



## Invited Review

# VA-ECMO in Cardiogenic Shock in Adults: Indications and Outcomes

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## Abstract

### Background

Use of veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) has become increasingly common as a means of providing hemodynamic support for patients in cardiogenic shock. Data regarding the efficacy of VA-ECMO are provided almost exclusively by single-center, retrospective analyses. These retrospective analyses vary significantly with regards to documentation of the underlying pathophysiologic process resulting in cardiogenic shock.

### Methods

Relevant published studies were identified by using a comprehensive search of English-language MEDLINE from 1966 to November 2015. Relevant references found cited in these studies were also analyzed. These studies were analyzed with regard to the indications the authors used for initiation of ECMO, as well as the outcomes for each indication in each individual study.

### Results

Analysis of multiple relevant studies regarding the indications for ECMO support demonstrated that there is a great deal of variability with regard to the use of different indications for initiation of ECMO support.

### Conclusions

Data regarding the efficacy of VA-ECMO is derived largely from single-center, retrospective analyses. In order to gain a better understanding of the efficacy of VA-ECMO in different patient populations, a more standardized format of documenting the indication for VA-ECMO should be used in centers that provide VA-ECMO. In general, all patients supported with VA-ECMO are in cardiogenic shock. In our experience, the underlying processes leading to cardiogenic shock can be classified as: cardiac arrest, acute decompensated congestive heart failure, acute on chronic congestive heart failure, myocardial infarction, acute

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pulmonary embolism, right ventricular failure not secondary to acute pulmonary embolism, and post-cardiotomy syndrome.

### **Keywords**

VA ECMO, extracorporeal membrane oxygenation; heart failure; cardiogenic shock

### **Abbreviations**

AVR -Aortic valve replacement

Bi-VAD Bi-ventricular assist device

CABG -Coronary artery bypass grafting

CI – confidence intervals

ECMO -Extra-corporeal membrane oxygenation

HIT -Heparin-induced thrombocytopenia

LV – left ventricle

LVAD - Left ventricular assist device

OR – odds ratio

RV – right ventricle

RVF – right ventricular failure

VA -Veno-arterial.

### **Introduction**

The first successful use of extra-corporeal membrane oxygenation (ECMO) for treatment of cardiogenic shock was described in 1973 (1). However, only recently has veno-arterial (VA) ECMO become a commonly used and, in some institutions, the preferred device for short term hemodynamic support in cardiac arrest or cardiogenic shock.

Cardiogenic shock, defined as low cardiac output with poor tissue perfusion and end-organ damage, is a grave condition. Spontaneous recovery is rarely possible. A typical definition of cardiogenic shock usually includes multiple hemodynamic parameters with some variability. Such parameters may include



cardiac index less than 2.0 L/min/m<sup>2</sup> with systolic blood pressure less than 100 mmHg and pulmonary capillary wedge pressure  $\geq$ 24 mmHg, and dependency on at least two inotropes or vasopressors with or without intra-aortic balloon pump support (2). With pharmacologic treatment, mortality is invariably high. In the SHOCK trial registry, patients with cardiogenic shock complicating an acute myocardial infarction (AMI) had in-hospital mortality of 60% (3).

By the data from the Nationwide Inpatient Sample database, ECMO use in adults has increased significantly since 2007. In 2002, the leading indication for initiation of VA-ECMO was post-cardiotomy syndrome (PCS) (56.9% of all cases). By 2012, the proportion of PCS as an indication for VA-ECMO decreased to 37.9% of cases, and cardiopulmonary failure as an indication increased from 3.9% (2002) to 11.1% (2012) (4).

There are several reasons behind the increased use of VA-ECMO. Cardiogenic shock and cardiac arrest, regardless of the underlying pathological condition, are conditions most frequently managed by cardiologists. Unlike some other devices, ECMO can be placed at the bedside or in the catheterization laboratory. Also, ECMO can be initiated not only by surgeons, but also interventional cardiologists. This increases access to this technology and the comfort level of using ECMO - not only by attending cardiologists but also cardiology fellows, who then begin practicing independently with an increased level of familiarity regarding the use of ECMO in critical situations.

Another factor contributing to the wide acceptance of ECMO technology is progress in other areas of mechanical circulatory support, particularly left ventricular assist devices (LVADs). With the ability to maintain adequate hemodynamics in patients using an LVADs for several years, it became possible to use ECMO not only as a bridge to recovery, but also as a bridge to more permanent therapies such as a long-term LVAD or cardiac transplant. ECMO provides sufficient hemodynamic support and allows time to recover end-organ function and decide if the patient is salvageable (2). Because ECMO can be a bridge to an LVAD, which can itself be a bridge to cardiac transplant, ECMO can serve as a bridge to bridge (4).

Unlike other percutaneous short term devices, such as intra-aortic balloon counterpulsation devices, the TandemHeart (CardiacAssist, Inc., Pittsburgh, Pennsylvania), and Impella (Abiomed, Danvers, Massachusetts), ECMO can support the left ventricle (LV), right ventricle (RV), or both. It is also useful in incessant ventricular tachycardia, when isolated LV support is usually insufficient due to inadequate filling by the RV, which is equally affected by the arrhythmia.

It can be predicted that the utilization of ECMO will only increase in years to come. We felt that it was useful to summarize the literature in terms of indications and outcomes of VA-ECMO in cardiogenic shock, and to discuss the classification of indications for ECMO that is currently in use.



## **Methods**

Relevant published studies were identified by using a comprehensive search of English-language PubMed from 1966 to November 2015 for the MeSH term “Heart Arrest” or text words “heart arrest” or “cardiac arrest” MeSH term “shock, cardiogenic” or text word “cardiogenic shock”, MeSH term “extracorporeal circulation” or text word “extracorporeal circulation”, or “extracorporeal membrane oxygenation”. In addition, the reference sections of the selected publications were manually screened for further relevant studies.

## **Cardiogenic shock and cardiac arrest**

One of the distinctions that must be made is whether VA-ECMO is used for cardiogenic shock or cardiac arrest. In fact, cardiac arrest can be considered an extreme form of cardiogenic shock. When trying to analyze the outcomes of VA-ECMO by indication, we found it difficult to separate cardiac arrest and cardiogenic shock. In acute myocardial infarction (AMI), cardiogenic shock develops due to a large portion of myocardium being affected by evolving ischemia and necrosis, which also leads to electric instability. If this results in ventricular fibrillation and cardiac arrest, and the ECMO is placed during resuscitation or immediately after restoration of spontaneous circulation, the case could either be classified as cardiogenic shock due to AMI, or as cardiac arrest/resuscitation. The physiology of AMI is different from cardiac arrest. On the other hand, cardiac arrest may result from other conditions, such as pulmonary embolism (PE), acute myocarditis, terminal chronic cardiomyopathy, right ventricular failure (RVF) due to a chronic pulmonary process, acute rejection after cardiac transplantation or PCS. If the inciting pathophysiology of those underlying conditions persists post-arrest, we should classify the cases of cardiac arrest by their underlying etiology. However, if we agree that cardiac arrest, once it occurs, has the distinctly different physiology of a dying organism, then perhaps all cardiac arrest/resuscitation cases should be analyzed separately, regardless of the inciting pathologic process.

In the past, authors of similar analyses have encountered same problem. Nichol et al. (5) performed a systematic review of case series in which ECMO was used for cardiogenic shock or cardiac arrest from 1966 to 2005. By their data, there was a 50% survival rate when ECMO was used for cardiogenic shock and a 44% survival rate when it was used in cardiac arrest, but a statistically significant heterogeneity was found within each patient group. Other authors, comparing outcomes in cardiac arrest versus cardiogenic shock, also reported better survival in the latter. There is also increasing data on the efficacy of ECMO implanted during cardiopulmonary resuscitation (CPR).

In the ESCLS registry, the definition of extracorporeal membrane oxygenation for adults in cardiac arrest (eCPR) is as follows: “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” (6). According to this definition, cases of ECMO facilitated cardiac arrest should be analyzed separately from cases of cardiogenic shock.



Per multi-institutional data from the Extracorporeal Life Support Organization (ELSO) registry, survival to hospital discharge in ECMO during CPR was 27% (6).

For the purpose of this review, we attempted to focus on cardiogenic shock rather than cardiac arrest. In many cases, though, it was nearly impossible to separate cardiogenic shock from cardiac arrest because the reported series often include both. In the tables throughout this manuscript, we indicated in the comments how many cases out of each cohort had ECMO initiated during CPR. Ideally, we think that all such cases should be taken out of their original subsets and analyzed as ECMO during CPR, or eCPR.

Like many therapies for critical conditions, ECMO is a difficult modality to study in a randomized controlled trial because the decision to utilize ECMO is commonly made instantaneously, not allowing time for research-specific procedures like randomization or informed consent. Because of this, information regarding the use of ECMO is obtained from registries. It is very important that registries documenting ECMO data follow some form of standard reporting that is clinically relevant.

The primary international registry regarding ECMO is maintained by the Extracorporeal Life Support Organization <http://www.else.org> (7), with the mission of providing support to institutions delivering ECLS through continuing education, guideline development, original research, publications, and maintenance of a comprehensive registry of patient data. Over 230 individual ECMO centers, including ours, enter data into this registry. Data are submitted to the registry by reporting centers using a standardized data collection form and include patient demographic information, diagnosis and procedure codes, pre-ECMO support details, ECMO indication and support details, adverse events, and patient outcomes (8).

The ELSO registry separates cardiac versus pulmonary runs, and VA versus veno-venous (VV) ECMO. Furthermore, within cardiac runs, it recognizes the following indications: cardiac arrest, cardiogenic shock, acute myocarditis, cardiomyopathy, congenital, and miscellaneous. Interestingly, not a single group of authors, analyzing their own data for publication, followed the same categories of indications for VA-ECMO in adults.

### **Conditions within Cardiogenic Shock**

In this section, we summarized the distribution of indications for VA-ECMO reported by different authors. The classifications of indications are extremely heterogeneous, making the analysis difficult. Besides assigning their cases to different subsets, authors sometimes exclude large groups other than cardiac arrest/CPR. As an illustration, one retrospective study reporting the outcomes of their 26 patients with cardiogenic shock classified indications into AMI, decompensated chronic heart failure (HF), cardiac arrest, and acute valvular pathology, but excluded post-cardiotomy shock (9). This is not an uncommon situation, but it skews the distribution of cases, making comparison between different institutions very difficult. One of the goals of this section is to



demonstrate the vast heterogeneity of reported indication and to present a evidence that there is a need for unified definitions and uniform classification of indications for ECMO in cardiogenic shock.

As an example, Abrams et al. (10) used the following cardiac indications for ECMO initiation: AMI, fulminant myocarditis, septic cardiomyopathy, decompensated pulmonary hypertension with RVF, bridge to VAD or heart transplantation, right ventricular support during LVAD implantation in biventricular failure, PE, PCS, and primary graft failure post-heart transplantation. Another group used different set of indications: AMI, acute HF, chronic HF, PCS, and PE. (11). When we analyzed our data, we used similar categories, with an addition of RVF due to chronic pulmonary disease. In general, it is difficult to identify even two studies where authors use similar classification for indications for VA-ECMO.

The highest level of evidence for all indications is cohort studies, which make the importance of the registries even greater. Categories of indications for VA-ECMO support are summarized in Table 1.

Burrell et al.(12) formed their cohort only from survivors, and therefore it was not comparable with other studies.

The most controversial category is HF. It can be acute or acute-on-chronic, and can be reported and analyzed together or separately. Differentiating cardiomyopathy from myocarditis is sometimes impossible, especially in the setting of an emergent situation. It seems reasonable to avoid using cardiomyopathy as an indication for ECMO, and to only differentiate acute or acute-on-chronic HF. All the cases of myocarditis will be then included in the acute HF group. Also, since congenital defects are so infrequent in the adult population, this group could be classified as “other/miscellaneous”. Also, the indication “bridge to transplant or LVAD” should be distributed among other categories, because patients bridged due to hemodynamic instability in the setting of multiple different underlying conditions.

The 2015 ECLS registry included the following categories: total (3406), cardiac arrest (283), acute myocarditis (51), cardiogenic shock (873), miscellaneous (1,785), congenital (163), cardiomyopathy (251). There are multiple problems with how the ECLS registry is categorized. It is clear that these diagnostic categories do not correlate with what investigators use clinically. Acute myocarditis and cardiomyopathy are similar indications. All disease processes result in cardiogenic shock. Lastly, if a miscellaneous group counts for half of the cases, it has to be divided into subtypes.

## **Outcomes in typical indications for VA-ECMO**

### **Mixed Subsets**

Many authors reported their outcomes for mixed cohorts of patients, where some patients were receiving CPR at the time of ECMO insertion. In AMI, when ECMO was inserted in the absence of ongoing CPR, survival to discharge reached 55%. Survival to discharge when ECMO was placed during CPR was 12.5%. However,



**Table 1. Classification/indications for VA-ECMO in Adults**

Author, Date Country	N	Car-diac arrest/ CPR	Acute MI	Acute myo-carditis or AHF	Post-cardio-tomy	Primary graft failure after heart trans-plant	PE	Acute on chronic HF	Other indications
Kolla(13) 1996 USA	27	9 (33.3%)		1 (3.7%)	7 (25.9%)	5 (18.5%)			Bridge to transplant 5 (18.5%)
Willms (14) 1997 USA	81	68 (84.0%)	3 (3.7%)		4 (4.9%)	2 (2.5%)		4 (4.9%) (dilated cardio-myopathy)	
Bowen (15) 2001, USA	23	15 (65%)	8 (34.8%)						
Hoefler (4) 2006 USA	131			58(44.3%) (acute HF)	62(47.3%)			11(8.4%)	
Combes (16) 2008 France	81		16 (19.8%)	16 (19.8%)	16 (19.8%)	10 (12.3%)		18 (22.2%) (dilated cardio-myopathy)	Other 5 (6.2%)
Liden(17) 2009 Sweden	52		9 (17.3%)	2 (3.8%)	33 (63.4%)				Other 8 (15.4%)
Bermudez (18) 2011 USA	42		33 (78.6%)					9 (21.4%)	
Barth (19) 2012 France	242				32 (13.2%)				112 (46.3%) Cir-culatory collapse 80 (33.1%) cardiogenic shock
Guenther (20) 2013 Germany	41		23 (56.1%)	13 (31.7%)					Other 5 (12.2%)
Chamogeorgakis (21) 2013, USA	61		32 (52.5%)					29(47.5) all HF	
Loforte (22) 2014, Italy	228		27 (11.8%)	6 (2.6%)	118 (51.8%)	37 (16.2%)		40 (17.5%)	
Truby (23) 2015 USA	179		46 (25.7%)	24 (13.4%) acute HF	70 (39.1%)	17(9.5%)			Other 22 (12.3%)
Tarzia (24) 2015 Italy	64		41 (64%)	6 (9.4%)				26 (56.3%)	Congenital defect 2 (3.1%)
Carroll (11) 2015 USA	123		35(28.5 %)	13 (10.6%)	26 (21.1%)		17 (13.8%)	15 (12.2%)	57 (46.3%) with cardiac arrest before ECMO 17(13.8%) other



the predicted survival for this cohort was less than 10% (25), so utilization of ECMO demonstrated benefit.

The largest series of ECMO recipients in a single institution was reported from the National Taiwan University Hospital, where ECMO was utilized for 607 patients (26). Unfortunately, there were no specific indications for ECMO support reported in this paper. The overall survival to discharge was 30.1%. Independent predictors of mortality included age, stroke, need for dialysis during ECMO, pre-ECMO infection, hypoglycemia, and alkalosis (26). Per other authors, independent predictors of intensive care unit death were the following: device insertion during CPR (OR = 20.68), 24 hour urine output < 500 mL (OR = 6.52), prothrombin activity < 50% (OR = 3.93), and female sex (OR = 3.89); myocarditis was associated with better outcomes (OR = .13) (16). Other factors associated with poor prognosis were older age, longer support time, decreased cardiac function at the baseline (27), higher lactate concentration, peripheral vascular disease, pre-operative chronic obstructive lung disease, ejection fraction, and renal dysfunction (11, 28).

### **Survival in Acute MI**

Outcomes in AMI were often reported with inclusion of patients suffering cardiac arrest in the setting of acute MI. Because, as previously mentioned, the outcomes are worse in the setting of cardiac arrest, the resulting numbers are difficult to interpret. In the tables below, all studies are retrospective and single center, unless indicated otherwise.

Almost all cohorts included patients that suffered cardiac arrest, which should increase mortality. The outcomes are very heterogeneous, with survival to hospital discharge ranging from 19% (29) to 87.5% (30). This last result was from very small series with only eight observations. Part of the heterogeneity may be due to the fact that there is a mixture of cardiogenic shock and cardiac arrest in the setting of AMI (Table 2).

ECMO was able to save patients even with potentially fatal complications of acute MI such as free wall rupture, ventricular septal defect, and mitral regurgitation due to papillary muscle rupture. Out of nine patients with such complications, four were discharged, three of them in good neurological condition (31).

In AMI, longer CPR time and support time, increased cardiac enzymes, lower ejection fraction, lower albumin, and major complications were risk factors of mortality (32).



**Table 2. Outcomes of VA-ECMO in Acute Myocardial Infarction**

Author, date	N	Survival On ECMO, %	Survival to discharge, %	Survival 30 days, %	Time on ECMO	Comments
Shawl, 1989 (30)	8	87.5	87.5	87.5		2 in cardiac arrest
Matsuwaka, 1996 (29)	16	87.5	19	37.5		AMI (n = 7), or post-infarction LV free wall rupture (n = 9)
Sheu, 2010 (33)	46			60.9		30 day survival without ECMO with similar hemodynamic 28%
Aiba, 2001 (34)	26	35	19.2			
Chen, 2006 (25)	36	69.4	33.3		108.5± 77.5 hrs	eCPR in all
Brunet, 2008 (35)	8	25	25			4 e CPR
Bermudez, 2011 (18)	33			64	69 hours (3–352)	Survival 48% at 1 and 2 years
Chung, 2011 (32)	20	70	50		3.8±4.0 days	CPR in 14 cases
Sakamoto, 2012 (36)	98	55.1	32.7		Mean 68.9 ± 62.7 hours	64 eCPR during
Negi, 2015 (37)	15	50	47	47	Mean 45 hours	5 after cardiac arrest
Esper, 2015 (38)	18		67		3.2 +/- 2.5 days	
Carroll*, 2015 (11)	35	50	28			14 eCPR

\* The data are presented as a graph only, we made our best estimate

### Survival in Heart Failure

There are several indications for ECMO within acute HF, and they are also reported inconsistently. Acute myocarditis (Table 3), acute HF, acute on chronic HF (Table 4), cardiomyopathy – all these terms are used in the ECMO literature, making the outcome comparison challenging. Septic cardiomyopathy is sometimes reported separately (Table 5). Several authors commented on higher survival rates in fulminant myocarditis than in other indications for ECMO (39). In the analysis from the ECLS registry, acute myocarditis was a favorable factor for survival (OR : 0.18; 95% confidence interval CI : 0.05 to 0.69) (6). It is important to remember that other categories such as AMI are not recognized as diagnostic entities by the registry.

Few authors reported the outcomes of acute on chronic HF as a separate category.



**Table 3. Outcomes of VA-ECMO in Fulminant Myocarditis**

Author, date	N	Survival On ECMO, %	Survival to discharge, %	Survival 30 days, %	Time on ECMO	Comments
Kawahito, 1998 (40)	6	83.3	83.3		200 ± 52 hours Range 32-399	
Kato, 1999 (41)	9	100	77.8	88.9	6.4 ± 2.2 days	
Asaumi, 2005 (42)	14	71	71	71	median 130 (42–171) h (max 12 days)	No further death in 3-5 years
Pages, 2009 (43)	6	83.3	83.3	83.3	13 ± 4 days	Outcomes are similar to biventricular assist device
Gariboldi, 2010 (44)	10		70		Median 12 days	
Carroll, 2015 (11)	13	80	70			Numbers are presented on the graph, we took our best estimate
Hsu, 2011 (45)	75		64		171.5 ± 121 hours	23 5 eCPR
Mirabel, 2011 (46)	35		68.6			5 eCPR
Wu, 2012 (47)	16		87.5			
Ishida, 2013 (48)	20		60			
Diddle, 2015 (8)			61			21% inserted during CPR Data from ELSO

**Table 4. Outcomes of VA-ECMO in Acute on Chronic HF**

Author, date	N	Survival on ECMO, %	Survival to discharge, %	Survival 30 days, %	Time on ECMO	Comments
Bermudez 2011 (18)	9			56	60 hours (1–274)	11% at 1 and 2 years
Carroll, 2015 (11)	15	47	40			Numbers are presented on the graph, we took our best estimate

**Table 5. Outcomes of VA-ECMO in septic cardiomyopathy**

Author, date	N	Survival On ECMO, %	Survival to discharge, %	Survival 30 days, %	Time on ECMO	Comments
Brechot, 2013 (49)	14	86	71			All 10 survivors alive after a median of 13 (3–43) months
Huang., 2013 (50)	52		15			21(40%) eCPR



When patients with cardiomyopathy were bridged with ECMO to recovery, LVAD or transplant, overall survival to discharge was 49%. 26% of these patients were transitioned to implantable VADs, 18% recovered sufficient native cardiac function, and 11% were bridged to transplantation. CPR at the time of implantation was an independent predictor of in-hospital mortality (odds ratio: 5.79;  $p = 0.022$ ) (18).

### **Survival in Right Ventricular Failure due to Chronic Lung Disease**

VA-ECMO is emerging as a cardiopulmonary support modality for RV failure due to chronic pulmonary disease, especially if there is a potentially reversible cause of exacerbation of a chronic process (such as acute pneumonia) or if ECMO serves as a bridge to transplant. Still, VV ECMO is a more common modality in this settings, and the outcomes are often reported for VV and VA-ECMO combined (51-54). In a single institution series, VA-ECMO was used in 6 patients with primary arterial pulmonary hypertension or pulmonary hypertension due to a congenital defect (in two cases, the artery was not, in fact, cannulated, but large atrial septal defects created the access to systemic arterial circulation). Both bridge to transplant patients were successfully weaned off ECMO and discharged home after lung transplant. Out of 4 patients who were placed on ECMO because of acute destabilization, 3 were in cardiac arrest. Three out of 4 survived to weaning off ECMO, and two survived to discharge (54). In the Hoopes et al.(53) paper, the indications for VA-ECMO included pulmonary fibrosis, cystic fibrosis, and pulmonary hypertension. Despite currently limited literature, this area will likely continue to expand, and it is reasonable to analyze it as a separate category (Table 6).

**Table 6. Outcomes of VA-ECMO in right ventricular failure due to chronic lung disease**

Author, date	N	Survival On ECMO,%	Sirvival to discharge,%	Survival 30 days, %	Time on ECMO	Comments
Ollson, 2010 (55)	5	60	60			All bridge to lung transplant
Hoopes, 2013 (53)	19	94.7	94.7			2 institutions
Rozenhweig, 2014 (54)	6	83.3	66.7			

### **Survival in Pulmonary embolism**

Massive PE with acute RV failure with circulatory collapse is another indication for VA-ECMO. Similar to other indications for VA-ECMO support, the information is coming from retrospective single center series (Table 7)



**Table 7. Outcomes of VA-ECMO in pulmonary embolism**

Author, date	N	Survival On ECMO,%	Survival to discharge,%	Survival 30 days, %	Time on ECMO	Comments
Kawahito, 2000 (56)		57	57	57	18-168 hours Mean 67.8±67.1	
Maggio, 2007 (57)	21		62		mean 113 ± 97 hours or 4.7 days	Eight were in active cardiac arrest.
Munakata, 2012 (58)	10			70	Mean 48 ± 44 hours Median 23 hours	9 in cardiac arrest
Akkanti, 2015 (59)	4	100	100			

### Survival in Post heart transplant for primary graft failure

The outcomes of VA-ECMO for post-heart transplant graft failure are shown in Table 8.

**Table 8. Outcomes of VA-ECMO in Primary Graft Failure after Heart Transplantation**

Author, date	N	Survival On ECMO,%	Survival to discharge, %	Time on ECMO	Comments
Ko, 2002 (60)	9	77.7	44.4		
Taghavi, 2004 (61)	13	77	54	72.4 ±61.6	RVF Comparing with RVAD, ECMO is better. Weaning (77% versus 13%; p< 0.001 )
Leprince, 2005 (62)	14	78.6	50	5 ± 2.5 days	3 with pulmonary HTN, 3 from marginal donors
Chou, 2006 (63)	19	84.2	52.6	157 +/- 129 hours.	Compared with data from VAD-supported PCAGF, ECMO had a better weaning and graft survival rates (p < 0.05)
Arpesella, 2008 (64)	11			9.1 +/- 6.9 days (range, 1-18 days)	
D'Alessandro, 2010 (65)	54	67	50		Patients treated with ECMO have the same 1-year conditional survival as patients not having suffered EGF: 94% at 3 years
Marasco, 2010 (66)	39	87	74.3		Comparison of survival in the 39 ECMO patients to the non-PGF patients (n = 185) showed a significantly worse survival in the ECMO group (p = 0.007). When those patients who died in the first 30 days were excluded, there was no difference in overall survival between groups (p = 0.73).

### Survival in Postcardiotomy cardiogenic shock

Post-cardiotomy cardiogenic shock is a rare but often fatal complication of cardiac surgery. In approximately 1% of all cases, patients cannot be weaned off cardiopulmonary bypass, and VA-ECMO is the only viable option for



hemodynamic support (39) (Table 9). Predictors of mortality included age, diabetes, and longer time on cardiopulmonary bypass (67).

**Table 9. Outcomes of VA-ECMO in Postcardiotomy Syndrome**

Author, date	N	Survival On ECMO, %	Survival to discharge, %	Survival 30 days, %	Time on ECMO	Comments
Magovern, 1994 (68)	21		57.1			
Kawahito, 1994 (69)	13	77			1 to 66 hr (mean 27.4 +/- 26.7),	
Wang, 1996 (70)	18	52.6	33.3			
Muehrcke, 1996 (71)	23	56.5	30.4		58.4 +/- 35.1 hours (range, 0.5 to 144 hours)	Including 4 post heart transplant
Kitamura, 1999 (72)	64	50	26.7			76.2% and 57.1% with biventricular bypass, 87.5% and 37.5% with isolated left ventricular bypass, and 60.0% and 40.0% with pulsatile left ventricular assistance
Sasaki(73)	9	66.7	55.5		84.3 +/- 6.3 hrs	
Hata, 2000 (74)	30	56.7	43.3			
Hayashi, 2000 (75)	9	100	66.7			
Ko, 2002 (60)	76	60.5	26.3		99±32 hours.	Including 9 post heart transplant, presented separately in the next table.
Doll, 2004 (76)	219	60	24	24	2.8 +/- 2.2 days	74% of the discharged alive in 5 years
Bakhtiary, 2008 (77)	45	55.5	29	47	6.4 ± 4.5 days	1 post heart transplant In 3 years, 22% of the initial cohort was alive
Liden, 2009 (17)	33		45		5.59±4.9days	
Elsharkawy, 2010 (67)	233		36			
Hsu, 2010 (78)	51	53	33	51		29% alive in 1 year
Carroll, 2015 (11)	26	50	24			Numbers are presented on the graph, we took our best estimate



### **ECMO to prevent acute right ventricular failure after LVAD implantation**

One of the newest indications for VA-ECMO is RVF after LVAD implantation, when the RV is potentially recoverable but needs time to adjust to new hemodynamic conditions (10). Although the numbers are likely small, this indication is so different from the others, that we think it should be collected and analyzed separately.

### **Outcomes by Indications**

As previously mentioned, patients supported with ECMO in the setting of both fulminant myocarditis and PE have good rates of survival. In one study, patients with PE (odds ratio 8.0, 95% confidence interval 2.00 to 31.99;  $p=0.01$ ) and acute cardiomyopathy (odds ratio 7.5, 95% confidence interval 1.69 to 33.27;  $p=0.01$ ) had a higher rate of survival than that of acute myocardial infarction, chronic cardiomyopathy, and miscellaneous etiologies compared to post-cardiotomy cardiogenic shock as a referent (11). However, in another cohort, survival in cardiomyopathy was worse than in AMI (18).

### **Proposed Classification of Indications for ECMO in Cardiogenic Shock**

Data regarding the efficacy of VA-ECMO is derived largely from single-center, retrospective analyses. In order to gain a better understanding of the efficacy of VA-ECMO in different patient populations, a more standardized format of documenting the indication for VA-ECMO should be used in centers that provide VA-ECMO. We believe that developing a more uniform and clinically relevant way of categorizing the indications for initiation of VA-ECMO support in patients with cardiogenic shock is essential to gaining a better understanding of which patient groups may or may not benefit from VA-ECMO support.

In general, all patients supported with VA-ECMO are in cardiogenic shock. Therefore, the underlying pathophysiologic process leading to cardiogenic shock should be identified and documented as the indication for VA-ECMO support in addition to cardiogenic shock. It has been our experience that the underlying processes leading to cardiogenic shock can be classified in the following categories: cardiac arrest, acute decompensated congestive heart failure, acute on chronic congestive heart failure, myocardial infarction, acute PE, RVF not secondary to acute PE, and PCS.

The cardiac arrest category is the most difficult to classify because patients who suffer cardiac arrest typically have another underlying process, such as AMI or acute PE, and the potential for meaningful recovery may depend on reversibility of the underlying process. However, patients who suffer cardiac arrest have a poorer prognosis than patients who are in cardiogenic shock due to a process such as AMI or acute PE in the absence of cardiac arrest. Therefore, we propose that patients should be classified in a group of cardiac arrest, regardless of the underlying cause of cardiac arrest. Both cardiac arrest and any other underlying process should be documented. In addition, if a patient is initiated on VA-ECMO while actively undergoing CPR, this should be documented as eCPR. This will help analyze the efficacy of initiating VA-ECMO support during CPR, which could potentially change future clinical practice.



The classification of acute decompensated heart failure should be used for patients with no history of heart failure who are in cardiogenic shock due to new-onset cardiomyopathy. This group would include patients such as those in cardiogenic shock due to fulminant myocarditis, stress-induced cardiomyopathy, viral cardiomyopathy, peripartum cardiomyopathy, etc. It is necessary to differentiate this group from patients suffering acute or chronic decompensated heart failure because the natural course of the disease process is very different due to higher potential to regain cardiac function. Patients with a history of chronic cardiomyopathy may be more likely to require more long-term mechanical support, such as a LVAD, or heart transplant, and would potentially demonstrate decreased benefit from VA-ECMO when compared to patients with no history of cardiomyopathy.

Patients in cardiogenic shock due to AMI should be classified into one category due to the distinct nature of this condition. Cardiac recovery in the setting of AMI is variable, and typically depends on the ability to provide timely revascularization. In addition, patients may suffer the inherent complications of AMI such as an unstable arrhythmia, acute mitral regurgitation, mechanical complications such as free wall rupture, etc. Not only should AMI be documented, but mechanical complications contributing to cardiogenic shock should be documented as well.

Patients with no history of left or right ventricular dysfunction who are in cardiogenic shock due to right heart failure in the setting of an acute PE should be separated from patients with chronic right ventricular dysfunction. Patients with acute PE and no underlying right or left ventricular dysfunction have a fairly reversible cause of cardiogenic shock, and would likely demonstrate increased benefit from VA-ECMO when compared to patients with chronic right ventricular dysfunction resulting from pulmonary arterial hypertension or pulmonary fibrosis, for example. Given the difficulty in treating or reversing these underlying conditions, patients with chronic, isolated RVF would likely demonstrate decreased benefit from VA-ECMO than patients with RVF due to acute PE with no underlying cardiomyopathy.

Patients who are supported with VA-ECMO in the setting of recent cardiac surgery should be classified into a separate group such as a PCS group. This group would include patients with recent coronary artery bypass grafting, valvular surgery, or any other cardiac surgery. Often, these patients cannot be weaned from cardiopulmonary bypass in the operating room, or may develop cardiogenic shock in the post-operative course due to complications or the natural sequela of critical illness. This group has demonstrated poor survival when supported with VA-ECMO in the setting of cardiogenic shock.

## **Conclusion**

The use of VA-ECMO to provide MCS in the setting of cardiogenic shock has become increasingly more common over the past several years. The decision to initiate VA-ECMO support typically occurs in an emergency setting, making it difficult to evaluate the efficacy of VA-ECMO support in a prospective, randomized controlled trial. The vast majority of objective evidence regarding the



efficacy of VA-ECMO support in the setting of cardiogenic shock comes from retrospective analyses in single-centers. In order to obtain data to help guide clinical practice regarding the decision to utilize VA-ECMO as a means of providing MCS, there should be a more uniform system of documentation of the underlying etiology of cardiogenic shock across centers that utilize VA-ECMO.

This review demonstrates the extensive variability in the documentation of the indications for MCS with VA-ECMO in the setting of cardiogenic shock across different centers utilizing VA-ECMO. We propose that the etiologies should include cardiac arrest, acute decompensated congestive heart failure, acute on chronic congestive heart failure, AMI, acute PE, RVF not secondary to acute pulmonary embolism, and PCS. We believe that these disease processes include the majority of disease processes causing cardiogenic shock and need for MCS, and that they differ with regard to pathophysiology, prognosis, and management. If centers providing support with VA-ECMO document the etiology of cardiogenic shock in a uniform manner, it will be possible to obtain more accurate and clinically relevant data regarding the efficacy of VA-ECMO in these patient populations, which may assist in guiding management strategies in patients with cardiogenic shock.



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