Predictors of Favourable Neurological Outcomes in a Territory-First E-CPR Program

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Abstract

Background: Extracorporeal cardiopulmonary resuscitation (E-CPR) is an alternative resuscitation method that has been associated with better survival and neurological outcomes in both in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA) compared with conventional cardiopulmonary resuscitation (CPR). This study aims to report the results of the territory-first E-CPR program at Queen Mary Hospital, and identify factors that predict favorable patient outcomes.

Methods: This is a single center, retrospective analysis of all patients who had OHCA or IHCA and were managed with E-CPR at Queen Mary Hospital from 2012-2020. The primary outcome was favorable neurological outcome at 3 months, defined as Cerebral Performance Categories scale 1 or 2. Secondary outcomes include ICU survival and hospital survival.

Results: From 2012-2020, a total of 102 patients received E-CPR – 48 (47.1%) were patients who suffered from OHCA, and 54 (52.9%) from IHCA. Of the 102 patients, 63 (61.8%) were diagnosed with myocardial infarction, 11 (10.8%) were diagnosed with acute myocarditis, and 5 (4.9%) were diagnosed with pulmonary embolism. 19 (18.6%) patients survived with favorable neurological outcome at 3 months. The overall 30-day survival was 32.3%, while ICU survival was 33.3%. Having a shockable first documented rhythm was the strongest predictor of favorable neurological outcome in both univariate ($p < 0.001$) and multivariate analysis (odds ratio 8.49; 95% CI, 1.76 to 40.93; $p = 0.008$). Patients with favorable neurological outcome were also more likely to have received percutaneous coronary intervention (PCI) after completion of E-CPR ($p = 0.007$), lower aspartate aminotransferase (AST) ($p = 0.003$) and bicarbonate ($p = 0.009$) levels within 24 hours after E-CPR, defibrillation during CPR ($p = 0.006$), and myocardial infarction as the cause of cardiac arrest ($p = 0.026$).

Introduction

E-CPR (extracorporeal cardiopulmonary resuscitation):

- An advanced resuscitation method incorporating the utility of veno-arterial extracorporeal membrane oxygenation (V-A ECMO) to achieve adequate circulation and organ perfusion in patients with refractory cardiac arrest (CA)
- Associated with improved survival rates and neurologic outcomes compared with conventional CPR for both patients with in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA). [1]
- A pilot randomized control trial in patients with OHCA showed that E-CPR resulted in significantly improved survival to hospital discharge. [2]

The first E-CPR program in Hong Kong for patients with refractory cardiac arrest was started in Queen Mary Hospital, a tertiary medical center in 2012.

Objectives:

1. Report the outcomes of the territory-first E-CPR program
2. Identify factors predicting favorable patient survival and neurological outcomes after E-CPR
3. Examine the utility of the SAVE score, ECPR score and the nECPR score in predicting patient outcomes

Methodology

Design: Single center retrospective analysis of patients who received E-CPR in Queen Mary Hospital

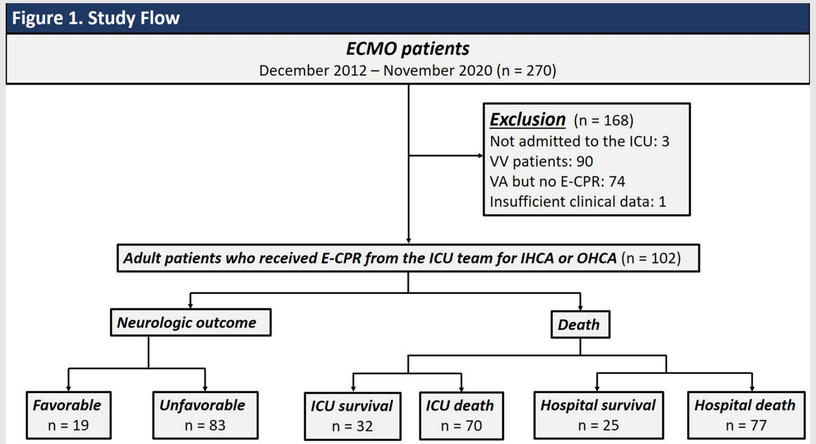
Study population: All adult patients who received E-CPR from the ICU team for IHCA or OHCA from Dec 2012 to Nov 2020

Primary outcome: 3-month neurological outcome*

Statistical analysis:
Predictors of favorable neurological outcome were selected a priori based on biological plausibility and literature review. Variables that were significantly associated with the outcome in univariate analyses were included in multivariable logistic regression. The performance of the SAVE and ECPR scores in predicting hospital mortality, and nECPR score in predicting favorable neurological outcome were assessed by logistic regression with the concordance C statistic.

* Defined as Cerebral Performance Categories (CPC) scale 1 or 2 [3]

Figure 1. Study Flow

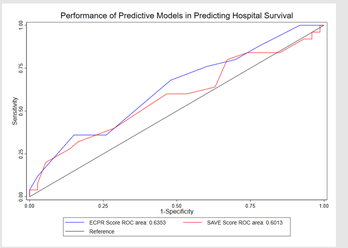


Characteristic	All patients (n = 102)	Favorable neurologic outcome (n = 19)	Unfavorable neurologic outcome (n = 83)	P-value
Age, years	54 (45 - 61)	54 (50 - 61)	55 (41 - 61)	0.76
Male	73 (72%)	15 (79%)	58 (70%)	0.36
APACHE II score	36.5 (31 - 40)	33 (29 - 38)	37 (33 - 40.5)	***0.014‡***
In-hospital cardiac arrest	54 (53%)	10 (53%)	44 (53%)	0.98
Shockable first documented rhythm	53 (52%)	17 (89%)	36 (43%)	***<0.001‡***
Defibrillation during CPR	63 (62%)	17 (89%)	46 (55%)	***0.006‡***
PCI after ECMO established	37 (36%)	12 (63%)	25 (30%)	***0.007‡***
First Mean Arterial Pressure post ECMO, mmHg	82 (55 - 100)	103 (86 - 125)	72 (53 - 94)	***0.009‡***
ECPR due to:				
· MI	63 (62%)	16 (84%)	47 (57%)	***0.026‡***
· Myocarditis	11 (11%)	1 (5%)	10 (12%)	0.390
· Pulmonary embolism	5 (5%)	0 (0%)	5 (6%)	0.273
Worst biochemistry results within 24 hours after E-CPR initiation				
pH	7.05 (6.91 - 7.17)	7.09 (6.99 - 7.20)	7.05 (6.89 - 7.17)	0.16
PaO2 (kPa)	10.8 (6.8 - 25.4)	10.3 (7.7 - 12.1)	11.3 (6.1 - 29.0)	0.52
Base excess (mmol/L)	-20 (-25.2 - -14.8)	-16.9 (-21.3 - -14)	-20.6 (-26 - -15)	***0.036***
Bicarbonate (mmol/L)	9.2 (6.3 - 12.1)	11.7 (9.5 - 12.6)	8.6 (5.6 - 11)	***0.009‡***
Lactate (mmol/L)	13.3 (10.7 - 20.4)	10.6 (8.6 - 17.0)	14.2 (10.9 - 20.9)	***0.041***
Creatinine (umol/L)	191 (137 - 255)	161 (127 - 231)	196.5 (144 - 267)	0.13
Troponin T (ng/L)	12120 (2964 - 37170)	10470 (5475 - 17300)	12480 (2021 - 42270)	0.91
ALT (U/L)	305 (150 - 598)	208 (127 - 366)	353 (150 - 719)	0.087
AST (U/L)	1013 (474 - 2050)	563 (408 - 872)	1225 (558 - 2535)	***0.003‡***
Platelet ($x10^9$/L)	110 (55 - 158)	133 (88 - 182)	106 (54 - 149)	0.17
White blood cells ($x10^9$/L)	17.5 (12.5 - 22.8)	18.4 (16.2 - 24.4)	16.5 (12.2 - 22.2)	0.18

Table 1. Baseline Characteristics of ECPR Patients

‡ indicates favorable neurologic outcomes

(a)



(b)

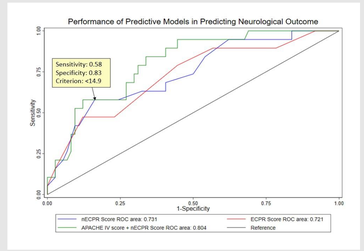


Figure 2. Receiver Operating Characteristic curves (ROC) of (a) SAVE score and ECPR score against hospital survival, (b) ECPR score, nECPR score, and nECPR score incorporating APACHE IV score against neurological outcome

Discussion

In this territory-first E-CPR program in Hong Kong, the rate of survival with favorable neurological outcome was 18.6% with a hospital survival of 24.5% and 30-day survival of 32.3%.

In our cohort the presence of a shockable first documented rhythm is the strongest predictor for favorable neurologic outcome in both univariate and multivariate analysis, with almost a 10-fold increase in the rate of favorable neurological outcome.

Our study found a strong correlation between high AST levels, a clinical marker of hypoxic hepatitis, within the first 24 hours after resuscitation and poor neurological outcome. Furthermore, AST may be useful in suggesting widespread tissue ischemia since it is present in multiple organs and tissues [4]. However, current literature on the use of AST as a marker of hypoxic damage due to CA is lacking. Further prospective studies may be required to explore the implications of high AST levels and patient outcomes after CA.

The nECPR score performed better at predicting 3-month neurological outcomes of E-CPR patients in our cohort than the ECPR score. Furthermore, we showed that incorporating the APACHE score in addition to the nECPR score improves the discrimination of the model. APACHE scores are routinely collected in ICU settings, and the combination of the two scores has better prognostic value in the care of E-CPR patients.

Conclusion

Among patients who received E-CPR, those who had a shockable rhythm at presentation, defibrillation during E-CPR, higher MAP after ECMO cannulation, lower AST or lactate, or higher bicarbonate or base excess values in the first 24 hours after E-CPR, cardiac arrest due to myocardial infarction, or PCI after E-CPR had better neurological outcomes. The nECPR score was useful in predicting neurological outcome after E-CPR, and incorporation of the APACHE IV score can improve the model's performance.

References

1: Wang GN, Chen XF, Qiao L, et al. Comparison of extracorporeal and conventional cardiopulmonary resuscitation: A meta-analysis of 2 260 patients with cardiac arrest. *World J Emerg Med*. 2017;8(1):5-11.
2: Yannopoulos D, Bartos J, Raveendran G, et al. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. *The Lancet (British edition).* 2020;396(10265):1807-1816.
3: Jennett B, Bond M. ASSESSMENT OF OUTCOME AFTER SEVERE BRAIN DAMAGE: A Practical Scale. *The Lancet.* 1975;305(7905):480-484.
4: Weibrecht K, Dayno M, Darling C, Bird SB. Liver Aminotransferases Are Elevated with Rhabdomyolysis in the Absence of Significant Liver Injury. *J Med Toxicol.* 2010;6(3):294-300.

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