OPEN

Use of Extracorporeal Membrane Oxygenation to Rescue Patients With Refractory Ventricular Arrhythmia in Acute Myocardial Infarction

Chih-Fan Yeh, MD, Chih-Hsien Wang, MD, Pi-Ru Tsai, BSc, Cho-Kai Wu, MD, PhD, Yen-Hung Lin, MD, PhD, and Yih-Sharng Chen, MD, PhD

Abstract: Refractory ventricular arrhythmia is a serious problem in acute myocardial infarction (AMI), with an extremely high mortality rate and limited effective treatment. Extracorporeal membrane oxygenation (ECMO) is useful to rescue patients with cardiopulmonary collapse. However, little is known about whether ECMO is a potential rescue technique for patients with refractory ventricular arrhythmia in AMI.

We retrospectively analyzed prospectively collected data on patients with AMI and refractory ventricular arrhythmia who underwent ECMO as rescue therapy and the bridge to revascularization from February 2001 to January 2013. Primary endpoint was mortality on index admission, and secondary endpoint was mortality on index admission or advanced brain damage at discharge.

A total of 69 (62 men) patients were enrolled in this study. During the index admission, 39 patients (56.5%) met primary endpoint, and 45 patients (65.2%) met secondary endpoint, respectively. In multivariate Cox regression analysis, both the presence of profound anoxic encephalopathy and acute renal failure requiring dialysis were significant predictive factors for both primary and secondary endpoints.

ECMO is a feasible rescue therapy and bridge to revascularization in patients with refractory ventricular arrhythmia in acute myocardial infarction. The presence of profound anoxic encephalopathy and acute renal failure requiring dialysis were significant prognostic factors.

(Medicine 94(30):e1241)

Abbreviations: AMI = acute myocardial infarction, ARF = acute renal failure, CABG = coronary artery bypass graft, CK = creatine kinase, ECMO = extracorporeal membrane oxygenation, E-CPR = ECMO-assisted cardiopulmonary resuscitation, PCI =

Editor: Alessandro Durante.

- Received: April 15, 2015; revised: June 25, 2015; accepted: July 3, 2015. From the Department of Internal Medicine (C-FY, C-KW, Y-HL); and Department of Surgery(C-HW, Y-SC, P-RT), National Taiwan University Hospital; and National Taiwan University College of Medicine, Taipei, Taiwan (Y-HL, Y-SC).
- Taiwan (Y-HL, Y-SC). Correspondence: Yen-Hung Lin, Department of Internal Medicine, National Taiwan University Hospital, No. 7, Chung-Shan S. Road, Taipei 100, Taiwan (e-mail: austinr34@gmail.com).
- This study was supported by National Taiwan University Hospital (grants NTUH 102-S2096, NTUH 103-M254, NTUH 103-S2447, NTUH 103-S2347), National Taiwan University (UN102–060), and Taiwan National Science Council (NSC 102–2314-B-002–078-MY3, MOST 103–2220-E-002-011).
- The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

This is an open access article distributed under the Creative Commons Attribution- NonCommercial License, where it is permissible to download, share and reproduce the work in any medium, provided it is properly cited. The work cannot be used commercially. ISSN: 0025-7974

DOI: 10.1097/MD.00000000001241

percutaneous coronary intervention, STEMI = ST elevation myocardial infarction.

INTRODUCTION

M ortality and complications associated with acute myocardial infarction (AMI) have gradually decreased in the era of reperfusion therapy.¹ However, the outcomes are still poor in patients with ventricular arrhythmia in AMI who need resuscitation.^{2,3} Refractory ventricular arrhythmia is even more challenging with an extremely high mortality rate.⁴ Current guidelines focus on medical and defibrillation therapy when facing ventricular arrhythmia in patients with AMI.^{5,6} However, the available treatment modalities for patients with refractory ventricular arrhythmia are still limited. Intraaortic balloon pump support is a possible solution in such circumstances, although the results have been reported to be unacceptable due to extremely high mortality rate.^{4,7}

Extracorporeal membrane oxygenation (ECMO) provides cardiopulmonary support and is used to rescue patients with cardiopulmonary collapse.^{8,9} In patients with AMI, ECMO is suggested for temporary support in those with acute heart failure with the potential for functional recovery following revascularization.⁷ In recent studies, ECMO has been reported to improve outcomes in patients with AMI with cardiogenic shock, and that early ECMO initiation yields better outcomes.¹⁰ Moreover, a previous study demonstrated a significant increase in survival using ECMO in patients with cardiogenic shock compared with intraaortic balloon pump support.⁴ The previous studies suggest that ECMO is a potential solution for patients with refractory ventricular arrhythmia in AMI. However, little is known about the efficacy of such treatment in these patients, and it has not been mentioned in current guidelines.^{5,6} Therefore, we assessed the efficacy of ECMO as rescue therapy and as a bridge to revascularization in patients with refractory ventricular arrhythmia in AMI.

METHODS

Setting and Population

The present study was conducted at National Taiwan University Hospital, a university-affiliated 2200-bed hospital in northern Taiwan. This hospital is also an ECMO referral center and tertiary medical center. We established a computerized case record form prospectively and collected the demographic data, clinical features, and outcomes of patients undergoing ECMO.⁸ Adult patients who required ECMO for AMI-induced refractory ventricular arrhythmia between February 2001 and January 2013 were included. The inclusion criteria were an age of 18 years or older, and those who received venoarterial ECMO for circulatory collapse despite

All authors have no conflicts of interest to disclose.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

conventional cardiopulmonary resuscitation and medical treatment, and a clinical diagnosis of AMI-induced refractory ventricular arrhythmia before ECMO. The exclusion criteria were those who did not receive coronary catheterization during this hospitalization, and who receive ECMO implantation during or after revascularization therapy. Primary endpoint was mortality on index admission. Secondary endpoint was mortality on index admission or advanced brain damage at discharge.

The institutional review board of National Taiwan University hospital approved the study and waived for the need of informed consent (Ref: 201409041RIN).

Definitions

The diagnosis of AMI was made by electrocardiography, medical history, and the presence of cardiac necrosis markers in serum. The definition of ST-elevation myocardial infarction (STEMI) was new ST elevation at the J point in at least 2 contiguous leads of $\geq 2 \, \text{mm} \, (0.2 \, \text{mV})$ in men or $\geq 1.5 \, \text{mm} \, (0.15 \, \text{mV})$ in women in leads V2–V3, and/or of $\geq 1 \, \text{mm} \, (0.1 \, \text{mV})$ in other contiguous chest leads or the limb leads. New or presumably new left bundle branch block was considered to be equivalent to STEMI.⁶ Refractory ventricular arrhythmia was defined as persistent ventricular arrhythmia even with the use of antiarrhythmia medications, cardioversion, and cardiopulmonary resuscitation.⁴

Venoarterial ECMO was delivered to the appropriate candidates when refractory ventricular arrhythmia occurred. ECMO-assisted cardiopulmonary resuscitation (E-CPR) was defined as the rescue process, while ECMO was used to obtain return of spontaneous circulation in the patients with cardiac arrest who were unresponsive to conventional cardiopulmonary resuscitation.¹¹ E-CPR will be performed only in 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 minutes.⁸ The duration of CPR was defined as the duration from the witnessed cardiac arrest to return of spontaneous circulation with ECMO.⁸ Advanced vessel disease was defined as left main disease or triple-vessel disease of the coronary artery.¹² Dialysis-dependent acute renal failure (ARF) was defined as de novo renal failure found on ECMO with necessity and indication for dialysis.^{13,14} Profound anoxic encephalopathy was defined as a comatose or vegetative status after the hemodynamic insult with abnormal brainstem reflexes and organic brain lesions identified by brain computed tomography.10 The functional status of the survivors after discharge was analyzed according Glasgow-Pittsburgh cerebral-performance categories to scores, with advanced brain damage at discharge defined as a score of 3-4.¹⁵

Clinical Management

Diagnostic coronary catheterization with ad hoc percutaneous coronary intervention (PCI) was the first interventional strategy given to the patients on ECMO to confirm and resolve culprit coronary lesions. The patients who experienced an unsatisfactory PCI (TIMI flow ≤ 2 after intervention) and those who had a coronary anatomy or clinical condition unsuitable for PCI received coronary artery bypass grafts (CABG). After the revascularization therapy, multidisciplinary therapies were delivered to support the injured organs. The consciousness level was evaluated every 12 hours after CPR, and neurological assessments with brain imaging studies were performed to check the cause of prolonged unconsciousness (>72 hours after ECMO initiation) or significant deterioration of the coma scale after stopping sedatives.^{11,16} Weaning off ECMO was attempted in the patients who showed myocardial improvements in periodical evaluations by echocardiography and other hemodynamic studies. Suitable candidates without myocardial recovery were listed for heart transplantation, and a short-term ventricular assisted device was considered if there was a long-waiting time to transplantation.¹⁷

The preprocedural demographics, characteristics of myocardial infarction, coronary lesions, E-CPR requirement and duration, type of coronary revascularization, common complications of ECMO, ECMO duration, and clinical outcomes were collected as previously reported.⁴

Statistical Analysis

Data were expressed as mean \pm standard deviation. Categorical variables were compared using the Chi-square or Fisher exact test, whereas continuous variables were compared using the Student *t*-test. Univariate Cox regression analysis was used to examine the possible factors affecting the primary or secondary endpoint. Determinants with a *P* value < 0.1 in univariate Cox regression analysis were then tested in multivariate Cox regression analysis with forward stepwise subset selection to identify independent factors predicting primary or secondary endpoint. Linear analysis was used for detecting the trend of difference among patients divided by peak creatine kinase (CK)-MB levels. All statistical analyses were performed using SPSS for Windows (Version 12.0, SPSS, Inc., IL). A *P* value less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 69 patients (62 men) were enrolled in this study, with a mean age of 57.8 years. The average total ECMO time was 92 hours and the average hospitalization duration was 20.8 days. The weaning rate of ECMO was 59.4% (n = 41). Primary endpoint was met in 39 patients (56.5%), and 30 patients (43.5%) survived to hospital discharge, of whom 6 had advanced brain damage at discharge. Forty five patients (65.2%) met secondary endpoint.

The clinical data are summarized in Table 1. Forty two patients (60.9%) had STEMI. The patients who received CABG had a higher percentage of advanced vessel disease and lower percentage of STEMI compared with those who received PCI. The other parameters were comparable between the patients who received PCI or CABG.

Primary Outcome Analysis: Mortality on Index Admission

In univariate Cox regression analysis, age (P = 0.017), peak CK-MB level (P = 0.034), and the presence of profound anoxic encephalopathy (P < 0.001), and dialysis-dependent ARF (P < 0.001) were the significant factors associated with mortality (Table 2).

In multivariate Cox regression analysis, the presence of profound anoxic encephalopathy (hazard ratio [HR] = 3.474, 95% confidence interval (CI): 1.720–7.015, P = 0.001) and dialysis-dependent ARF (HR = 3.543, 95% CI: 1.450–8.656, P = 0.006) were the independent factors significantly associated with mortality (Table 3).

	PCI $(N = 49)$	CABG $(N=20)$	P Value
Demographic data			
Age, years	57.6	58.8	0.736
Sex, male	44 (90%)	18 (90%)	0.98
Diabetes mellitus	16 (33%)	9 (45%)	0.333
Hypertension	28 (57%)	7 (35%)	0.095
End-stage renal disease requiring dialysis	1 (2%)	0 (0%)	0.52
Previous CAD	12 (24%)	8 (40%)	0.198
Previous MI	3 (6%)	3 (15%)	0.235
Previous stroke	4 (8%)	1 (5%)	0.646
Clinical condition			
Advanced vessel disease on coronary angiogram	26 (53%)	16 (80%)	0.013^{*}
STEMI	35 (71%)	7 (35%)	0.015^{*}
Pre-ECMO CPR	21 (43%)	13 (65%)	0.095
ECMO-support CPR,	42 (86%)	16 (80%)	0.556
CPR duration, min	50.8	48.3	0.757
Peak CK-MB level, U/L	639.4	601.1	0.804
Duration on ECMO, hours	88.4	101	0.547
Presence of profound anoxic encephalopathy	24 (49%)	8 (40%)	0.497
Presence of vascular complication on ECMO	22 (45%)	10 (50%)	0.700
Presence of dialysis-dependent ARF	31 (63%)	12 (60%)	0.800
Mortality on the index admission	27 (55%)	12 (60%)	0.710
Discharge with advanced brain damage	6 (12%)	0 (0%)	0.171
Mortality on index admission or advanced brain damage at discharge	33 (67%)	12 (60%)	0.561

TABLE 1. Demographic Data and Clinical Condition of Patients Undergoing Different Revascularization Strategy

ARF = acute renal failure, CABG = coronary artery bypass graft, CAD = coronary artery disease, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal membrane oxygenation, MI = myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction.

Secondary Endpoint Analysis: Mortality on Index Admission or Advanced Brain Damage at Discharge

In univariate Cox regression analysis, age (P = 0.047), and the presence of anoxic encephalopathy (P < 0.001) and dialysisdependent ARF (P = 0.021) were the significant factors associated with secondary endpoint (Table 4). In multivariate Cox regression analysis, the presence of anoxic encephalopathy (HR = 3.838, 95% CI: 1.999–7.368, P < 0.001) and dialysisdependent ARF (HR = 2.233, 95% CI: 1.118–4.461, P = 0.023) were the independent factors significantly associated with secondary endpoint (Table 5).

Comparison of Early and Late Phase of Study

For the evaluation of possible influence by the improvement of ECMO techniques and patients care during these years, we divided patients into 2 groups (enrolled in early 6 years vs late 6 years). In baseline characteristics, these 2 groups were similar except more patients with hypertension (P < 0.001) in the late group. Patients enrolled in late 6 years had a significantly lower mortality (P < 0.001) and a better outcome in secondary endpoint (P = 0.003) (Table 6).

Comparison of Groups Divided by Peak CK-MB

We divided patients into 3 groups according to the peak CK-MB concentrations. There was an insignificant trend in patients from low to high peak CK-MB levels for clinical outcomes (*P* of trend = 0.100 in primary endpoint, and *P* of trend = 0.178, in secondary endpoint, respectively) (Table 7).

DISCUSSION

The major findings of this study are: ECMO is feasible as a bridging tool for revascularization in patients with AMI and refractory ventricular arrhythmia; the crucial factors associated with clinical outcomes in this group of patients include the presence of profound anoxic encephalopathy and dialysisdependent ARF.

Primary ventricular arrhythmia affects 2.3% to 8.0% of patients with AMI.^{18,19} AMI-induced refractory ventricular arrhythmia, which is resistant to traditional antiarrhythmic medications and cardiac defibrillation, may involve a large area of infarction or multivessel disease with a high ischemic burden and is associated with a very poor prognosis.²⁰ The available treatment modalities for these patients are still limited. Intraaortic balloon pump support is a possible solution, however, the results have been reported to be unacceptable due to the extremely high mortality rate.^{4,7} ECMO provides cardiopulmonary support and is frequently used to rescue patients with cardiopulmonary collapse.^{8,21} Therefore, it should also be a reasonable treatment of choice for patients with refractory ventricular arrhythmia. A previous case report showed that early ECMO installation may be helpful in terminating refractory ventricular arrhythmia.²² In AMI-induced ventricular arrhythmia, ECMO installation has been reported to significantly improve the 30-day (61%) and 1-year (53.85%) survival rate.⁴ However, a definitive conclusion cannot be made due to the small number of patients. Despite the increasing use of ECMO, it is not currently mentioned as a possible solution or bridging tool for refractory ventricular arrhythmia in the guidelines.^{5,6,23} In our hospital with a high volume of ECMO use, we

Factors	β (95% CI)	P Value	
Male	1.299 (0.506, 3.334)	0.587	
Age, years	1.032 (1.006, 1.058)	0.017	
Diabetes mellitus	1.339 (0.707, 2.534)	0.370	
Hypertension	0.810 (0.428, 1.532)	0.517	
Baseline end-stage renal disease requiring dialysis	4.105 (0.542, 31.087)	0.172	
Previous CAD	1.195 (0.611, 2.339)	0.602	
Previous MI	1.766(0.723, 4.313)	0.212	
Previous stroke	1.908 (0.671, 5.420)	0.225	
Advanced vessel disease on coronary angiogram	1.417 (0.717, 2.801)	0.316	
STEMI	0.823 (0.431, 1.571)	0.555	
Pre-ECMO CPR	1.258 (0.663, 2.388)	0.483	
ECMO-assisted CPR	1.623 (0.628, 4.193)	0.318	
CRP duration, min	1.012 (0.988, 1.036)	0.327	
Duration on ECMO, hours	0.998 (0.994, 1.003)	0.418	
Pre-ECMO lactate, mg/dl	0.961 (0.860, 1.074)	0.488	
Pre-ECMO white cell count, K/µL	1.000 (1.000,1.000)	0.213	
Pre-ECMO hematocrit, %	1.014 (0.974, 1.055)	0.506	
Pre-ECMO platelet number, K/µL	0.997 (0.993, 1.002)	0.240	
Pre-ECMO creatinine, mg/dL	1.004 (0.867, 1.163)	0.955	
Peak CK-MB level, U/L	1.000 (1.000, 1.001)	0.034	
Revascularization modality			
PCI versus CABG	1.047 (0.528, 2.076)	0.895	
Presence of profound anoxic encephalopathy	3.254 (1.662, 6.372)	0.001	
Presence of vascular complication of ECMO	1.494 (0.792, 2.819)	0.215	
Presence of dialysis-dependent ARF	4.146 (1.728, 9.946)	0.001	

TABLE 2. Univariate Cox Regression Analysis for the Prediction of Mortality in ECMO Recipients (n = 69)

ARF = acute renal failure, CABG = coronary artery bypass graft, CAD = coronary artery disease, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal membrane oxygenation, MI = myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction.

demonstrated a similar survival rate (43%) using ECMO as a bridging tool for revascularization in patients with refractory ventricular arrhythmia because of AMI. This study is the first to focus on the role of ECMO in patients with AMI and refractory ventricular arrhythmia. According to our findings, ECMO seems to be a feasible tool to terminate refractory ventricular arrhythmia and as a bridge to revascularization.

The mechanisms of improvement of refractory ventricular arrhythmia after ECMO implantation are complex. In patients with refractory ventricular arrhythmia, the failure of conversion to a normal rhythm causes further poor perfusion of the myocardium, elevated ventricular end-diastolic pressures, profound ventricular dysfunction, and circulatory collapse. These conditions make the heart resistant to medical therapy and further electrical conversion.²⁴ Venoarterial-ECMO can

TABLE 3. Multivariate Cox Regression Analysis for the Prediction of Mortality in ECMO Recipients (n = 69)

Factors	β (95% CI)	P Value	
Presence of profound anoxic encephalopathy	3.474 (1.720, 7.015)	0.001	
Presence of dialysis-dependent ARF	3.543 (1.450, 8.656)	0.006	

Excluded parameters: age and peak CK-MB level. ARF = acute renal failure, CI = confidence interval.

decompress the heart, maintain coronary circulation, increase cardiac output, preserve systemic organ perfusion, and improve the condition of acidosis/hypoxia.^{24,25} It provides better cardiac and general conditions, which make successful cardiac conversion possible.

ECMO has also been reported to have good results for the treatment of similar conditions such as AMI-related cardiogenic shock. According to the SHOCK trial, successful early revascularization improved the long-term survival of patients with AMI-related cardiogenic shock.²⁶ It has also been reported that early ECMO-assisted primary PCI improved 30-day clinical outcomes in patients with STEMI complicated with profound cardiogenic shock.²⁷ Therefore, ECMO seems to be a reasonable choice to act as a bridge to revascularization in patients with refractory ventricular arrhythmia.

In the presented study, our patients enrolled in late 6 years had better clinical outcome. The reasons for this result probably are the learning process in the initial stage of ECMO setup in such emergent and critical condition, better devices of ECMO launched in the market in modern era. Among patients enrolled in late 6 years, the survival rate was 71% and more than half patients (58%) discharged without advanced brain damage. According to these positive results, it would emphasize our conclusion in modern era that "ECMO" is a reasonable and feasible rescue tool and a bridge to revascularization in patients with refractory ventricular arrhythmia in AMI.

The factors affecting survival in patients with ECMO have been studied for a long time, and recent data have focused on patients with AMI-related cardiogenic shock.^{27–31} Pre-ECMO

	β (95% CI)	P Value	
Male	3.538 (0.400, 31.265)	0.256	
Age	1.024 (1.000, 1.048)	0.047	
Diabetes mellitus	1.250 (0.683, 2.287)	0.469	
Hypertension	0.926 (0.510, 1.682)	0.802	
Baseline end-stage renal disease requiring dialysis	4.105 (0.542, 31.087)	0.172	
Previous CAD	1.118 (0.597, 2.092)	0.728	
Previous MI	1.433 (0.592, 3.468)	0.424	
Previous stroke	1.875 (0.661, 5.319)	0.238	
Advanced vessel disease on coronary angiogram	0.927 (0.795, 1.081)	0.334	
STEMI	0.818 (0.447, 1.498)	0.515	
Pre-ECMO CPR	1.061 (0.586, 1.921)	0.844	
ECMO-assisted CPR	1.517 (0.636, 3.620)	0.347	
CPR duration, minutes	1.015 (0.989, 1.042)	0.272	
Duration on ECMO, hours	0.997 (0.993, 1.002)	0.260	
Pre-ECMO lactate, mg/dL	0.956 (0.865, 1.057)	0.380	
Pre-ECMO white cell count, K/µL	1.000 (1.000, 1.000)	0.110	
Pre-ECMO hematocrit, %	1.025 (0.987, 1.064)	0.195	
Pre-ECMO platelet number, K/µL	0.998 (0.994, 1.001)	0.244	
Pre-ECMO creatinine, mg/dL	0.968 (0.834, 1.123)	0.668	
Peak CK-MB level, U/L	1.000 (1.000, 1.001)	0.119	
Revascularization modality			
PCI versus CABG	1.217 (0.626, 2.368)	0.563	
Presence of profound anoxic encephalopathy	3.860 (2.012, 7.403)	< 0.001	
Presence of vascular complication of ECMO	1.407 (0.778, 2.545)	0.259	
Presence of dialysis-dependent ARF	2.254 (1.133, 4.483)	0.021	

TABLE 4. Univariate Cox Regression Analysis for the Prediction of Mortality or Advanced Brain Damage at Discharge in the ECMO Recipients (n = 69)

ARF = acute renal failure, CABG = coronary artery bypass graft, CAD = coronary artery disease, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal membrane oxygenation, MI = myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction.

serum lactate level, CPR duration, door-to-balloon time, requirement for E-CPR, profound anoxic encephalopathy, and age >60 years have been reported to be risk factors.^{4,11,30} When limiting the strategy of myocardial revascularization to ECMO in early PCI with CABG as a complementary reperfusion method, a high pre-ECMO serum lactate level, unsuccessful angioplasty, asystole or pulseless electrical activity before ECMO introduction, ECMO-related complications, age >60 years, and profound anoxic encephalopathy have been reported to be the proposed factors affecting survival.^{11,30,31} However, no study has focused on survival in patients with AMI-related refractory ventricular arrhythmia who undergo ECMO. We found that the presence of profound anoxic encephalopathy

TABLE 5. Multivariate Cox Regression Analysis for the Prediction of Mortality or Advanced Brain Damage in the ECMO Recipients (n = 69)

Factors β (95% CI)		P Value	
Presence of profound anoxic encephalopathy	3.838 (1.999, 7.368)	< 0.001	
Presence of dialysis- dependent ARF	2.233 (1.118, 4.461)	0.023	

Excluded parameters: age. ARF = acute renal failure, CI = confidence interval, ECMO = extracorporeal membrane oxygenation.

and dialysis-dependent ARF were the factors affecting survival, which is consistent with previous studies. $^{11}\,$

Peak CK-MB levels are useful in estimating infarct size and predicting clinical outcomes in patients with AMI.³² In the presented study, peak CK-MB levels were significantly associated with mortality in univariate Cox regression analysis (Table 2), but not in multivariate Cox regression analysis (Table 3). Furthermore, there was only an insignificant trend in patients from low to high peak CK-MB levels for the primary and secondary endpoints. There were several possible reasons for the difference of our study from the previous one. First, the number of patients was small which might weaken the power of analysis. Second, the rise of CK-MB levels might not only due to myocardial infarction itself. Cardiac resuscitation might also contribute. Third, multiple factors were associated with prognosis of patients receiving ECMO including underling cardiac condition, CPR duration, and CPR quality. These factors might also influence the predictive power of CM-MB levels on prognosis. Further studies with a larger patient number are needed to investigate the relations between peak CK-MB levels and clinical outcomes in patients with refractory ventricular arrhythmia in AMI.

Neurological complication is the most serious morbidity and often causes a heavy economical burden on the patient's family. Therefore, we set secondary endpoint as the composite of mortality and advanced brain damage. We found that the presence of profound anoxic encephalopathy and dialysisdependent ARF were the factors associated with secondary endpoint. To the best of our knowledge, no previous study

	Early 6 years (N = 24)	Late 6 years (N = 45)	P Value
Demographic data			
Age, years	59.0	57.4	0.618
Sex, male	21 (88%)	41 (91%)	0.636
Diabetes mellitus	5 (21%)	20 (44%)	0.052
Hypertension	4 (17%)	31 (69%)	< 0.001
End-stage renal disease requiring dialysis	0 (0%)	1 (2%)	0.462
Previous CAD	3 (13%)	17 (38%)	0.028
Previous MI	2 (8%)	4 (9%)	0.938
Previous stroke	2 (8%)	3 (7%)	0.799
Presence of profound anoxic encephalopathy	13 (54%)	19 (42%)	0.343
Presence of vascular complication on ECMO	10 (42%)	22 (49%)	0.567
Presence of dialysis-dependent ARF	18 (75%)	25 (56%)	0.112
Mortality on the index admission	19 (79%)	13 (29%)	< 0.001
Discharge with advanced brain damage	0 (0%)	6 (13%)	0.085
Mortality on index admission or advanced brain damage at discharge	19 (79%)	19 (42%)	0.003

TABLE 6. Comparison of Early and Late Phase of Study

ARF = acute renal failure, CAD = coronary artery disease, ECMO = extracorporeal membrane oxygenation, MI = myocardial infarction.

TABLE 7. Comparison of Groups Divided by Peak CK-MB

	First Tertile (N = 23)	Second Tertile (N = 23)	Third Tertile (N = 23)	P Value
Demographic data				
Age, years	60.3	57.7	55.9	0.477
Sex, male	19 (83%)	21 (91%)	22 (96%)	0.329
Diabetes mellitus	14 (61%)	8 (35%)	3 (13%)	0.003
Hypertension	16 (70%)	10 (43%)	9 (39%)	0.083
End-stage renal disease requiring dialysis	1 (4%)	0 (0%)	0 (0%)	0.363
Previous CAD	9 (39%)	4 (17%)	7 (30%)	0.262
Previous MI	3 (13%)	1 (4%)	2 (9%)	0.578
Previous stroke	3 (13%)	1 (4%)	1 (4%)	0.422
Presence of profound anoxic encephalopathy	9 (39%)	11 (48%)	12 (52%)	0.665
Presence of vascular complication on ECMO	11 (48%)	10 (43%)	11 (48%)	0.943
Presence of dialysis-dependent ARF	12 (52%)	13 (57%)	18 (78%)	0.148
Mortality on the index admission	10 (43%)	12 (52%)	17 (74%)	0.100
Discharge with advanced brain damage	2 (9%)	3 (13%)	1 (4%)	0.578
Mortality on index admission or advanced brain damage at discharge	12 (52%)	15 (65%)	18 (78%)	0.178

ARF = acute renal failure, CAD = coronary artery disease, CK = creatine kinase, ECMO = extracorporeal membrane oxygenation, MI = myocardial infarction.

focusing on AMI with ECMO support has included neurological sequelae. Hence, the results of this study may be a reference for clinicians to predict more realistic clinical outcomes, not only focusing on survival.

Limitations

First, this is a retrospective study, and the data source of this study is only from a single medical center with a high volume of ECMO cases. Second, there is no control group (such as similar patients receiving intraaortic balloon pump) in this study. Further prospective case–control or randomized study is needed for evaluation the effect of ECMO in these patients. Third, only 3 patients receive therapeutic hypothermia in this study (data not shown), and it is hard to evaluate the impact of hypothermia to clinical outcomes.

CONCLUSION

ECMO is a reasonable and feasible rescue tool and a bridge to revascularization in patients with refractory ventricular arrhythmia in AMI. The presence of profound anoxic encephalopathy and ARF requiring dialysis were significant prognostic factors.

ACKNOWLEDGMENTS

The authors thank National Taiwan University Hospital (grants NTUH 102-S2096, NTUH 103-M254, NTUH 103-S2447, NTUH 103-S2347), National Taiwan University (UN102–060), and Taiwan National Science Council (NSC 102–2314-B-002–078-MY3, MOST 103–2220-E-002-011) for the support.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

REFERENCES

- ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both or neither among 17,187 patients with suspected acute myocardial infarction: ISIS-2. *J Am Coll Cardiol.* 1988;12 (suppl A):3A–13A.
- Thompson CA, Yarzebski J, Goldberg RJ, et al. Changes over time in the incidence and case-fatality rates of primary ventricular fibrillation complicating acute myocardial infarction: perspectives from the Worcester Heart Attack Study. *Am Heart J.* 2000;139:1014–1021.
- Mehta RH, Starr AZ, Lopes RD, et al. Incidence of and outcomes associated with ventricular tachycardia or fibrillation in patients undergoing primary percutaneous coronary intervention. *JAMA*. 2009;301:1779–1789.
- Tsao NW, Shih CM, Yeh JS, et al. Extracorporeal membrane oxygenation-assisted primary percutaneous coronary intervention may improve survival of patients with acute myocardial infarction complicated by profound cardiogenic shock. J Crit Care. 2012;27:2012;530:e531–e511.
- Steg PG, James SK, et al., Task Force on the management of STseamiotESoC. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J.* 2012;33:2569–2619.
- 6. American College of Emergency P, Society for Cardiovascular A, Interventions, et al.. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61:e78–e140.
- Task Force on Myocardial Revascularization of the European Society of Cardiology, the European Association for Cardio-Thoracic Surgury, European Association for Percutaneous Cardiovascular Intervention, et al. Guidelines on myocardial revascularization. *Eur J Cardiothorac Surg.* 2010;38(Suppl):S1–S52.
- 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;372:554–561.
- Kagawa E. Extracorporeal cardiopulmonary resuscitation for adult cardiac arrest patients. World J Crit Care Med. 2012;1:46–49.
- Wu MY, Lee MY, Lin CC, et al. Resuscitation of non-postcardiotomy cardiogenic shock or cardiac arrest with extracorporeal life support: the role of bridging to intervention. *Resuscitation*. 2012;83:976–981.
- Wu MY, Tseng YH, Chang YS, et al. Using extracorporeal membrane oxygenation to rescue acute myocardial infarction with cardiopulmonary collapse: the impact of early coronary revascularization. *Resuscitation*. 2013;84:940–945.
- Takeishi Y, Chiba J, Abe S, et al. Noninvasive identification of left main and three-vessel coronary artery disease by thallium-201 single photon emission computed tomography during adenosine infusion. *Ann Nucl Med.* 1994;8:1–7.
- Tsai CW, Lin YF, Wu VC, et al. SAPS 3 at dialysis commencement is predictive of hospital mortality in patients supported by extracorporeal membrane oxygenation and acute dialysis. *Eur J Cardiothorac Surg.* 2008;34:1158–1164.
- Chen YC, Tsai FC, Fang JT, et al. Acute kidney injury in adults receiving extracorporeal membrane oxygenation. J Formos Med Assoc. 2014.
- Prohl J, Rother J, Kluge S, et al. Prediction of short-term and longterm outcomes after cardiac arrest: a prospective multivariate approach combining biochemical, clinical, electrophysiological, and neuropsychological investigations. *Crit Care Med.* 2007;35:1230– 1237.

- Chen YS, Chao A, Yu HY, et al. Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. J Am Coll Cardiol. 2003;41:197–203.
- Chen YS, Yu HY, Huang SC, et al. Extracorporeal membrane oxygenation support can extend the duration of cardiopulmonary resuscitation. *Crit Care Med.* 2008;36:2529–2535.
- Dhurandhar RW, MacMillan RL, Brown KW. Primary ventricular fibrillation complicating acute myocardial infarction. *Am J Cardiol.* 1971;27:347–351.
- Pantridge JF, Geddes JS. A mobile intensive-care unit in the management of myocardial infarction. *Lancet.* 1967;2:271–273.
- Volpi A, Cavalli A, Santoro L, et al. Incidence and prognosis of early primary ventricular fibrillation in acute myocardial infarction – results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-2) database. *Am J Cardiol.* 1998;82:265–271.
- Wang CH, Chen YS, Ma MH. Extracorporeal life support. Curr Opin Crit Care. 2013;19:202–207.
- Cohen MI, Gaynor JW, Ramesh V, et al. Extracorporeal membrane oxygenation for patients with refractory ventricular arrhythmias. J Thorac Cardiovasc Surg. 1999;118:961–963.
- 23. Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American Academy of Family Physicians, Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;57:215–367.
- Tsai FC, Wang YC, Huang YK, et al. Extracorporeal life support to terminate refractory ventricular tachycardia. *Crit Care Med.* 2007;35:1673–1676.
- Lawson WE, Koo M. Percutaneous Ventricular Assist Devices and ECMO in the Management of Acute Decompensated Heart Failure. *Clin Med Insights Cardiol.* 2015;9(Suppl 1):41–48.
- Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should we emergently revascularize occluded coronaries for cardiogenic shock. N Engl J Med. 1999;341:625–634.
- 27. Sheu JJ, Tsai TH, Lee FY, et al. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary intervention improved 30-day clinical outcomes in patients with ST-segment elevation myocardial infarction complicated with profound cardiogenic shock. *Crit Care Med.* 2010;38:1810–1817.
- Chen JS, Ko WJ, Yu HY, et al. Analysis of the outcome for patients experiencing myocardial infarction and cardiopulmonary resuscitation refractory to conventional therapies necessitating extracorporeal life support rescue. *Crit Care Med.* 2006;34:950–957.
- Bermudez CA, Rocha RV, Toyoda Y, et al. Extracorporeal membrane oxygenation for advanced refractory shock in acute and chronic cardiomyopathy. *Ann Thorac Surg.* 2011;92:2125–2131.
- Kim H, Lim SH, Hong J, et al. Efficacy of veno-arterial extracorporeal membrane oxygenation in acute myocardial infarction with cardiogenic shock. *Resuscitation*. 2012;83:971–975.
- Sakamoto S, Taniguchi N, Nakajima S, et al. Extracorporeal life support for cardiogenic shock or cardiac arrest due to acute coronary syndrome. *Ann Thorac Surg.* 2012;94:1–7.
- 32. Dohi T, Maehara A, Brener SJ, et al. Utility of peak creatine kinase-MB measurements in predicting myocardial infarct size, left ventricular dysfunction, and outcome after first anterior wall acute myocardial infarction (from the INFUSE-AMI trial). *Am J Cardiol.* 2015;115:563–570.