

Post-cardiac Arrest Care Update 2021

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Disclosures of COIs

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|----------------------------|--|
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2020 JRC GLs;
2020 ILCOR organ donation statement |

What is Post-cardiac Arrest Care?

Post-cardiac Arrest Syndrome (PCAS):

4 Key Components

- **Post-Cardiac Arrest Brain injury**
- **Post-Cardiac Arrest Myocardial Dysfunction**
- **Systemic Ischemia/Reperfusion Response**
- **Persistent Precipitating Pathology**

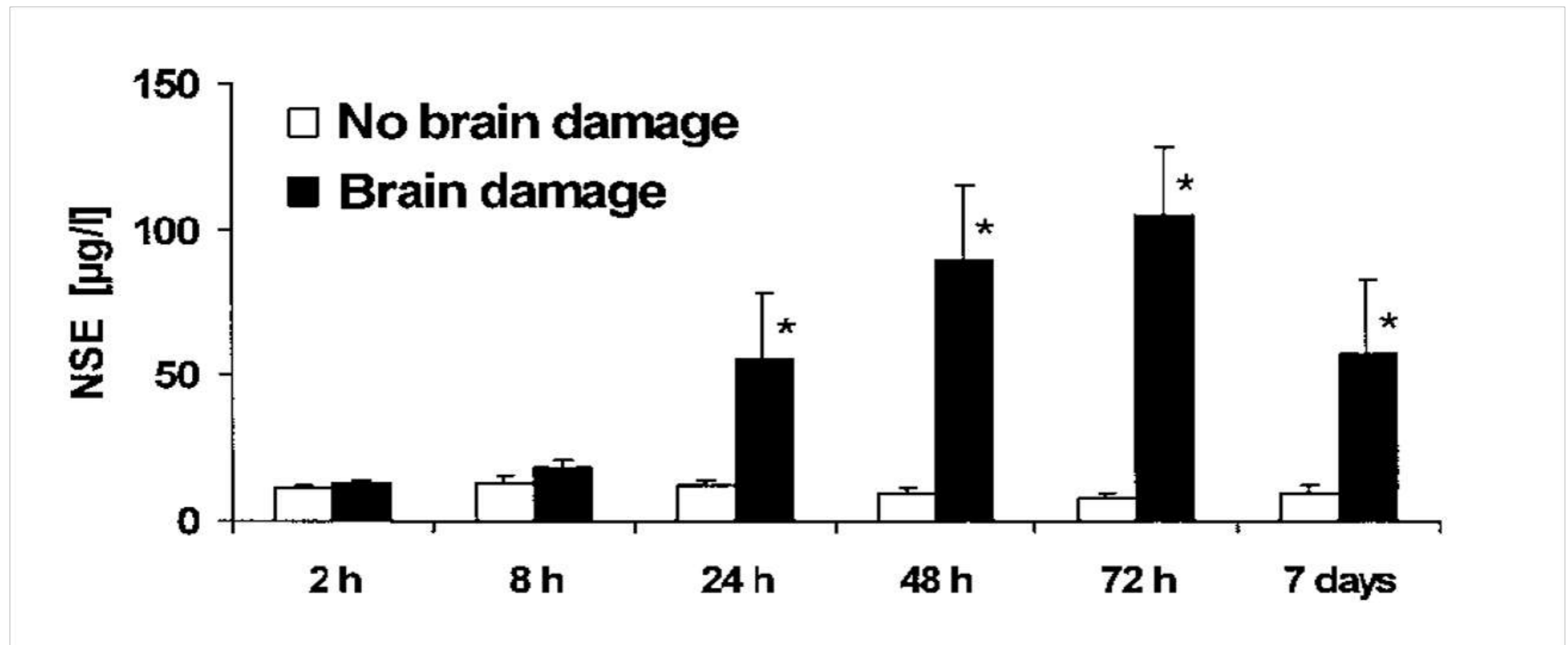
Post-Cardiac Arrest Syndrome

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Serum Neuron-Specific Enolase (NSE) is a Biomarker of Neuronal Death After Cardiac Arrest

The Timing of NSE Release Suggests that Neuronal Death is Delayed for up to 24 Hours and Persists for Days

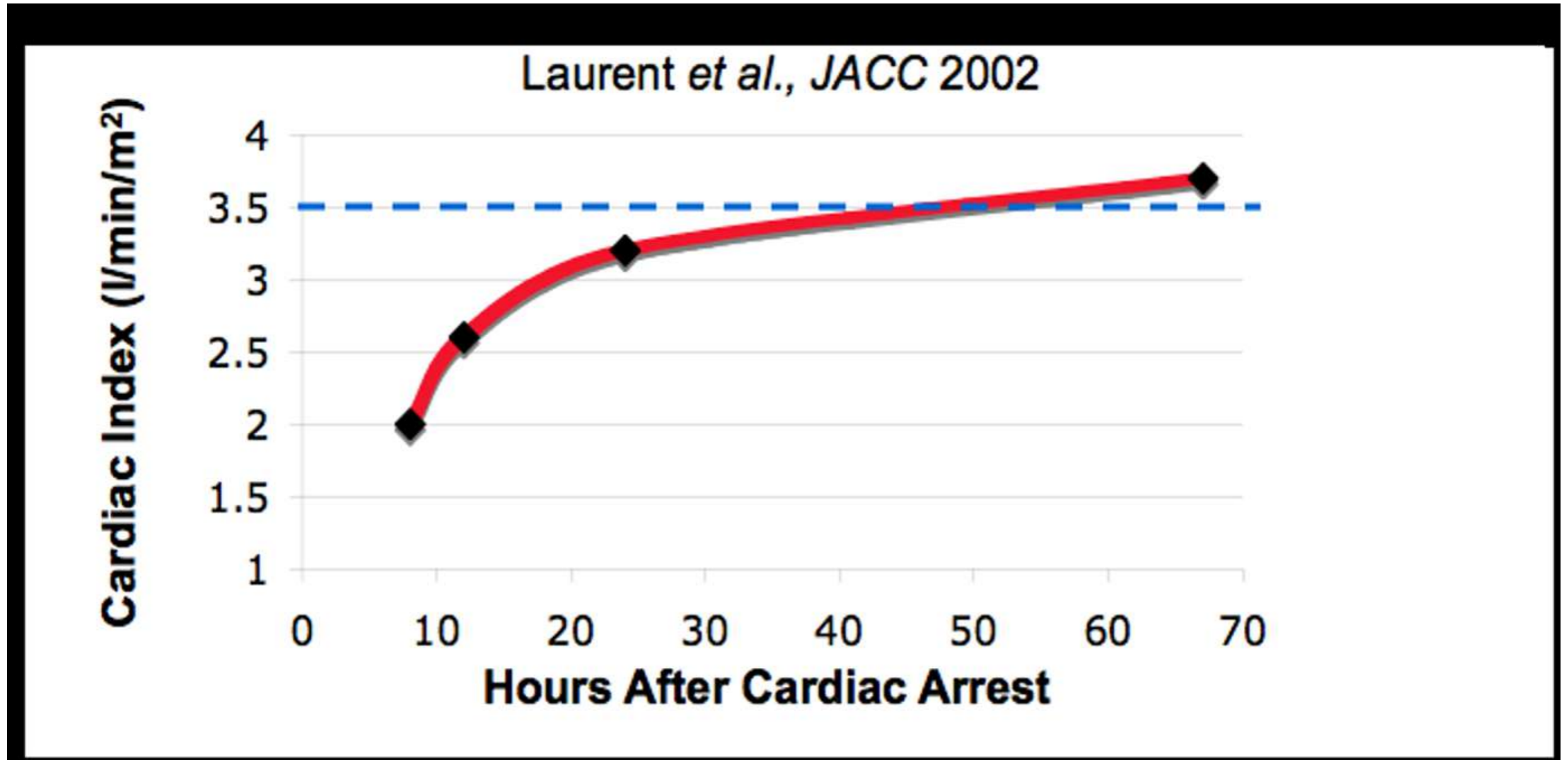


Post-Cardiac Arrest Syndrome

4 Key Components

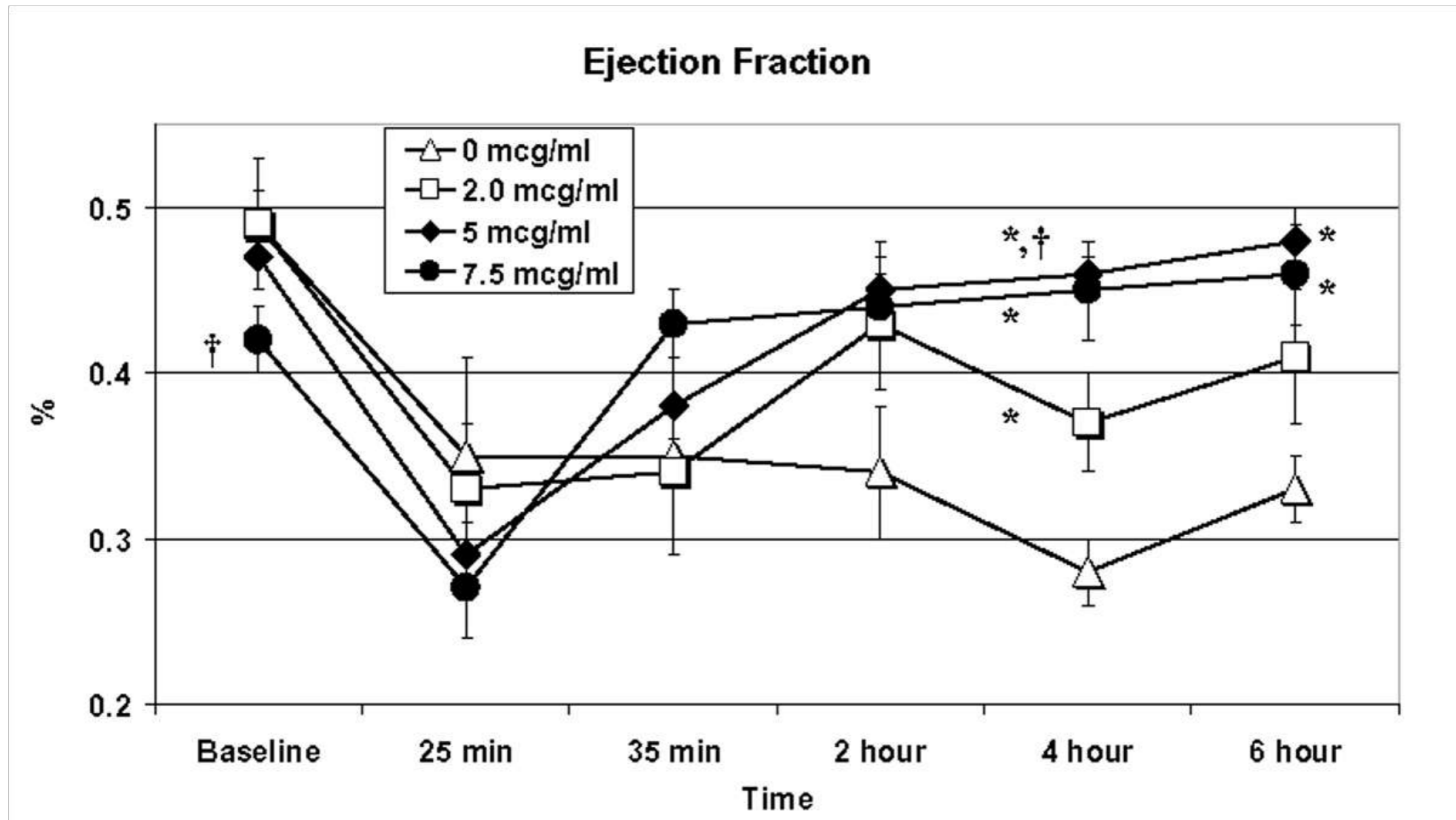
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Myocardial Function is Reversibly Depressed for 24 to 72 hours after Cardiac Arrest



Post-Cardiac Arrest Myocardial Dysfunction is Responsive to Inotropic Therapy

Vazquez et al., Resuscitation, 2004



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Systemic Ischemia/Reperfusion Response:

- **Cytokine Elevations (Sepsis-Like Syndrome ?)**

Cytokine levels in PCAS are not so high as sepsis.

- **Activated Intravascular Coagulation in PCAS (Wada T. Front Med. 2017):**

Increased TAT (thrombin-anti-thrombin complex): intravascular thrombin formation

Elevated PAI-1: inhibition in fibrinolysis, producing intravascular thrombi.

...A Potential Indication of Anti-coagulation Therapy for PCAS

- **Endothelial Damages in PCAS (Gando S. et al., *ICM*, 2000; J Thromb Haemost. 2019).....might link to organ hypoperfusion after ROSC.**

...Therapeutic Modulation for Coagulation after ROSC could have potential.

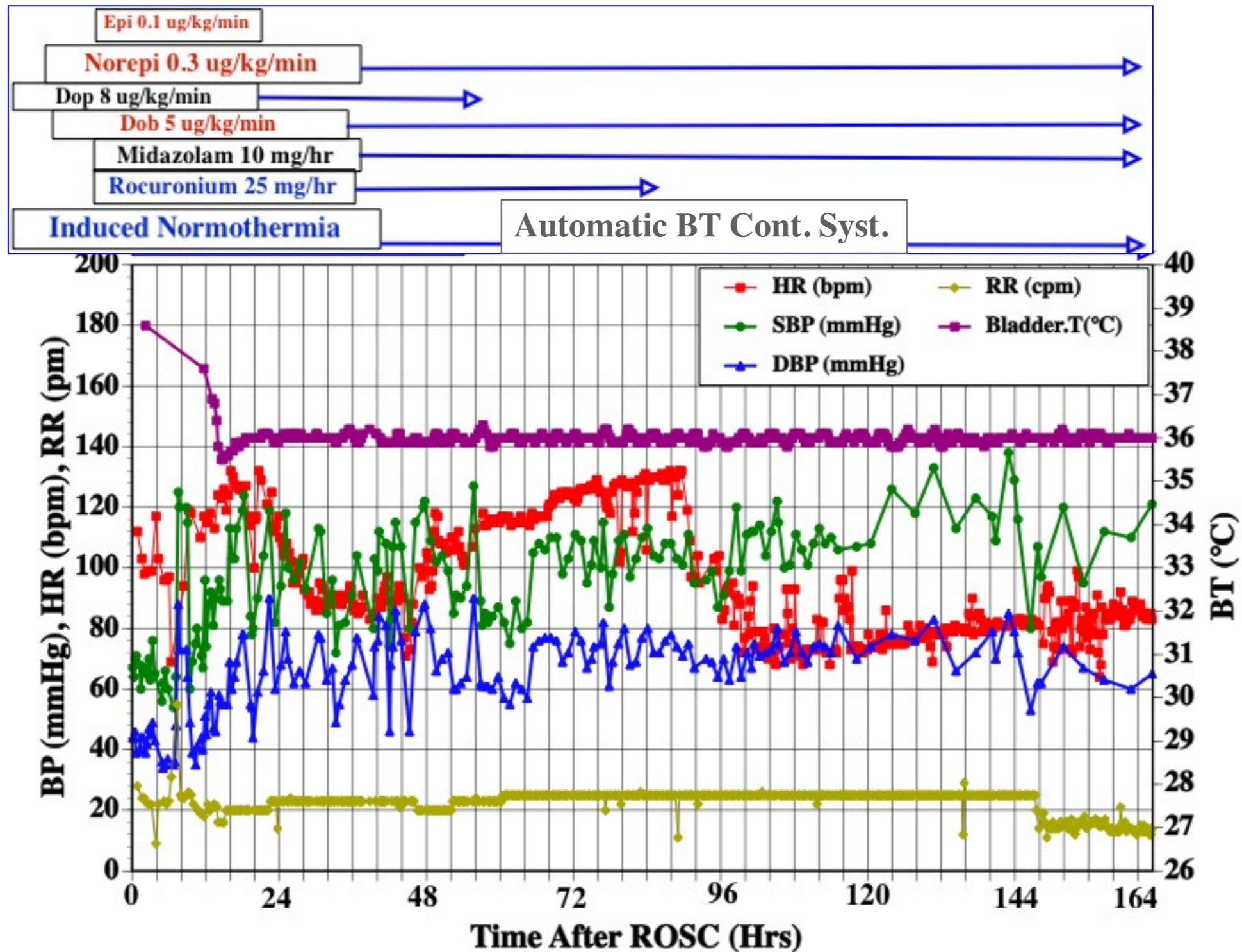
TTM at 36 °C for a Sepsis-associated IHCA

70 Y-O-M in a coma after ROSC from IHCA due to Septic Shock

- Four hours after ICU admission, the patient fell into CPA from VF.
- So, a nurse made an **RRS (Rapid Response System)** call to an emergency physician. He did CPR and **16 minutes** later the patient had an ROSC.
- Even after the ROSC, he was unresponsive and had very unstable hemodynamics, **so the physician decided to do induced normothermia at 36°C using the Arctic Sun™.Prevention of hyperthermia**

70 Y-O-M in a coma PCAS pt from SEPSIS

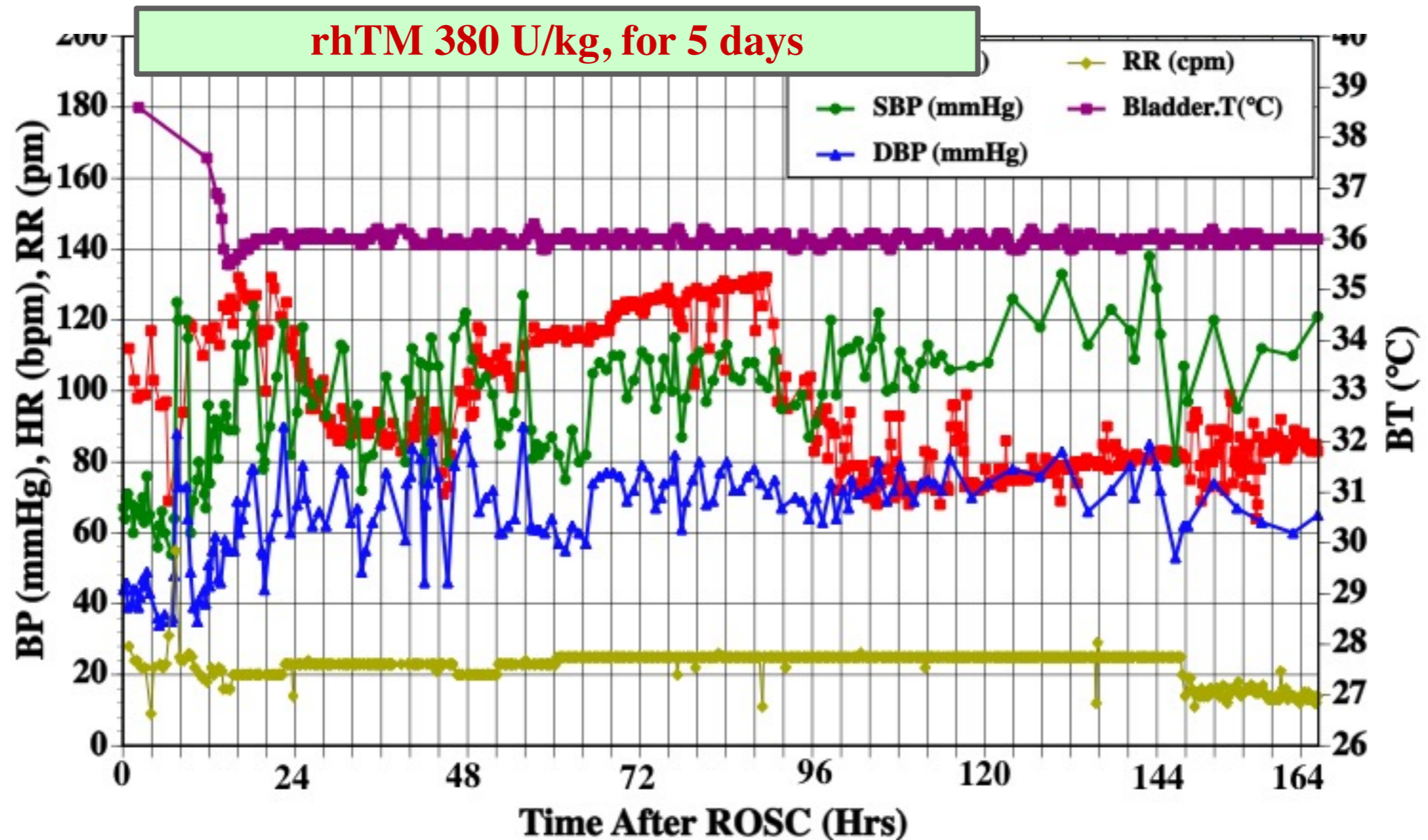
APACHE II 31, VF Arrest time 16 min: **Induced Normothermia** **CPC 1**



70 Y-O-M in a coma after ROSC from IHCA

Severe Sepsis from pneumonia: APACHE II 31.....CPC 1

APTT	84.3 sec.	71.2	69.9	54	42.3	36.5
TAT	9.1 ug/L	4.9	1.8	1.0		
PIC	2.4 ng/ml	0.5	0.4	0.8		
Plat.	13.5 (x10 ⁴)	7.6	4.9	3.9	4.6	6.8



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

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ABSTRACT

Background The incidence of acute coronary artery occlusion in survivors of out-of-hospital cardiac arrest and the role of reperfusion therapy. We therefore performed a study of coronary angiography in survivors of out-of-hospital cardiac arrest.

Methods In 1996, coronary angiography was performed in 100 consecutive patients who had survived out-of-hospital cardiac arrest.

Results Significant coronary artery disease was found in 26%. Coronary angiography was clinically successful in 20%.

relative contraindication to thrombolytic therapy. Furthermore, it may be difficult to establish a clinical

- 48% of post-cardiac arrest patients had acute coronary occlusion

- 26% of patients with acute coronary occlusion in this study did not have ST-elevation

artery disease in survivors of out-of-hospital cardiac arrest. The incidence of acute coronary artery occlusion in survivors of out-of-hospital cardiac arrest was 48%. The incidence of acute coronary artery occlusion in survivors of out-of-hospital cardiac arrest was 48%. The incidence of acute coronary artery occlusion in survivors of out-of-hospital cardiac arrest was 48%.

OHCA survivors, STEMI or Others?

JRC GLs 2020 Recommendation (adopted 2015 GLs)

- **For STEMI:**

We strongly recommend emergent CAG and PCI despite the very low level of evidences.

- **For non-STEMI and other types of ACS:**

We suggest emergent or elective CAG, with an elective PCI, despite the low level of evidences.

Post-Cardiac Arrest Syndrome

Therapeutic Strategies

- Mild Therapeutic Hypothermia
- Early Coronary Revascularization
- Early Hemodynamic Optimization
- Controlled Reoxygenation
- Glucose Control
- High-Volume Hemofiltration

TTM

The main topics of the JRC GLs 2020 include:

- 1) Oxygen administration or Carbon Dioxide adjustment after ROSC**
- 2) Circulatory Management**
- 3) Target Temperature Management (TTM)**
- 4) Issue of Epilepsy after ROSC**
- 5) Prognostication**

ILCOR CoSTR 2021

Temperature Management in Adult CA: ALS SR

ILCOR suggests actively **preventing fever by targeting a temperature ≤ 37.5** for patients who remain comatose after ROSC from cardiac arrest (weak recommendation, low certainty evidence).

Whether **subpopulations of cardiac arrest patients may benefit from targeting hypothermia** at 32–34°C remains uncertain.

Comatose patients with mild hypothermia after ROSC should not be actively warmed to achieve normothermia (good practice statement).

JRC Comments on ILCOR TTM CoSTR 2021

For ILCOR Recommendation in Conclusions:

1. The proposed statement regarding the active prevention of fever less than or equal to 37.5°C:

It is quite limited **since only half of the patients** in the normothermic group used temperature control devices in the TTM 2 study (Dankiewicz 2021, 2283).

Our concern is that more physicians **become less cautious in temperature management** than after the previous TTM in 2013, Nielsen Shock.

This could further worsen the neurological outcomes of ROSC patients around the world.

JRC Comments on ILCOR TTM CoSTR 2021

For ILCOR Recommendation in Conclusions:

Another practical concern regarding the statement:

Just controlling the BT to less than or equal to 37.5°C after ROSC:so, the body temperature might vary between 35 and 37.5°C.

We indicate the body temperature variations should be **limited after ROSC for at least 48 h.**

Furthermore, TTM should actively target **one BT level between 33 and 37.5°C** in comatose patients after ROSC using temperature management devices.

JRC Comments on ILCOR TTM CoSTR 2021

ILCOR Justification in Conclusions:

A huge variation in reported survival outcomes of the current Utstein-style recommendations for OHCA across nations and regions, as reported by ILCOR (Kiguchi 2020, 39).

Only two RCTs of TTM were not effective in improving the neurological outcomes after ROSC (Nielsen 2013; Dankiewicz 2021).

RCTs in patients with heterogenous backgrounds and severity should be careful on the evaluation for the results (Callaway 2020, e208215; Nishikimi 2021, e741).

Comments on ILCOR TTM CoSTR 2021

Benjamin Abella

The statement "Whether subpopulations of cardiac arrest patients may benefit from targeting hypothermia at 32-34°C remains uncertain. " feels **too weak a statement**, as it essentially **discards a very well performed positive multicenter trial (Hyperion), and newer severity of illness data (Callaway, 2020; Nishikimi, 2021).**

I would recommend "RCT and cohort data exist suggesting a potential role for targeting hypothermia at 32-34°C to **improve neurologic outcome in selected subpopulations**" - **this seems to be more appropriately....**

ALS TF: The ALS task Force considered the two publications and considered giving a stronger statement for the use of hypothermia at 32-34°C in some subpopulations – **however our systematic review of the available evidence did not identify any subpopulation** for which hypothermia at 32-34°C improves any important or critical outcomesThe CoSTR statement represents the consensus of the ALS Task Force and states that there is uncertainty about this issue.

ALS TF response to Dr. Hiroshi Nonogi (JRC comments):

Thank you for this response. Recommendations 1. We agree that temperature control in cardiac arrest survivors should not be abandoned all together. This will require all National Councils to spread this message to clinicians involved in the care of post cardiac arrest survivors.

Whether there has been harm from a decrease in the use of hypothermia after ROSC is uncertain. Two observational studies have looked at this [1. Salter, R., et al., Crit Care Med, 2018. 2. Nolan, J.P., et al., Resuscitation, 2021.]

The first study from Australia and New Zealand found no significant difference in the slope or “stepwise change” after the publication of the TTM1 trial. This is the most appropriate analysis for a before/after study.

.....

**Changes in Temperature Management of Cardiac Arrest Patients
Publication of the Target Temperature Management Trial. Ryan
Salter, et al., Niklas Nielsen. Crit Care Med. 2018
Nov;46(11):1722-1730. ANZICS-CORE.**

Objectives: Hypotheses:

TTM at 36°C was rapidly adopted in Australian and New Zealand ICUs.

1) Temporal reductions in mortality would be seen and would have accelerated after publication of the target temperature management trial.

Design: Retrospective cohort study (January 2005 to December 2016). Patients: 16,252 adult patients from 140 hospitals admitted to ICU after out-of-hospital cardiac arrest.

Results: **Lowest temperature in the first 24 hours in ICU** in pre- and post-TTM trial patients was **$33.80 \pm 1.71^{\circ}\text{C}$ and $34.70 \pm 1.39^{\circ}\text{C}$** (absolute difference, **0.98°C [99% CI, 0.89 - 1.06°C]).**

In-hospital mortality rate decreased by 1.3 [99% CI, -1.8 to -0.9] percentage points per year from January 2005 until December 2013; increased by 0.6 [99% CI, -1.4 to 2.6] percentage points per year from January 2014 until December 2016 (change in slope 1.9 percentage points per year [99% CI, -0.6 to 4.4]).

Fever occurred in 568 (12.8%) of 4,450 pre-TTM trial patients and 853 (16.5%) of 5,184 post-TTM trial patients (**odds ratio, 1.35 [99% CI, 1.16-1.57]**).

Conclusions: The average lowest temperature of post-cardiac arrest patients in the first 24 hours in ICU **rose** after publication of the TTM trial. This change was associated with **an increased frequency of fever not seen in the TTM trial.**

The importance of a concept of “High-Quality TTM” has been recently posed from western countries.

We have already realized this concept from the 1990s, so we have done for unconscious cardiac arrest survivors:

- 1) Very fine body-temperature management**
- 2) Circulatory adjustment**
- 3) Control of infection, and/or coagulofibrinolysis.**

When evaluating TTM studies, we should be aware of these methodological points also in the future.

Furthermore, also when adopting ILCOR recommendations on TTM 2021, we need to consider these points carefully.