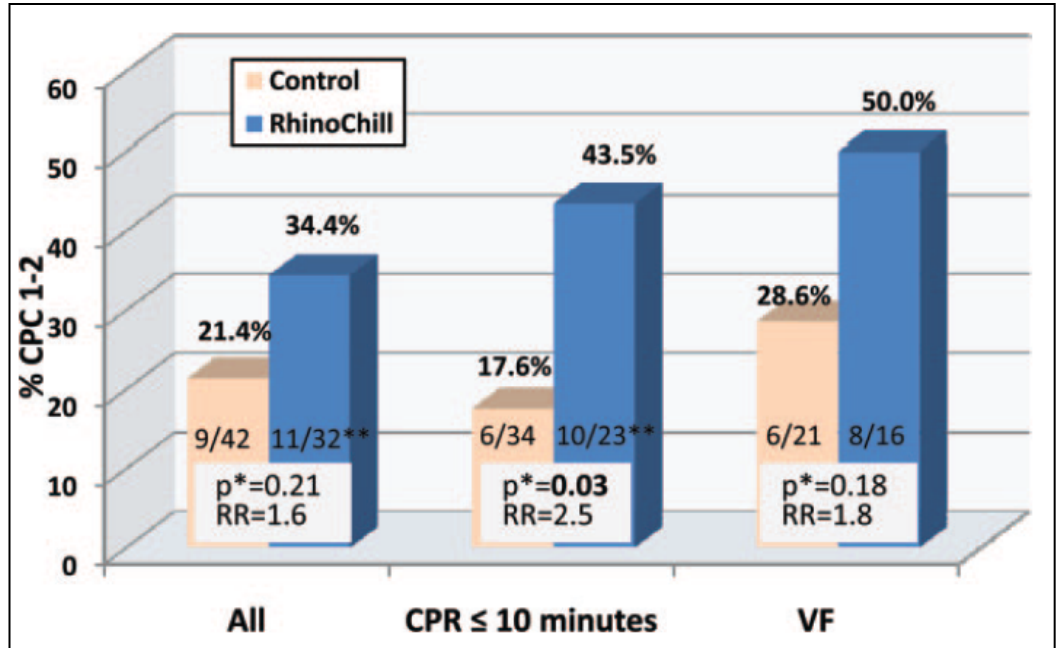
Circulation 2010





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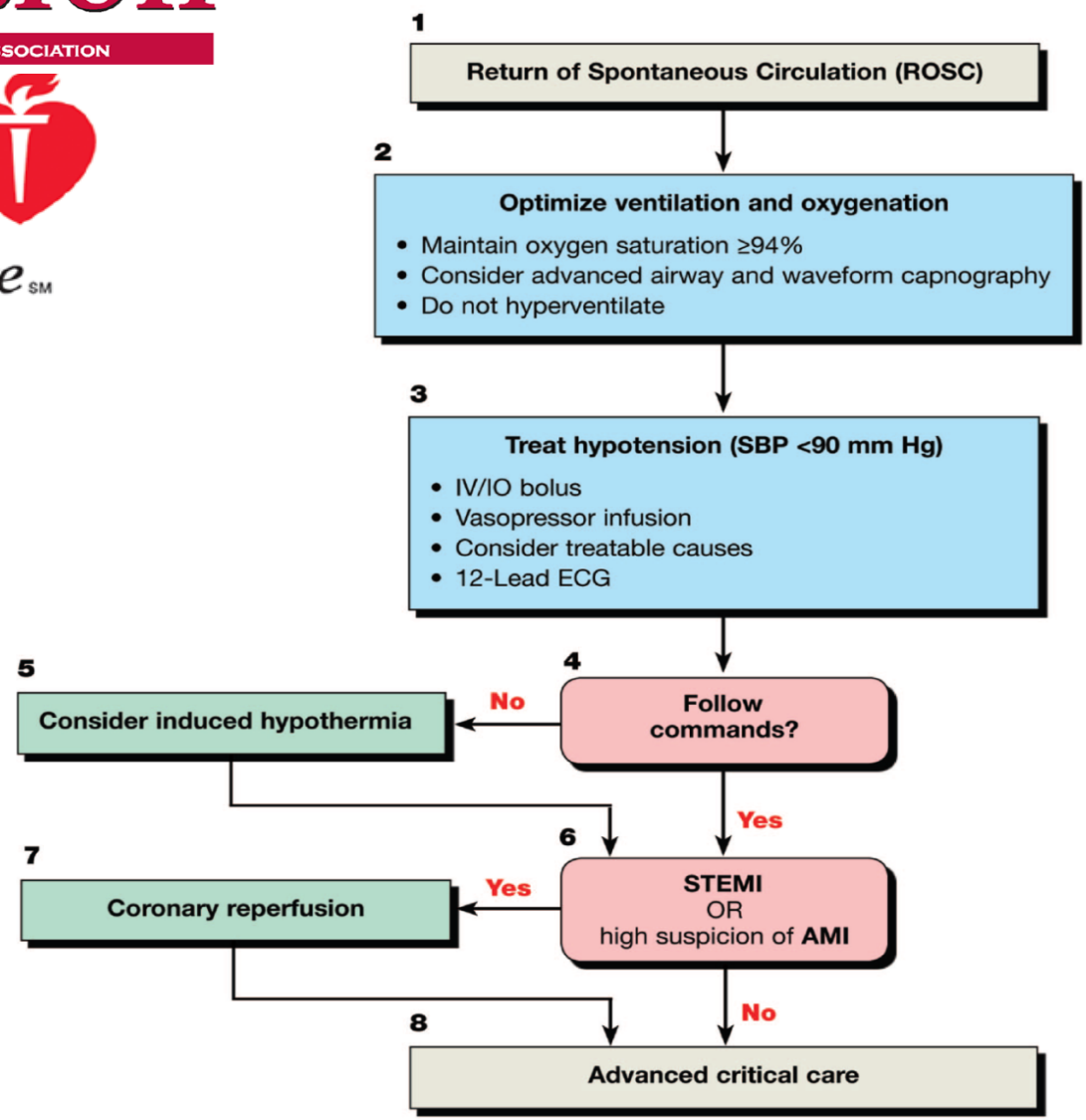
Adult Immediate Post–Cardiac Arrest Care



Doses/Details

Ventilation/Oxygenation
Avoid excessive ventilation. Start at 10-12 breaths/min and titrate to target P_{ETCO_2} of 35-40 mm Hg.
When feasible, titrate F_{IO_2} to minimum necessary to achieve Spo_2 ≥94%.

IV Bolus
1-2 L normal saline or lactated Ringer's.
If inducing hypothermia, may use 4°C fluid.

Epinephrine IV Infusion:
0.1-0.5 mcg/kg per minute (in 70-kg adult: 7-35 mcg per minute)

Dopamine IV Infusion:
5-10 mcg/kg per minute

Norepinephrine IV Infusion:
0.1-0.5 mcg/kg per minute (in 70-kg adult: 7-35 mcg per minute)

Reversible Causes
- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

Recommendations “up to date”…

European Resuscitation Council

Resuscitation. 2010 Oct;81(10)

American Heart Association

Circulation. 2010 Nov 2;122(18 Suppl 3)

International Liaison Committee on Resuscitation (ILCOR)