Hypothermie thérapeutique après arrêt cardiaque récupéré

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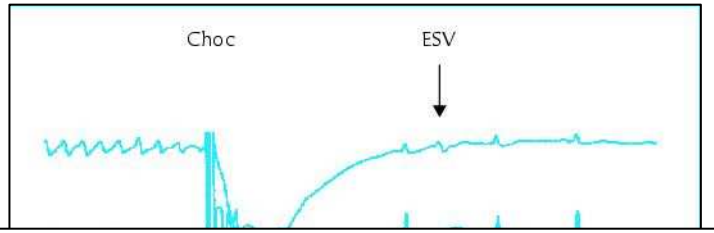
Pronostic sombre…

- 500 000/an en Europe,

  50 000/an en France
- Massage cardiaque: 1 arrêt/5
- 5% des ACR sortent vivants de l’hôpital
- 21 à 33% des ACR admis à l’hôpital sortent vivants de l’hôpital, dont 20 à 30% avec des séquelles neuro (données « historiques »)



Resuscitation 81 (2010) 1219–1276

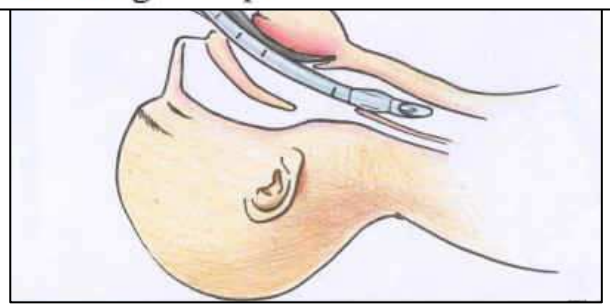
Contents lists available at ScienceDirect

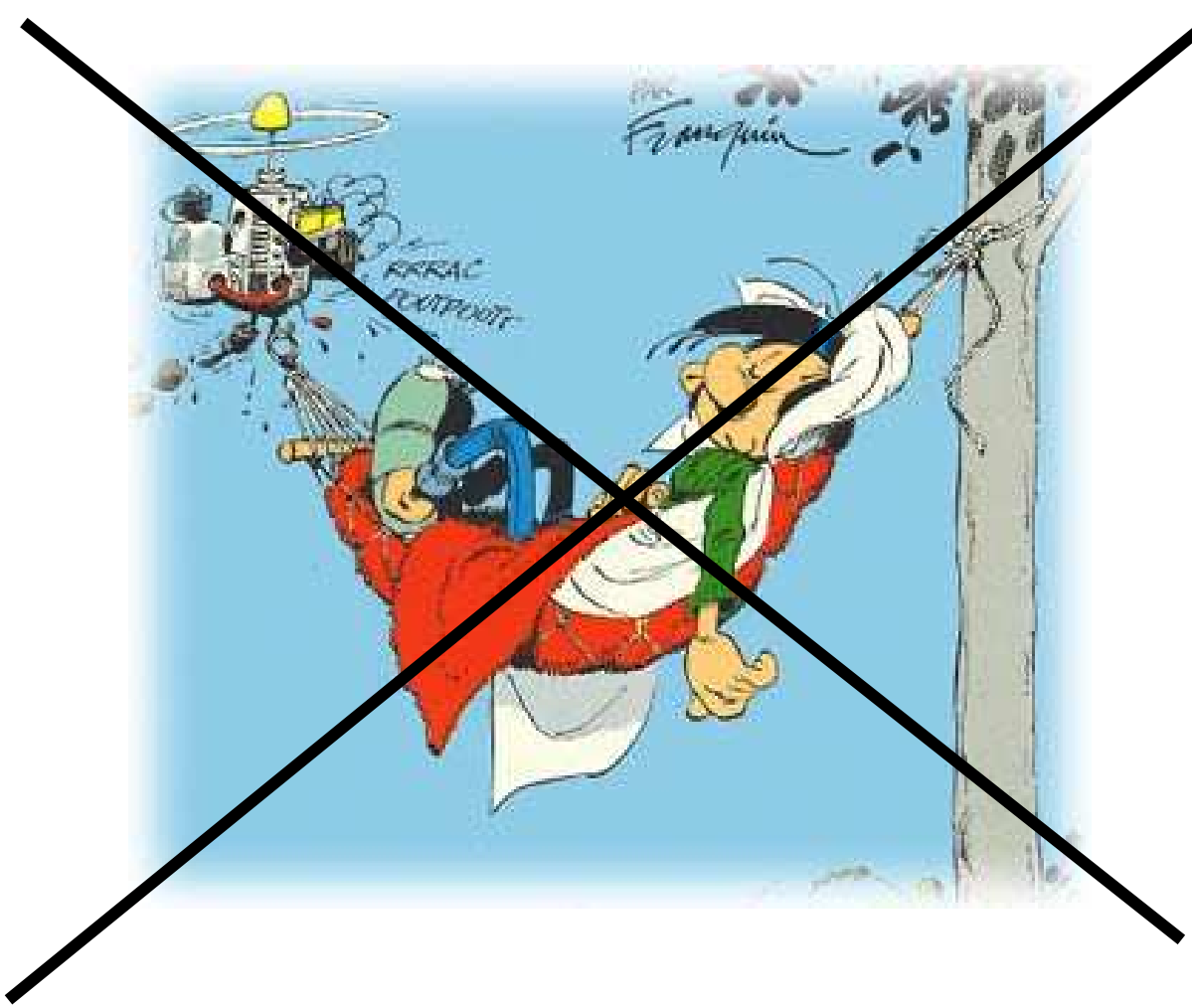
Resuscitation

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

European Resuscitation Council Guidelines for Resuscitation 2010 Section 1. Executive summary

Jerry P. Nolan[a,*], Jasmeet Soar[b], David A. Zideman[c], Dominique Biarent[d], Leo L. Bossaert[e], Charles Deakin[f], Rudolph W. Koster[g], Jonathan Wyllie[h], Bernd Böttiger[i], on behalf of the ERC Guidelines Writing Group[1]





Danger!!: le SPAC menace…

Syndrome post arrêt cardiaque

Syndrome	Pathophysiology	Clinical manifestation	Potential treatments
Post-cardiac arrest brain injury	• Impaired cerebrovascular autoregulation • Cerebral oedema (limited) • Postischaemic neurodegeneration	• Coma • Seizures • Myoclonus • Cognitive dysfunction • Persistent vegetative state • Secondary Parkinsonism • Cortical stroke • Spinal stroke • Brain death	• Therapeutic hypothermia[177] • Early haemodynamic optimization • Airway protection and mechanical ventilation • Seizure control • Controlled reoxygenation (SaO_2 94%-96%) • Supportive care

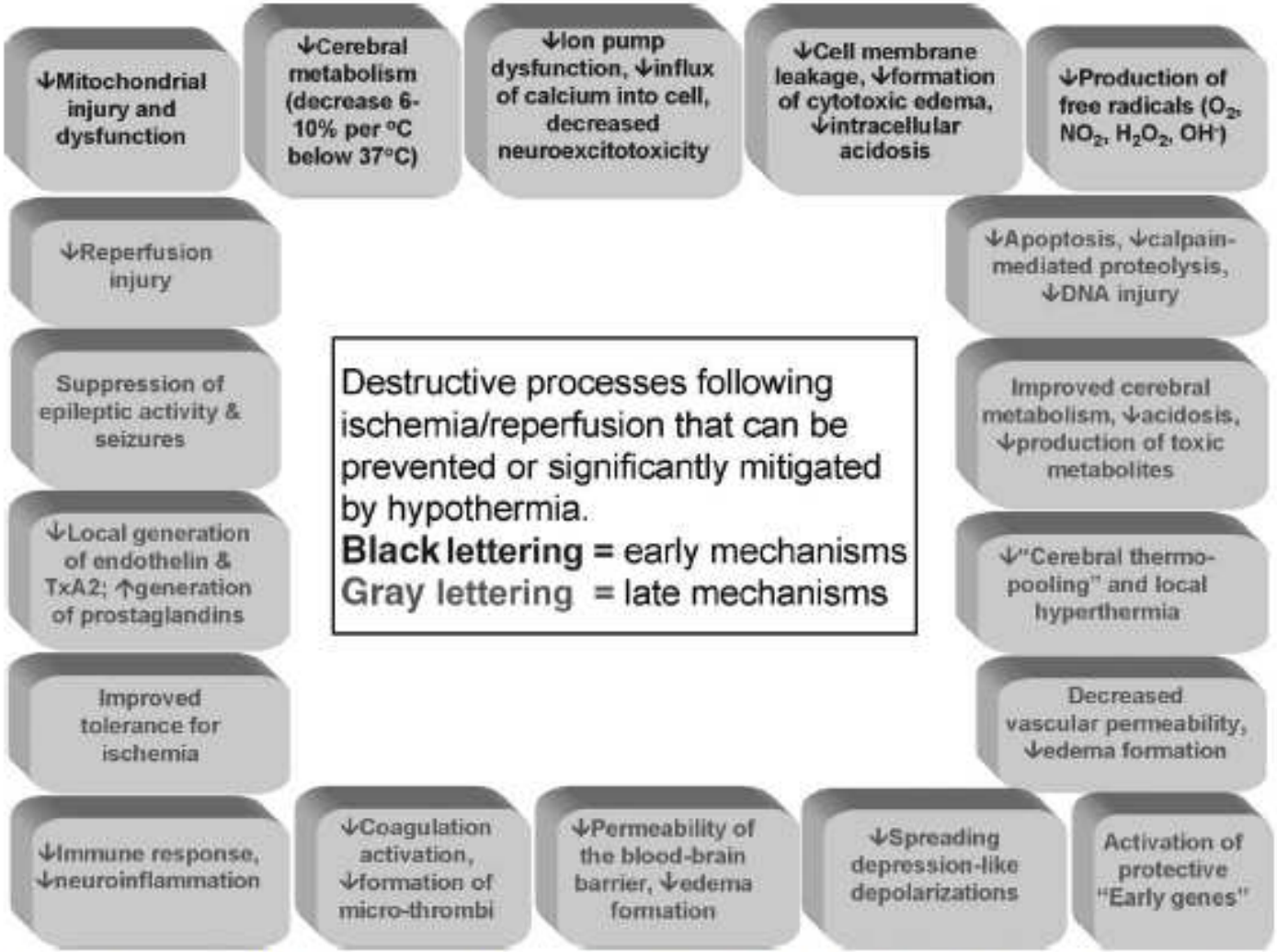
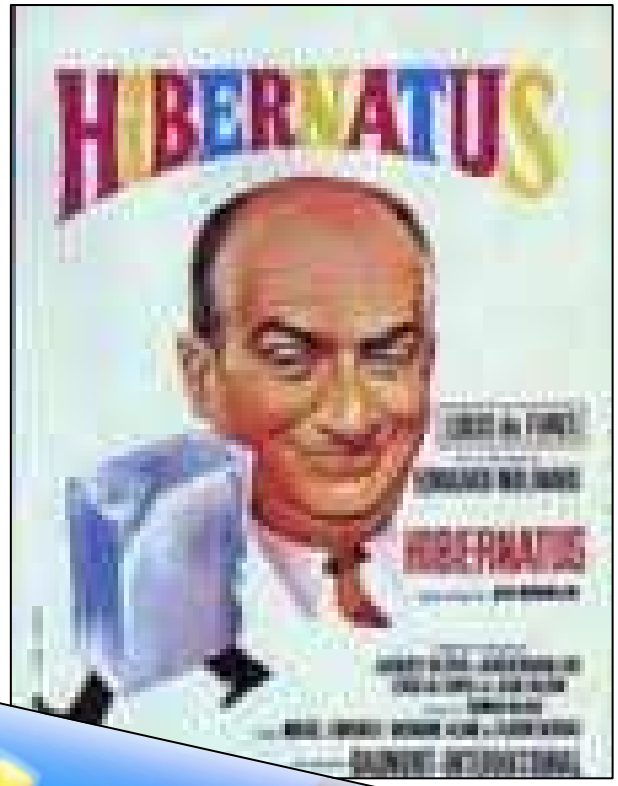


Figure 1. Schematic depiction of the mechanisms underlying the protective effects of mild to moderate hypothermia. *TxA2*, thromboxane A2.

KH Polderman. Crit Care Med 2009


HIBERNATUS


Mr.Freeze


HIBERNATUS

Une vieille technique…

Treatment	Number of Experiments	Percentage of Recovery
None	12	25%
Hypothermia 32–34° C. 18–36 hours	12	83%

Williams GR Jr, Spencer FC. The clinical use of hypothermia following cardiac arrest. *Ann Surg* 1958; **148:** 462–68.

Body Systems	Physiological Changes	Medical Treatment
Cutaneous and muscular	Cutaneous vasoconstriction, Shivering (≤35°C–30°C)	Prevent bedsores Prevent and treated shivering (pharmacologic treatment ± skin warming in awake patients)
Cardiovascular		
HR	Tachycardia (≥36→35°C, briefly for induction): related to the increase in venous return to the heart caused by a shift in circulatory volume from peripheral to core compartment, leading to a reflex increase in HR might be exacerbated when patient is not sedated enough and/or shivering response not overcome Bradycardia (≤35°C): further pronounced as core temperature drop (at 33°C, normal HR will be 45 to 55 beats/min) caused by a decrease in the rate of diastolic repolarization in the cells of the sinus node as well as prolongation of the duration of action potentials and a mild decrease in the speed of myocardial impulse conduction Slight hypertension (≤34°C, ~10 mm Hg more): due to hypothermia-induced vasoconstriction of peripheral arteries and arterioles Association with hypotension due to: hypovelemia related to "cold diuresis" post-cardiac arrest syndrome and its systemic inflammatory response	None unless symptomatic
Blood pressure	Primary cardiac cause	Wean vasopressors, administer analgesics and sedation if needed
	Increase when HR decreased (mild HT)	Avoiding or correcting hypovolemia by fluid administration
	Decrease when temp <30°C or artificial HR increased (chronotropic drugs or pacing)	± Vasopressors
	Decrease in cardiac output (≤35°C) in relation with HR decrease	± Etiologic treatment
	Increase central venous pressure (≤35°C)	Prevent overcooling and avoid excessive heart stimulation
Myocardial contractility	Mild arrhythmia in some patients (≤32°C) Tachyarrhythmias beginning by atrial fibrillation (≤28°C–30°C)	None unless symptomatic or hypotensive
Cardiac output	Prolonged PR, QRS, and QT intervals (≤33°C)	
	Rare Osborne's J waves in mild hypothermia	
Arrhythmia		Prevent overcooling and electrolytes disorders
		Re-warm slowly to avoid hyperkalemia in rewarming phase
ECG changes		None

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Immunologic	Impaired neutrophil function, suppression of pro-inflammatory mediator release (≤35°C) Leukopenia and impaired leukocyte function (≤33°C)	Take measure to prevent infection (especially pneumonia); antibiotic prophylaxis
Hematologic	Thrombopenia, thrombopathy Impaired coagulation cascade (≤35°C)	Usually none
Metabolic	Decrease metabolic demands (30°C–35 °C): Decrease carbon dioxide production Decrease oxygen consumption	Frequent blood gases (used temperature corrected value) especially in induction phase and ventilation parameters management
Endocrine	Insulin resistance (≤35°C)	Insulin administration to maintain appropriate glucose level
Gastrointestinal	Decrease motility (≤35°C)	Delayed feeding after HT
Neurological	Decrease consciousness (≤30°C–31°C) in awake patient	
Renal	Increase diuresis, tubular dysfunction (≤35°C) Electrolytes loss and disorders (≤35°C)	Monitor urine output and replace fluid if needed Prevent and monitor blood electrolytes disorders (usually every 6–8 h)
Drug metabolism	Reduce in cytochrome P450 activity Slowing of numerous liver enzymes Usually reduced clearance of numerous medications such as sedative or neuromuscular blocking agents (≤35°C)	Adjust infusion rates, use preferentially bolus dose rather than increasing infusion dose

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G.D. Curfman

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The Hypothermia after Cardiac Arrest Study Group
Free Full Text

Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia 557-563
S.A. Bernard and Others

- Étude multicentrique, randomisée
- 275 patients (FV/TV)…sur 3551 screenés
- Hypothermie 32-34°dans les 4 heures, pendant 24h
- Critère 1^{aire}: évolution neuro favorable à 6 mois (Pittsburgh 1 ou 2)

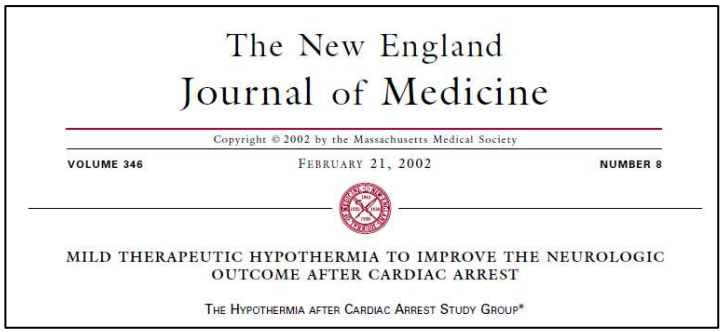

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.

CHARACTERISTIC	NORMOTHERMIA (N=138)	HYPOTHERMIA (N=137)
Age — yr		
Median	59	59
Interquartile range	49–67	51–69*
Female sex — no./total no. (%)	32/138 (23)	33/137 (24)
Medical history — no./total no. (%)		
Diabetes	26/138 (19)	11/135 (8)
Coronary heart disease	59/138 (43)	43/135 (32)
Cerebrovascular disease	11/138 (8)	10/135 (7)
NYHA class III or IV†	16/132 (12)	14/130 (11)
Location of cardiac arrest — no./total no. (%)		
Home	70/138 (51)	69/135 (51)
Public place	53/138 (38)	48/135 (36)
Other‡	15/138 (11)	18/135 (13)
Arrest witnessed — no./total no. (%)§	136/138 (99)	134/137 (98)
Presumed cardiac origin of arrest — no./total no. (%)§	135/138 (98)	135/137 (99)
Ventricular fibrillation or pulseless ventricular tachycardia — no./total no. (%)§	132/138 (96)	133/137 (97)
Basic life support provided by bystander — no./total no. (%)	68/138 (49)	59/137 (43)
Interval between collapse and restoration of spontaneous circulation — min¶		
Median	22	21
Interquartile range	17–33	15–28
Total epinephrine dose — mg		
Median	3	3
Interquartile range	1–6	1–5*
Hypotension after resuscitation — no./total no. (%)	68/138 (49)	75/137 (55)
Subsequent nonfatal arrest — no./total no. (%)	11/138 (8)	15/137 (11)
Thrombolysis after resuscitation — no./total no. (%)	24/133 (18)	27/135 (20)

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THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

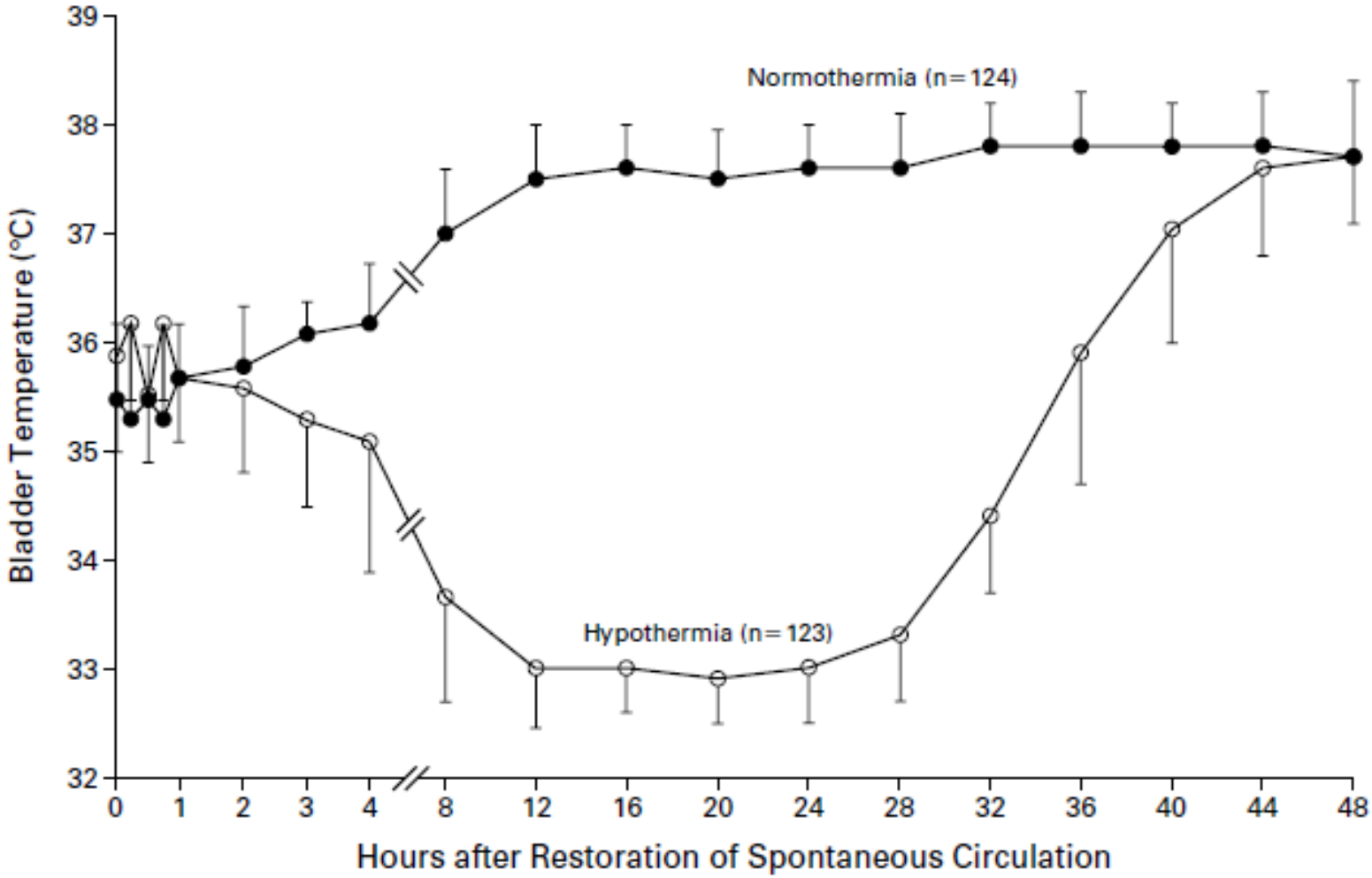

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TABLE 2. NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

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

*The risk ratio was calculated as the rate of a favorable neurologic outcome or the rate of death in the hypothermia group divided by the rate in the normothermia group. CI denotes confidence interval.

†Two-sided P values are based on Pearson's chi-square tests.

‡A favorable neurologic outcome was defined as a cerebral-performance category of 1 (good recovery) or 2 (moderate disability). One patient in the normothermia group and one in the hypothermia group were lost to neurologic follow-up.

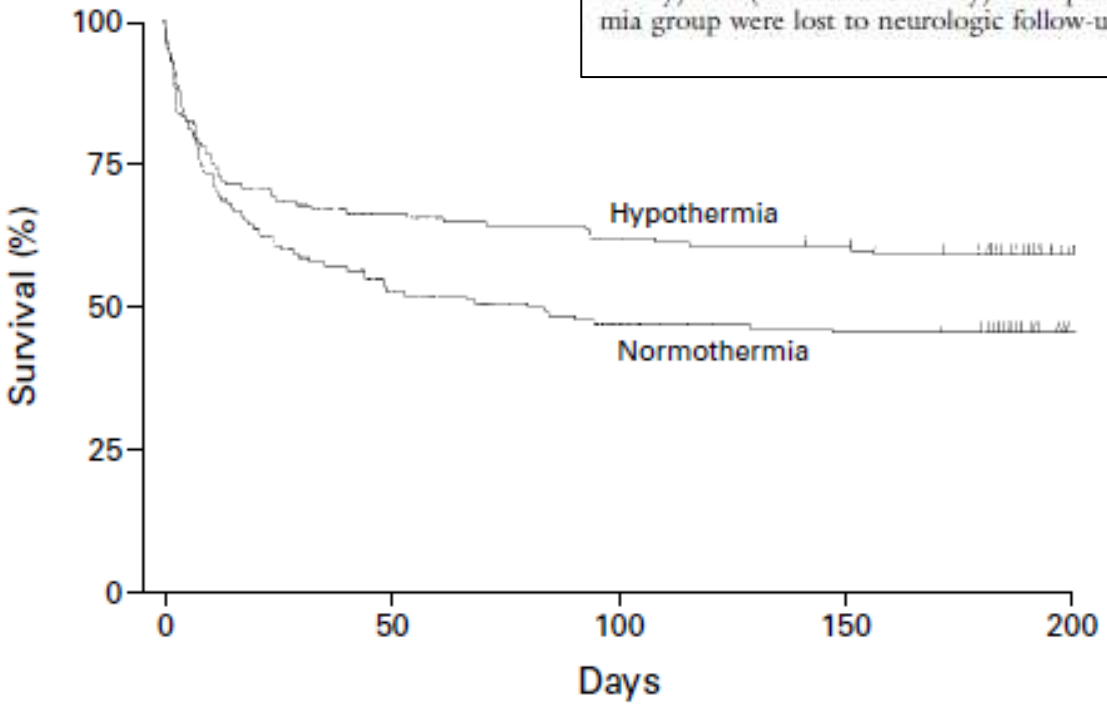

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TABLE 4. COMPLICATIONS DURING THE FIRST SEVEN DAYS AFTER CARDIAC ARREST.*

COMPLICATION	NORMOTHERMIA	HYPOTHERMIA
	no./total no. (%)	
Bleeding of any severity†	26/138 (19)	35/135 (26)
Need for platelet transfusion	0/138	2/135 (1)
Pneumonia	40/137 (29)	50/135 (37)
Sepsis	9/138 (7)	17/135 (13)
Pancreatitis	2/138 (1)	1/135 (1)
Renal failure	14/138 (10)	13/135 (10)
Hemodialysis	6/138 (4)	6/135 (4)
Pulmonary edema	5/133 (4)	9/136 (7)
Seizures	11/133 (8)	10/136 (7)
Lethal or long-lasting arrhythmia	44/138 (32)	49/135 (36)
Pressure sores	0/133	0/136

*None of the comparisons between the two groups, performed with the use of Pearson's chi-square test, indicated significant differences.

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THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

- Étude australienne randomisée
- 77 patients (FV/TV)
- HypoT 33° dans les 2 h, pendant 12 h
- Exclusion: choc cardiogénique, cause extra cardiaque possible
- Critère 1^{aire}: sortie vivant de l'hôpital avec pas/peu de séquelle neuro (CPC 1 ou 2)

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.

TABLE 1. CLINICAL CHARACTERISTICS OF THE 77 PATIENTS WITH ANOXIC BRAIN INJURY WHO WERE ELIGIBLE FOR RANDOMIZATION.*

CHARACTERISTIC	HYPOTHERMIA (N=43)	NORMOTHERMIA (N=34)	P VALUE
Age (yr)			0.55
Median	66.8	65.0	
Range	49–89	41–85	
Male sex (%)	58	79	0.05
Arrest witnessed (%)	95	94	0.81
Bystander performed cardiopulmonary resuscitation (%)	49	71	0.05
Time from collapse to emergency-medical-services call (min)	2.1±1.9	2.7±3.0	0.32
Time from call to emergency-medical-services arrival (min)	7.9±3.1	8.3±2.8	0.60
Time from arrival to first DC shock (min)	2.5±2.2	2.0±1.2	0.22
Time from first shock to return of spontaneous circulation (min)	13.6±11.2	12.1±7.9	0.48
Time from collapse to return of spontaneous circulation (min)	26.5±12.9	25.0±8.9	0.54
Number of DC shocks	4.2±3.0	4.1±3.2	0.87
Dose of epinephrine (mg)	2.2±2.1	2.2±1.9	0.97

*Plus–minus values are means ±SD. DC denotes direct current.

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TABLE 2. PHYSIOLOGICAL AND HEMODYNAMIC VALUES.*

VARIABLE	TREATMENT GROUP	ADMISSION TO ED	ADMISSION TO ICU	6 HR	12 HR	18 HR	24 HR
Number of patients	Hypothermia	43	39	39	39	39	38
	Normothermia	34	33	32	32	32	31
Temperature (°C)	Hypothermia	35.0±1.18	33.3±0.98†	32.7±1.19†	33.1±0.89†	36.0±1.24†	37.4±0.85†
	Normothermia	35.5±0.90	36.0±0.76†	37.1±0.75	37.4±0.58†	37.3±0.56†	37.3±0.59†
	P value‡	0.02	<0.001	<0.001	<0.001	<0.001	0.60
Mean arterial blood pressure (mm Hg)	Hypothermia	90.4±18.89	108.7±20.89†	97.0±14.92	89.5±13.16	88.8±9.17	89.1±12.9
	Normothermia	87.2±21.46	94.4±18.80	92.2±13.00	90.8±14.16	91.3±12.96	92.1±11.76
	P value‡	0.51	0.02	0.16	0.82§	0.38	0.24
Pulse (per minute)	Hypothermia	97±22.5	82±21.6§	72±17.1§	70±17.6	80±18.2§	89±17.9†
	Normothermia	105±30.4	100±17.0	100±21.9	94±17.9	97±16.8	99±15.5
	P value‡	0.18	0.001	<0.001	<0.001	<0.001	0.02
Cardiac index (liters/min/m² of body-surface area)¶	Hypothermia		2.0 (1.2–4.4)	2.1 (0.9–4.2)	2.4 (0.8–4.9)	2.9 (1.5–7.3)§	3.4 (1.6–6.8)§
	Normothermia		2.6 (1.4–5.5)	2.7 (1.4–6.1)	3.2 (1.2–6.1)	3.3 (1.5–5.8)	3.0 (1.8–5.7)
	P value‡		0.01	0.16	0.10	0.12	0.54
Systemic vascular resistance (dyn-sec·cm^{-5})¶	Hypothermia		2213 (599–4645)	1808 (836–4531)	1564 (439–4280)	1198 (402–2833)§	987 (551–2500)§
	Normothermia		1356 (481–2545)	1278.5 (346–2841)	1056 (340–3163)	964 (479–2204)†	1072 (591–1998)
	P value‡		0.02	<0.001	0.002	0.23	0.50

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	P value‡	0.02	<0.001	<0.001	<0.001	<0.001	0.60
Mean arterial blood pressure (mm Hg)	Hypothermia	90.4±18.89	108.7±20.89†	97.0±14.92	89.5±13.16	88.8±9.17	89.1±12.9
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Number of patients	Hypothermia	43	39	39	39	39	38
	Normothermia	34	33	32	32	32	31
Temperature (°C)	Hypothermia	35.0±1.18	33.3±0.98†	32.7±1.19†	33.1±0.89†	36.0±1.24†	37.4±0.85†
	Normothermia	35.5±0.90	36.0±0.76†	37.1±0.75	37.4±0.58†	37.3±0.56†	37.3±0.59†
	P value‡	0.02	<0.001	<0.001	<0.001	<0.001	0.60
Mean arterial blood pressure (mm Hg)	Hypothermia	90.4±18.89	108.7±20.89†	97.0±14.92	89.5±13.16	88.8±9.17	89.1±12.9
	Normothermia	87.2±21.46	94.4±18.80	92.2±13.00	90.8±14.16	91.3±12.96	92.1±11.76
	P value‡	0.51	0.02	0.16	0.82§	0.38	0.24
Pulse (per minute)	Hypothermia	97±22.5	82±21.6§	72±17.1§	70±17.6	80±18.2§	89±17.9†
	Normothermia	105±30.4	100±17.0	100±21.9	94±17.9	97±16.8	99±15.5
	P value‡	0.19	0.001†	<0.001†	<0.001†	<0.001†	0.02
Cardiac index (liters/min/m² of body-surface area)¶	Hypothermia		2.0 (1.2–4.4)	2.1 (0.9–4.2)	2.4 (0.8–4.9)	2.9 (1.5–7.3)§	3.4 (1.6–6.8)§
	Normothermia		2.6 (1.4–5.5)	2.7 (1.4–6.1)	3.2 (1.2–6.1)	3.3 (1.5–5.8)	3.0 (1.8–5.7)
	P value‡		0.01	0.16	0.10	0.12	0.54
Systemic vascular resistance (dyn-sec·cm^{-5})¶	Hypothermia		2213 (599–4645)	1808 (836–4531)	1564 (439–4280)	1198 (402–2833)§	987 (551–2500)§
	Normothermia		1356 (481–2545)	1278.5 (346–2841)	1056 (340–3163)	964 (479–2204)†	1072 (591–1998)
	P value‡		0.02	<0.001	0.002	0.23	0.50

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.

TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

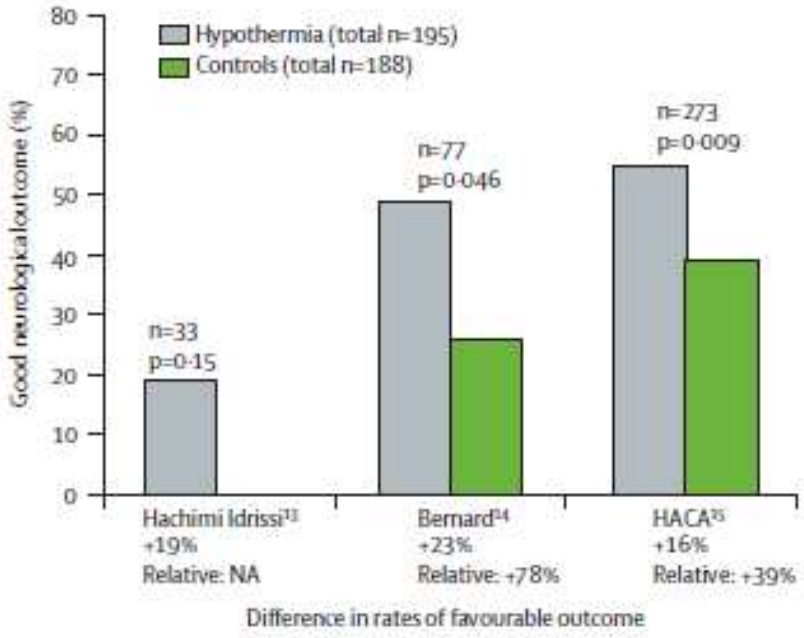
OUTCOME*	HYPOTHERMIA (N=43)	NORMOTHERMIA (N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing facility)	0	1
Severe disability, unconscious (discharged to a long-term nursing facility)	0	1
Death	22	23

*The difference between the rates of a good outcome (normal or with minimal or moderate disability) in the hypothermia and the normothermia groups (49 percent and 26 percent, respectively) was 23 percentage points (95 percent confidence interval, 13 to 43 percentage points; P=0.046). The unadjusted odds ratio for a good outcome in the hypothermia group as compared with the normothermia group was 2.65 (95 percent confidence interval, 1.02 to 6.88; P=0.046). The odds ratio for a good outcome in the hypothermia group as compared with the normothermia group, after adjustment by logistic regression for age and time from collapse to return of spontaneous circulation, was 5.25 (95 percent confidence interval, 1.47 to 18.76; P=0.011).

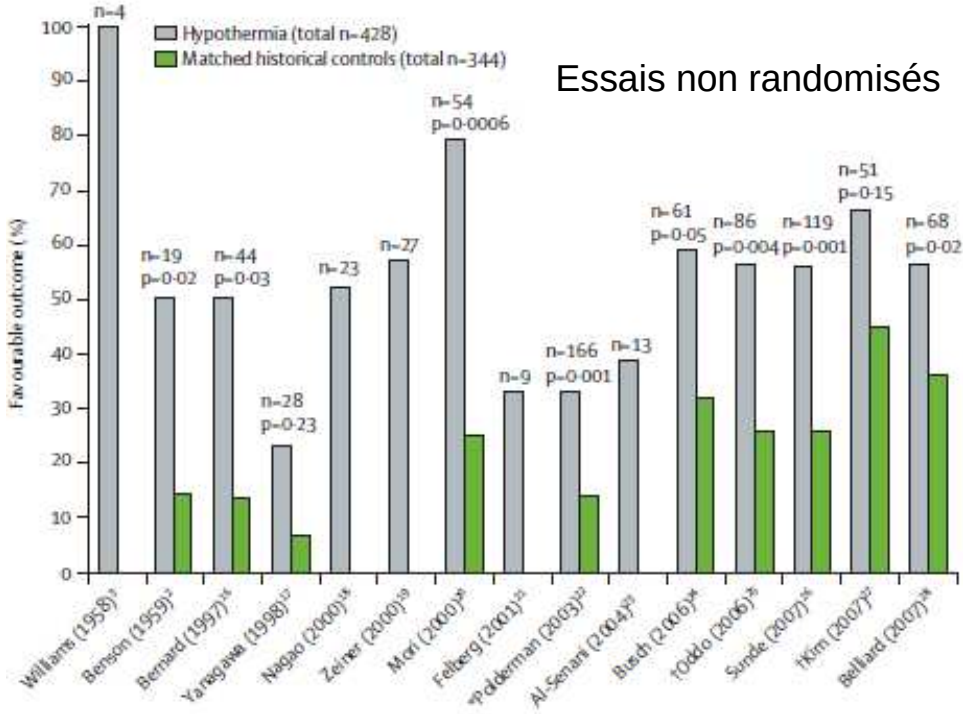
TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

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.

Donc…ça marche!!



Essais randomisés



Essais non randomisés

Poldermann. Lancet 2008

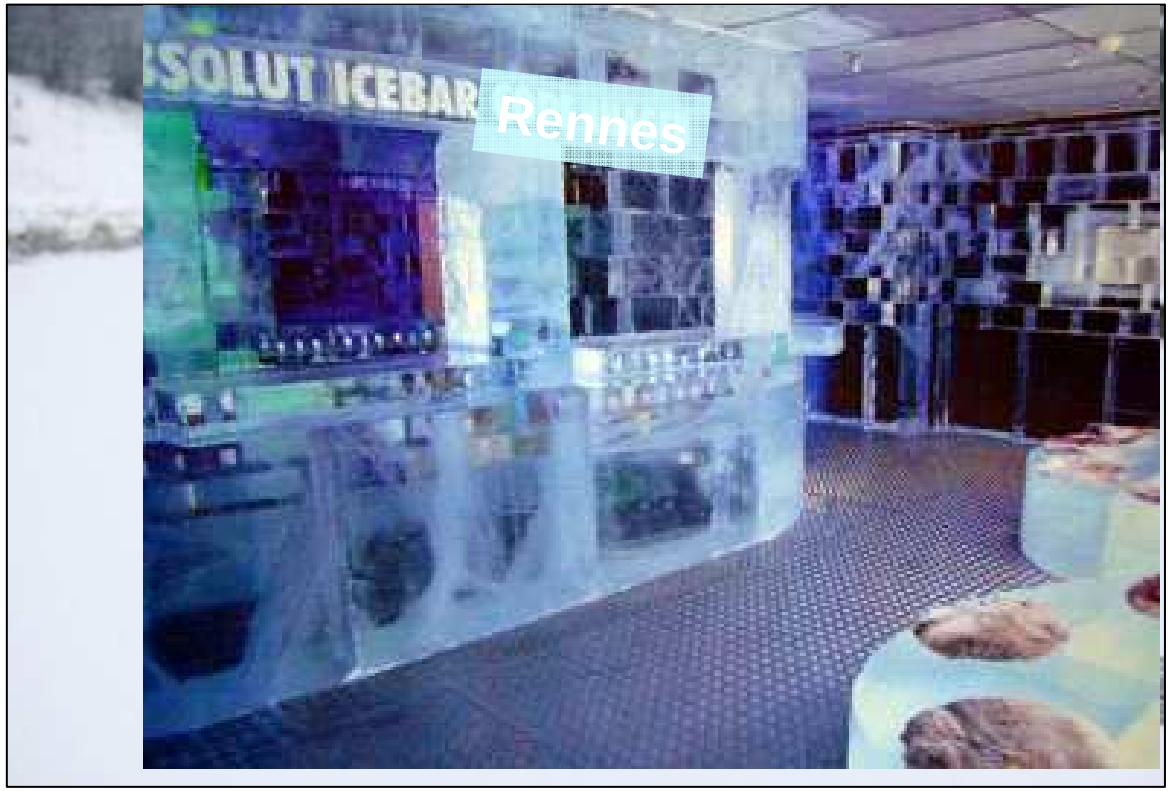
Nombre de patients à traiter pour permettre 1 amélioration neurologique à la sortie de l'hôpital: 6…

Holzer M et al. Crit Care Med 2005

En pratique:

- ✓ *comment faire?*
- ✓ *quand la débuter?*
- ✓ *pour qui?*

Comment faire?



Comment faire?

- 3 phases

✓ *induction de l'hypoT* → *SAMU*

✓ *maintien de l'hypoT*

✓ *réchauffement*

} → USIC/Réa

Comment faire?

- Les techniques possibles

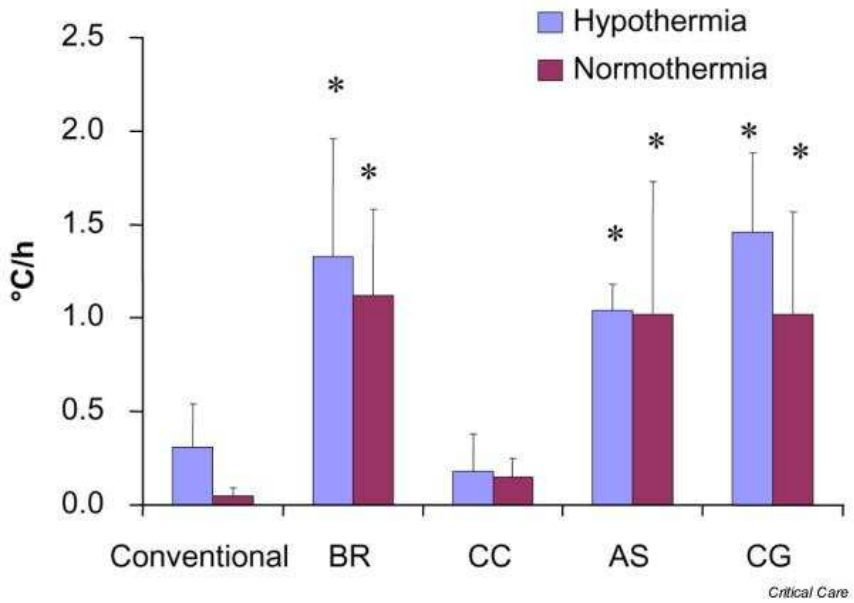
✓ *perfusion glacée*: très efficace pour l'induction mais généralement insufisant

30 ml/kg de SSI 4℃ ⟶ Température centrale ↘ de 1.5℃

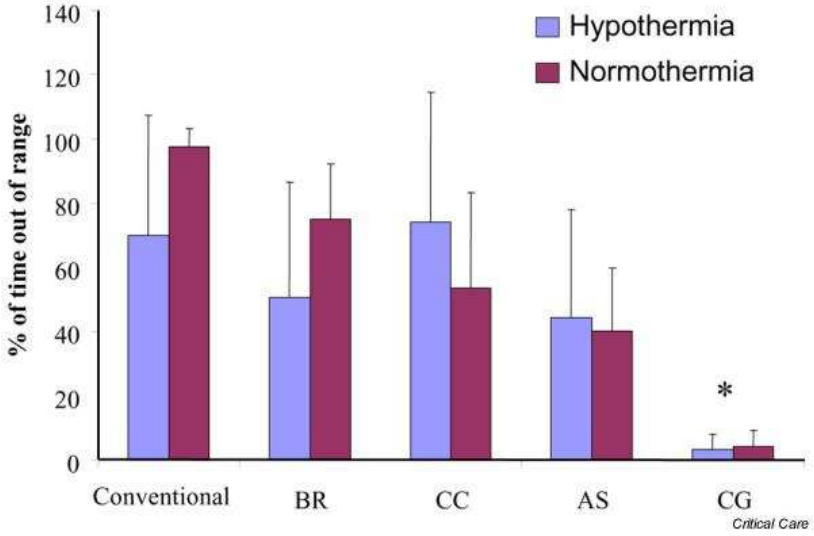
✓ *refroidissement externe (glace, tunnel de froid, matelas):* très efficace, pb de la maitrise de la température

✓ *méthodes endovasculaires:* voie centrale, coût, disponibilité machine

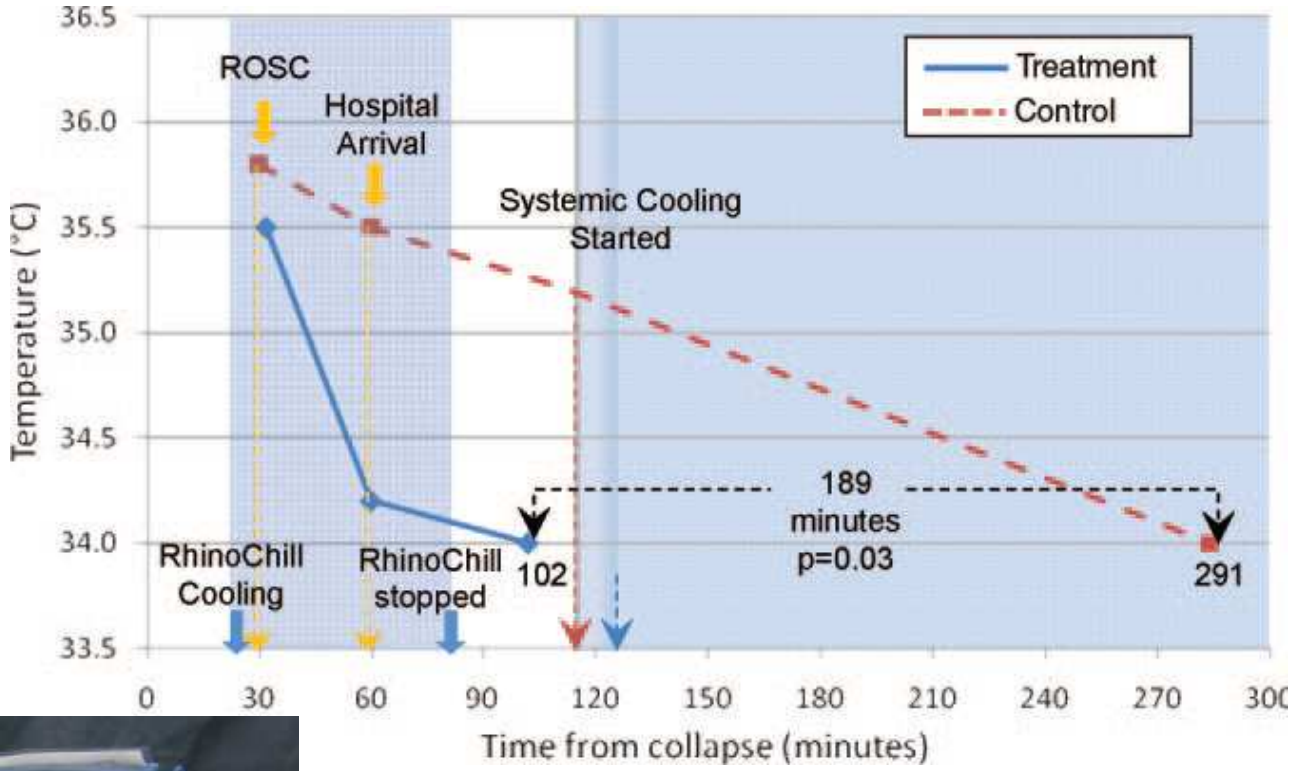
✓ *autres techniques: lavage gastrique glacé, casque refroidissant, immersion dans l'eau glacée, refroidissement trans nasal…*

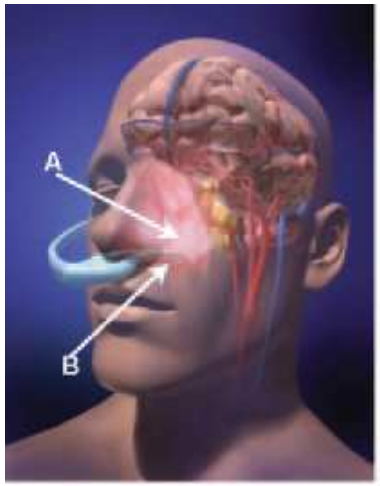


Conventional, conventional cooling with ice cold fluids and ice/coldpacks
BR, water-circulating cooling system
CC, air-circulating cooling system
AS, gel-coated cooling system
CG, intravascular cooling system

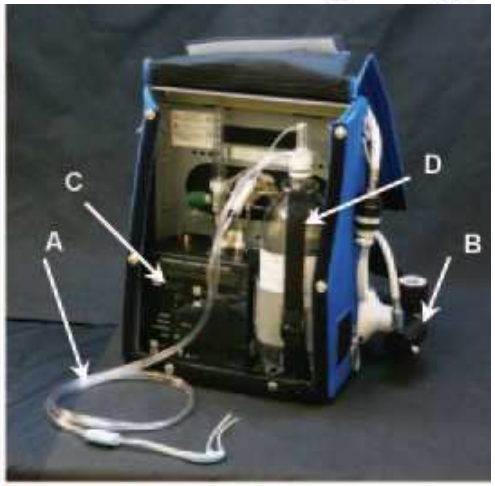


Hoedemaekers CW. Crit Care 2007





A: coolant spray
B: nasal catheter



A: nasal catheter
B: oxygen tank
C: control unit
D: coolant bottle

PRINCE study group. Circulation 2010

Quand la débuter?

- Chez le chien…

	normoT n=6	**hypoT immédiate** n=6	**hypoT décalée (15min.)** n=6
Délai ROSC-T≤34°C	-	6 min.	29 min.
Score neuro déficitaire (0% normal, 100% mort cérébrale)	44±4%	19±15%*	38±9%
Score histo de dégats cérébraux	150±32	81±13*	107±17*

p<0.05 vs groupe 1

Kuboyama K. Crit Care Med 1993

- Chez l'homme…

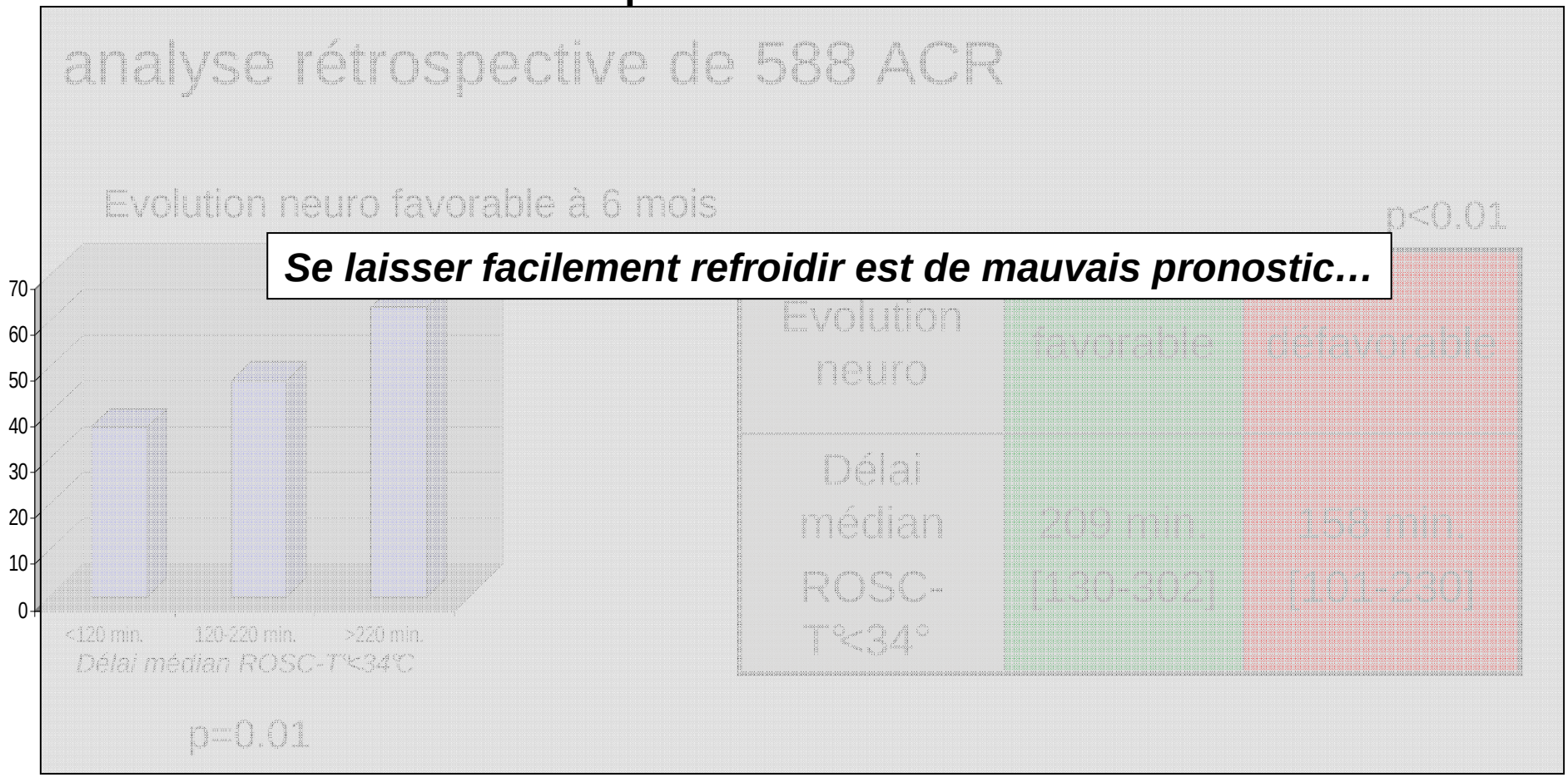
After the return of spontaneous circulation had been accomplished outside the hospital, eligible patients were randomly assigned to hypothermia or normothermia according to the day of the month, with patients assigned to hypothermia on odd-numbered days. For these patients, the paramedics began measures in the field to initiate hypothermia by removing the patient's clothing and applying cold packs (CoolCare, Cheltenham, Victoria, Australia) to the patient's head and torso. The treatment of patients assigned to normothermia followed usual prehospital treatment protocols.

Variable	Treatment Group	Admission to ED	Admission to ICU	6 Hr	12 Hr	18 Hr	24 Hr
Number of patients	Hypothermia	43	39	39	39	39	38
	Normothermia	34	33	32	32	32	31
Temperature (°C)	Hypothermia	35.0±1.18	33.3±0.98†	32.7±1.19†	33.1±0.89†	36.0±1.24†	37.4±0.85†
	Normothermia	35.5±0.90	36.0±0.76†	37.1±0.75	37.4±0.58†	37.3±0.56†	37.3±0.59†
	P value‡	0.02	<0.001	<0.001	<0.001	<0.001	0.60

Bernard. NEJM 2002

Quand la débuter?

- Attention aux interprétations « hâtives »…



Haugk et al. Critical Care 2011

Des données « pour »…

		Outcome		
	All (N=49)	Good (N=28)	Poor (N=21)	P*
Starting T, °C	35.7 [35.0–36.2]	35.3 [34.8–36.0]	36.0 [35.1–36.5]	.040
T after 1 h, °C	34.5 [33.9–35.0]	34.1 [33.5–34.7]	34.6 [34.3–35.3]	.025
Coldest T, °C	33.0 [32.8–33.0]	33.0 [32.9–33.0]	33.0 [32.6–33.2]	.941
T after rewarming, °C	36.5 [36.1–37.0]	36.5 [36.0–37.0]	36.4 [36.2–36.6]	.468

Variables with predictive value for the neurologic outcome of CA patients after MTH

	OR	95% Confidence interval	P
Age (per increment by 1 year)	.86	.76–.97	.012
BMI (per increment by 1.0 kg/m^2)	.49	.30–.79	.004
Asystole as initial rhythm (yes/no)	.01	.00–.32	.010
Thrombolysis during CPR (yes/no)	.02	.00–.71	.031
TCT (per increment by 1 h)	.73	.45–.98	.013
TTT (per increment by 1 h)*	.69	.51–.98	.037

OR, confidence intervals, and P values are derived from a stepwise forward logistic regression model with good neurologic outcome as dependent variable and all of the following as independent variables: age, sex, bystander CPR, BMI, time to CPR, out-of-hospital arrest, asystole, thrombolysis, PCI, time to cooling, TTT, TCT, starting T, T after 1 h, coldest T.

- Étude prospective observationnelle
- 49 ACR

Wolff B. Int J Card 2009

Des données « contre »…

Contents lists available at SciVerse ScienceDirect

Resuscitation

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

Clinical paper

Early- versus late-initiation of therapeutic hypothermia after cardiac arrest: Preliminary observations from the experience of 17 Italian intensive care units☆

The Italian Cooling Experience (ICE) Study Group[a]

-Étude prospective observationnelle
-174 ACR, délai médian no+low flow = 20 min.
-HypoT débutée précocément (<2h après l'ACR)
vs tardivement (>2h après l'ACR)

Des données « contre »…

		TH (*n* = 122)	Early-TH (*n* = 79)	Late-TH (*n* = 42)	*P*-value[a]
Patient characteristics					
Age	yrs	66 [54–77]	65 [54–75]	66 [52–73]	0.96
Male sex	*n* (%)	88/122 (72.1%)	57/79 (72.2%)	31/42 (73.8)	0.85
SAPS II (ICU admission)		62 [52–77]	64 [55–73]	56 [47–67.5]	0.03
GCS (ICU admission)		3 [3–4]	3 [3–4]	3 [3–4]	0.27
Cardiac arrests					
Presentation rhythm					
VF/VT	*n* (%)	74/116 (63.8%)	48/78 (61.5%)	26/37 (70.3%)	0.36
PEA/asystole	*n* (%)	42/116 (36.2%)	30/78 (38.5%)	11/37 (29.7%)	0.36
Out-of-hospital cardiac arrests	*n* (%)	100/122 (82.0%)	65/79 (82.3%)	34/42 (81.0%)	0.86
Rescue timing					
Arrest-BLS	min	5 [1–9]	3 [1–8]	6.5 [2.5–10]	0.10
Arrest-ALS	min	10 [5–14]	8 [5–12]	11.5 [5–18]	0.05
Arrest-ROSC	min	20 [10–30]	20 [10–30]	17.5 [8–32]	0.46
Therapeutic hypothermia					
Hypothermia timing					
Arrest-start hypothermia	min	90 [50–160]	60 [34–90]	191 [160–255]	<0.01
Arrest-34 °C	min	240 [140–358]	180 [100–284]	410 [300–490]	<0.01
Duration of hypothermia	h	24 [24–26]	24 [24–25]	24 [24–26.5]	0.46
Interruptions of hypothermia	*n* (%)	10/122 (8.2%)	6/79 (7.6%)	4/42 (9.5%)	0.74
Cooling device					
Ice packs	*n* (%)	37/117 (31.6%)	21/76 (27.6%)	16/40 (40.0%)	0.17
Cold fluid infusions	*n* (%)	92/117 (78.6%)	65/76 (85.5%)	27/40 (67.5%)	0.02
Air cooling	*n* (%)	37/117 (31.6%)	26/76 (34.2%)	11/40 (27.5%)	0.46
Circulating water blande	*n* (%)	34/117 (29.1%)	26/76 (34.2%)	7/40 (17.5%)	0.06
Intravenous device	*n* (%)	10/117 (8.6%)	4/76 (5.3%)	6/40 (15.0%)	0.08

ICE study group. Rescuscitation. In press

Des données « contre »…

		TH (n = 122)	Early-TH (n = 79)	Late-TH (n = 42)	P-value[b]
Intensive care unit discharge					
Mortality	n (%)	47/121 (38.8%)	37/78 (47.4%)	10/42 (23.8%)	0.01
Cerebral performance category[a]	median [IQR]	1 [1–3]	1 [1–2]	1 [1–3]	0.57
Hospital discharge					
Mortality	n (%)	58/113 (51.3%)	45/77 (58.4%)	12/35 (34.3%)	0.02
Cerebral performance category[a]	median [IQR]	1 [1–1]	1 [1–1]	1 [1–2]	0.25
1 month					
Mortality	n (%)	57/112 (50.9%)	44/74 (59.5%)	12/37 (32.4%)	0.007
Cerebral performance category[a]	median [IQR]	1 [1–2]	1 [1–1]	1 [1–2]	0.14
6 month					
Mortality	n (%)	61/112 (54.5)	45/74 (60.8%)	15/37 (40.5%)	0.04
Cerebral performance category[a]	median [IQR]	1 [1–1]	1 [1–1]	1 [1–2]	0.43

ICE study group. Rescuscitation. In press

Des données « neutre »…

- Registre scandinave
- 986 arrêts traités par hypoT
- aucune incidence sur le pronostic neuro des délais:

• avant initiation de l'hypoT

• pour atteindre l'objectif thermique

Nielsen N. Acta Anesthe. Scandinavia 2009

Pas facile l'*evidence based medicine !!*

Table 2 **Sample size calculation using mortality as an endpoint**

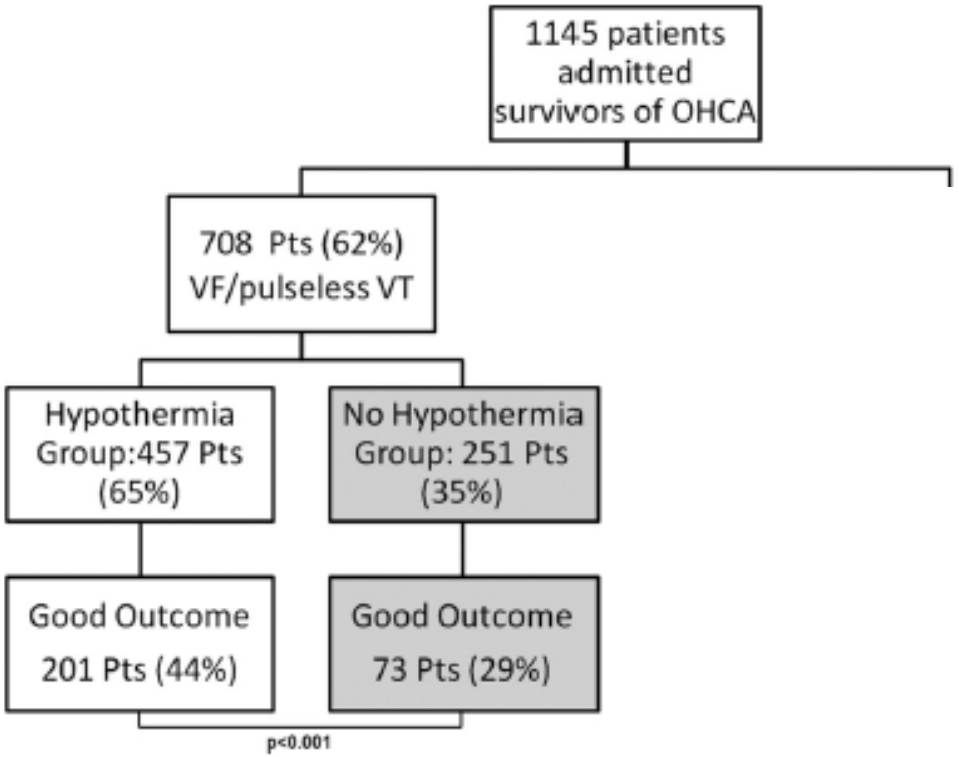
Estimated mortality standard treatment group (%)	45.0	45.0	45.0	45.0	45.0	45.0	45.0	45.0
Estimated mortality new treatment group (%)	42.5	40.0	37.5	35.0	32.5	30.0	27.5	25.0
Absolute mortality reduction (%)	2.5	5.0	7.5	10.0	12.5	15.0	17.5	20.0
Power (%)	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0

Thiele H. European Heart J. 2011

Pour qui?

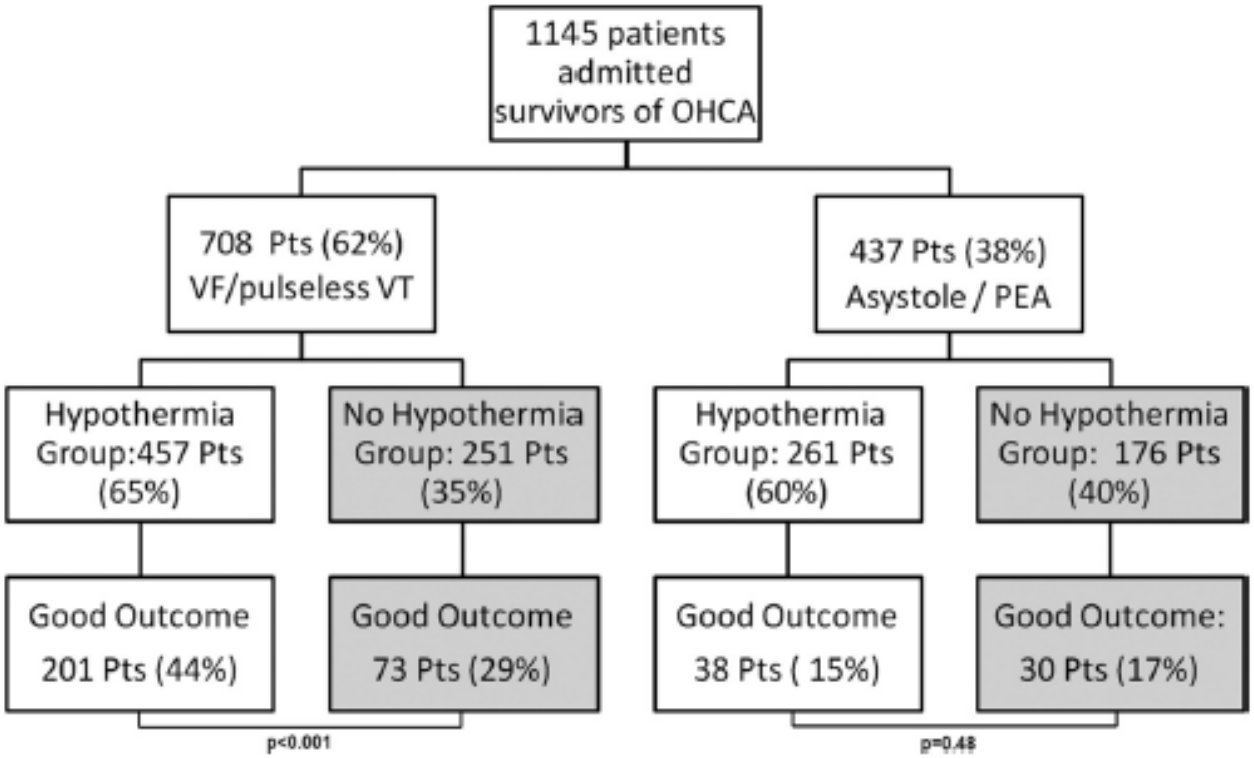
- Patient comateux au décours de la réa…
- Les FV ou TV hémodynamiquement inefficaces (« rythmes choquables »)
- Et pour les autres rythmes ??

  - asystolie
  - dissociation électro-mécanique?



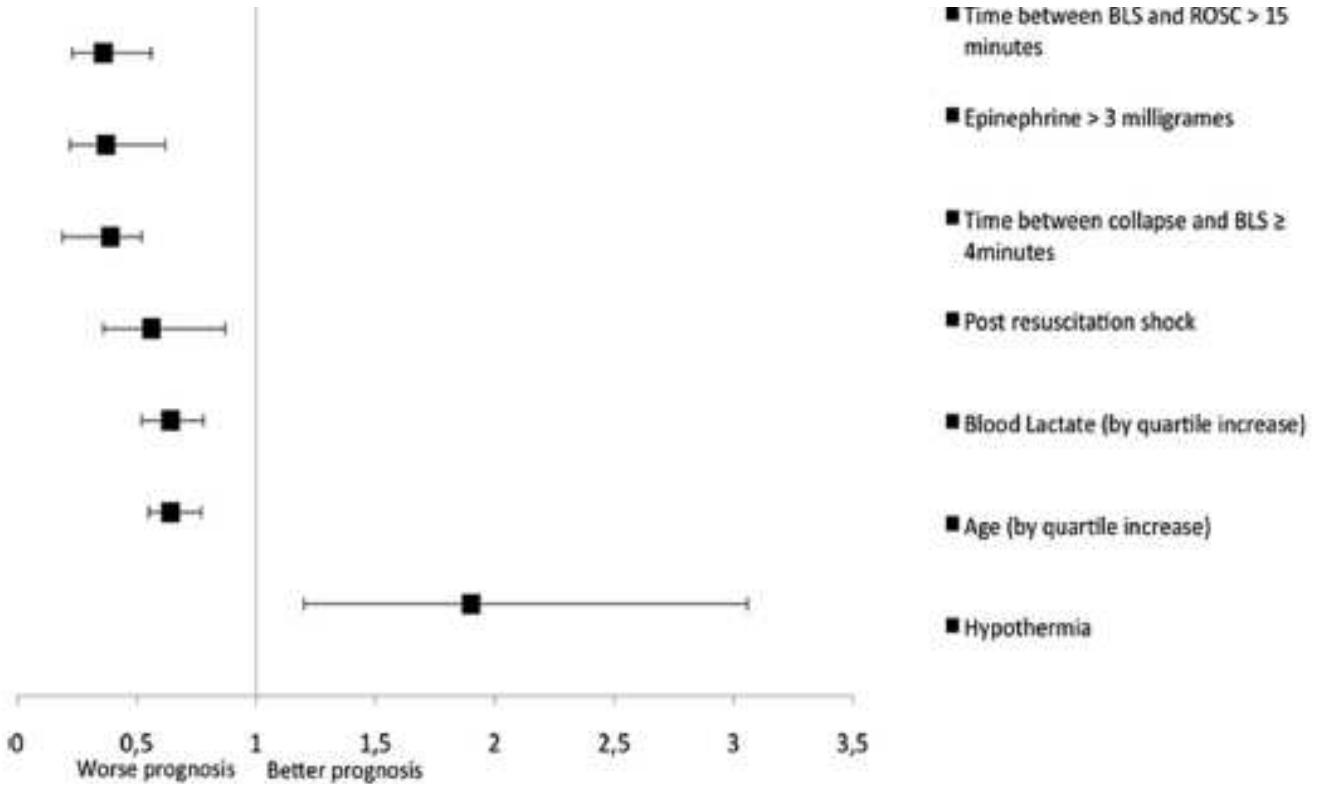
Registre parisien (Cochin)

Dumas F. Circulation 2011



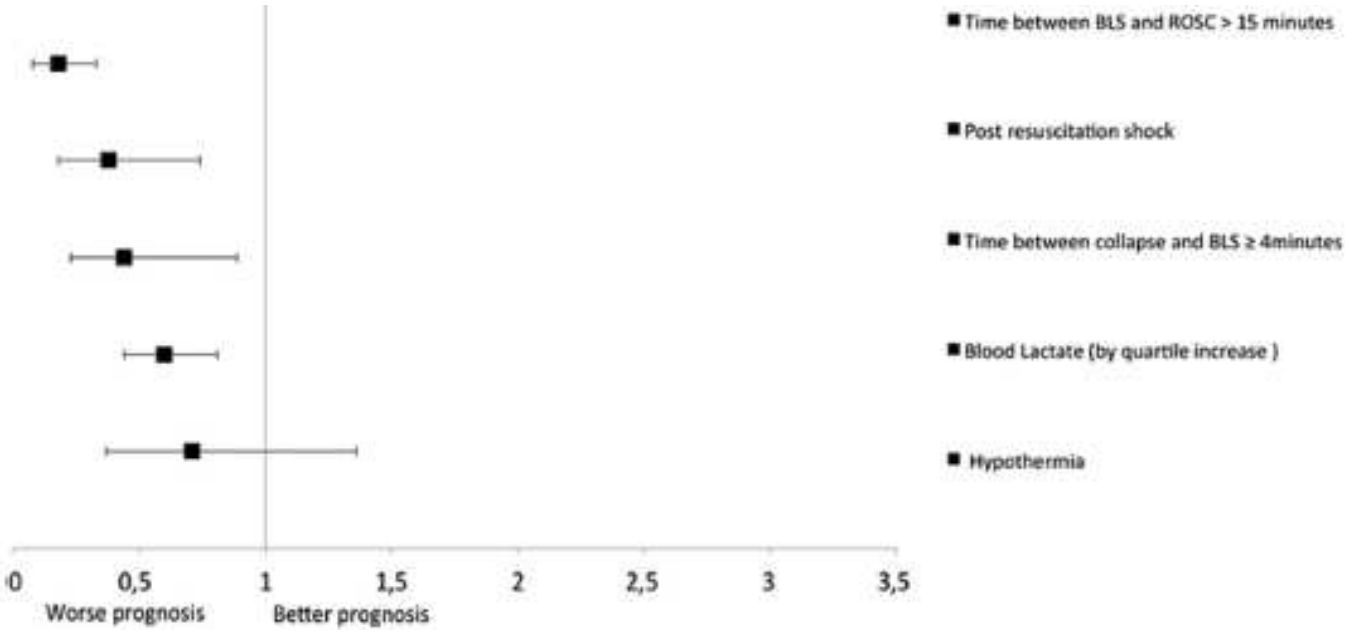
Registre parisien (Cochin)

Dumas F. Circulation 2011



Rythmes <u>choquables</u>

Dumas F. Circulation 2011



Rythmes <u>non choquables</u>

Dumas F. Circulation 2011

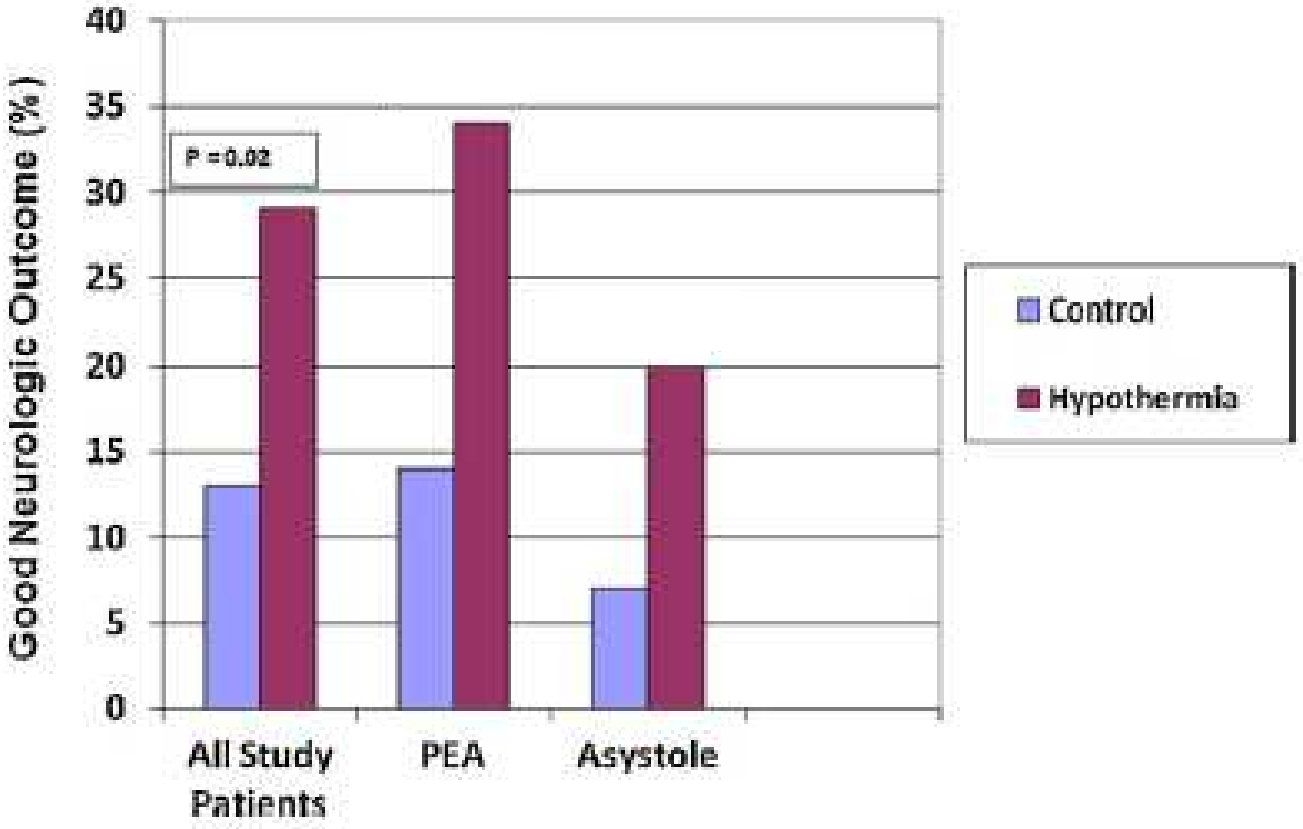
- Registre rétrospectif monocentrique américain
- 100 ACR sur rythmes non choquables
    - 48 avant mise en place de l'hypoT (groupe contrôle)
    - 52 après (groupe hypoT)

Baseline characteristics of the study population in the hypothermia and control groups.

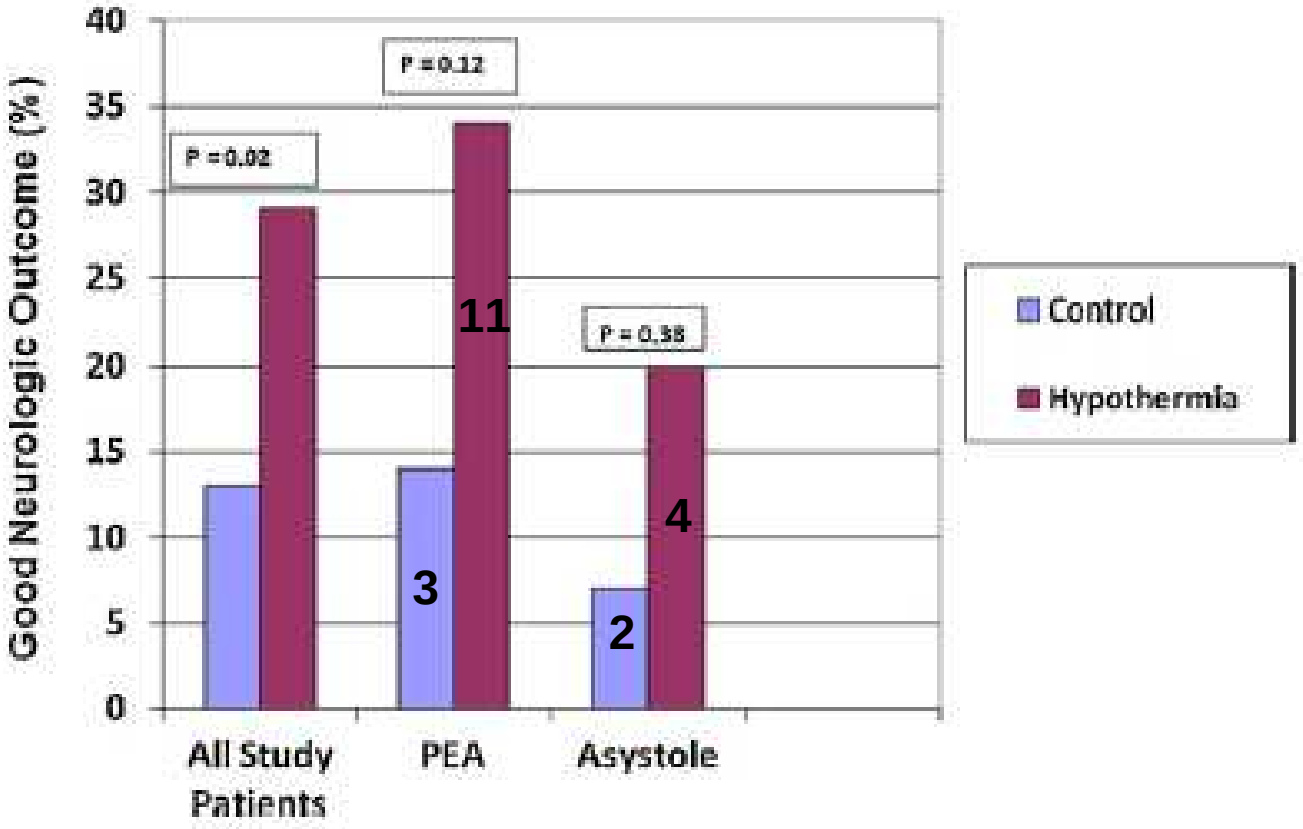
Characteristic	Hypothermia group ($n=52$)	Control group ($n=48$)	P value
Age (years)			
Median	58	68	0.074
Interquartile range	50–73	52–75	
Gender, female (%)	35	48	0.22
Whites (%)	46	44	0.34
History of CAD (%)	35	27	0.52
History of CM (%)	31	35	0.67
History of HTN (%)	67	63	0.68
History of ESRD(%)	8	6	0.78
History of DM (%)	44	35	0.42
Asystole (%)	39	56	0.10
PEA (%)	62	44	0.10
In-hospital (%)	37	60	**0.017**
Time of ROSC (min)			
Median	19	14	0.36
Inter quartile range	10–30	7–22	
Witnessed arrest (%)	69	90	**0.015**
Bystander CPR (%)	39	56	0.10

SD, standard deviation; CAD, coronary artery disease; DM, diabetes mellitus; CM, cardiomyopathy; ESRD, end-stage renal disease; HTN, hypertension; ROSC, return of speontaneous circulation; PEA, pulseless electrical activity; CPR, cardio-pulmonary resuscitation.

Lundbye JD. Resuscitation 2012



Lundbye JD. Resuscitation 2012



Lundbye JD. Resuscitation 2012

	Effective	Level of evidence*	Evidence for efficacy or lack of efficacy of hypothermia
Cardiopulmonary resuscitation in patients with witnessed arrests and ROSC within 60 min			
Initial rhythm VT or VF	Yes	I	Two RCTs,[14,15] one additional RCT underpowered to reach statistical significance,[13] much supporting evidence[16–28]
Initial rhythm asystole or PEA	Probably	III	Data from several non-randomised trials, many animal studies[4–6,13,22]
Cardiopulmonary resuscitation in unwitnessed arrests	Unknown	IV	Animal studies and case reports only

Poldermann. Lancet 2008

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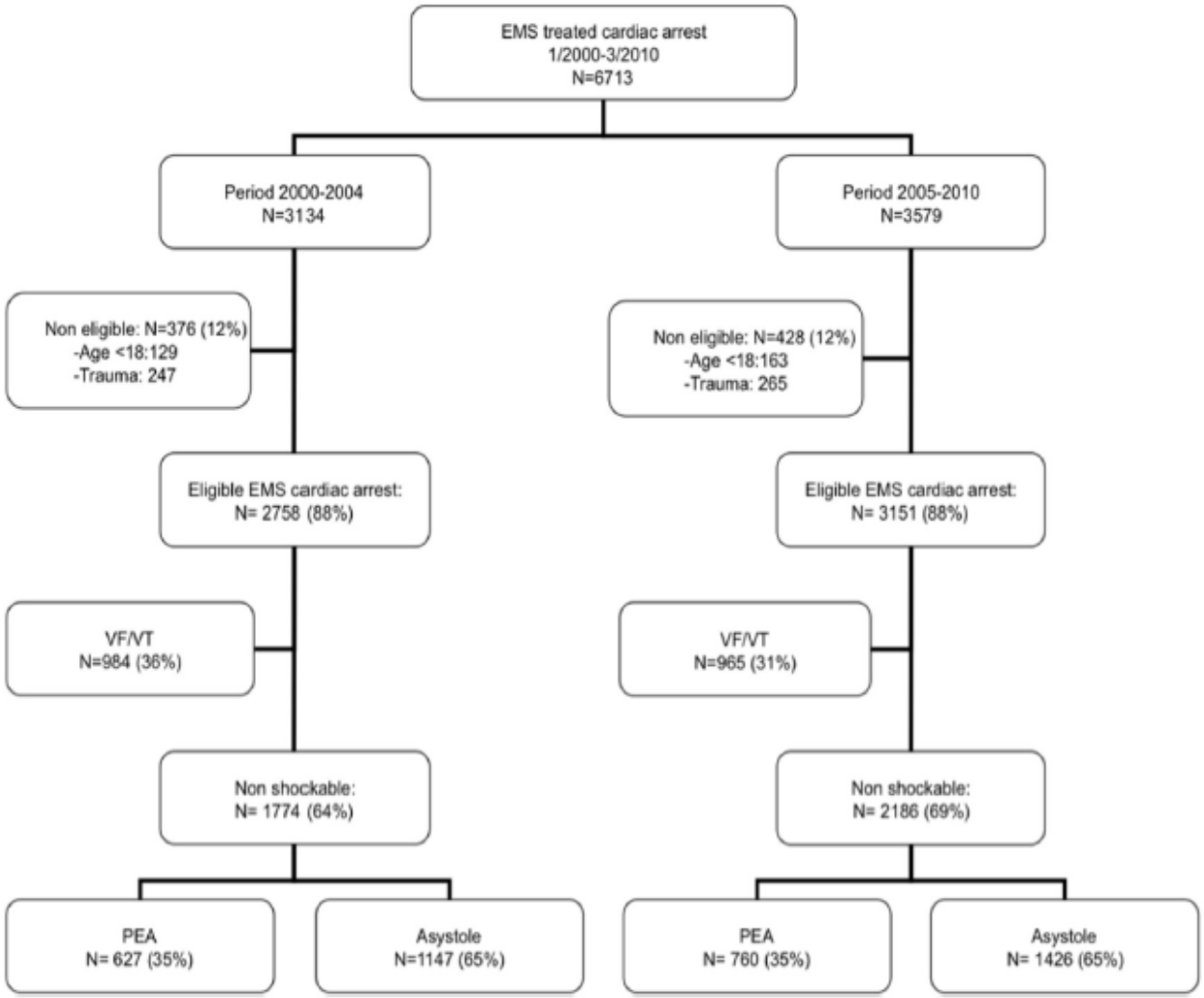
Impact of Changes in Resuscitation Practice on Survival and Neurological Outcome After Out-of-Hospital Cardiac Arrest Resulting From Nonshockable Arrhythmias

Peter J. Kudenchuk, Jeffrey D. Redshaw, Benjamin A. Stubbs, Carol E. Fahrenbruch, Florence Dumas, Randi Phelps, Jennifer Blackwood, Thomas D. Rea and Mickey S. Eisenberg

Circulation 2012, 125:1787-1794: originally published online April 2, 2012



Kudenchuk PJ. Circulation 2012

	Control Period, 2000–2004 (n=1774)	Intervention Period, 2005–2010 (n=2186)	Odds Ratio (95% Confidence Interval)			
			Unadjusted	*P*	Adjusted*	*P*
Overall						
ROSC at hospital arrival, n (%)	471 (26.6)	742 (33.9)	1.42 (1.24–1.63)	<0.001	1.50 (1.29–1.74)	<0.001
Survival to hospital discharge, n (%)	82 (4.6)	149 (6.8)	1.51 (1.14–1.99)	0.004	1.53 (1.14–2.05)	0.004
Good neurological outcome, n (%)†	60 (3.4)	112 (5.1)	1.59 (1.15–2.20)	0.005	1.56 (1.11–2.18)	0.01
1-mo survival, n (%)	73 (4.1)	135 (6.2)	1.53 (1.14–2.05)	0.004	1.54 (1.14–2.10)	0.006
1-y survival, n (%)	48 (2.7)	106 (4.9)	1.83 (1.29–2.59)	0.001	1.85 (1.29–2.66)	0.001
Patients with ROSC at hospital arrival	471	742				
Survival to hospital discharge			1.19 (0.88–1.61)	0.25	1.29 (0.94–1.76)	0.11
Good neurological outcome†			1.21 (0.86–1.70)	0.27	1.32 (0.93–1.89)	0.12
1 mo survival			1.22 (0.89–1.66)	0.23	1.30 (0.94–1.81)	0.11
1 y survival			1.47 (1.02–2.11)	0.04	1.60 (1.10–2.34)	0.02
Patients who survived to hospital discharge	82	149				
1-mo survival			1.19 (0.49–2.88)	0.70	1.33 (0.50–3.54)	0.56
1-y survival			1.75 (1.0–3.07)	0.05	2.05 (1.10–3.83)	0.02

Kudenchuk PJ. Circulation 2012

L'expérience rennaise

Unité de Soins Intensifs Cardiologiques			
Protocole : Hypothermie contrôlée après arrêt circulatoire sur trouble du rythme ventriculaire			
Codification du document	: 3.3.3	Rédacteurs	: G LEURENT (CCA), R GERVAIS (CCA)
Date d'application	: 01022008	Approbateurs	: M BEDOSSA (PH), H LE BRETON (PU PH)
N° de version du document	: 1	Gestionnaire	:
Destinataires du document		: Médecins et IDE des Urgences Cardiologiques et des Soins intensifs de Cardiologie et seniors de garde	

But et objet

Maintien d'une hypothermie contrôlée entre 32 et 34°C pendant 24 heures, au décours d'un arrêt circulatoire sur trouble du rythme ventriculaire, afin d'améliorer le pronostic neurologique du patient.

Cette hypothermie est à mettre en place dans les 4 à 8 heures qui suivent l'admission dans le service. Elle permet un taux de récupération neurologique complet ou satisfaisant à 6 mois d'environ 50%, contre environ 30% lorsqu'elle n'est pas réalisée.

Inclusion

Patient ayant fait un trouble du rythme ventriculaire compliqué d'arrêt cardio respiratoire, choqué par le défibrillateur semi-automatique ou par le SMUR,

et premières manœuvres de réanimation réalisées moins de 15 minutes après l'arrêt circulatoire,

et récupération d'une hémodynamique moins d'une heure après l'arrêt circulatoire,

et situation hémodynamique contrôlée à l'arrivée à l'USIC,

et absence de récupération neurologique après le choc et à l'arrivée aux soins intensifs (évaluer selon la sédation éventuellement reçue).

L'expérience rennaise

Actions et méthodes

1°/ sédation et curarisation :

midazolam : 0,125 mg/kg/heure IVSE,
morphine : 0,05 à 0,1 mg /kg/heure IVSE,
Une fois la cédation efficace : cis-atracurium (Nimbex®) : bolus IVD 0,1mg/kg puis 0,15 mg/kg/heure IVSE (prévention des frissons).

2°/ moyen de refroidissement externe

patient nu, corps recouvert d'un drap humide,
packs de glace ou vessie de glace sur le torse, l'abdomen, autour du crâne, racine des membres,
Cuvette de glaçon entre les jambes,
Ventilateur à l'extrémité du lit,
Couvrir l'ensemble avec un drap sec : « **tunnel de froid** ».

3°/ moyen de refroidissement interne

perfusion de sérum physiologique frais (réfrigérateur) : 500 mL à 1000 mL sur une heure.

4°/ objectifs de réanimation

Pression artérielle moyenne entre 90 et 100 mmHg **(privilégier la noradrénaline si besoin d'inotrope)**
PaO2 100 mmHg, PaCO2 40 mmHg
Normoglycémie

5°/ réchauffement (au bout de 24H)

Arrêt des méthodes de refroidissement.
Réchauffement actif par « bair hugger » jusqu'à 37°C.
Quand 37°C atteint (habituellement en 6 à 8 heures), arrêt de la curarisation, puis secondairement de la sédation.

6°/ Surveillance biologique particulière

Bilan de coagulation complet (TP-INR, TCA, Facteur V, D-Dimères, fibrinogène), NFS-plaquettes et enzymes pancréatiques toutes les 6 heures

L'expérience rennaise

- 4 ans, 70 patients traités en USIC par hypoT pour arrêt extra hospitalier
- âge: 59±14; hommes: 60 (86%))
- délais: *no flow* 4.2 ±6 minutes

  low flow 23 ±16 minutes
- 56 TV/FV (80%)

L'expérience rennaise

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- âge: 59±14; hommes: 60 (86%))
- délais: *no flow* 4.2 ±6 minutes,

  low flow 23 ±16 minutes
- 56 TV/FV (80%)

→ 35 (50%) CPC 1-2 à la sortie

L'expérience rennaise

		Good outcome Group n=35	**Poor outcome Group n=35**	**p**
Clinical	Male	29 (83%)	31 (89%)	0,73
	Age	55,6 ±12	63,1±14	**0,018**
	Current smoker	21 (60%)	25 (71%)	0,3
	Known cardiopathy	17 (48%)	24 (69%)	0,089
Anamnesis and management of the OHCA	Time of occurring (8am-8pm)	28 (80%)	21 (60%)	0,23
	Location: public place	15 (43%)	21 (60%)	0,12
	Witnessed	35 (100%)	29 (83%)	**0,025**
	"No flow" delay (minutes)	2,5 ±3,5	5,9 ±6,8	**0,017**
	"Low flow" delay (minutes)	17 ±13,7	28 ±16,8	**0,007**
	VF or pulseless VT as first rhythm	29 (83%)	27 (77%)	0,76
	Number of electric shock	3,4 ±3	3,8 ±3,6	0,68
	Dose of adrenaline (mg)	2,6 ±3,7	4,6 ±6	**0,012**
	Delay between OHCA and beginning of hypothermia (minutes)	166 ±90	225 ±108	0,08
Coronary status	Coronary angiography realised	31 (89%)	26 (74%)	0,21
	Coronary artery disease on the admission angiography	25 (81%)	19 (73%)	0,5
	STEMI	20 (80%)	16 (84%)	1
	Angioplasty	21 (60%)	7 (20%)	**0,0001**
Biomarkers at the admission	Troponin (ng/ml)	8,3 ±25	6,2 ±19	0,9
	Lactate blood (mmol/l)	2,8 ±1,7	4,7 ±3,4	**0,006**

Et ailleurs ??…

- Enquête en 02-03/2011 auprès de 105 SAMU (100% de réponse)
- 32 (30%) pratiquent l'hypoT (perf. glacée++)

  16 (15%) ont un protocole écrit

Leurs messages:

✓ tant qu'à remplir…

✓ création de « cardiac arrest centers »

Yordanov Y. Rescuscitation; in press

Discussion

- Cyclosporine: PHRC en cours…

Discussion

- Bilan étiologique de l’ACR

 place de la coro « systématique » et de l’angioplastie?

IMMEDIATE CORONARY ANGIOGRAPHY IN SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST

CHRISTIAN M. SPAULDING, M.D., LUC-MARIE JOLY, M.D., ALAIN ROSENBERG, M.D., MEHRAN MONCHI, M.D., SIMON N. WEBER, M.D., JEAN-FRANÇOIS A. DHAINAUT, M.D., PH.D., AND PIERRE CARLI, M.D.

-84 ACR sans cause évidente à cet ACR

- Coro systématique

Spaulding C. NEJM 1997

CHARACTERISTIC	VALUE
Male sex — no. (%)	70 (82)
Mean (±SD) age — yr	55.5±11.5
History of coronary artery disease or surgery — no. (%)†	17 (20)
Risk factors for coronary artery disease — no.‡	
0	34
1	38
2	10
3	2
4	1
Location of out-of-hospital cardiac arrest — no. (%)	
At home	28 (33)
At work	16 (19)
Other	41 (48)
Chest pain before arrest — no. (%)	28 (33)
Bystander-initiated CPR — no. (%)	68 (80)
Median interval between cardiac arrest and CPR — min (10th–90th percentile)	3 (1–10)
Median interval between cardiac arrest and CPR by EMSP — min (10th–90th percentile)	10 (5–60)
Median interval between cardiac arrest and return of spontaneous circulation — min (10th–90th percentile)	25 (10–98)
Median interval between cardiac arrest and arrival at hospital — min (10th–90th percentile)	110 (65–160)
First rhythm recorded on preadmission electrocardiogram — no. (%)	
Ventricular fibrillation	61 (72)
Ventricular tachycardia	18 (21)
Asystole	2 (2)
Sinus rhythm	3 (4)
Atrioventricular block	1 (1)
Electrocardiographic changes after return to sinus rhythm — no. (%)§	
ST-segment elevation	36 (42)
ST-segment depression	8 (9)
Left bundle-branch block	18 (21)
Right bundle-branch block	2 (2)
No specific ST or T patterns	10 (12)
Normal ST segment and T wave	11 (13)

Spaulding C. NEJM 1997

VARIABLE	VALUE
Normal coronary arteries — no. (%)	17 (20)
Clinically insignificant coronary artery disease (≤50 percent stenosis) — no. (%)	7 (8)
Clinically significant coronary artery disease — no. (%)	60 (71)
Single-vessel disease	22
Two-vessel disease	13
Three-vessel disease	24
Isolated left main coronary artery disease	1
Left ventricular ejection fraction — %	33.9±10.5
Left ventricular end-diastolic pressure — mm Hg	25.3±9.5

TABLE 3. TYPES OF CORONARY-ARTERY LESIONS AND RESULTS OF PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA) IN THE 60 PATIENTS WITH CLINICALLY SIGNIFICANT CORONARY ARTERY DISEASE.

VARIABLE	VALUE
Type II lesion — no. (%)	18 (30)
IIA	7
IIB	11
Type I lesion — no. (%)	2 (3)
Recent coronary-artery occlusion — no. (%)	40 (67)
PTCA attempted — no.	37
Median interval between admission and PTCA — min (10th–90th percentile)	32 (18–55)
Median duration of procedure — min (10th–90th percentile)	62 (40–120)
PTCA successful — no.	28
Stent implanted — no.	5
Intraaortic balloon inserted — no.	9

Spaulding C. NEJM 1997

TABLE 4. RELATION BETWEEN ST-SEGMENT ELEVATION, CHEST PAIN BEFORE CARDIAC ARREST, AND RECENT CORONARY-ARTERY OCCLUSION IN THE 84 PATIENTS WHO UNDERWENT CORONARY ANGIOGRAPHY.*

VARIABLE	NO. OF PATIENTS	NO. WITH RECENT CORONARY-ARTERY OCCLUSION (%)
ST-segment elevation and chest pain		
Present	15	13 (87)
Absent	69	27 (39)
ST-segment elevation or chest pain		
Present	49	31 (63)
Absent	35	9 (26)

*ST-segment elevation was defined as an elevation of more than 1 mm in two contiguous leads.

Douleur et ST+
- VPP 0.87
- VPN 0.61

Douleur ou ST+
- VPP 0.63
- VPN 0.74

Spaulding C. NEJM 1997

Table 1 Post-cardiac arrest syndrome: pathophysiology, clinical manifestations, and potential treatments.

Syndrome	Pathophysiology	Clinical manifestation	Potential treatments
Post-cardiac arrest brain injury	• Impaired cerebrovascular autoregulation • Cerebral oedema (limited) • Postischaemic neurodegeneration	• Coma • Seizures • Myoclonus • Cognitive dysfunction • Persistent vegetative state • Secondary Parkinsonism • Cortical stroke • Spinal stroke • Brain death	• Therapeutic hypothermia[177] • Early haemodynamic optimization • Airway protection and mechanical ventilation • Seizure control • Controlled reoxygenation (SaO_2 94%-96%) • Supportive care
Post-cardiac arrest myocardial dysfunction	• Global hypokinesis (myocardial stunning) • Reduced cardiac output • ACS	• Early revascularization of AMI[171,373] • Hypotension • Dysrhythmias • Cardiovascular collapse	• Early haemodynamic optimization • Intravenous fluid[97] • Inotropes[97] • IABP[13,160] • LVAD[161] • ECMO[161]
Systemic ischaemia/ reperfusion response	• Systemic inflammatory response syndrome • Impaired vasoregulation • Increased coagulation • Adrenal suppression • Impaired tissue oxygen delivery and utilisation • Impaired resistance to infection	• Ongoing tissue hypoxia/ischaemia • Hypotension • Cardiovascular collapse • Pyrexia (fever) • Hyperglycaemia • Multiorgan failure • Infection	• Early haemodynamic optimization • Intravenous fluid • Vasopressors • High-volume haemofiltration[374] • Temperature control • Glucose control[220] • Antibiotics for documented infection
Persistent precipitating pathology	• Cardiovascular disease (AMI/ACS, cardiomyopathy) • Pulmonary disease (COPD, asthma) • CNS disease (CVA) • Thromoboembolic disease (PE) • Toxicologic (overdose, poisoning) • Infection (sepsis, pneumonia) • Hypovolaemia (haemorrhage, dehydration)	• Specific to aetiology, but complicated by concomitant PCAS	• Disease-specific interventions guided by patient condition concomitant PCAS

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; IABP, intra-aortic balloon pump; LVAD, left ven device; EMCO, extracorporeal membrane oxygenation; COPD, chronic obstructive pulmonary disease; CNS, central nervous cerebrovascular accident PE, pulmonary embolism; and PCAS, post-cardiac arrest syndrome.

Recommandation européennes Resuscitation 2008

The majority of out-of-hospital cardiac arrest patients have coronary artery disease.[656,657] Acute changes in coronary plaque morphology occur in 40–86% of cardiac arrest survivors and in 15–64% of autopsy studies.[658] It is well recognised that post-cardiac arrest patients with ST elevation myocardial infarction (STEMI) should undergo early coronary angiography and percutaneous coronary intervention (PCI) but, because chest pain and/or ST elevation are poor predictors of acute coronary occlusion in these patients,[659] this intervention should be considered in all post-cardiac arrest patients who are suspected of having coronary artery disease.[629,633,659–665] Several studies indicate that the combination of therapeutic hypothermia and PCI is feasible and safe after cardiac arrest caused by acute myocardial infarction.[629,633,638,665,666]

European Resuscitation Council Guidelines for Resuscitation 2010

- 111 ACR, dont 50 ST+
- 61 survivants

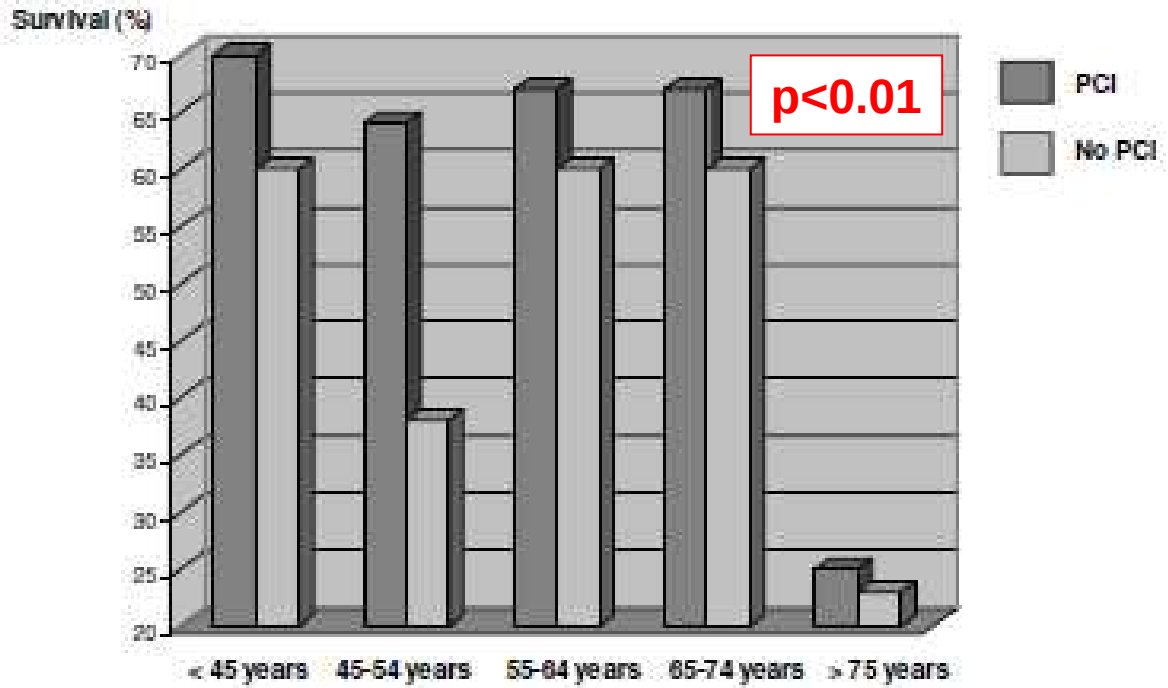

Figure 3 Survival according to whether a percutaneous coronary intervention (PCI) was performed in the different study groups.

Cronier P. Critical Care 2011

L'expérience rennaise

		Good outcome Group n=35	**Poor outcome Group n=35**	**p**
Clinical	Male	29 (83%)	31 (89%)	0,73
	Age	55,6 ±12	63,1±14	**0,018**
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Registre parisien PROCAT (01/03-12/08)

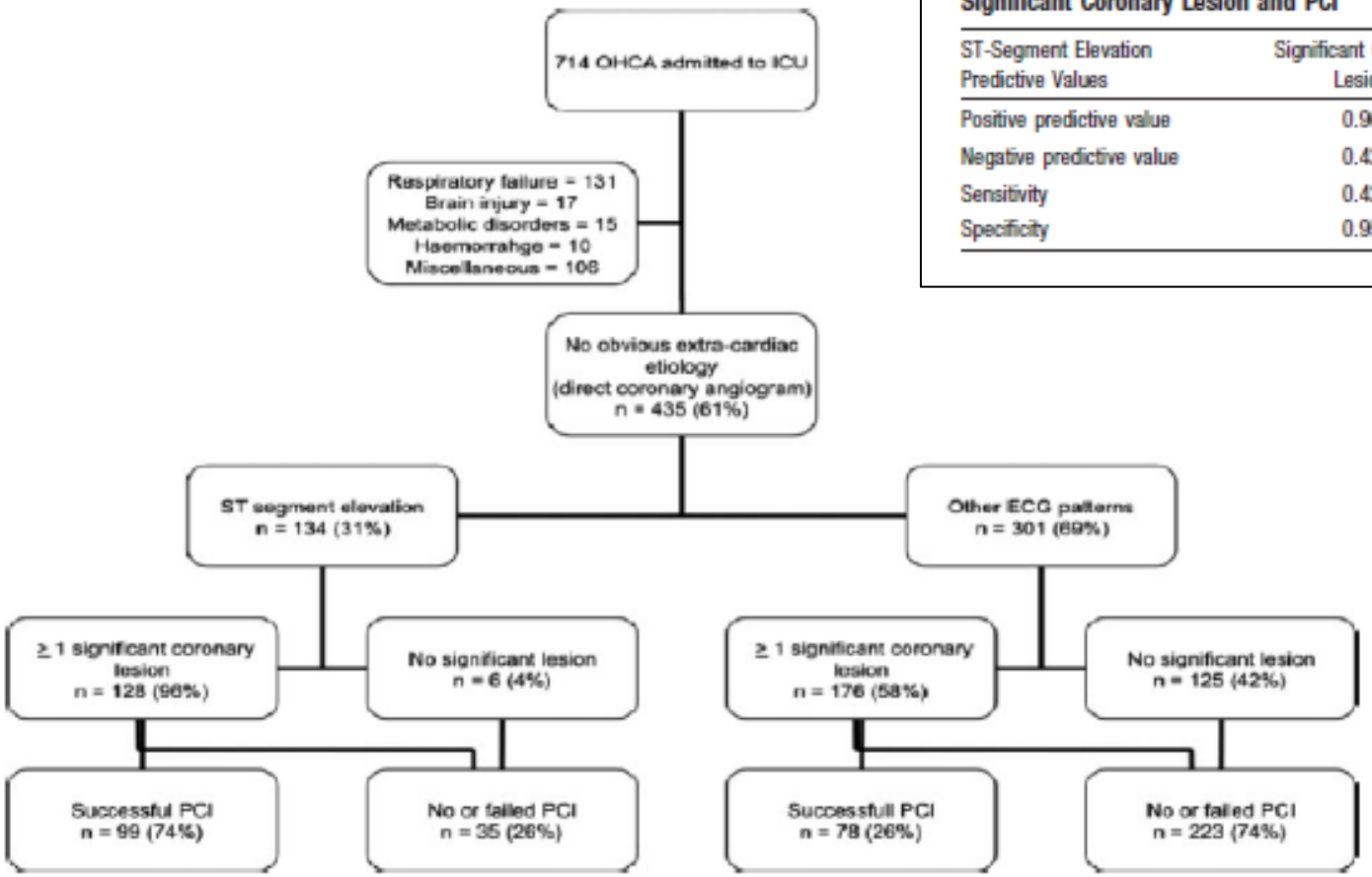


Table 2. Predictive Values of ST-Segment Elevation for Significant Coronary Lesion and PCI

ST-Segment Elevation Predictive Values	Significant Coronary Lesion	Significant PCI
Positive predictive value	0.96	0.74
Negative predictive value	0.42	0.74
Sensitivity	0.42	0.56
Specificity	0.95	0.83

Dumas F. CCI 2010

Registre parisien PROCAT (01/03-12/08)

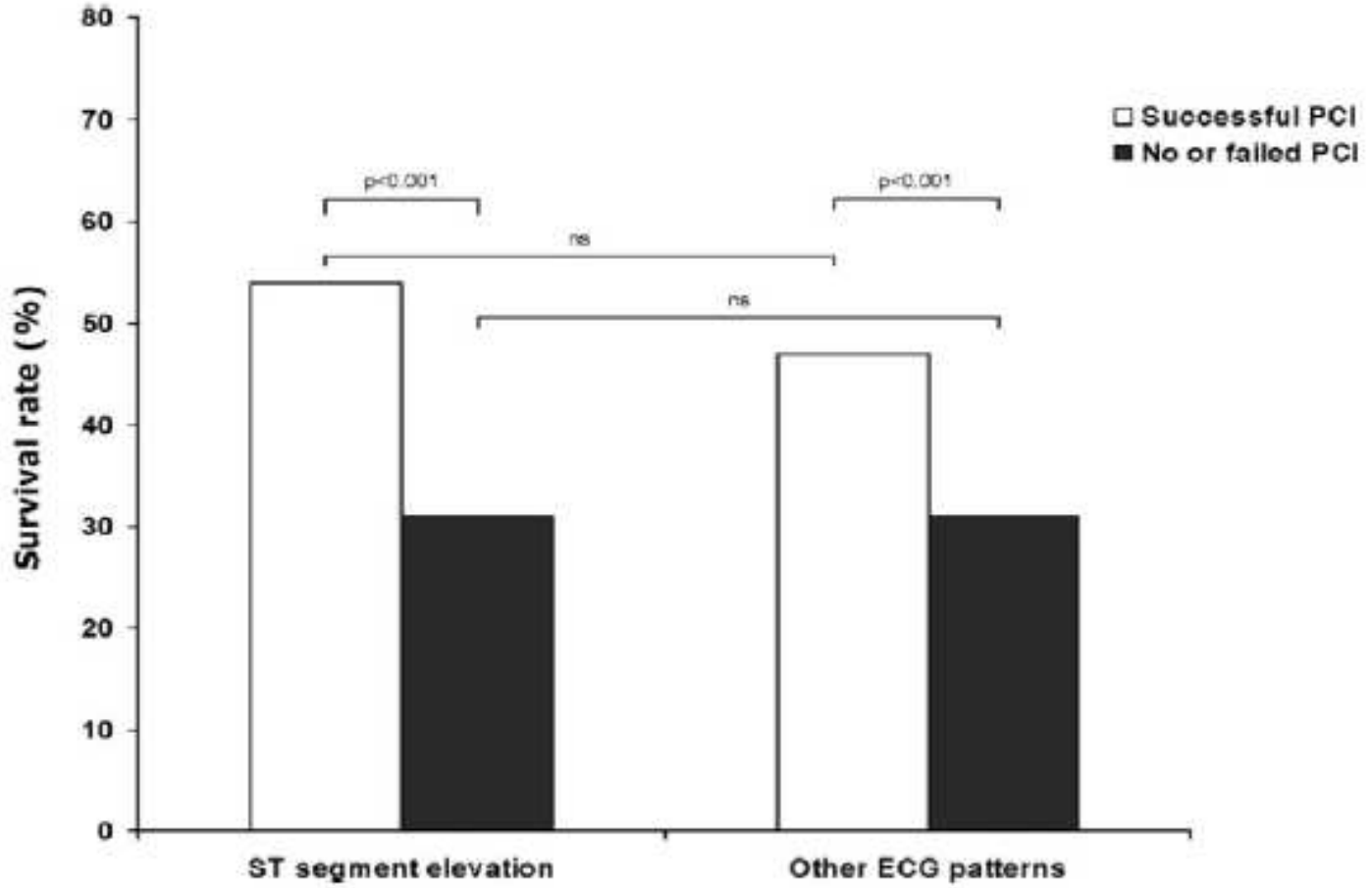


Figure 2. Survival rates according to the performance and outcome of PCI. ns indicates not significant.

Dumas F. CCI 2010

Registre parisien PROCAT (01/03-12/08)

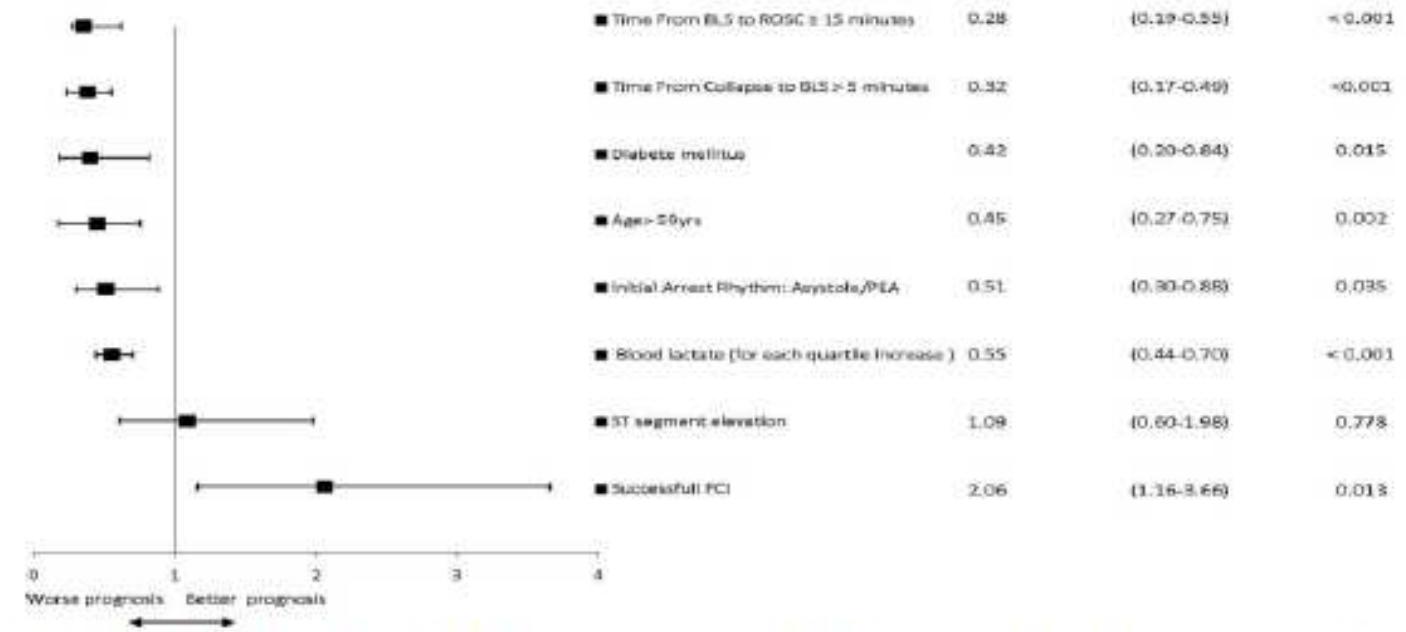


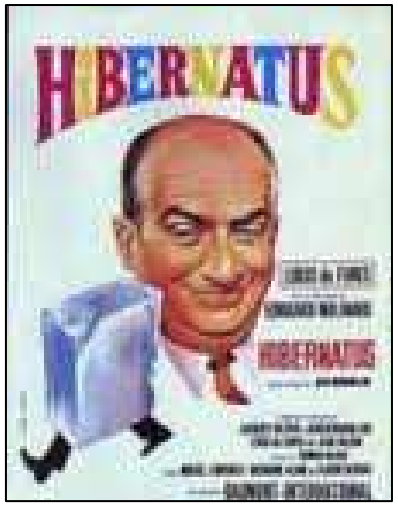
Figure 3. Multivariable logistic regression analysis of early predictors of survival in patients with OHCA without obvious extracardiac causes. PEA indicates pulseless electrical activity.

Dumas F. CCI 2010

Coro+/-ATC post ACR

- Faisable
- N’augmente pas les délais intra hospitaliers de prise en charge
- Incontournable: ischémie responsable de l’ACR, réduction de la dysfonction myocardique post-ACR, +/-pose CPBIA

Conclusion
« *take home message* »



- Efficacité de l'hypoT:

- prouvée pour les ACR sur VF/TV

- possible pour les autres causes d'ACR

- Perf. de SSI glacé dès que possible