Hypothermic Resuscitation

Beyond „Therapeutic:“: Intraarrest Hypothermia to Mitigate Reperfusion Injury after Cardiac Arrest

1st International Critical Care and Emergency Medicine Congress
Istanbul, 11/6-8/2013

HYPOTHERMIC RESUSCITATION

(non-official) definitions

Protective Hypothermia:

Hypothermia induced before cardiac arrest (CA)

Not feasible for sudden CA

Preservative Hypothermia:

Hypothermia induced during cardiac arrest before reperfusion

Resuscitative or therapeutic Hypothermia:

Hypothermia after restoration of spontaneous circulation

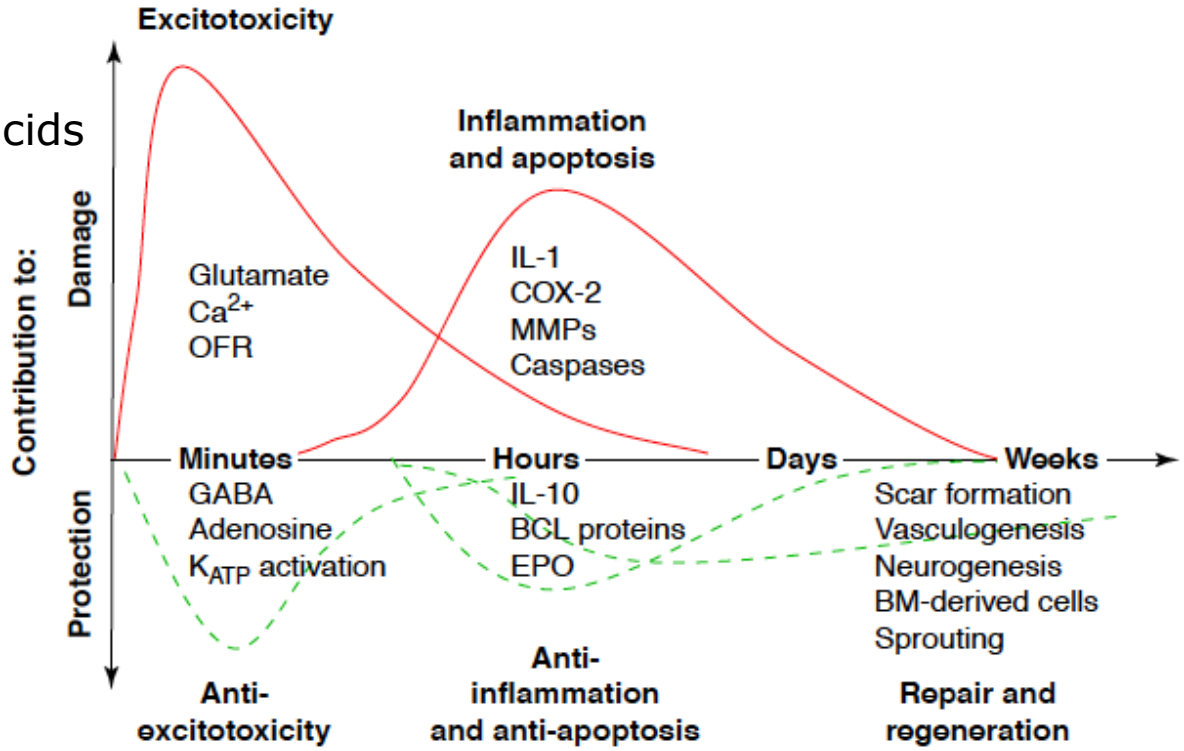
HYPOTHERMIC RESUSCITATION

timeline of reperfusion injury

hypothesis: the initial phase of reperfusion is crucial

early mechanisms of reperfusion injury:

- calcium overload
- excitotoxicity amino acids
- ROS



Dirnagl U et al. TINS 2003

COOLING TECHNIQUES

how to induce hypothermia in a no flow state

surface cooling

- circulation needed
- cold capillary blood from skin cools the core
- ineffective during cardiac arrest

cooling during circulation and arrest

- 90 kg human sized swine
- cooling with -40°C cold gas
- brain temperatures

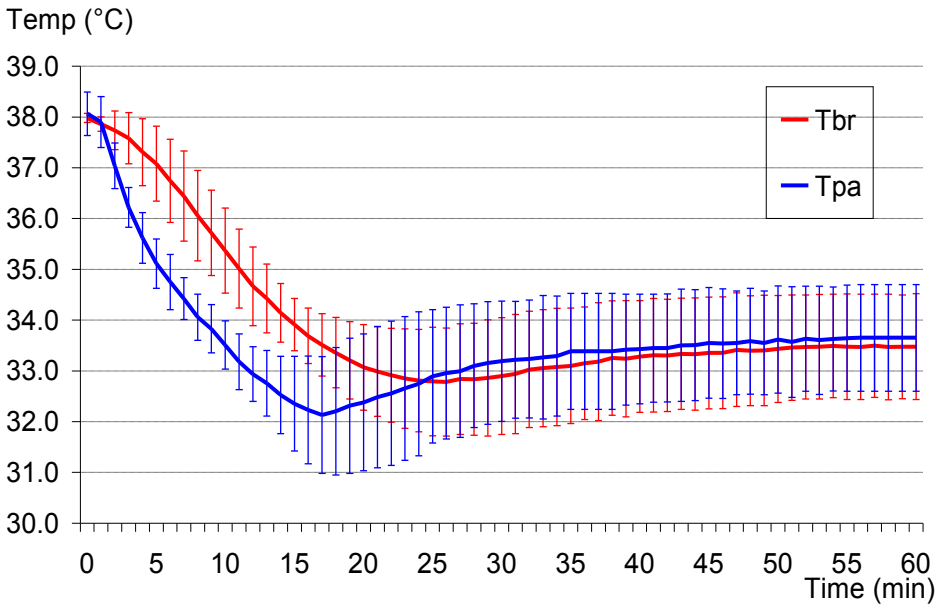
Bayegan et al. Resuscitation 2004 (abstract)

SURFACE COOLING

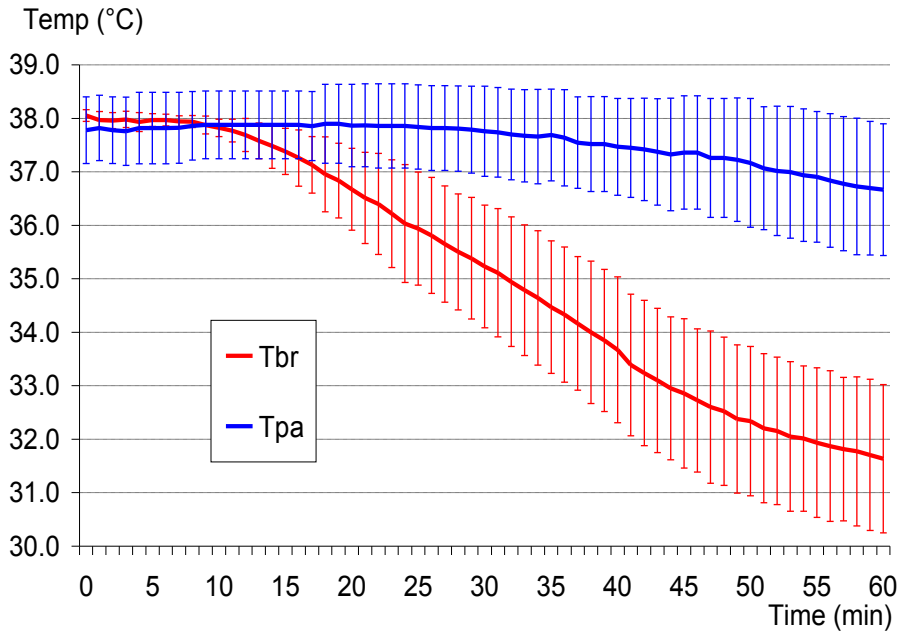
beating heart vs. cardiac arrest

cold gas:

beating heart



cardiac arrest



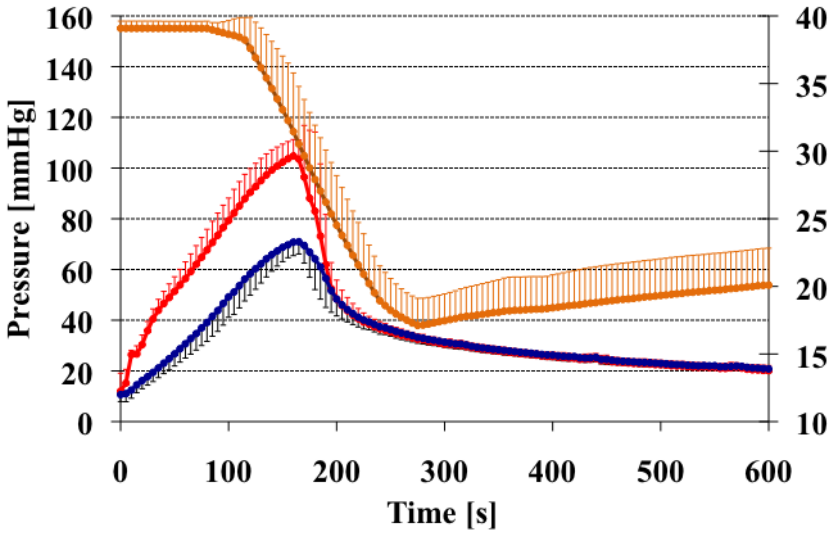
Bayegan et al. Resuscitation 2004 (abstract)

INVASIVE COOLING

aortic flush, extracorporeal circulation

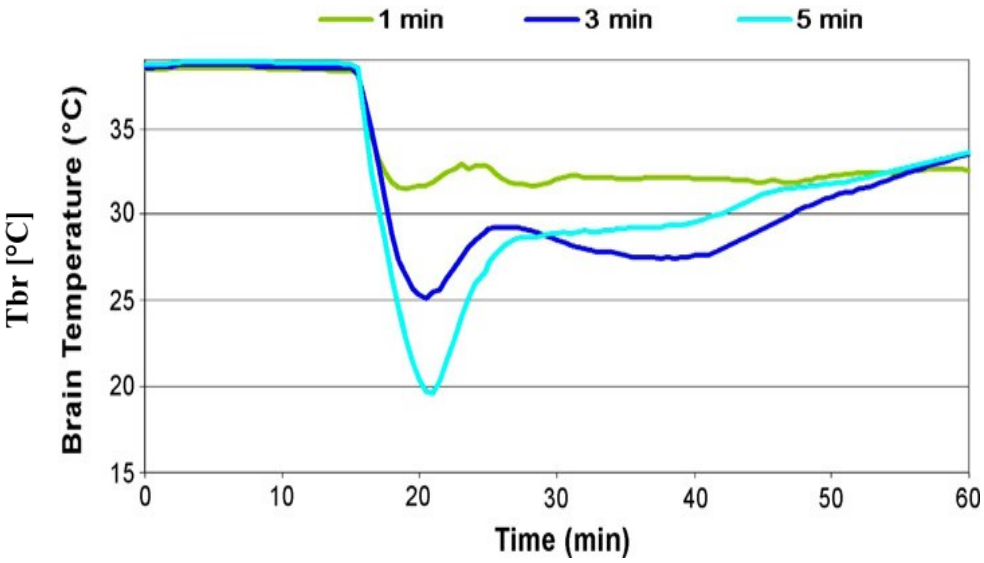
cardiac arrest:

aortic flush, cold saline 100 ml/kg



Janata a et al *Crit Care Med*. 2006

ECMO with heat exchanger



Outcome after resuscitation using controlled rapid extracorporeal cooling, Weihs et al Resuscitation 2010.

HYPOTHERMIC RESUSCITATION

ice cold iv. saline during resuscitation

- 33 patients
- 2L 4°C cold saline 0.9% over 30 min during ACLS
- ΔTesophagus -2.1°C
- median time to reach <34°C after ROSC: 16 minutes
- 1 patient developed pulmonary edema
- survival to discharge: 4/33 (12%)

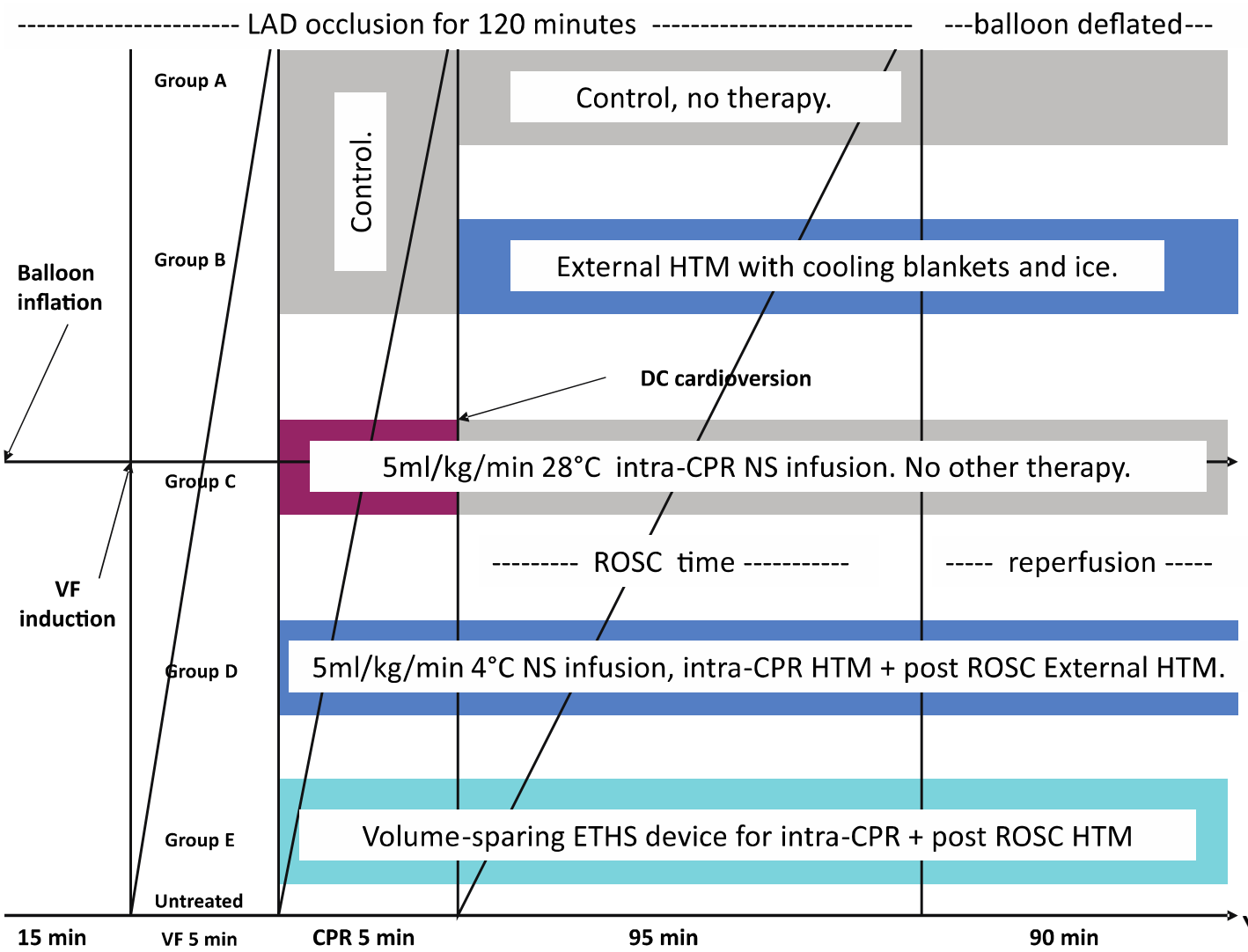
Conclusion:

- 2L cold saline during ACLS is feasible, effective and safe

Mild hypothermia during advanced life support. Bruel et al. Critical Care 2008.

HYPOTHERMIC RESUSCITATION

ice cold iv. saline during resuscitation



Yannopoulos et al.

HYPOTHERMIC RESUSCITATION

ice cold iv. saline during resuscitation

46 pigs, LAD-occlusion cardiac arrest model

CoPP = coronary perfusion pressure (diastolic aortic pressure minus diastolic right atrial pressure during CPR)

SBP = systolic blood pressure

	A	B	C	D	E
	No intervention	Surface cooling post ROSC	25 ml/kg 28°C iv saline intra-arrest	25 ml/kg 4°C iv saline intra-arrest	Cooling catheter intra-arrest
ROSC	56%		13%	55%	100%
SBP, mmHg	100		102	11	113
CoPP, mmHg	21		13	15	21

Intra–Cardiopulmonary Resuscitation Hypothermia With and Without Volume Loading in an Ischemic Model of Cardiac Arrest. Yannopoulos et al, Circulation 2009.

HYPOTHERMIC RESUSCITATION

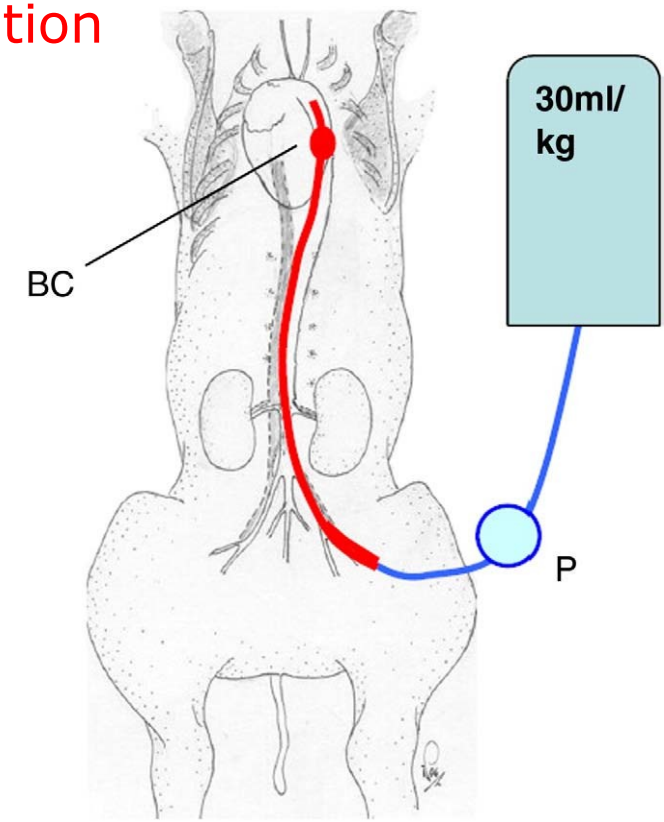
ice cold intra-arterial saline during resuscitation

24 pigs, electrical vf-cardiac arrest model

15 min cardiac arrest

A	B	C
ACLS, no intervention	30 ml/kg 38°C iv saline intra-arrest	30 ml/kg 4°C iv saline intra-arrest

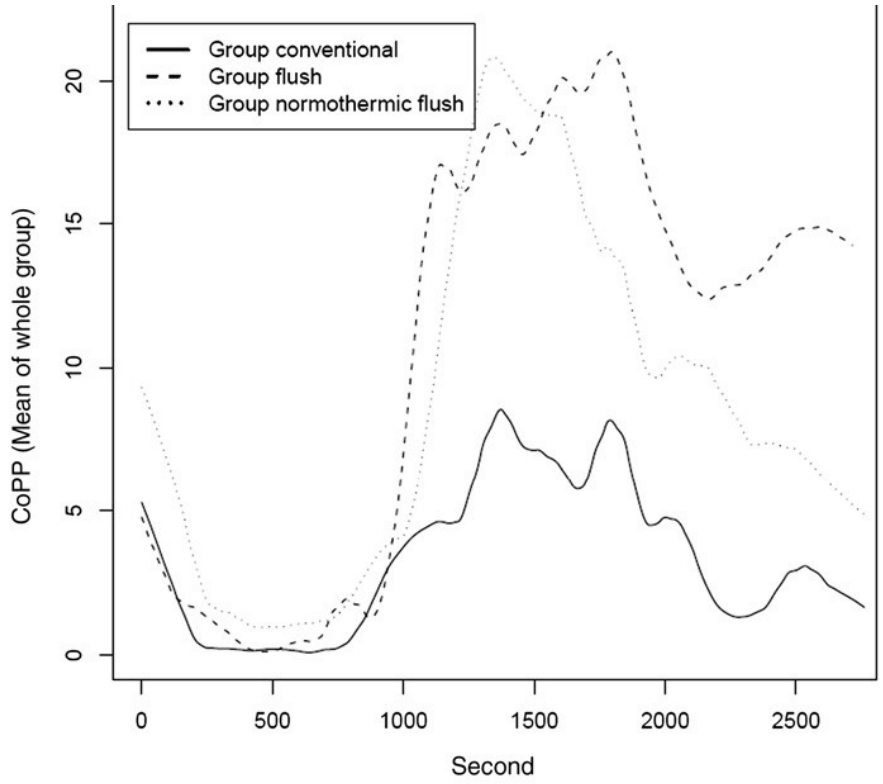
Outcome	Conventional	Hypothermic Flush	Normothermic Flush
OPC 1		●	●
OPC 2		●●	
OPC 3			●
OPC 4			
OPC 5			●
No Rosc	●●●●●●●●	●●●●●	●●●●●
ROSC	0	3	3
Survival to 9 days	0	3	2
NDS %	-	0,6,13	0,49

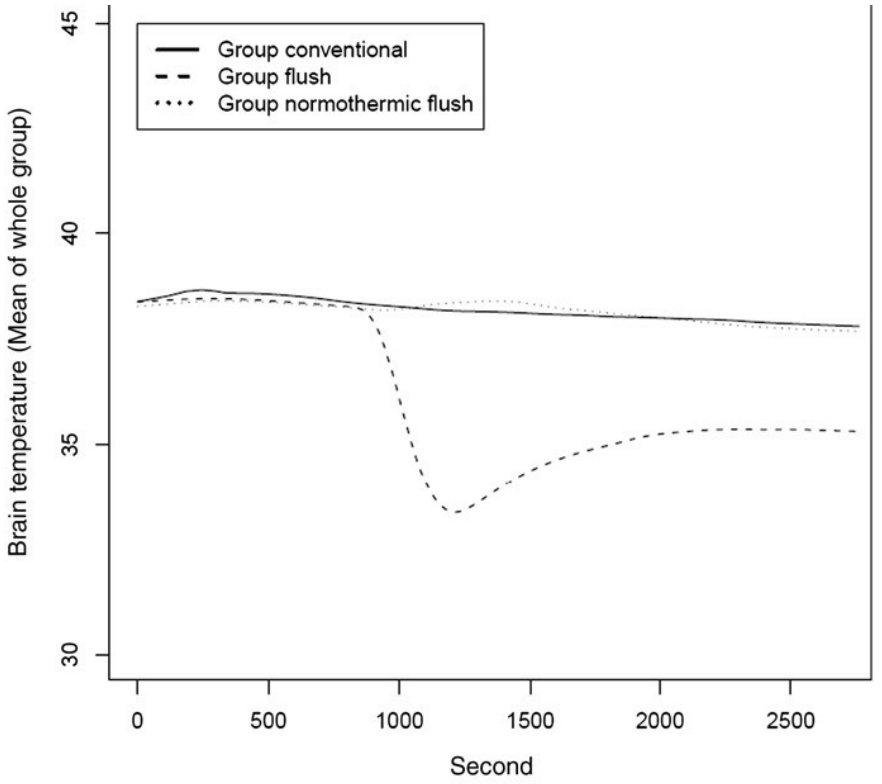


Weihs et al, Am. J. Em. Med. 2009.

HYPOTHERMIC RESUSCITATION

ice cold intra-arterial saline during resuscitation





Rapid induction of hypothermia with a small volume aortic flush during cardiac arrest in pigs
Weihs et al, Am. J. Em. Med. 2009.

LOCAL SURFACE COOLING

nasopharyngeal cooling

- **Hypothesis: a coolant into the nasal cavity will cool adjacent tissues – including the brain**

- 16 pigs weighing 40±3kg
- 15 min VF
- 5-15 min of ACLS
- randomization to nasal cooling vs normothermia prior to shock

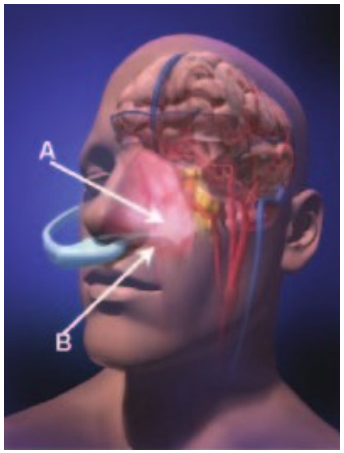
Intra-Arrest Transnasal Evaporative Cooling: A Randomized, Prehospital, Multicenter Study. Castrén et al. Circulation 2010.

LOCAL SURFACE COOLING

nasopharyngeal cooling with rhinochill

- 93 patients during arrest, cooled with transnasal cooling, compared to 101 control patients
- ΔTtympanic ROSC-admission: 1.3°C
- Safe, some local side effects
- **Reliability of Ttympanic?**
- Good outcome (CPC1-2):

  cooling group 11/93 (12%) control group: 9/101 (9%)



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Extracorporeal CPR (E-CPR)

cooling with cardiopulmonary bypass during ca

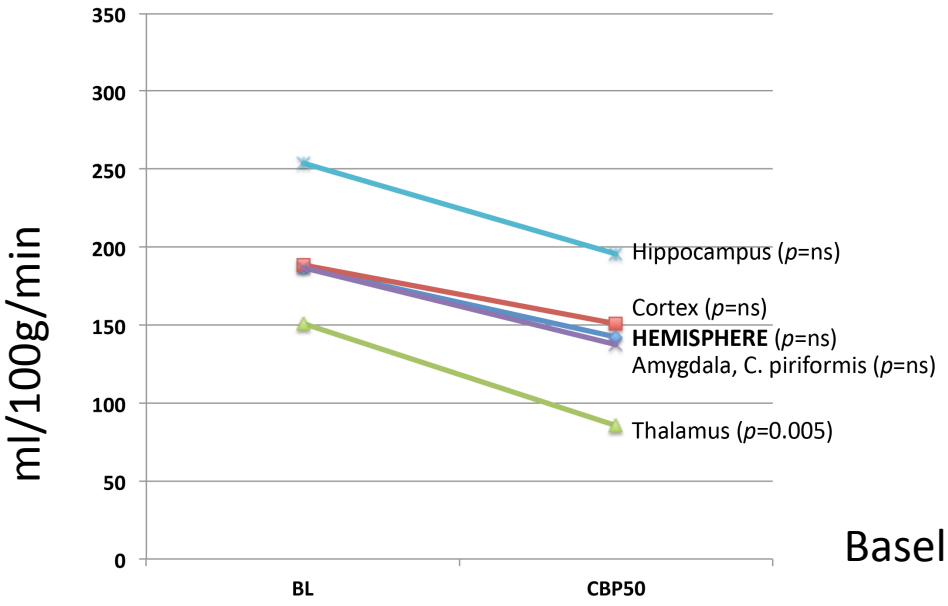
Probability of ROSC decreases over time

Overall Hypothesis:

- support the heart for prolonged time periods
- achieve critical organ perfusion more reliably than chest compressions
- resuscitate the patients after prolonged periods of CA
- induce hypothermia rapidly

E-CPR

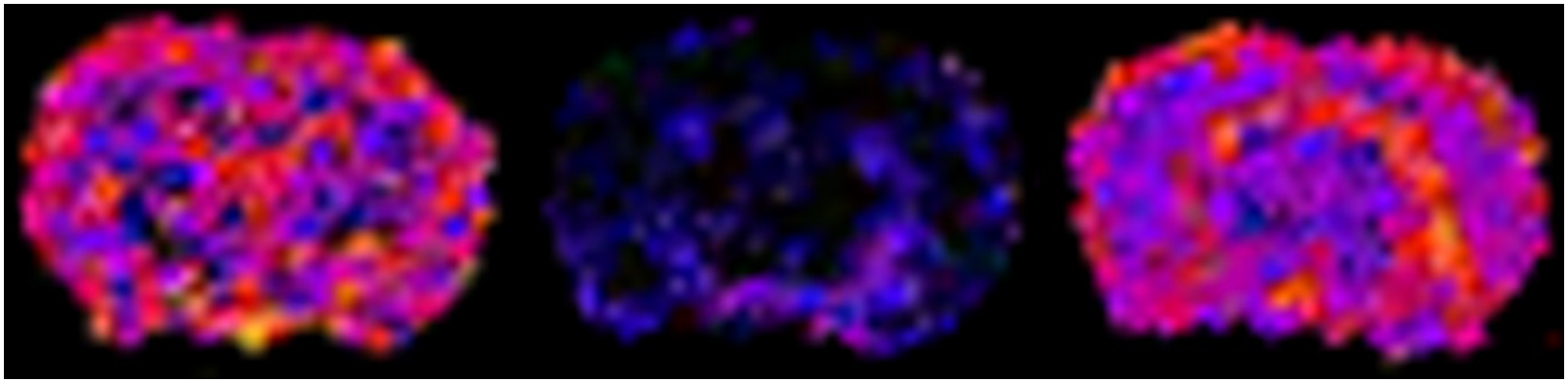
brain perfusion with E-CPR after 10 min ca in rats



Cerebral blood flow with spin label MRI:

Hemispheric CBF by E-CPR is 76% of baseline

Baseline – 10 min Cardiac Arrest – CPB 50 ml/min



HYPOTHERMIA AND E-CPR

for refractory cardiac arrest – perfusion and cooling

1-year experience of Erasme Hospital, Brussels

Inclusion criteria:

(a) witnessed cardiac arrest with immediate CPR (<5 min from call to chest compression)

(b) refractory CA, as defined by the absence of ROSC after 10 min of Advanced Life Support (ALS)

(c) age less than 65 years and no major co-morbidity

(d) the ability to initiate ECMO within 1 h from arrest

Extracorporeal life support associated with hypothermia and normoxemia in refractory cardiac arrest. Fagnoul et al, Resuscitation 2013

E-CPR

for refractory cardiac arrest

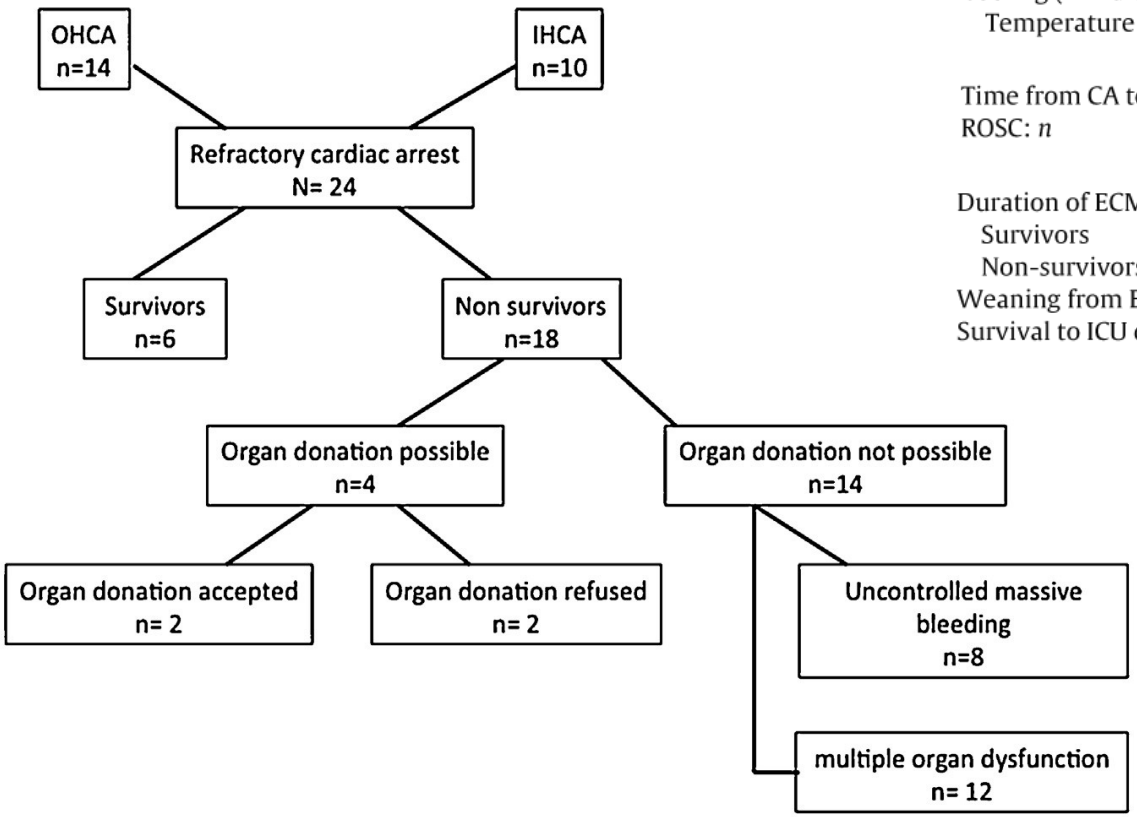
Methods:

- mechanical CPR with Lucas
- 30 ml ice cold saline/kg during CPR
- veno-arterial ECMO
- heat exchanger to maintain 33°C for 24 h
- PCI after ECMO implantation

Extracorporeal life support associated with hypothermia and normoxemia in refractory cardiac arrest. Fagnoul et al, Resuscitation 2013

E-CPR

for refractory cardiac arrest



General characteristics of the patients ($n = 24$) and cardiac arrest data.

Age: years	48 [38–55]
Male: *n*	14
Location of cardiac arrest	
In hospital: *n*	10
Out hospital: *n*	14
By-stander CPR: *n*	22
Cardiac arrest to ALS time (min)	10 [5–15]
Initial recorded rhythm: *n*	
VF/VT	10
PEA/asystole	14
Mechanical chest compression: *n*	22
Cooling (IV fluids/intranasal cooling): *n*	16
Temperature at ECMO initiation: (°C)	32.3 ± 2.9
Time from CA to ECMO (min)	58 [45–70]
ROSC: *n*	18
Duration of ECMO (Hours)	48 [2–66]
Survivors	96 [54–172]
Non-survivors	3.5 [2–48]
Weaning from ECMO; *n* (%)	7 (29%)
Survival to ICU discharge *n* (%)	6 (25%)

EPR
EMERGENCY PRESERVATION AND RESUSCITATION
Definition

„Torpor“ (lat. Erstarrung)

Reduced metabolic rate to protect the organism during adversity (harsh climate, low availability of food – or ischemia)

EPR, SA

A hibernation-like state, induced in animals that normally do not hibernate to protect the organism during adversity (shock, ischemia)

Safar and Bellamy 1984

“preservation of viability of the organism for transport and repair during circulatory arrest of 2 h or longer, followed by delayed resuscitation to survival without brain damage”

EPR

induction by hypothermia

- Metabolism is reduced by 5% to 8% /°C temperature reduction

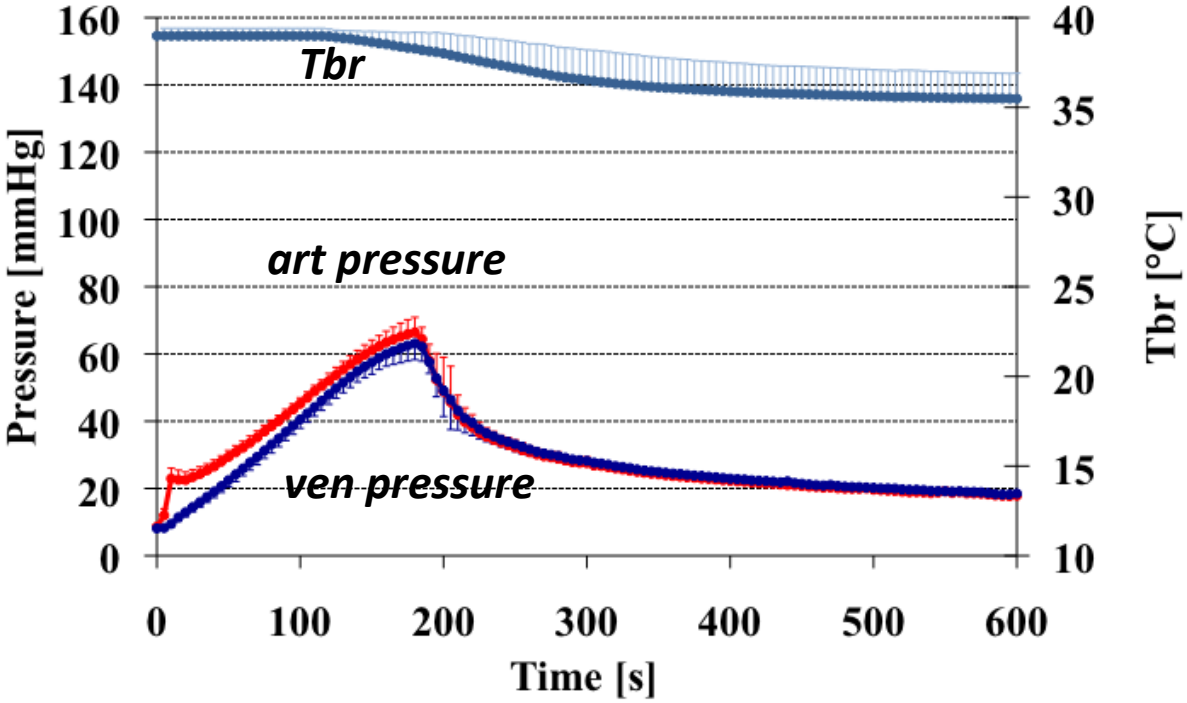
Rosomoff et al, Am J Physiol 1954
Lanier et al, J Neurosurg Anesthesiol 1995

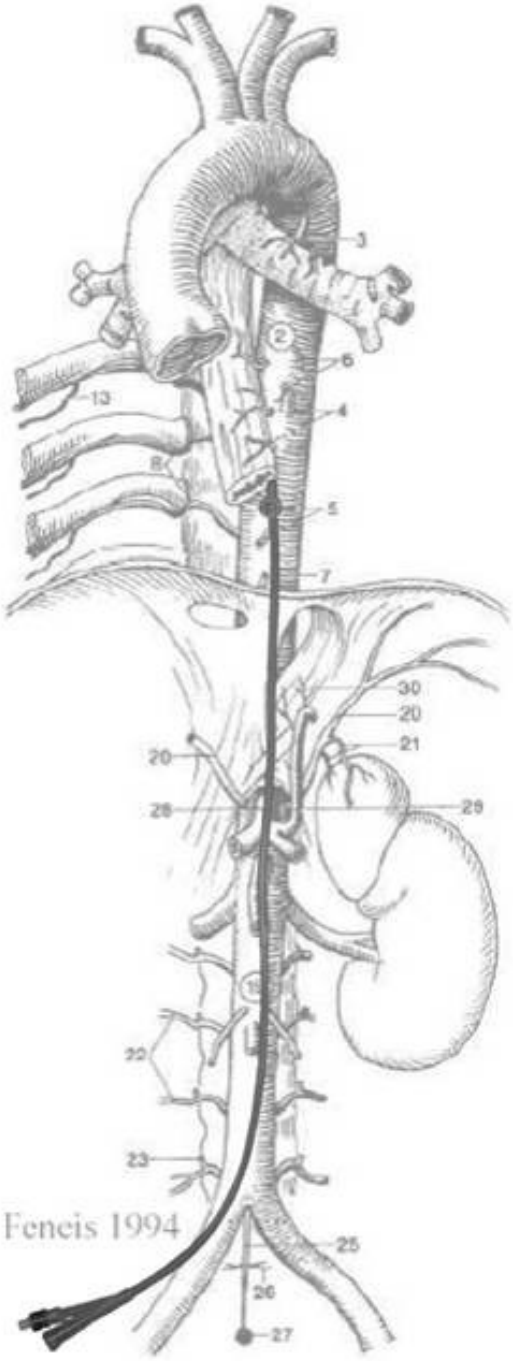
EPR

in vfib-cardiac arrest

Swine after 10 min of VF-CA

Aortic flush (100 ml/kg) via balloon catheter





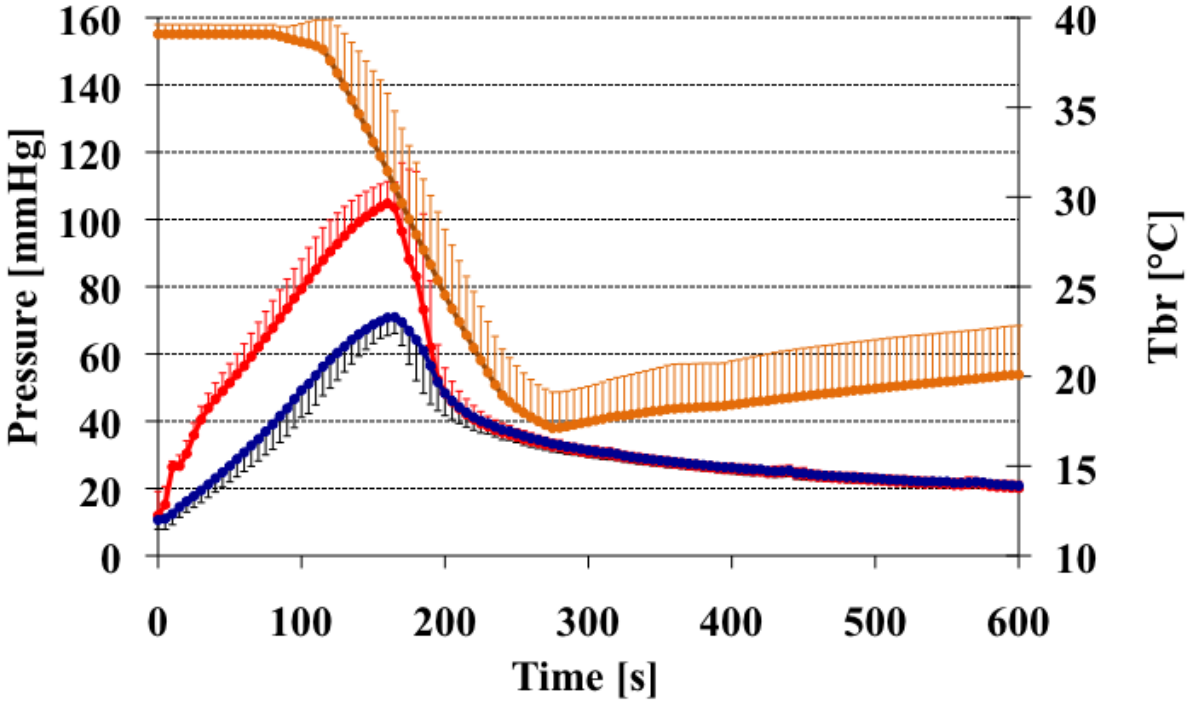
EPR

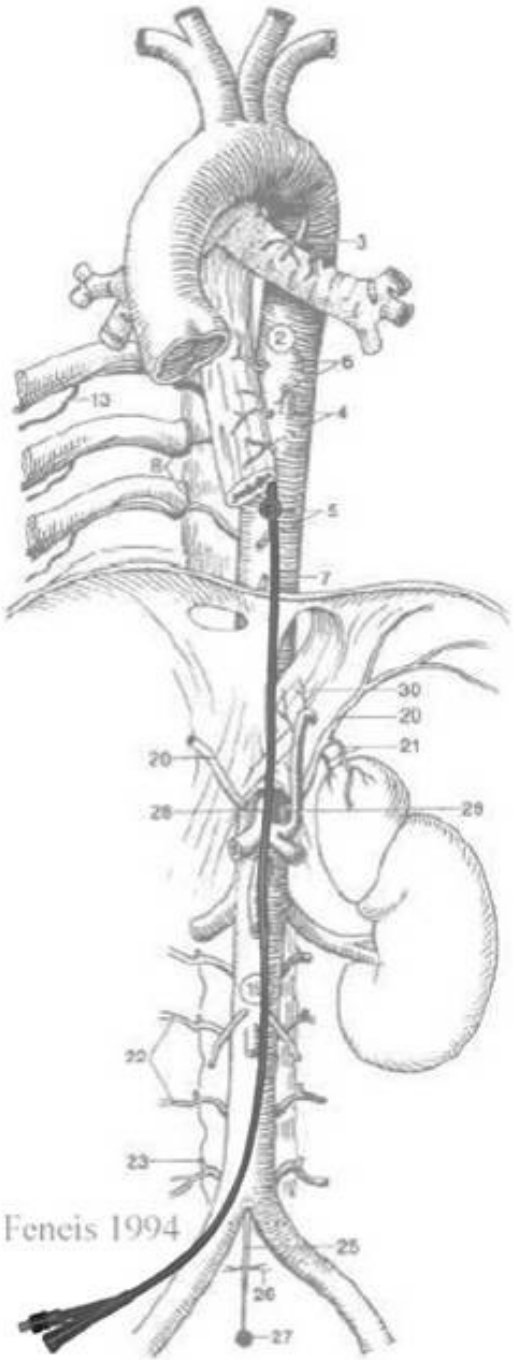
flush technique

Saline + Vasopressin 1.2 IU/kg

Cooling rate 4.8°C/min

Cooling effect 6.0°C/L flush





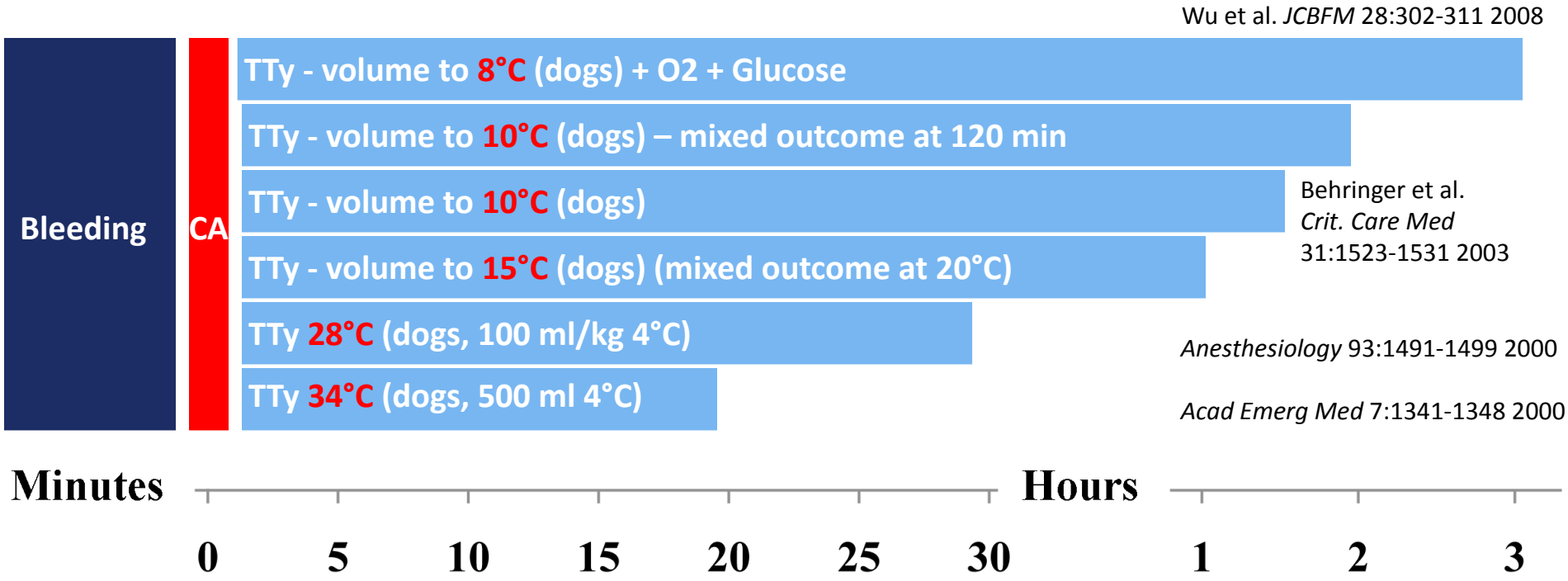
Janata a et al *Crit Care Med*. 2006 Jun;34(6):1769-74.

EPR

target temperature

Which temperature buys how much time?

Groups with predominantly favourable outcome after ExCA.



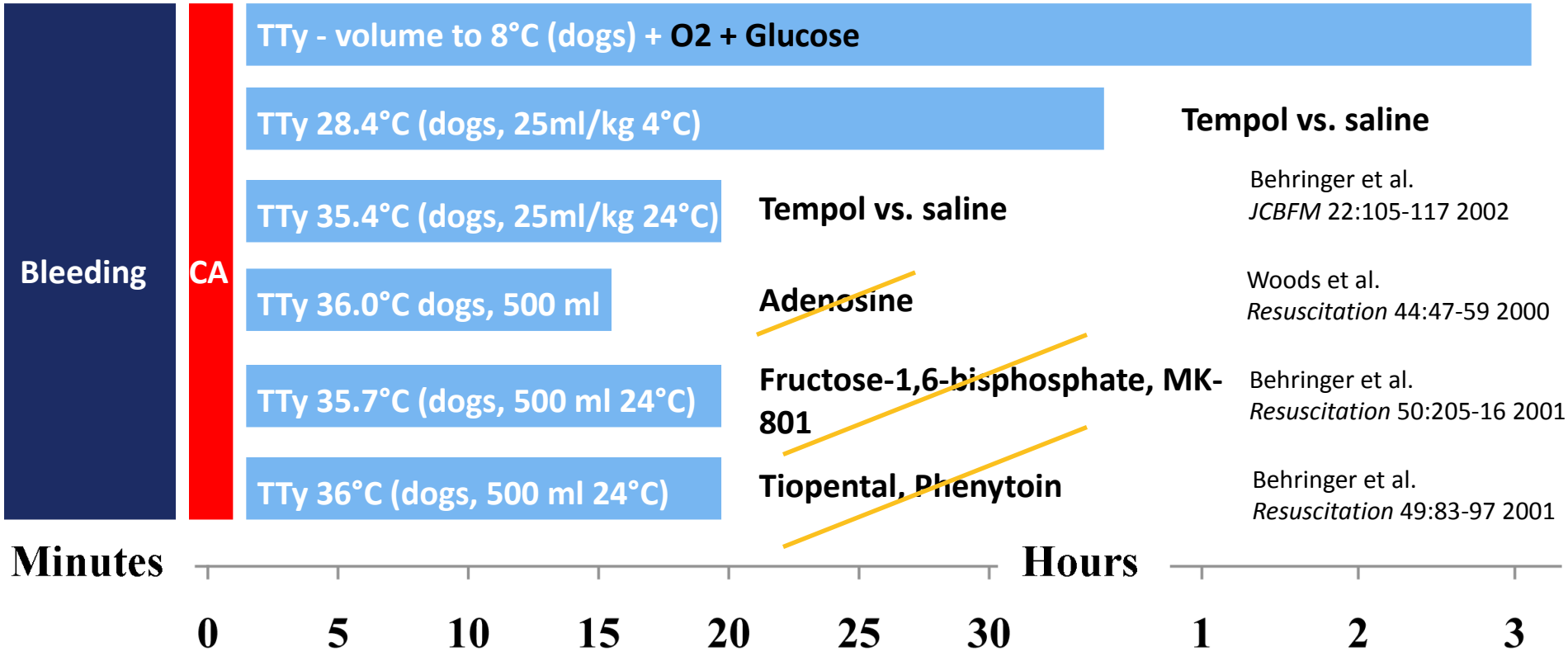
EPR

flush cocktails – additions to improve protection

Antioxidant Tempol improves neurologic recovery vs. saline

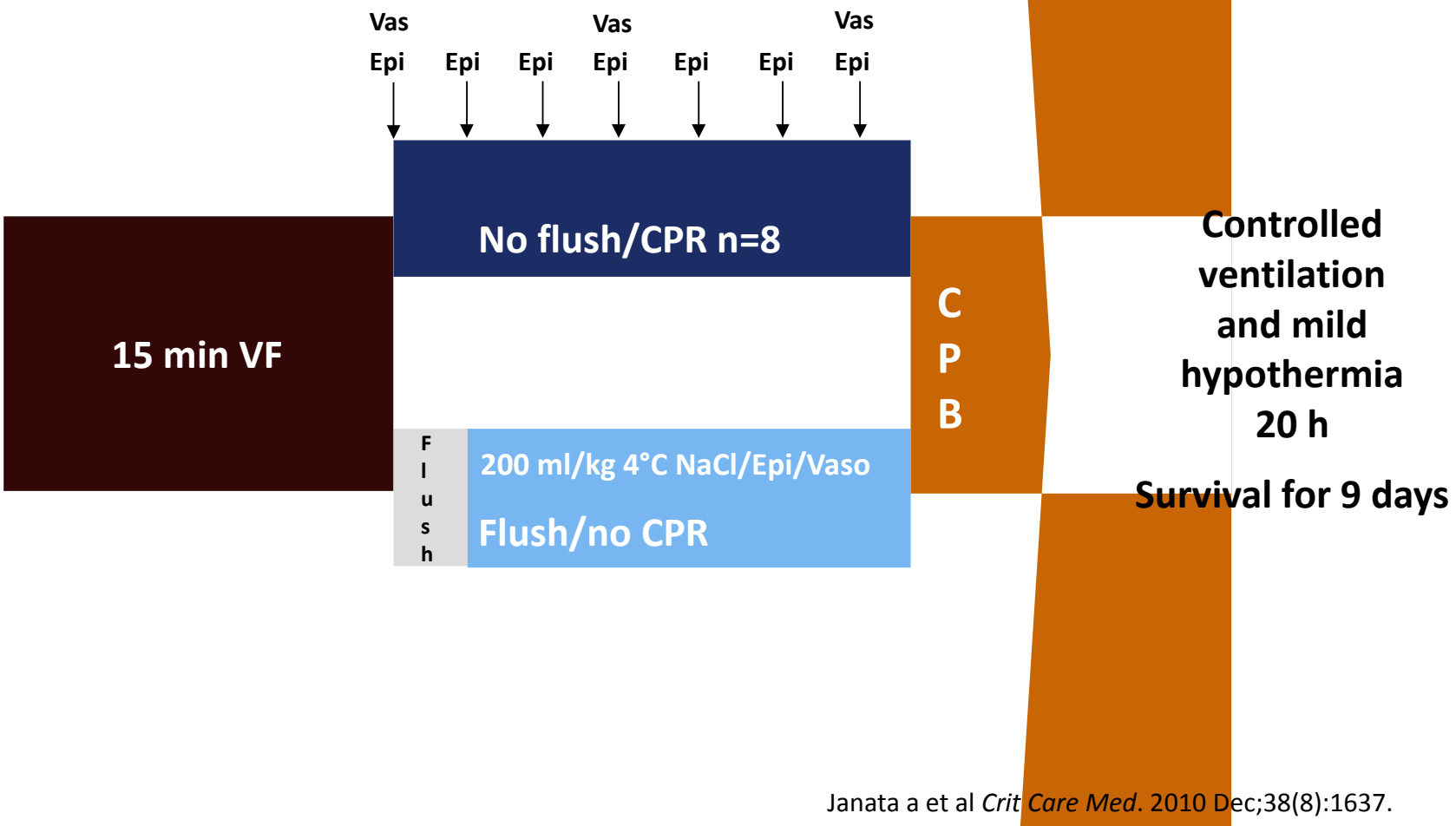
water-soluble, inexpensive, commercially available, penetrates the blood-brain-barrier

Wu et al. *JCBFM* 28:302-311 2008



EPR

after prolonged vf in pigs



Janata a et al *Crit Care Med*. 2010 Dec;38(8):1637.

EPR

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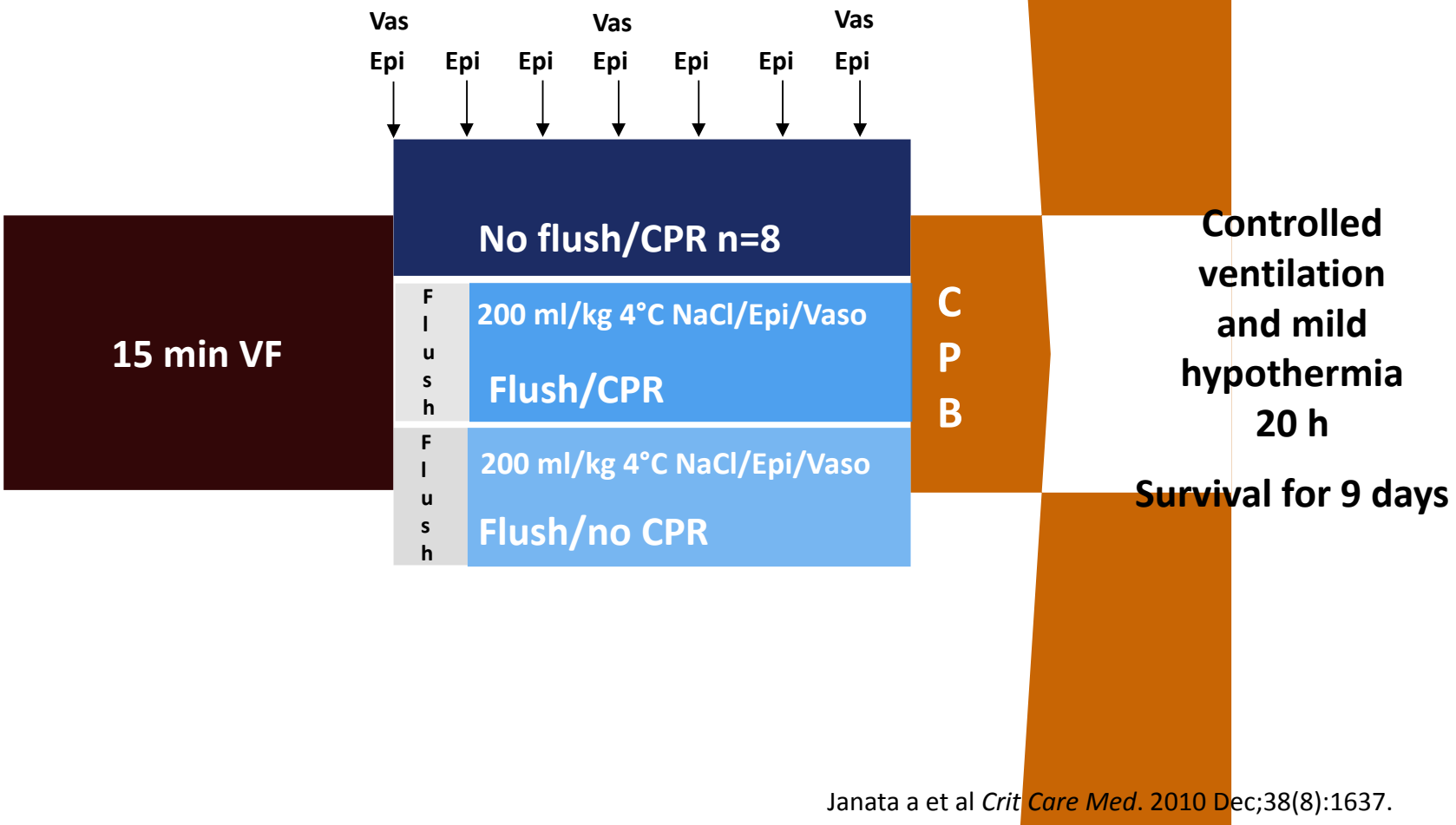

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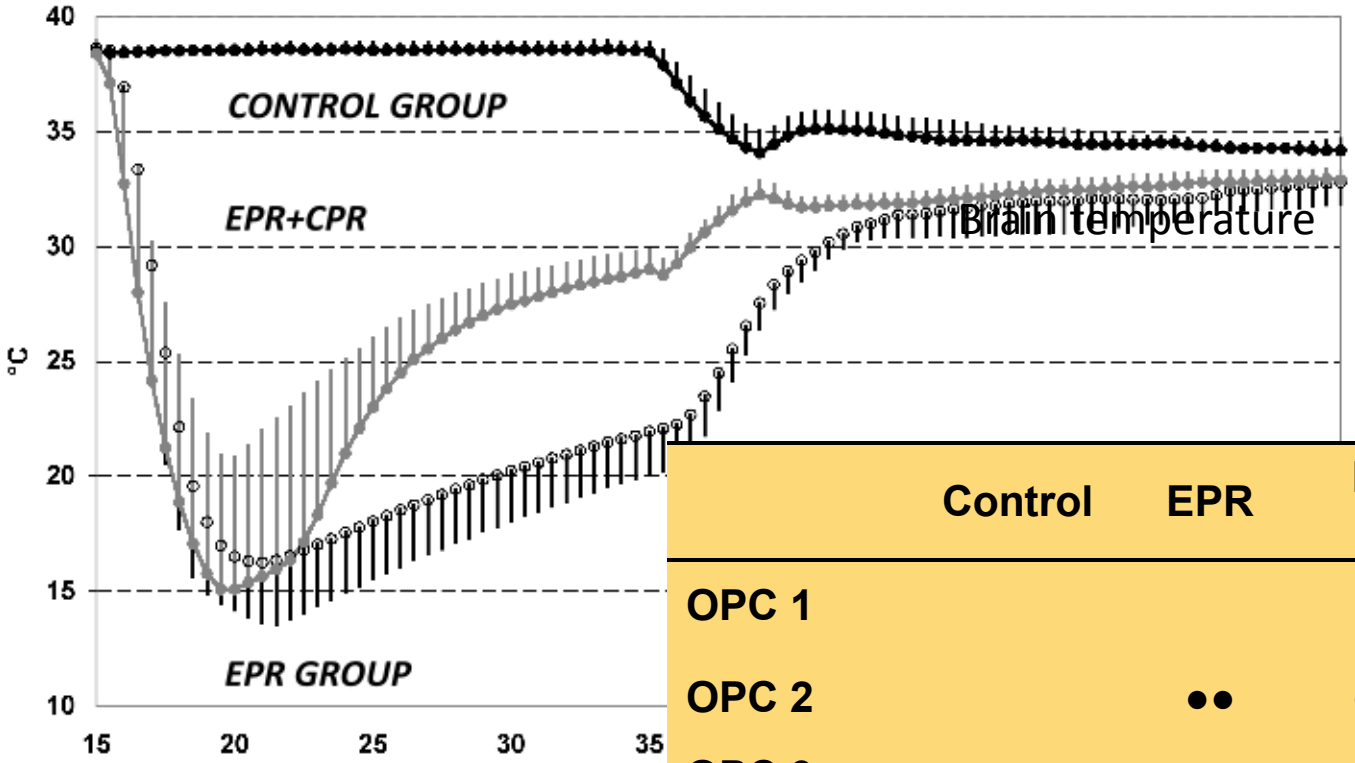

	Control	EPR	EPR-CPR
OPC 1			●●
OPC 2		●●	●●●●
OPC 3	●	●●●	●
OPC 4			
OPC 5	●●●	●●	●
No ROSC	●●●●	●	

Janata a et al *Crit Care Med*. 2010 Dec;38(8):1637.

HYPOTHERMIC RESUSCITATION

SUMMARY

Need for more data

Venous volume load and CoPP?

Feasible for vf ca?

Combination with invasive resuscitation methods.

EPR+E-CPR?

HYPOTHERMIC RESUSCITATION

EMCOOLS
EASY EFFICIENT PATIENT COOLING

Thank You.