Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis

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Summary

Background Extracorporeal life-support as an adjunct to cardiac resuscitation has shown encouraging outcomes in patients with cardiac arrest. However, there is little evidence about the benefit of the procedure compared with conventional cardiopulmonary resuscitation (CPR), especially when continued for more than 10 min. We aimed to assess whether extracorporeal CPR was better than conventional CPR for patients with in-hospital cardiac arrest of cardiac origin.

Methods We did a 3-year prospective observational study on the use of extracorporeal life-support for patients aged 18–75 years with witnessed in-hospital cardiac arrest of cardiac origin undergoing CPR of more than 10 min compared with patients receiving conventional CPR. A matching process based on propensity-score was done to equalise potential prognostic factors in both groups, and to formulate a balanced 1:1 matched cohort study. The primary endpoint was survival to hospital discharge, and analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00173615.

Findings Of the 975 patients with in-hospital cardiac arrest events who underwent CPR for longer than 10 min, 113 were enrolled in the conventional CPR group and 59 were enrolled in the extracorporeal CPR group. Unmatched patients who underwent extracorporeal CPR had a higher survival rate to discharge (log-rank p<0·0001) and a better 1-year survival than those who received conventional CPR (log rank p=0·007). Between the propensity-score matched groups, there was still a significant difference in survival to discharge (hazard ratio [HR] 0·51, 95% CI 0·35–0·74, p<0·0001), 30-day survival (HR 0·47, 95% CI 0·28–0·77, p=0·003), and 1-year survival (HR 0·53, 95% CI 0·33–0·83, p=0·006) favouring extracorporeal CPR over conventional CPR.

Interpretation Extracorporeal CPR had a short-term and long-term survival benefit over conventional CPR in patients with in-hospital cardiac arrest of cardiac origin.

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Introduction

Sudden cardiac arrest still has a low survival rate despite the introduction of cardiopulmonary resuscitation (CPR),[1] and this rate has remained unchanged since 1993.[2,3] Investigations have also shown that survival rate declines rapidly when the duration of CPR exceeds 10 min, and even more rapidly if it exceeds 30 min.[3–5]

Extracorporeal life-support as a device for cardiac resuscitation was proposed in the early 1960s.[6] Advances in technology have allowed such treatment to be deployed rapidly, and several descriptive series investigations have shown encouraging outcomes in patients with cardiac arrest.[7–9] Despite promising results in paediatric patients,[10–12] no comparative data have been assessed in adult groups undergoing CPR assisted with extracorporeal life-support.

Since protracted conventional CPR has been associated with high immediate mortality,[4,5] we did a prospective observational study, between 2004 and 2006, of adults with in-hospital cardiac arrest of cardiac origin who received CPR of more than 10 min. We also aimed to assess whether the survival benefit of extracorporeal CPR over conventional CPR seen in previous studies[7–9] might have been due to selection bias.

Methods
Setting

National Taiwan University Hospital, in Taipei, is an extracorporeal life-support referral centre.[13–15] The CPR team consisted of a senior medical resident, several junior residents, a respiratory therapist, a head nurse, and several registered nurses from the intensive care unit. Each member of the CPR team is certified for advanced cardiac life-support. According to American Heart Association guidelines,[16] we established an internet-based Utstein style registry system to prospectively obtain all data for in-hospital cardiac arrest since 2003 (webpanel 1). A registered nurse was responsible for data collection. Each event was reviewed

See Online for webpanel 1

and discussed by the IHCA (in-hospital cardiac arrest) task force committee to discover the possible cause of cardiac arrest at the end of the hospital treatment (webpanel 2). The task force consisted of cardiovascular surgeons, anaesthetists, and critical care specialists under the direct supervision of the Centre of Quality Management, which has supervised 70–100 extracorporeal life-support procedures a year for the past 5 years. Patients surviving to discharge were followed-up for at least a year. In-hospital and out-of-hospital information was traced and placed online with authorised access.[5]

Patients

We included adults with in-hospital cardiac arrest of cardiac origin (as established by two independent committees), aged between 18 and 75 years, who underwent CPR for longer than 10 min between Jan 1, 2004, and Dec 31, 2006 (webfigures 1 and 2). An in-hospital cardiac arrest was deemed to be of cardiac origin if there was evidence of raised cardiac enzymes before CPR, sudden collapse without obvious causes, sudden collapse with pre-existing cardiovascular disease, or other expressions approved by the task force committee. Only patients who underwent witnessed arrest of cardiac origin and CPR duration (defined as the interval from beginning CPR to return of spontaneous circulation or death) for more than 10 min were recruited in the study cohort. Those who received extracorporeal life-support with CPR were assigned to the extracorporeal CPR group, and those who did not to the conventional CPR group.

Exclusion criteria that were applied to both groups were: CPR of less than 10 min; age over 75 years; previously known severe irreversible brain damage; terminal malignancy; a traumatic origin with uncontrolled bleeding; non-cardiac arrest; and those who previously signed "Do not attempt resuscitation".[7]

Conventional CPR was stopped when spontaneous circulation returned and was maintained for 20 min. The decision to discontinue unsuccessful CPR (no return of spontaneous circulation for 30 min) was made after communication with the family. Exclusion criteria applying only to the extracorporeal CPR group were those who were not weaned from cardiopulmonary bypass due to post-cardiotomy shock requiring transition to extracorporeal life-support, and those who experienced shock necessitating extracorporeal life-support in an elective condition.

Procedures

Doctors in our institute were taught to regard extracorporeal life-support as an option in prolonged CPR. The decision to call the extracorporeal life-support team was made by the attending doctors in charge. Average duration from the call to team arrival was 5–7 min during the day and 15–30 min during the night shift. In general, if return of spontaneous circulation was

sustained for more than 20 min after the team arrived, extracorporeal life-support would not be installed. If return of spontaneous circulation was continued for less than 20 min, the team would wait at least 10 min and begin extracorporeal life-support in case of reoccurrence of arrest. 10–15 min was usually needed to set up extracorporeal life-support. Oral permission was obtained immediately, and written informed consent was later collected from the relatives. The study was approved by the institutional review board.

The equipment and management have been reported previously.[7] The principal component of the extra-corporeal CPR circuit was a heparin-bonded surface circuit including a centrifugal pump and hollow-fibre oxygenator (Medtronic, Anaheim, USA). The circuit was pre-organised without priming and was primed with saline containing 2 U/mL of heparin when the extracorporeal CPR call was initiated. We did not apply the bridge tube between the arterial and venous lines, and it was reconnected to the circuit when weaning was

	Extracorporeal CPR group (N=59)	Conventional CPR group (N=113)
Men, n (%)	50 (84·7)	73 (64·6)
Age (year)		
Mean (SD)	57·4 (12·5)	60·3 (13·3)
Median (range)	61·5 (18–74)	65 (19–75)
Age >60 years, n (%)	34 (57·6)	67 (63·5)
Pre-existing comorbidity, n (%)		
Diabetes	22 (37·3)	39 (34·5)
Hypertension	29 (49·2)	51 (45·1)
Dyslipidaemia	10 (17·0)	5 (4·4)
Malignancy	5 (8·5)	15 (13·3)
Lung insufficiency	2 (3·4)	12 (10·6)
Stroke	10 (17·0)	8 (7·1)
Chronic renal disease	5 (8·5)	21 (18·6)
Cardiovascular disease	37 (62·7)	58 (51·3)
Chronic hepatitis	2 (3·4)	10 (8·9)
Causes of arrest, n (%)		
Acute coronary syndrome	37 (62·7)	80 (70·8)
Congestive heart failure	6 (10·2)	18 (15·9)
Myocarditis	5 (8·5)	2 (1·8)
Post-cardiotomy	7 (11·9)	0
Pulmonary embolism	1 (1·7)	0
Unspecified cardiac causes	3 (5·1)	13 (11·5)
Department type, n (%)		
Internal medicine	37 (62·7)	78 (69·0)
Surgery	22 (37·3)	33 (29·2)
Other		2 (1·8)
Inotropic equivalent, μg/kg per min before CPR, n (%)	55 (93·2)	43 (38·1)
Mean (SD)	55·9 (65·6)	24·7 (29·0)
Median (range)	40 (2·4–324)	14·8 (1·7–150)

Table 1: Baseline characteristics of the extracorporeal CPR group and the conventional CPR group

	Extracorporeal CPR group, N (%)	Conventional CPR group, N (%)	p (extracorporeal vs conventional CPR)
N	59	113	
Witnessed	59 (100)	113 (100)	
Defibrillation*	59 (100)	74 (65·5)	
Left ventricle decompression	3 (5·1)	0	
Time period of CPR episode			0·04
Period A (0701 h–1500 h)	19 (32·2)	34 (30·0)	
Period B (1501 h–2300 h)	33 (55·9)	47 (41·6)	
Period C (2301 h–700 h)	7 (11·9)	32 (28·3)	
CPR location			0·07
Intensive care unit/operating room/ catheterisation laboratory	33 (55·9)	45 (39·8)	
Emergency room/ward	26 (44·1)	64 (56·6)	
Other	..	4 (3·5)	
First documented rhythm			0·08
Ventricular tachycardia/ventricular fibrillation	29 (49·2)	36 (31·9)	
Pulseless electrical activity	17 (28·8)	46 (40·7)	
Asystole	13 (22·0)	31 (27·4)	
Intubated before arrest	39 (66·1)	77 (68·1)	0·86
ROSC (ROSB)	55 (93·2)	63 (55·8)	<0·0001
CPR duration			
N	59	113	
Mean (SD), min	52·8 (37·2)	42·7 (31·1)	0·08
Median (range)	40 (16–251)	32 (11–180)	
Available maximal lactic acid level in 24 h			
N	54	20	
Mean (SD)	12·7 (6·2)	6·2 (5·5)	<0·0001
Median (range)	12·0 (2·4–39·7)	3·7 (1·1–20)	
Subsequent intervention			
Yes	36 (61·0)	14 (12·4)	<0·0001
Revascularisation	26 (44·1)	6 (6·4)	<0·0001
Ventricular assist device	3 (5·1)	0 (0)	0·04
Heart transplantation	5 (8·5)	0 (0)	0·004
Extracorporeal life support		3 (3·1)	
Reperfusion for distal limb	15 (25·4)	..	<0·0001
Other	9 (15·3)†	6 (5·3)‡	0·04
Hospital stay after CPR (day)			
N	55	44	
Mean	20·3 (21·8)	25·4 (39·5)	0·44
Median (range)	12 (1–93)	12·0 (1–174)	

ROSB=return of spontaneous heart beating (for extracorporeal CPR group). ROSC=return of spontaneous circulation (for conventional CPR group). *Defibrillation before or during CPR. †Valve replacement 3. ‡Tapping 3, pacing 2, dissecting aortic aneurysm graft 1.

Table 2: CPR and post-CPR variables in the extracorporeal CPR group and the conventional CPR group

attempted if necessary. To avoid possible distal malperfusion, we applied an antegrade reperfusion catheter for distal limb perfusion when the mean pressure of the superficial femoral artery was below 50 mm Hg.[17] Left heart decompression was required to unload the left ventricular end-diastolic pressure in case of persistent lung oedema with frothy sputum for 12 h under high-dose catecholamine. The extracorporeal life-

support circuit was connected to a temperature controller within 2 h of beginning extracorporeal circulation to maintain normothermia. No hypothermia was applied.

Since extracorporeal CPR patients were supported by artificial circulation, we defined the return of spontaneous heart (ventricular) beating after extracorporeal CPR compared with return of spontaneous circulation in conventional CPR. Inotropic equivalent (IE), using the equation IE (μg/kg per min)=dopamine+dobutamine+100×epinephrine+100×norepinephrine+100×isoproterenol+15×milrinone, was used to roughly estimate the severity of the pre-arrest status.[13] Daily echocardiography was essential to estimate myocardial recoverability and to detect possible thrombus formation within the left ventricle.

Weaning, defined as successful separation from extracorporeal life-support without mortality in 12 h, was not attempted until 72 h after initiation. Ventricular assist device and heart transplantation were alternatives in the absence of contraindications when weaning was unsuccessful in 5–7 days. Cessation of extracorporeal life-support was considered if severe neurological impairment persisted for more than 7 days without signs of recovery.

Consciousness status was assessed every 12 h. The functional status of survivors (1 and 2=good neurological outcome vs 3 and 4=poor) after discharge from hospital was analysed according to the Glasgow-Pittsburgh cerebral–performance categories (CPC) score.[18] The patient was regarded as discharged on the day of death (CPC 5), or at the end of the hospital course when they went home with good neurological outcome (CPC 1 or 2) or to a nursing home with poor neurological outcome (CPC 3 or 4).

The primary endpoint was survival to hospital discharge. The difference in survival curves, assessed at 30 days and 1 year, was used as the secondary endpoint. Other parameters, such as the proportion of return of spontaneous heart beat or return of spontaneous circulation, the cumulative survival rate at 24 h, 3 days, 14 days, 30 days, 6 months, and 1 year, were summarised.

Propensity score methods

Propensity score matching is a method used to balance observed covariates in the two treatment groups.[19–21] In this study, the propensity score was the conditional probability for getting extracorporeal CPR, as a binary dependent variable, under a set of measurements. Age, sex, initial cardiac rhythm, time point of CPR, CPR duration, the presence of comorbidities were added into a non-parsimonious multivariable logistic regression model to predict the effect of extracorporeal life-support. The predicted probability derived from the logistic equation was used as the propensity score for each individual.

Extracorporeal and conventional CPR patients were pooled and sorted according to their propensity score

in ascending order. The selection process began from the first two cases with the lowest propensity score. If one underwent extracorporeal CPR and the other underwent conventional CPR, both were selected as a matched pair. If this was not the case, then four cases were included. If there were two extracorporeal CPR and two conventional CPR cases, the four were selected as two matched pairs. In the same way, extracorporeal CPR and conventional CPR cases were matched by their propensity score in 1:1, 2:2, 3:3, or 4:4 blocks. A patient who did not have a suitable match within the acceptable rank range was excluded from further analysis, and the matching process moved down the sort list until all possible matched pairs were included. The selected patients formed well-matched 1:1 pairs in both groups (extracorporeal CPR-M and conventional CPR-M).

Statistical analysis

Categorical variables were compared with χ^2 test (or Fisher's exact test) and continuous variables with Student's t test. The survival time to discharge was defined as the duration from the day of CPR to the day of discharge, either dead or alive. A case that survived to discharge was regarded as censored (non-event) on the day of discharge. Log-rank test was used to compare the survival difference between the extracorporeal and conventional CPR groups. In the observational cohort, extracorporeal CPR status and covariates (age, sex, initial rhythm, CPR duration, CPR timing, and CPR location) were added into a Cox regression model to estimate the hazards.

Kaplan-Meier curves, with follow-up of up to 30 days and 1 year, were plotted to show survival trend. Log-rank test and Cox regression model were used to compare the hazard between the two matched groups. Hazard ratio, 95% CI, and p value were reported. The survival time was defined as the duration from CPR to death in the mortality cases, and in the survivors as the duration from CPR to censorship—ie, discharge, 30 days, and 1 year. A p value of less than 0·05 was regarded as significant.

A logistic regression model was used for the propensity match using SPSS version 13.0 (SPSS, Chicago, USA). Odds ratio (OR) and p values were used to represent the probability that a patient would receive extracorporeal life-support. Propensity scores in both extracorporeal and conventional CPR groups were used to draw box-plots. If two-thirds of conventional CPR patients died and extracorporeal CPR resulted in a 50% risk reduction, we estimated that 35 patients in either group would be needed to achieve 80% statistical power (given α=0·05). After the 1:1 matched groups were assembled, the primary and secondary endpoints were compared accordingly.

This trial is registered with ClinicalTrials.gov, NCT00173615.

	Extracorporeal CPR group	Conventional CPR group
N	59	113
Duration of extracorporeal membrane oxygenation (h)		
Mean (SD)	110 (128)	..
Median (range)	69 (2–771)	..
Weaned off extracorporeal membrane oxygenation, n (%)	29 (49·2)	..
CPC status at discharge		
1 or 2*, n (%)	14 (23·7)	12 (10·6)
Odds ratio (95% CI, p value)	2·6 (95% CI 1·1–6·7, p=0·02*)	2·6 (95% CI 1·1–6·7, p=0·02*)
CPC status at 1 year		
1 or 2, n (%)	9 (15·3)	10 (8·9)
Odds ratio (95% CI, p value)	1·9 (95% CI 0·6–5·4, p=0·20)	1·9 (95% CI 0·6–5·4, p=0·20)

CPC=Cerebral–performance category score. *p<0·05.

Table 3: Outcome of the extracorporeal CPR group and conventional CPR group
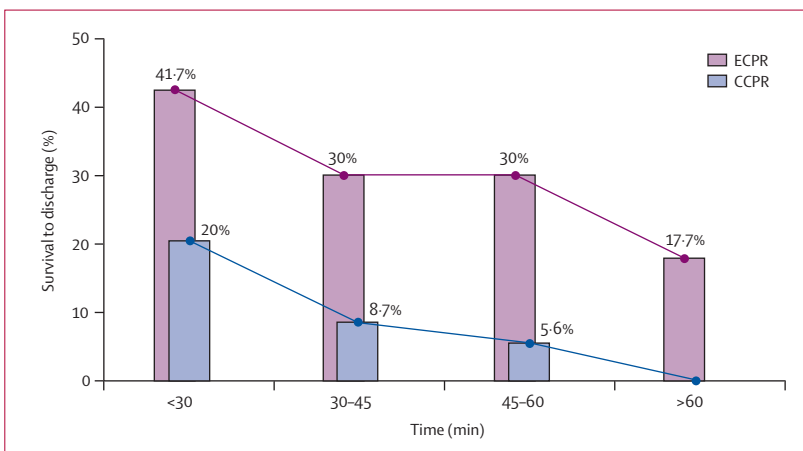
Figure 1: Relation between CPR duration and the survival rate to discharge
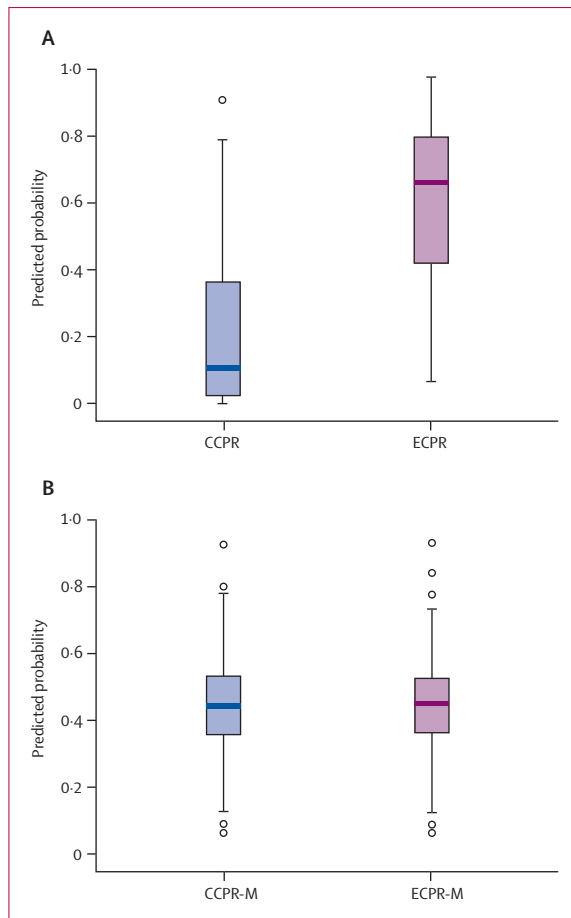ECPR=extracorporeal CPR. CCPR=conventional CPR.

	Hazard ratio	95% CI	p
Ventricular tachycardia/ventricular fibrillation	0·58	0·40–0·83	0·003
Use of extracorporeal membrane oxygenation	0·50	0·33–0·74	0·001
CPR duration (+1 min)	1·007	1·003–1·011	0·002
Age (+1 year)	1·01	0·99–1·02	0·07
Men	1·04	0·72–1·5	0·83
Period C (midnight)	1·05	0·71–1·5	0·82
Intensive scenario	1·1	0·78–1·6	0·58

Intensive scenario=intensive care unit, operating room, or catheterisation room.

Table 4: Multivariate Cox regression analysis for the factors associated with the survival to hospital discharge

Role of the funding source

The funding source had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Figure 2: **Propensity analysis**
Distribution of propensity scores in (A) the conventional CPR and extracorporeal CPR groups, and (B) the matched conventional CPR (CCPR-M) and extracorporeal CPR (ECPR-M) groups.

Results

Of the 975 patients with in-hospital cardiac arrest events recorded during the 36-month observational study, 113 received conventional CPR and 59 received extracorporeal CPR, according to the selection criteria (webfigures 1 and 2). The baseline characteristics of both groups are shown in table 1, and CPR and post-CPR variables are shown in table 2. CPR duration did not significantly differ between the two groups (p=0·08). CPR call occurred less frequently in period C (2301 h–0700 h) in the extracorporeal group (p=0·04). The first documented rhythm of ventricular tachycardia or ventricular fibrillation was higher in the extracorporeal CPR group than in the conventional CPR group, but the distribution of ventricular tachycardia or ventricular fibrillation, pulseless electrical activity, and asystole were not significant (p=0·08). Return of spontaneous beating in the extracorporeal group was higher than return of spontaneous circulation in the conventional group, despite a longer CPR duration (table 2).

More subsequent interventions were done in the extracorporeal group than in the conventional group. These interventions included revascularisation, implantation of a ventricular assist device, and heart transplantation (table 2). Three patients in the conventional group required extracorporeal life-support because of persistent shock after return of spontaneous circulation, the interval between extracorporeal life-support and return of spontaneous circulation being 24 (SD 12) h. They were analysed in the conventional group (intention to treat). The length of hospital stay after CPR was similar between groups.

At discharge, the extracorporeal group had a roughly 20% increase in survival rate and better neurological outcome compared with the conventional group (table 3). The adverse relation between CPR duration and the survival rate to discharge is shown in figure 1.

17 patients in the extracorporeal group (28·8%) and 14 patients (12·3%) in the conventional group survived to discharge. The cumulative survival rate in the extracorporeal group was 93·2% (at 24 h), 76·3% (3 days), 44·1% (14 days), 33·9% (30 days), 28·8% (6 months), and 18·6% (1 year; 11 survivors). In the conventional group, the cumulative survival was 38·1% (at 24 h), 31·0% (3 days), 21·2% (14 days), 15·0% (30 days), 11·5% (6 months), and 9·7% (1 year; 11 survivors). Kaplan-Meier analysis showed a survival benefit favouring the extracorporeal group over the conventional group at discharge (log-rank p<0·0001), and also at 30 days (p=0·003) and 1 year (p=0·007). Multivariate Cox regression model analysis indicated that extracorporeal life-support use and first documented rhythm of ventricular tachycardia or ventricular fibrillation were positively associated with the survival to discharge, and CPR duration was negatively associated (table 4). When the interaction between return of spontaneous beating in the extracorporeal group and return of spontaneous circulation in the conventional group was added to the model, the new variable was not associated with the survival (p=0·50). This finding suggested a lack of survival benefit in the return of spontaneous beating responders over the return of spontaneous circulation responders.

There were six late deaths in the extracorporeal group between 6 and 12 months; the causes were underlying malignancy (two), progressive heart failure (two), and another sepsis episode (two). In the conventional group, three late deaths occurred in 12 months, one related to a persistent cardiac event and two to pneumonia.

In the propensity score assignment, extracorporeal life-support was found to be positively associated with an increase in CPR time (OR 1·01 per min, p=0·05), initial presentation with ventricular tachycardia or ventricular fibrillation (OR 2·5, p=0·04 compared with pulseless electrical activity and OR 2·4, p=0·07 compared with asystole), the presence of dyslipidaemia (OR 4·9, p=0·02), previous cardiovascular or cerebrovascular events (OR 3·5, p=0·03), and negatively associated with

increased age (OR 0·98 per year, p=0·03) and the presence of end-stage renal disease (OR 0·18, p=0·009). Mean propensity score was 0·60 (SD 0·24) in the extracorporeal group and 0·20 (0·23) in the conventional group (p<0·0001; figure 2A).

The propensity score-matching process selected 46 patients from the extracorporeal CPR-M group and the other 46 from the conventional CPR-M group for further analysis. No case in conventional CPR-M received extracorporeal life-support later in the course. Propensity score was 0·43 (SD 0·18) in the extracorporeal CPR-M group and 0·44 (0·18) in the conventional CPR-M group (p=0·94; figure 2B). Baseline characteristics, including initial cardiac rhythm, CPR duration, and subsequent percutaneous coronary intervention, were similar in the two groups (table 5).

The return of spontaneous beating rate in the extracorporeal CPR-M group was statistically higher than the return of spontaneous circulation rate in the conventional CPR-M group (p<0·0001). 15 cases in the extracorporeal CPR-M group (32·6%) and eight cases in the conventional CPR-M group survived to discharge (17·4%). Kaplan-Meier analysis showed a survival benefit favouring extracorporeal CPR-M over conventional CPR-M at discharge (HR 0·51, 95% CI 0·35–0·74, p<0·0001). Neurological outcome (categorised into CPC 1/2, CPC 3/4, and death) showed no difference at discharge (p=0·09, table 5).

The cumulative survival rate was 65·2% (at 24 h), 52·2% (3 days), 37·0% (14 days), 34·8% (30 days), 32·6% (6 months), and 19·6% (1 year; nine survivors) in the extracorporeal CPR-M group and 41·3% (24 h), 34·8% (3 days), 23·9% (14 days), 17·4% (30 days), 15·2% (6 months), and 13·0% (1 year; six survivors) in the conventional CPR-M group. Survival analysis with the Kaplan-Meier plot showed a better survival in the extracorporeal CPR-M group at the end of 30 days (log-rank p=0·042) and at 1 year (log-rank p=0·003; figure 3). The hazard ratio of extracorporeal CPR over conventional CPR was 0·47 (95% CI 0·28–0·77, p=0·003) if the survival curves were trimmed at 30 days. Extracorporeal CPR still showed a survival benefit at the end of 1 year (HR 0·53, 95% CI 0·33–0·83, p=0·006). Neurological outcome showed no difference at 1 year (p=0·27, table 5).

Discussion

Our observational study focusing on adult in-hospital cardiac arrest of cardiac origin in a single institute has shown a survival benefit in patients receiving extracorporeal CPR compared with those receiving conventional CPR. Although randomisation is, in theory, the proper way to take account of unknown confounders, propensity analysis has still shown a short-term and long-term survival benefit favouring extracorporeal CPR when known confounding factors were matched.

Extracorporeal circulation had previously been applied in several critical conditions, including acute respiratory distress syndrome, cardiogenic or postcardiotomy shock, and bridge to ventricular assist device, transplantation,

	Extracorporeal CPR-M (N=46)	Conventional CPR-M (N=46)	p
Baseline characteristics			
Age (mean [SD])	57 (14)	55 (15)	0·64
CPR duration (min)	53 (41)	47 (33)	0·44
Men, n (%)	39 (85)	40 (87)	0·76
Initial rhythm, n (%)			0·81
Ventricular tachycardia/ventricular fibrillation	21 (45·7)	19 (41·3)	
Pulseless electrical activity	15 (32·6)	18 (39·1)	
Asystole	10 (21·7)	9 (19·6)	
Causes of arrest*, n (%)			
Acute coronary syndrome	28 (60·8)	33 (71·7)	
Congestive heart failure	5 (10·9)	9 (19·6)	
Myocarditis	5 (10·9)	1 (2·2)	
Post-cardiotomy	4 (8·7)	0	
Pulmonary embolism	1 (2·2)	0	
Unspecified cardiac causes	3 (6·5)	3 (6·5)	
Diabetes	15 (32·6)	15 (32·6)	1·00
Hypertension	17 (37·0)	22 (47·8)	0·29
Dyslipidaemia	5 (10·9)	4 (8·7)	0·73
Malignancy	4 (8·7)	3 (6·5)	0·69
Chronic obstructive pulmonary disease	2 (4·3)	2 (4·3)	1·00
Cerebrovascular accidents	6 (13·0)	5 (10·9)	0·75
Abnormal liver function	2 (4·3)	3 (6·5)	0·65
Haemodialysis	5 (10·9)	4 (8·7)	0·73
Documented heart disease	24 (52·2)	30 (65·2)	0·39
Location (intensive care unit/operating room/catheterisation room)	25 (54·4)	24 (52·2)	0·83
Period C (midnight)	7 (15·2)	10 (21·8)	0·65
Department			0·56
Medicine	30 (65·2)	31 (67·4)	
Surgery	16 (34·8)	14 (30·4)	
Other	0	1 (2·2)	
Subsequent percutaneous coronary intervention	8 (17·4)	3 (6·5)	0·11
Clinical endpoints			
ROSB/ROSC†, n (%)	42 (91·3)	24 (52·2)	<0·001‡
Neurological outcome			
CPC status at discharge	n (%)	n (%)	
1 or 2	14 (30·4)	7 (15·2)	0·09
3 or 4	1 (2·2)	1 (2·2)	0·09
5 (death)	31 (67·4)	38 (82·6)	0·09
CPC status at 1 year	n (%)	n (%)	
1 or 2	9 (19·5)	5 (10·8)	0·27
3 or 4	1 (2·2)	1 (2·2)	0·27
5 (death)	36 (78·3)	40 (87·0)	0·27

ROSC=return of spontaneous circulation for conventional CPR-M. ROSB=return of spontaneous beating for extracorporeal CPR-M. *p=0·10. †Odds ratio 9·6 (95% CI 3·0–31·2). ‡p<0·05.

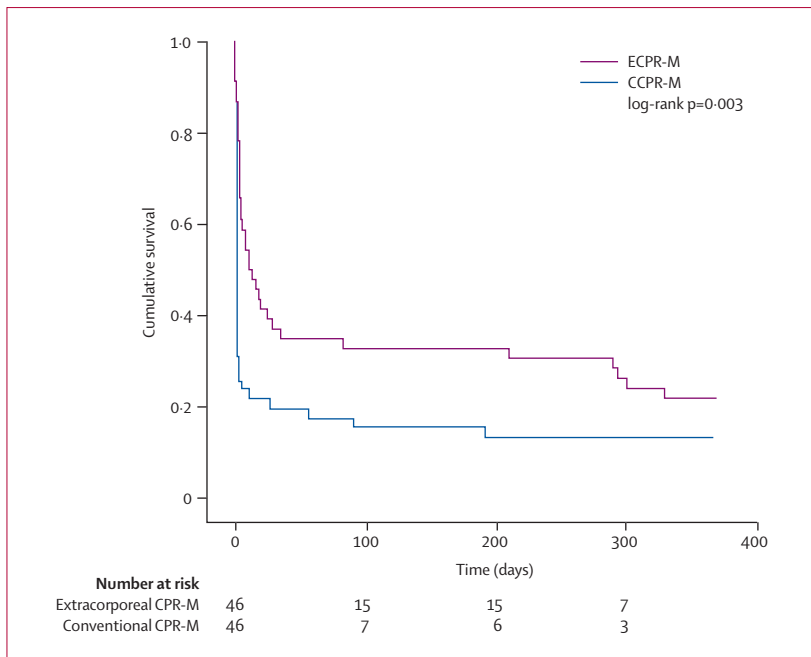*Table 5:* Propensity analysis baseline characteristics and clinical endpoints

Figure 3: Kaplan-Meier plot of the survival curves in the extracorporeal CPR-M and conventional CPR-M groups for 1 year

or next decision.[13,15,22–25] The improving results in various applications have encouraged the use of extracorporeal life-support in cardiac arrested patients and offered better neurological preservation.[7,10,26,27] However, comparison with results derived from conventional CPR in different institutions with heterogeneous causes might be of restricted applicability.

In our study, longer CPR duration was associated with poor prognosis. Compared with ventricular tachycardia or ventricular fibrillation as the initial rhythm, those who showed pulseless electrical activity or asystole had higher mortality. This finding suggests that the main factors associated with outcome are baseline condition, underlying cause, and the rapid response of the CPR team.[28] The effect of extracorporeal life-support on improving survival of patients with in-hospital cardiac arrest of cardiac origin was still prominent after these clinical conditions were adjusted in the observational study (table 4) or matched by propensity analysis (figure 3). Extracorporeal CPR reduced mortality risk by up to 1 year using the highly technique-dependent invasive procedure. This resuscitative method is reasonable for patients suffering from refractory cardiac arrest.

Could patients who showed signs of return of spontaneous circulation after relentless CPR further benefit from extracorporeal life-support? In our study, the interaction effect between return of spontaneous beating in the extracorporeal group and return of spontaneous circulation in the conventional group on survival was not significant. We tried to assemble another set of propensity-score matched subgroups between the

extracorporeal CPR responders and conventional CPR responders, but the preliminary result did not show a survival difference. Since only a small proportion of the original registry was included in the subgroup analysis, further examination into the most suitable application of extracorporeal life-support in patients with return of spontaneous circulation after conventional CPR is warranted.

The quality of CPR might not have been well controlled between the two groups.[29,30] Although the propensity-score approach could reduce selection bias and confounding factors inherent in the observational study, a key limitation is that bias could remain if there are unmeasured or unknown confounders that are not incorporated into the propensity score.

The difference in subsequent interventions in the conventional and extracorporeal groups could be attributed to some extent to observer bias (which might have occurred even in a randomised study if it is not blinded). We tried to reduce observer bias by locating (or relocating) the patients in both groups to the intensive care unit. A subsequent decision was made according to their clinical condition, not simply to their life-support status. Conversely, fewer patients in the conventional CPR group could survive to definite therapy. The greater number of subsequent investigations in the extracorporeal CPR group was also attributed to the differential effect of intervention. In the propensity analysis, later percutaneous coronary intervention was similar in the extracorporeal CPR-M group and conventional CPR-M group (table 5).

Previous studies have suggested that applying mild hypothermia (34°C) for 24 or 48 h in patients receiving extracorporeal life-support was both feasible and safe. Since our observational cohort was started in 2003, the institutional review board did not approve the use of hypothermia at its experimental stage. However, therapeutic hypothermia is currently recommended in cardiac arrest of cardiac origin. Further research should stress the additive or synergistic effect of hypothermia in extracorporeal CPR for adult cardiac patients.

Extracorporeal CPR might be recommended for adult in-hospital cardiac arrest patients of cardiac origin who have undergone CPR for more than 10 min and could provide a short-term and long-term survival advantage. Although the observed survival benefit of extracorporeal CPR over conventional CPR is in part attributed to selection bias, the use of propensity analysis that equalised potential prognostic predictors has shown a beneficial effect in short-term and long-term survival with extracorporeal life-support. There was no significant difference in survival between return of spontaneous beating from extracorporeal CPR and return of spontaneous circulation from conventional CPR. Further studies will be needed to identify potential subgroups in in-hospital cardiac arrest patients who could benefit from extracorporeal CPR.

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