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# Venoarterial extracorporeal membrane oxygenation for cardiogenic shock: a retrospective analysis based on the etiology of shock

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## Abstract

### Background

We performed a retrospective analysis to evaluate the efficacy of VA-ECMO support in cardiogenic shock based on various etiologies.

### Methods

We retrospectively analyzed 99 patients supported with VA-ECMO from January 1, 2012 to January 1, 2015. Outcomes included survival to discontinuation of VA-ECMO support and survival to hospital discharge. The etiologies of cardiogenic shock included cardiac arrest (CPR), acute myocardial infarction (AMI), decompensated congestive heart failure (CHF), pulmonary embolism (PE), right



ventricular failure (RVF) not secondary to an acute pulmonary embolism, and post-cardiotomy syndrome (PCS). The PCS group was used as a reference group; odds ratios were estimated and Fisher's exact tests were performed to compare each other group to the reference.

### **Results**

Patients supported with VA-ECMO due to PE and CHF had better survival to hospital discharge (83.3% and 54.2%, with  $p = 0.003$  and  $p = 0.011$ , respectively) versus the PCS group (7.7%). The PE, CHF, and AMI groups had statistically improved survival to VA-ECMO discontinuation. There was no statistically significant difference in survival to VA-ECMO discontinuation or hospital discharge in four subgroup analyses.

### **Conclusions**

Patients supported with VA-ECMO in cardiogenic shock due to PE or CHF demonstrated increased rates of survival to hospital discharge when compared to the PCS group. This study also highlights the need for a more uniform system of categorizing etiologies of cardiogenic shock.

**Keywords:** Venoarterial extracorporeal membrane oxygenation, refractory cardiogenic shock, heart failure, pulmonary embolism, mechanical circulatory support

### **Introduction**

Extracorporeal membrane oxygenation (ECMO), also known as extracorporeal life support (ECLS), has been available as a life-saving means of supporting respiratory or cardiac function since the 1970's.<sup>1,2</sup> The first successful use of venoarterial ECMO (VA-ECMO) was reported in 1972.<sup>3</sup> The first successful use of ECMO for treatment of cardiogenic shock was in 1973.<sup>4</sup> However, during this era there was no proven survival advantage over conventional management, largely due to high complication rates.<sup>1,2</sup> There has been a renewed interest in the use of ECMO for cardiopulmonary disease<sup>5,6</sup>, mostly due to technological advances, improved risk-benefit profile<sup>6-9</sup>, and increasing evidence and experience.<sup>5,6</sup>

ECMO is an invasive technique that allows for the oxygenation of deoxygenated blood. Deoxygenated blood is drained from the venous system, pumped through an oxygenator, and then re-infused to the patient. This allows for the exchange of carbon dioxide and oxygen. Veno-venous ECMO (VV-ECMO) can be used to bypass the lung and oxygenate blood when only respiratory support is necessary.<sup>10</sup> VA-ECMO bypasses both the heart and lungs, and thus can be utilized to provide both circulatory and respiratory support to patients with significantly impaired cardiac function, with or without impaired gas exchange.<sup>11</sup>

The primary goal of this analysis was to evaluate the efficacy of VA-ECMO support for cardiogenic shock based on the underlying etiology, and to identify patient populations that derive the most benefit from VA-ECMO support. Outcomes evaluated included survival to VA-ECMO decannulation and survival to hospital



discharge. In addition, we evaluated these outcomes in the following subgroups: cardiogenic shock due to primarily right ventricular failure vs. primarily left ventricular failure, peripheral vs. central VA-ECMO access site, VA-ECMO cannulation performed by cardiothoracic surgery (CTS) vs. interventional cardiology, and post-cannulation management by either the cardiology critical care service vs. other critical care services.

## **Methods**

Following institutional review board approval, data were collected by a combination of chart review of our institution's electronic medical record and data collected by the members of the mechanical circulatory support (MCS) team. Cases in which only VV-ECMO was used were excluded. For individual patients who were cannulated multiple times during one admission, each cannulation was counted as one initiation of VA-ECMO. Data regarding date of death were obtained via our institution's inpatient and outpatient medical records, as well as an internet search of the Social Security Death Index and obituaries.

All patients were thought to be in cardiogenic shock as a primary indication for VA-ECMO initiation. Distinguishing the etiology of cardiogenic shock proved difficult because it was very common for patients to have multiple pathologic processes contributing to shock. We defined the following groups for etiologies of cardiogenic shock: cardiac arrest and subsequent cardiopulmonary resuscitation (CPR), acute myocardial infarction (AMI), decompensated congestive heart failure (CHF), acute pulmonary embolism (PE), right ventricular failure (RVF) not secondary to an acute pulmonary embolism, and post-cardiotomy syndrome (PCS).

The patients in the CPR group were found to be in cardiogenic shock post cardiac arrest or with ongoing CPR. The cardiac arrest event for each patient was secondary to a variety of primary etiologies, including but not limited to AMI, PE, hypoxic respiratory failure, RVF, primary arrhythmia, and PCS. The patients in the AMI group were thought to have had an acute coronary thrombosis resulting in either a ST segment elevation myocardial infarction (STEMI) or non-ST segment elevation myocardial infarction (NSTEMI) with subsequent cardiogenic shock. The patients in the CHF group had varying etiologies of decompensated heart failure. The majority of this group had known severe, acute on chronic CHF. This group also included less frequent etiologies of acute decompensated heart failure such as peripartum cardiomyopathy, acute myocarditis, and stress-induced cardiomyopathy secondary to a pheochromocytoma. The patients in the PCS group underwent CTS for a variety of reasons. The majority of these patients developed cardiogenic shock following coronary artery bypass grafting (CABG) or valvular surgery, and failed weaning from cardiopulmonary bypass in the operating room. Some of these patients had undergone cardiac surgery for less frequent reasons such as carcinoid syndrome with valvular involvement or orthotopic heart transplant. The PE group included patients that were in cardiogenic shock secondary to acute, massive PE. The RVF group included patients with pulmonary conditions ranging from primary arterial pulmonary hypertension to pulmonary hypertension secondary to interstitial lung disease, but did not include patients with acute PE.



For survival to decannulation, each episode of VA-ECMO cannulation was used, resulting in 106 events for analysis. For survival to hospital discharge the number of individual patients was used, resulting in 99 events. Because some individual patients were placed on VA-ECMO multiple times for different etiologies of cardiogenic shock, the sum total of individuals cannulated for each etiology of cardiogenic shock was 102 as opposed to 99.

Historically, PCS was the most common indication for the utilization of VA-ECMO. The Nationwide Inpatient Sample database reports that the PCS group comprised 80% of all ECMO utilizations, and that cardiogenic shock comprised 16% in 1998. In 2009, 40% of ECMO initiations were due to PCS and 39% were due to cardiogenic shock.<sup>12</sup> Comprising the PCS group of all patients who failed weaning from cardiopulmonary bypass in the perioperative setting is consistent with other similar retrospective analyses.<sup>11,13,14</sup> Because PCS is historically the most common indication for VA-ECMO initiation, and this group had the lowest rate of survival to decannulation and hospital discharge, the PCS group (n = 13) was used as a reference group for calculating estimated odds ratios (OR) and accompanying 95% confidence intervals (CI). This method has been used by Carrol et al. in a similar retrospective analyses.<sup>14</sup> Fisher's exact test was used to acquire p-values.

When the necessary information was available in the electronic medical record, we further analyzed survival by separating occurrences of VA-ECMO into subgroups: cardiogenic shock due to primarily left ventricular failure vs. primarily right ventricular failure; peripheral vs. central access for VA-ECMO; VA-ECMO initiation performed by either CTS vs. an interventional cardiologist; and primary management post-cannulation by either the critical care cardiology service vs. other services.

The six main groups were compared on age and gender using one-way analysis of variance and a version of Fisher's exact test for larger contingency tables, respectively.

A p-value less than 0.05 was regarded as statistically significant. Data analysis was performed using Excel 2013 and SAS Version 9.3.

## **Results**

Between January 1, 2012, and January 1, 2015, VA-ECMO was initiated to provide support for cardiogenic shock in 99 patients on 106 occasions at our institution. Of these 99 individual patients, 67 (67.7%) were male and 32 (32.3%) were female. The mean  $\pm$ SD age was  $51.3 \pm 14.9$  years. The groups with the lowest mean age were the CHF and RVF groups, with mean ages of approximately 49 years. The groups with the highest mean age were the AMI and PE groups, with mean ages of approximately 57 years. However, the variation in mean ages across groups was not significant ( $p = 0.527$ ). All groups were in their majority male, with the exception of the PE group, which was evenly divided in gender. The variation in gender ratios across groups was not significant ( $p = 0.597$ ). The baseline characteristics are summarized in Table 1.



**Table 1. Baseline characteristics: mean age and gender for each group.**

	Mean Age (SD)	Male (%)	Female (%)
Total	51.3 (14.9)	67 (67.7%)	32 (32.3%)
CPR	49.8 (15.1)	25 (78.1%)	7 (21.9%)
AMI	57.4 (10.8)	8 (72.7%)	3 (27.3%)
CHF	48.8 (15.9)	16 (66.7%)	8 (33.3%)
PE	56.5 (13.8)	3 (50.0%)	3 (50.0%)
RVF	48.5 (14.6)	9 (56.3%)	7 (43.8%)
PCS	53.3 (18.0)	9 (69.2%)	4 (30.8%)

Note: Some persons belonged to more than one group. Within each row, however, each person is counted only once.

Results regarding rates of survival to ECMO discontinuation and survival to hospital discharge are furnished in Table 2 and Table 3, respectively.

**Table 2. Survival to decannulation, using post-cardiotomy syndrome as the reference group**

	Total # Cannulations		Survived to Decannulation		OR (survival) (95% CI)	p-value	OR (dying) (95% CI)
	N	%	N	%			
Total	106	100.0%	55	51.9%			
CPR	32	30.2%	12	37.5%	2.00 (0.46-8.74)	0.492	0.50 (0.11-2.19)
AMI	13	12.3%	9	69.2%	7.50 (1.31-43.0)	0.047	0.13 (0.02-0.76)
CHF	26	24.5%	20	76.9%	11.1 (2.29-54.0)	0.002	0.09 (0.02-0.44)
PE	6	5.7%	5	83.3%	16.7 (1.36-204.0)	0.041	0.06 (0.05-0.73)
RVF	16	15.1%	6	37.5%	2.00 (0.39-10.3)	0.454	0.50 (0.10-2.58)
PCS	13	12.3%	3	23.1%	1.00 (reference)		1.00 (reference)

Note: OR = estimated odds ratio, CI = confidence interval.



**Table 3. Survival to hospital discharge, using post-cardiotomy syndrome as the reference group**

	# Individuals Cannulated		Survived to Discharge		OR (survival)	p-value	OR (dying)
	N	%	N	%	(95% CI)		(95% CI)
Total	99	100.0%	36	36.4%			
CPR	32	32.3%	9	28.1%	4.70 (0.53-41.6)	0.238	0.21 (0.02-1.89)
AMI	11	11.1%	5	45.5%	10.0 (0.94-105.9)	0.061	0.10 (0.01-1.06)
CHF	24	24.2%	13	54.2%	14.18 (1.58-127.0)	0.011	0.07 (0.01-0.63)
PE	6	6.1%	5	83.3%	60.0 (3.10-1160)	0.003	0.02 (0.001-0.32)
RVF	16	16.2%	4	25.0%	4.00 (0.39-41.2)	0.343	0.25 (0.02-2.58)
PCS	13	13.1%	1	7.7%	1.00 (reference)		1.00 (reference)

Note: Some persons belonged to more than one group. Within each row, however, each person is counted only once. OR = estimated odds ratio, CI = confidence interval.

For the 106 occurrences of VA-ECMO initiation, survival to weaning of VA-ECMO support occurred on 55 (51.9%) occasions. Survival to hospital discharge occurred for 36 of the 99 (36.4%) individual patients.

For the PCS group (the reference group) survival to ECMO decannulation occurred in three of the 13 events (23.1%) of ECMO initiation. Only one of the 13 (7.7%) patients initiated on VA-ECMO survived to hospital discharge.

The AMI, CHF, and PE groups had significantly higher rates of survival to ECMO decannulation than the reference group. For the 13 initiations of VA-ECMO in the AMI group, nine (69.2%) survived to ECMO decannulation ( $p = 0.047$ ). For the 26 initiations in the CHF group, 20 (76.9%) survived ( $p = 0.002$ ). For the six initiations in the PE group, five (83.3%) survived ( $p = 0.041$ ).

The CHF and PE groups had significantly higher rates of survival to hospital discharge than the reference group. For the CHF group, 13 of the 24 (54.2%) individuals supported with VA-ECMO survived to hospital discharge ( $p = 0.011$ ). For the PE group, five of six (83.3%) individuals survived ( $p = 0.003$ ). Of note, all patients in the PE group who survived to ECMO decannulation survived to hospital discharge.

Additional analyses were performed to evaluate other factors in relation to survival to VA-ECMO decannulation and survival to hospital discharge. These factors included whether the patient was in cardiogenic shock due to primarily left ventricular failure vs. primarily right ventricular failure, central vs. peripheral VA-ECMO access, VA-ECMO cannulation performed by CTS vs. interventional cardiology, and post-cannulation management by the cardiovascular critical care team vs. a different inpatient service. There was no significant difference in survival to ECMO discontinuation or survival to hospital discharge between any of these groups. The results appear in Table 4 and Table 5.



**Table 4. Subgroup analysis of survival to VA-ECMO discontinuation**

	Total # Cannulations	Survived to Decannulation (n, %)		OR Survival (95%, CI)	p-value	OR Death (95%, CI)
LV Failure	70	37	52.9%	1.35 (0.59-3.09)	0.531	0.74 (0.32-1.71)
RV Failure	33	15	45.5%	1.00 (reference)		1.00 (reference)
Peripheral	74	36	48.6%	0.63 (0.27-1.49)	0.387	1.58 (0.67-3.75)
Central	30	18	60.0%	1.00 (reference)		1.00 (reference)
CTS	91	44	48.4%	0.47 (0.15-1.48)	0.266	2.14 (0.68-6.74)
Interventional Cardiology	15	10	66.7%	1.00 (reference)		1.00 (reference)
CCU	41	20	48.8%	0.92 (0.42-2.02)	1.000	1.08 (0.5-2.37)
Other	65	33	50.8%	1.00 (reference)		1.00 (reference)

Note: OR = estimated odds ratio, CI = confidence interval.

**Table 5. Subgroup analysis of survival to hospital discharge**

	# Individuals Cannulated	Survived to Discharge (n, %)		OR Survival (95%, CI)	p-value	OR Death (95%, CI)
LV Failure	66	22	33.3%	0.73 (0.31-1.75)	0.507	1.37 (0.57-3.27)
RV Failure	32	13	40.6%	1.00 (reference)		1.00 (reference)
Peripheral	71	25	35.2%	0.72 (0.30-1.77)	0.497	1.38 (0.57-3.37)
Central	28	12	42.9%	1.00 (reference)		1.00 (reference)
CTS	85	28	32.9%	0.43 (0.14-1.31)	0.152	2.33 (0.77-7.06)
Interventional Cardiology	15	8	53.3%	1.00 (reference)		1.00 (reference)
CCU	39	14	35.9%	0.95 (0.41-2.18)	1.000	1.05 (0.46-2.42)
Other	62	23	37.1%	1.00 (reference)		1.00 (reference)

Note: Some persons belonged to more than one group. Within each row, however, each person is counted only once. OR = estimated odds ratio, CI = confidence interval.



## Discussion

In a retrospective analysis of patients with cardiogenic shock placed on VA-ECMO we found that there were 106 events in 99 individual patients, 36.4% of which survived to hospital discharge.

Survival to VA-ECMO decannulation was better in the AMI, CHF, and PE groups when compared to the PCS group. Also, more patients with CHF and PE survived to discharge.

There were no statistically significant survival differences in patients in cardiogenic shock due to primarily left ventricular failure vs. right ventricular failure, central ECMO cannulation vs. peripheral ECMO cannulation, ECMO cannulation performed by CTS vs. interventional cardiology, or post-cannulation management by the cardiology critical care service vs. other inpatient services.

This retrospective analysis was performed to identify patient populations that may derive greater benefit from VA-ECMO as a means of providing MCS for patients in cardiogenic shock. We grouped patients supported by VA-ECMO by the underlying etiology of cardiogenic shock to compare rates of survival to VA-ECMO discontinuation and survival to hospital discharge.

Data demonstrating the efficacy of VA-ECMO support in the setting of cardiogenic shock largely comes from retrospective analyses such as this.<sup>14-17</sup> There is considerable variability in the documentation of the etiologies of cardiogenic shock in the VA-ECMO literature.<sup>15</sup> For example, in the Extracorporeal Life Support Organization (ELSO) ECLS Registry Report from January 2015, patients placed on ECLS for cardiac causes were grouped into the following categories: congenital defect, cardiac arrest, cardiogenic shock, cardiomyopathy, myocarditis, and other. In this system, more patients were included in the “other” group (1,785) than all other groups combined (1,621).<sup>18</sup> Because of this variability, it is difficult to evaluate the efficacy of VA-ECMO in the setting of cardiogenic shock across different institutions. To better evaluate the efficacy of VA-ECMO in cardiogenic shock due to specific pathological processes, a more uniform system to categorize patients in cardiogenic shock is necessary.

Our grouping system consisting of CPR, AMI, CHF, RVF, PE, and PCS is efficient and intuitive, both separating clinically different etiologies of cardiogenic shock and representing the vast majority of patients in cardiogenic shock. The benefit of such a system is that these specific etiologies of cardiogenic shock differ in their pathophysiology, management, and prognosis. Carroll et al. used a similar system with the following etiologies: AMI, PE, acute cardiomyopathy, chronic cardiomyopathy, post-cardiotomy shock, or other. In this system, patients that suffered cardiac arrest were placed into a group based on the underlying pathologic process causing cardiac arrest, and placed in the “other” group if no underlying process was identified.<sup>14</sup>

Patients who undergo CPR create difficulty with regard to classification. The ECLS registry defines extracorporeal membrane oxygenation for adults in cardiac arrest (eCPR) as the following: “extracorporeal life support (ECLS) used as part of initial resuscitation from cardiac arrest. Patients who are hemodynamically unstable and placed on ECLS without cardiac arrest are not considered E-CPR”.<sup>18</sup>



These patients typically undergo CPR due to a variety of underlying pathologic processes, such as AMI and PE. However, the fact that they suffer from cardiac arrest generally worsens their prognosis. In addition, these patients may not be in cardiogenic shock until they undergo cardiac arrest. Therefore, we assigned them their own group in our classification system. However, an argument can be made that these patients should be grouped based on the etiology of cardiac arrest. Also, there may be benefit in further dividing patients in the CHF group into patients with acute on chronic CHF and patients with acute decompensated CHF with no history of cardiomyopathy. Examples of patients that would fit in the latter division include those suffering from fulminant myocarditis or peripartum cardiomyopathy. Acutely decompensated CHF patients with no history of cardiomyopathy may be more likely to have a better prognosis due to potential reversibility, which may result in increased benefit to temporary support with VA-ECMO.

This analysis has limitations. It is retrospective as opposed to a prospective randomized controlled trial. However, the decision to initiate VA-ECMO support in these cases occurred in emergent situations, and in general VA-ECMO is initiated because patients are deemed to be at great risk of not surviving without it. The emergent nature of VA-ECMO initiation makes it difficult to propose a prospective randomized controlled trial, necessitating retrospective analyses which would benefit from a more uniform system of documentation across institutions.

Another limitation is the relatively small number of patients in some of the cardiogenic shock etiology groups, even though the total of 99 patients supported with VA-ECMO over a three-year period is a substantial number for a single institution. The fact that survival to VA-ECMO decannulation and hospital discharge in the PE group was found to be significantly better than in the reference group, notwithstanding the small sample size in the PE group, highlights the effectiveness of VA-ECMO in this setting. In addition, the relatively small numbers of patients in some groups demonstrates the need for increased uniformity across institutions, so that data may be pooled for meta-analysis.

Even with its limitations, this analysis provides valuable data regarding patients supported with VA-ECMO in cardiogenic shock. In particular, it demonstrates significantly increased rates of survival to hospital discharge in the CHF and PE groups versus PCS patients. In addition, we have proposed a classification system that can be used across institutions, so that larger numbers of patients can be pooled for meta-analysis to gain a better understanding of the efficacy of VA-ECMO use for specific etiologies of cardiogenic shock.

## **Conclusions**

In patients with cardiogenic shock and supported with VA-ECMO, the PCS group had the worst prognosis, with only 7.7% surviving to discharge. Patients with CHF and PE have the best prognosis, with 54.2% and 83.3% surviving to discharge, respectively. Prognosis was especially favorable for PE, where everyone who survived to decannulation was discharged alive. Our analysis underscores the need for functional, intuitive, and uniform classification of indications for VA-ECMO.



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