CONGRESSO NAZIONALE IRC 2023

Vicenza

Italian Resuscitation Conference 2023

20 • 21 OTTOBRE

Vicenza Convention Centre

LA RIVOLUZIONE DEI SISTEMI

IRC | Italian Resuscitation Council

LA FORMULA MAGICA PER IL POST ROSC: QUESTIONE DI TARGET

Erik Roman-Pognuz MD, PhD
UNITs Università di Trieste

UNIVERSITÀ DEGLI STUDI DI TRIESTE

Italian Resuscitation Council

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LA RIVOLUZIONE DEI SISTEMI

Why interventions have consistently failed in clinical trials despite promising results in experimental models?

https://directpoll.com/r?XDbzPBd3ixYqg8pEsI9oo4Yx5F8TvGfYEe5WxUw

Why interventions have consistently failed in clinical trials despite promising results in experimental models?

Complexity of Real-World Settings

Translation Challenges

Heterogeneity in Cardiac Arrest Cases

One size NOT fits all solution

OUT OF HOSPITAL CHALLENGES
after cardiac arrest

A Closer Look on CA

1. Statistics : 300,000 annually

2. The Challenge of ICU & Survival Rates

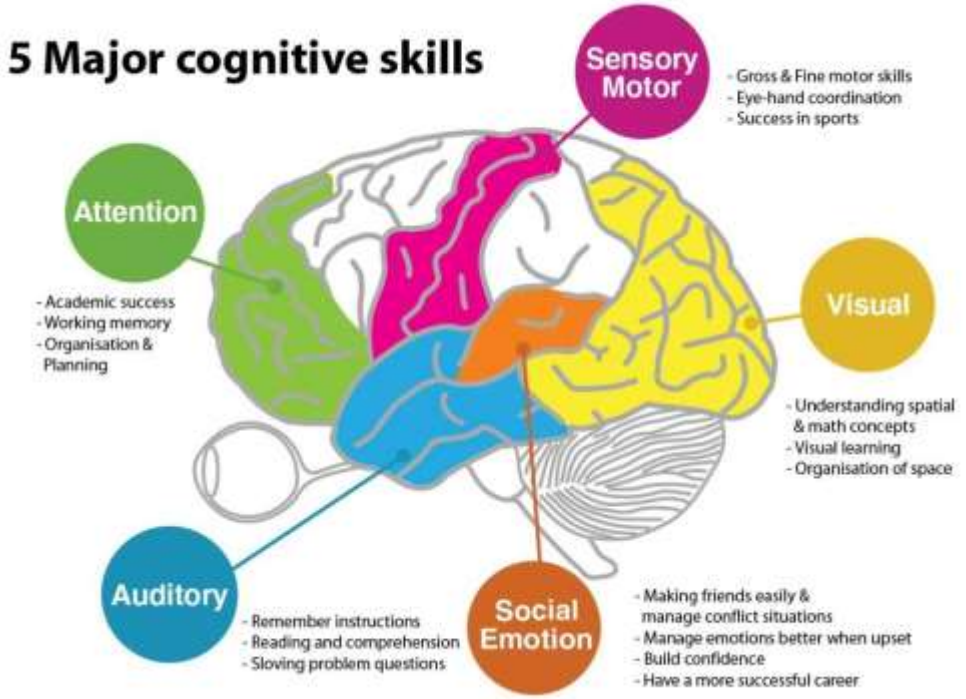
3. Neurological Outcomes

30-55% discharged alive

CPC, GOS, mRS
10% severe disability

OUT OF HOSPITAL CHALLENGES after CA

HIDDEN COGNITIVE IMPAIRMENTS



Resuscitation 80 (2009) 297–305

Contents lists available at ScienceDirect

Resuscitation

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

Review article

Cognitive impairments in survivors of out-of-hospital cardiac arrest: A systematic review☆

Véronique R.M.P. Moulaert[a,*], Jeanine A. Verbunt[a,b], Caroline M. van Heugten[c,d], Derick T. Wade[a,e]

- **50%** of survivors
- lower quality of life and increased caregiver strain.

What's the targets?

CHALLENGING
THE STATUS QUO

Innovative approches

SEDATION
TEMPERATURE
PRESSURE

SEDATION

RANDOMISED TRIALS

Deep sedation vs light sedation

Continuing Medical Education Article

Randomized trial of light versus deep sedation on mental health after critical illness*

Miriam M. Treggiari, MD, PhD, MPH; Jacques-André Romand, MD, FCCM; N. David Yanez, PhD; Steven A. Deem, MD; Jack Goldberg, PhD; Leonard Hudson, MD; Claudia-Paula Heidegger, MD; Noel S. Weiss, MD, DrPH

Daily Interruptions and Light **SED**
Less ventilation days & ICU's stays

Interrupt sedation vs light sedation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nonsedation or Light Sedation in Critically Ill, Mechanically Ventilated Patients

Hanne T. Olsen, M.D., Helene K. Nedergaard, M.D., Ph.D.,

Non-sedation group has more ventilator-free days

Not replicate in the subsequent multicenter

SEDATION

DEEP SEDATION IN TTM

Reduce discomfort and side effects
Facilitate the cooling process

Oddo et al. Critical Care (2016) 20:128
DOI 10.1186/s13054-016-1294-5

Critical Care

REVIEW Open Access

Optimizing sedation in patients with acute brain injury

Mauro Oddo[1,2*], Ilaria Alice Crippa[3,4,5], Sangeeta Mehta[6], David Menon[7], Jean-Francois Payen[8], Fabio Silvio Taccone[5] and Giuseppe Citerio[3,4]

LIMITED RANDOMIZED DATA

The New England
Journal of Medicine

Volume 314 FEBRUARY 13, 1986 Number 7

RANDOMIZED CLINICAL STUDY OF THIO
OF CARD
BRAIN RESUSCITATION CL

Seizure prophylactic

Brain protective

1986 Trial involging a single dose of thiopental

No outcome difference

CA trials have consequently targeted **DEEP** SEDATION

SEDATION IN VENTILATION

SEDATION

PROS

Ventilator synchrony, comfort, reduce agitation

Neurochem Res. 2015 December ; 40(12): 2583–2599. doi:10.1007/s11064-015-1581-6.

The Glymphatic System – A Beginner's Guide

Nadia Aalling Jessen[1], **Anne Sofie Finmann Munk**[1], **Iben Lundgaard**[1], and **Maiken Nedergaard**
University of Rochester Medical Center, School of Medicine and Dentistry, 601 Elmwood Ave, Box 645, Rochester, NY 14642

Neuro metabolic waste

Seizure management

CONS

Inconclusive mortality impact

ORIGINAL ARTICLE

Treating Rhythmic and Periodic EEG Patterns in Comatose Survivors of Cardiac Arrest

Barry J. Ruijter, M.D., Ph.D., Hanneke M. Keijzer, M.Sc., Marleen C. Tjepkema-Cloostermans, Ph.D., Michiel J. Bläns, M.D., Albertus Beishuizen, M.D., Ph.D., Selma C. Tromp, M.D., Ph.D., Erik Scholten, M.D., Janneke Horn, M.D., Ph.D., Anne-Fleur van Rootselaar, M.D., Ph.D., Marjolein M. Admiraal, Ph.D., Walter M. van den Bergh, M.D., Ph.D., Jan-Willem J. Elting, M.D., Ph.D., et al., for the TELSTAR Investigators*

Pneumonia, circulatory compromise, delayed awakening & ICU stay

Conflicting for and against deep sedation in the first days

BALANCING ACT

SEDATION

Published in final edited form as:
Resuscitation. 2019 June ; 139: 308–313. doi:10.1016/j.resuscitation.2019.02.031.

Early withdrawal of life support after resuscitation from cardiac arrest is common and may result in additional deaths

Teresa L May[1,2], Robin Ruthazer[2], Richard R Riker[1], Hans Friberg[3], Nainesh Patel[4], Eldar

Intensive Care Med (2020) 46:1803–1851
https://doi.org/10.1007/s00134-020-06198-w

SYSTEMATIC REVIEW

Prediction of poor neurological outcome in comatose survivors of cardiac arrest: a systematic review

Claudio Sandroni[1,2], Sonia D'Arrigo[1*], Sofia Cacciola[1], Cornelia W. E. Hoedemaekers[3], Marlijn J. A. Kamps[4],

Interference neurological prognostication

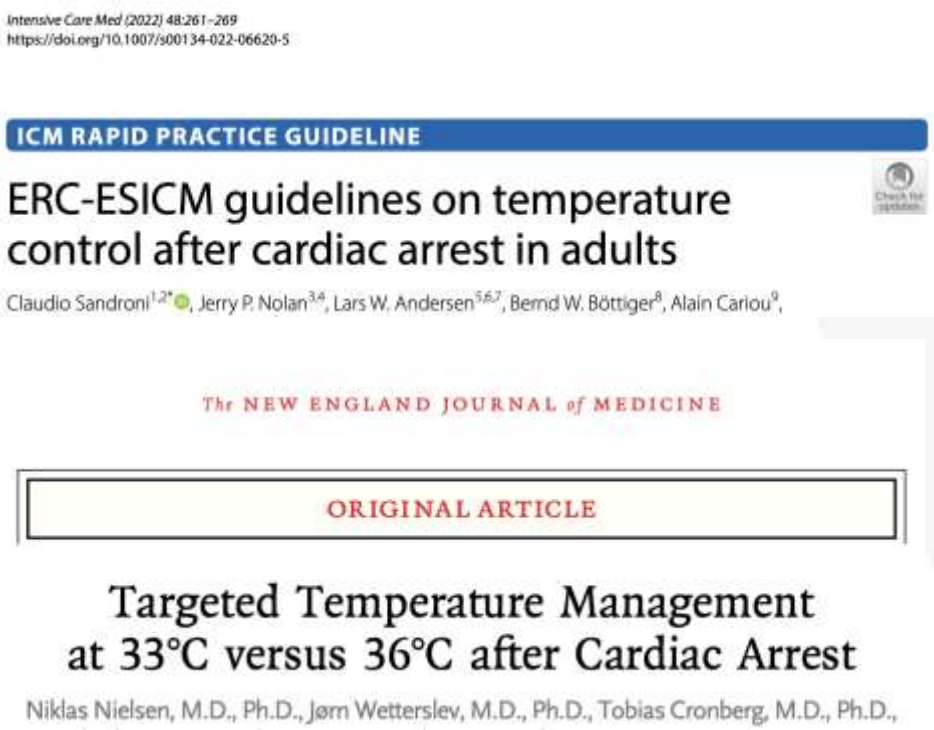
Confounds clinical examination and EEG-patterns

Sedation potentially increase the risk of **adverse effects**

TEMPERATURE

Active TEMPERATURE MANAGEMENT

Grounded in animal data, supported by clinical observations



Intensive Care Med (2022) 48:261–269
https://doi.org/10.1007/s00134-022-06620-5

ICM RAPID PRACTICE GUIDELINE

ERC-ESICM guidelines on temperature control after cardiac arrest in adults

Claudio Sandroni[1,2*], Jerry P. Nolan[3,4], Lars W. Andersen[5,6,7], Bernd W. Böttiger[8], Alain Cariou[9],

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D.,

Fever prevention, limited evidence

Global practice variability

Similar outcomes

- survival
- functional status
- health-related quality of life (HRQoL)
- cognitive impairment

Pivotal role but questions on its optimal parameters and long terms effects persist

TEMPERATURE

TTM2 AND BEYOND

1900 - 33 vs normothermia

ORIGINAL ARTICLE

Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

Josef Dankiewicz, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D., Gisela Lilja, O.T., Ph.D., Janus C. Jakobsen, M.D., Ph.D., Helena Levin, M.Sc., Susann Ullén, Ph.D., Christian Rylander, M.D., Ph.D., Matt P. Wise, M.B., B.Ch., D.Phil., Mauro Oddo, M.D., Alain Cariou, M.D., Ph.D., Jan Bělohlávek, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D., et al., for the TTM2 Trial Investigators*

Circulation

Volume 146, Issue 18, 1 November 2022; Pages 1357-1366

https://doi.org/10.1161/CIRCULATIONAHA.122.060106

American Heart Association.

ORIGINAL RESEARCH ARTICLE

Temperature Control After In-Hospital Cardiac Arrest: A Randomized Clinical Trial

Sebastian Wolfrum, MD*, Kevin Roedl, MD*, Alexia Hanebutte, MD, Rüdiger Pfeifer,

TTM2's neutral results, mirroring TTM1

Subnormal temperatures doesn't provide benefits

33°C for 24 hours

No decrease mortality or improve functional outcomes.

TEMPERATURE

META-ANALYSIS FINDINGS

Systematic Review | Published: 13 August 2021

Targeted temperature management following out-of-hospital cardiac arrest: a systematic review and network meta-analysis of temperature targets

Shannon M. Fernando, Pietro Di Santo, Behnam Sadeghirad, Jean-Baptiste Lascarrou, Bram Rochwerg, Rebecca Mathew, Mypinder S. Sekhon, Laveena Munshi, Eddy Fan, Daniel Brodie, Kathryn M. Rowan, Catherine L. Hough, Shelley L. McLeod, Christian Vaillancourt, Sheldon Cheskes, Niall D. Ferguson, Damon C. Scales, Claudio Sandroni, Jerry P. Nolan & Benjamin Hibbert

Intensive Care Medicine **47**, 1078–1088 (2021) | Cite this article

Moderate or deep hypothermia may be **harm**

Intensive Care Med (2022) 48:261–269
https://doi.org/10.1007/s00134-022-06620-5

ILCOR

ICM RAPID PRACTICE GUIDELINE

ERC-ESICM guidelines on temperature control after cardiac arrest in adults

Claudio Sandroni[1,2*], Jerry P. Nolan[3,4], Lars W. Andersen[5,6,7], Bernd W. Böttiger[8], Alain Cariou[9],

TTM at 32-34°C did not result in improved outcomes

GL were **updated** to recommend **JUST** active fever prevention

The emphasis shifted from cooling to maintaining normothermia and **actively preventing fever**

TEMPERATURE

FEVER

Linked to higher mortality **risk**

Recommend to **treat** based on Non RCT

> Intensive Care Med. 2018 Feb;44(2):227-230. doi: 10.1007/s00134-017-4969-8. Epub 2017 Oct 22.

Fever control

Paul J Young [1 2], Niklas Nielsen [3 4], Manoj Saxena [5 6]

Affiliations + expand

PMID: 29058053 DOI: 10.1007/s00134-017-4969-8

Directly harms neuro impaired patients?

Epiphenomenon?

Active prevention is beneficial?

UNRESOLVED QUESTION

FINNRESUSCI

FEVER PREVALENCE

Intensive Care Med (2013) 39:826–837
DOI 10.1007/s00134-013-2868-1

ORIGINAL

Jukka Vaahersalo
Pamela Hiltunen
Marjaana Tiainen
Tuomas Oksanen
Kirsi-Maija Kaukonen

Therapeutic hypothermia after out-of-hospital cardiac arrest in Finnish intensive care units: the FINNRESUSCI study

- **45%** of OHCA **not TTM** had fever
- **High fever < 5%**
- **No difference** in outcomes

Multicenter Study > Crit Care Resusc. 2015 Jun;17(2):129-34.

A multicentre audit of temperature patterns after traumatic brain injury

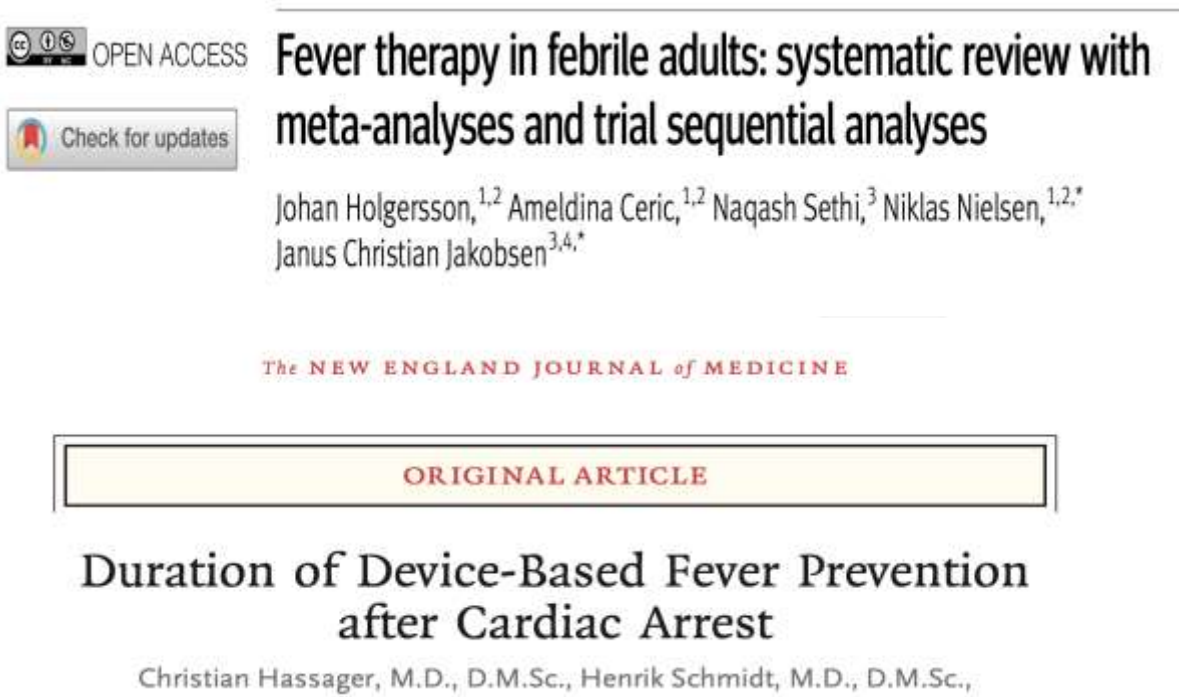
Manoj K Saxena [1], Colman Taylor [2], Naomi Hammond [2], Paul Young [3], Jayanthi Mysore [2], Laurent Billot [2], Ashleigh Myburgh [2], John Myburgh [4]

Similar prevalence in SAH & TBI

Fever is not a predominant factor influencing outcomes

TEMPERATURE

FEVER THERAPY



OPEN ACCESS

Check for updates

Fever therapy in febrile adults: systematic review with meta-analyses and trial sequential analyses

Johan Holgersson,[1,2] Ameldina Ceric,[1,2] Naqash Sethi,[3] Niklas Nielsen,[1,2,*] Janus Christian Jakobsen[3,4,*]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Duration of Device-Based Fever Prevention after Cardiac Arrest

Christian Hassager, M.D., D.M.Sc., Henrik Schmidt, M.D., D.M.Sc.,

No evidence on mortality

Device vs no device

No difference on mortality

Fever therapy may **not provide** a benefit on all-cause mortality

REDEFINE TARGETS

PRESSURE

PRESSION MEANS PERFUSION?

MAP > 65 mmHg in CA

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 7, 2020
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PUBLISHED BY ELSEVIER

Optimum Blood Pressure in Patients With Shock After Acute Myocardial Infarction and Cardiac Arrest

Koen Ameloot, MD,[a,b,c,*] Pekka Jakkula, MD, PhD,[d,*] Johanna Hästbacka, MD, PhD,[d] Matti Reinikainen, MD, PhD,[e]

Observational data

Safety target ranging from 85 to 100 mmHg

Potential **organ protective** effects

NEUROPROTECTION

PRESSURE

COMACARE Trial

Intensive Care Med (2021) 47:39–48
https://doi.org/10.1007/s00134-020-06218-9

ORIGINAL

Neurofilament light as an outcome predictor after cardiac arrest: a post hoc analysis of the COMACARE trial

Lauri Wihersaari[1], Nicholas J. Ashton[2,3,4,5], Matti Reinikainen[1], Pekka Jakkula[6], Ville Pettilä[6], Johanna Hästbacka[6],

Surrogate endpoints:
Biomarkers, MRI scans

MAP targets on VF
65-75 VS 80-100 mmHg

No difference NSE

NFL significant reductions in the higher MAP group

Potential benefits of higher MAP target

NEUROPROTECTION

PRESSURE

NEUROPROTECT Study

Randomized Controlled Trial > Eur Heart J. 2019 Jun 7;40(22):1804-1814.
doi: 10.1093/eurheartj/ehz120.

Early goal-directed haemodynamic optimization of cerebral oxygenation in comatose survivors after cardiac arrest: the Neuroprotect post-cardiac arrest trial

Koen Ameloot [1 2 3], Cathy De Deyne [3 4], Ward Eertmans [3 4], Bert Ferdinande [1],

MAP targets on any rhithm
65-70 VS 85-100 mmHg

Optimize SvO2 (inotropes, flids, RBC)

No difference MRI
in follow up

NEUROPROTECTION

PRESSURE

NEUROPROTECT Study

+

COMACARE Trial

Combining analysis in MI and vasopressor need

Higher MAP turns to **lower hsTNT**

Potential reduction of MI, HR and arrithmias

Potential myocardial protection on higher MAP target

PRESSURE

Higher MAP is safe?

> Resuscitation. 2021 Nov:168:199-205. doi: 10.1016/j.resuscitation.2021.08.037. Epub 2021 Aug 27.

Increasing mean arterial pressure or cardiac output in comatose out-of-hospital cardiac arrest patients undergoing targeted temperature management: Effects on cerebral tissue oxygenation and systemic hemodynamics

Johannes Grand [1], Sebastian Wiberg [2], Jesper Kjaergaard [2], Michael Wanscher [3],

Works both with and without chronic hypertension? Or any other PMH?

targeting a higher MAP to mitigate the risk of inadequate CBF in the early post-arrest phase.

BOX Trial

ORIGINAL ARTICLE

Blood-Pressure Targets in Comatose Survivors of Cardiac Arrest

Jesper Kjaergaard, M.D., D.M.Sc., Jacob E. Møller, M.D., D.M.Sc., Henrik Schmidt, M.D., D.M.Sc., Johannes Grand, M.D., Ph.D., Simon Mølstrøm, M.D., Britt Borregaard, R.N., Ph.D., Søren Vene, M.D., Laura Sarkisian, M.D., Ph.D., Dmitry Mamaev, M.D., Lisette O. Jensen, M.D., D.M.Sc., Benjamin Nyholm, M.D., Dan E. Høfsten, M.D., Ph.D., et al.

COMACARE Trial

Possible benefits of a higher MAP target in patients with ST elevation

CONCLUSIONS

KEY TAKEAWAY

In brain-injured depth, duration and benefits of sedation are uncertain

Active temperature optimal parameters and long-term effects remain unclear

Meta-analysis change recent GL, focusing on preventing fever rather than cooling.

Fever is common in OHCA , but its exact effect on long-term outcomes is unclear

Treating post-cardiac arrest fever it's still unresolved matter

Recent trials indicating benefits from higher MAP targets for neuroprotection.

NEXT STEP?

STEP CARE

1. Continuous sedation for 36 h or minimal sedation (**SEDCARE**)

2. Fever management with or without a TTM device for 72 h (**TEMPCARE**)

3. A mean arterial pressure target of > 85mmHg or > 65mmHg for 36 hours (**MAPCARE**)

Follow-up: mortality, functional outcome and quality of life

1. Detailed cognitive outcome with focus on patients and caregivers

2. Prognostication to identify and validate early and accurate instruments and algorithm

3. Biobank with blood samples at 0, 24, 48, and 72 hours after the cardiac arrest