Clinical outcomes after rescue extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest

Tae Sun Ha,[1] Jeong Hoon Yang,[1,2] Yang Hyun Cho,[3] Chi Ryang Chung,[1] Chi-Min Park,[1] Kyeongman Jeon,[1,4] Gee Young Suh[1,4]

[1]Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[2]Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[3]Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[4]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Correspondence to
Dr Jeong Hoon Yang, Department of Critical Care Medicine and Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 135-710, South Korea; jhysmc@gmail.com

Received 9 March 2015
Revised 25 March 2016
Accepted 11 June 2016
Published Online First 29 June 2016

To cite: Ha TS, Yang JH, Cho YH, *et al. Emerg Med J* 2017;**34**:107–111.

ABSTRACT

Aim Extracorporeal cardiopulmonary resuscitation (ECPR) has been shown to have survival benefit in patients who had in-hospital cardiac arrest (IHCA). However, limited data are available on the role of extracorporeal membrane oxygenation (ECMO) for out-of-hospital cardiac arrest (OHCA). Therefore, we aimed to investigate clinical outcomes and predictors of in-hospital mortality in patients who had OHCA and who underwent ECPR.

Methods From January 2004 to December 2013, 235 patients who received ECPR were enrolled in a retrospective, single-centre, observational registry. Among those, we studied 35 adult patients who had OHCA. The primary outcome was in-hospital mortality.

Results Among 35 patients with a median age of 55 years (IQR 45–64), 29 (82.9%) of whom were male, ECMO implantation was successful in all and 10 patients (28.6%) lived to be discharged from the hospital. In 18 cases (51.4%), first monitored rhythms were identified as ventricular tachycardia/ventricular fibrillation, that is, shockable rhythm. There were no differences between in-hospital survivors and non-survivors regarding median time of arrest to cardiopulmonary resuscitation (CPR) (survivors: 23.5 min (IQR 18.8–27.3) vs non-survivors: 20.0 min (IQR 15.0–24.5); p=0.41) and median time of CPR to ECMO pump-on (survivors: 61.0 min (IQR 39.8–77.8) vs non-survivors 50.0 min (IQR 44.0–72.5); p=0.50). In 23 cases (65.7%), ischaemic heart disease was diagnosed and successful revascularisation was achieved in a significantly higher proportion of the survivor group (8/10 (80.0%)) than the non-survivor group (8/25 (32.0%)) (p=0.02). Witnessed arrest (HR=3.96; 95% CI 1.38 to 11.41; p=0.01), bystander CPR (HR=4.05; 95% CI 1.56 to 10.42; p=0.004) and successful revascularisation (HR=2.90; 95% CI 1.23 to 6.86; p=0.02) were independent predictors of survival-to-discharge in patients who had OHCA in univariate Cox regression analysis.

Conclusion Survival rate for ECPR in the setting of OHCA remains poor. Our findings suggest that ECMO implantation should be very carefully considered in highly selected patients who had OHCA with little no-flow time and a reversible cause.

Key messages

What is already known on this subject?

- Survival rates after out-of-hospital cardiac arrest have remained unchanged or improved only slightly over the past few decades.
- Extracorporeal cardiopulmonary resuscitation should be considered for in-hospital patients in cardiac arrest.

What might this study add?

- Survival rate for extracorporeal cardiopulmonary resuscitation in the setting of out-of-hospital cardiac arrest is poor.
- Predictors of survival to discharge in patients with out-of-hospital cardiac arrest were witnessed arrest, prehospital bystander cardiopulmonary resuscitation and successful revascularization.

INTRODUCTION

Cardiopulmonary resuscitation (CPR) of patients who had out-of-hospital cardiac arrest (OHCA) remains a critical situation with high immediate mortality despite the improvement in resuscitation methods and the spread of automatic defibrillator. Recent studies have shown that survival rates after OHCA have remained unchanged or improved only slightly over the past few decades.[1–3] Extracorporeal membrane oxygenation (ECMO) in the setting of CPR, sometimes called extracorporeal CPR (ECPR), has been suggested as a therapeutic option in refractory cardiac arrest.[4] ECMO can achieve normal oxygen delivery by providing sufficient perfusion of vital organs during treatment of the cause of cardiac arrest, thereby effectively reducing the 'no-flow time'.[5] The American Heart Association proposed that ECPR should be considered for in-hospital patients in cardiac arrest when the duration of no-flow arrest is brief and the conditions leading to the cardiac arrest are reversible or amenable to heart transplantation or revascularisation.[6] Recent studies reported that early application of ECMO improved the prognosis of prolonged cardiac arrest in the context of in-hospital cardiac arrest (IHCA) compared with conventional CPR alone.[7] However, limited data are available on the role of ECMO for OHCA. Therefore, we investigated clinical outcomes and predictors of survival-to-discharge of patients who had OHCA and who underwent ECPR.

METHODS

Study population

We retrospectively analysed our ECMO data registry of 35 patients treated with ECMO for refractory OHCA among 696 patients treated with ECMO life support at Samsung Medical Center (a 1960-bed, university-affiliated, tertiary hospital in 10.36 million residents city Seoul, Korea) from January 2004 to December 2013. Exclusion criteria were as follows: IHCA, unrelated CPR, age <18 years, terminal malignancies or expected lifespan of <1 year and veno-veno-type ECMO. This study received Institutional Review Board approval and informed consent was waived. Clinical, laboratory and outcome data were collected by a trained study coordinator using a standardised case report form. All cardiac arrest-related data, including location of arrest, first monitored arrest rhythm, resuscitation time and use of a defibrillator, were collected from the emergency medical services. Similarly, past medical history, onset time and/or elapsed time of cardiac arrest, circumstances of cardiac arrest and information on bystander CPR were collected through interview with members of the family and witnesses to the arrest. Initially, all patients were treated by emergency room physicians without interruption of treatment until ECMO implantation.

Definition and outcomes

The use of ECMO was considered for patients who underwent prolonged CPR (>10 min) without sustained return of spontaneous circulation (ROSC). Definition of sustained ROSC was continuous maintenance of spontaneous circulation for ≥20 min. ECPR was defined as intention-to-treat with haemodynamic ECMO support during cardiac massage regardless of interim ROSC.[8] Successful revascularisation was defined as final residual stenosis of <20% of the vessel diameter with thrombolysis in myocardial infarction flow grade of ≥2 after revascularisation as assessed by visual estimation of the angiograms.[9] Cerebral performance category (CPC) scores were obtained from medical records and scored on the day of discharge from the hospital. Good neurological status was defined as a CPC score of 1 or 2.[2] The primary outcome was survival-to-discharge and the secondary outcome was a CPC score of 1 or 2.

ECMO system and management

Percutaneous cannulation of the femoral vein and artery was performed mostly using Seldinger technique by the attending staff interventional cardiologist or cardiovascular surgeon, without interruption of chest compression. Femoral cut-down procedures were performed when it was difficult to puncture the femoral artery percutaneously, such as patients with peripheral artery disease or severe obesity. The Capiox Emergency Bypass System (Terumo, Tokyo, Japan) was used in all cases. Vascular cannula size was 14–18 Fr for artery and 21–28 Fr for vein. Anticoagulation was accomplished by bolus injection of unfractionated heparin, followed by continuous intravenous infusion of heparin to maintain an activated clotting time between 150 and 200 s. After ECMO initiation, pump blood flow rate was set above 2.2 L/min/body surface area (m^2) initially and was adjusted subsequently to maintain a mean arterial pressure (MAP) of above 65 mm Hg. BP was monitored continuously through an arterial catheter and ABG analysis was performed in the artery of the right arm to estimate cerebral oxygenation. Additional fluids, blood transfusion and/or catecholamines (norepinephrine, epinephrine or dobutamine) were supplied to maintain intravascular volume and/or to achieve a MAP of >65 mm Hg, if necessary. If hypoperfusion of the leg was suspected, as noted on physical examination and Doppler ultrasound of the femoral artery, an additional 7–9 Fr percutaneous catheter distal to the ECMO arterial cannula was placed into the superficial femoral artery.

Statistical analysis

Results are reported as medians and quartiles (IQRs) or percentages. Continuous variables were compared using the Mann-Whitney U test and categorical data were analysed using χ^2 test or Fisher's exact test as appropriate. Univariate Cox regression analysis was used to determine independent predictors of in-hospital mortality. Multivariate Cox regression analysis was inappropriate due to the small sample size. Survival curves were constructed using Kaplan-Meier estimates and compared with the log-rank test. All tests were two-tailed and a p value <0.05 was considered statistically significant. Statistical tests were performed using SPSS software (V.18.0; SPSS, Chicago, Illinois, USA) for Windows.

RESULTS

Baseline and arrest characteristics

Between January 2004 and December 2013, a total of 235 patients received ECPR for cardiac arrest, including 200 patients who had IHCA and 35 patients who had OHCA. Figure 1 summarises the patient flow in this study. Baseline characteristics of our study populations are summarised in table 1. There were no significant differences in baseline characteristics between survivors and non-survivors. All survivors were male and younger than 65 years. Arrest and resuscitation characteristics of patients are shown in table 2. The most common cause of OHCA was cardiogenic origin. Of the 10 OHCA survivors, 7 had a shockable rhythm (ventricular fibrillation and /or ventricular tachycardia) on the initial ECG and 29 patients who had OHCA were witnessed arrest (82.9%). Bystander CPR were performed in nine (90.0%) of the survivors compared with six (24.0%) of the non-survivors (p=0.001). There was no significant difference in arrest-to-hospital arrival time (survivors: 23.5 min (IQR 18.8–27.3) vs non-survivors 20.0 min (IQR 15.0–24.5); p=0.41) and hospital arrival-to-ECMO implantation time (survivors: 61.0 min (IQR 39.8–77.8) vs non-survivors 50.0 min (IQR 44.0–72.5); p=0.50) between the two groups. However, survivors had a high prevalence of successful revascularisation as compared with non-survivors (8(80.0%) vs 8(32.0%), p=0.02). All patients in the survivor group (100%) and three patients in the

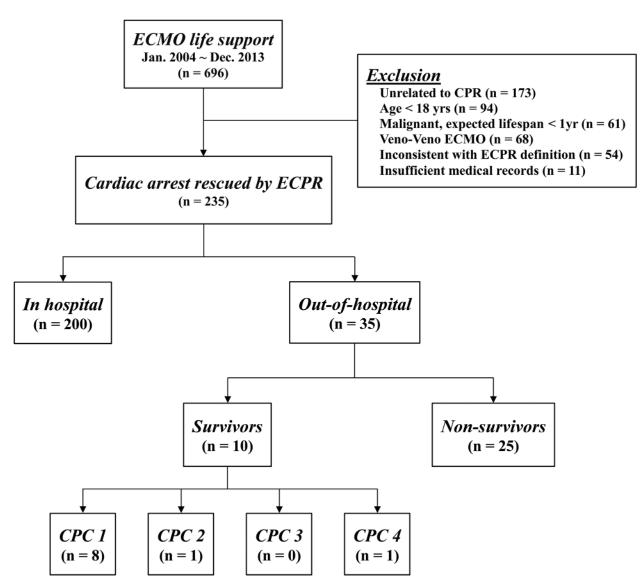

Figure 1 Flow chart showing patient selection. CPC: cerebral performance category; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation.

 Ha TS, et al. Emerg Med J 2017;34:107–111. doi:10.1136/emermed-2015-204817

non-survivor group (12.0%) were successfully weaned from ECMO (p<0.001). Bleeding complications at the cannulation site of ECMO developed in 13 patients (37.1%) and limb ischaemia occurred in one patient (2.8%) in the survivor group. No differences in proportion of patients requiring either continuous renal replacement treatment or intra-aortic balloon pump counterpulsation were found between the two groups (p=1.00 and p=0.32, respectively).

Table 1 Baseline clinical characteristics of the patients

Variables	Non-survivors (n=25)	Survivors (n=10)	p Value
Age ≥65 (years)	7 (28.0%)	0 (0%)	0.08F
Gender (male)	19 (76.0%)	10 (100%)	0.15F
Comorbidities			
Diabetes	4 (16.0%)	2 (16.0%)	1.00F
Hypertension	8 (32.0%)	1 (10.0%)	0.24F
Dyslipidaemia	5 (20.0%)	1 (10.0%)	0.65F
Current smoker	7 (28.0%)	4 (40.0%)	0.98F
Previous myocardial infarction	5 (20.0%)	2 (20.0%)	1.00F
Previous PCI	3 (12.0%)	2 (20.0%)	0.61F
Previous stroke	2 (8.0%)	0 (0%)	1.00F
Previous CKD	1 (4.0%)	0 (0%)	1.00F

CKD, chronic kidney disease; F, Fisher's exact test; PCI, percutaneous coronary intervention.

Clinical outcomes and predictors of survival-to-discharge

Of the 13 of 35 patients (37.1%) who were successfully weaned from ECMO, 10 (76.9%) lived to be discharged from the hospital. The CPC scores of patients at discharge were as following: eight patients (80.0%) were discharged with a CPC score of 1, one patient (10.0%) had a CPC score of 2 (moderate disability) and one patient (10.0%) was in a vegetative state (CPC score of 4) (p<0.001) (figure 1). Cox regression analysis was performed to determine predictors of survival-to-discharge (table 3). Significant univariate predictors of survival-to-discharge were witnessed arrest (HR=3.96; 95% CI 1.38 to 11.41; p=0.01), bystander CPR (HR=4.05; 95% CI 1.56 to 10.42; p=0.004) and successful revascularisation (HR=2.90; 95% CI 1.23 to 6.86; p=0.02). Kaplan-Meier curves also showed favourable survival for those patients who received prehospital bystander CPR (p<0.001) and those in whom successful revascularisation was achieved (p=0.004) (figure 2).

DISCUSSION

In the present study, we investigated clinical outcomes and predictors of survival-to-discharge in patients who had OHCA and who underwent ECPR as a rescue procedure. survival-to-discharge was observed in 10 patients (28.6%) and the neurological course of in-hospital survivors was relatively good. Predictors of survival-to-discharge in this patient population were witnessed arrest, prehospital bystander CPR and successful revascularisation.

Table 2 Arrest and resuscitation characteristics of the patients

Variables	Non-survivors (n=25)	Survivors (n=10)	p Value
Arrest cause			0.38F
Cardiogenic shock	16 (64.0%)	10 (100%)	
Septic shock	1 (4.0%)	0 (0%)	
Hypovolemic shock	1 (4.0%)	0 (0%)	
Respiratory deterioration	0 (0%)	0 (0%)	
Neurogenic shock	2 (8.0%)	0 (0%)	
Unknown	5 (20.0%)	0 (0%)	
First monitored arrest rhythm			0.34F
Asystole	8 (32.0%)	1 (10.0%)	
Pulseless electrical activity	6 (24.0%)	2 (20.0%)	
VF/pulseless VT	11 (44.0%)	7 (70.0%)	
Witnessed arrest	19 (76.0%)	10 (100%)	0.15F
Bystander CPR	6 (24.0%)	9 (90.0%)	0.001F
Time limits, median (IQR)			
Arrest to hospital time (min)	20.0 (15.0–24.5)	23.5 (18.8–27.3)	0.41
Hospital to ECMO (min)	50.0 (44.0–72.5)	61.0 (39.8–77.8)	0.50
Arrest to ECMO (min)	72.0 (57.0–91.5)	82.0 (65.3–104.8)	0.61
ROSC before ECMO pump-on	13 (52.0%)	8 (80.0%)	0.25F
Fluoroscopic guidance	8 (32.0%)	6 (60.0%)	0.15F
Successful revascularisation	8 (32.0%)	8 (80.0%)	0.02F
ECMO-related complications			
Bleeding at the cannulation site	8 (32.0%)	5 (50.0%)	0.44F
Limb ischaemia	0 (0%)	1 (10.0%)	0.29F
Use of CVVH	7 (28.0%)	3 (30.0%)	1.00F
IABP	3 (12.0%)	3 (30.0%)	0.32F
ECMO weaning success	3 (12.0%)	10 (100%)	<0.001F
ICU stay (days)	13.0±52.8	25.8±41.9	0.52
ECMO duration time, hours (IQR)	35.0 (4.5–94.3)	52.0 (37.8–58.3)	0.07

Data are shown as n (%) or median (IQR).
CPR, cardiopulmonary resuscitation; CVVH, continuous veno-venous hemofiltration; ECMO, extracorporeal membrane oxygenation; F, Fisher's exact test; IABP, intra-aortic balloon pump; ICU, intensive care unit; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 3 Predictors of survival-to-discharge in patients who had OHCA and who underwent ECPR

	Univariate analysis	
Variables	**Unadjusted HR (95% CI)**	**p Value**
Age (compared with <65 years)	1.72 (0.71 to 4.12)	0.23
Witnessed arrest	3.96 (1.38 to 11.41)	0.01
Bystander CPR	4.05 (1.56 to 10.42)	0.004
ROSC before ECMO	2.24 (1.00 to 5.02)	0.05
Pre-arrest rhythm (compared with asystole)		
PEA	0.95 (0.33 to 2.75)	0.93
VT/VF	0.57 (0.23 to 1.43)	0.23
Fluoroscopic guidance	2.25 (0.95 to 5.29)	0.06
Successful revascularisation	2.90 (1.23 to 6.86)	0.02

CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Encouraging survival rates in patients with refractory cardiac arrest illustrates the usefulness of ECMO.[10–12] The ECMO pump can immediately generate sufficient blood flow in adult patients after cannulation of the artificial circuit, while conventional chest compression results in a cardiac output of only 25%–30% of normal, even when performed under optimal conditions.[13] Thus, rapid ECMO initiation in refractory cardiac arrest supports organ, cerebral and myocardial perfusion, oxygenation and improves metabolic state after circulatory arrest.[14] Consequently, restoration of cerebral and coronary circulation by mechanical haemodynamic support could stabilise haemodynamic status and increase the chance of survival. However, to date, most studies on the benefits of ECMO have been performed in patients who had IHCA; the few studies conducted on patients who had OHCA have reported various survival rates ranging between 4% and 36%, with most reported rates lower than those documented for patients who had IHCA.[7 15 16] Therefore, we investigated clinical outcomes in patients who had OHCA and who underwent ECPR and the rate of survival-to-discharge of patients who had OHCA and who were rescued with ECPR was 28.6%.

Recent studies have reported better survival rates with reduced time delay to ECMO implantation.[15 17–19] Leick *et al*[3] showed that door-to-ECMO implantation time was an independent predictor of 30-day mortality in patients who had OHCA. However, in our study, the median time of arrest to ECMO was not significantly different between survivors and non-survivors. Hollenberg *et al*[1] reported that witnessed arrest cases and a shockable rhythm were significant predictors of increased survival. However, neither witnessed arrest nor shockable rhythm were significant determinants of survival in patients who had OHCA following ECMO. It is uncertain why there were differences in predictors between previous studies and our study; this may be due to a lack of statistical power owing to small sample size in our study as well as previous studies.

In the present study, significant predictors of in-hospital mortality in patients who had OHCA were bystander CPR and successful revascularisation. Avalli *et al*[5] showed that no-flow and low-flow times were higher in patients who had OHCA than in patients who had IHCA and could therefore be a major determinant of the difference in survival between survivors and non-survivors. In a recent study by Wissenberg *et al*,[20] bystander CPR was the only factor associated with a good outcome. Consequently, bystander CPR can reduce no-flow time, which has great potential for decreasing the mortality rate of patients who had OHCA. The current American Heart Association proposed that ECPR for patients should be considered when the duration of the no-flow is brief.[6] Therefore, we propose that ECPR should be actively considered for patients who had OHCA with bystander CPR. In addition, Mollmann *et al*[21] investigated whether early coronary angiography in resuscitated patients with an unknown underlying cause of cardiac arrest could reduce mortality rates. They reported favourable long-term outcomes and suggested that early invasive therapy after CPR, irrespective of the underlying cause of cardiac arrest, reduced mortality and improved prognosis. Similarly, our study showed that successful revascularisation is another important determinant of survival-to-discharge in patients who had OHCA; actually, the survival-to-discharge rate of patients who

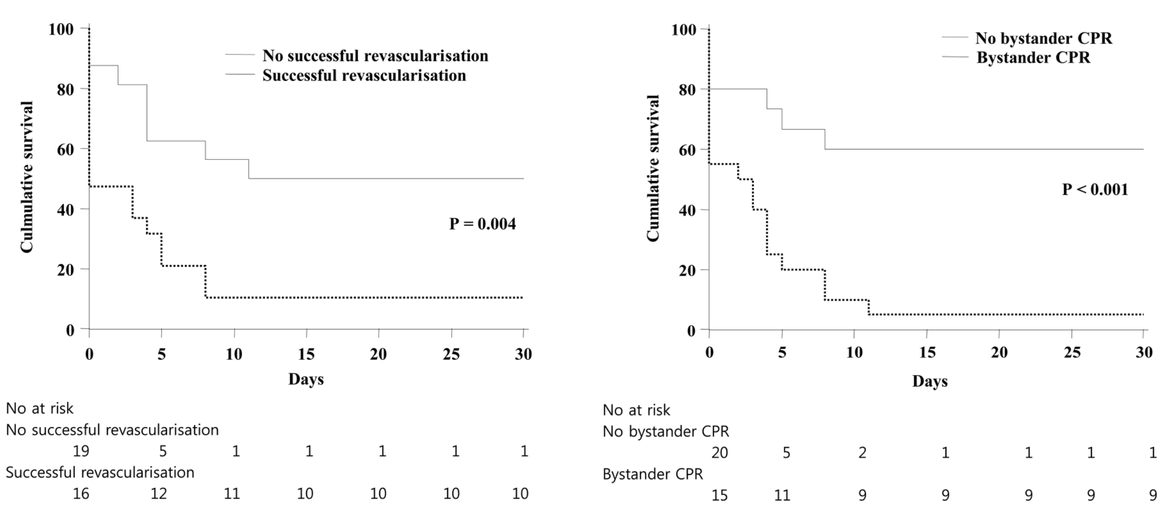

Figure 2 Kaplan-Meier survival curves of patients who had out-of-hospital cardiac arrest and who underwent extracorporeal cardiopulmonary resuscitation. (A) Kaplan-Meier curves of no bystander cardiopulmonary resuscitation (CPR) (dashed line) versus bystander CPR groups (solid line). (B) Kaplan-Meier curves of the non-revascularised group (dashed line) versus the successful revascularisation by percutaneous coronary intervention after extracorporeal membrane oxygenation group (solid line).

received emergency revascularisation was 50.0%, which is comparable with that of recent studies, which reported acceptable survival rates of 55%–67%.[22 23]

In our recent study, which is about developing a risk prediction model for survival-to-discharge in patients who had IHCA and who had undergone ECMO, age less than 66 years is considered a good risk predictor for survival-to-discharge of patients who had IHCA and who underwent ECPR.[24] In addition, Schmidt *et al*[25] demonstrated that age less than 63 years is identified as pre-ECMO prognosis factors of in-hospital survival. Similarly, in the present study, all patients aged 65 years and more belong to non-survival group. Therefore, a younger age patient who had OHCA might be one of the factors to be considered active to receive ECPR.

Our study had several limitations. First, we investigated a small number of patients from a single centre; thus, the patient cohort was heterogeneous. Furthermore, it was a non-randomised observational study and had a retrospective study design. In particular, the outcome in patients who had OHCA and who underwent ECPR was not compared with OHCA with conventional care. The survival-to-discharge (28.6%) in our study is higher compared with those of patients who had OHCA with conventional care ranging from 7.6% to 10.8% in previous studies.[3 11 20] There is possible confounding by indication in the analysis of the association between the ECPR and survival. When the ethical aspects of CPR are considered, however, randomised trial of resuscitation strategy is very difficult in clinical practice. However, all consecutive patients who had OHCA treated with ECMO were prospectively included in a single-centre registry and continuing data collection will improve the generalisability of our findings. Second, in our centre, therapeutic hypothermia was not applied in all patients who had OHCA and who underwent ECPR and we did not investigate the additive or synergistic effect of hypothermia in the setting of higher tissue perfusion with mechanical haemodynamic support. Third, an important limitation of this study is the lack of data on the quality of bystander CPR. However, evaluating the quality of CPR before emergency department arrival is not feasible. Fourth, we did not evaluate laboratory parameters during ECMO support to confirm haemodynamic improvement. Finally, our sample size is too small to build a robust multiple Cox model, adjusting for all other covariates. Although the sample size is small, this study is based on 10 years of experience with our patients' cohort data. Therefore, our results should be interpreted as suggestive and not conclusive that ECPR is definitely more effective than conventional CPR, which require further study.

CONCLUSION

Survival rate of patients who had OHCA and who underwent ECPR was poor. Witnessed arrest, bystander CPR and successful revascularisation were predictors of survival-to-discharge in patients who had OHCA and who underwent ECPR. These findings suggest that ECMO implantation should be very carefully considered in highly selected patients who had OHCA with little no-flow time and a reversible cause.

Contributors TSH planned the study and performed data collection. He also analysed the data and wrote the article. JHY as corresponding author is responsible for the overall content as guarantor. YHC, C-MP, CRC, KJ and GYS supervised the study, such as its design and coordination. All authors read and approved the final manuscript.

Competing interests None declared.

Ethics approval Institutional review and ethics board of the Samsung Medical Center, Sungkyunkwan University School of Medicine.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Hollenberg J, Herlitz J, Lindqvist J, *et al*. Improved survival after out-of-hospital cardiac arrest is associated with an increase in proportion of emergency crew--witnessed cases and bystander cardiopulmonary resuscitation. *Circulation* 2008;118:389–96.

2 Nagata T, Abe T, Noda E, *et al*. Factors associated with the clinical outcomes of paediatric out-of-hospital cardiac arrest in Japan. *BMJ Open* 2014;4:e003481.

3 Leick J, Liebetrau C, Szardien S, *et al*. Door-to-implantation time of extracorporeal life support systems predicts mortality in patients with out-of-hospital cardiac arrest. *Clin Res Cardiol* 2013;102:661–9.

4 Mattox KL, Beall AC Jr. Resuscitation of the moribund patient using portable cardiopulmonary bypass. *Ann Thorac Surg* 1976;22:436–42.

5 Avalli L, Maggioni E, Formica F, *et al*. Favourable survival of in-hospital compared to out-of-hospital refractory cardiac arrest patients treated with extracorporeal membrane oxygenation: an Italian tertiary care centre experience. *Resuscitation* 2012;83:579–83.

6 ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2005;112:IV1–203.

7 Le Guen M, Nicolas-Robin A, Carreira S, *et al*. Extracorporeal life support following out-of-hospital refractory cardiac arrest. *Crit Care* 2011;15:R29.

8 Shin TG, Choi JH, Jo IJ, *et al*. Extracorporeal cardiopulmonary resuscitation in patients with inhospital cardiac arrest: a comparison with conventional cardiopulmonary resuscitation. *Crit Care Med* 2011;39:1–7.

9 Godino C, Bassanelli G, Economou FI, *et al*. Predictors of cardiac death in patients with coronary chronic total occlusion not revascularized by PCI. *Int J Cardiol* 2013;168:1402–9.

10 Chen YS, Lin JW, Yu HY, *et al*. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. *Lancet* 2008;372:554–61.

11 Sasson C, Rogers MA, Dahl J, *et al*. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes* 2010;3:63–81.

12 Stub D, Byrne M, Pellegrino V, *et al*. Extracorporeal membrane oxygenation to support cardiopulmonary resuscitation in a sheep model of refractory ischaemic cardiac arrest. *Heart Lung Circ* 2013;22:421–7.

13 Barsan WG, Levy RC. Experimental design for study of cardiopulmonary resuscitation in dogs. *Ann Emerg Med* 1981;10:135–7.

14 Gilmore CM, Rea TD, Becker LJ, *et al*. Three-phase model of cardiac arrest: time-dependent benefit of bystander cardiopulmonary resuscitation. *Am J Cardiol* 2006;98:497–9.

15 Ferrari M, Hekmat K, Jung C, *et al*. Better outcome after cardiopulmonary resuscitation using percutaneous emergency circulatory support in non-coronary patients compared to those with myocardial infarction. *Acute Card Care* 2011;13:30–4.

16 Kuilman M, Bleeker JK, Hartman JA, *et al*. Long-term survival after out-of-hospital cardiac arrest: an 8-year follow-up. *Resuscitation* 1999;41:25–31.

17 Morimura N, Sakamoto T, Nagao K, *et al*. Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: a review of the Japanese literature. *Resuscitation* 2011;82:10–14.

18 Shin TG, Jo IJ, Sim MS, *et al*. Two-year survival and neurological outcome of in-hospital cardiac arrest patients rescued by extracorporeal cardiopulmonary resuscitation. *Int J Cardiol* 2013;168:3424–30.

19 Sunde K, Pytte M, Jacobsen D, *et al*. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation* 2007;73:29–39.

20 Wissenberg M, Lippert FK, Folke F, *et al*. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. *JAMA* 2013;310:1377–84.

21 Mollmann H, Szardien S, Liebetrau C, *et al*. Clinical outcome of patients treated with an early invasive strategy after out-of-hospital cardiac arrest. *J Int Med Res* 2011;39:2169–77.

22 Gorjup V, Radsel P, Kocjancic ST, *et al*. Acute ST-elevation myocardial infarction after successful cardiopulmonary resuscitation. *Resuscitation* 2007;72:379–85.

23 Reynolds JC, Callaway CW, El Khoudary SR, *et al*. Coronary angiography predicts improved outcome following cardiac arrest: propensity-adjusted analysis. *J Intensive Care Med* 2009;24:179–86.

24 Park SB, Yang JH, Park TK, *et al*. Developing a risk prediction model for survival to discharge in cardiac arrest patients who undergo extracorporeal membrane oxygenation. *Int J Cardiol* 2014;177:1031–5.

25 Schmidt M, Burrell A, Roberts L, *et al*. Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. *Eur Heart J* 2015;36:2246–56.