Con il patrocinio di

REGIONE LIGURIA

IRC Italian Resuscitation Council

CONGRESSO NAZIONALE IRC 2017

13 · 14 OTTOBRE

DALL'EVIDENZA **AI TRATTAMENTI FUTURI**

CENTRO CONGRESSI MAGAZZINI DEL COTONE

PORTO ANTICO GENOVA

Dall'evidenza ai Trattamenti Futuri

Francesca Fumagalli, MSc

IRCCS- Istituto di Ricerche Farmacologiche Mario Negri

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

13 E 14 OTTOBRE
CENTRO CONGRESSI MAGAZZINI DEL COTONE
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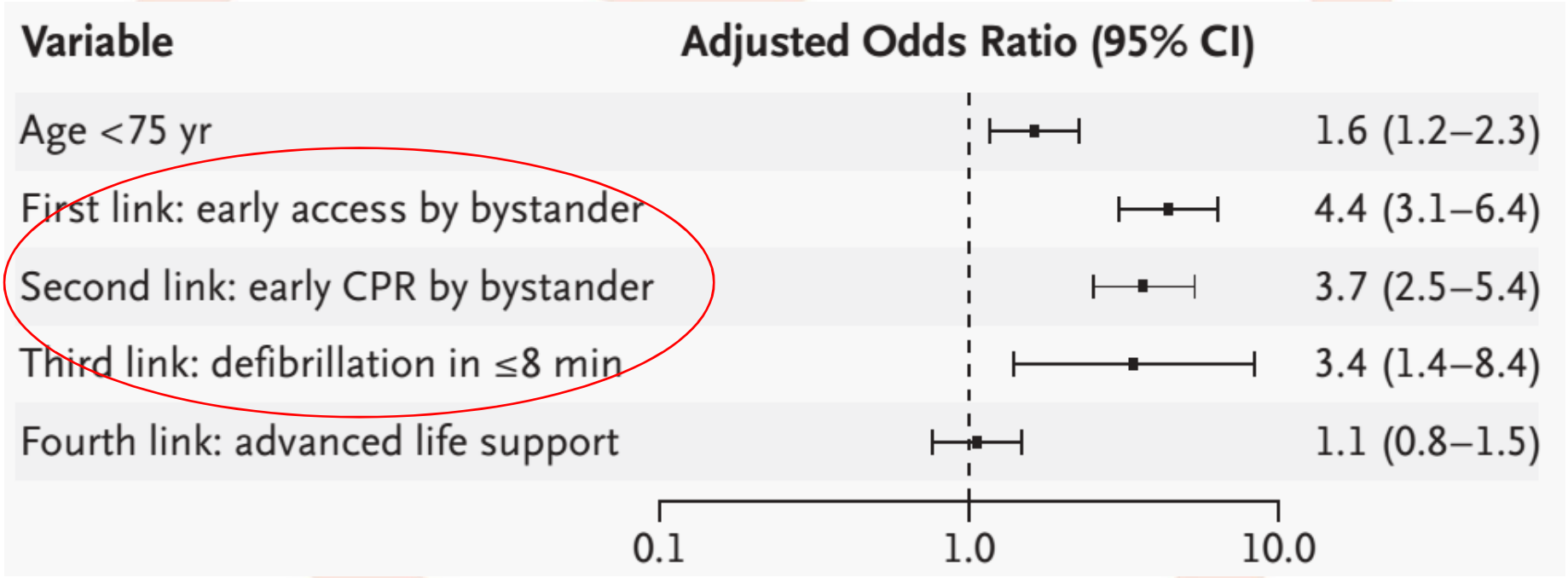
IRC Italian Resuscitation Council

Chain of survival

BLS- ALS

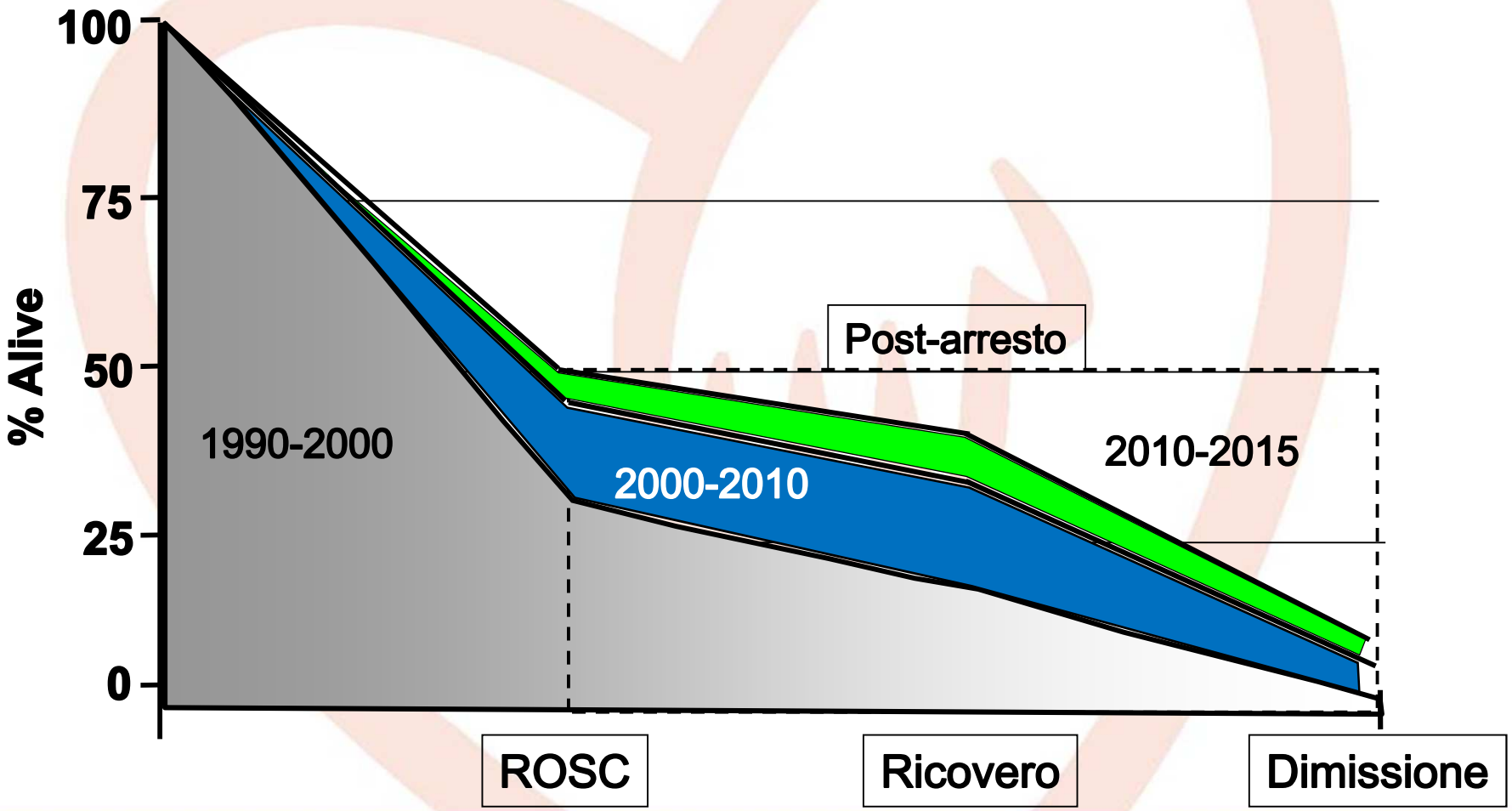
POST RESUSCITATION CARE

Catena della Sopravvivenza & Sopravvivenza



Stiell IG et al N Engl J Med 2004;351:647-56

Outcome dell'Arresto Caridaco



Linee- guida *post resuscitation care*

Intensive Care Med (2015) 41:2039–2056
DOI 10.1007/s00134-015-4051-3

CONFERENCE REPORTS AND EXPERT PANEL

Jerry P. Nolan
Jasmeet Soar
Alain Cariou
Tobias Cronberg
Véronique R. M. Moulaert
Charles D. Deakin
Bernd W. Bottiger
Hans Friberg
Kjetil Sunde
Claudio Sandroni

European Resuscitation Council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care

Definiscono lo standard di trattamento del paziente post arresto

EUROPEAN RESUSCITATION COUNCIL

ESICM EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Agenda:

- Progressi recenti nei trattamento dell’arresro cardiaco
- Progressi recenti nei trattamenti POST ROSC

1. Riconoscimento precoce dell'arresto cardiaco

Table 2. Fitted Logistic Regression Model for Survival and Favorable Functional Outcome

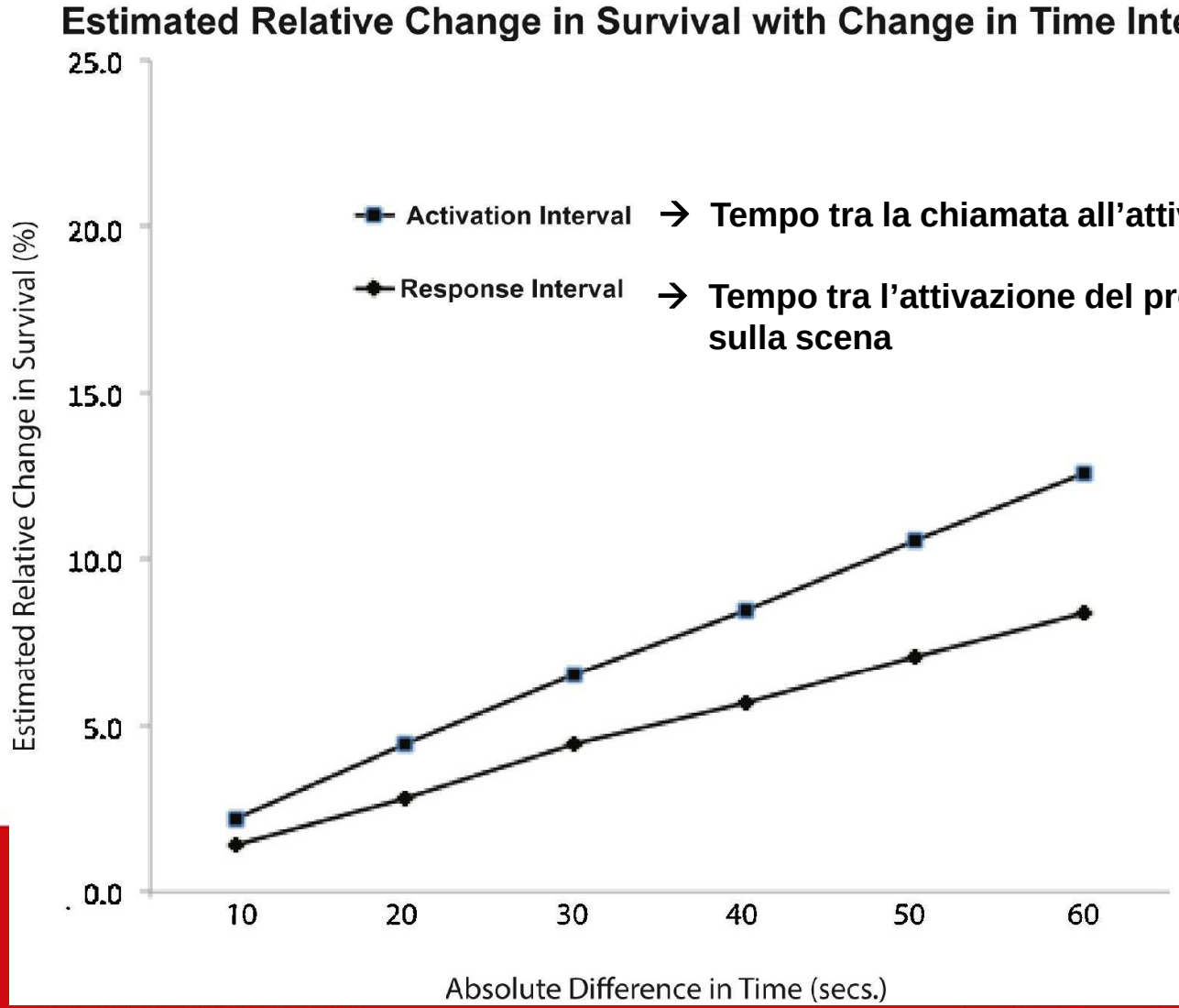
	Survival		Favorable Functional Outcome	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Phase				
P1	1 [Reference]	.02	1 [Reference]	.01
P2	1.47 (1.08-2.02)		1.68 (1.13-2.48)	
Sex				
Male	0.73 (0.54-0.99)	.046	0.71 (0.48-1.04)	.08
Female	1 [Reference]		1 [Reference]	
Age, 1-y increase	0.98 (0.97-0.99)	<.001	0.98 (0.97-0.99)	<.001
Bystander-witnessed arrest				
No	1 [Reference]	<.001	1 [Reference]	<.001
Yes	2.72 (2.02-3.66)		2.75 (1.91-3.96)	
Shockable initial rhythm				
No	1 [Reference]	<.001	1 [Reference]	<.001
Yes	5.94 (4.41-8.00)		8.37 (5.78-12.10)	
Location of arrest				
Residential	1 [Reference]	.07	1 [Reference]	.004
Public	1.41 (0.98-2.05)		1.86 (1.22-2.83)	
Patient transported to cardiac receiving center				
No	1 [Reference]	.007	1 [Reference]	<.001
Yes	1.53 (1.12-2.09)		2.23 (1.48-3.38)	

Abbreviations: OR, odds ratio; P1, phase 1; P2, phase 2.

Bobrow et al., JAMA Cardiol. 2016.

Ruolo dell'operatore di centrale nel guidare il riconoscimento del CA e l'esecuzione delle manovre di rianimazione

2. Rapida attivazione dei soccorsi



Activation Interval → **Tempo tra la chiamata all'attivazione del provider**

Response Interval → **Tempo tra l'attivazione del provider e l'arrivo sulla scena**

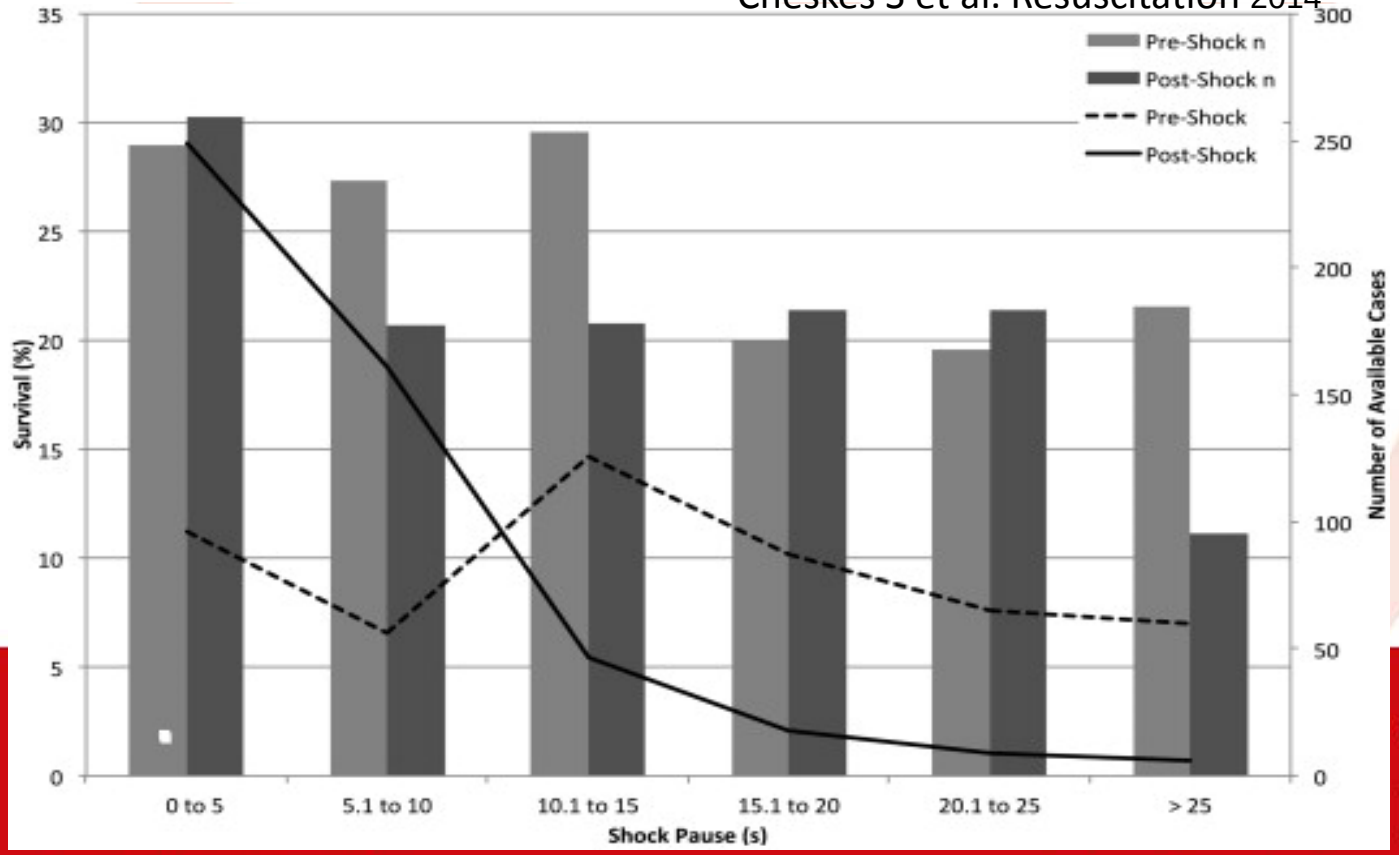
Nichol G., Resuscitation 2014

1. Bystander RCP di qualità- Reduce pre-shock pause

Clinical paper

The impact of peri-shock pause on survival from out-of-hospital shockable cardiac arrest during the Resuscitation Outcomes Consortium PRIMED trial☆

Cheskes S et al. Resuscitation 2014



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2. Bystander RCP di qualità- Optimal chest compression depth

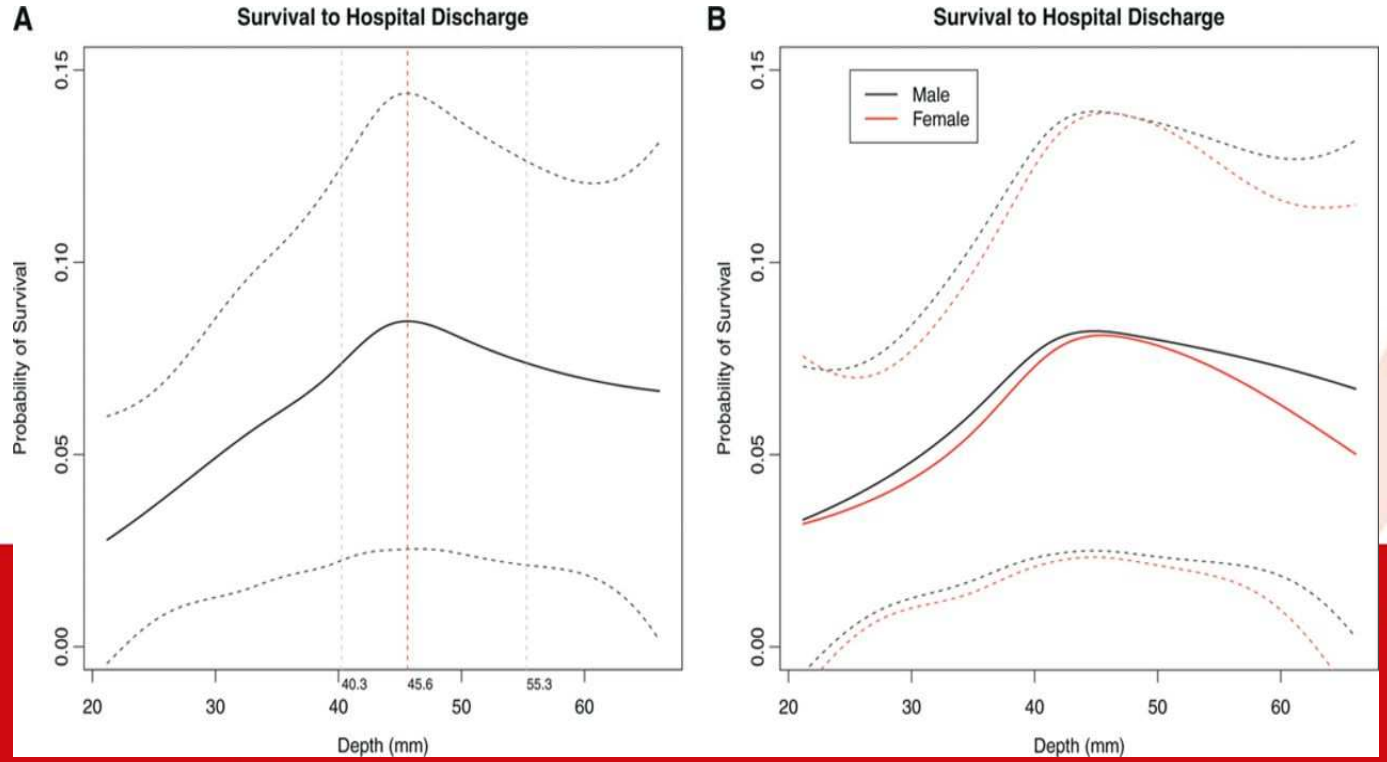
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

2014

American Heart Association.

What is the Optimal Chest Compression Depth During Out-of-Hospital Cardiac Arrest Resuscitation of Adult Patients?

Ian G. Stiell, Siobhan P. Brown, Graham Nichol, Sheldon Cheskes, Christian Vaillancourt, Clifton W. Callaway, Laurie J. Morrison, James Christenson, Tom P. Aufderheide, Daniel P. Davis, Cliff Free, Dave Hostler, John A. Stouffer and Ahamed H. Idris
and the Resuscitation Outcomes Consortium (ROC) Investigators



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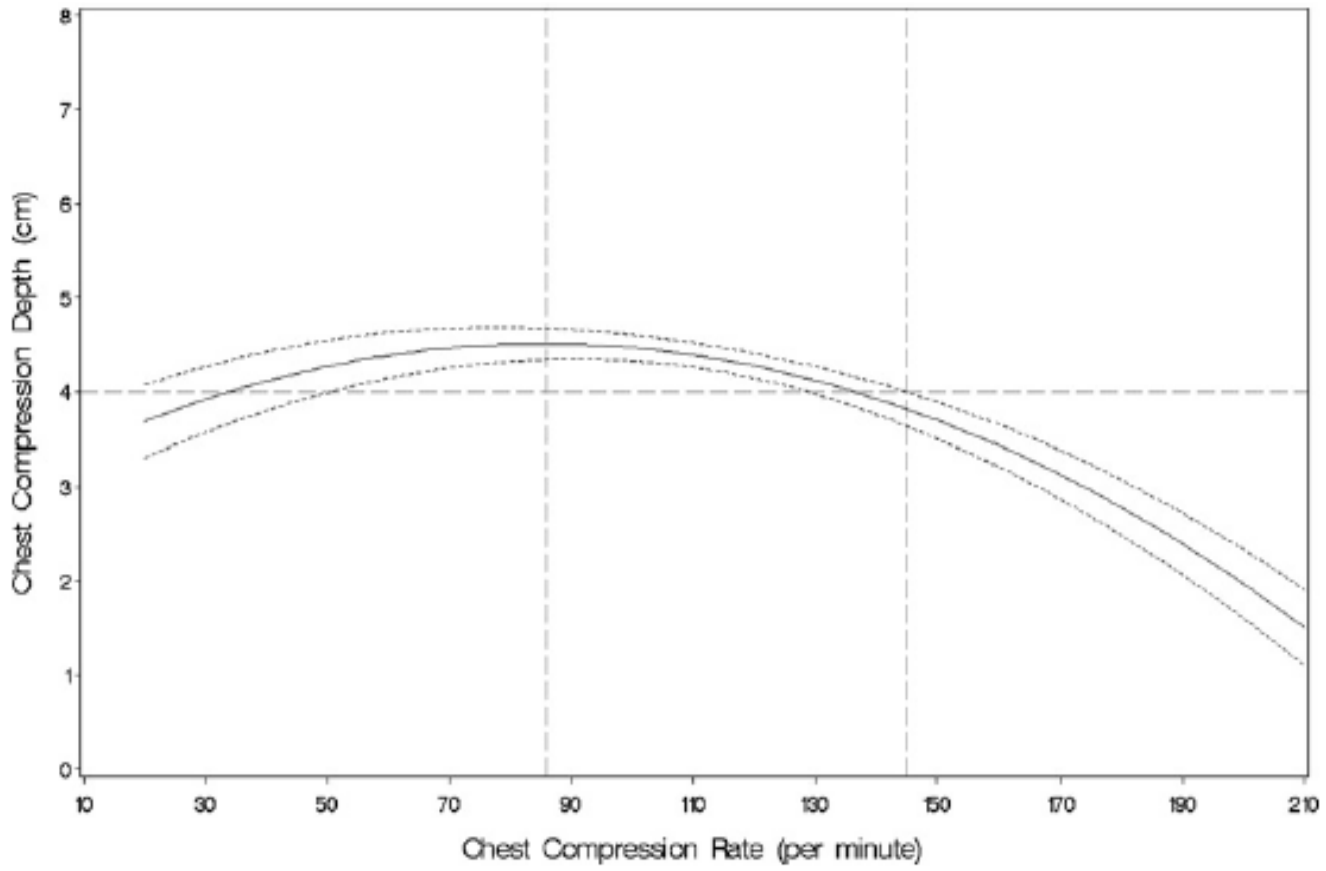
2. Bystander RCP di qualità- Optimal chest compression rate

Excessive chest compression rate is associated with insufficient compression depth in prehospital cardiac arrest☆

Koenraad G. Monsieurs[a,b,*], Melissa De Regge[c], Kristof Vansteelandt[d], Jeroen De Smet[e], Emmanuel Annaert[e], Sabine Lemoyne[e], Alain F. Kalmar[f], Paul A. Calle[b]



Resuscitation 2012

IRC Italian Resuscitation Council

3. Monitoraggio Emodinamico durante RCP

Hemodynamic Directed Cardiopulmonary Resuscitation Improves Short-Term Survival From Ventricular Fibrillation Cardiac Arrest*

Stuart H. Friess, MD[1]; Robert M. Sutton, MD, MSCE[2]; Utpal Bhalala, MD[3]; Matthew R. Maltese, PhD[2]; Maryam Y. Naim, MD[2]; George Bratinov, MD[2]; Theodore R. Weiland III, BS[2]; Mia Garuccio[2]; Vinay M. Nadkarni, MD, MS[2]; Lance B. Becker, MD[4]; Robert A. Berg, MD[2]

Resuscitation. 2014 August ; 85(8): 983–986. doi:10.1016/j.resuscitation.2014.04.015.

Hemodynamic–directed cardiopulmonary resuscitation during in–hospital cardiac arrest*

Robert M. Sutton[a], Stuart H. Friess[b], Matthew R. Maltese[a], Maryam Y. Naim[a], George Bratinov[a], Theodore R. Weiland[a], Mia Garuccio[a], Utpal Bhalala[c], Vinay M. Nadkarni[a], Lance B. Becker[d], and Robert A. Berg[a,*]

Resuscitation. 2014 September ; 85(9): 1298–1303. doi:10.1016/j.resuscitation.2014.05.040.

Hemodynamic Directed CPR Improves Cerebral Perfusion Pressure and Brain Tissue Oxygenation

Stuart H. Friess, MD[1], Robert M. Sutton, MD MSCE[2], Benjamin French, PhD[3], Utpal Bhalala, MD[4], Matthew R. Maltese, PhD[2], Maryam Y. Naim, MD[2], George Bratinov, MD[2], Silvana Arciniegas Rodriguez, MD[2], Theodore R. Weiland III, BS[2], Mia Garuccio[2], Vinay M. Nadkarni, MD MS[2], Lance B. Becker, MD[5], and Robert A. Berg, MD[2]

Resuscitation. 2013 May ; 84(5): 696–701. doi:10.1016/j.resuscitation.2012.10.023.

Hemodynamic Directed CPR Improves Short-term Survival from Asphyxia-Associated Cardiac Arrest

Robert M. Sutton, MD MSCE[1], Stuart H. Friess, MD[1], Utpal Bhalala, MD[1], Matthew R. Maltese, PhD[1], Maryam Y. Naim, MD[1], George Bratinov, MD[1], Dana Niles, MS[1], Vinay M. Nadkarni, MD MS[1], Lance B. Becker, MD[2], and Robert A. Berg, MD[1]

3. Monitoraggio Emodinamico durante RCP

- ***CPP > 20 mmHg***
- $EtCO_2$ > 20 mmHg
- Pressione arteriosa diastolica > 25 to 30 mmHg

Meaney PA et al. Circulation 2013

3. Monitoraggio Emodinamico durante RCP

Ottimizzazione della RCP sulla base della risposta di ciascun paziente (cause, comorbidità, differenze individuali)

3. Farmaci

Adrenalina

Summary of Research

The diagram below shows a summary of the research studies that have looked at the effect of adrenaline on survival to hospital discharge and risk of brain damage:

	Adrenaline made **no difference to survival** Jacobs et al, 2011	Adrenaline was associated with a **worse survival** rate Dumas et al, 2014	
Adrenaline was associated with a **better survival** rate in a subgroup with a non-shockable heart rhythm Nakahara et al, 2013	Adrenaline made **no difference to survival** or to the risk of severe brain damage Machida et al, 2012	Adrenaline was associated with a **worse survival** rate Herlitz et al, 1995	Adrenaline was associated with a **worse survival** rate and increased risk of **severe brain damage** Olasveengen et al, 2012
	Adrenaline made **no difference to survival** Woodhouse et al, 1995	Adrenaline was associated with a **worse survival** rate Holmberg et al, 2002	Adrenaline was associated with a **worse survival** rate and increased risk of **severe brain damage** Hagihara et al, 2012
	Adrenaline made **no difference to survival** Ong et al, 2007	Adrenaline made **no difference to survival**, but increased the risk of **severe brain damage** Hayashi et al, 2012	

As you can see above, only one study showed an increase in survival and therefore a benefit to patients. The rest of the studies show either no difference in the chance of survival or harm when adrenaline is used.

3. Farmaci

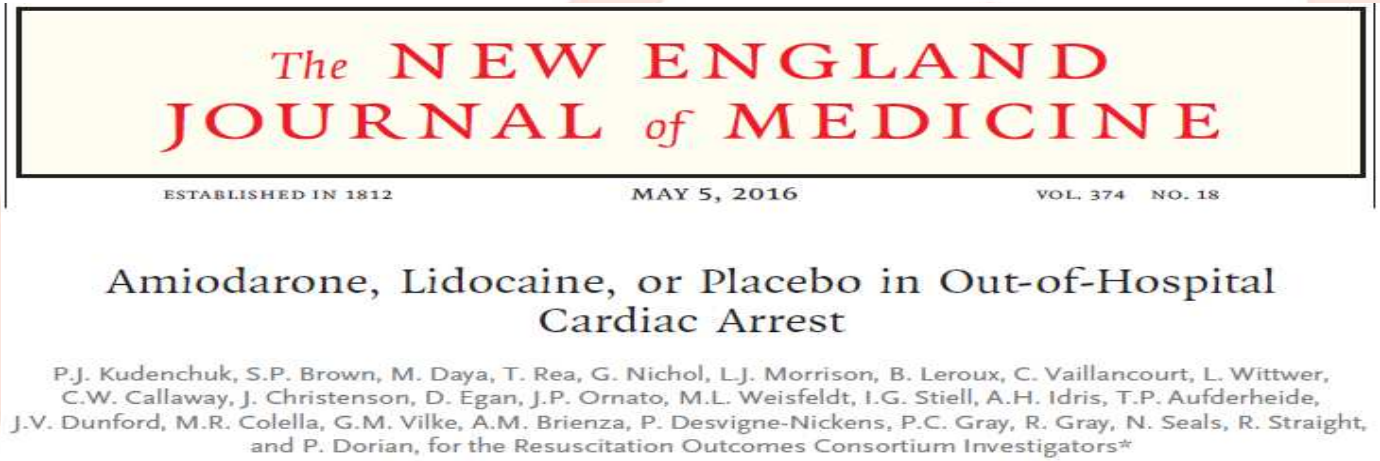
Adrenalina

PARAMEDIC2
The Adrenaline Trial

Prehospital **A**ssessment of the **R**ole of **A**drenaline: **M**easuring the **E**ffectiveness of **D**rug administration **I**n **C**ardiac arrest

- Randomised, placebo-controlled trial
- Primary endpoint : 30-day survival
- Sample size: 8000 patients
- Conclusion: end 2018

3. Farmaci
Farmaci antiaritmici



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 5, 2016 VOL. 374 NO. 18

Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest

P.J. Kudenchuk, S.P. Brown, M. Daya, T. Rea, G. Nichol, L.J. Morrison, B. Leroux, C. Vaillancourt, L. Wittwer, C.W. Callaway, J. Christenson, D. Egan, J.P. Ornato, M.L. Weisfeldt, I.G. Stiell, A.H. Idris, T.P. Aufderheide, J.V. Dunford, M.R. Colella, G.M. Vilke, A.M. Brienza, P. Desvigne-Nickens, P.C. Gray, R. Gray, N. Seals, R. Straight, and P. Dorian, for the Resuscitation Outcomes Consortium Investigators*

3026 patients randomized, double-blind trial, we compared parenteral amiodarone (n=974), lidocaine (n=993), and saline placebo (n=1059)

3. Farmaci
Farmaci antiaritmici

Table 3. Outcomes According to Trial Group in the Per-Protocol Population.*

Outcome	Amiodarone (N=974)	Lidocaine (N=993)	Placebo (N=1059)
Primary outcome: survival to discharge — no./total no. (%)†	237/970 (24.4)	233/985 (23.7)	222/1056 (21.0)
Secondary outcome: modified Rankin score ≤3 — no./total no. (%)‡	182/967 (18.8)	172/984 (17.5)	175/1055 (16.6)
Mechanistic (exploratory) outcomes			
Return of spontaneous circulation at ED arrival — no./total no. (%)	350/974 (35.9)	396/992 (39.9)	366/1059 (34.6)
Admitted to hospital — no. (%)	445 (45.7)	467 (47.0)	420 (39.7)

Gli effetti dei farmaci dipendono anche dal momento in cui vengono somministrati

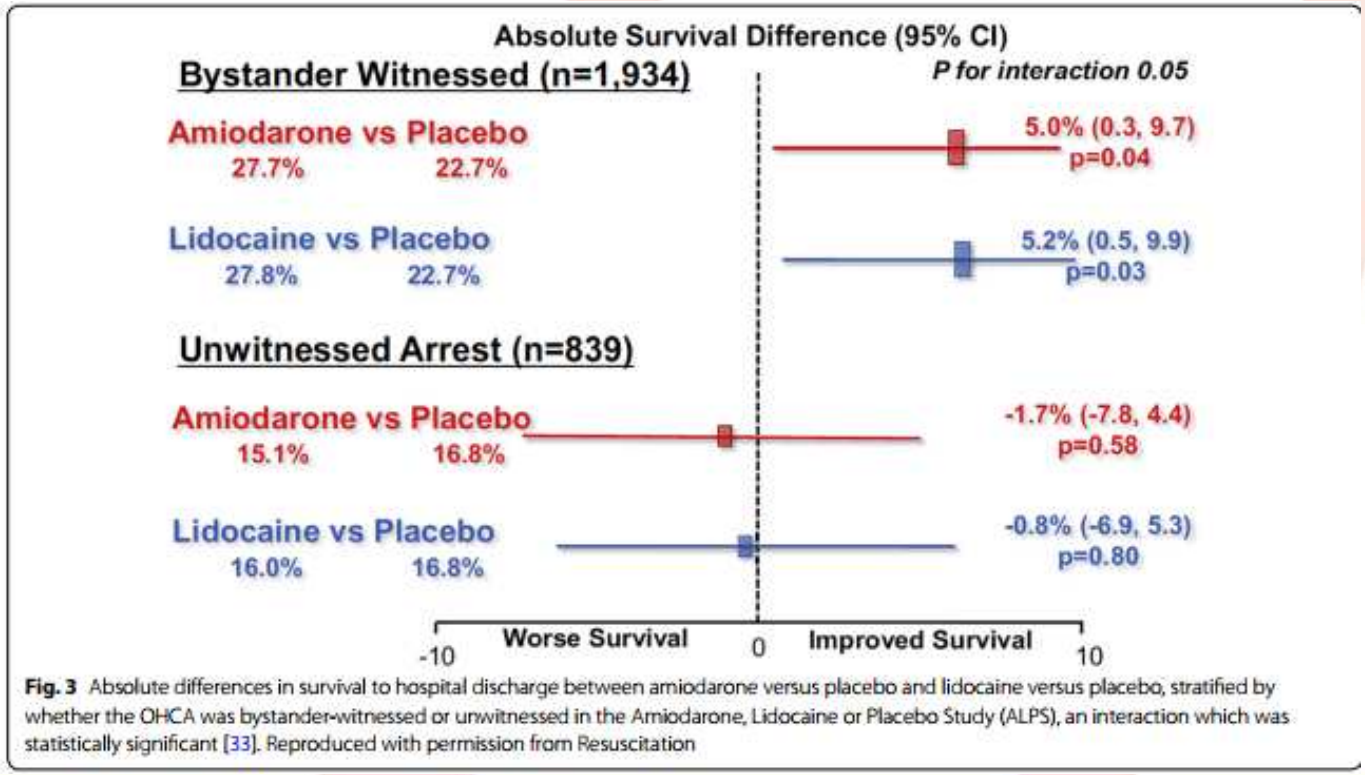


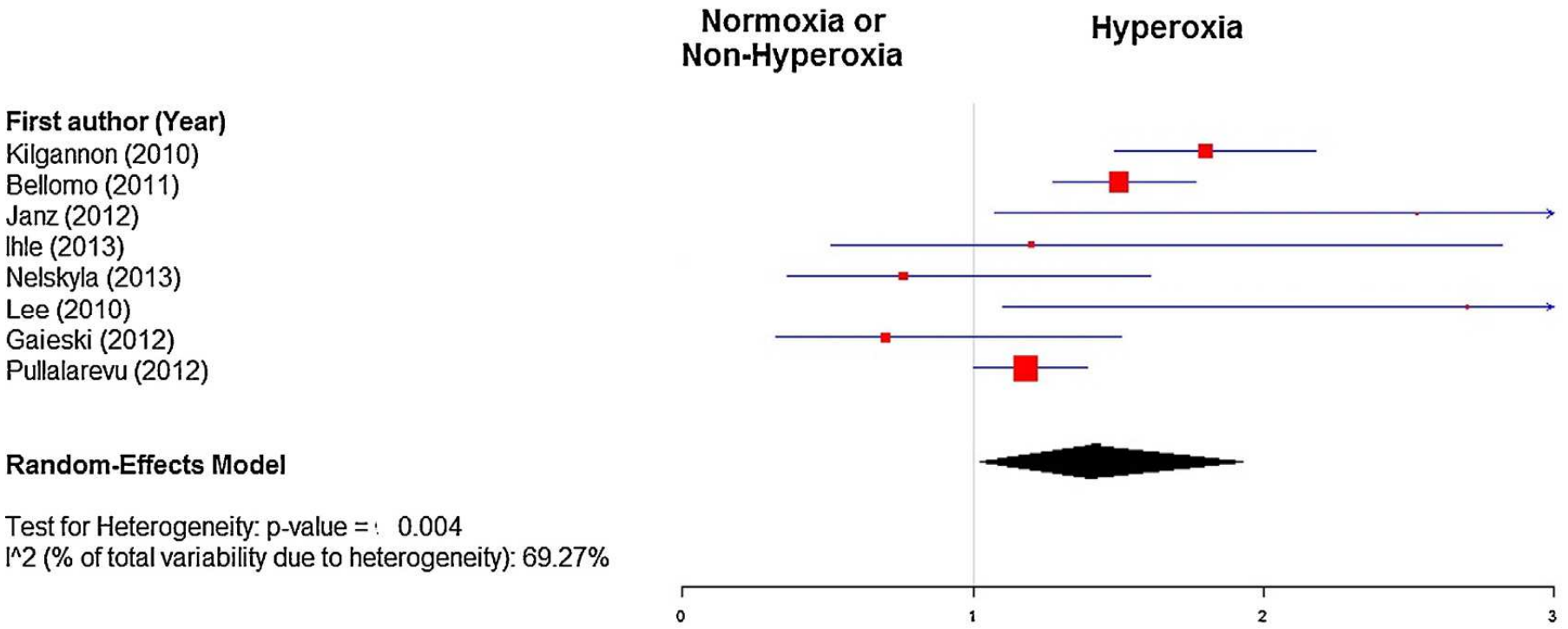
Fig. 3 Absolute differences in survival to hospital discharge between amiodarone versus placebo and lidocaine versus placebo, stratified by whether the OHCA was bystander-witnessed or unwitnessed in the Amiodarone, Lidocaine or Placebo Study (ALPS), an interaction which was statistically significant [33]. Reproduced with permission from Resuscitation

Chain of survival

BLS- ALS

POST RESUSCITATION CARE

Oxygenation after cardiac arrest: meta-analysis of human studies



Wang CH et al. Resuscitation 2014;85:1142-8

O_2

Post Resuscitation Care
- to restore quality of life

- Kuisma M, Resuscitation 2006 → ossigenzione accettabile nei pazienti ventilati con 30% O2 vs 100% O2 immediatamente dopo ROSC.

- Young P, Resuscitation 2014 → studio interrotto per valori troppo bassi di ossigeno nel sangue nei pazienti con normossia.

Studio di Fase 3: target SpO2 di 90-94% immediatamente dopo ROSC

START RECRUITING

Arterial Blood Gas Tensions After Resuscitation From Out-of-Hospital Cardiac Arrest: Associations With Long-Term Neurologic Outcome*

Jukka Vaahersalo, MD[1]; Stepani Bendel, MD, PhD[2]; Matti Reinikainen, MD, PhD[3]; Jouni Kurola, MD, PhD[4]; Marjaana Tiainen, MD, PhD[5]; Rahul Raj, BM[1]; Ville Pettilä, MD, PhD[1]; Tero Varpula, MD, PhD[1]; Markus B. Skrifvars, MD, PhD, FCICM[1]; for the FINNRESUSCI Study Group

409 patients - CPC ≤ 2 at 12 months

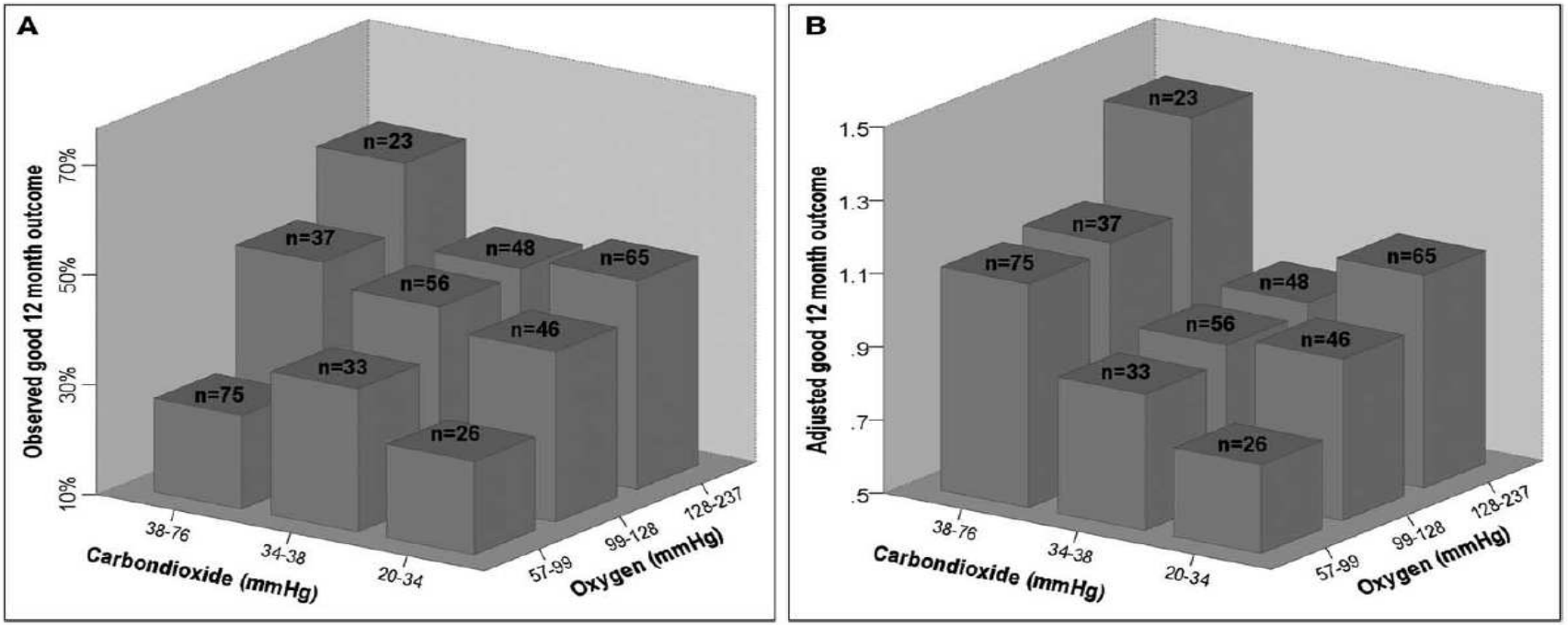


Figure 3. Mean values of Pao_2 and $Paco_2$ and observed (**A**) and adjusted (observed per predicted) (**B**) good neurologic outcome at 12 mo.

CO_2

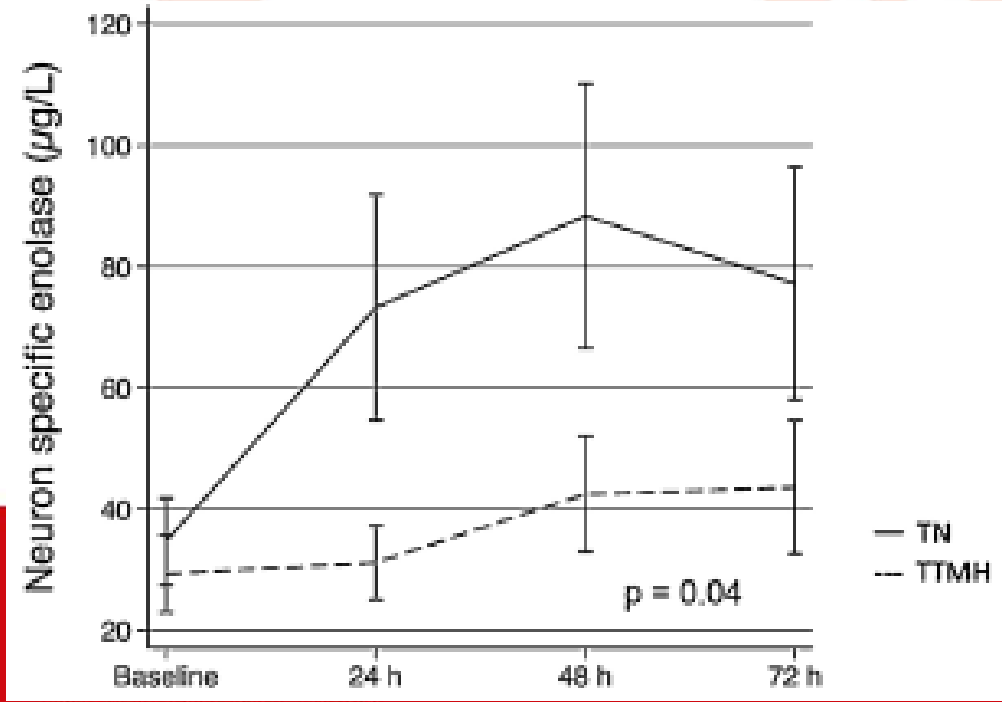
Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

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



CO_2

Evitare ipocapnia

- Si riduce metabolismo e produzione CO_2 a 33°C
- Ipocapnia = ipoperfusione cerebrale (con resistenze vascolari già aumentate dopo ROSC).

Studio di Fase 3: normocapnia vs ipercapnia (50-55 mmHg) dopo ricovero in ICU

START RECRUITING

Coronarografia precoce nei pazienti non STEMI

- Pazienti con ST-elevation post ROSC → Coronarografia precoce (occlusione della coronaria è generalmente la causa dell'arresto) → clinical benefit.
- Pazienti senza ST- elevation post ROSC → ?????

Coronarografia precoce nei pazienti non STEMI

Early coronary angiography after ROSC	Feasibility study—cardiac arrest survivors without ST-elevation randomised to acute coronary angiography versus routine care (DISCO study, NCT02309151)	Feasibility for multiple outcomes Recruiting
	Feasibility study—cardiac arrest survivors without ST-elevation randomised to acute coronary angiography versus standard care (PEARL study, NCT02387398)	Safety and feasibility Recruiting
	Cardiac arrest survivors without ST-elevation randomised to transfer to a cardiac arrest centre and urgent coronary catheterisation versus transfer to a district general hospital (ARREST trial, ISRCTN96585404)	All-cause mortality at 30 days Recruiting
	Emergency versus delayed coronary angiogram in survivors of OHCA with no obvious non-cardiac cause of arrest (EMERGE trial—NCT02876458)	Survival with no or minimal neurological sequel at 180 days Recruiting

Gestione della temperatura

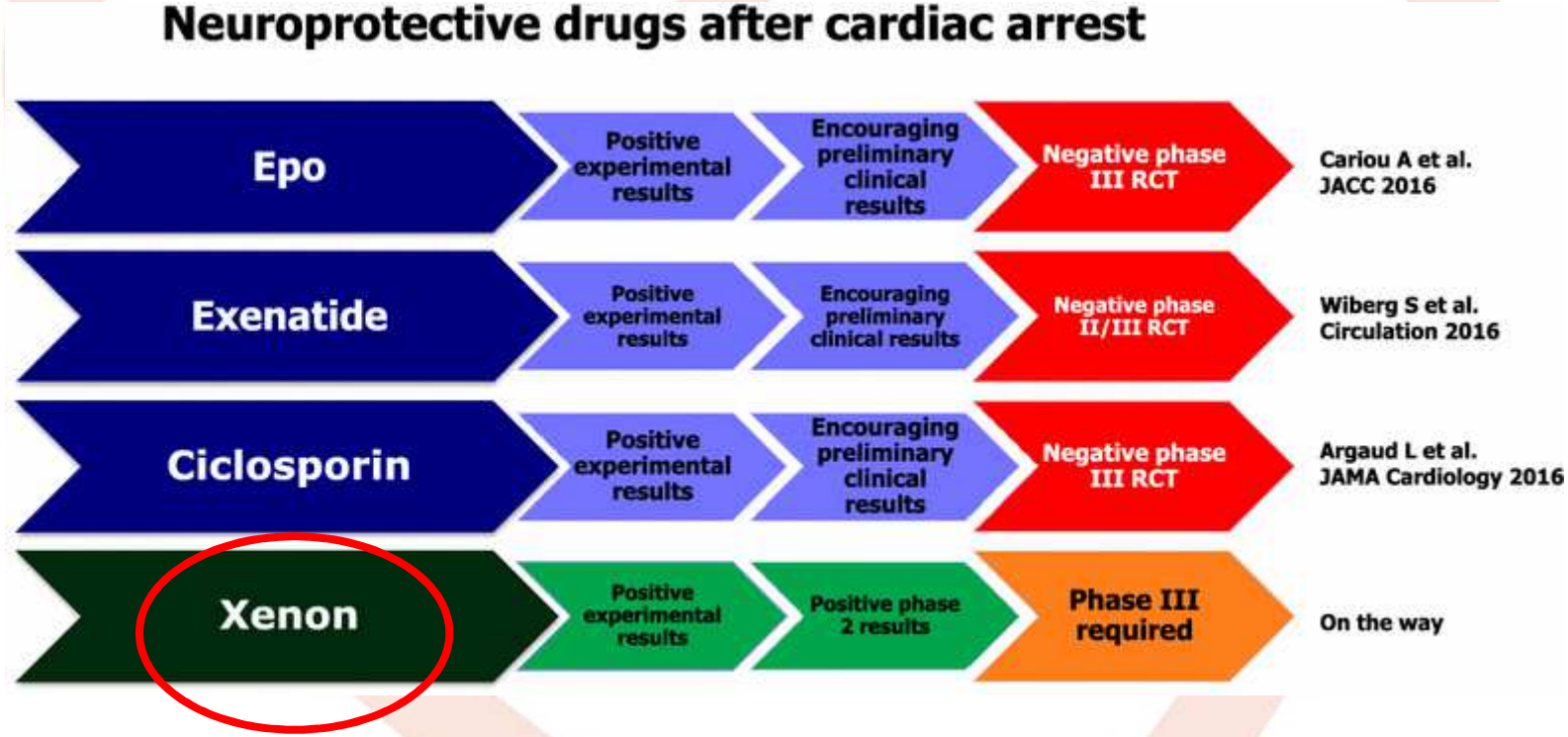
Targeted temperature management and pharmacological neuroprotection	Mild induced hypothermia (33 °C) versus fever control (≤37.8 °C) only (TTM-2, NCT02908308)	Mortality at 6 months Not yet recruiting
	Targeted temperature management after non-shockable cardiac arrest: 32.5–33.5 °C versus 36.5–37.5 °C (NSE-HYPERION study, NCT02722473)	NSE values day 1 to day 3 Recruiting

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 Arrest
A Randomized Clinical Trial

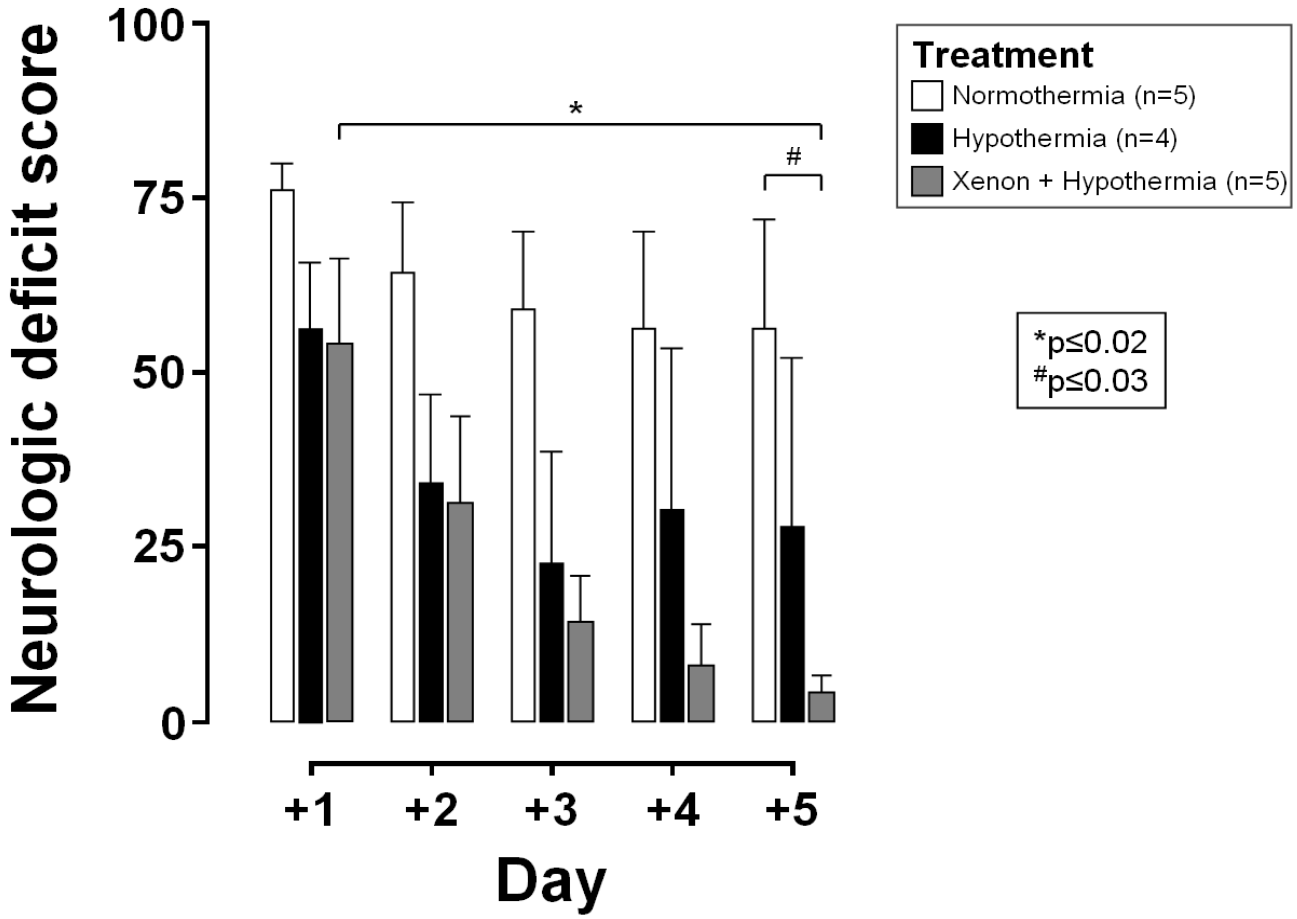
Hans Kirkegaard, MD, PhD, DMSci, DEAA, DLS; Eldar Søreide, MD, PhD, FERC; Inge de Haas, MD; Ville Pettilä, MD, PhD, EDIC; Fabio Silvio Taccone, MD, PhD; Urmet Arus, MD; Christian Storm, MD, PhD; Christian Hassager, MD, DMSc; Jørgen Feldbæk Nielsen, MD, DMSci; Christina Ankjær Sørensen, MD; Susanne Ilkjær, MD, PhD; Anni Nørgaard Jeppesen, MD; Anders Morten Grejs, MD, PhD; Christophe Henri Valdemar Duez, MD; Jakob Hjort, MPH; Alf Inge Larsen, MD, PhD, FESC; Valdo Toome, MD; Marjaana Tiainen, MD, PhD; Johanna Hästbacka, MD, PhD; Timo Laitio, MD, PhD; Markus B. Skrifvars, MD, PhD, EDIC, FCICM

Nuovi farmaci neuroprotettivi



Neurologic Critical Care

Combining xenon and mild therapeutic hypothermia preserves neurological function after prolonged cardiac arrest in pigs*



Fries 2012 Crit Care Med

Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Inhaled Xenon on Cerebral White Matter Damage in Comatose Survivors of Out-of-Hospital Cardiac Arrest
A Randomized Clinical Trial

Inhaled xenon combined with hypothermia (33°C) for 24 hours (n = 55 in the xenon group) or hypothermia treatment alone (n = 55 in the control group).

Table 2. Results of Diffusion Tensor Magnetic Resonance Imaging in the Complete Case Population

	Unadjusted Mean (SD)		Mean Difference (95% CI)		*P* Value	
Global Values	Xenon Group (n = 48)	Control Group (n = 49)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Fractional anisotropy	0.433 (0.028)	0.419 (0.033)	0.014 (0.002 to 0.026)	0.016 (0.005 to 0.027)	.03	.006
Type of diffusivity, 10^{-3} mm^2/s						
Axial	1.190 (0.052)	1.199 (0.051)	−0.009 (−0.030 to 0.012)	−0.011 (−0.031 to 0.010)	.40	.30
Radial	0.598 (0.051)	0.619 (0.062)	−0.021 (−0.043 to 0.002)	−0.024 (−0.046 to −0.003)	.08	.03
Mean	0.795 (0.050)	0.812 (0.056)	−0.017 (−0.038 to 0.005)	−0.020 (−0.040 to 0.0007)	.13	.06

[a] Data are adjusted for age, sex, and site.

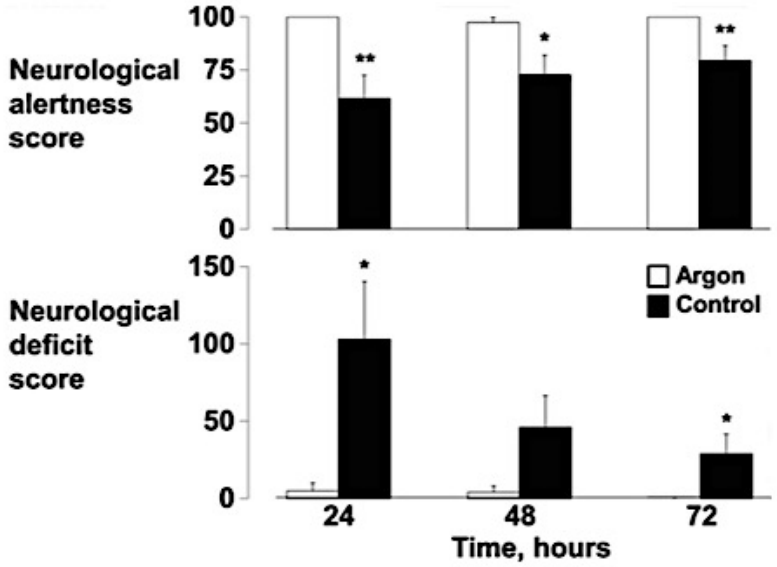
POSTRESUSCITATION TREATMENT WITH ARGON IMPROVES EARLY NEUROLOGICAL RECOVERY IN A PORCINE MODEL OF CARDIAC ARREST

Giuseppe Ristagno,* Francesca Fumagalli,* Ilaria Russo,* Simona Tantillo,† Davide Danilo Zani,‡§ Valentina Locatelli,‡§ Marcella De Maglie,§‖ Deborah Novelli,* Lidia Staszewsky,* Tarcisio Vago,¶ Angelo Belloli,‡§ Mauro Di Giancamillo,‡§ Michael Fries,** Serge Masson,* Eugenio Scanziani,§‖ and Roberto Latini*

*IRCCS–Istituto di Ricerche Farmacologiche "Mario Negri," Milan; †Ospedale Maggiore, Bologna; ‡Polo Veterinario di Lodi, §University of Milan, ‖Fondazione Filarete, and ¶Endocrininology Laboratory, Luigi Sacco Hospital, Milan, Italy; and **Department of Anesthesia and Intensive Care, Aachen University, Germany

8 min of untreated cardiac arrest

4 h post-resuscitation treatment with 70% argon



Migliore recupero neurologico

- Argon does not produce anesthesia at atmospheric pressure
- It is the third most abundant element in the atmosphere with a fraction of 0.93% (>CO_2)
- 100-fold more cost-effective (≈ 9cent/L)
- It can be administered by inhalation by means of open-circuit systems (mask)

Coburn M, Crit Care Med 2012

CP*Ar* study

Cardio**P**ulmonary resuscitation with ***Ar***gon study

in cardiac arrest patients

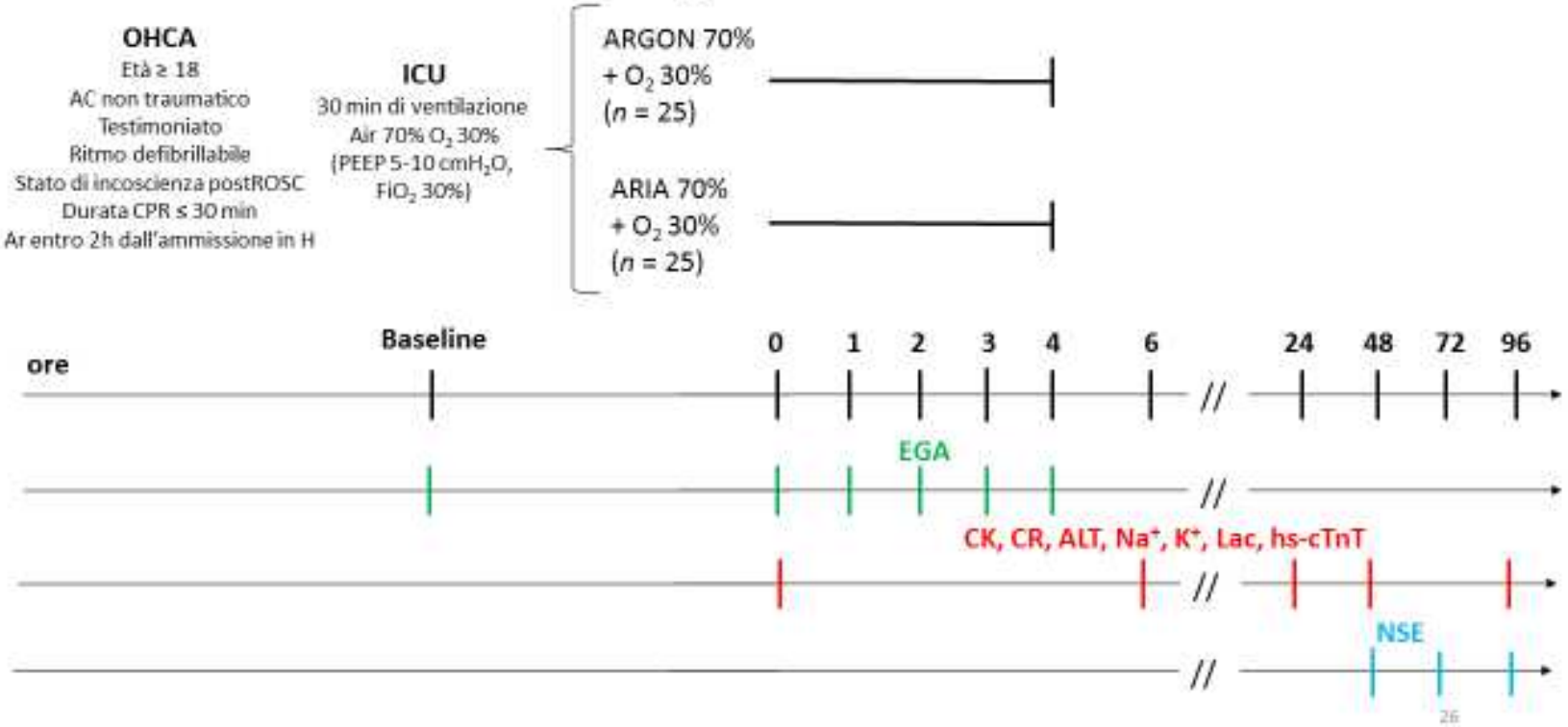
In attesa dell'approvazione da parte dei comitati etici

Scopo

Identificare eventuali effetti avversi della ventilazione con argon nei pazienti rianimati da arresto cardiaco extra-ospedaliero.

Protocollo

Disegno dello studio



Protocollo

Endpoints

Primario

- **Eventi avversi correlabili all'Argon**:
  - Impossibilità a ventilare con PEEP 5-10 cmH_2O, FiO_2 30%, SpO_2 > 95%
  - Ipotensione arteriosa non responsiva a trattamento
  - Aritmie maligne

Secondari

- **Effetti dell'Ar su:**
  - hs-cTnT, NSE
  - Sopravvivenza e CPC alla dimissione dalla TI e a 1 mese

Protocollo

Conclusioni

- Confermare che la ventilazione con Ar è sicura e possibile

- Ottenere dati sull'outcome necessari per uno studio di fase II

Grazie

13 E 14 OTTOBRE

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