3rd SRFAC Townhall

Beyond ROSC

– Update on Post-Cardiac Arrest Management in the ICU

Presented by
Dr Chia Yew Woon
Cardiologist-Intensivist
Chair, National TTM Workgroup

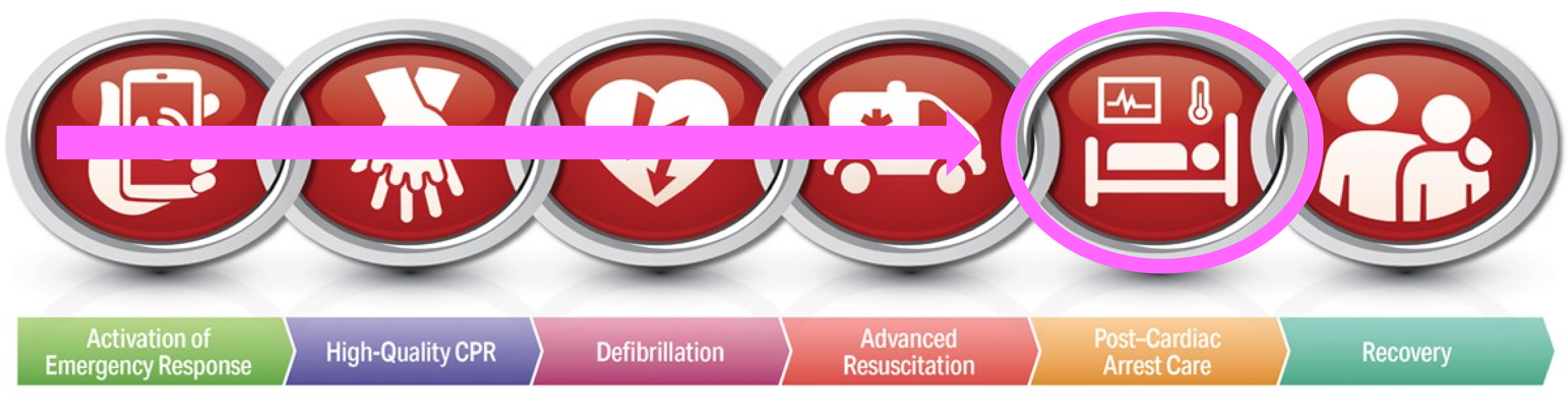
SRFAC

Disclosures

- None related to this presentation.

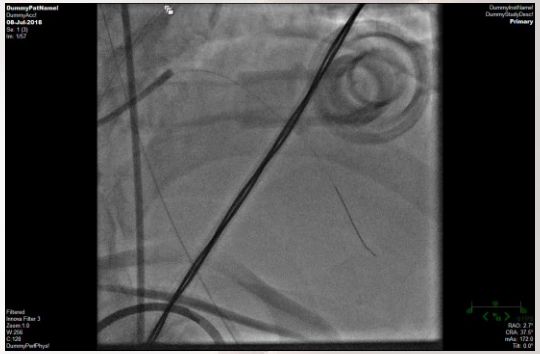
SRFAC

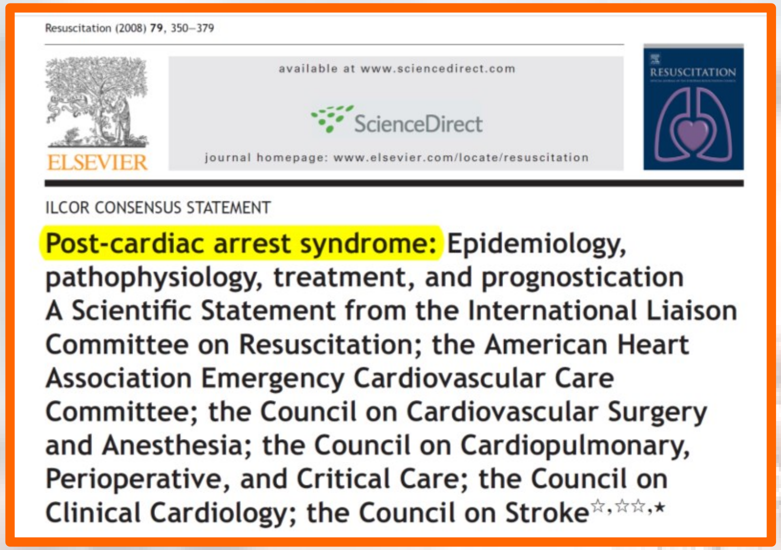
Chain of Survival



Raina M. Merchant. Circulation. Part 1: Executive Summary: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, Volume: 142, Issue: 16_suppl_2, Pages: S337-S357, DOI: (10.1161/CIR.0000000000000918)

SRFAC





Resuscitation (2008) 79, 350–379

available at www.sciencedirect.com

ScienceDirect

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

ELSEVIER

RESUSCITATION

ILCOR CONSENSUS STATEMENT

Post-cardiac arrest syndrome: Epidemiology, pathophysiology, treatment, and prognostication A Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke☆,☆☆,★

ROSC!

Now what??!!

SRFAC

Resuscitation (2008) 79, 350–379
available at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/resuscitation
ELSEVIER
RESUSCITATION

ILCOR CONSENSUS STATEMENT

Post-cardiac arrest syndrome: Epidemiology, pathophysiology, treatment, and prognostication
A Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke☆,☆☆,★

Resuscitation 80 (2009) 418–424
Contents lists available at ScienceDirect
Resuscitation
journal homepage: www.elsevier.com/locate/resuscitation
ELSEVIER
RESUSCITATION

Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest☆,☆☆

David F. Gaieski[a,b,*], Roger A. Band[a,b], Benjamin S. Abella[a,b], Robert W. Neumar[a,b], Barry D. Fuchs[c], Daniel M. Kolansky[d], Raina M. Merchant[a,b], Brendan G. Carr[a,b], Lance B. Becker[a,b], Cheryl Maguire[e], Amandeep Klair[a], Julie Hylton[a], Munish Goyal[a,b]

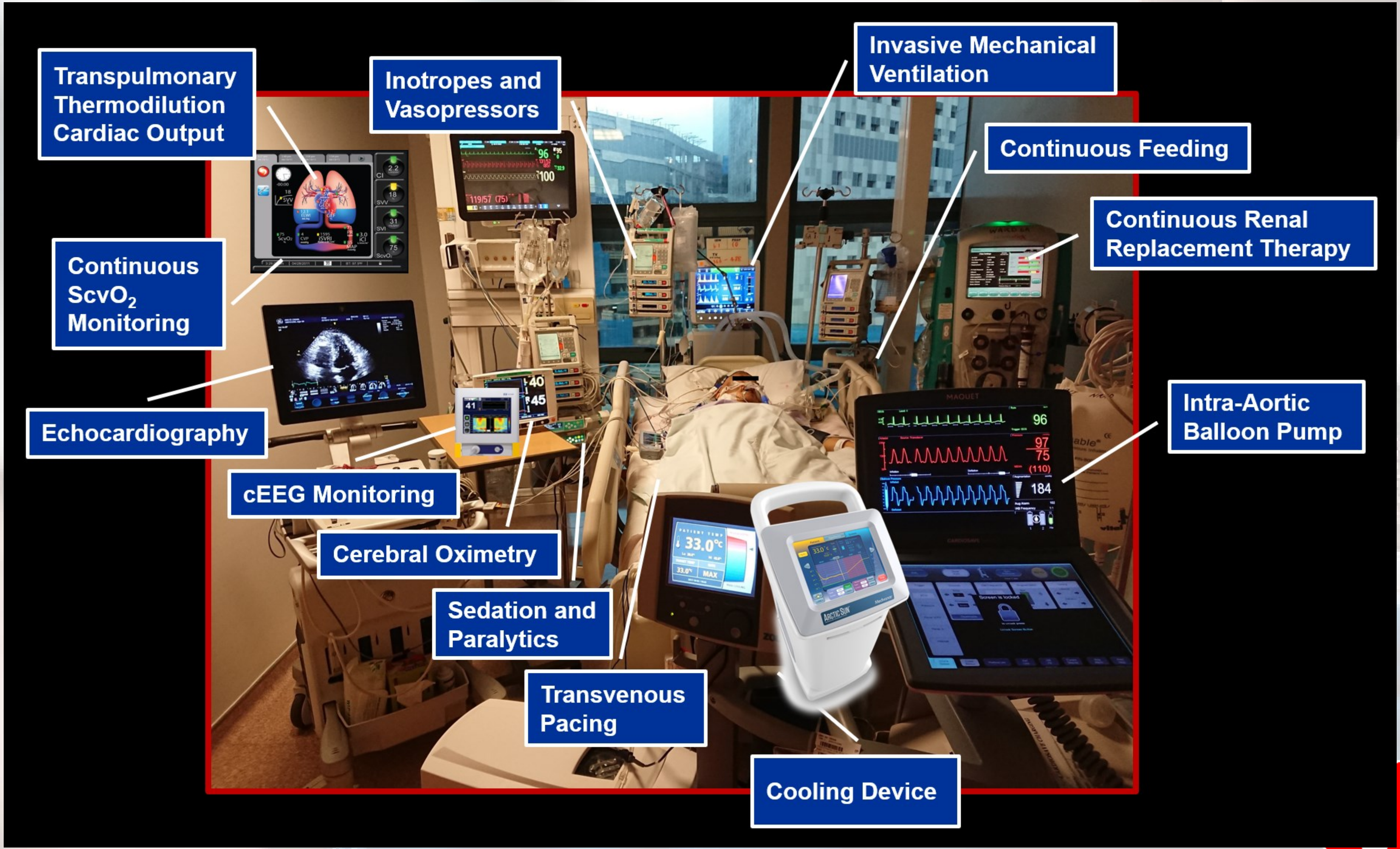
[a] Department of Emergency Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA 19104, USA
[b] Center for Resuscitation Science, University of Pennsylvania School of Medicine, Philadelphia, PA 19104, United States
[c] Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA 19104, United States
[d] Department of Internal Medicine, Division of Cardiology, University of Pennsylvania School of Medicine, Philadelphia, PA 19104, United States
[e] University of Pennsylvania School of Nursing, Nurse Manager, Medical Intensive Care Unit, United States

PCAS

1. Post-cardiac arrest **brain injury**
2. Post-cardiac arrest **myocardial dysfunction**
3. Systemic **ischaemic-reperfusion syndrome**
4. Persistence of **precipitating pathology**

SRFAC

Post-Cardiac Arrest Syndrome (PCAS)



SRFAC

Consensus Recommendations

Review Article

Singapore Med J 2017; 58(7): 408-410
doi: 10.11622/smedj.2017067

Therapeutic temperature management (TTM): post-resuscitation care for adult cardiac arrest, with recommend

Siew Hon
Colin Ye

Circulation

Adult Advanced Life

2020 International Consensus
and Emergency Cardiovascular
Recommendations

Circulation

Part 3: Adult Basic and Advanced Life Support

2020 America
Resuscitation

RESUSCITATION 161 (2021) 220 –269

ELSEVIER

Available online at www.sciencedirect.com

Resuscitation

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

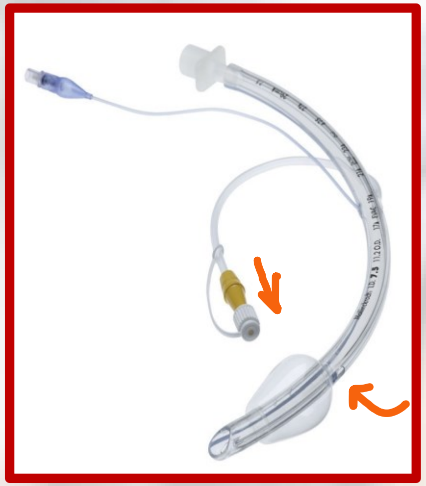
EUROPEAN RESUSCITATION COUNCIL

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care☆

Check for updates

A (Airway)

- Suggest **ETT with subglottic secretion drainage** ↑VAP



Review Article

Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: A systematic review and meta-analysis*

John Muscedere, MD, FRCPC; Oleksa Rewa, MD; Kyle Mckechnie, MD; Xuran Jiang, Msc; Denny Laporta, MD, FRCPC; Daren K. Heyland, MD, FRCPC

Study or Subgroup	SSD Events	SSD Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Mahul 1992	9	70	21	75	6.2%	0.46 [0.23, 0.93]	1992
Valles 1995	14	76	25	77	9.5%	0.57 [0.32, 1.01]	1995
Metz 1998	5	10	10	14	6.3%	0.70 [0.35, 1.41]	1998
Kollef 1999	8	160	15	183	4.5%	0.61 [0.27, 1.40]	1999
Bo 2000	8	35	15	33	6.1%	0.50 [0.25, 1.03]	2000
Smulders 2002	3	75	12	75	2.1%	0.25 [0.07, 0.85]	2002
Girou 2004	5	8	6	10	5.7%	1.04 [0.50, 2.18]	2004
Liu 2006	14	41	30	45	13.9%	0.51 [0.32, 0.82]	2006
Lorente 2007	11	140	31	140	7.4%	0.35 [0.19, 0.68]	2007
Yang 2008	12	48	20	43	9.1%	0.54 [0.30, 0.97]	2008
Bouza 2008	12	331	19	359	6.2%	0.69 [0.34, 1.39]	2008
Zheng 2008	9	30	16	31	7.5%	0.58 [0.31, 1.11]	2008
Lacherade 2010	25	169	42	164	15.6%	0.58 [0.37, 0.90]	2010
Total (95% CI)		**1193**		**1249**	**100.0%**	**0.55 [0.46, 0.66]**	
Total events	135		262				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 7.78$, df = 12 (P = 0.80); $I^2 = 0\%$
Test for overall effect: Z = 6.57 (P < 0.00001)

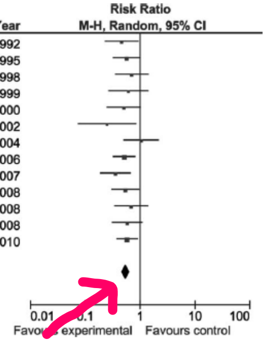


Figure 1. Rate of ventilator-associated pneumonia between groups with subglottic secretion and without subglottic secretion. *M-H*, Mantel-Henszel; *SSD*, subglottic secretion drainage; *CI*, confidence interval.

Study or Subgroup	SSD Events	SSD Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bouza 2008	12	331	19	359	18.4%	0.69 [0.34, 1.39]
Kollef 1999	8	160	15	183	13.3%	0.61 [0.27, 1.40]
Lacherade 2010	25	169	42	164	46.3%	0.58 [0.37, 0.90]
Lorente 2007	11	140	31	140	22.0%	0.35 [0.19, 0.68]
Total (95% CI)		**800**		**846**	**100.0%**	**0.54 [0.40, 0.73]**
Total events	56		107			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.23$, df = 3 (P = 0.53); $I^2 = 0\%$
Test for overall effect: Z = 3.99 (P < 0.0001)

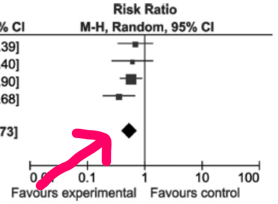


Figure 2. Rate of ventilator-associated pneumonia between groups with subglottic secretion and without subglottic secretion in studies of high methodologic quality. *M-H*, Mantel-Henszel; *SSD*, subglottic secretion drainage; *CI*, confidence interval.

SRFAC

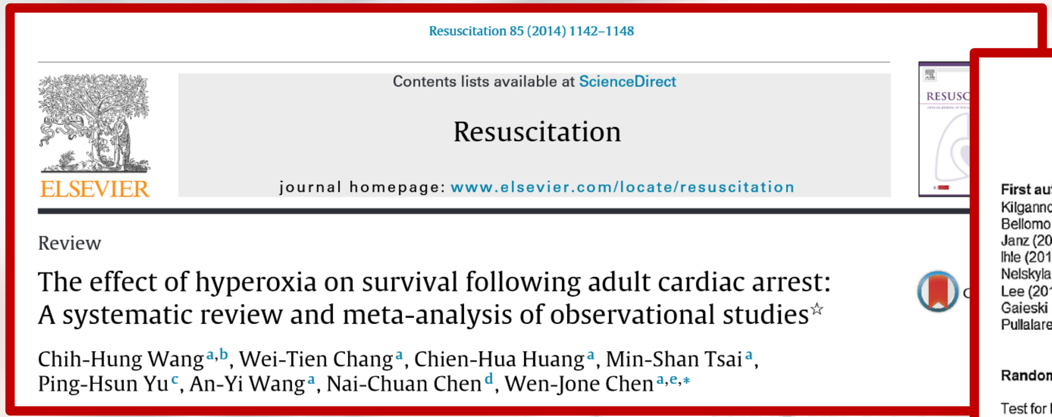
B (Breathing) – O_2

- **Hypoxaemia** (PaO_2 < 60 mmHg)

→ risks further cardiac arrest, secondary brain injury

- **Hyperoxaemia** (PaO_2 > 300 mmHg)

→ causes oxidative stress, worsens neurological injury


Resuscitation 85 (2014) 1142–1148

Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

Review

The effect of hyperoxia on survival following adult cardiac arrest: A systematic review and meta-analysis of observational studies☆

Chih-Hung Wang[a,b], Wei-Tien Chang[a], Chien-Hua Huang[a], Min-Shan Tsai[a], Ping-Hsun Yu[c], An-Yi Wang[a], Nai-Chuan Chen[d], Wen-Jone Chen[a,e,*]

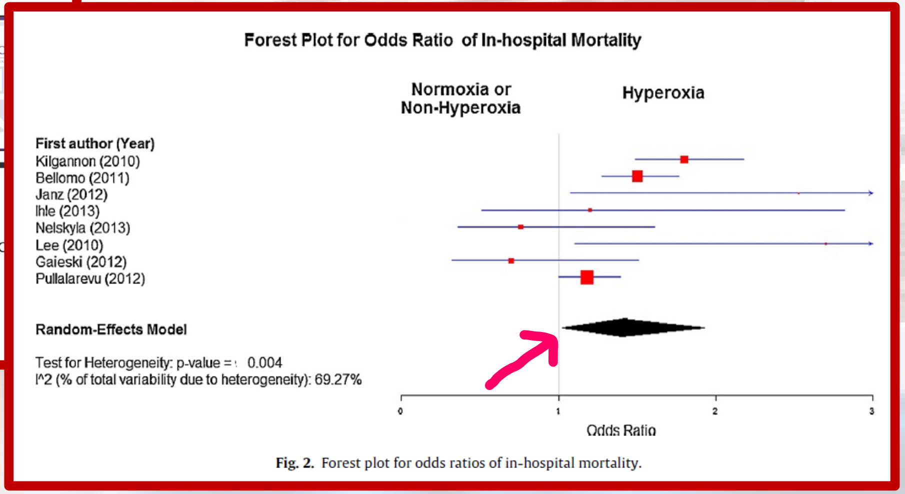


Fig. 2. Forest plot for odds ratios of in-hospital mortality.

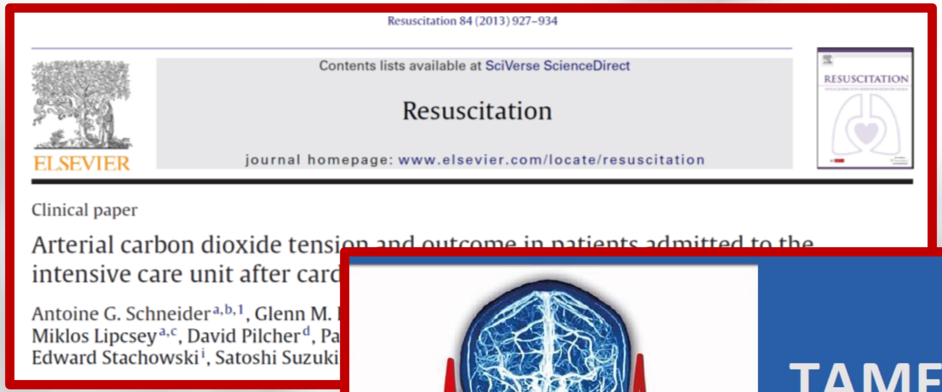
- **Target SpO_2 94 to 98%**
- High PEEP may reduce cerebral venous drainage

→ increasing CBV, ICP

→ **suggest PEEP ≤ 10 cmH_2O**

SRFAC

B (Breathing) – CO_2


Resuscitation 84 (2013) 927–934

Contents lists available at SciVerse ScienceDirect

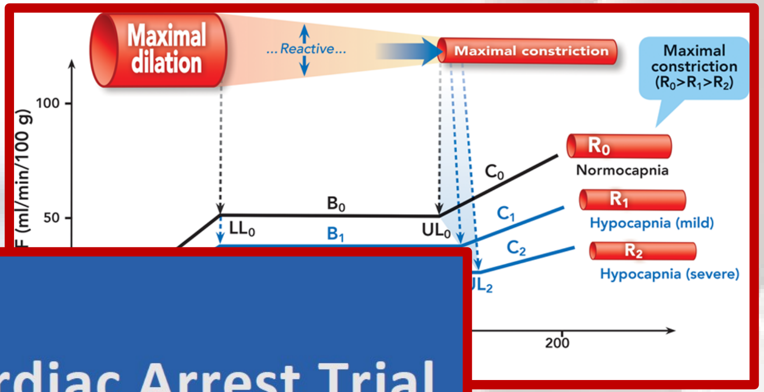
Resuscitation

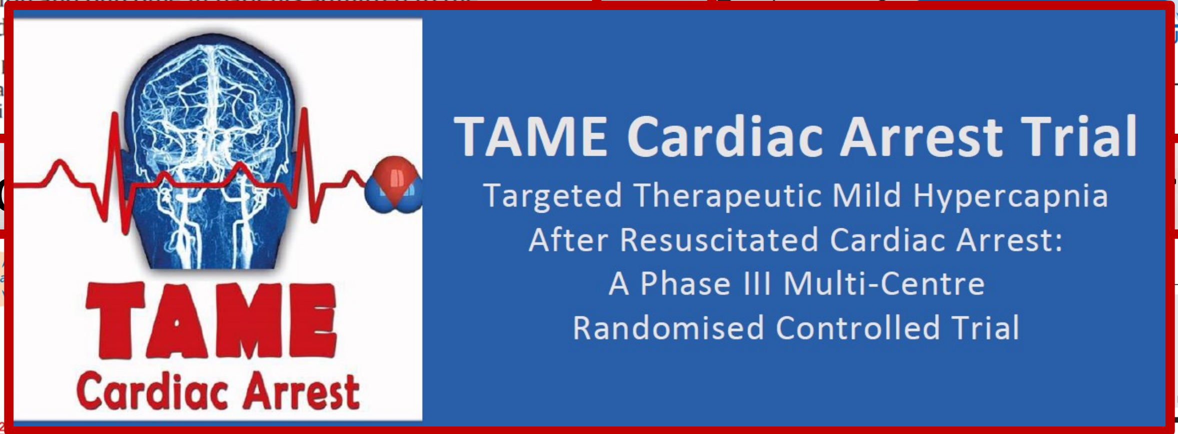
journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

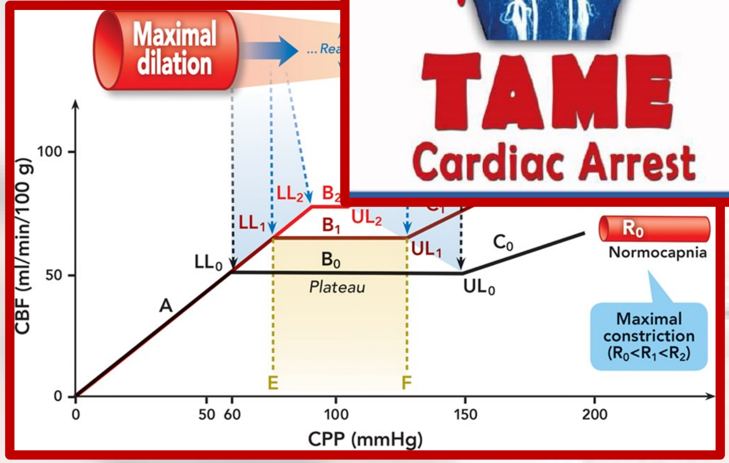
Arterial carbon dioxide tension and outcome in patients admitted to the intensive care unit after card

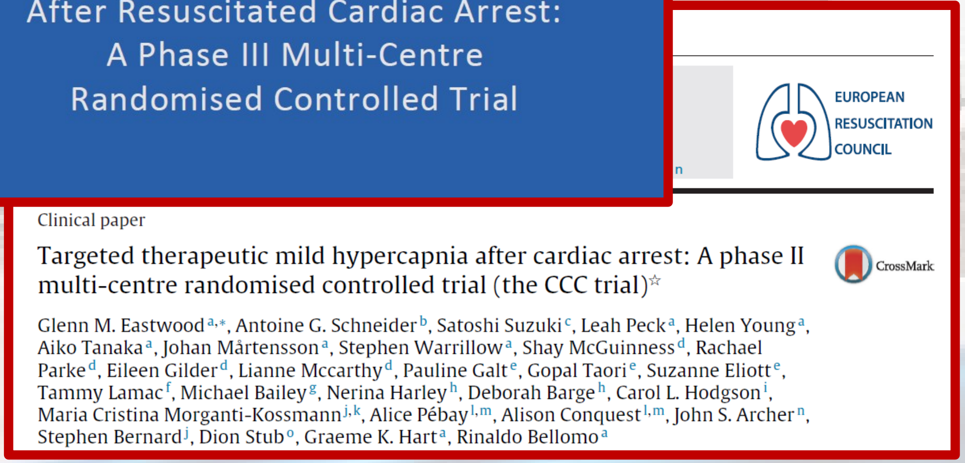
Antoine G. Schneider[a,b,1], Glenn M.
Miklos Lipcsey[a,c], David Pilcher[d], Pa
Edward Stachowski[i], Satoshi Suzuki





• **Hypocapnia** → c … al blood flow



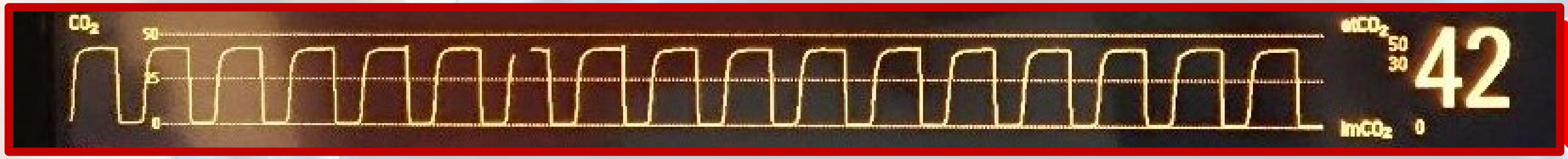

EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Targeted therapeutic mild hypercapnia after cardiac arrest: A phase II multi-centre randomised controlled trial (the CCC trial)☆

Glenn M. Eastwood[a,*], Antoine G. Schneider[b], Satoshi Suzuki[c], Leah Peck[a], Helen Young[a], Aiko Tanaka[a], Johan Mårtensson[a], Stephen Warrillow[a], Shay McGuinness[d], Rachael Parke[d], Eileen Gilder[d], Lianne Mccarthy[d], Pauline Galt[e], Gopal Taori[e], Suzanne Eliott[e], Tammy Lamac[f], Michael Bailey[g], Nerina Harley[h], Deborah Barge[h], Carol L. Hodgson[i], Maria Cristina Morganti-Kossmann[j,k], Alice Pébay[l,m], Alison Conquest[l,m], John S. Archer[n], Stephen Bernard[j], Dion Stub[o], Graeme K. Hart[a], Rinaldo Bellomo[a]

• **Mild hypercapnia** → increases cerebral blood flow but risk of increasing ICP



SRFAC

B (Breathing) – Ventilation Strategies

- **Lung protective ventilation strategies**
  - Low tidal volume 6 to 8 mls/kg PBW (↓volutrauma),
  - Plateau pressure ≤ 30 cmH_2O (↓barotrauma)
- Continuous infusion of NMBA may reduce mortality

Resuscitation 84 (2013) 1728–1733

Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

Clinical Paper, Clinical

Continuous neuromuscular blockade is associated with decreased mortality in post-cardiac arrest patients☆

Justin D. Salciccioli[a,1], Michael N. Cocchi[a,b,1], Jon C. Rittenberger[c,1], Mary Ann Peberdy[h,1], Joseph P. Ornato[d,1], Benjamin S. Abella[e,1], David F. Gaieski[e,1], John Clore[d,1], Shiva Gautam[f,1], Tyler Giberson[a,1], Clifton W. Callaway[c,1], Michael W. Donnino[a,g,*,1]

Table 3
Outcomes according to use or non-use of early, sustained NMB in post-CA subjects.

Outcome	Total	24 h NMB	No NMB	*P*-Value
Survivor MV (days)	4 (3–6)	5 (3–6)	4 (2–6)	0.53
Survivor ICU LOS (days)	7 (5–10)	8 (6–8)	6 (4–10)	0.31
Survivor hospital LOS (days)	13 (9–19)	15.5 (11–18)	12.5 (8–20)	0.42
Hospital survival *n* (%)	52 (47)	14 (78)	38 (41)	0.005
Favorable Functional Status (MR[a] 0 – 3) *n* (%)	35 (32)	9 (50)	26 (28)	0.07

MV, mechanical ventilation; ICU, intensive care unit; LOS, length of stay; MR, modified rankin.

[a]Modified Rankin Scale[14]. 0, no symptoms at all; 1, no significant disability despite symptoms; able to carry out all usual duties and activities; 2, slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance; 3, moderate disability requiring some help, but able to walk without assistance; 4, moderate severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance; 5, severe disability; bedridden, incontinent and requiring constant nursing care and attention; 6, Death.

SRFAC

C (Circulation) – ?Cath

Resuscitation 83 (2012) 1427–1433

Contents lists available at SciVerse ScienceDirect

Resuscitation

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

Clinical paper

Acute coronary angiography in patients resuscitated from out-of-hospital cardiac arrest—A systematic review and meta-analysis☆

Jacob Moesgaard Larsen*, Jan Ravkilde

Department of Cardiology and Centre for Cardiovascular Research, Aalb

Resuscitation 85 (2014) 657–663

Contents lists available at ScienceDirect

Resuscitation

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

Clinical Paper

Early coronary angiography and induced hypothermia are associated with survival and functional recovery after out-of-hospital cardiac arrest☆

Clifton W. Callaway[a,*], Robert H. Schmicker[b], Siobhan P. Brown[b], J. Michael Albrich[c], Douglas L. Andrusiek[d], Tom P. Aufderheide[e], James Christenson[d], Mohamud R. Daya[f], David Falconer[g], Ruchika D. Husa[h], Ahamed H. Idris[i], Joseph P. Ornato[j], Valeria E. Rac[g], Thomas D. Rea[b], Jon C. Rittenberger[a], Gena Sears[b], Ian G. Stiell[k], ROC Investigators

Canadian Journal of Cardiology ■ (2017) 1–15

Systematic Review/Meta-analysis

Does Early Coronary Angiography Improve Survival After out-of-Hospital Cardiac Arrest? A Systematic Review With Meta-Analysis

Michelle Welsford, MD,[a,b] Matthias Bossard, MD,[c,d] Colleen Shortt, PhD,[b] Jodie Pritchard, MD, MPH,[e] Madhu K. Natarajan, MD, MSc,[c,f] and Emilie P. Belley-Côté, MD, MSc[e,f]

- 59 to 71% of OHCA patients, <u>without</u> an obvious non-cardiac cause, have an acute coronary lesion on cath
- ST elevation on ECG post-ROSC → **cath**

SRFAC

C (Circulation) – ?Cath

Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation and the American Heart Association, Inc.
Published by Elsevier Inc.
Vol. 61, No. 4, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.11.019

PRACTICE GUIDELINE

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

A Report of the American College of Cardiology Foundatio
American Heart Association Task Force on Practice Guideli

Evaluation and Management of Patients With STEMI and Out-of-Hospital Cardiac Arrest

I IIa IIb III
B

Therapeutic hypothermia should be started as soon as possible in comatose patients with STEMI and out-of-hospital cardiac arrest caused by VF or pulseless VT, including patients who undergo primary PCI.

I IIa IIb III
B

Immediate angiography and PCI when indicated should be performed in resuscitated out-of-hospital cardiac arrest patients whose initial ECG shows STEMI.

SRFAC

C (Circulation) – ?Cath

ESC
European Society of Cardiology
European Heart Journal (2018) 39, 119–177
doi:10.1093/eurheartj/ehx393
ESC GUIDELINES

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Recommendations	Class	Level
A primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an ECG consistent with STEMI.	I	B
Targeted temperature management is indicated early after resuscitation of cardiac arrest patients who remain unresponsive.	I	B
Urgent angiography (and PCI if indicated) should be considered in patients with resuscitated cardiac arrest without diagnostic ST-segment elevation but with a high suspicion of ongoing myocardial ischaemia.	IIa	C

SRFAC

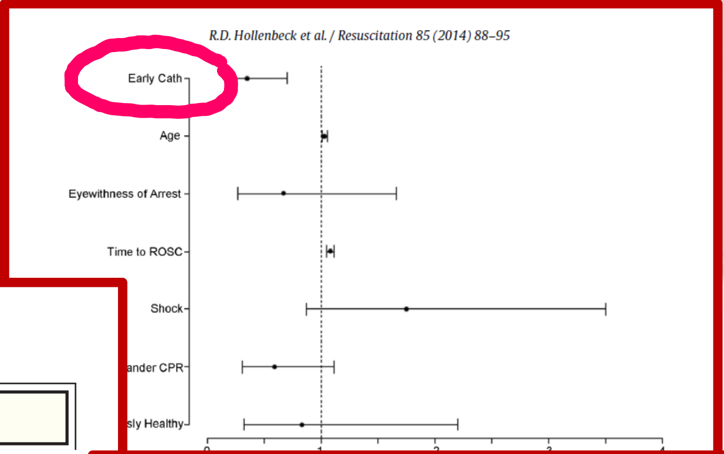
C (Circulation) – ?Cath

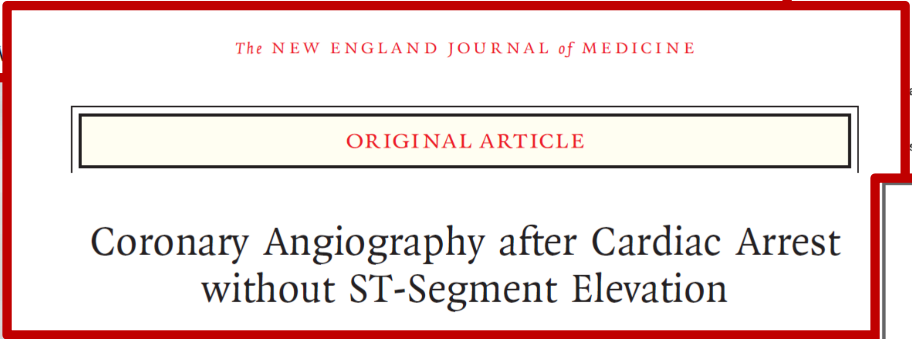

Resuscitation 85 (2014) 88–95
Contents lists available at ScienceDirect
Resuscitation
journal homepage: www.elsevier.com/locate/resuscitation

Clinical Paper

Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI☆

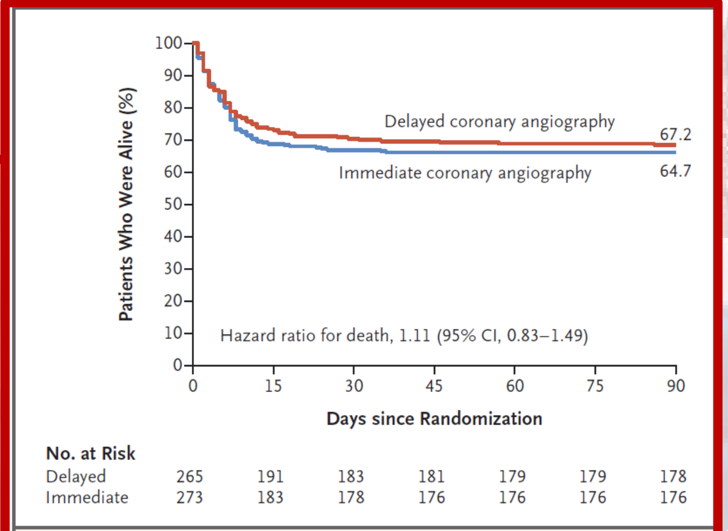
Ryan D. Hollenbeck[a,*,1]
Nainesh C. Patel[c], Paul V




The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary Angiography after Cardiac Arrest without ST-Segment Elevation



No. at Risk							
Delayed	265	191	183	181	179	179	178
Immediate	273	183	178	176	176	176	176

Figure 1. Kaplan–Meier Estimates of Survival among Patients Who Underwent Immediate or Delayed Coronary Angiography after Cardiac Arrest.
There was no significant difference between the two groups in overall survival at 90 days.

- No ST elevation on ECG
  - → ***consider*** **cath**
  - → **especially if haemodynamic or electrical instability**

SRFAC

C (Circulation) – ?Cath

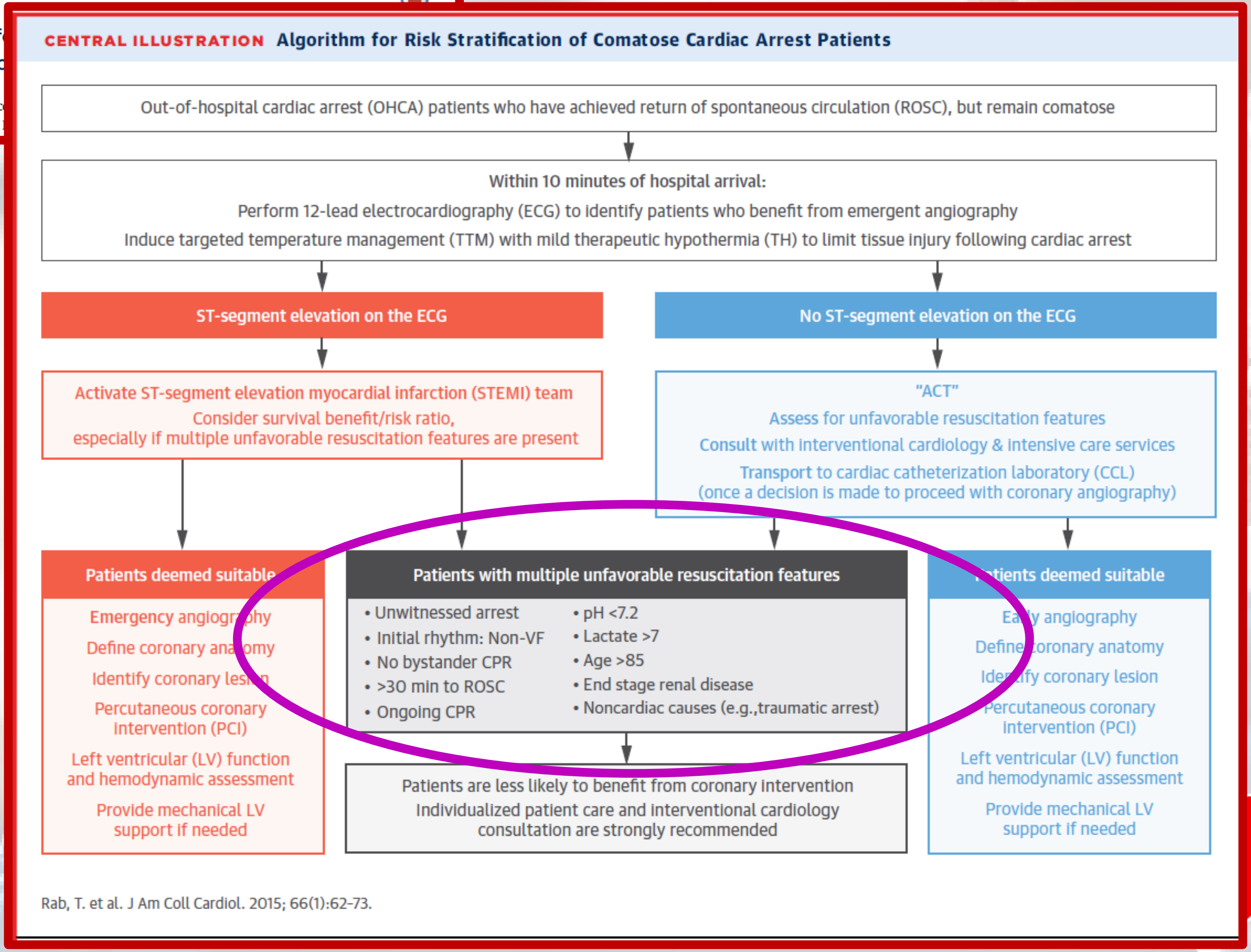

THE PRESENT AND FUTURE

COUNCIL PERSPECTIVES

Cardiac Arrest

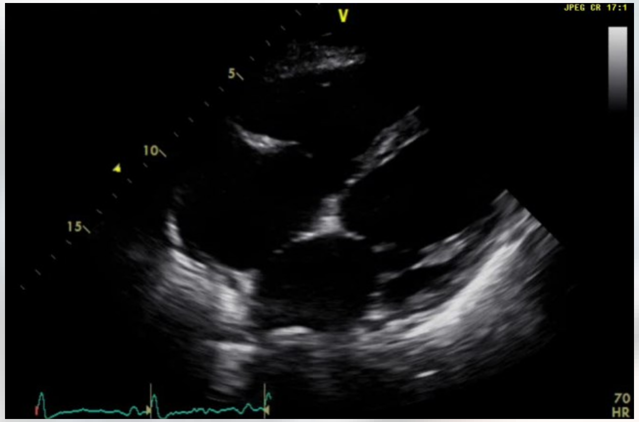
A Treatment Algorithm f
Procedures in the Resusc

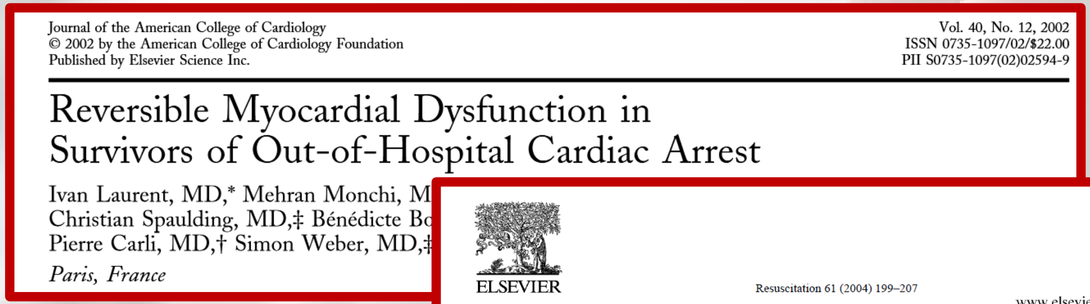
Tanveer Rab, MD,* Karl B. Kern, MD,† Jac
Michael McDaniel, MD,|| Neal W. Dickert,



SRFAC

C (Circulation) – Haemodynamic Monitoring



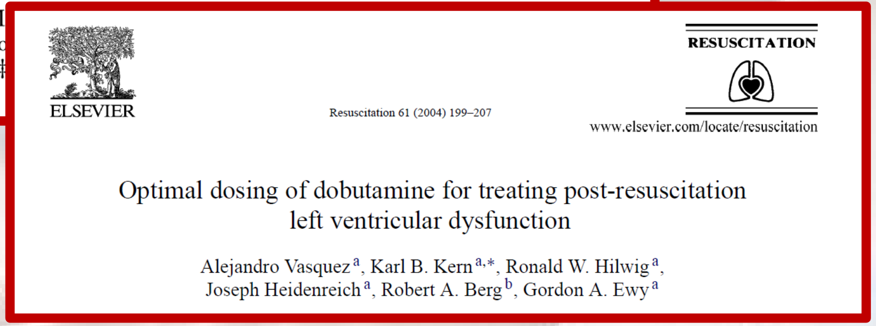


Journal of the American College of Cardiology
© 2002 by the American College of Cardiology Foundation
Published by Elsevier Science Inc.

Vol. 40, No. 12, 2002
ISSN 0735-1097/02/$22.00
PII S0735-1097(02)02594-9

Reversible Myocardial Dysfunction in Survivors of Out-of-Hospital Cardiac Arrest

Ivan Laurent, MD,* Mehran Monchi, M
Christian Spaulding, MD,‡ Bénédicte Bo
Pierre Carli, MD,† Simon Weber, MD,‡
Paris, France



ELSEVIER

Resuscitation 61 (2004) 199–207

RESUSCITATION

www.elsevier.com/locate/resuscitation

Optimal dosing of dobutamine for treating post-resuscitation left ventricular dysfunction

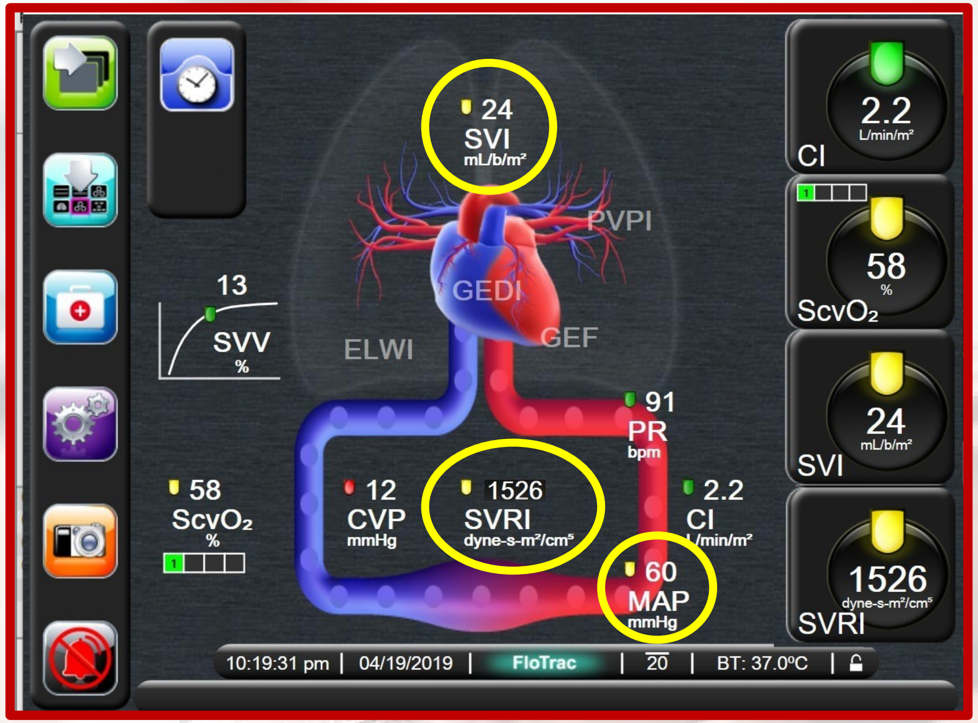
Alejandro Vasquez[a], Karl B. Kern[a,*], Ronald W. Hilwig[a], Joseph Heidenreich[a], Robert A. Berg[b], Gordon A. Ewy[a]

Perfusion
- Pressure – MAP
- Flow – CO, $ScvO_2$, CO_2 gap

- All patients should have an arterial line
  - **Continuous pressure** (MAP) monitoring
  - **Continuous flow** (CO) monitoring e.g. pulse contour analysis, $ScvO_2$

SRFAC

C (Circulation) – Haemodynamic Support



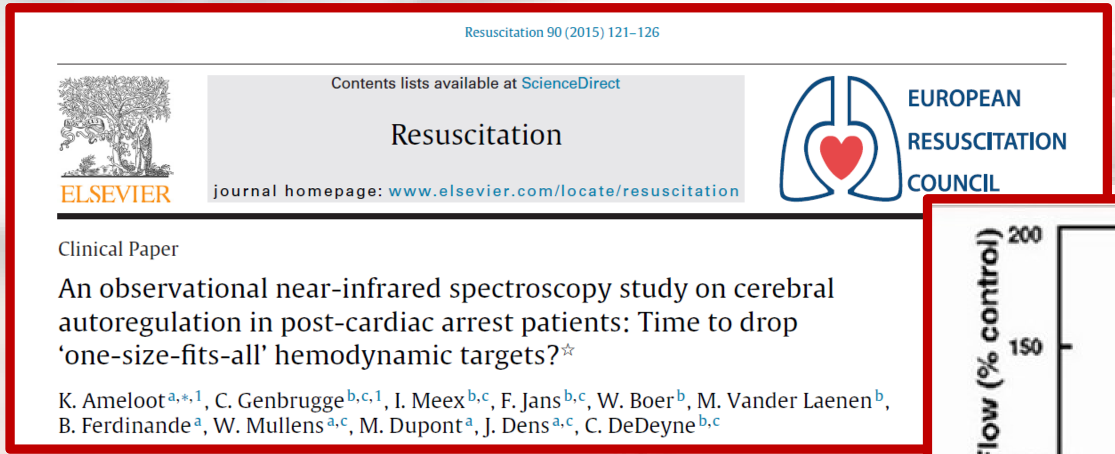
- Consider **Noradrenaline** to achieve hemodynamic targets (less arrhythmogenic)
- If uptitration of Noradrenaline results in a drop in SVI/CI/ScvO$_2$

→ consider low dose **Dobutamine** 3 to 5 mcg/kg/min

SRFAC

C (Circulation) – MAP Target

- Optimal MAP target should be **<u>individualised</u>**
  - Consider baseline BP, evidence of ↑ ICP or AKI
  - In PCAS, cerebral autoregulation impaired
    → CBF varies directly with **CPP (= MAP – ICP)**


Resuscitation 90 (2015) 121–126

Contents lists available at ScienceDirect

Resuscitation

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

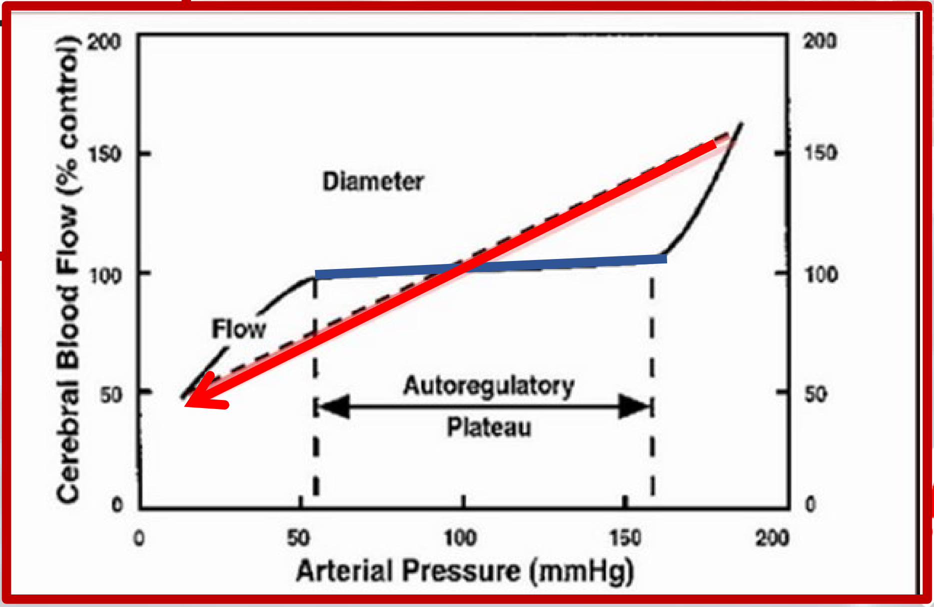
ELSEVIER

EUROPEAN RESUSCITATION COUNCIL

Clinical Paper

An observational near-infrared spectroscopy study on cerebral autoregulation in post-cardiac arrest patients: Time to drop 'one-size-fits-all' hemodynamic targets?☆

K. Ameloot[a,*,1], C. Genbrugge[b,c,1], I. Meex[b,c], F. Jans[b,c], W. Boer[b], M. Vander Laenen[b], B. Ferdinande[a], W. Mullens[a,c], M. Dupont[a], J. Dens[a,c], C. DeDeyne[b,c]



SRFAC

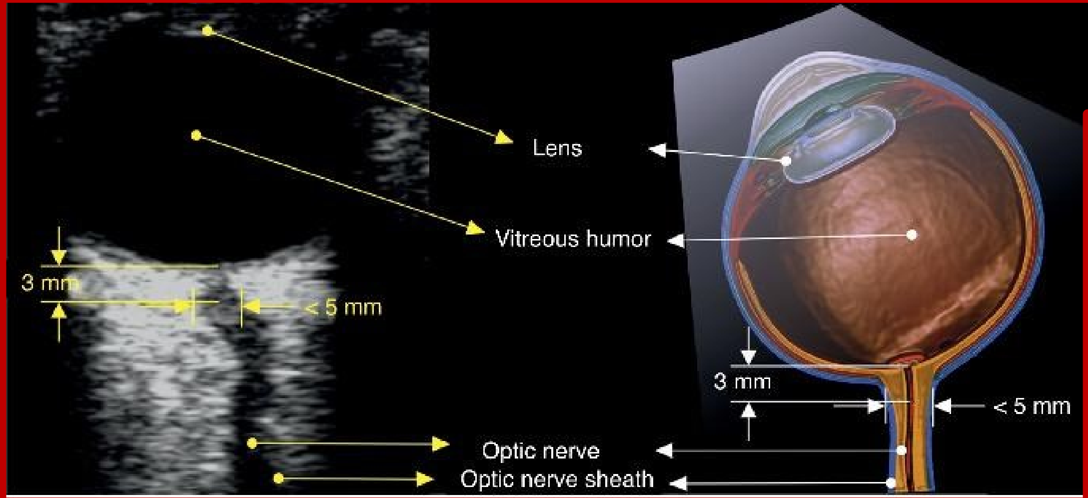
C (Circulation) – MAP Target

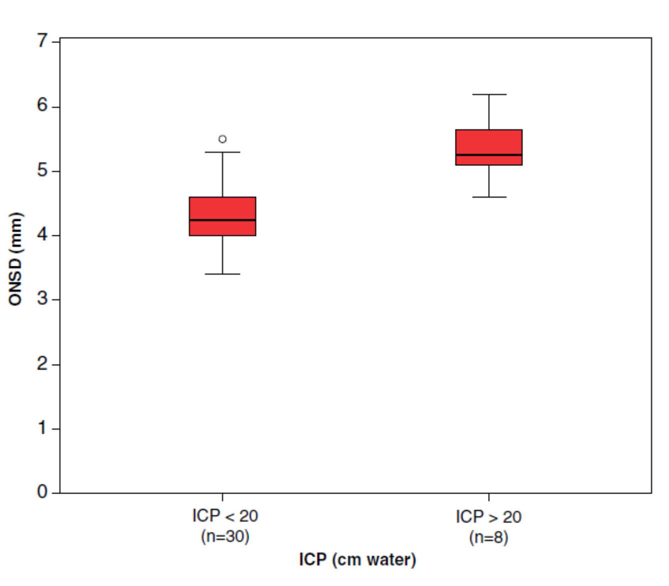
- Estimate ICP
  - From CT Head and ultrasound optic nerve sheath diameter (ONSD)

BRIEF REPORT

Correlation of Optic Nerve Sheath Diameter with Direct Measurement of Intracranial Pressure

Heidi Harbison Kimberly, MD, Sachita





- Ultrasound ONSD > 5 mm ~ ICP > 20 mmHg
- **Target MAP 80 to 85 mmHg**

D (Neurology) – Sedation

- Sedation reduces cerebral oxygen consumption ($CMRO_2$)
- Sedation reduces shivering during induced hypothermia
- Metabolism of sedatives and NMBA reduced with hypothermia

→ suggest using short acting drugs which allows earlier and more reliable neurological assessment

Intensive Care Med (2012) 38:959–967
DOI 10.1007/s00134-012-2540-1

ORIGINAL

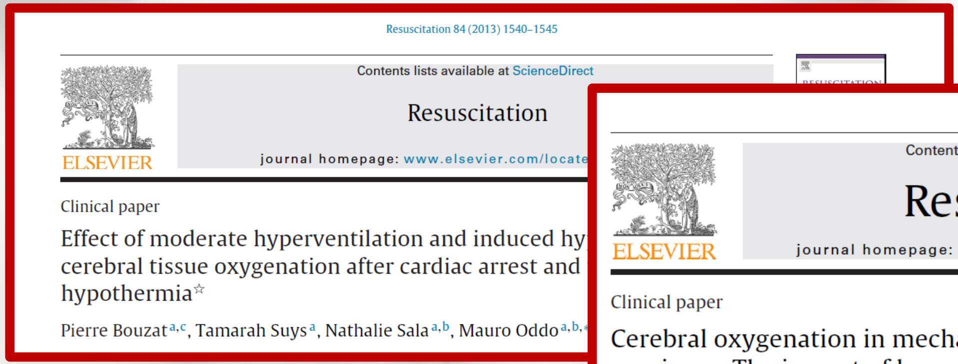
Thor W. Bjelland
Ola Dale
Kjell Kaisen
Bjørn O. Haugen
Stian Lydersen
Kristian Strand
Pål Klepstad

Propofol and remifentanil versus midazolam and fentanyl for sedation during therapeutic hypothermia after cardiac arrest: a randomised trial

- Consider **Remifentanil** +/- **Propofol**

SRFAC

D (Neurology) – Cerebral Oximetry


Resuscitation 84 (2013) 1540–1545

Contents lists available at ScienceDirect

Resuscitation

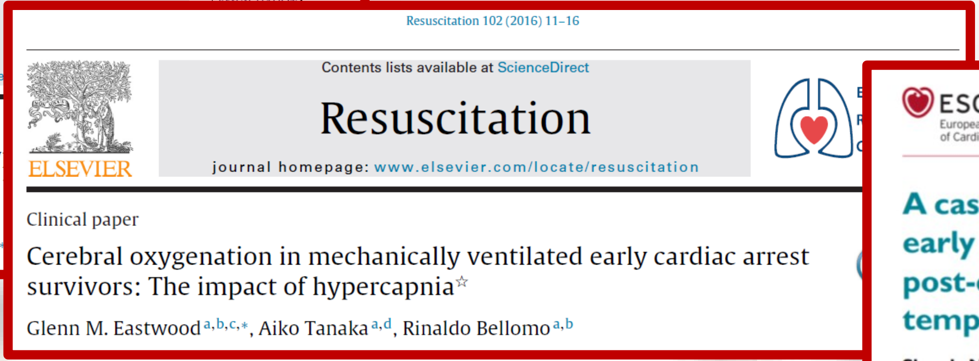
journal homepage: www.elsevier.com/locate

ELSEVIER

Clinical paper

Effect of moderate hyperventilation and induced hy
cerebral tissue oxygenation after cardiac arrest and
hypothermia☆

Pierre Bouzat[a,c], Tamarah Suys[a], Nathalie Sala[a,b], Mauro Oddo[a,b,]


Resuscitation 102 (2016) 11–16

Contents lists available at ScienceDirect

Resuscitation

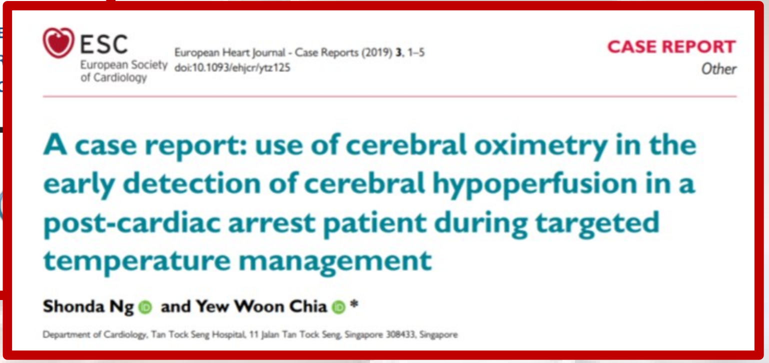
journal homepage: www.elsevier.com/locate/resuscitation

ELSEVIER

Clinical paper

Cerebral oxygenation in mechanically ventilated early cardiac arrest survivors: The impact of hypercapnia☆

Glenn M. Eastwood[a,b,c,*], Aiko Tanaka[a,d], Rinaldo Bellomo[a,b]


ESC European Society of Cardiology

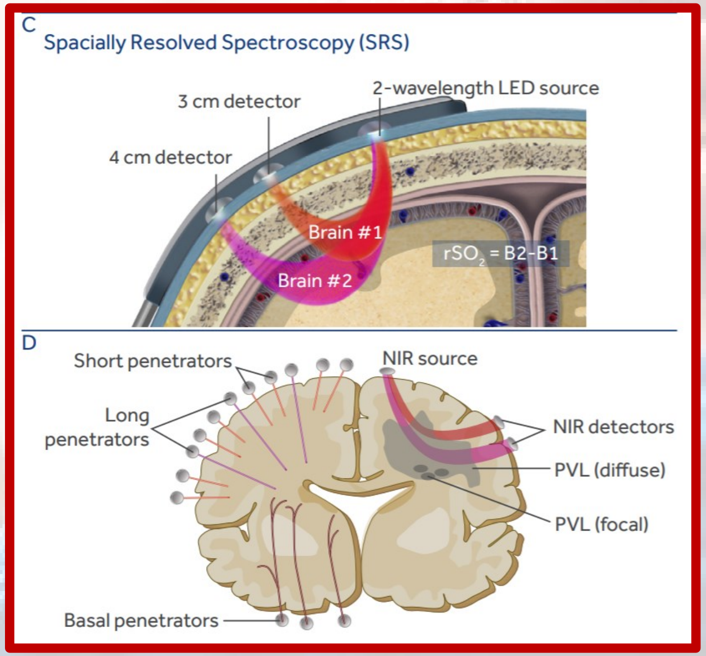
European Heart Journal - Case Reports (2019) 3, 1–5
doi:10.1093/ehjcr/ytz125

CASE REPORT
Other

A case report: use of cerebral oximetry in the early detection of cerebral hypoperfusion in a post-cardiac arrest patient during targeted temperature management

Shonda Ng and Yew Woon Chia *

Department of Cardiology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433, Singapore



D (Neurology) – continuous EEG

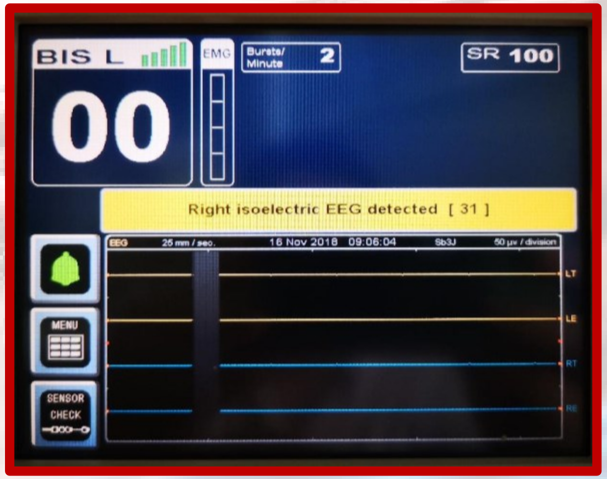
Neurology. 1980 Dec;30(12):1292-7.

Neurologic prognosis after cardiopulmonary arrest: III. Seizure activity.

Snyder BD, Hauser WA, Loewenson RB, Leppik IE, Ramirez-Lassepas M, Gumnit RJ.

- Occurs in 1/3 of patients who remain comatose after ROSC

→ suggest cEEG especially patients on NMBA



- Seizures increases $CMRO_2$ and may cause secondary brain injury
- Consider **Levetiracetam** and/or **Sodium Valproate**

SRFAC

D (Neurology) – Temperature Control

Articles

Mechanisms of action, physiological effects, and complications of hypothermia

Kees H. Polderman, MD

Background: Mild to moderate hypothermia (32–35°C) is the first treatment with proven efficacy for postischemic neurological injury. In recent years important insights have been gained into the mechanisms underlying hypothermia's protective effects; in addition, physiological and pathophysiological changes associated with cooling have become better understood.

Objective: To discuss hypothermia's mechanisms of action, to review (patho)physiological changes associated with cooling, and to discuss potential side effects.

Design: Review article.

Interventions: None.

Main Results: A myriad of destructive processes unfold in injured tissue following ischemia–reperfusion. These include excitotoxicty, neuroinflammation, apoptosis, free radical production, seizure activity, blood–brain barrier disruption, blood vessel leakage, cerebral thermopooling, and numerous others. The severity of this destructive cascade determines whether injured cells will survive or die. Hypothermia can inhibit or mitigate all of these mechanisms, while stimulating protective systems such as early gene activation. Hypothermia is also effective in mitigating intracranial hypertension and reducing brain edema. Side effects include immunosuppression with increased infection risk, cold diuresis and hypovolemia, electrolyte disorders, insulin resistance, impaired drug clearance, and mild coagulopathy. Targeted interventions are required to effectively manage these side effects. Hypothermia does not decrease myocardial contractility or induce hypotension if hypovolemia is corrected, and preliminary evidence suggests that it can be safely used in patients with cardiac shock. Cardiac output will decrease due to hypothermia-induced bradycardia, but given that metabolic rate also decreases the balance between supply and demand, is usually maintained or improved. In contrast to deep hypothermia (≤30°C), moderate hypothermia does not induce arrhythmias; indeed, the evidence suggests that arrhythmias can be prevented and/or more easily treated under hypothermic conditions.

Conclusions: Therapeutic hypothermia is a highly promising treatment, but the potential side effects need to be properly managed particularly if prolonged treatment periods are required. Understanding the underlying mechanisms, awareness of physiological changes associated with cooling, and prevention of potential side effects are all key factors for its effective clinical usage. (Crit Care Med 2009; 37[Suppl.]:S186–S202)

Key Words: hypothermia; normothermia; fever; mechanisms; neuroprotection; side effects; neurological injury; cardiac arrest; traumatic brain injury

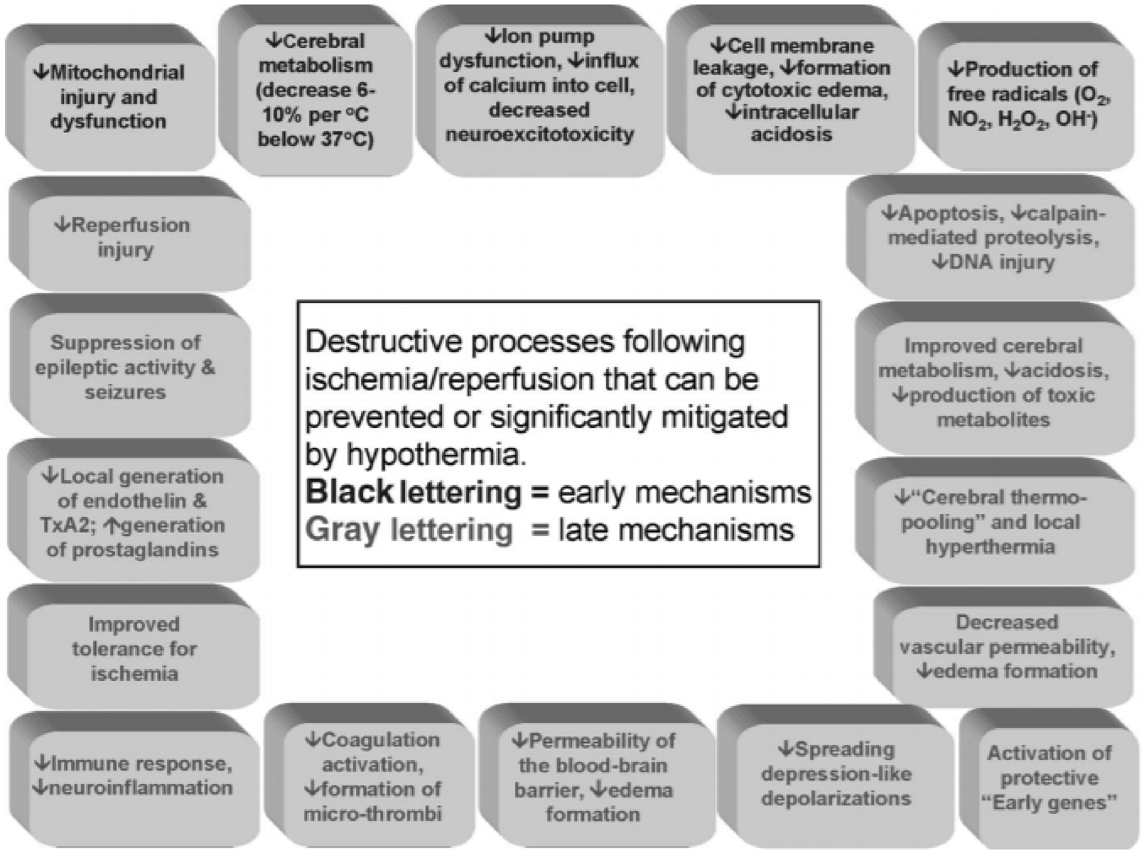


Figure 1. Schematic depiction of the mechanisms underlying the protective effects of mild to moderate hypothermia. *TxA2*, thromboxane A2.

D (Neurology) – TTM @ Hypothermia?

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.

The New England Journal of Medicine

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

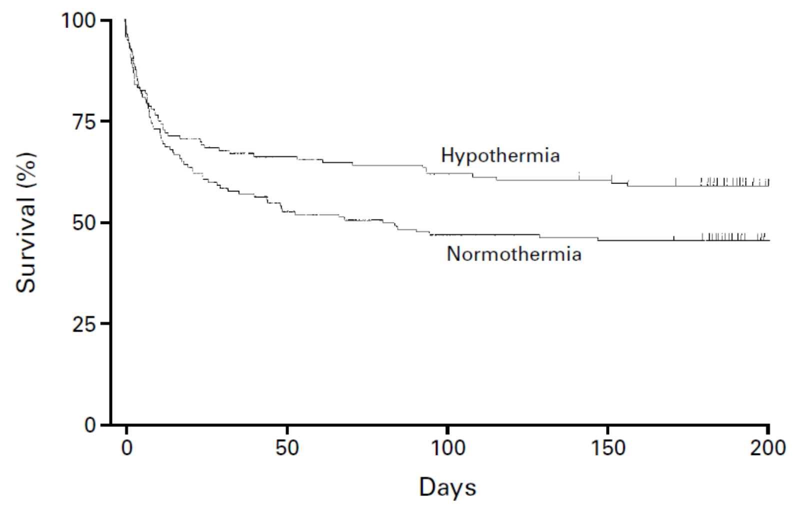
MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

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

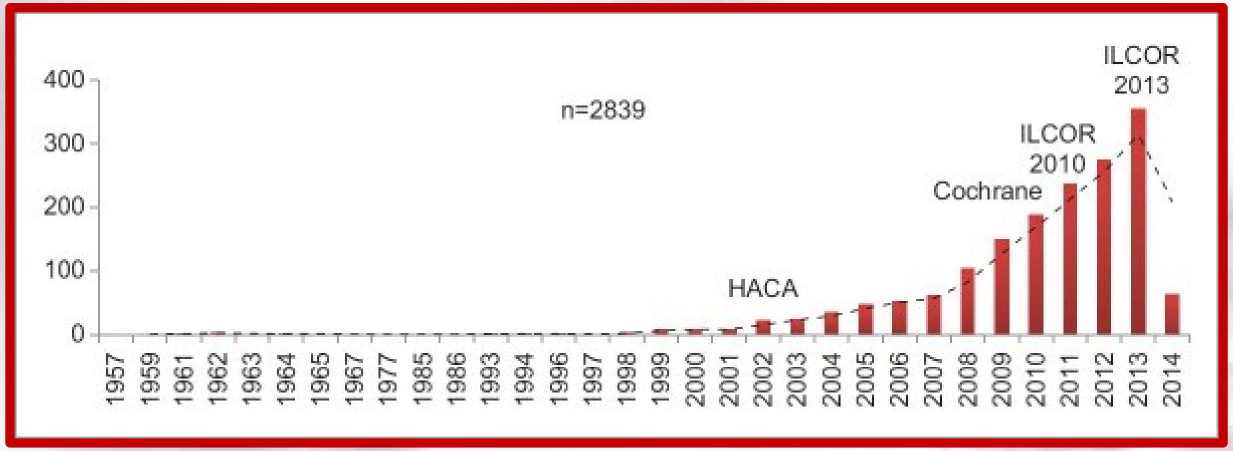
OUTCOME*	HYPOTHERMIA (N=43)	NORMOTHERMIA (N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing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



SRFAC

D (Neurology) – TTM @ Hypothermia?



Saigal S, et al. *Indian J Crit Care Med* 2015; 19:537-46

Part 9: Post–Cardiac Arrest Care

2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Mary Ann Peberdy, Co-Chair*; Clifton W. Callaway, Co-Chair*; Robert W. Neumar; Romergryko G. Geocadin; Janice L. Zimmerman; Michael Donnino; Andrea Gabrielli; Scott M. Silvers; Arno L. Zaritsky; Raina Merchant; Terry L. Vanden Hoek; Steven L. Kronick

- Core Temperature Measurement If Comatose
  - Rationale: Minimize brain injury and improve outcome
  - Prevent hyperpyrexia >37.7°C
  - Induce therapeutic hypothermia if no contraindications
  - Cold IV fluid bolus 30 mL/kg if no contraindication
  - Surface or endovascular cooling for 32°C–34°C×24 hours
  - After 24 hours, slow rewarming 0.25°C/hr

SRFAC

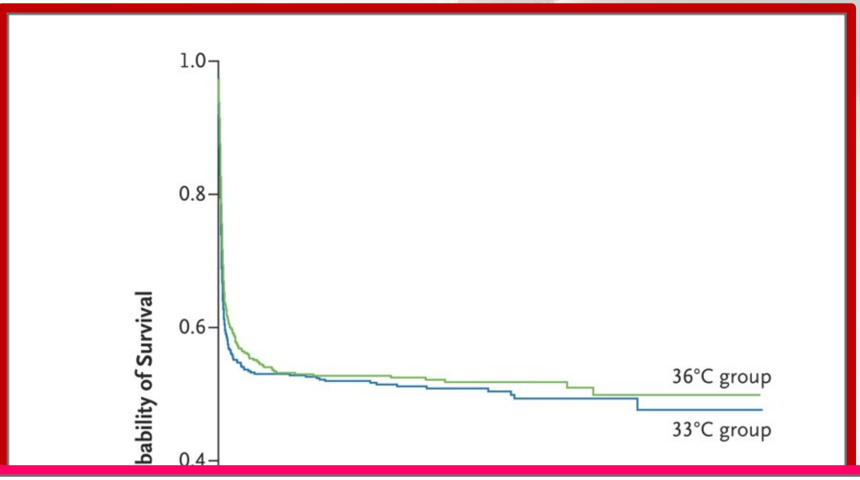
D (Neurology) – TTM @ Normothermia?

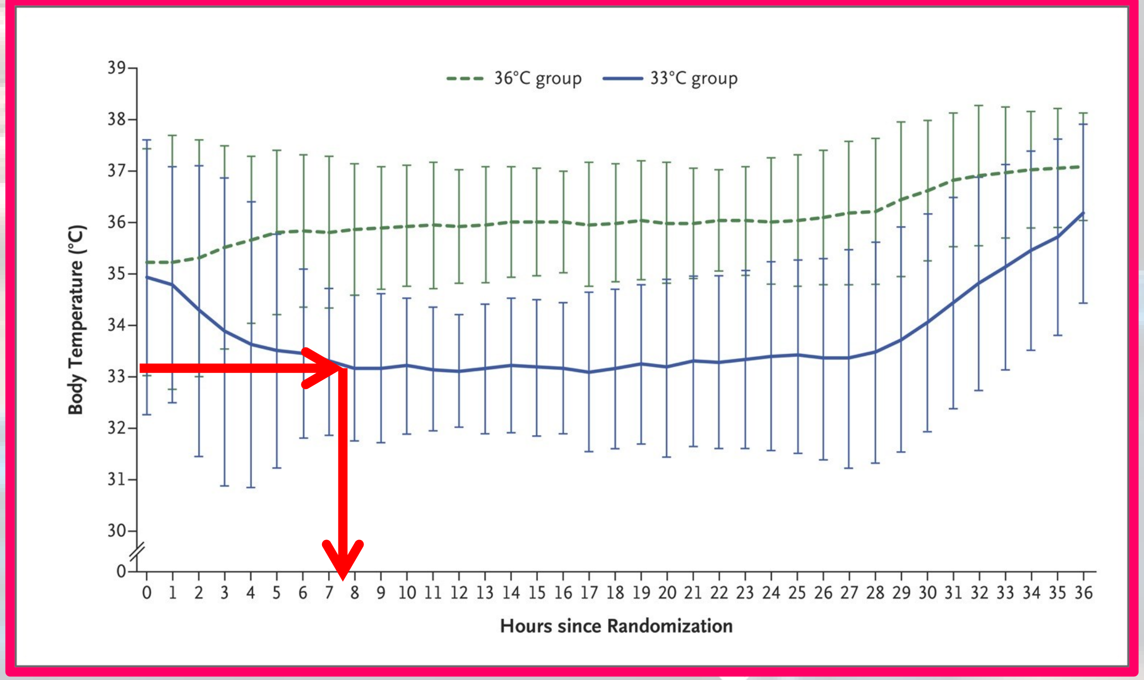
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Bystander performed CPR — no. (%)	344 (73)	339 (73)
First monitored rhythm — no. (%)†		
Shockable rhythm	375 (79)	377 (81)
Ventricular fibrillation	349 (74)	356 (77)
Nonperfusing ventricular tachycardia	12 (3)	12 (3)
Unknown rhythm but responsive to shock	5 (1)	5 (1)
Perfusing rhythm after bystander-initiated defibrillation	9 (2)	4 (1)
Asystole	59 (12)	54 (12)
Pulseless electrical activity	37 (8)	28 (6)
Unknown first rhythm, not responsive to shock or not shocked	2 (<0.5)	6 (1)
Time from cardiac arrest to event — min‡		
Start of basic life support		
Median	1	1
Interquartile range	0–2	0–2
Start of advanced life support		
Median	10	9
Interquartile range	6–13	5–13
Return of spontaneous circulation		
Median	25	25
Interquartile range	18–40	16–40





D (Neurology) – TTM @ Normothermia?

Resuscitation 113 (2017) 39–43

Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Changing target temperature from 33 °C to 36 °C in the ICU management of out-of-hospital cardiac arrest: A before and after study☆

Janet E. Bray[a,b,c,*], Dion Stub[a,b,d,e,f], Jason E. Bloom[b], Louise Segan[a,b], Biswadev Mitra[a,b], Karen Smith[a,d,g,h], Judith Finn[a,c], Stephen Bernard[a,b,d]

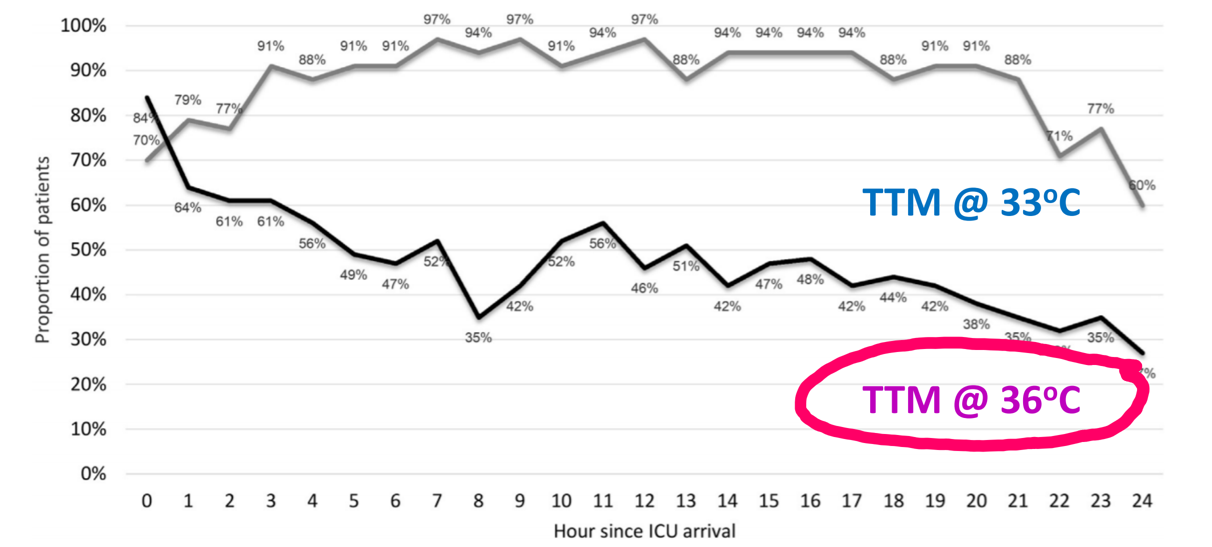
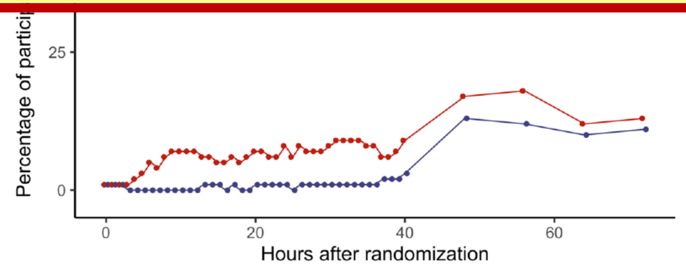


Fig. 1. The proportion of patients at target temperature for each hour of the first day of intensive care stay by the 33 °C (grey line) and 36 °C (black line) TTM periods.

ttm2

Figure S5. Percentage of participants who were febrile per hour

group and 428 of 931 patients (46%) in the normothermia group received cooling with a device. Among patients who received cooling, the types of devices used in each treatment group were similar (70% surface and 30% intravascular in the hypothermia group and 69% surface and 31% intravascular in the normothermia group).



The figure depicts the percentage of participants who had a recorded body temperature above 37.7°C at each time point (0-72 hours after randomization, bladder measurement). The denominator is the total number of participants with a bladder measurement at each time point.

D (Neurology) – TTM @ Normothermia?

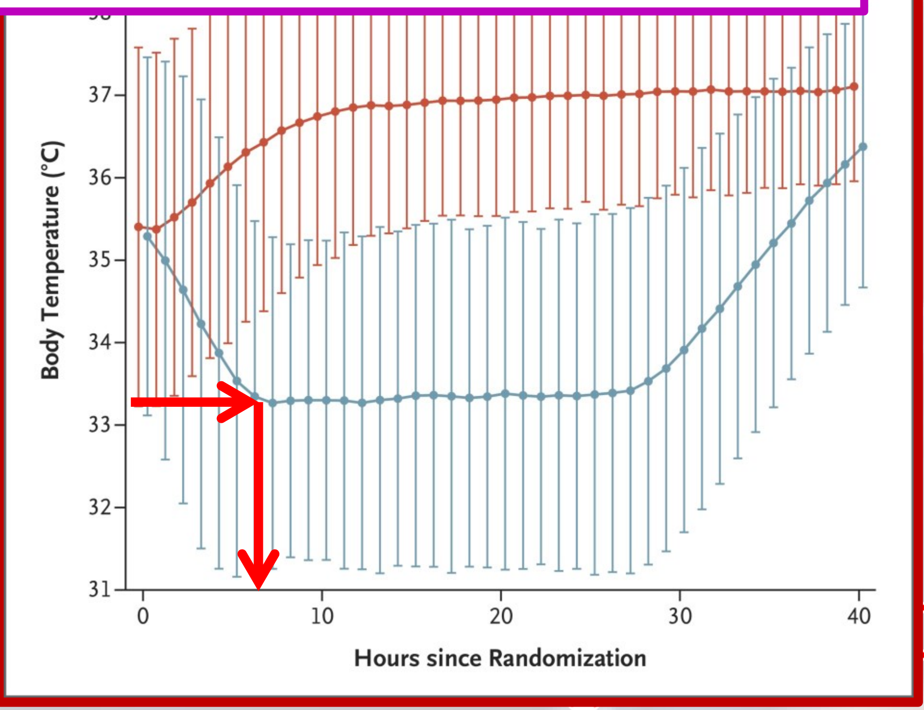
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

Bystander-witnessed cardiac arrest	850 (9	
Bystander-performed CPR	759 (82)	728 (78)
First monitored rhythm — no. (%)		
Shockable rhythm	671 (72)	700 (75)
Ventricular fibrillation	576 (62)	585 (63)
Nonperfusing ventricular tachycardia	31 (3)	29 (3)
ROSC after bystander-initiated defibrillation	24 (3)	41 (4)
Unknown rhythm, shock administered	40 (4)	45 (5)
Nonshockable rhythm	259 (28)	231 (25)
Pulseless electrical activity	117 (13)	113 (12)
Asystole	124 (13)	100 (11)
Unknown rhythm, no shock administered	18 (2)	18 (2)
Median time from cardiac arrest to sustained ROSC (IQR) — min§	25 (16–40)	25 (17–40)
Median time from cardiac arrest to randomization — min (IQR)	136 (103–170)	133 (99–17

Choose a temperature target between 33 to 36°C, achieve that ASAP and maintain consistently. Aim 33°C if possible.



D (Neurology) – TTM for non-shockable rhythm

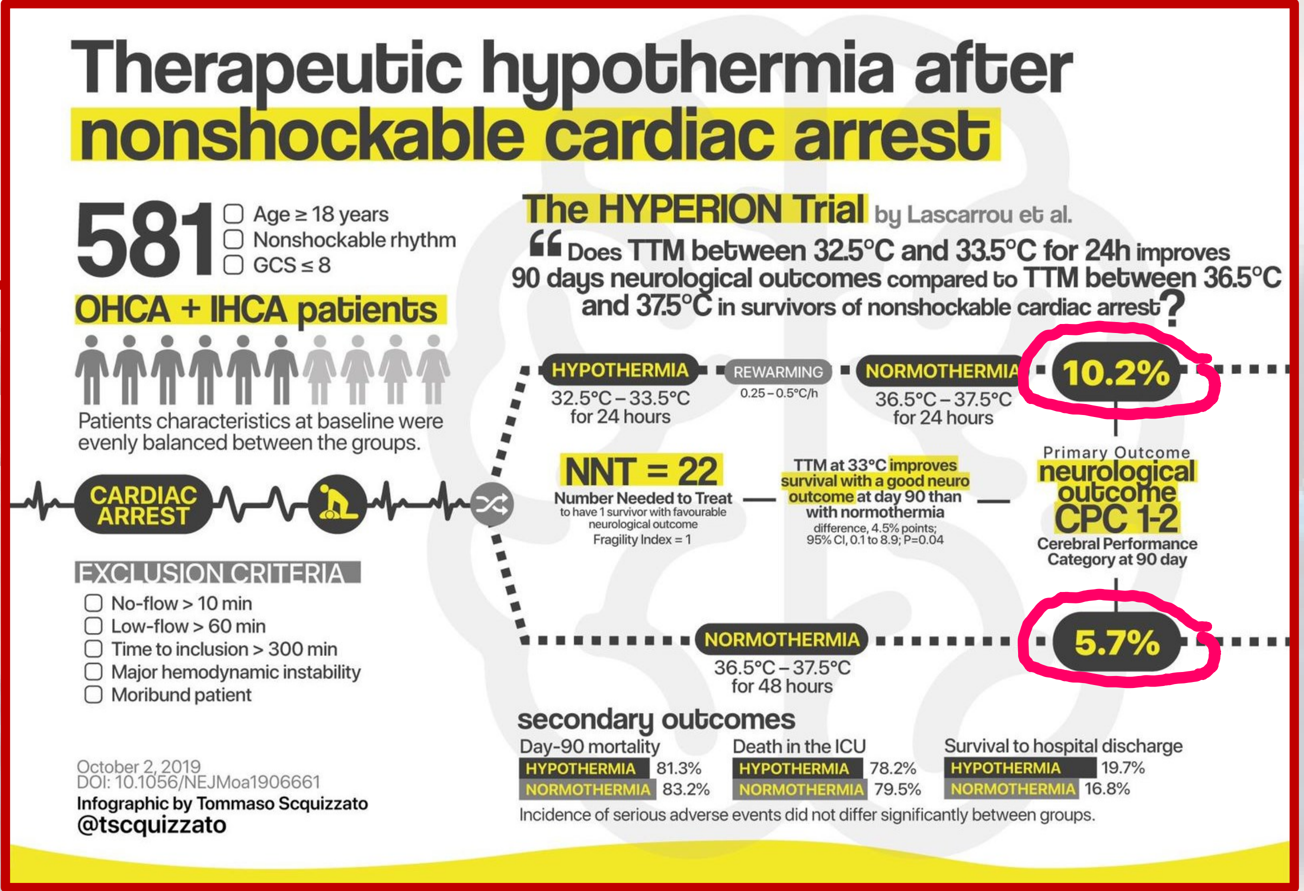
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm

J.-B. Lascarrou, H. Merdji, A. Le Gouge, G. Colin, G. Grillet, P. Girardie, E. Coupez, P.-F. Dequin, A. Cariou, T. Boulain, N. Brule, J.-P. Frat, P. Asfar, N. Pichon, M. Landais, G. Plantefeve, J.-P. Quenot, J.-C. Chakarian, M. Sirodot, S. Legriel, J. Letheulle, D. Thevenin, A. Desachy, A. Delahaye, V. Botoc, S. Vimeux, F. Martino, B. Giraudeau, and J. Reignier, for the CRICS-TRIGGERSEP Group*

The Brain does not care how the Heart stops!



D (Neurology) – How to Cool?

Resuscitation 124 (2018) 14–20

Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

Clinical paper

Efficacy of different cooling technologies for therapeutic temperature management: A prospective intervention study☆

Petra ...
Jon C. ...

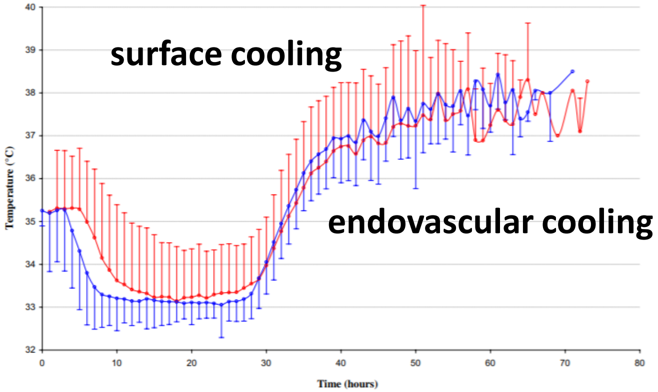


Figure 2. Temperature distribution during the targeted temperature management (TTM) phase (eg, within the first 3 days after cardiac arrest). Data are expressed as mean±SD. The times to reach the 34°C and 33°C target temperatures were significantly shorter in the endovascular group (blue line) than in the external group (red line). The stability of temperature values was significantly better in the endovascular group during the maintenance phase of the TTM.

Resuscitation Science

Endovascular Versus External Targeted Temperature Management for Patients With Out-of-Hospital Cardiac Arrest

A Randomized, Controlled Study

Nicolas Deye, MD; Alain Cariou, MD, PhD; Patrick Girardie, MD; Nicolas Pichon, MD; Bruno Megarbane, MD, PhD; Philippe Midez, MD; Jean-Marie Tonnelier, MD; Thierry Boulain, MD; Hervé Outin, MD; Arnaud Delahaye, MD; Aurélie Cravoisy, MD;

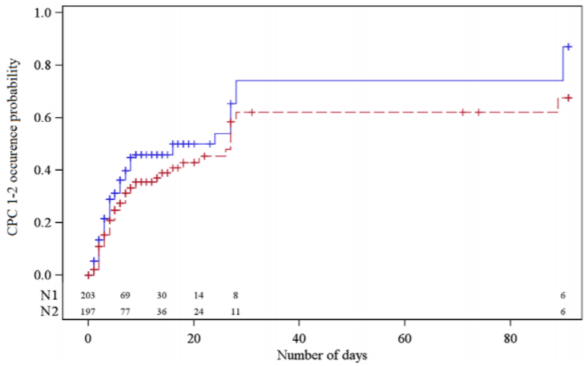


Figure 3. Cumulative incidence of favorable outcome (eg, occurrence of Cerebral Performance Categories [CPC] 1 and 2) within 90 days after cardiac arrest. CPC 1 and 2 denote a favorable neurological outcome (eg, survival without major neurological sequelae). The dotted red line depicts the external group; and the blue line, the endovascular group. The number of patients at risk corresponds to N1 in the external group and to N2 in the endovascular group. Log-rank test, P=0.052.

D (Neurology) – How Long to Cool?

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Targeted Temperature Management for 48 vs 24 Hours and Neurologic Outcome After Out-of-Hospital Cardiac A
A Randomized Clinical Trial

Hans Kirkegaard, MD, PhD, DMSci, DEAA, DLS; Eldar Søreide, MD, PhD,
Urmet Arus, MD; Christian Storm, MD, PhD; Christian Hassager, MD, D
Susanne Ilkjær, MD, PhD; Anni Nørgaard Jeppesen, MD; Anders Morte
Alf Inge Larsen, MD, PhD, FESC; Valdo Toome, MD; Marjaana Tiainen,
Timo Laitio, MD, PhD; Markus B. Skrifvars, MD, PhD, EDIC, FCICM

Cool for <u>at least</u> 24 hours, for patients with longer "no flow"/"low flow" time or raised ICP, consider longer duration

Figure 2. Core Temperature of the Intervention

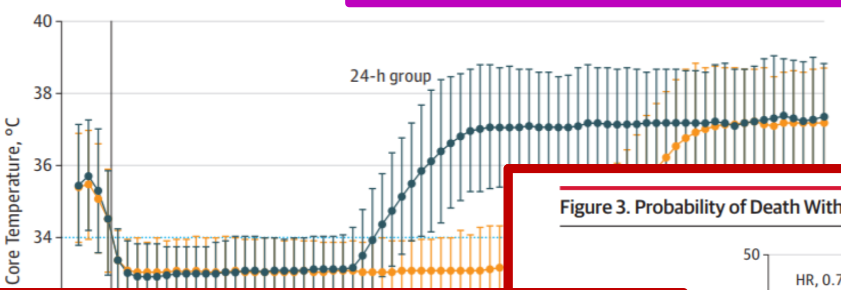
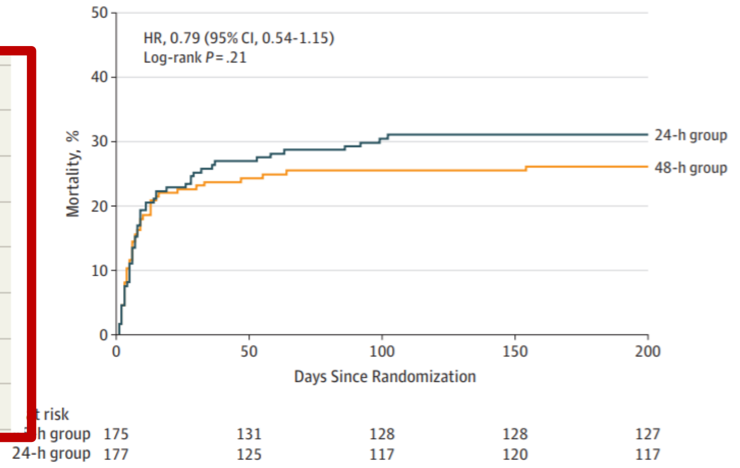


Figure 3. Probability of Death With Standard and Prolonged Targeted Temperature Management.



Resuscitation factors		
Bystander-initiated CPR	147 (84)	144 (82)
Shockable rhythm	160 (91)	152 (86)
AED used	38 (22)	43 (24)
Time to basic life support, median (IQR), min[a]	1 (0-2)	1 (0-2)
Time to advanced life support, median (IQR), min[c]	[illegible] (5-11)	[illegible] (5-11)
Time to return of spontaneous circulation, median (IQR)[d]	20 (15-30)	21 (16-[illegible])
Mechanical chest compression used	43 (25)	47 (27)

D (Neurology) – How to Rewarm?

Resuscitation 84 (2013) 1245–1249
Contents lists available at ScienceDirect
Resuscitation
journal homepage: www.elsevier.com/locate/resuscitation
ELSEVIER

Clinical paper

Assessment of risk factors for post-rewarming "rebound hyperthermia" in cardiac arrest patients undergoing therapeu

S.A. Winters[a,*], K.H. Wolf[b], S.A. Kettinger[a], E.K. Seif[a], J.S
[a] Michigan State University College of Human Medicine, Grand Rapids, MI, United States

Table 3
Compilation of results from modified Rankin scale classification.

Modified Rankin score					
	2	3	4	5	6
6.06%)	10 (10.1%)	8 (8.08%)	19 (19.2%)	10 (10.1%)	40 (40.4%)
4.76%)	2 (4.76%)	1 (2.38%)	5 (11.9%)	4 (9.52%)	27 (64.3%)

Resuscitation 84 (2013) 1734–1740
Contents lists available at ScienceDirect
Resuscitation
journal homepage: www.elsevier.com/locate/resuscitation
ELSEVIER

Clinical paper

Post-hypothermia fever is associated with increased mortality after out-of-hospital cardiac arrest☆

John Bro-Jeppesen[a,*], Christian Hassager[a], Michael Wanscher[b], Helle Søholm[a], Jakob H. Thomsen[a], Freddy K. Lippert[c], Jacob E. Møller[a], Lars Køber[a], Jesper Kjaergaard[a]
[a] Department of Cardiology, The Heart Centre, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark
[b] Department of Cardiothoracic Anaesthesia, The Heart Centre, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark
[c] Emergency Medical Services, The Capital Region of Denmark, Copenhagen, Denmark

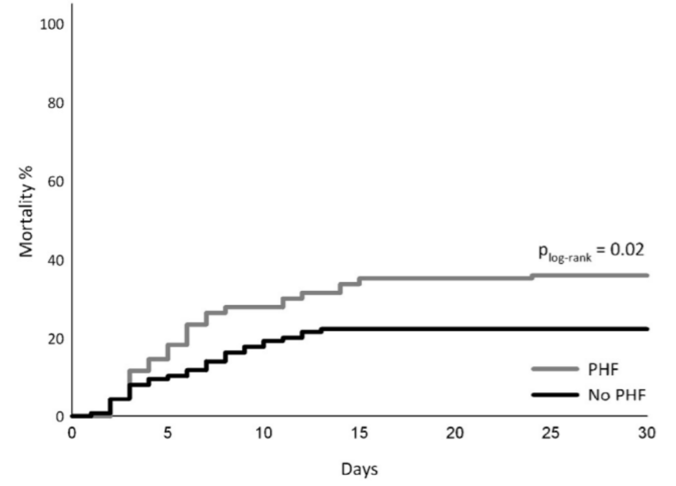


Fig. 2. Kaplan–Meier 30-days mortality plot. The curves represent mortality rates according to development of PHF (≥38.5 °C), log-rank 0.02. OHCA, PHF, Post-hypothermia fever.

SRFAC

E (Electrolytes) & F (Fluids)

- Avoid hyponatremia which may worsen cerebal edema
- Suggest lower potassium (3 to 3.5 mmol/L) while on induced hypothermia to prevent rebound hyperkalaemia during re-warming
- Check ABG and electrolytes 6 hourly while on hypothermia therapy

- Avoid hypotonic solutions
- Consider **PlasmaLyte A** or **Lactated Ringer's**

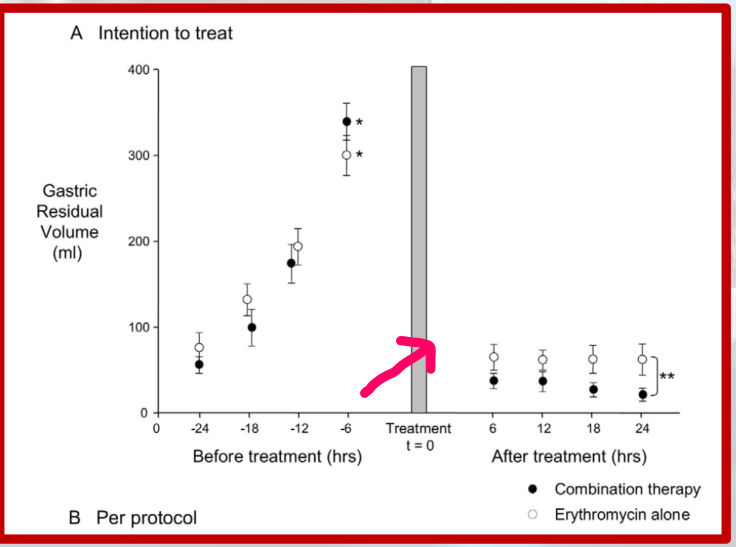
SRFAC

G (Gastrointestinal & Glucose)

- Early enteral feeding to reduce infectious complications
- Beware of gastroparesis and prolonged intestinal transit time during hypothermia
- High gastric residual volume → **Metoclopramide** and **Erythromycin**

Prokinetic therapy for feed intolerance in critical illness: One drug or two?

Nam Q. Nguyen, MBBS (Hons), FRACP; Marianne Chapman, BMBS, FANZCA, FJFICM; Robert J. Fraser, MBBS, FRACP, PhD; Laura K. Bryant, BHSc; Carly Burgstad, BHSc (Hons); Richard H. Holloway, MBBS, FRACP, MD



- Suggest ECG for QT prolongation while on both hypothermia and Erythromycin

SRFAC

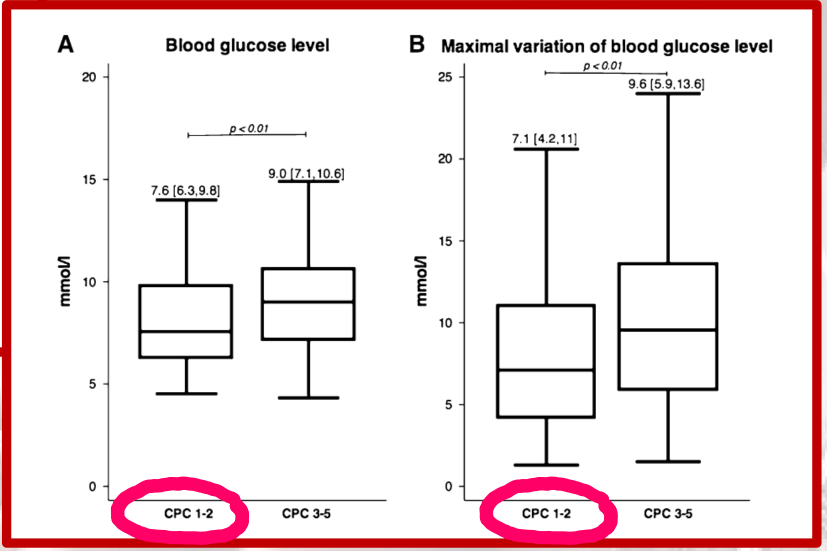
G (Gastrointestinal & Glucose)

Intensive Care Med
DOI 10.1007/s00134-014-3269-9

ORIGINAL

Fabrice Daviaud
Florence Dumas
Nadège Demars
Guillaume Geri
Adrien Bouglé
Tristan Morichau-Beauchant
Yên-Lan Nguyen
Wulfran Bougouin
Frédéric Pène
Julien Charpentier
Alain Cariou

Blood glucose level and outcome after cardiac arrest: insights from a large registry in the hypothermia era



- Both low and high blood glucose worsen neurological outcomes
- Hypothermia associated with higher blood glucose and increases glucose variability → increases mortality and worsens neurological outcomes for survivors
- **Target blood glucose 6 to 10 mmol/L**

→ Consider IV Insulin

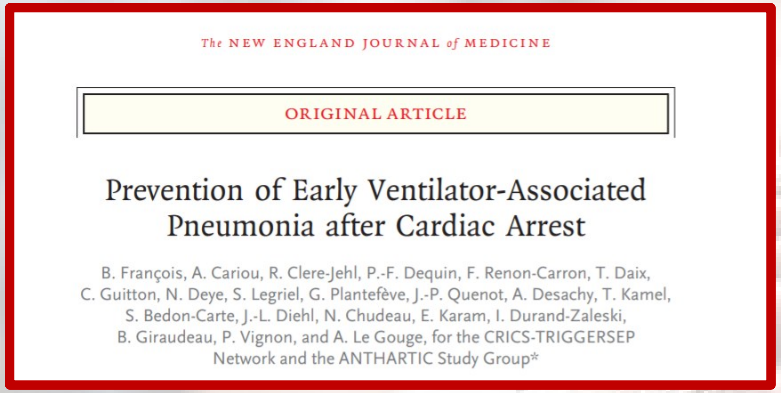
SRFAC

H (Haematology)

- Hypothermia causes **mild coagulopathy** but no clinically significant bleeding
- Use **pneumatic calf compressors**, instead of Enoxaparin, for DVT prophylaxis

I (Infectious Diseases)

- Immune paresis with hypothermia → higher incidence of respiratory tract infections
- No current recommendation for prophylactic antibiotics



The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Prevention of Early Ventilator-Associated Pneumonia after Cardiac Arrest

B. François, A. Cariou, R. Clere-Jehl, P.-F. Dequin, F. Renon-Carron, T. Daix, C. Guitton, N. Deye, S. Legriel, G. Plantefève, J.-P. Quenot, A. Desachy, T. Kamel, S. Bedon-Carte, J.-L. Diehl, N. Chudeau, E. Karam, I. Durand-Zaleski, B. Giraudeau, P. Vignon, and A. Le Gouge, for the CRICS-TRIGGERSEP Network and the ANTHARTIC Study Group*

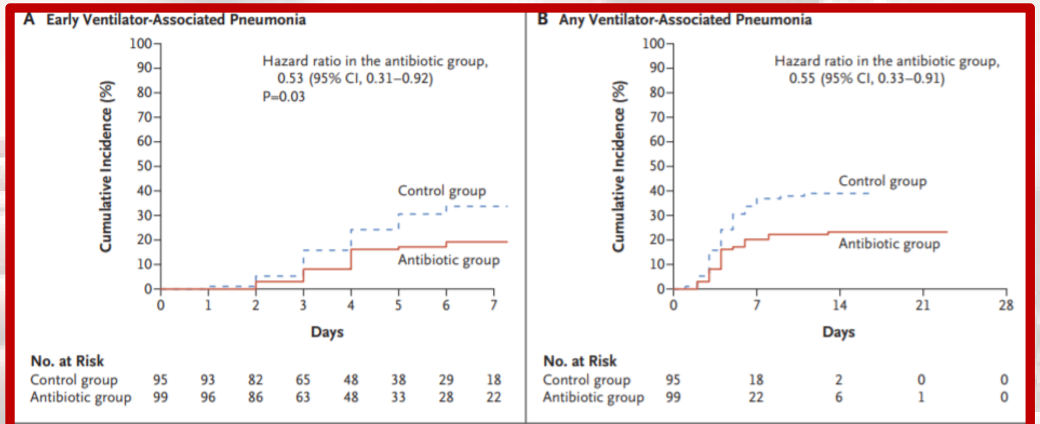


Figure 2. Cumulative Incidence of Ventilator-Associated Pneumonia.

…ulative incidence curves of early ventilator-associated pneumonia (during the first 7 days of hospitalization) (Panel A) and any ven…r-associated pneumonia (Panel B) were compared with the use of the Fine–Gray approach between patients assigned to receive …xicillin–clavulanate (1 g and 200 mg, respectively) three times a day for 2 days (antibiotic group) and those assigned to receive pla… (control group).

- Check Procalcitonin

SRFAC

Neuroprognostication

"Are You Sure She Will Not Recover?" Multimodal Prognostication Provides Increased Certainty About Poor Outcomes Prediction*

- **Delayed multi-modal strategy**
  - Clinical examination
  - Somatosensory evoked potentials
  - Electroencephalogram
  - Cerebral imaging (CT/MRI)
  - Biomarkers
- Clearance of sedative drugs and NMBAs reduced by up to 30% at a core body temperature of 34°C
- Neuroprognostication should be delayed to **72 hours after rewarming completed**

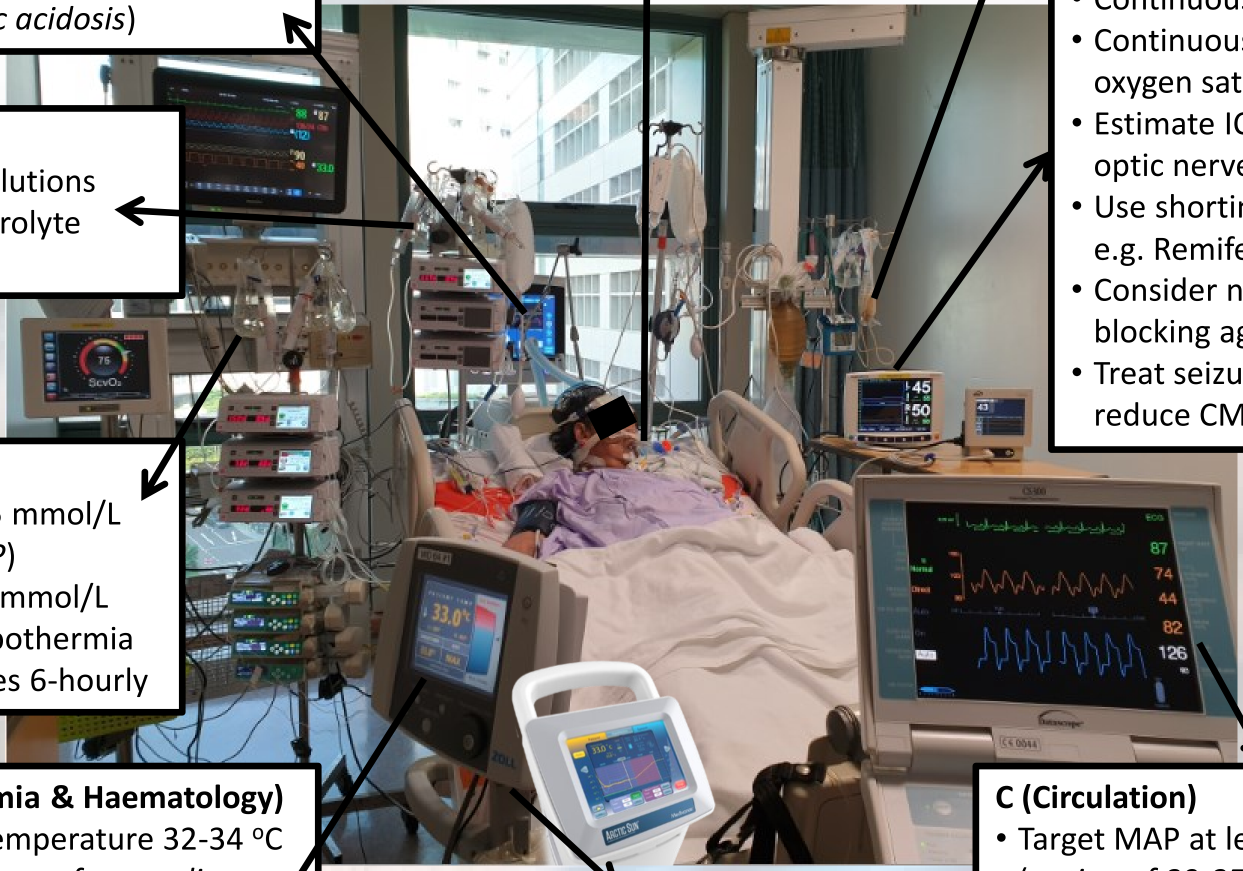
SRFAC

B (Breathing)
- Target SpO_2 94-98% (*with lowest FiO_2*)
- Avoid PEEP > 10 cmH_2O (*which may reduce cerebral venous drainage*)
- Target $PaCO_2$ 35-45 mmHg (*option of 50-55 mmHg if no raised ICP or severe metabolic acidosis*)

A (Airway)
- Use ETT with subglottic secretion drainage to reduce VAP (*increased incidence during induced hypothermia*)

G (Gastrointestinal & Glucose)
- Start trophic enteral feeding early
- Target blood glucose 6-10 mmol/L

F (Fluids)
- Avoid hypotonic solutions
- Use balanced electrolyte solutions



D (Disability) – Neurology
- Continuous EEG monitoring
- Continuous cerebral regional oxygen saturation monitoring
- Estimate ICP using ultrasound optic nerve sheath diameter
- Use shorting acting sedatives e.g. Remifentanil $\pm$ Propofol
- Consider neuromuscular blocking agent infusion
- Treat seizures aggressively to reduce $CMRO_2$

E (Electrolytes)
- Target Na^+ 140-145 mmol/L (*higher if raised ICP*)
- Tolerate K^+ 3.0-3.5 mmol/L during induced hypothermia
- Monitor electrolytes 6-hourly

H (Hypo/Hyperthermia & Haematology)
- Target core body temperature 32-34 ^oC (*use intravascular or surface cooling devices with continuous temperature feedback*)
- Use pneumatic calf compressors for DVT prophylaxis (*mild coagulopathy during induced hypothermia*)

I (Infectious Diseases)
- Use antimicrobial-impregnated central venous catheters
- Screen for infection if systemic vascular resistance persistently low

C (Circulation)
- Target MAP at least 65 mmHg (*option of 80-85 mmHg if chronic hypertension or raised ICP to optimise cerebral perfusion pressure, KIV Noradrenaline*)
- Monitor CO, $ScvO_2$ and $Pcv\text{-}aCO_2$ gap (*KIV Dobutamine or Milrinone*)

SRFAC

1. Care of PCAS patients requires a multi-organ approach to improve neurologically intact survival.

2. Quality of post-resuscitation care influences final outcomes.

3. Need to be systematic in the management of the post-cardiac arrest syndrome.

If a cardiac arrest patient is “fortunate” enough to be successfully resuscitated, he/she deserves the best chance for a good long-term outcome.

SRFAC

The End

Contact me

yew_woon_chia@ttsh.com.sg

SRFAC