Resüsitasyonda yeni ne var?

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Resuscitation

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Simulation and education

A 10-s rest improves chest compression quality during hands-only cardiopulmonary resuscitation: A prospective, randomized crossover study using a manikin model☆

Mun Ki Min[a], Seok Ran Yeom[b,*], Ji Ho Ryu[a], Yong In Kim[a], Maeng Real Park[a], Sang Kyoon Han[b], Seong Hwa Lee[b], Suck Ju Cho[b]

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ARTICLE INFO

Article history:
Received 5 October 2012
Received in revised form 30 January 2013
Accepted 31 January 2013

Keywords:
Hands-only CPR
Chest compression
Fatigue

ABSTRACT

Objectives: This study was designed to assess changes in cardiopulmonary resuscitation (CPR) quality and rescuer fatigue when rescuers are provided with a break during continuous chest compression CPR (CCC-CPR).

Methods: The present prospective, randomized crossover study involved 63 emergency medical technician trainees. The subjects performed three different CCC-CPR methods on a manikin model. The first method was general CCC-CPR without a break (CCC), the second included a 10-s break after 200 chest compressions (10/200), and the third included a 10-s break after 100 chest compressions (10/100). All methods were performed for 10 min. We counted the total number of compressions and those with appropriate depth every 1 min during the 10 min and measured mean compression depth from the start of chest compressions to 10 min.

Results: The 10/100 method showed the deepest compression depth, followed by the 10/200 and CCC methods. The mean compression depth showed a significant difference after 5 min had elapsed. The percentage of adequate compressions per min was calculated as the proportion of compressions with appropriate depth among total chest compressions. The percentage of adequate compressions declined over time for all methods. The 10/100 method showed the highest percentage of adequate compressions, followed by the 10/200 and CCC methods.

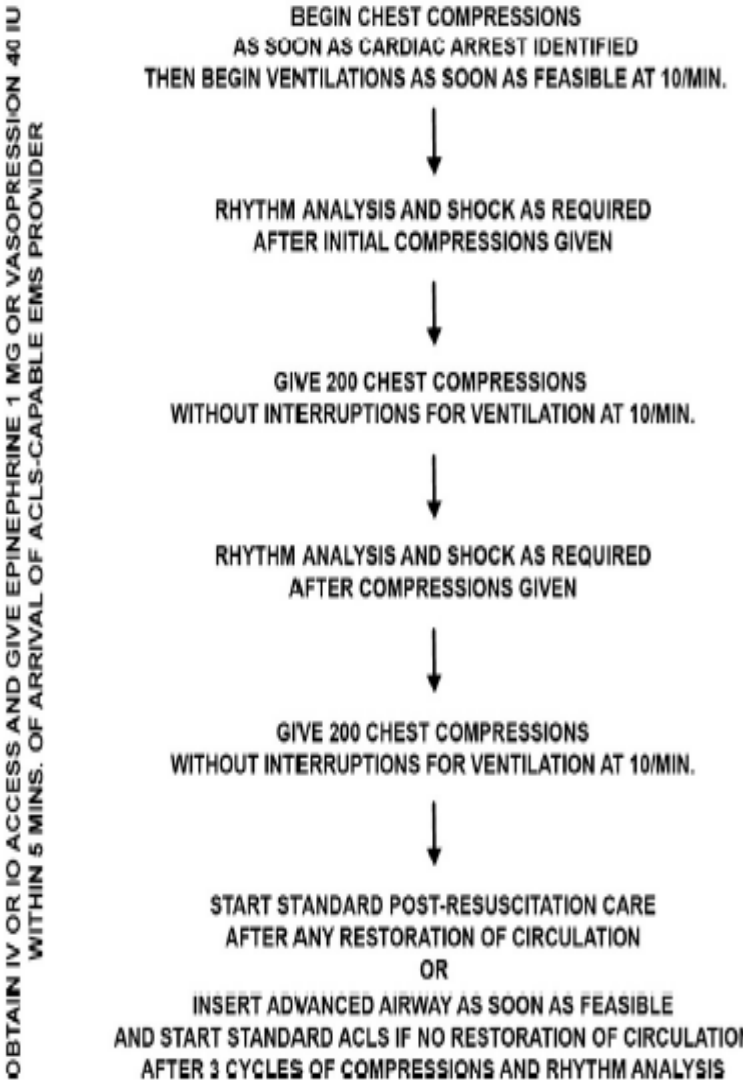
Conclusion: When rescuers were provided a rest at a particular time during CCC-CPR, chest compression quality increased compared with CCC without rest. Therefore, we propose that a rescuer should be provided a rest during CCC-CPR, and specifically, we recommend a 10-s rest after 100 chest compressions.

A randomized trial of continuous versus interrupted chest compressions in out-of-hospital cardiac arrest: Rationale for and design of the Resuscitation Outcomes Consortium Continuous Chest Compressions Trial

Siobhan P. Brown, PhD,[a] Henry Wang, MD,[b] Tom P. Aufderheide, MD, MSc,[c] Christian Vaillancourt, MD, MSc, FRCP (C),[d] Robert H. Schmicker, MSc,[a] Sheldon Cheskes, MD, CCFP (EM), FCFP,[e] Ron Straight, BGS, MEd,[f] Peter Kudenchuk, MD,[a] Laurie Morrison, MD, MSc, FRCP (C),[c] M. Riccardo Colella, DO, MPH,[c] Joseph Condle, MSc,[g] George Gamez, EMT-P,[h] David Hostler, PhD,[g] Tami Kayea, EMT-P,[h] Sally Ragsdale, ARNP,[a] Shannon Stephens, EMT-P,[b] and Graham Nichol, MD, MPH, FRCP (C)[a], The ROC Investigators *Seattle, WA; Birmingham, AL; Milwaukee, WI; Ottawa, ON, Toronto, ON, Vancouver, BC; Pittsburgh, PA; Dallas, TX*

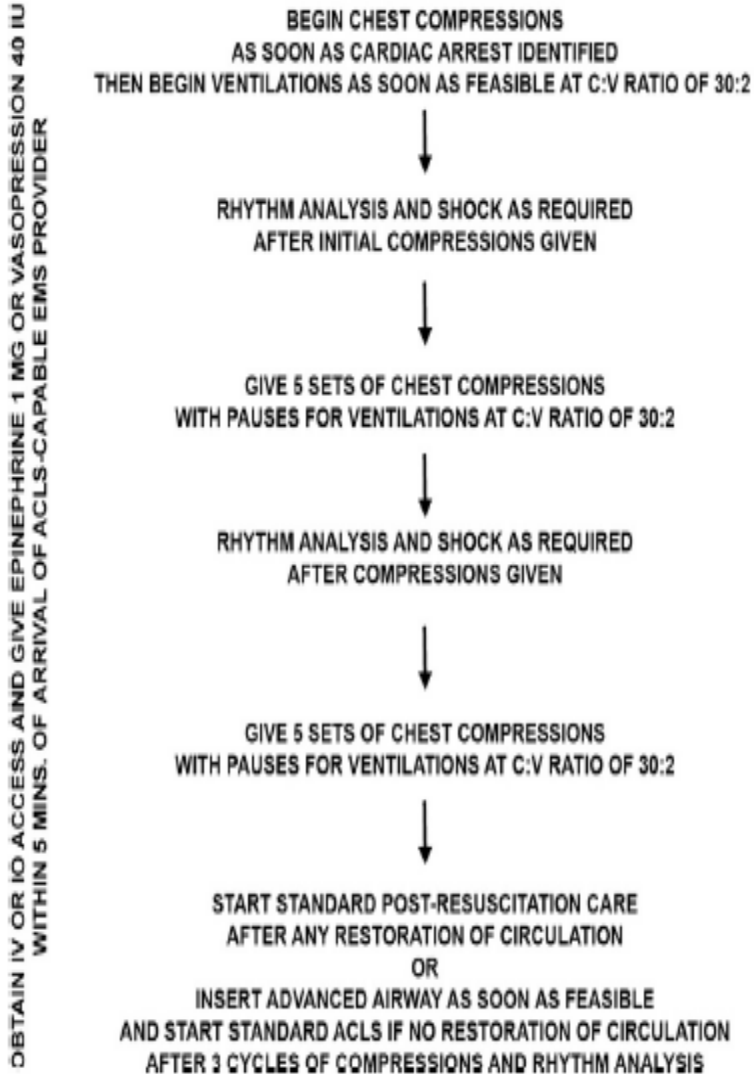
The Resuscitation Outcomes Consortium is conducting a randomized trial comparing survival with hospital discharge after continuous chest compressions without interruption for ventilation versus currently recommended American Heart Association cardiopulmonary resuscitation with interrupted chest compressions in adult patients with out-of-hospital cardiac arrest without obvious trauma or respiratory cause. Emergency medical services perform study cardiopulmonary resuscitation for 3 intervals of manual chest compressions (each ~2 minutes) or until restoration of spontaneous circulation. Patients randomized to the continuous chest compression intervention receive 200 chest compressions with positive pressure ventilations at a rate of 10/min without interruption in compressions. Those randomized to the interrupted chest compression study arm receive chest compressions interrupted for positive pressure ventilations at a compression:ventilation ratio of 30:2. In either group, each interval of compressions is followed by rhythm analysis and defibrillation as required. Insertion of an advanced airway is deferred for the first ≥6 minutes to reduce interruptions in either study arm. The study uses a cluster randomized design with every-6-month crossovers. The primary outcome is survival to hospital discharge. Secondary outcomes are neurologically intact survival and adverse events. A maximum of 23,600 patients (11,800 per group) enrolled during the post-run-in phase of the study will provide ≥90% power to detect a relative change of 16% in the rate of survival to discharge, 8.1% to 9.4% with overall significance level of 0.05. If this trial demonstrates improved survival with either strategy, >3,000 premature deaths from cardiac arrest would be averted annually. (Am Heart J 2015;169:334-341.e5.)

Figure 2



Treatment in intervention group.

Figure 3



Treatment in control group.

Conclusions

A large randomized trial is underway to compare survival with hospital discharge after CCCs versus currently recommended CPR with ICCs at a rate of 30 compressions to 2 ventilations in patients with OHCA. If this trial demonstrates a significant improvement in survival with either strategy, it is estimated that >3,000 premature deaths from cardiac arrest would be averted in the United States alone.

Optimal chest compression rate in cardiopulmonary resuscitation: a prospective, randomized crossover study using a manikin model

Seong Hwa Lee[a], Ji Ho Ryu[b], Mun Ki Min[b], Yong In Kim[b], Maeng Real Park[b], Seok Ran Yeom[a], Sang Kyoon Han[a] and Seong Wook Park[a]

Objectives When performing cardiopulmonary resuscitation (CPR), the 2010 American Heart Association guidelines recommend a chest compression rate of at least 100 min^{-1}, whereas the 2010 European Resuscitation Council guidelines recommend a rate of between 100 and 120 min^{-1}. The aim of this study was to examine the rate of chest compression that fulfilled various quality indicators, thereby determining the optimal rate of compression.

Methods Thirty-two trainee emergency medical technicians and six paramedics were enrolled in this study. All participants had been trained in basic life support. Each participant performed 2 min of continuous compressions on a skill reporter manikin, while listening to a metronome sound at rates of 100, 120, 140, and 160 beats/min, in a random order. Mean compression depth, incomplete chest recoil, and the proportion of correctly performed chest compressions during the 2 min were measured and recorded.

Results The rate of incomplete chest recoil was lower at compression rates of 100 and 120 min^{-1} compared with that at 160 min^{-1} ($P=0.001$). The numbers of compressions that fulfilled the criteria for high-quality CPR at a rate of 120 min^{-1} were significantly higher than those at 100 min^{-1} ($P=0.016$).

Conclusion The number of high-quality CPR compressions was the highest at a compression rate of 120 min^{-1}, and increased incomplete recoil occurred with increasing compression rate. However, further studies are needed to confirm the results. *European Journal of Emergency Medicine* 00:000–000

European Journal of Emergency Medicine 2015, 00:000–000

Keywords: basic life support, quality, rate of chest compression, resuscitation

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Received 13 July 2014 Accepted 12 January 2015

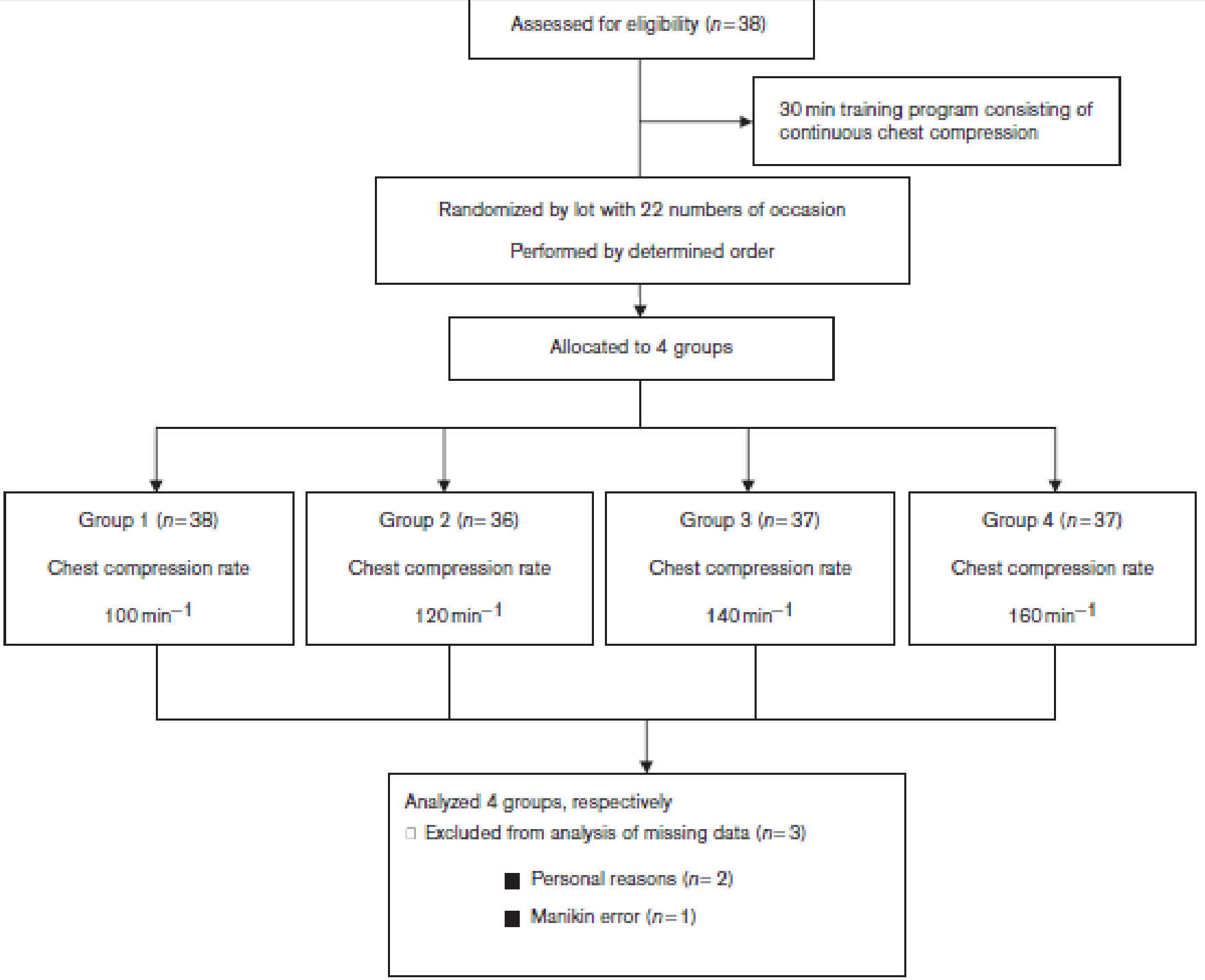
Assessed for eligibility (n=38)
30 min training program consisting of continuous chest compression
Randomized by lot with 22 numbers of occasion
Performed by determined order
Allocated to 4 groups
Group 1 (n=38)
Chest compression rate
100 min−1
Group 2 (n=36)
Chest compression rate
120 min−1
Group 3 (n=37)
Chest compression rate
140 min−1
Group 4 (n=37)
Chest compression rate
160 min−1
Analyzed 4 groups, respectively
Excluded from analysis of missing data (n=3)
Personal reasons (n=2)
Manikin error (n=1)

Table 2 Factors associated with quality of chest compression at rates from 100 to 160 min^{-1}

	100 min^{-1}	120 min^{-1}	140 min^{-1}	160 min^{-1}	*P* value
Total numbers of compression delivered for 2 min	199.0 (199.0–201.0)	240.0 (239.0–240.0)	279.0 (278.0–280.0)	318.0 (310.3–320.0)	0.000
Numbers of compression fulfilled the criteria of high-quality CPR	132.0[a] (50.5–199.0)	233.5[b] (98.5–239.0)	226.0[a,b] (48.5–277.5)	182.5[a,b] (52.0–312.0)	0.016
Numbers of incomplete chest recoil	0.0[a] (0.0–0.0)	0.0[a] (0.0–0.0)	0.0[a,b] (0.0–4.5)	1.0[b] (0.0–15.5)	0.001
Proper depth compressions/total compressions (%)	65.0 (26.4–99.5)	97.7 (40.4–99.6)	81.0 (17.3–99.7)	58.2 (16.3–99.4)	0.646
Mean depth for 2 min (mm)	51.5 (46.8–58.0)	55.0 (48.3–58.0)	53.0 (45.0–58.5)	51.0 (44.8–57.8)	0.760
The proportion of participants who fulfilled compression depth criteria [*n*/*N* (%)]	9/38 (23.7)	9/36 (25.0)	7/37 (18.9)	1/36 (2.8)	0.052

CPR, cardiopulmonary resuscitation.
[a,b]The same letters indicate nonsignificant differences between groups on the basis of Bonferroni correction.

Conclusion

We found that the number of high-quality CPR compressions was highest at a compression rate of 120 min^{-1} and increased incomplete recoil occurred with the increasing compression rate. However, additional clinical studies are needed to confirm these results.

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RESUS-6328; No. of Pages 6

ARTICLE IN PRESS

Resuscitation xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Resuscitation

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Clinical Paper

Mechanical chest compressions improved aspects of CPR in the LINC trial☆

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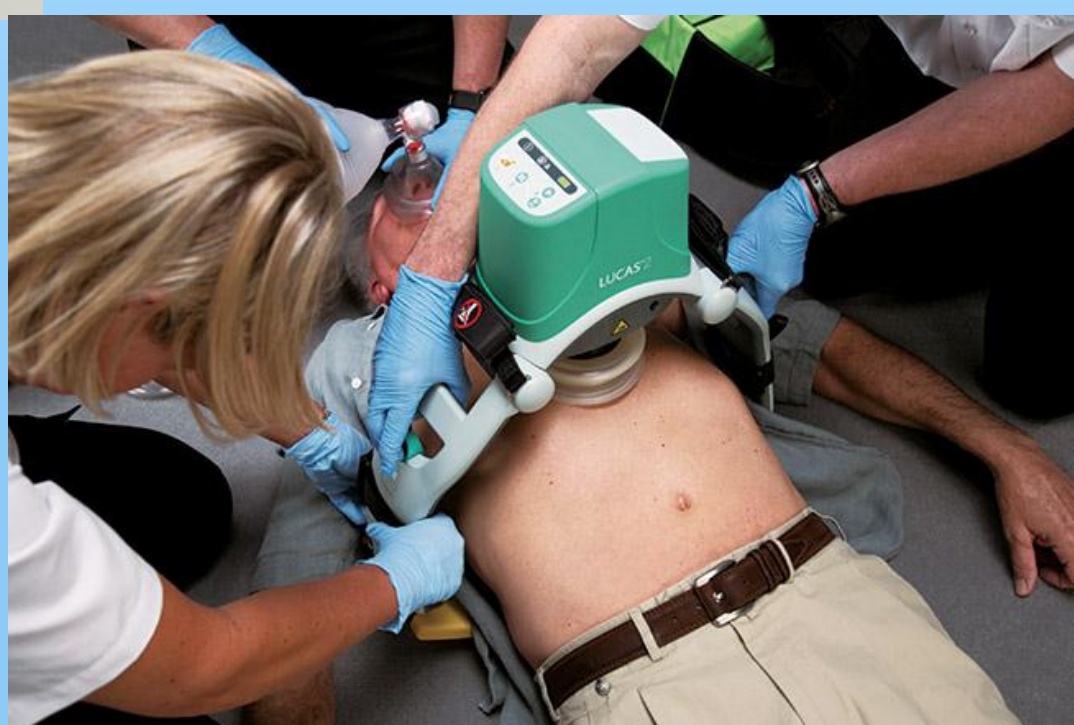

4. Discussion

In this study, we examined the CPR process in a subset of the patients randomized to mechanical and manual CPR protocols from the LINC trial. Our main finding was that patients in the mechanical CPR group had significantly higher chest compression fractions than patients in the manual CPR group. Furthermore, perishock pauses were eliminated in the majority of patients in the mechanical CPR group by delivering shocks during ongoing compressions.

The CCF achieved in each arm of this study was over 79%, comparable with the high end of values reported in literature.[16–18] This

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Journal of the Chinese Medical Association xx (2015) 1–4

www.jcma-online.com

Original Article

Effectiveness of mechanical chest compression for out-of-hospital cardiac arrest patients in an emergency department

Ching-Kuo Lin [a,b,c], Mei-Chin Huang [d], Yu-Tung Feng [e], Wei-Hsuan Jeng [a,b,c], Te-Cheng Chung [a,b,c], Yu-Wa Lau [a,b,c], Kuang-I. Cheng [f,g,*]

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Received August 30, 2014; accepted November 7, 2014

Abstract

Background: To increase the chance of restoring spontaneous circulation, cardiopulmonary resuscitation (CPR) with high-quality chest compressions is needed. We hypothesized that, in a municipal hospital emergency department, the outcome in nontraumatic out-of-hospital cardiac arrest patients treated with standard CPR followed by mechanical chest compression (MeCC) was not inferior to that followed by manual chest compression (MaCC). The purposes of the study were to test our hypothesis and investigate whether the use of MeCC decreased human power demands for CPR.

Methods: A total of 455 consecutive out-of-hospital cardiac arrest patients of presumed cardiac etiology were divided into two groups according to the chest compressions they received (MaCC or MeCC) in this retrospective review study. Human power demand for CPR was described according to the Basic Life Support/Advanced Cardiovascular Life Support guidelines and the device handbook. The primary endpoint was recovery of spontaneous circulation during resuscitation, and the secondary endpoints were survival to hospital admission and medical human power demands.

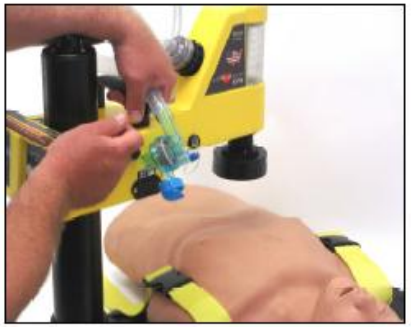
Results: In this study, recovery of spontaneous circulation was achieved in 33.3% of patients in the MeCC group and in 27.1% in the MaCC group ($p = 0.154$), and the percentages of patients who survived hospitalization were 22.2% and 17.6%, respectively ($p = 0.229$). A ratio of 2:4 for the human power demand for CPR between the groups was found. Independent predictors of survival to hospitalization were ventricular fibrillation/pulseless ventricular tachycardia as initial rhythm and recovery of spontaneous circulation.

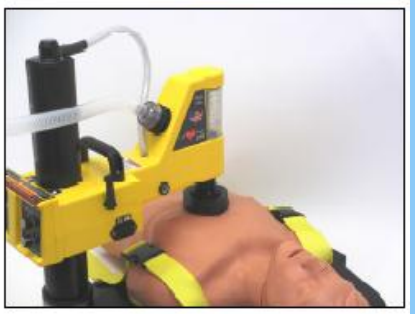
Conclusion: No difference was found in early survival between standard CPR performed with MeCC and that performed with MaCC. However, the use of the MeCC device appears to promote staff availability without waiving patient care in the human power-demanding emergency departments of Taiwan hospitals.

LIFE-STAT® CPR

Model 1008MII
Mechanical CPR System
Instructions for Use (IFU) Manual

(Part Number REF 16005)





Enhanced Perfusion During Advanced Life Support Improves Survival With Favorable Neurologic Function in a Porcine Model of Refractory Cardiac Arrest

Guillaume Debaty, MD[1,2]; Anja Metzger, PhD[3]; Jennifer Rees, PhD[1]; Scott McKnite, BS[3]; Laura Puertas, MD, PhD[3]; Demetris Yannopoulos, MD[1]; Keith Lurie, MD[3]

Objective: To improve the likelihood for survival with favorable neurologic function after cardiac arrest, we assessed a new advanced life support approach using active compression-decompression cardiopulmonary resuscitation plus an intrathoracic pressure regulator.

Design: Prospective animal investigation.

Setting: Animal laboratory.

Subjects: Female farm pigs ($n = 25$) (39 ± 3 kg).

Interventions: Protocol A: After 12 minutes of untreated ventricular fibrillation, 18 pigs were randomized to group A–3 minutes of basic life support with standard cardiopulmonary resuscitation, defibrillation, and if needed 2 minutes of advanced life support with standard cardiopulmonary resuscitation; group B–3 minutes of basic life support with standard cardiopulmonary resuscitation, defibrillation, and if needed 2 minutes of advanced life support with active compression-decompression plus intrathoracic pressure regulator; and group C–3 minutes of basic life support with active compression-decompression cardiopulmonary resuscitation plus an impedance threshold device, defibrillation, and if needed 2 minutes of advanced life support with active compression-decompression plus intrathoracic pressure regulator. Advanced life support always included IV epinephrine

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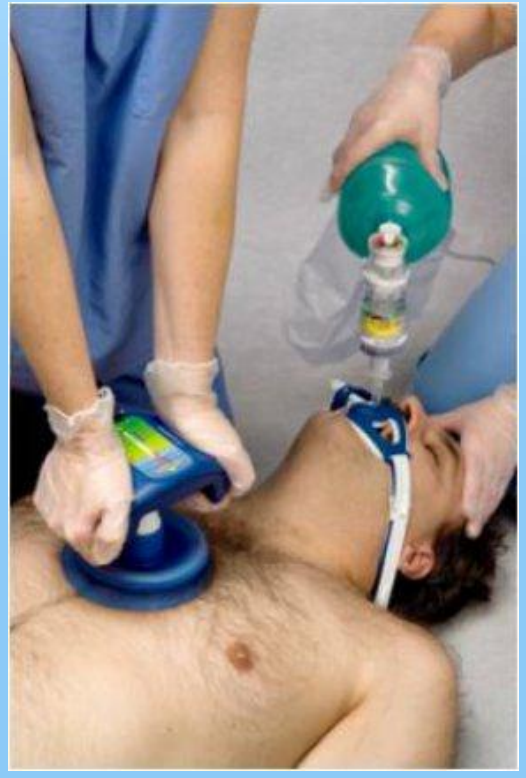
Supported, in part, by the National Institutes of Health (grant, 1R43HL110517).

Impedance threshold device (ITD)

- Concept. Lower intrathoracic pressure in the chest during the decompression phase of CPR enhances venous return to the thorax.
- Design. Each time the chest wall recoils following a compression, the ITD transiently blocks air/oxygen from entering the lungs, creating a small vacuum in the chest, resulting in improved pre-load.



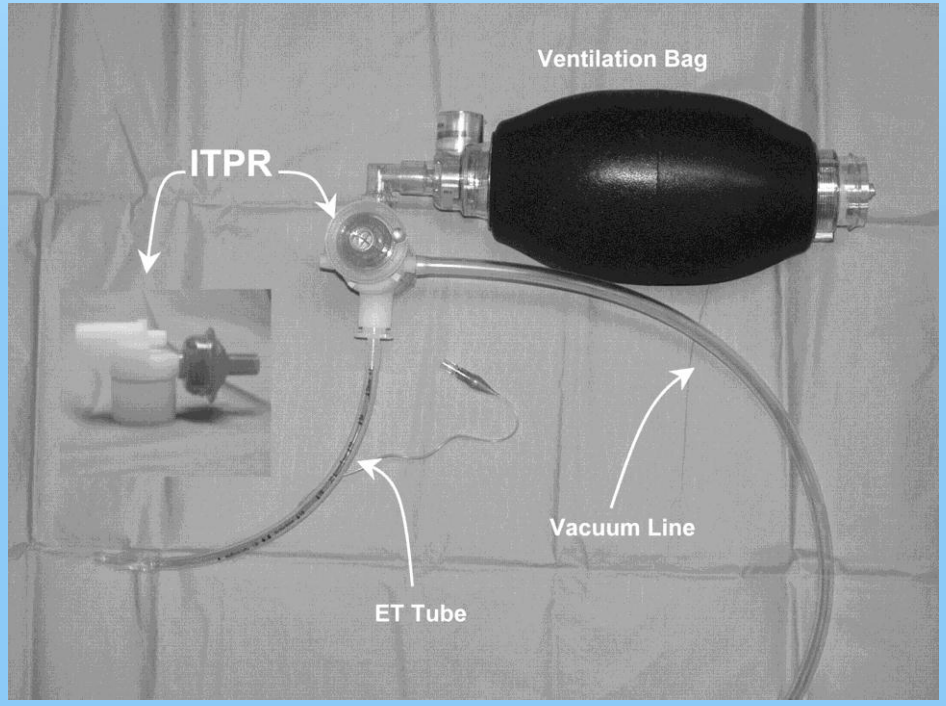


TABLE 1. Summary of Hemodynamic Variables, Survival Rates, Defibrillation Attempts, and Epinephrine Use During Basic Life Support and Advanced Life Support in Groups A, B, and C

Group of CPR	Measure	Baseline	BLS 2 Min 30 CPR	ALS 5 Min CPR	ROSC 1 Hr	No. of Shocks	ROSC at BLS	ROSC BLS + ALS	24-Hr Survival
		n = 18	*n* = 18	*n* = 16	*n* = 13				
Group A	SBP	102±20	54±9	74±23	47	6	0/6	1/6	1/6
BLS: standard	DBP	76±17	31±11	44±12	32				
ALS: standard	CPP	77±18	26±12	36±12	25				
	CBF	240±69	27±12	25±9	99				
	$ETco_2$	39±2	21±5	22±8	43				
	Airway pressure maximum	2.6±0.4	2.2±2.4	2.2±2.1	3.1				
	Airway pressure minimum	1.5±0.4	−0.3±1.4	−0.3±1.2	1.8				
Group B	SBP	103±16	85±29	119±28[a]	80±9	6±6	0/6	6/6[a]	6/6[a]
BLS: standard	DBP	71±14	33±18	56±19	44±8				
ALS: ACD-ITPR	CPP	68±20	29±17	50±16	44±8				
	CBF	243±53	25±22	37±28	163±48				
	$ETco_2$	40±1	28±8	41±9[a]	45±4				
	Airway pressure maximum	2.9±0.8	1.3±0.9	−4.2±3.2[a]	3.2±0.6				
	Airway pressure minimum	1.7±0.4	−0.9±0.4	−11.3±1.8[a]	1.5±0.8				
Group C	SBP	107±18	97±23[a]	117±15[a]	106±25[a]	5±4	2/6	6/6[a]	6/6[a]
BLS: ACD plus impedance threshold device	DBP	77±18	43±19	57±6	63±15				
ALS: ACD-ITPR	CPP	76±17	37±19	46±11	59±16[a]				
	CBF	273±80	42±22	37±18	208±70				
	$ETco_2$	40±1	43±10[a]	42±4[a]	45±5				
	Airway pressure maximum	3.1±0.5	4.3±2.5	−1.9±6	3.3±0.7				
	Airway pressure minimum	2±0.4	−10.5±0.8[a,b]	−12.3±2.1[a]	1.7±0.8				

CPR = cardiopulmonary resuscitation, BLS = basic life support, ALS = advanced life support, ROSC = return of spontaneous circulation, SBP = systolic blood pressure, DBP = diastolic blood pressure, CPP = coronary perfusion pressure, CBF = carotid blood flow, $ETco_2$ = end-tidal Co_2, ACD = active compression-decompression, ITPR = intrathoracic pressure regulator.

[a] $p < 0.05$ compared with group A.

[b] $p < 0.05$ compared with group B.

Airway pressure was measured between positive pressure ventilation. Values are shown as mean ± SD. All pressures are in mm Hg and all flows in mL/min.

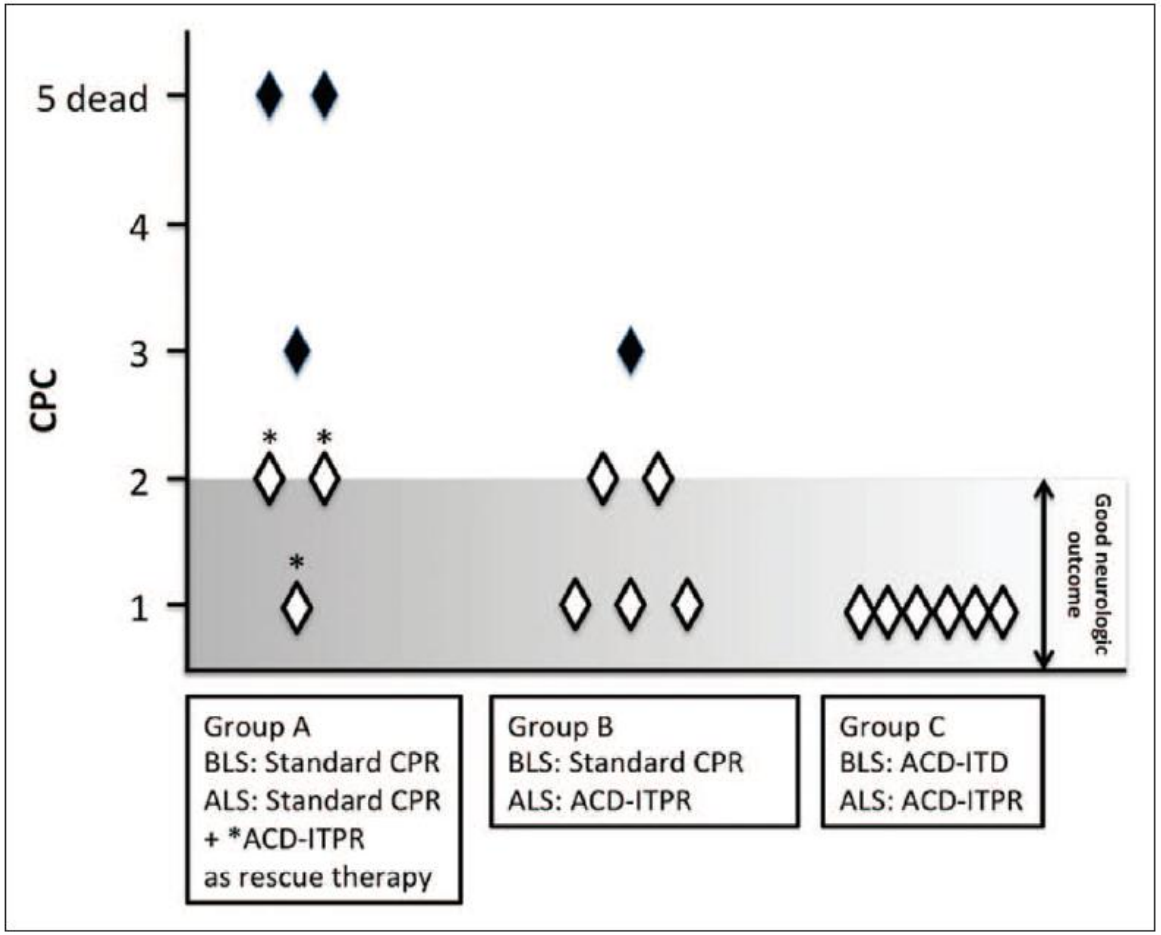
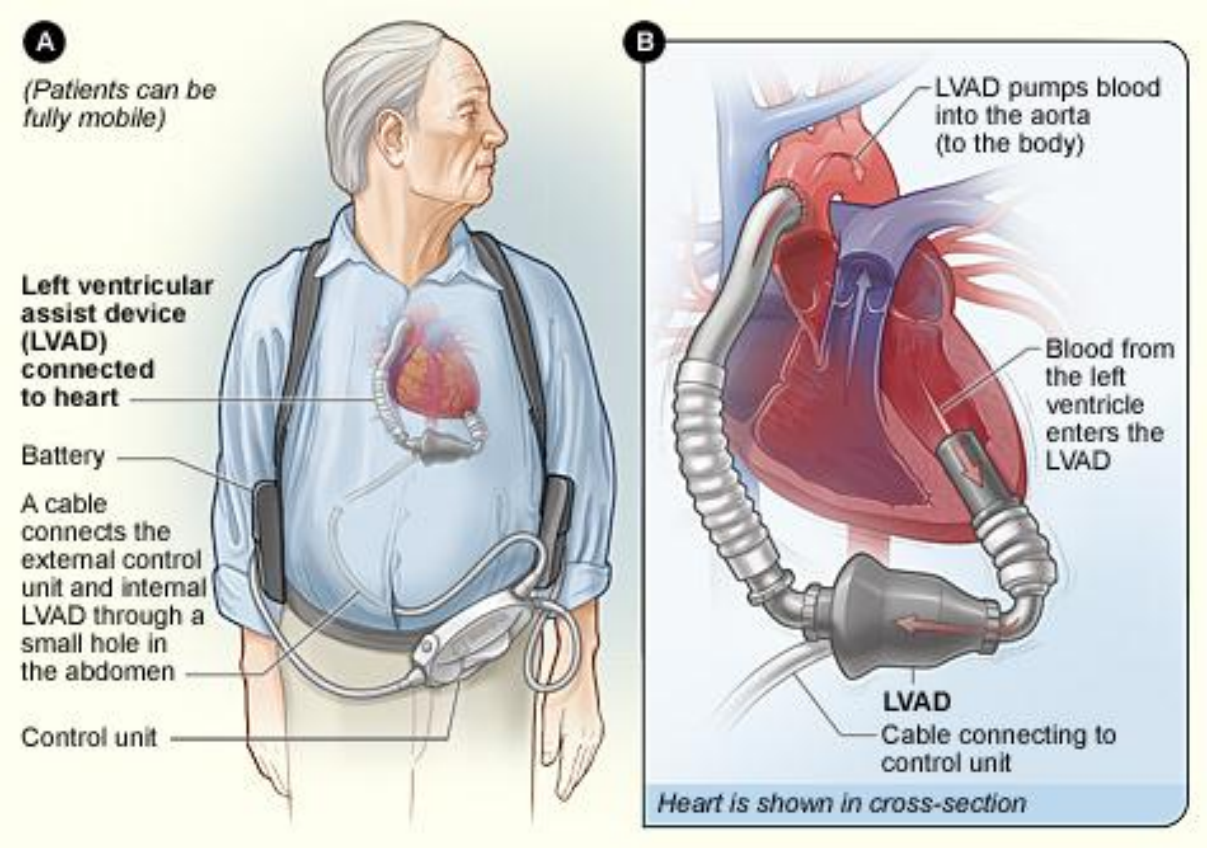


Figure 2. Twenty-four-hour Cerebral Performance Category (CPC) score (1= normal, 2 = mild deficit, 3 = severe deficit, 4 = coma, and 5 = dead). CPC is significantly different between groups ($p = 0.001$). ACD = active compression-decompression, ALS = advanced life support, BLS = basic life support, CPR = cardiopulmonary resuscitation, ITD = impedance threshold device, ITPR = intrathoracic pressure regulator.

CONCLUSION

Use of ACD-ITPR during ALS improved hemodynamics, ROSC rates, and neurological favorable survival, the primary study endpoint, compared with conventional ALS using standard CPR. ACD-ITPR also significantly improved brain blood flow compared with ACD-ITD. These positive findings provide strong support for further ALS research with ACD-ITPR.



Crit Care. 2015 Dec;19(1):864. doi: 10.1186/s13054-015-0864-2. Epub 2015 Mar 26.

Doubling survival and improving clinical outcomes using a left ventricular assist device instead of chest compressions for resuscitation after prolonged cardiac arrest: a large animal study.

Derwall M[1], Brücken A, Bleilevens C, Ebeling A, Föhr P, Rossaint R, Kern KB, Nix C, Fries M.

CONCLUSIONS:

In a model of prolonged cardiac arrest, the use of iCPR instead of sCPR improved CPP and doubled ROSC rates, translating into improved clinical outcomes.

CRITICAL CARE

EDITORIAL

Cerebral tissue saturation, the next step in cardiopulmonary resuscitation management?

Cornelia Genbrugge[1,2*], Willem Boer[2], Ingrid Meex[1,2], Frank Jans[1,2], Jo Dens[1,3] and Cathy De Deyne[1,2]

The goal of cardiopulmonary resuscitation (CPR) is to preserve the pre-arrest neurological state by maintaining sufficient cerebral blood flow and oxygenation, but the predictors thereof remain largely unknown. Despite recent attempts to improve the quality of basic and advanced life support, no monitored link to the neurological and physiological response of these CPR efforts has been established. The difficult decision to end pre-hospital resuscitation efforts is currently based on the circumstances of cardiac arrest, length of resuscitation efforts (if available), knowledge of pre-morbid physiological reserves, and (if present) end-tidal carbon dioxide ($ETCO_2$) measurement. $ETCO_2$ is currently the only parameter proven to correlate with the likelihood of return of spontaneous circulation (ROSC), although the prediction of long-term outcome based on $ETCO_2$ values has not been established [1,2]. To measure $ETCO_2$ adequately, invasive airway management is necessary and measured values are influenced by differ-

cerebrovascular accident [6] was observed, and accordingly two landmark studies [7,8] showed that a goal-directed protocol preventing cerebral desaturation resulted in a decrease in length of intensive care unit and hospital stay, lower incidence of major organ morbidity and mortality, and decreased risk of cognitive decline [4-8].

Almost 20 years after the first published study on cerebral saturation monitoring during CPR, a revival of cerebral saturation measurement during CPR is taking place. Recent published research measures cerebral saturation in patients with ongoing CPR at arrival to the emergency department, but different cerebral saturation devices and different methods for analysis of NIRS data are used. The latest research on NIRS in the CPR setting focuses on two main questions.

Firstly, can cerebral saturation values predict ROSC or neurological outcome? Ito and colleagues [9] observed higher initial cerebral saturation values for patients with

CRITICAL CARE

EDITORIAL

Cerebral tissue saturation, the next step in cardiopulmonary resuscitation management?

Cornelia Genbrugge[1,2*], Willem Boer[2], Ingrid Meex[1,2], Frank Jans[1,2], Jo Dens[1,3] and Cathy De Deyne[1,2]

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In conclusion, preliminary data suggest that monitoring of cerebral saturation during CPR seems a likely predictor of both ROSC and neurological outcome and that it might have a role guiding CPR interventions. Although the current knowledge, obtained from small observational studies, is limited, both the further development of NIRS devices and the likely execution of well-designed large blinded observational trials, particularly in the difficult environment of out-of-hospital CPR, bode well for the future. A real-time monitoring tool providing vital information on the neurological and physiological response to CPR efforts and with predictive value for neurological outcome seems

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Milrinone and esmolol decrease cardiac damage after resuscitation from prolonged cardiac arrest

F. Zoerner[1,2], F. Lennmyr[3], L. Wiklund[1], C. Martijn[4] and E. Semenas[1]

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Conflicts of interest
The authors confirm that there are no conflicts of interest.

Funding
Financial support from the Laerdal Foundation for Acute Medicine is gratefully acknowledged.

Submitted 29 December 2014; accepted 30 December 2014; submission 5 August 2014.

Citation
Zoerner F, Lennmyr F, Wiklund L, Martijn C, Semenas E. Milrinone and esmolol decrease cardiac damage after resuscitation from prolonged cardiac arrest. Acta Anaesthesiologica Scandinavica 2015

doi: 10.1111/aas.12480

Background: Long-term survival after cardiac arrest (CA) due to shock-refractory ventricular fibrillation (VF) is low. Clearly, there is a need for new pharmacological interventions in the setting of cardiopulmonary resuscitation (CPR) to improve outcome. Here, hemodynamic parameters and cardiac damage are compared between the treatment group (milrinone, esmolol and vasopressin) and controls (vasopressin only) during resuscitation from prolonged CA in piglets.

Methods: A total of 26 immature male piglets were subjected to 12-min VF followed by 8-min CPR. The treatment group ($n = 13$) received i.v. (intravenous) boluses vasopressin 0.4 U/kg, esmolol 250 μg/kg and milrinone 25 μg/kg after 13 min, followed by i.v. boluses esmolol 375 μg/kg and milrinone 25 μg/kg after 18 min and continuous esmolol 15 μg/kg/h infusion during 180 min reperfusion, whereas controls ($n = 13$) received equal amounts of vasopressin and saline. A 200 J monophasic counter-shock was delivered to achieve resumption of spontaneous circulation (ROSC) after 8 min CPR. If ROSC was not achieved, another 200 J defibrillation and bolus vasopressin 0.4 U/kg would be administered in both groups. Direct current shocks at 360 J were applied as one shot per minute over maximally 5 min. Hemodynamic variables and troponin I as a marker of cardiac injury were recorded.

Results: Troponin I levels after 180 min reperfusion were lower in the treatment group than in controls ($P < 0.05$). The treatment group received less norepinephrine ($P < 0.01$) and had greater diuresis ($P < 0.01$). There was no difference in survival between groups.

Conclusion: The combination of milrinone, esmolol and vasopressin decreased cardiac injury compared with vasopressin alone.

高渗盐水在心搏骤停动物模型心肺复苏中应用疗效的 Meta 分析

李伟　徐军　谈定玉　于学忠

【摘要】 **目的**　系统评价高渗盐水（HS）对心搏骤停动物模型心肺复苏（CPR）的有效性。**方法**　分别检索美国国立医学图书馆 PubMed 数据库、荷兰医学文摘 EMBASE 数据库 1966 年 1 月 1 日至 2014 年 9 月 30 日，以及万方数据库、中国知网 1990 年 1 月 1 日至 2014 年 9 月 30 日，有关 HS 对心搏骤停模型动物干预作用的随机对照研究。HS 组于 CPR 开始即刻给予 HS，剂量、浓度不限；NS 组于 CPR 开始即刻给予等量生理盐水（NS）。采用 RevMan 5.3 软件对 HS 应用于心搏骤停模型动物 CPR 的自主循环恢复率（ROSC），心搏骤停前及 CPR 期间血钠水平，CPR 时及 ROSC 后 90 min 时的平均动脉压（MAP）、冠状动脉灌注压（CPP）进行 Meta 分析。**结果**　最终纳入 8 篇文献，Meta 分析显示，与 NS 组相比，HS 组可提高 ROSC 率〔相对危险度（*RR*）=1.23，95% 可信区间（95%*CI*）=1.05～1.43，*P*=0.010〕、CPR 期间血钠水平〔加权均数差（*WMD*）=17.44，95%*CI*=12.57～22.31，*P*<0.01〕及 ROSC 后 90 min 时的 MAP（*WMD*=4.81，95%*CI*=1.58～8.03，*P*=0.003），但心搏骤停前血钠水平（*WMD*=0.78，95%*CI*=−0.26～1.82，*P*=0.14）、CPR 时 MAP（*WMD*=5.43，95%*CI*=−0.74～11.59，*P*=0.08）、CPR 时 CPP（*WMD*=6.82，95%*CI*=−5.54～19.19，*P*=0.28）、ROSC 后 90 min 时 CPP（*WMD*=−0.77，95%*CI*=−10.33～8.80，*P*=0.88〕差异均无统计学意义。漏斗图显示，入选文章发表偏倚不大。**结论**　HS 能够提高 CPR 时 ROSC 率，并提高 CPR 期间血钠水平及 ROSC 后 90 min 时的 MAP。

【关键词】 心肺复苏；　心搏骤停；　高渗盐水；　Meta 分析

The efficacy of hypertonic saline treatment in cardiopulmonary resuscitation in animal model with cardiac arrest: a Meta-analysis

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【Abstract】 Objective To evaluate the efficacy of hypertonic saline (HS) treatment in cardiopulmonary resuscitation (CPR) in animal models of cardiac arrest (CA). **Methods** PubMed and EMBASE data were retrieved from January 1st, 1966 to September 30th, 2014, and Wanfang data and CNKI were searched from January 1st, 1990 to September 30th, 2014 for randomized controlled trials (RCTs) regarding CPR intervention of CA animal models with HS. HS was intravenously infused at the initiation of CPR in HS group, without limiting its dosage or concentration. The same volume of normal saline (NS) was given in NS group. Meta-analysis concerning the rate of restoration of spontaneous circulation (ROSC), the serum sodium concentration before CA and during CPR, and related hemodynamic parameters, including mean arterial pressure (MAP) and coronary perfusion pressure (CPP) at the immediate beginning of CPR and 90 minutes after ROSC was conducted by RevMan 5.3 software. **Results** A total of 8 RCTs were included. Meta-analysis showed that compared with NS group, the rate of ROSC [relative risk (*RR*) = 1.23, 95% confidence interval (95%*CI*) = 1.05–1.43, $P = 0.010$], serum sodium concentration during CPR [weight mean difference (*WMD*) = 17.44, 95%*CI* = 12.57–22.31, $P < 0.01$], and the level of MAP at 90 minutes after ROSC (*WMD* = 4.81, 95%*CI* = 1.58–8.03, $P = 0.003$) were significantly improved in HS group. There was no significant statistic difference in other hemodynamic parameters, including serum sodium concentration before CA (*WMD* = 0.78, 95%*CI* = –0.26–1.82, $P = 0.14$), MAP (*WMD* = 5.43, 95%*CI* = –0.74–11.59, $P = 0.08$) and CPP at the immediate beginning of CPR (*WMD* = 6.82, 95%*CI* = –5.54–19.19, $P = 0.28$), and CPP at 90 minutes after ROSC (*WMD* = –0.77, 95%*CI* = –10.33–8.80, $P = 0.88$) between two groups. It was showed by funnel chart that bias was not significant in the published articles. **Conclusion** This systematic review indicates that HS infusion is followed by an improved ROSC rate, serum sodium concentration during CPR, and MAP at 90 minutes after ROSC in animal models of CA.

【Key words】 Cardiopulmonary resuscitation; Cardiac arrest; Hypertonic saline; Meta-analysis

DOI: 10.3760/cma.j.issn.2095-4352.2015.03.008

Shock, Publish Ahead of Print
DOI: 10.1097/SHK.0000000000000357

Evaluation of Cyclosporine A as a Cardio- and Neuroprotective Agent After Cardiopulmonary Resuscitation in a Rat Model

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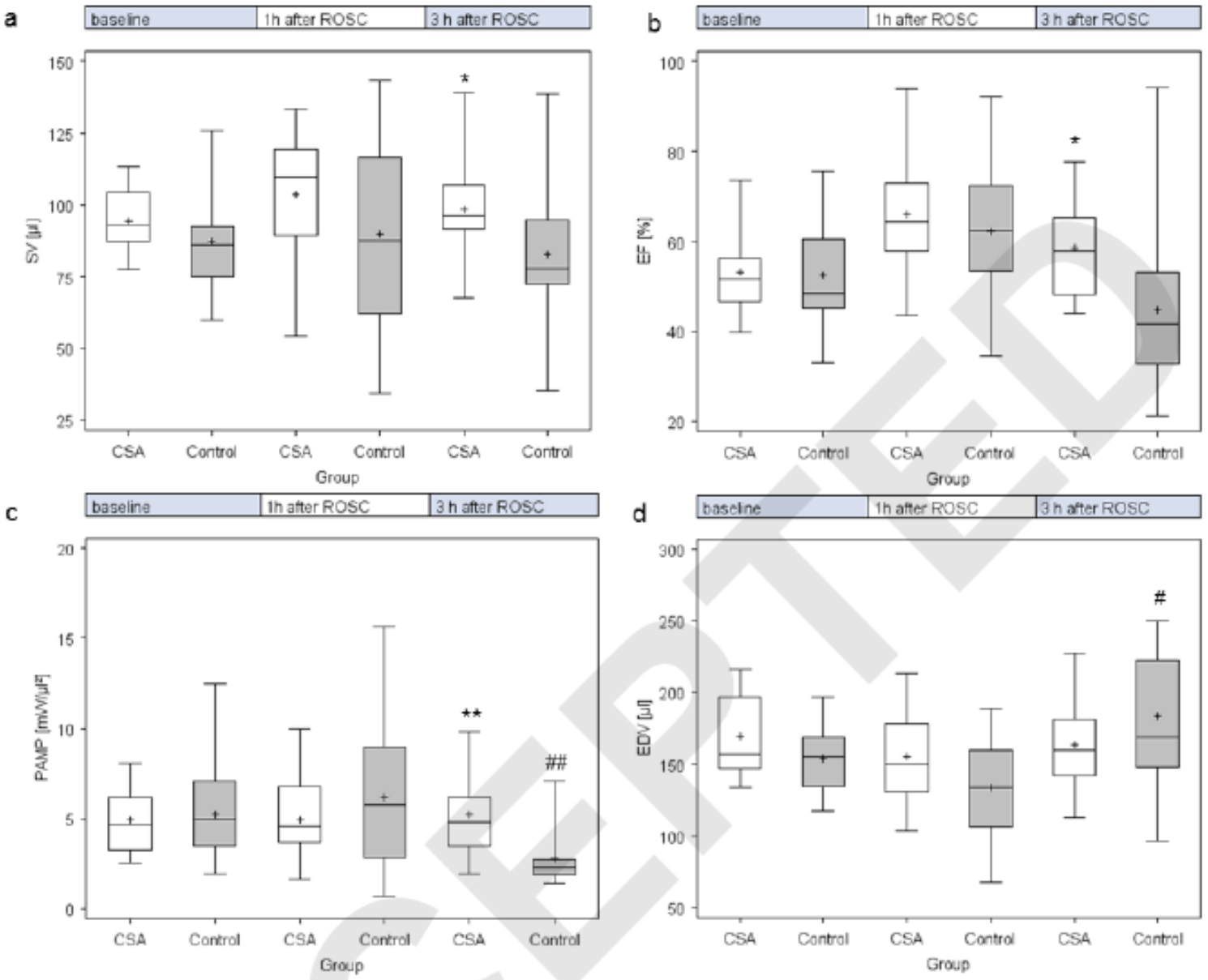
Figure 2


a
baseline
1h after ROSC
3 h after ROSC
SV [µl]
150
125
100
75
50
25
*
CSA
Control
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Control
CSA
Control
Group
b
baseline
1h after ROSC
3 h after ROSC
EF [%]
100
80
60
40
20
*
CSA
Control
CSA
Control
CSA
Control
Group
c
baseline
1h after ROSC
3 h after ROSC
PAMP [mV/µl²]
20
15
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5
0
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CSA
Control
CSA
Control
CSA
Control
Group
d
baseline
1h after ROSC
3 h after ROSC
EDV [µl]
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#
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Control
CSA
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CSA
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Group

Figure 4

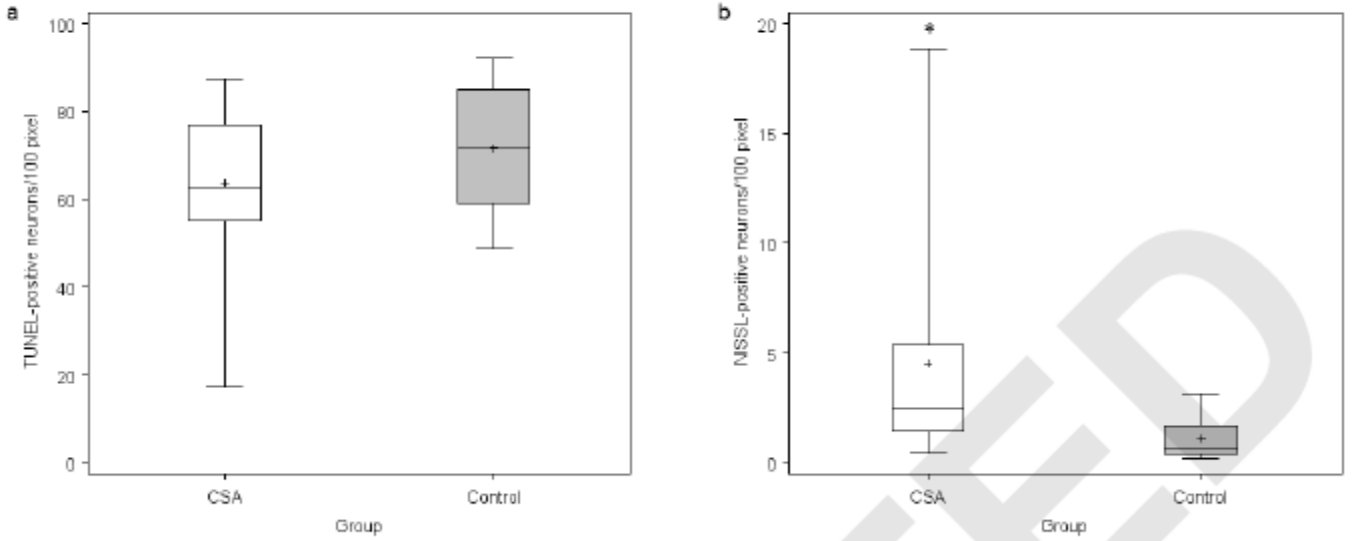
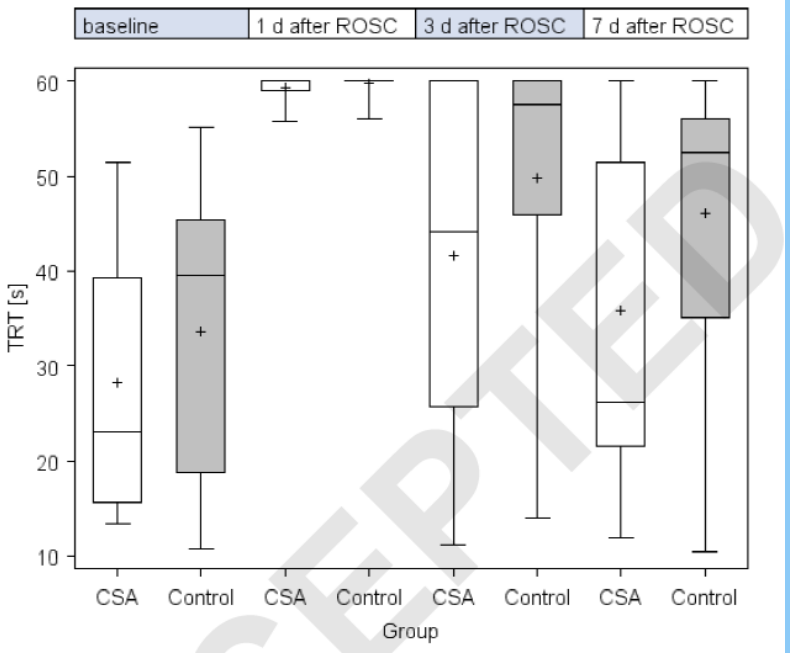


Figure 5



Shock, Publish Ahead of Print
DOI: 10.1097/SHK.0000000000000367

Role of Endoplasmic Reticulum Stress in Brain Damage after Cardiopulmonary Resuscitation in Rats

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Conclusion: Our findings suggested that ER stress and the associated apoptotic pathways were activated in the hippocampus after resuscitation. Administration of Sal 30 min prior to CPR ameliorated neurological dysfunction 24 h after CA, possibly through the inhibition of ER stress following post-resuscitation brain injury.

Sal is a selective inhibitor of the eukaryotic translation initiation factor 2 subunit α (eIF-2α) dephosphorylation. Enhanced eIF-2α phosphorylation attenuates the initiation of translation for most mRNAs, which reduces protein synthesis and allows cells to restore their protein folding capacity and recover from ER stress (25, 26). In the present study, we administered Sal prior to CA to investigate its effects on brain injury after resuscitation. Our results demonstrated that Sal could significantly alleviate the ultrastructural damages, cell apoptosis and neurological dysfunction that occur following CA. Our findings were also supported by the results of a previous study showing that Sal decreases neurocyte death and reduces infarct volume after focal cerebral ischemia (17). In addition, we found that Sal pretreatment enhanced

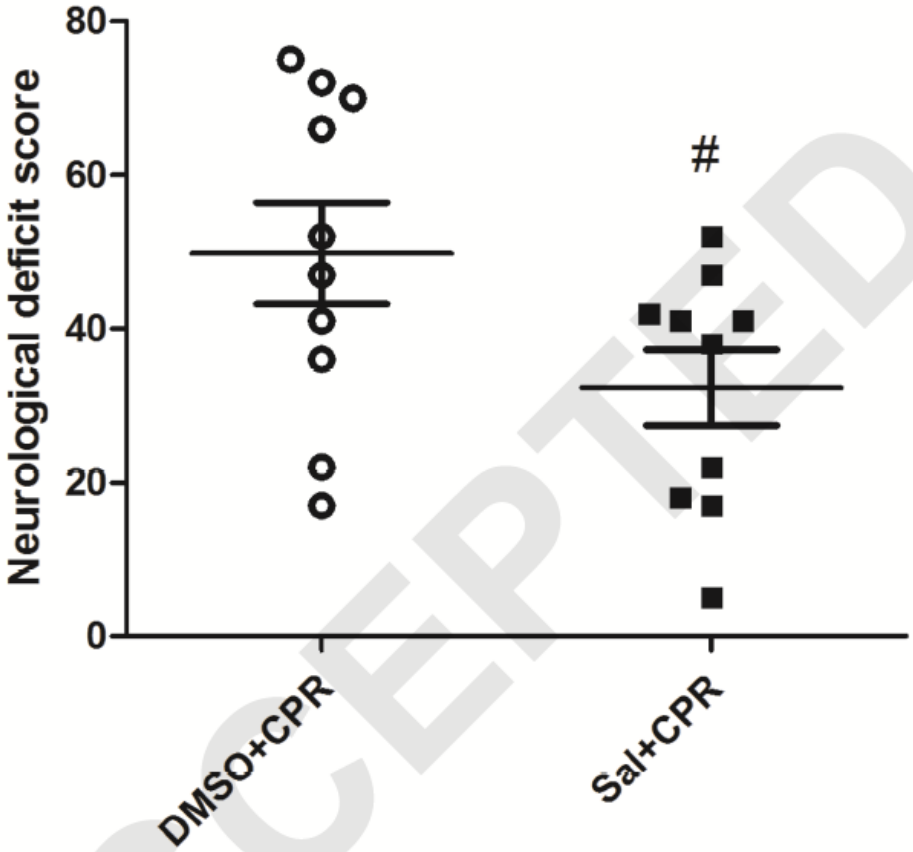
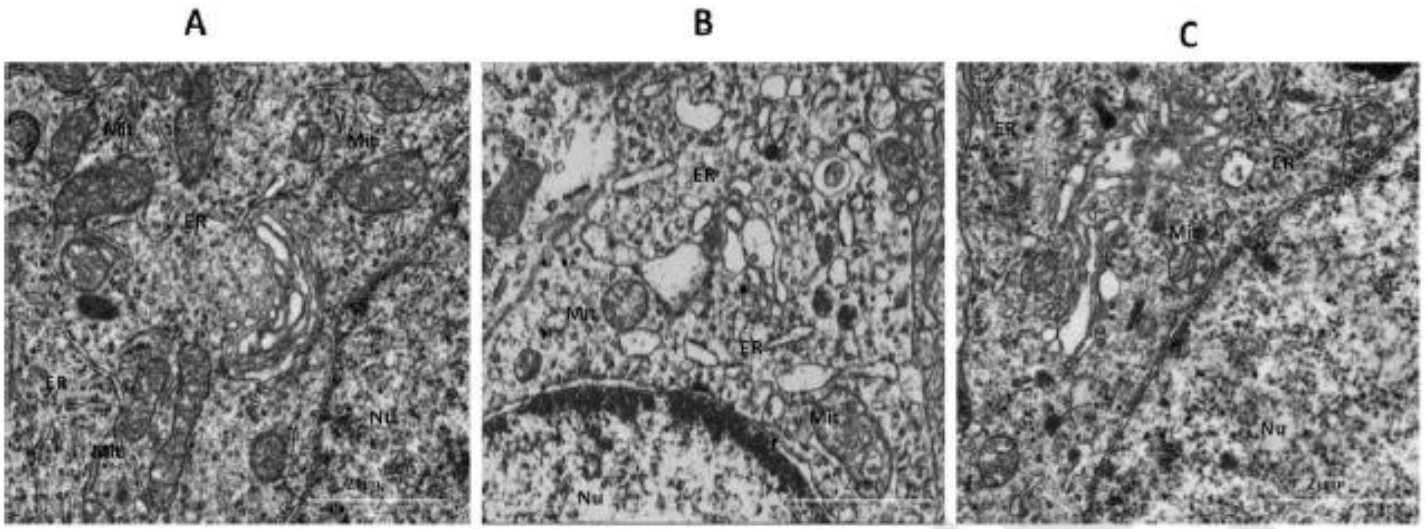


Fig 3

The neurological deficit scores in the DMSO+CPR and the Sal+CPR groups 24 h after resuscitation. Sal improved neurological outcomes 24 h after CPR. $^{\#}P< 0.05$ vs the DMSO+CPR group.

Figure 4



Epinephrine Administration in Lipid-Based Resuscitation in a Rat Model of Bupivacaine-Induced Cardiac Arrest

Optimal Timing

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Background and Objectives: The medical community commonly uses lipid emulsion combined with epinephrine in local anesthetic–induced cardiac arrest, but the optimal timing of epinephrine administration relative to lipid emulsion is currently unknown and needs to be determined.

Methods: Thirty adult male Sprague-Dawley rats were subjected to bupivacaine-induced asystole and were then randomly divided into 3 groups. The temporal administration of epinephrine varied in each group: (1) immediately after the completion of the initial bolus of lipid emulsion therapy (postILE0); (2) immediately after cardiac arrest before the initial bolus of lipid emulsion (preILE); or (3) 1 minute after the completion of the initial bolus of lipid emulsion (postILE1). External chest compression was administered until the return of spontaneous circulation or the end of a 20-minute resuscitation period.

Results: The postILE0, preILE, and postILE1 groups displayed different survival rates (100%, 30%, and 40%; $P = 0.003$). After return of spontaneous circulation, the rate–pressure product of the postILE0 group was higher than that of the postILE1 group ($P < 0.001$). Wet-to-dry lung weight ratio of preILE and postILE1 groups was higher than that of the postILE0 group ($P < 0.05$). The rate of damaged alveoli of the postILE0 group was lower than those of the preILE ($P = 0.001$) and postILE1 ($P < 0.001$) groups. Concentrations of bupivacaine in the cardiac tissues of the postILE0 group were lower than that of the postILE1 group ($P = 0.01$).

Conclusions: In the rat model of bupivacaine-induced cardiac arrest, the optimal timing for the administration of epinephrine to produce best outcomes of successful cardiopulmonary resuscitation is immediately after the completion of the lipid emulsion bolus. This optimal timing/therapeutic window is of paramount importance.

(*Reg Anesth Pain Med* 2015;40: 00–00)

rine during cardiopulmonary resuscitation. The American Heart Association's advanced cardiac life support executive summary is now deemphasizing drugs for advanced cardiac life support in favor of quality and uninterrupted chest compression. Nonetheless, in day-to-day medical practice, epinephrine has retained a clinical priority in the treatment of cardiac arrest,[2,3] especially in the face of local anesthetic–induced cardiac arrest.[4,5]

The primary mechanism of action of epinephrine is on the α-receptor response,[6–8] thereby leading to increased coronary vascular pressure. Lipid administration delays the peak effect of epinephrine[9] and prolongs its duration of action on mean arterial pressure (MAP) but does not alter the peak increase in MAP or the heart rate (HR). Our recent work[10] demonstrated that a combination of lipid emulsion with epinephrine was superior to the administration of lipid emulsion alone with regard to successful resuscitation.

No study thus far has addressed epinephrine's temporal administration in association with that of a lipid emulsion bolus when used during local anesthetic–induced cardiac arrest. Therefore, we did a preliminary experimental exploration of this association. Our results suggest that administering intravenous epinephrine immediately after an intravenous bolus of lipid emulsion facilitated the best resuscitation outcome. In view of these findings, we designed an investigator-blinded randomized study using a rat model of bupivacaine-induced cardiac arrest. We hypothesized that (1) a dose of epinephrine administered immediately after a bolus of lipid emulsion in bupivacaine-induced cardiac arrest (asystole) would have a higher survival, a lower cardiac bupivacaine concentration, and lower rates of pulmonary hemorrhage than the

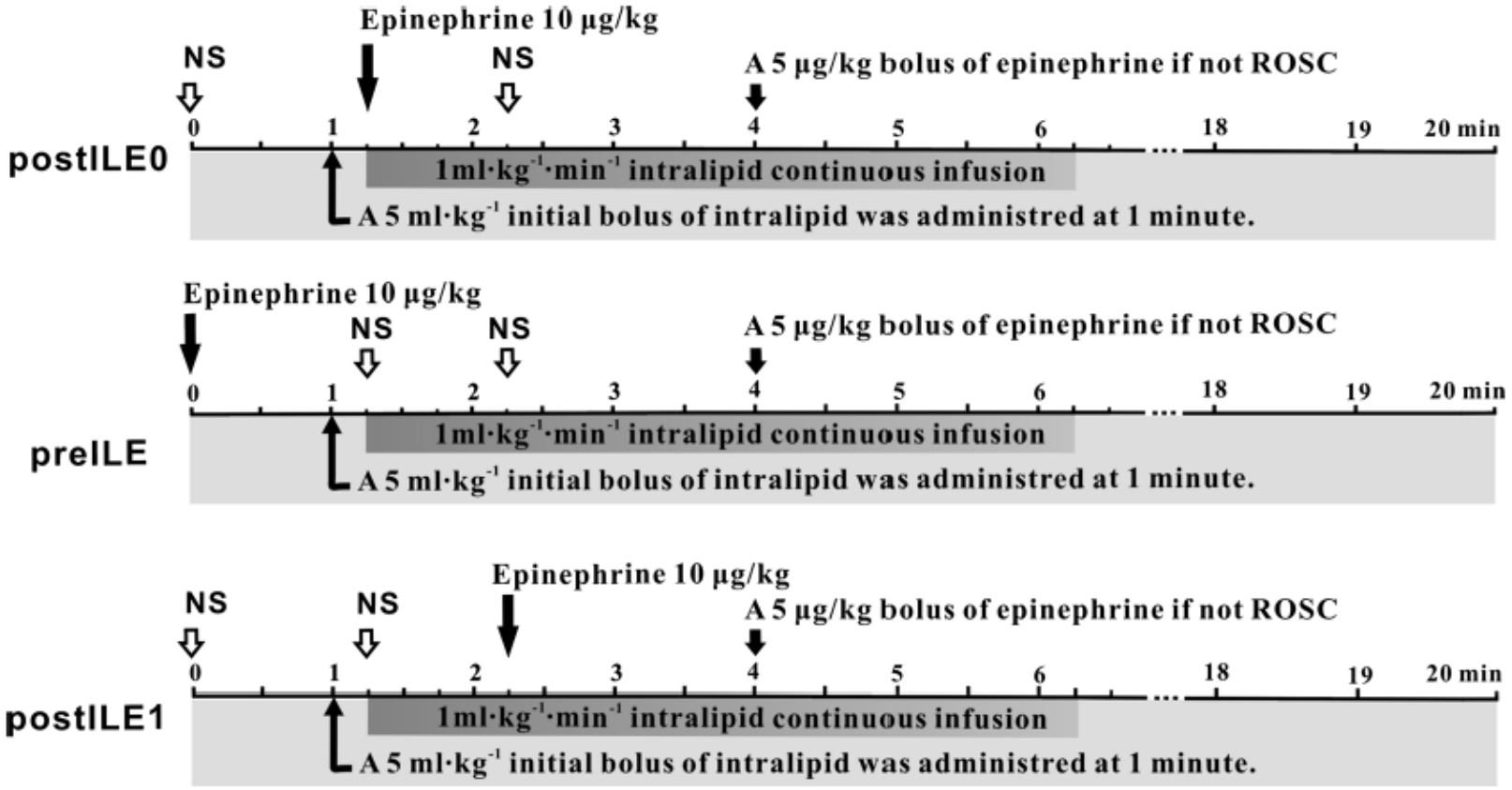

FIGURE 1. Timeline to the recovery of cardiac arrest. Cardiac arrest is time 0. At 1 minute, all groups were injected with a 5-mL/kg bolus of 30% lipid emulsion (Intralipid) for 15 seconds, followed by a continuous infusion of 1 mL/kg per minute for 5 minutes. A 5-μg/kg bolus of epinephrine is administered at 4 minutes if there was no ROSC and repeated at 2-minute intervals until ROSC or the end of the observation period of 20 minutes. ROSC indicates return of spontaneous circulation; NS, normal saline; postILE0, epinephrine administered immediately after lipid emulsion initial bolus; preILE, epinephrine administered immediately after cardiac arrest; postILE1, epinephrine administration delayed until 1 minute after conclusion of the lipid emulsion initial bolus.

TABLE 2. Resuscitation Outcomes for PreILE, PostILE0, and PostILE1 Groups

	PostILE0 (n = 10)	PreILE (n = 10)	PostILE1 (n = 10)
Rate of ROSC, %	100% (10)	50% (5)	50% (5)
Survival rate, %	100% (10)	30% (3)	40% (4)
Time to return of pulse, s	94 ± 20*	89 ± 12*	117 ± 33
Time to ROSC, s	228 ± 54*†	188 ± 67	275 ± 89
The time of administration of epinephrine to return of pulse	38 ± 24†	88 ± 12	57 ± 33†
The time of administration of epinephrine to ROSC, s	168 ± 54*†	188 ± 67	215 ± 89
Epinephrine cumulative dose, μg/kg	15 (15, 20)	37.5 (15, 50)	35 (15, 50)

Normal distributed data are given as mean ± SD, whereas non-normal distributed data are expressed as median and interquartile values. The postILE0, preILE, and postILE1 groups displayed differences in the rate of ROSC ($P = 0.03$; postILE0 vs preILE, $P = 0.033$; postILE0 vs postILE1, $P = 0.033$; preILE vs postILE1, $P = 1$) and survival rate ($P = 0.003$; postILE0 vs preILE, $P = 0.003$; postILE0 vs postILE1, $P = 0.011$; preILE vs postILE1, $P = 1$). The postILE0, preILE, and postILE1 groups displayed differences in time to return of pulse ($P = 0.012$); postILE0 versus preILE, $P = 0.287$; postILE0 versus postILE1, $P = 0.038$; preILE versus postILE1, $P = 0.006$. The postILE0, preILE, and postILE1 groups displayed differences in time to ROSC ($P = 0.01$); postILE0 versus preILE, $P = 0.042$; postILE0 versus postILE1, $P = 0.002$; preILE versus postILE1, $P = 0.794$. The postILE0, preILE, and postILE1 groups displayed differences in the first medication time to first heartbeat ($P < 0.001$); postILE0 versus preILE, $P < 0.001$; postILE0 versus postILE1, $P = 0.093$; preILE versus postILE1, $P = 0.047$. The postILE0, preILE, and postILE1 groups displayed differences in the time of administration of epinephrine to ROSC ($P = 0.002$); postILE0 versus preILE, $P = 0.007$; postILE0 versus postILE1, $P = 0.002$; preILE versus postILE1, $P = 0.904$. ROSC indicates return of spontaneous circulation; postILE0, immediately after lipid emulsion initial bolus; preILE, immediately after cardiac arrest, before lipid emulsion initial bolus; postILE1, delaying 1 minute after lipid emulsion initial bolus. *$P < 0.05$ versus postILE1; †$P < 0.05$ versus preILE.

TABLE 3. Arterial Blood Gas Parameters, Wet-To-Dry Lung Weight Ratio, and Bupivacaine Content at 20 Minutes

	PostILE0 (n = 10)	PreILE (n = 10)	PostILE1 (n = 10)
pH	6.99 ± 0.13	6.90 ± 0.09	6.84 ± 0.09*
$PaCO_2$, mm Hg	87 ± 25	88 ± 13	95 ± 22
Base excess, mmol/L	−11 ± 6	−16 ± 4*	−17 ± 4*
HCO_3^-, mmol/L	21 ± 5	17.3 ± 2.9*	16 ± 3*
Lactate, mmol/L	7.9 ± 3.3	9.8 ± 3.1	10.9 ± 2.2
PaO_2, mm Hg	62 (43, 74)	38 (21, 68)	32 (28, 46)
Wet-to-dry lung weight ratio	5.8 ± 0.5	6.8 ± 0.6*	7.1 ± 1.3*
Plasma bupivacaine content, µg/mL	14.4 ± 3.0	15.7 ± 2.5	17.4 ± 4.2
Myocardial bupivacaine content, µg/g	8.5 ± 1.7	9.7 ± 1.5	11.2 ± 2.7*

Normal distributed data are given as mean ± SD, whereas non-normal distributed data are expressed as median and interquartile values. The postILE0, preILE, and postILE1 groups displayed differences in pH ($P = 0.013$); pH value at postILE1 group was lower than postILE0 group ($P = 0.004$). The postILE0, preILE, and postILE1 groups displayed differences in BE ($P = 0.019$); preILE versus postILE0, $P = 0.032$; postILE1 versus postILE0, $P = 0.008$. The postILE0, preILE, and postILE1 groups displayed differences in HCO_3^- ($P = 0.035$); preILE versus postILE0, $P = 0.048$; postILE1 versus postILE0, $P = 0.015$. The postILE0, preILE, and postILE1 groups displayed differences in wet-to-dry lung weight ratios (5.8 ± 0.5, 6.8 ± 0.6, and 7.1 ± 1.3, respectively; postILE0 vs preILE, $P = 0.04$; postILE0 vs postILE1, $P = 0.008$). Significance differences were demonstrated between the postILE0, preILE, and postILE1 groups in myocardial bupivacaine content. Bupivacaine content of the postILE0 group in cardiac tissue was lower than that of the postILE1 group ($P = 0.01$, n = 10 for each group). No significant differences were demonstrated between the 3 groups in arterial blood plasma. PostILE0 indicates immediately after lipid emulsion initial bolus; preILE, immediately after cardiac arrest, before lipid emulsion; postILE1, delaying 1 minute after lipid emulsion initial bolus. *$P < 0.05$ versus postILE0.

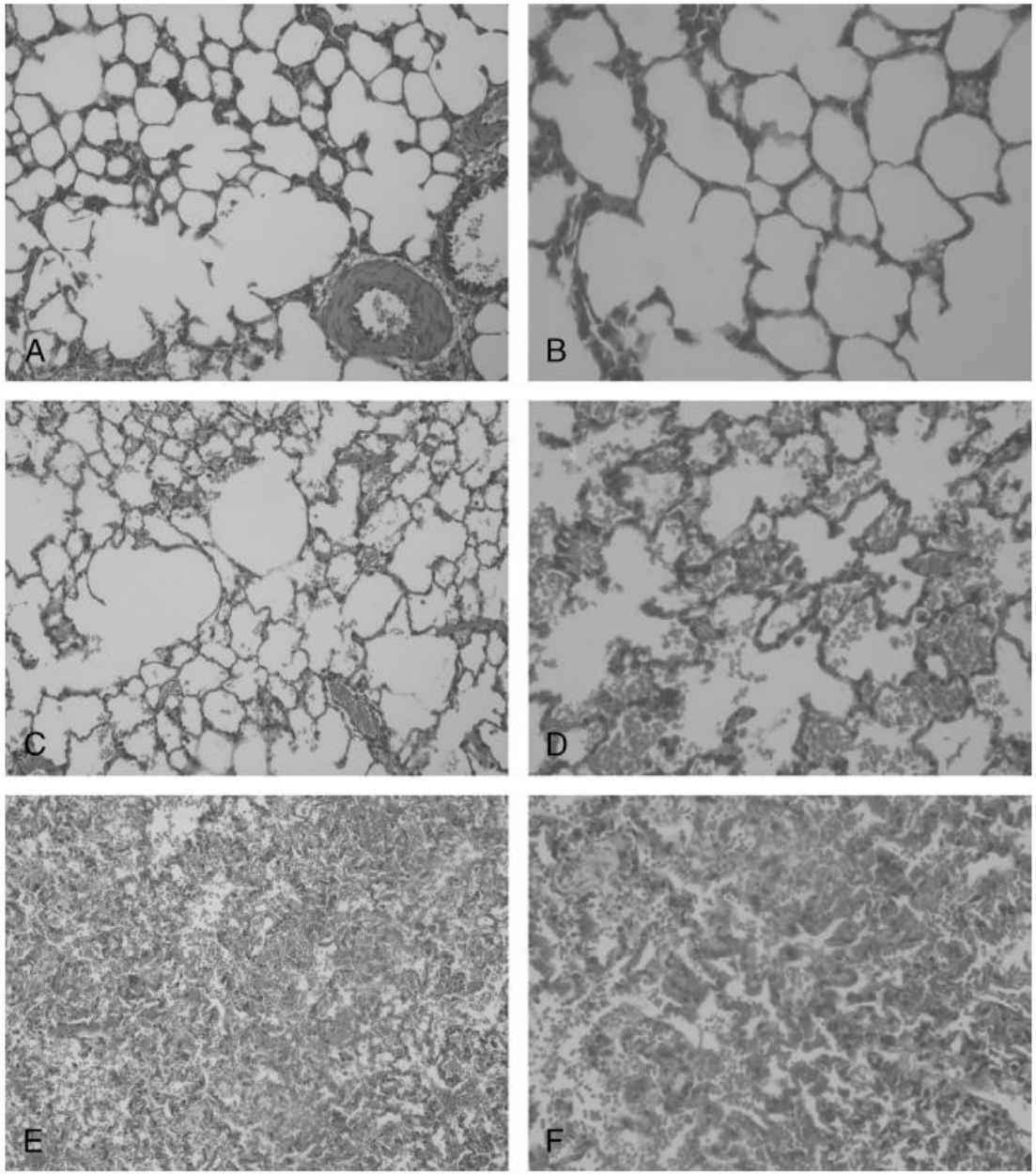

FIGURE 3. The light microscopy view of the right middle lobe in the postILE0 (A, B), postILE1 (C, D), and preILE (E, F) groups. A, Structure of alveoli are normal (magnification, 200×). B, There is no accumulation of leukocytes or erythrocytes observed in the alveoli (magnification, 400×). C, Near-normal alveoli are identified (magnification, 200×). D, There are numerous erythrocytes observed in the alveoli (magnification, 400×). E, Most of the alveoli are destroyed, and their structures are significantly altered (magnification, 200×). F, There are numerous erythrocytes evident accompanying the damaged alveolar framework (magnification, 400×).

Shock, Publish Ahead of Print
DOI: 10.1097/SHK.0000000000000337

Effects of Ghrelin on Post-resuscitation Brain Injury in a Rat Model of Cardiac Arrest

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Ghrelin is a novel gastrointestinal hormone that is known to induce a positive energy balance by stimulating food intake while decreasing adipose usage.(6) Previous studies have demonstrated ghrelin's neuroprotective effects in a series of models of neuronal injury.(7) In a rat model of traumatic brain injury, ghrelin treatment increased survival and facilitated function recovery by suppressing inflammation and apoptosis.(8, 9) In a rat model of pilocarpine-induced seizures, ghrelin attenuated hippocampal neuronal damage with a decreased ratio of Bcl-2/Bax and inhibited caspase-3 activation.(10) Particularly, in models of

Ghrelin,

- improved neurological function 48 h and 72 h after ROSC
- treated rats exhibited histological improvement 72 h after ROSC
- prevented apoptosis in the hippocampal CA1 sector 72 h after ROSC
- decreased the level of oxidative stress in the hippocampus 6 h after ROSC

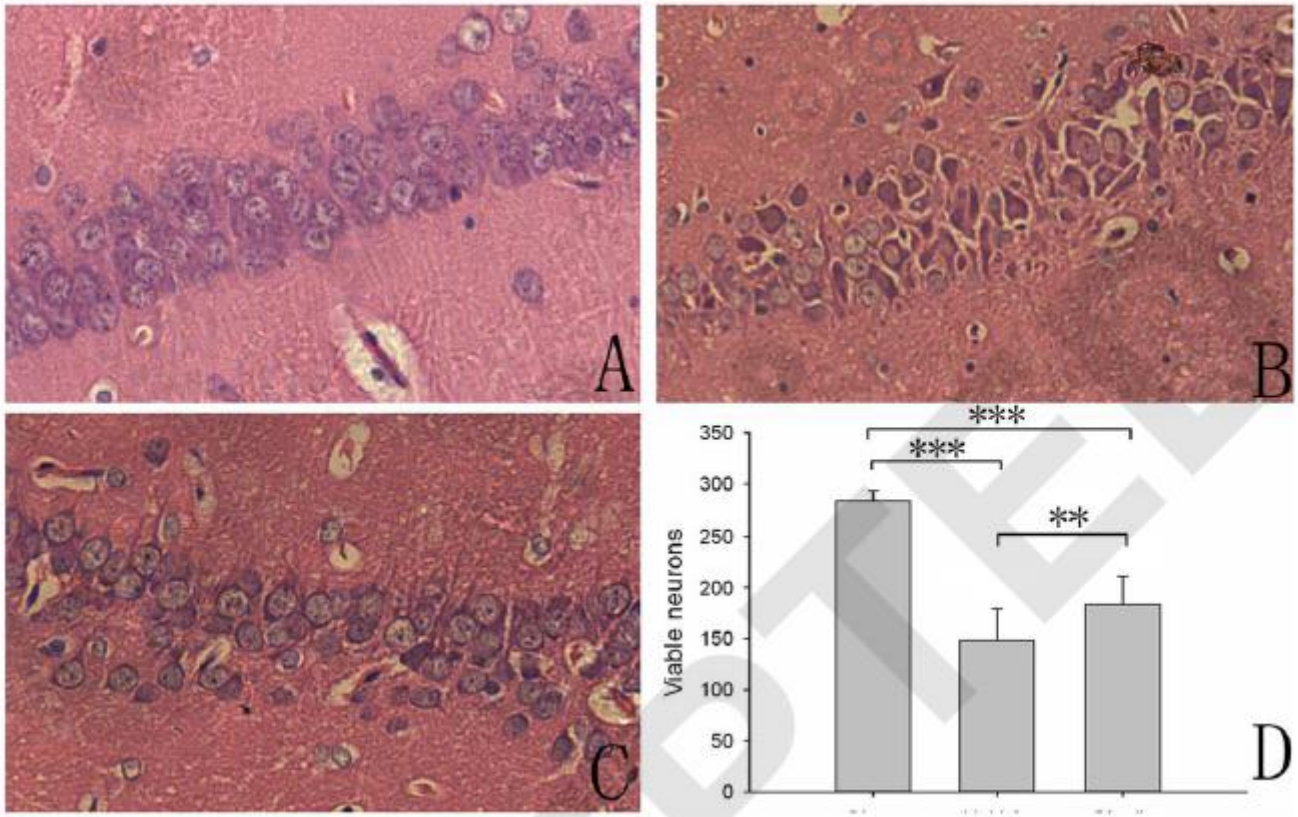

Figure 2 Effect of ghrelin on histological changes 72 h after ROSC (return of spontaneous circulation) in hippocampal CA1 sector.

The representative histological images of hippocampal CA1 sector by HE staining in sham (A), vehicle (B) and ghrelin (C) group were showed. (D)The amount of viable neurons was signifcantly more in the ghrelin group than that in the vehicle group. (***P＜0.001, **P＜0.01, by student's t-test).

Hydrogen-Rich Saline Improves Survival and Neurological Outcome After Cardiac Arrest and Cardiopulmonary Resuscitation in Rats

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BACKGROUND: Sudden cardiac arrest is a leading cause of death worldwide. Three-fourths of cardiac arrest patients die before hospital discharge or experience significant neurological damage. Hydrogen-rich saline, a portable, easily administered, and safe means of delivering hydrogen gas, can exert organ-protective effects through regulating oxidative stress, inflammation, and apoptosis. We designed this study to investigate whether hydrogen-rich saline treatment could improve survival and neurological outcome after cardiac arrest and cardiopulmonary resuscitation, and the mechanism responsible for this effect.

METHODS: Sprague-Dawley rats were subjected to 8 minutes of cardiac arrest by asphyxia. Different doses of hydrogen-rich saline or normal saline were administered IV at 1 minute before cardiopulmonary resuscitation, followed by injections at 6 and 12 hours after restoration of spontaneous circulation, respectively. We assessed survival, neurological outcome, oxidative stress, inflammation biomarkers, and apoptosis.

RESULTS: Hydrogen-rich saline treatment dose dependently improved survival and neurological function after cardiac arrest/resuscitation. Moreover, hydrogen-rich saline treatment dose dependently ameliorated brain injury after cardiac arrest/resuscitation, which was characterized by the increase of survival neurons in hippocampus CA1, reduction of brain edema in cortex and hippocampus, preservation of blood-brain barrier integrity, as well as the decrease of serum S100β and neuron-specific enolase. Furthermore, we found that the beneficial effects of hydrogen-rich saline treatment were associated with decreased levels of oxidative products (8-iso-prostaglandin F2α and malondialdehyde) and inflammatory cytokines (tumor necrosis factor-α, interleukin-1β, and high-mobility group box protein 1), as well as the increased activity of antioxidant enzymes (superoxide dismutase and catalase) in serum and brain tissues. In addition, hydrogen-rich saline treatment reduced caspase-3 activity in cortex and hippocampus after cardiac arrest/resuscitation.

CONCLUSIONS: Hydrogen-rich saline treatment improved survival and neurological outcome after cardiac arrest/resuscitation in rats, which was partially mediated by reducing oxidative stress, inflammation, and apoptosis. (Anesth Analg 2014;119:368–80)

Experimental Design

Experiment 1: Effects of Hydrogen-Rich Saline Treatment on Survival and Neurological Outcome After Cardiac Arrest/ Resuscitation in Rats

Experiment 2: Effects of Hydrogen-Rich Saline Treatment on Brain Edema, Brain Injury, and Blood-Brain Barrier After Cardiac Arrest/Resuscitation in Rats

Experiment 3: Effects of Hydrogen-Rich Saline Treatment on Oxidative Stress, Inflammatory Cytokines, and Apoptosis in Serum and Brain Tissues After Cardiac Arrest/ Resuscitation in Rats

Caspase-3 Activity

Caspase-3 activation, widely accepted as a reliable indicator for cell apoptosis, was measured at 24 hours after restoration of spontaneous circulation or sham operation (Fig. 11). Eight animals in the sham group, 6 in the control group, 7 in the HS-5 group, and 8 in the HS-10 group were analyzed. Control animals showed a significant increase of caspase-3 activity in cortex and hippocampus ($P = 0.0003$ versus sham group), which was reduced by hydrogen-rich saline treatment ($P = 0.0008$ versus control group). This result suggests that hydrogen-rich saline treatment ameliorates neuron apoptosis after cardiac arrest/resuscitation.

DISCUSSION

In the present study, we investigated the protective effects of hydrogen-rich saline treatment in a rat model of asphyxia-induced cardiac arrest and its associated mechanisms. Here, we found that IV injection of hydrogen-rich saline dose dependently improves survival and neurological function after cardiac arrest/resuscitation. Moreover, hydrogen-rich saline treatment significantly ameliorated brain injury after cardiac arrest/resuscitation. Furthermore, we found that the beneficial effects of hydrogen-rich saline treatment were associated with decreased levels of oxidative products (8-iso-prostaglandin F2α and malondialdehyde) and inflammatory cytokines (TNF-α, IL-1β, and HMGB1), as well as the increased activity of antioxidant enzymes (superoxide dismutase and catalase) in serum and brain tissues. In addition, hydrogen-rich saline treatment reduced caspase-3 activity in cortex and hippocampus after cardiac arrest/resuscitation.

Asphyxia-induced cardiac arrest is a well-characterized model to study cellular and molecular changes after cardiac arrest/resuscitation.[23,24,27] In this study, using this model, we found that cardiac arrest/resuscitation-challenged rats had significant mortality and brain injury, which is consistent with previous studies.[23,24,27] Nevertheless, hydrogen-rich saline treatment increased the rate of successful resuscitation. Hydrogen gas improved resuscitation perhaps through regulating heart and brain function, or nervous reflex. However, detailed mechanisms of this effect are still unclear.

Cardiac arrest/resuscitation results in significant mortality after initial resuscitation due in most cases to ischemia and reperfusion-induced brain injury and to a lesser degree myocardial dysfunction.[1] The rate of oxidative metabolism in brain is high. Reactive oxygen species are massively produced in the brain after ischemia, and oxidative stress has been regarded as a fundamental mechanism of brain damage after cardiac arrest/resuscitation.[4] Reactive oxygen species include many types such as superoxide anion, hydroxyl radicals, hydrogen peroxide, and so on. Despite their cytotoxic effects, superoxide anion and hydrogen peroxide have an important physiological role at low concentration, which function as regulatory signaling molecules that are involved in numerous signal transduction pathways and regulate biological processes such as apoptosis and cell proliferation.[29] However, hydroxyl radicals are the strongest reactive oxygen species and react indiscriminately with nucleic acids, lipids, and proteins.[6] More importantly, there is no known detoxification system for hydroxyl radicals in vivo. Therefore, scavenging hydroxyl radicals is a critical antioxidant process, which may be a good method for improving the survival and neurological outcome after cardiac arrest/resuscitation.

Interestingly, many studies have demonstrated that hydrogen gas exerts therapeutic antioxidant activity by selectively reducing hydroxyl radicals and effectively

Contents lists available at SciVerse ScienceDirect

Resuscitation

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

Experimental paper

The neuroprotective effects of intraperitoneal injection of hydrogen in rabbits with cardiac arrest☆,☆☆

Guoqing Huang[a,b,d], Jun Zhou[c,d], Wei Zhan[a], Yan Xiong[a], Chunlin Hu[a], Xiangmin Li[b], Xin Li[a], Yingqing Li[a], Xiaoxing Liao[a,*]

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ARTICLE INFO

Article history:
Received 9 July 2012
Received in revised form 11 October 2012
Accepted 18 October 2012

Keywords:
Cardiac arrest
Cardiopulmonary resuscitation
Oxidative stress
Hydrogen

ABSTRACT

Objective: The purpose of this study was to investigate the neuroprotective effects of intraperitoneal injection of hydrogen (H_2) in rabbits with cardiac arrest (CA).
Methods: A rabbit model of CA was established by the delivery of alternating current between the esophagus and chest wall to induce ventricular fibrillation. Before CA, the animals were randomly divided into four groups: a sham group (no CA), a CA group, a CA + low dose (10 ml/kg) H_2 group (CA + H_2 group 1), and a CA + high dose (20 ml/kg) H_2 group (CA + H_2 group 2). In the first experiment, animals were observed for 72 h after the restoration of spontaneous circulation (ROSC). The neurological scores were assessed at 24, 48 and 72 h after ROSC. The rabbits that survived until 72 h were sacrificed using an overdose of anesthetic, and the brain tissues were collected and Nissl-stained to observe nerve cell damage in the hippocampal CA1 area. In addition, TUNEL assay was performed to detect apoptosis. In the second experiment, animals were observed for 6 h after ROSC. Blood samples and brain hippocampal tissues were collected, and differences in oxidative stress indicators were compared among the four groups.
Results: Intraperitoneal injection of H_2 improved the 72-h survival rate and neurological scores, reduced neuronal injury and inhibited neuronal apoptosis. Intraperitoneal injection of H_2 reduced oxidative stress indicators in the plasma and hippocampal tissues and enhanced antioxidant enzyme activity. No significant difference was observed between the two CA groups treated with different doses of H_2.
Conclusions: Intraperitoneal injection of H_2 is a novel hydrogen administration method and can reduce cerebral ischemia-reperfusion injury and improve the prognosis of cardiopulmonary cerebral resuscitation in a rabbit model of CA.

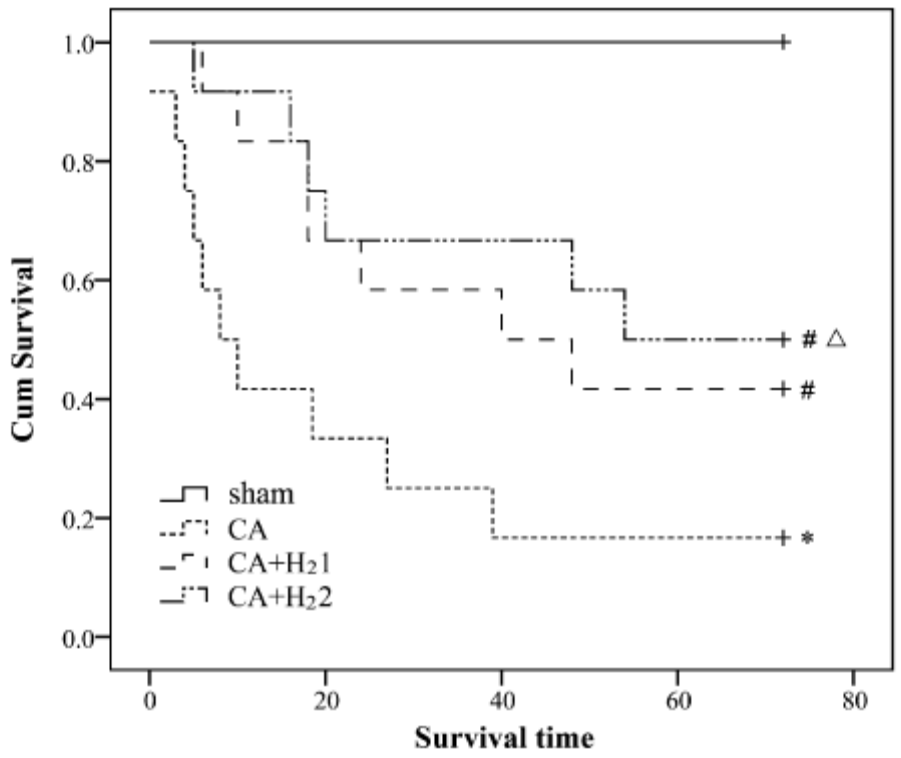


Fig. 1. Survival curves for the 4 groups. $^{\#}P < 0.05$ and $^{*}P < 0.01$ vs. the sham group revealed by Kaplan–Meier survival analysis; $^{\triangle}P < 0.05$ vs. the CA group.

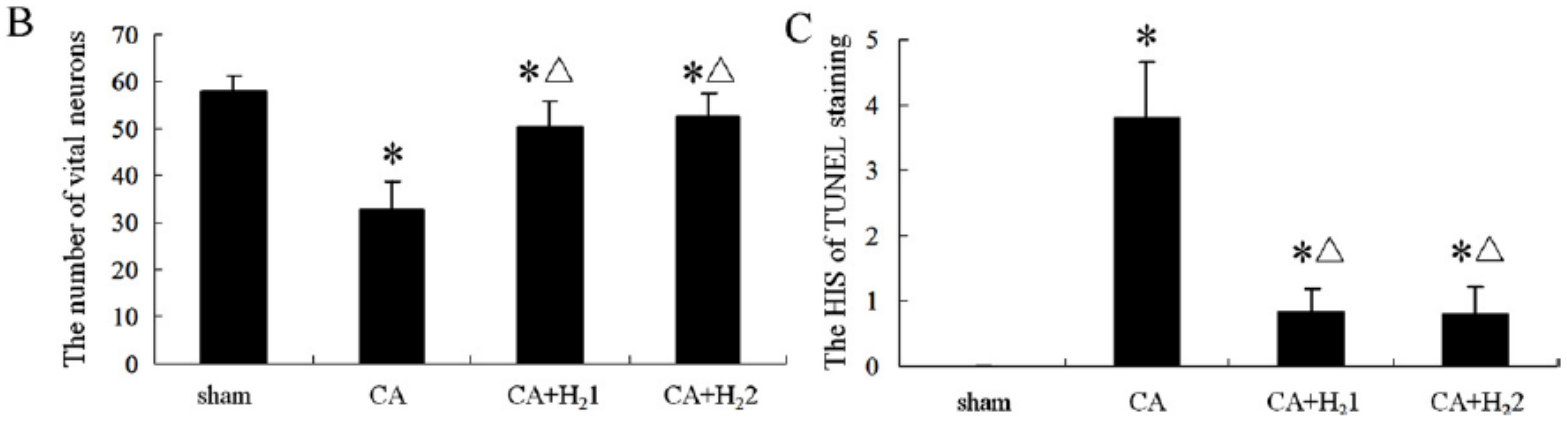


Fig. 3. Nissl staining and TUNEL staining of the hippocampal CA1 area in the 4 groups. (A) The pathological changes in CA1 region; (B) the number of vital neurons; (C) the HIS of TUNEL staining. $^{*}P<0.01$ vs. the sham group; $^{\triangle}P<0.05$ vs. the CA group. Bar = 50 μm.

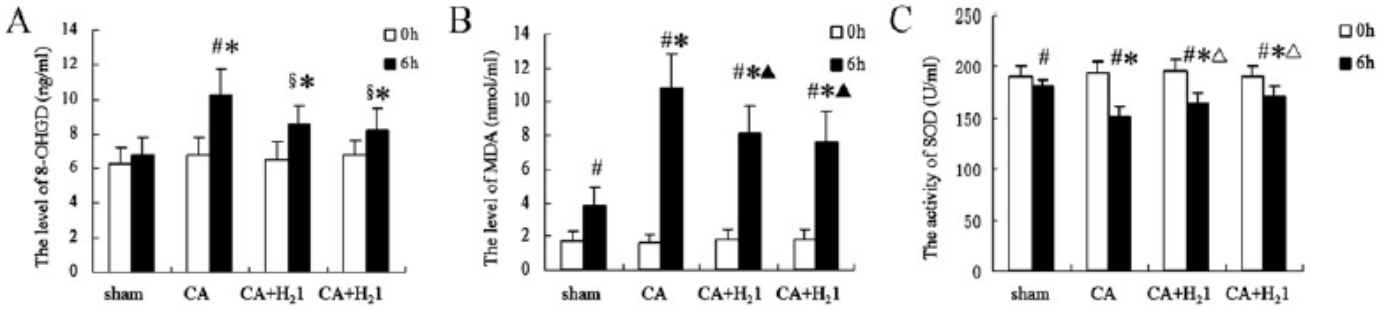


Fig. 4. The biochemical parameters in sera of rabbits from the 4 groups. The level of: (A) 8-OHGD, (B) MDA; (C) the activity of SOD. $^{\#}P<0.01$ of the self-control before and after treatment; $^{\S}P<0.05$ of the self-control before and after treatment; $^{*}P<0.01$ vs. the sham group at the same time point revealed by the LSD test; $^{\triangle}P<0.05$ and $^{\blacktriangle}P<0.01$ vs. the CA group at the same time point revealed by the LSD test.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D. for the ProMISe Trial Investigators

N Engl J Med 2015; 372:1301-1311 | April 2, 2015 | DOI: 10.1056/NEJMoa1500896

BACKGROUND

Early, goal-directed therapy (EGDT) is recommended in international guidelines for the resuscitation of patients presenting with early septic shock. However, adoption has been limited, and uncertainty about its effectiveness remains.

METHODS

We conducted a pragmatic randomized trial with an integrated cost-effectiveness analysis in 56 hospitals in England. Patients were randomly assigned to receive either EGDT (a 6-hour resuscitation protocol) or usual care. The primary clinical outcome was all-cause mortality at 90 days.

RESULTS

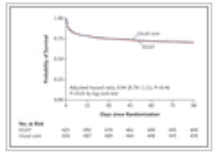
We enrolled 1260 patients, with 630 assigned to EGDT and 630 to usual care. By 90 days, 184 of 623 patients (29.5%) in the EGDT

MEDIA IN THIS ARTICLE

FIGURE 1

Enrollment and Outcomes.

FIGURE 2



Kaplan–Meier Survival Estimates.

The NEW ENGLAND JOURNAL of MEDICINE

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RESULTS

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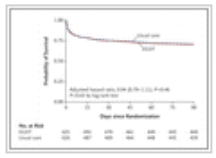
CONCLUSIONS

In patients with septic shock who were identified early and received intravenous antibiotics and adequate fluid resuscitation, hemodynamic management according to a strict EGDT protocol did not lead to an improvement in outcome. (Funded by the United Kingdom National Institute for Health Research Health Technology Assessment Programme; ProMISe Current Controlled Trials number, ISRCTN36307479.)



Kaplan–Meier Survival Estimates.

Extracorporeal membrane oxygenation for critically ill adults (Review)

Tramm R, Ilic D, Davies AR, Pellegrino VA, Romero L, Hodgson C

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2015, Issue 1

http://www.thecochranelibrary.com

Main results

We included four RCTs that randomly assigned 389 participants with acute respiratory failure. Risk of bias was low in three RCTs and high in one RCT. We found no statistically significant differences in all-cause mortality at six months (two RCTs) or before six months (during 30 days of randomization in one trial and during hospital stay in another RCT). The quality of the evidence was low to moderate, and further research is very likely to impact our confidence in the estimate of effects because significant changes have been noted in ECMO applications and treatment modalities over study periods to the present.

Two RCTs supplied data on disability. In one RCT survival was low in both groups but none of the survivors had limitations in their daily activities six months after discharge. The other RCT reported improved survival without severe disability in the intervention group (transfer to an ECMO centre ± ECMO) six months after study randomization but no statistically significant differences in health-related quality of life.

In three RCTs, participants in the ECMO group received greater numbers of blood transfusions. One RCT recorded significantly more non-brain haemorrhage in the ECMO group. Another RCT reported two serious adverse events in the ECMO group, and another reported three adverse events in the ECMO group.

Clinical heterogeneity between studies prevented meta-analyses across outcomes. We found no completed RCT that had investigated ECMO in the context of cardiac failure or arrest. We found one ongoing RCT that examined patients with acute respiratory failure and two ongoing RCTs that included patients with acute cardiac failure (arrest).

Authors' conclusions

Extracorporeal membrane oxygenation remains a rescue therapy. Since the year 2000, patient treatment and practice with ECMO have considerably changed as the result of research findings and technological advancements over time. Over the past four decades, only four RCTs have been published that compared the intervention versus conventional treatment at the time of the study. Clinical heterogeneity across these published studies prevented pooling of data for a meta-analysis.

We recommend combining results of ongoing RCTs with results of trials conducted after the year 2000 if no significant shifts in technology or treatment occur. Until these new results become available, data on use of ECMO in patients with acute respiratory failure remain inconclusive. For patients with acute cardiac failure or arrest, outcomes of ongoing RCTs will assist clinicians in determining what role ECMO and ECPR can play in patient care.

Extracorporeal Membrane Oxygenation for Resuscitation and Cardiac Arrest Management

Massimo Massetti, MD[a], Mario Gaudino, MD[a,*], Stefano De Paulis, MD[b], Andrea Scapigliati, MD[b], Franco Cavaliere, MD[b]

KEYWORDS

• ECMO • Cardiac arrest • Cardiopulmonary resuscitation • ECMO network

KEY POINTS

- The integration of extracorporeal membrane oxygenation (ECMO) technology into current strategies for cardiopulmonary resuscitation seems promising.
- Even in the absence of randomized trials and with a limited level of scientific evidence, several investigators have reported sound clinical benefits with the application of extracorporeal circulatory support in patients after cardiac arrest, both in and out of the hospital.
- ECMO support should be accompanied by a strategy of end-organ protection and (ideally) treatment.
- The recently developed concept of ECMO network extends the potential benefits of ECMO therapy to primary care centers and remote locations and is likely to grow considerably in the near future.

Tsukahara et al. Journal of Intensive Care (2014) 2:68
DOI 10.1186/s40560-014-0068-x

JOURNAL OF INTENSIVE CARE

RESEARCH Open Access

Current experience and limitations of extracorporeal cardiopulmonary resuscitation for cardiac arrest in children: a single-center retrospective study

Kohei Tsukahara[1,2*], Chiaki Toida[1] and Takashi Muguruma[1]

Abstract

Background: There are few reports detailing the importance of extracorporeal membrane oxygenation (ECMO) for pediatric cardiac arrest in Japan. We investigated the status and issues surrounding extracorporeal cardiopulmonary resuscitation (ECPR) at our institution.

Methods: Patients aged <15 years who underwent ECPR between April 1, 2003 and March 31, 2012 were eligible. The characteristics, cannulation site, durations of cardiopulmonary resuscitation (CPR), cannulation procedure, and ECMO, and neurologic outcomes were retrospectively reviewed. A favorable neurologic outcome was defined as Pediatric Cerebral Performance Categories 1 and 2.

Results: A total of 21 ECPR events were identified. The median CPR and cannulation durations were 60 and 25 min, respectively. Central and peripheral access sites were employed in 15 and six cases, respectively. Five of the 21 patients (24%) were successfully weaned from ECMO and three of the 21 (14%) survived. Two of the three survivors had a favorable neurologic outcome.

Conclusions: The mortality of patients undergoing ECPR at our institution was low. However, about 10% of all patients had a favorable neurologic outcome, which suggests that ECPR may be effective in pediatric cardiac arrest patients.

Keywords: Pediatric intensive care, Cardiac arrest, Extracorporeal membrane oxygenation, Extracorporeal cardiopulmonary resuscitation

European Heart Journal
Acute Cardiovascular Care
EUROPEAN SOCIETY OF CARDIOLOGY®

Review

European Heart Journal: Acute Cardiovascular Care
2(2) 118–126

DOI: 10.1177/2048872613484687
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Venous-arterial extracorporeal membrane oxygenation for refractory cardiac arrest: a clinical challenge

Chiara Lazzeri[1], Pasquale Bernardo[1], Andrea Sori[1], Lisa Innocenti[1], Pierluigi Stefano[2], Adriano Peris[3], Gian F Gensini[1] and Serafina Valente[1]

Abstract

Guidelines stated that extracorporeal membrane oxygenation (ECMO) may improve outcomes after refractory cardiac arrest (CA) in cases of cardiogenic shock and witnessed arrest, where there is an underlying circulatory disease amenable to immediate corrective intervention. Due to the lack of randomized trials, available data are supported by small series and observational studies, being therefore characterized by heterogeneity and controversial results. In clinical practice, using ECMO involves quite a challenging medical decision in a setting where the patient is extremely vulnerable and completely dependent on the medical team's judgment. The present review focuses on examining existing evidence concerning inclusion and exclusion criteria, and outcomes (in-hospital and long-term mortality rates and neurological recovery) in studies performed in patients with refractory CA treated with ECMO. Discrepancies can be related to heterogeneity in study population, to differences in local health system organization in respect of the management of patients with CA, as well as to the fact that most investigations are retrospective. In the real world, patient selection occurs individually within each center based on their previous experience and expertise with a specific patient population and disease spectrum. Available evidence strongly suggests that in CA patients, ECMO is a highly costly intervention and optimal utilization requires a dedicated local health-care organization and expertise in the field (both for the technical implementation of the device and for the intensive care management of these patients). A careful selection of patients guarantees optimal utilization of resources and a better outcome.

- In patients with refractory CA, ECMO is a highly costly intervention and optimal utilization requires a dedicated local health-care organization and expertise in the field (both for the technical implementation of the device and for the intensive care management of these patients). The health-care pathways of patients suffering from CA (both IHCA and OHCA) should be locally organized in detail in order to avoid wasting of time and to guarantee the optimal resource utilization. An ECMO center can be implemented only where a cardiac surgery unit is available and an ECMO team (including an intensivist trained in acute cardiac patient care, a cardiac surgeon, a cardiopulmonary technician) has to be available 24 h/7 d.

Outcomes (survival and neurological function) of CA patients treated with ECMO are strictly dependent on two factors: (a) expertise of the ECMO team (in technical skills for implantation and, especially, in intensive care); (b) a careful selection of patients. That is why the impact of ECMO implantation in CA patients can be considered a clinical challenge, since it is strictly linked to the 'clinical selection of patients', and not only to technically skills. Though in this emergency setting it is quite difficult to gain information concerning historical data of the patient, inclusion and exclusion criteria are of paramount importance. The following exclusion criteria should be considered: previous severe neurologic damage, current intracranial hemorrhage, malignancy in the terminal stage, irreversible organ failure leading to CA when no physiological benefit could be expected despite maximal therapy (i.e. hepatic failure), aortic dissection, severe peripheral arterial disease, and patients who previously signed 'do-not-resuscitate' orders. Inclusion criteria should be as follows: (a) age <75 years; (b) estimated interval of ≤15 min from the time of collapse to CPR with or without witnessed CA, independently of rhythm of presentation; (c) failure to achieve ROSC within 20 min of conventional CPR administered by medical personnel. Written informed consent for ECPR was obtained from family members, to justify that they

- The most important target to be pursed in CA patients treated with ECMO is to identify the 'reversible cause' (i.e. drowning, drug intoxication, hypothermia, Takotsubo Syndrome, myocarditis, acute coronary syndrome) of CA since it has to be treated in due time and the ECMO device gives us the opportunity (time) to do it. In other terms, i.e. in a patient with CA treated with ECMO if acute coronary syndrome is suspected, coronary angiography and eventually mechanical revascularization can be performed after ECMO implantation and initiation of hypothermia.

- When the ‘reversible cause’ of CA is identified and treated, management of ECMO patients mainly consists of organ support therapies (i.e. renal replacement therapy) and, most importantly, serial neurological assessments (by means of electroencephalogram (EEG) and somato-sensory evoked potentials). Neurological evaluations, since the first 12–24 h, play a pivotal role in the risk assessment of these patients. For example, the identification of EEG patters of brain death raises serious doubts for continuing on ECMO support.

- ECMO futility. Due to the lack of recommendations and guidelines, the decision not to implant ECMO is a hard decision which, in the real world, has to be taken in quite a short time. Taking into account available data and our experience, ECMO is not to be implanted in the presence of even one exclusion criteria or whenever the ECMO team is not alerted in due time. On the other hand, two factors may trigger the decision to stop ECMO: (a) the evidence of brain death; (b) the fact that, in lack of recovery, the patient is not considered eligible for transplantation.

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

Cardiopulmonary Resuscitation Support Application on a Smartphone

– Randomized Controlled Trial –

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Background: This simulation trial aimed to compare the quality of cardiopulmonary resuscitation (CPR) with and without the newly-developed CPR support application on smartphones.

Methods and Results: In this trial, participants were randomly assigned to either the CPR support application group or the control group, stratified by sex and previous CPR training. Participants' CPR skills were evaluated by a 2-min case-based scenario test using the Leardal Resusci Anne PC Skillreporting Manikin System®. The outcome measures were the proportion of chest compressions performed in each group and the number of total chest compressions and appropriate chest compressions performed during the 2-min test period. A total of 84 participants were enrolled and completed the protocol. All participants in the CPR support application group performed chest compressions, compared with only 31 (75.6%) in the control group (P<0.001). Among participants who performed chest compressions during the 2-min test period, the number of total chest compressions was significantly higher in the CPR support application group than in the control group (211.6±29.5 vs. 77.0±43.3, P<0.001). The number of appropriate chest compressions tended to be greater in the CPR support application group than in the control group, although it was statistically insignificant (30.3±57.3 vs. 17.2±28.7, P=0.246).

Conclusions: In this cohort of laypersons, the newly-developed CPR support application for smartphones contributed to increasing the implementation rate and the number of total chest compressions performed and may assist in improving the survival rate for out-of-hospital cardiac arrests (UMIN000004740).

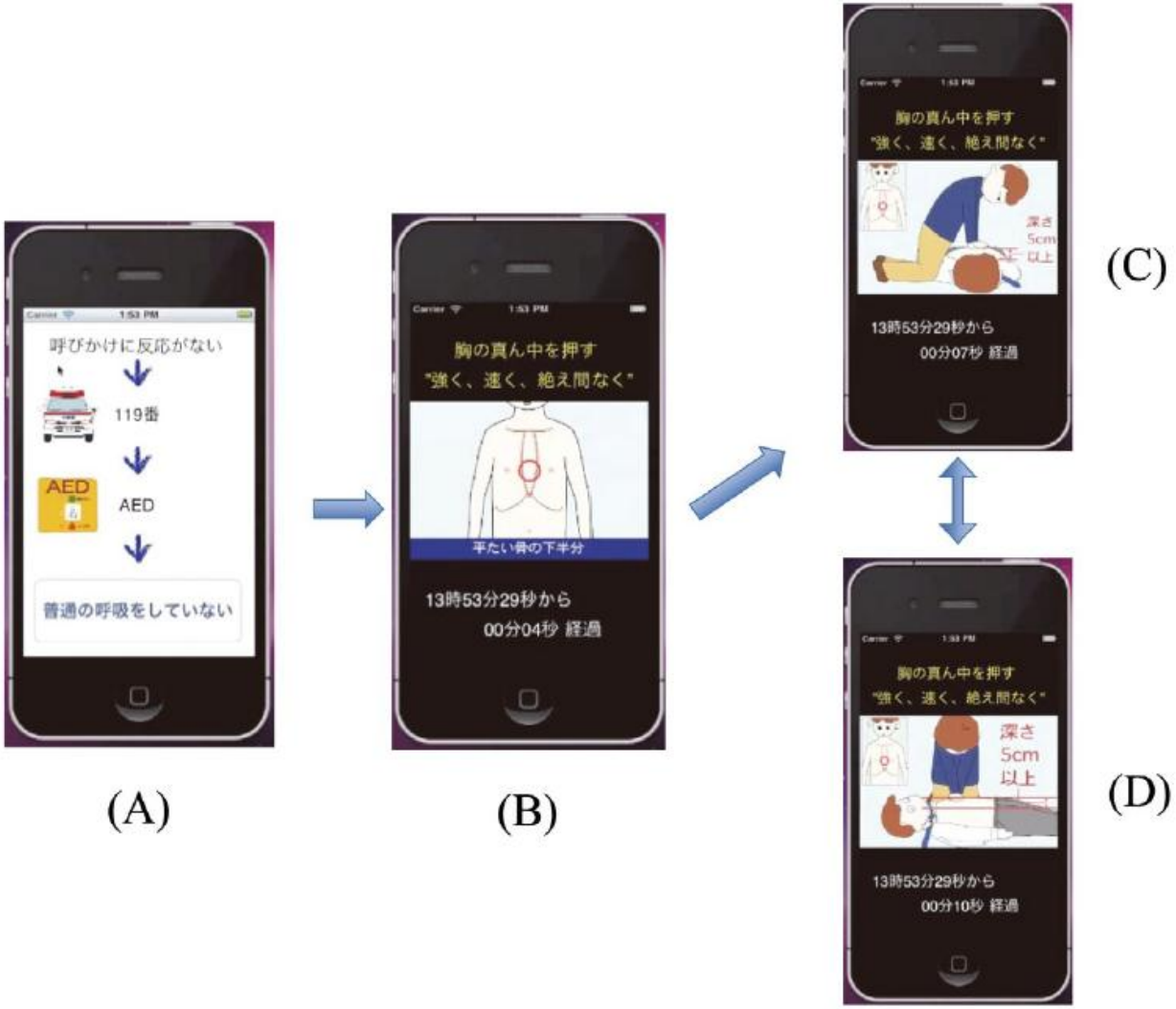

Figure 1. An overview of the smartphone application for cardiopulmonary resuscitation (CPR) support. (**A**) Response check, emergency call to 119 (in Japan) and request for an AED, and breathing check. (**B**) Hand position. Messages read: "Push the center of chest. Push hard, quickly, and without interruption." Progress time from start of CPR is shown at the bottom of the image in (**C**,**D**). Compression depth. Message reads: "At least 5 cm depth." (**B**–**D**) Metronome rhythm of 110 beats/min.

Table 3. Resuscitation Skills of the Participants in a Study of a Newly-Developed Support Application on Smartphones According to Prior Training in CPR

	CPR trained			Not CPR trained		
	CPR support application group (n=27)	Control group (n=25)	P value	CPR support application group (n=16)	Control group (n=16)	P value
Activation of EMS, n (%)						
Call 119 (in Japan)	20 (74.1)	14 (56.0)	0.141	9 (56.2)	5 (31.2)	0.143
Call for AED	18 (66.7)	6 (24.0)	0.002	8 (50.0)	3 (18.8)	0.068
Chest compressions performed, n (%)	27 (100.0)	20 (80.0)	0.020	16 (100.0)	11 (68.8)	0.043
Chest compressions during 2-min test period, n, mean±SD*						
Total chest compressions	211.0±33.9	91.6±44.1	<0.001	212.8±21.1	50.6±27.4	<0.001
Appropriate chest compressions	39.5±64.4	17.4±31.0	0.163	14.6±39.9	16.8±25.3	0.874
Chest compressions with correct hand position	119.2±89.4	46.2±42.3	0.002	91.8±99.0	36.1±17.1	0.078
Chest compressions with appropriate depth	70.3±74.2	49.5±53.1	0.291	57.9±73.8	22.9±35.7	0.158
Compression depth (mm)	36.2±9.0	39.5±9.8	0.237	32.9±9.4	31.6±15.2	0.785
Resuscitation time course (s), mean±SD						
Time to first chest compression or first ventilation	39.9±18.3	32.0±14.2	0.114	32.3±16.8	24.6±12.1	0.201
Time to chest compression	39.9±18.3	33.5±15.6	0.215	32.3±16.8	27.6±13.2	0.438
Time without chest compression	5.7±14.6	60.7±22.6	<0.001	2.2±2.7	69.4±24.0	<0.001

*Calculated only for those who performed chest compressions. Abbreviations as in Tables 1,2.

A Randomized Controlled Trial of a CPR and Intubation Video Decision Support Tool for Hospitalized Patients

Areej El-Jawahri, MD[1,2], Susan L. Mitchell, MD, MPH[2,3], Michael K. Paasche-Orlow, MD, MPH[4], Jennifer S. Temel, MD[1,2], Vicki A. Jackson, MD[1,2], Renee R. Rutledge, MD[5], Mihir Parikh, MD[6], Aretha D. Davis, MD, JD[2,7], Muriel R. Gillick, MD[2,8], Michael J. Barry, MD[1,2], Lenny Lopez, MD, MPH[1,2], Elizabeth S. Walker-Corkery, MPH[1], Yuchiao Chang, PhD[1,2], Kathleen Finn, MD[1,2], Christopher Coley, MD[1,2], and Angelo E. Volandes, MD, MPH[1,2]

[1]Hematology-Oncology Department, Massachusetts General Hospital, Boston, MA, USA; [2]Harvard Medical School, Boston, MA, USA; [3]Hebrew Senior Life Institute for Aging Research, Boston, MA, USA; [4]Boston University, Boston, MA, USA; [5]Oregon Health & Sciences University, Portland, OR, USA; [6]University of California San Francisco, San Francisco, CA, USA; [7]Mount Auburn Hospital, Cambridge, MA, USA; [8]Harvard Pilgrim Health Care Institute, Boston, MA, USA.

PARTICIPANTS: One hundred and fifty seriously ill hospitalized patients over the age of 60 with an advanced illness and a prognosis of 1 year or less were included. Mean age was 76 and 51 % were women.

INTERVENTION: Three-minute video describing CPR and intubation plus verbal communication of participants' preferences to their physicians (intervention) (N=75) or control arm (usual care) (N=75).

MAIN MEASURES: The primary outcome was participants' preferences for CPR and intubation (immediately after viewing the video in the intervention arm). Secondary outcomes included: orders to withhold CPR/intubation, documented discussions with providers during hospitalization, and participants' knowledge of CPR/ intubation (five-item test, range 0–5, higher scores indicate greater knowledge).

RESULTS: Intervention participants (vs. controls) were more likely not to want CPR (64 % vs. 32 %, p <0.0001) and intubation (72 % vs. 43 %, p<0.0001). Intervention participants (vs. controls) were also more likely to have orders to withhold CPR (57 % vs. 19 %, p<0.0001) and intubation (64 % vs.19 %, p<0.0001) by hospital discharge, documented discussions about their preferences (81 % vs. 43 %, p<0.0001), and higher mean knowledge scores (4.11 vs. 2.45; p<0.0001).