Predictors of in-hospital mortality and midterm outcomes of patients successfully weaned from venoarterial extracorporeal membrane oxygenation

Federico Sertic, MD,[a] Lexy Chavez, BS,[a] Dieynaba Diagne, MPH,[a] Thomas Richards, PhD,[a] Joyce Wald, MD,[b] Michael Acker, MD,[a] Edo Birati, MD,[b] Eduardo Rame, MD,[b] and Christian Bermudez, MD[a]

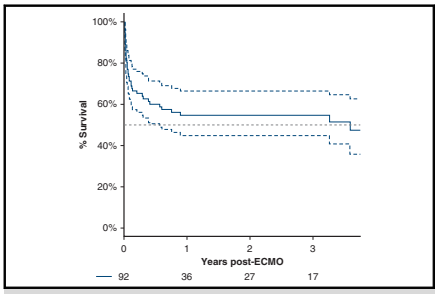
ABSTRACT

Objectives: There is limited evidence to guide the decision to proceed with weaning from venoarterial extracorporeal membrane oxygenation, and approximately 30% of patients weaned "successfully" do not survive to hospital discharge. We evaluated predictors of in-hospital mortality and midterm outcomes of patients successfully weaned from venoarterial extracorporeal membrane oxygenation after support for cardiogenic shock, surviving more than 24 hours after weaning, with the aim of improving patient selection for durable weaning.

Methods: We performed a retrospective analysis of 92 patients supported on venoarterial extracorporeal membrane oxygenation and successfully weaned between January 2013 and February 2018. Survival was estimated by the Kaplan–Meier method. Predictors of in-hospital mortality were identified using a Cox proportional hazards model and an Akaike information criterion–selected multivariate model.

Results: Overall survival at hospital discharge was 64.2%; survival was 54.6% 1 year after support and 51.4% 3 years after support. A history of diabetes, previous myocardial infarction, prolonged extracorporeal membrane oxygenation support, and hypoxemia at extracorporeal membrane oxygenation weaning were independent predictors of in-hospital mortality. At midterm follow-up, New York Heart Association class I heart function was observed in 53% of patients, class II in 19%, class III in 16%, and class IV in 12%. Average left ventricular ejection fraction was 46.5% ± 18.2%, and 50% of the patients had been readmitted to the hospital because of heart failure.

Conclusions: Durable extracorporeal membrane oxygenation weaning with acceptable midterm functional status is obtainable in well-selected patients. Previous myocardial infarction, diabetes, prolonged extracorporeal membrane oxygenation support, and pulmonary dysfunction strongly predicted in-hospital mortality after venoarterial extracorporeal membrane oxygenation weaning. In this high-risk situation, other heart replacement therapies should be considered. (J Thorac Cardiovasc Surg 2021;161:666-78)



Midterm outcomes of patients weaned from ECMO.

CENTRAL MESSAGE

Durable and sustained ECMO weaning, with acceptable midterm echocardiographic and functional status, is obtainable after support for CS in appropriately selected patients.

PERSPECTIVE

Limited information is available on the outcomes of patients weaned from ECMO. Patients with comorbidities, previous MI, low ejection fraction, residual valvular abnormalities, prolonged ECMO support, and hypoxemia at the time of weaning may have a high risk of in-hospital mortality. Other heart replacement options should also be considered in this patient population.

See Commentary on page 679.

The use of venoarterial extracorporeal membrane oxygenation (VA-ECMO) and other short-term circulatory assist devices to support patients in refractory cardiogenic shock (CS) has rapidly increased in the United States over the last decade.[1] VA-ECMO is frequently the first line of support in patients with advanced hemodynamic derangement

From the [a]Department of Surgery and Division of Cardiovascular Surgery and [b]Department of Medicine and Division of Cardiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pa.

Date and number of Institutional Review Board approval: #824927. Approved: May 17, 2016.

Read at the 99th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, May 4-7, 2019.

Received for publication May 5, 2019; revisions received Oct 11, 2019; accepted for publication Nov 19, 2019; available ahead of print Dec 14, 2019.

Address for reprints: Christian Bermudez, MD, 3400 Spruce St, Philadelphia, PA 19104 (E-mail: Christian.bermudez@uphs.upenn.edu).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.11.106

Abbreviations and Acronyms

CS = cardiogenic shock
DM = diabetes mellitus
ECMO = extracorporeal membrane oxygenation
FiO2 = fraction of inspired oxygen
HF = heart failure
HRT = heart replacement therapy
LV = left ventricular
LVAD = left ventricular assist device
LVEF = left ventricular ejection fraction
MAP = mean arterial pressure
MI = myocardial infarction
NYHA = New York Heart Association
PaO2 = partial pressure of oxygen
RV = right ventricle
VA-ECMO = venoarterial extracorporeal membrane oxygenation
VV-ECMO = venovenous extracorporeal membrane oxygenation

Scanning this QR code will take you to the article title page to access supplementary information. To view the AATS Annual Meeting Webcast, see the URL next to the webcast thumbnail.

and is used to support patients with cardiopulmonary failure due to various etiologies[2-6] as a bridge to recovery or bridge to advanced replacement therapies, including left ventricular assist devices (LVADs)[7] and heart transplantation.[8,9] Under ideal circumstances, after a few days of extracorporeal membrane oxygenation (ECMO) support to allow hemodynamic and metabolic stabilization, the patient can be weaned and separated from the ECMO circuit if there are consistent signs recovery of cardiopulmonary function.

Although clinical use of ECMO in this setting has rapidly increased,[10] there is limited evidence to guide the decision to proceed with an uncomplicated weaning from ECMO that will result in a durable survival free from heart failure (HF). In a recent analysis of the Extracorporeal Life Support Organization registry, 55% of adult patients supported with VA-ECMO for cardiac failure survived to ECMO discontinuation or removal, but only 41% survived to hospital discharge.[10] The ability to successfully wean patients from VA-ECMO without the use of other advanced therapies is complex, with success rates varying from 30% to 60% depending on the etiology necessitating support and the center's expertise.[11-16] When assessing the timing and ability to wean from ECMO, hemodynamics, end-organ function, pulmonary blood oxygenation, metabolic status, and echocardiographic assessments must be considered. Despite increasing experience, weaning is often performed without defined guidelines.[16]

Even when successful weaning from ECMO is achieved, a positive outcome for the patient does not necessarily follow. Indeed, approximately 30% of patients "successfully" weaned from support do not survive to hospital discharge,[10,17,18] and limited information is available regarding the factors associated with a sustained and durable weaning from support. Therefore, we sought to evaluate predictors of in-hospital mortality and midterm outcomes of patients successfully weaned from VA-ECMO with the aim of improving patient selection for weaning.

MATERIALS AND METHODS

Patients and Data Collection

We performed a retrospective analysis of a prospectively collected database of patients who were supported on VA-ECMO and were "successfully" weaned from support between January 2013 and February 2018 at our institution. The definition of successful weaning has been arbitrary and considered by some to be survival for at least 30 days after ECMO removal.[12,16] This criterion has been rarely used clinically, however, and would exclude a significant number of patients who die of progressive HF or other complications during hospitalization. For this reason, we decided to decrease this time frame, and ECMO weaning was considered "successful" if the patient survived more than 24 hours after weaning to decannulation.

Of 480 adult patients supported on VA-ECMO for CS, we included 92 patients (19.2%) with primary cardiac disease—acute myocardial infarction (MI), postcardiotomy shock, primary graft dysfunction after heart transplant, acute-on-chronic HF, refractory ventricular tachycardia, and myocarditis—who were weaned from ECMO and survived more than 24 hours. We excluded 289 patients who died on ECMO support and 28 patients who died within 24 hours of ECMO weaning because this was often palliative or the consequence of lack of candidacy to reinitiate ECMO or other mechanical support (Table E1). We also excluded 28 patients supported and weaned from ECMO for nonprimary cardiac diseases including shock due to pulmonary embolism, sepsis, major bleeding with hemodynamic collapse, primary graft dysfunction after lung transplant, extracorporeal cardiopulmonary resuscitation with an unclear cause, and hypoxic cardiac arrest caused by aspiration pneumonia. Forty-three patients who failed ECMO weaning and underwent heart replacement therapy (HRT) (LVAD or heart transplant) are presented separately (Figure 1).

Patient clinical information, including hemodynamic, echocardiographic, and ECMO data, was collected at different time points including at the time of ECMO implantation, before weaning (before decannulation), and at follow-up. New York Heart Association (NYHA) functional status[19] was determined by patient interview. This study was approved by our Institutional Review Board (# 824927).

Extracorporeal Membrane Oxygenation Management and Weaning Strategy

The ECMO circuit consisted of a centrifugal Rotaflow pump (MAQUET, Rastatt, Germany) with a hollow-fiber Quadrox D oxygenator (MAQUET) or the Cardiohelp integrated system (MAQUET). Peripheral cannulation was performed through the femoral vessels, and a distal perfusion cannula was inserted routinely in the superficial femoral artery for distal perfusion of the limb as per institutional protocol.[20] Central

ADULT

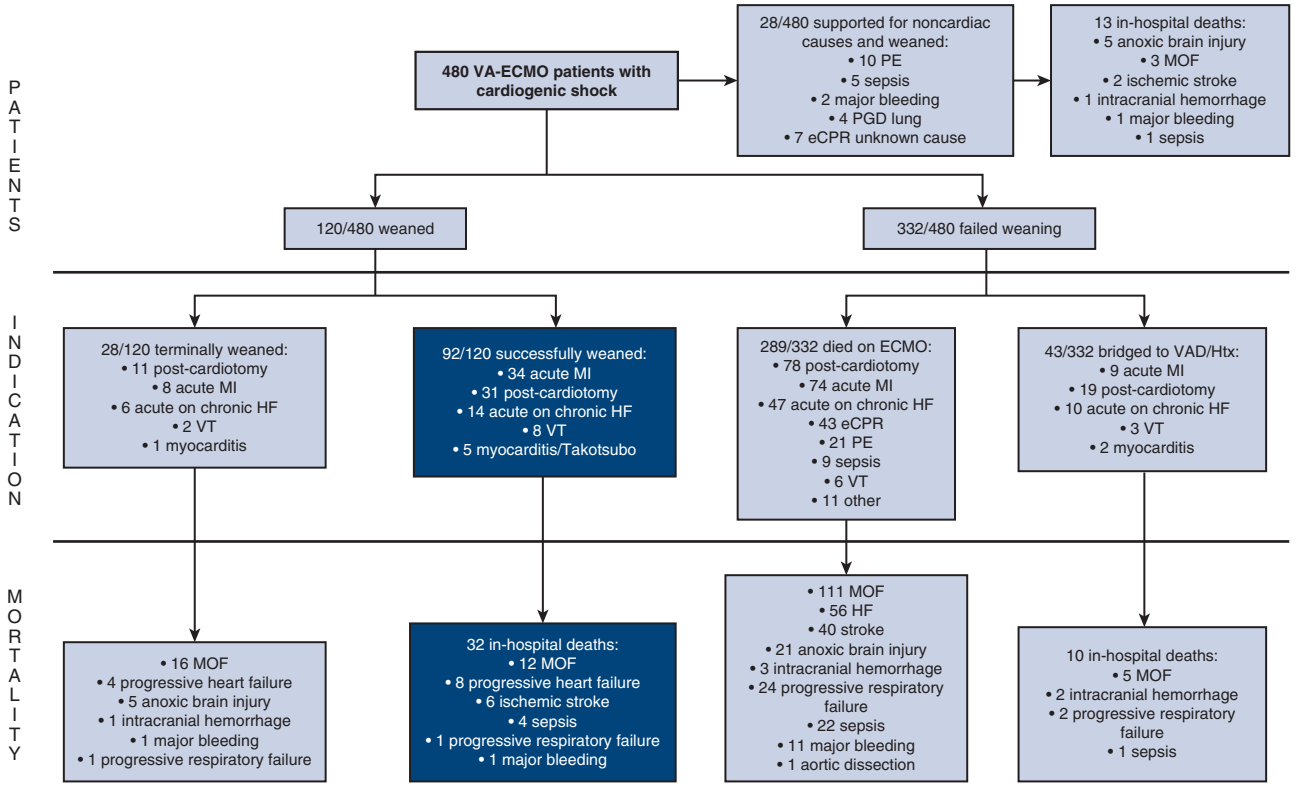


FIGURE 1. Study flow chart with study group in orange. *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation; *PGD*, primary graft dysfunction; *eCPR*, extracorporeal cardiopulmonary resuscitation; *MOF*, multiorgan failure; *MI*, myocardial infarction; *VT*, ventricular tachycardia; *VAD/Htx*, ventricular assist device/heart transplant; *HF*, heart failure.

cannulation was performed through the aorta and right atrium. At our institution, peripheral cannulation is the strategy of choice in most patients. However, central cannulation is used in the majority of patients postcardiotomy at the discretion of the attending surgeon. ECMO flow was started at a rate equal to or greater than the patient's anticipated cardiac output (typically 2.2 L/min/m^2 or 4-6 L/min). Active left ventricular (LV) decompression was considered in the presence of severe LV dilation, detected by echocardiographic imaging, with signs of increased LV filling pressures, as detected by a Swan-Ganz catheter, associated severe mitral regurgitation, and clinical or radiologic signs of significant pulmonary congestion. In 16 of the 92 patients (17.4%), an LV unloading strategy was used (11 with direct LV venting and 5 with Impella axial flow pump; ABIOMED, Danvers, Mass).

Weaning trials were supervised by an attending surgeon, a critical care specialist or HF cardiologist, a perfusionist, and the nursing staff. A weaning trial was performed when the patient was deemed hemodynamically and clinically stable after ECMO implantation and 24 hours or more of support. Typically, weaning trials are attempted after 2 or 3 days of support and repeated every 24 to 48 hours until a decision regarding the ability to successfully wean the patient from ECMO was made. Patients were considered acceptable candidates for weaning in the presence of a pulsatile arterial waveform, mean arterial pressure (MAP) greater than 60 mm Hg on no or low-dose inotropes (epinephrine <5 μg/min, dopamine <6 μg/min, and milrinone <0.375 μg/min) and vasopressors (vasopressin <0.02 μg/min and norepinephrine <5 μg/min), central venous pressure less than 17 mm Hg, pulmonary capillary wedge pressure less than 18 mm Hg, pulse pressure less than 40 mm Hg, satisfactory metabolic status (lactate <2.0 mmol/L), and satisfactory hepatic function (transaminases <100 U/L). Normal renal function was not mandatory, and often these patients would be on continuous renal replacement therapy because of acute kidney injury. A partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2) threshold was not specified in our weaning protocol, although patients with persistent acute lung injury or hypoxemia requiring high FiO2 would be considered for transition to venovenous ECMO (VV-ECMO). Weaning was usually considered after revascularization in patients with acute MI or after electrophysiologic ablation treatment in patients with an arrhythmic etiology of CS.

During the formal weaning trial, echocardiography was performed to continuously assess cardiac function. By using an arterial line and a Swan-Ganz catheter, which was inserted in every patient, to monitor arterial pulse pressure and cardiac output, the ECMO flow was progressively reduced by halving it every 5 to 10 minutes. A 75% reduction of the original flow or a minimum flow of 1 L/min is achieved over 20 minutes using this protocol. During reduction of flow, appropriate anticoagulation was ensured, targeting an activated partial thromboplastin time between 50 and 70 seconds. Heparin boluses were given if necessary. If hemodynamic instability developed, as indicated by systolic arterial pressure less than 100 mm Hg, MAP less than 60 mm Hg, or significant elevation of the central venous pressure (>18-20 mm Hg) on moderate inotropic support, the weaning trial was stopped, and the ECMO flow was increased back to 100% of the original flow. ECMO removal was considered when cardiac function was fully or partially recovered on minimal ECMO support. Generally, a left ventricular ejection fraction (LVEF) greater than 25% to 30% in the absence of severe valvular regurgitation (mitral or tricuspid) was required. Not infrequently, less strict criteria would be considered by different providers considering the overall clinical situation of the patients and whether they were poor candidates for advanced long-term support (LVAD) or transplantation. If hemodynamic parameters, arterial blood gases, and echocardiographic assessment remained satisfactory throughout the trial, patients deemed acceptable weaning candidates were scheduled

TABLE 1. Patient demographics, extracorporeal membrane oxygenation characteristics, and baseline metabolic and hemodynamic parameters at extracorporeal membrane oxygenation placement

Characteristic	Overall (n = 92)	Survivors (n = 60)	Nonsurvivors (n = 32)	*P* value
Sex				.48
Male	64 (69.6%)	40 (66.7%)	24 (75.0%)	
Female	28 (30.4%)	20 (33.3%)	8 (25%)	
Age, y (range)	61.4 (18.3-83.0)	62.0 (18.3-81.3)	60.5 (23.1-83.0)	.76
BMI, kg/m^2 (range)	28.3 (18.3-56.5)	28.7 (18.3-56.5)	28.0 (18.5-44.1)	.72
Diabetes, n (%)	34 (37.0%)	17 (28.3%)	17 (53.1%)	.02
CKD, n (%)	26 (28.3%)	14 (23.3%)	12 (37.5%)	.22
CAD, n (%)	69 (75.0%)	41 (68.3%)	28 (87.5%)	.04
Previous MI, n (%)	39 (42.4%)	19 (31.7%)	20 (62.5%)	<.01
Previous cardiac surgery, n (%)	35 (38.0%)	25 (41.7%)	10 (31.2%)	.37
VA-ECMO indication, n (%)				.84
Acute MI	34 (37.0%)	23 (38.3%)	11 (34.4%)	
Postcardiotomy	31 (33.7%)	20 (33.3%)	11 (34.4%)	
Decompensated chronic HF	14 (15.2%)	7 (11.7%)	7 (21.9%)	
VT	8 (8.7%)	6 (10.0%)	2 (6.2%)	
Myocarditis	4 (4.3%)	3 (5.0%)	1 (3.1%)	
Takotsubo	1 (1.1%)	1 (1.7%)	0 (0.0%)	
VA-ECMO configuration, n (%)				.56
Peripheral	77 (83.7%)	49 (81.7%)	28 (87.5%)	
Central	15 (16.3%)	11 (18.3%)	4 (12.5%)	
LV unloading, n (%)	16 (17.4%)	11 (18.3%)	5 (15.6%)	.74
Surgical vent	11	7	4	
Impella	5	4	1	
IABP while on VA-ECMO, n (%)	35 (38%)	22 (36.7%)	13 (40.6%)	.71
Total number of inotropes/vasopressors on VA-ECMO, n	1.8 ± 0.9	1.7 ± 0.9	1.9 ± 0.9	.45
Duration of ECMO support, d (range)	5.0 (1-45.0)	4.0 (1-26.0)	6.0 (1-45.0)	.13
PaO2, mm Hg (range)	130.5 (41.0-738.0)	177 (41-738)	103 (46-593)	.57
PCO2, mm Hg (range)	38 (20-99)	38 (20-99)	38 (25-61)	.92
pH (range)	7.3 (7.0-7.6)	7.3 (7.0-7.6)	7.4 (7.1-7.5)	.55
Lactate, mmol/L (range)	3.0 (0.3-17.0)	3.1 (0.3-14.3)	3.0 (0.6-17.0)	.94
Hb, g/dL (range)	10.7 (6.2-17.8)	10.8 (7.4-17.8)	10.1 (6.2-15.6)	.42
WBC count (range)	13.6 (4.3-29.1)	13.3 (5.3-29.1)	15.6 (4.3-27.7)	.74
Platelets count (range)	186 (15-431)	186 (15-405)	187 (78-431)	.59
Creatinine, mg/dL (range)	1.3 (0.2-9.5)	1.1 (0.5-5.6)	1.5 (0.2-9.5)	.04
ALT, U/L (range)	38 (6-6803)	32 (6-6803)	93 (13-1071)	.21
AST, U/L (range)	64 (9-7523)	50 (9-7523)	99.5 (22.0-4231)	.16
Bilirubin, mg/dL (range)	1.0 (0.3-15.4)	1.1 (0.4-15.4)	0.9 (0.3-7.3)	.87
MAP, mm Hg (range)	65 (24-87)	67 (24-86)	60 (53-87)	.32
Heart rate, beats/min (range)	86 (47-125)	86 (47-118)	87 (61-125)	1.00
CVP, mm Hg (range)	20 (3-37)	19.5 (4-32)	21 (3-37)	.63
mPAP, mm Hg (range)	31.2 (11.0-104.0)	31.2 (11.0-62.7)	32.0 (18.3-104.0)	.50
LVEF, %*	21.2% ± 16.8%	21.6% ± 16.9%	20.5% ± 16.8%	.37

(Continued)

TABLE 1. Continued

Characteristic	Overall (n = 92)	Survivors (n = 60)	Nonsurvivors (n = 32)	*P* value
RV dysfunction, n (%)*				.62
None	14 (25%)	13 (32.5%)	2 (12.6%)	
Mild	17 (30.4%)	9 (22.5%)	8 (50.0%)	
Moderate	15 (26.8%)	11 (27.5%)	3 (18.7%)	
Severe	10 (17.8%)	7 (17.5%)	3 (18.7%)	

BMI, Body mass index; *CKD*, chronic kidney disease; *CAD*, coronary artery disease; *MI*, myocardial infarction; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *HF*, heart failure; *VT*, ventricular tachycardia; *LV*, left ventricle; *IABP*, intra-aortic balloon pump; *PaO2*, partial pressure of oxygen; *PCO2*, partial pressure of carbon dioxide; *Hb*, hemoglobin; *WBC*, white blood cell; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *MAP*, mean arterial pressure; *CVP*, central venous pressure; *mPAP*, mean pulmonary arterial pressure; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle. *Available in 56 patients.

for elective decannulation in the operating room unless there was a need for urgent ECMO removal (eg, circuit clotting, limb ischemia). While in the operating room, another 10 to 20 minutes of monitoring was allowed to ensure hemodynamic stability while recirculating the ECMO circuit.

After hemodynamically stability was ensured, the patient was decannulated, and the cannulation sites were surgically repaired using an open technique to prevent vascular complications with potentially catastrophic consequences. Before peripheral decannulation, anticoagulation was stopped in the operating room. Before central decannulation, anticoagulation was stopped 2 hours before the operating room time. Patients who repeatedly failed weaning trials were considered for other heart replacement options or terminal weaning.

Statistical Analysis

Continuous variables are presented as median with range or mean ± standard deviation. Categoric variables are presented as percentages. Statistical variance between survivors and nonsurvivors was assessed using the chi-square test for categoric variables and the Wilcoxon signed-rank test for continuous variables. Survival curves were estimated by the Kaplan–Meier method. Predictors of in-hospital mortality were identified by a Cox proportional hazards model and by an Akaike information criterion–selected multivariate model. Statistical analyses were conducted using the R environment for statistical computing and graphics (R Foundation for Statistical Computing, Vienna, Austria, 2018).

RESULTS

During the study period, 92 patients with CS were supported with VA-ECMO and then weaned from support. Their median age was 61.4 years (range, 18.3-83.0). Of the 92 patients, 60 survived to hospital discharge (65.2%) and 32 did not (34.8%). Patients who did not survive to hospital discharge had a higher prevalence of diabetes mellitus (DM) ($P = .02$), coronary artery disease ($P = .04$), and history of MI ($P < .01$). Indications for VA-ECMO included acute MI (37.0%), postcardiotomy shock (33.7%), decompensated chronic HF (15.2%), refractory ventricular tachycardia (8.7%), and other (5.4%). Survival in patients with LV unloading was 70.6% versus 64% of those without LV unloading ($P = .61$). Metabolic, hemodynamic, and echocardiographic parameters were comparable between survivors and nonsurvivors at the time of ECMO placement, except for higher creatinine at ECMO placement in the nonsurvivors ($P = .04$) (Table 1).

At ECMO weaning, metabolic, hemodynamic, and echocardiographic parameters were still similar between the survivors and the nonsurvivors except that patients who did not survive to discharge had lower PaO2/FiO2 ($P < .001$) (Table 2). Median duration of ECMO support was 5 days (1-45), median ICU stay was 17 days (3-125), and median hospital stay was 24 days (3-126). Analysis of echocardiographic parameters at ECMO placement and ECMO weaning showed a significant improvement in LVEF ($P < .01$) and the degree of mitral and tricuspid valve regurgitation ($P < .01$). ECMO support did not significantly improve right ventricular function ($P = .52$) (Table E2).

Overall survival at hospital discharge was 65.2%. Overall 1-year survival was 54.6%, and 3-year survival was 51.4% (Figure 2, *A*). Survival conditional to hospital discharge was 84% at both 1 year and 3 years postsupport (Figure 2, *B*). There was no significant difference in midterm survival after weaning based on the indication for ECMO (Figure 2, *C*). The most common complications were acute kidney injury requiring dialysis (27.2%), bleeding requiring transfusion (22.8%), pneumonia (27.2%), and tracheostomy placement (36.9%). The most common causes of in-hospital death were multiorgan failure (37.3%), HF (25.4%), and stroke (18.6%) (Table 3). We performed a subanalysis according to LVEF (>30% vs ≤30%), because LVEF is a standard criterion that is typically used to consider a patient for ECMO weaning. Patients with an ejection fraction 30% or less (severe LV dysfunction) at the time of weaning had significantly lower survival than those with LVEF greater than 30% (mild or moderate dysfunction) ($P = .03$) (Figure 2, *D*).

In a multivariate model, a history of DM, a prior MI, prolonged ECMO support, and hypoxemia at ECMO weaning were identified as independent predictors of in-hospital mortality in patients successfully weaned from ECMO (Table 4). A linear mortality increase was seen with longer ECMO support with an inflexion point at 13.5 days associated with 80% mortality. A univariate model identified several additional factors associated with in-hospital mortality, including LVEF less than 45% at ECMO weaning and any degree of mitral regurgitation at ECMO weaning (Table 4).

At the time of last follow-up (median, 2.14 years; 95% confidence interval, 1.69-2.99), 37 patients were alive and 32 patients completed a study interview. NYHA class I

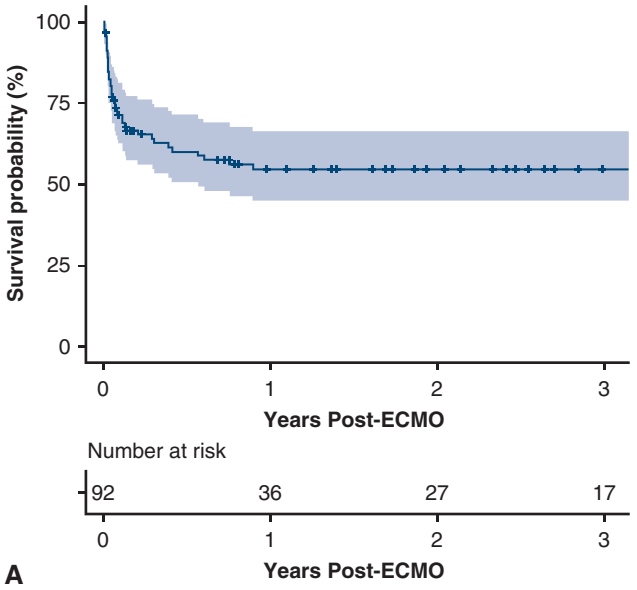
TABLE 2. Comparison of metabolic, hemodynamic, and echocardiographic parameters at extracorporeal membrane oxygenation weaning

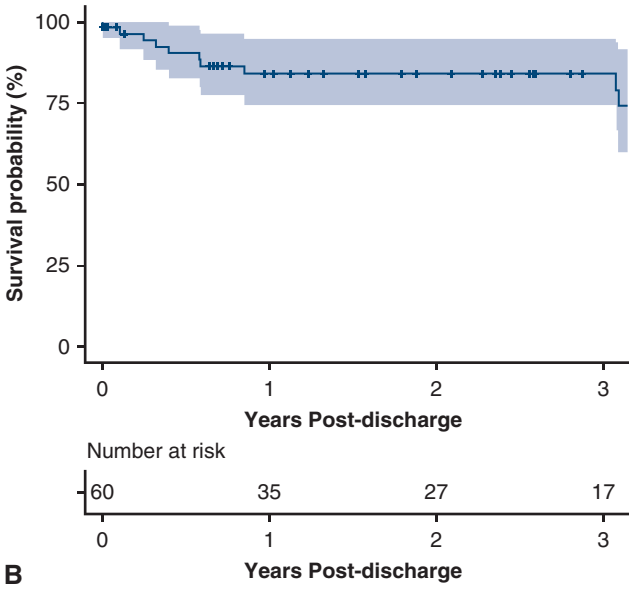
Characteristic	Overall (n = 92)	Survivors (n = 60)	Nonsurvivors (n = 32)	*P* value
PaO2, mm Hg (range)	139.0 (41.0-541.3)	168 (79.0-543.0)	94.0 (41.0-362.0)	<.01
FiO2, % (range)	40.0 (21.0-100.0)	45.0 (21.0-100.0)	40.0 (21.0-100.0)	.95
PaO2/FiO2 (range)	294.0 (69.0-1086.0)	337.5 (172.0-1086.0)	205.0 (69.0-595.0)	<.01
PCO2, mm Hg (range)	39.0 (26.0-61.0)	39.0 (26.0-61.0)	37.0 (26.0-52.0)	.52
pH (range)	7.43 (7.28-7.61)	7.42 (7.28-7.61)	7.44 (7.28-7.57)	.13
Lactate, mmol/L (range)	1.1 (0.3-10.4)	1.0 (0.3-9.9)	1.1 (0.4-10.4)	.75
Hb, g/dL (range)	8.3 (5.9-11.9)	8.2 (5.9-11.9)	8.4 (6.3-10.7)	.54
WBC count (range)	14.2 (3.5-41.2)	14.2 (6.3-39.8)	13.7 (3.5-41.2)	.93
Platelets count (range)	82.0 (29.0-355.0)	78.0 (29.0-355.0)	90.0 (47.0-229.0)	.18
Creatinine, mg/dL (range)	1.15 (0.36-9.40)	1.27 (0.36-9.40)	0.94 (0.37-7.68)	.24
ALT, U/L (range)	39.0 (5.0-627.0)	38.0 (7.0-527.0)	40.0 (5.0-627.0)	.82
AST, U/L (range)	56.0 (16.0-1809.0)	62.0 (21.0-403.0)	42.0 (16.0-1809.0)	.40
Bilirubin, mg/dL (range)	1.4 (0.3-13.5)	1.6 (0.3-13.5)	1.1 (0.3-9.2)	.10
MAP, mm Hg (range)	88.0 (63.0-129.0)	93.0 (63.0-129.0)	83.0 (64.0-108.0)	.25
Heart rate, beats/min (range)	91 (62-129)	93 (64-117)	90 (62-129)	.78
CVP, mm Hg (range)	16 (5-27)	15 (5-24)	17 (7-27)	.51
mPAP, mm Hg (range)	26 (12-104)	25 (12-58)	24 (17-104)	.20
IABP at weaning, n (%)	25 (27.2%)	18 (30%)	7 (21.9%)	.40
Total number of inotropes/vasopressors at weaning	0.7 ± 0.9	0.6 ± 0.8	0.9 ± 1.0	.10
LVEF, %*	33.9% ± 17.9%	36.3% ± 17.8%	28.9% ± 16.9%	.09
RV dysfunction*				.28
None	23 (30.7%)	19 (35.2%)	4 (19.1%)	
Mild	18 (24.0%)	13 (24.1%)	5 (23.9%)	
Moderate	23 (30.7%)	17 (31.5%)	6 (28.5%)	
Severe	11 (14.6%)	5 (9.2%)	6 (28.5%)	
Mitral regurgitation*				.51
None	40 (53.4%)	29 (58.0%)	11 (44%)	
Mild	24 (32.0%)	15 (30.0%)	9 (36.0%)	
Moderate	10 (13.3%)	6 (12.0%)	4 (16.0%)	
Severe	1 (1.3%)	0 (0.0%)	1 (4.0%)	
Tricuspid regurgitation†				.06
None	37 (53.6%)	29 (63.0%)	8 (34.8%)	
Mild	24 (34.8%)	14 (30.5%)	10 (43.5%)	
Moderate	4 (5.8%)	2 (4.3%)	2 (8.7%)	
Severe	4 (5.8%)	1 (2.2%)	3 (13.0%)	

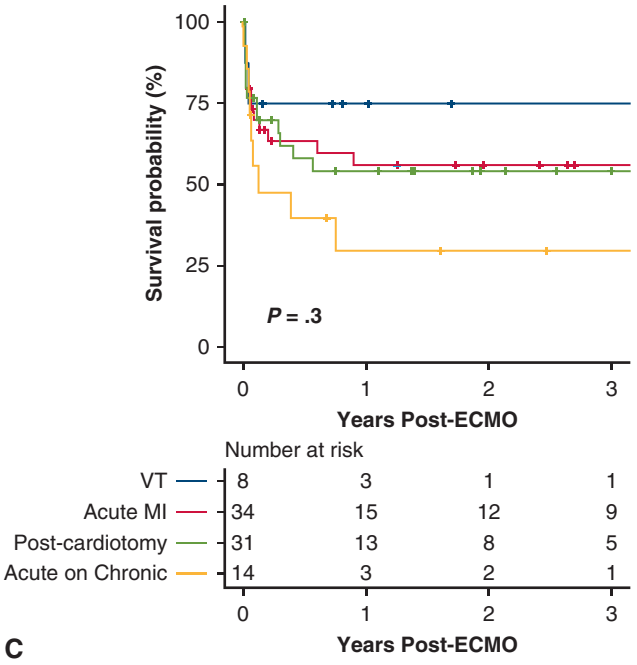
PaO2, Partial pressure of oxygen; *FiO2*, fraction of inspired oxygen; *PCO2*, partial pressure of carbon dioxide; *Hb*, hemoglobin; *WBC*, white blood cell; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *MAP*, mean arterial pressure; *CVP*, central venous pressure; *mPAP*, mean pulmonary arterial pressure; *IABP*, intra-aortic balloon pump; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle. *n = 75. †n = 69.

functional status was observed in 53% of patients, class II was observed in 19% of patients, class III was observed in 16% of patients, and class IV was observed in 12% of patients (Table 3). Half of the patients (50%, 16/32) had at least 1 readmission to the hospital because of their cardiac condition. In 22 patients who completed echocardiographic follow-up (median, 1.98 years, 95% confidence interval, 1.40-3.02 years), the average LVEF was 46.5% ± 18.2%, and a significant and sustained improvement in both LVEF ($P < .01$) and right ventricular function ($P = .03$) was observed (Figure E1).

Survival was also examined in 43 patients who failed ECMO weaning and underwent HRT (29 LVADs and 14 heart transplants) (Table 5). The patients who received HRT had 74.2% survival at 1 year and 64.8% survival at 3 years, which was significantly higher than for the patients who were weaned from ECMO and did not receive HRT ($P = .03$) (Figure E2).







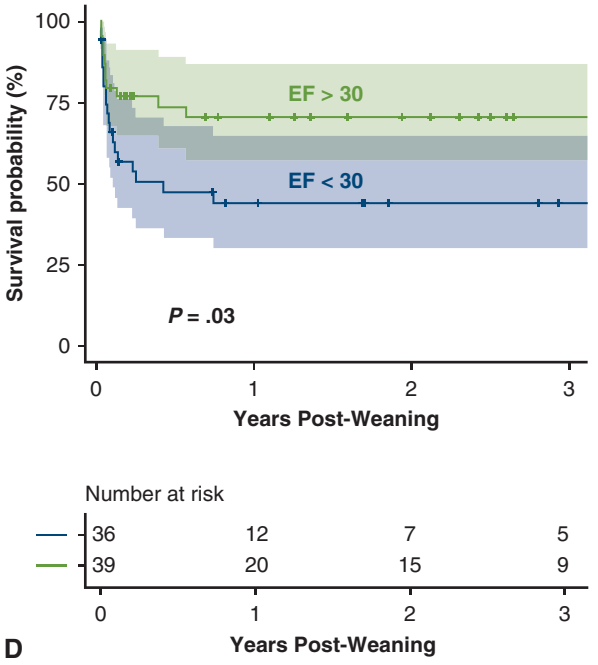


FIGURE 2. Survival after ECMO weaning of patients treated with VA-ECMO for CS. A, Kaplan–Meier curve showing a decrease in overall survival at midterm follow-up of 92 patients successfully weaned from VA-ECMO after CS. B, Kaplan–Meier curve showing a smaller decrease in survival conditional to hospital discharge at midterm follow-up of 60 of 92 patients weaned from VA-ECMO after CS. C, Kaplan–Meier curve showing no significant difference in survival by ECMO indication at midterm follow-up: acute MI (95% CI, 41-77) versus postcardiotomy shock (95% CI, 39-76) versus acute-on-chronic HF decompensation (95% CI, 12-72) versus refractory ventricular tachycardia (95% CI, 50-100) ($P = .3$). D, Kaplan–Meier curve showing better survival at midterm follow-up in patients who were successfully weaned from VA-ECMO after CS with an ejection fraction greater than 30% versus patients who were successfully weaned from VA-ECMO after CS with an ejection fraction 30% or less ($P = .03$). *ECMO*, Extracorporeal membrane oxygenation.

DISCUSSION

In this study, we retrospectively evaluated patients in CS supported with VA-ECMO and ''successfully'' weaned from support at our institution. We reviewed factors leading to in-hospital mortality after ECMO weaning and midterm outcomes, including clinical and echocardiographic considerations. Ours is the first study to provide insight specifically into patients who are weaned from ECMO due to cardiac recovery with midterm functional status, echocardiographic, and survival analysis. We identified

TABLE 3. Hospital course, complications, causes of death, and follow-up

Perioperative variable	Value
ICU stay (range)	17 d (3-125)
Hospital stay (range)	24 d (3-126)
Complications, n (%)*	
AKI requiring dialysis	25 (27.2%)
Bleeding requiring transfusion	21 (22.8%)
Stroke	7 (7.6%)
SSI	16 (17.4%)
Pneumonia	25 (27.2%)
Mesenteric ischemia	2 (2.2%)
Limb ischemia requiring fasciotomy	1 (1.1%)
DVT	15 (15.2%)
PEG	9 (9.8%)
Tracheostomy	34 (36.9%)
Causes of in-hospital death, n (%)†	
MOF	12 (37.5%)
HF	8 (25.0%)
Stroke	6 (18.6%)
Sepsis	4 (12.5%)
Respiratory failure	1 (3.1%)
Major bleeding	1 (3.1%)
Follow-up	**Value**
LVEF‡	46.5% ± 18.2%
RV dysfunction‡	
None	11 (50.0%)
Mild	6 (27.3%)
Moderate	4 (18.2%)
Severe	1 (4.5%)
Mitral regurgitation‡	
None	14 (63.7%)
Mild	4 (18.2%)
Moderate	3 (13.6%)
Severe	1 (4.5%)
Tricuspid regurgitation‡	
None	12 (54.5%)
Mild	6 (27.3%)
Moderate	2 (9%)
Severe	2 (9%)
NYHA class§	
I	17 (53.1%)
II	6 (18.8%)
III	5 (15.6%)
IV	4 (12.5%)

ICU, Intensive care unit; *AKI*, acute kidney injury; *SSI*, surgical site infection; *DVT*, deep vein thrombosis; *PEG*, percutaneous gastrostomy; *MOF*, multiorgan failure; *HF*, heart failure; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle; *NYHA*, New York Heart Association. *N = 92. †N = 32. ‡n = 22. §n = 32.

pre-existing comorbidities, such as diabetes and prior MI, as well as prolonged duration of ECMO support as risk factors for early in-hospital mortality (Video 1).

Other studies have focused on weaning strategies and predictors for successful weaning from support.[11,12,15,16,21-23] However, there is limited evidence available on the risk factors leading to mortality after ECMO weaning and the longer-term clinical and cardiac functional outcomes of patients who were successfully weaned from VA-ECMO and survive to hospital discharge. Only 2 studies have studied at this patient population.[17,18] Chang and colleagues,[17] in a series of 119 adult and pediatric patients successfully weaned from VA-ECMO (96/119) or VV-ECMO (23/119), identified urine output on the second day after ECMO decannulation, MAP, and Sequential Organ Failure Assessment score on the day of ECMO removal as predictors for in-hospital mortality using a multivariate model. García-Gigorro and colleagues,[18] in a retrospective follow-up cohort study of 31 patients weaned from VA-ECMO that included patients who underwent HRT, demonstrated that age and acute MI were the strongest predictors for in-hospital mortality. Survival at 30 days, 1 year, and 3 years was 59%, 46%, and 41%, respectively. Our study differed from these prior studies, because we only included patients with refractory CS due to a cardiac condition and supported with VA-ECMO and excluded patients who failed weaning and underwent HRT from the risk analysis.

An important finding of our study was the strong influence of comorbidities (DM and previous MI), prolonged ECMO support, and hypoxemia at the time of weaning as predictors of in-hospital mortality. As in our study, Pappalardo and colleagues[12] found that patients who died after weaning had a longer ECMO support than patients who survived to hospital discharge (8 vs 4 days), suggesting the importance of an early assessment for other advanced therapies if cardiac function does not improve.

Pulmonary dysfunction at the time of weaning had a strong correlation with poor outcomes in our study, suggesting that ECMO weaning should be avoided in the presence of existing pulmonary complications, including pulmonary congestion. Aissaoui and colleagues[16] suggested that weaning from VA-ECMO should be avoided when the PaO2/FiO2 ratio is less than 100, and patients otherwise presenting with improved cardiac function should be converted to VV-ECMO. A study by Boulate and colleagues[24] suggested that VA-ECMO is associated with a number of risk factors that could lead to acute lung injury in patients who undergo LVAD placement after ECMO support. In their study, 15 of 55 patients developed severe acute lung injury after LVAD implantation with PaO2/FiO2 less than 200, which was associated with mortality in 90% of the patients. The presence of increased pulmonary dysfunction as a risk factor for poor outcomes in patients undergoing VA-ECMO was also suggested by Pappalardo and colleagues[25] in a recent study assessing the efficacy of VA-ECMO in combination with an Impella device (ABIOMED) to unload the LV. In our series, only 5 patients were converted to VV-ECMO; 3 of them survived to discharge. Considering the weight of pulmonary dysfunction as a risk factor for mortality in our study, the

TABLE 4. Univariate and Akaike information criterion–selected multivariate model for predictors of in-hospital mortality

Variable	Univariate analysis		AIC-selected multivariate model*
	OR (95% CI)	*P* value	OR (95% CI)
Age	1.009 (0.98-1.04)	.6	
Sex (male)	1.5 (0.6-3.9)	.4	
BMI	1.004 (0.9-1.07)	.9	
DM	2.9 (1.2-7)	.01	3.06 (1.0-13.7)
Chronic kidney disease	1.9 (0.7-5)	.1	
History of coronary artery disease	3.2 (1.0-10.5)	.03	
Previous MI	3.6 (1.5-8.8)	.004	4.45 (1.0-21.1)
Previous cardiac surgery	0.6 (0.2-1.5)	.3	
ECMO indication		.7	
Acute MI	Reference		
Postcardiotomy	1.1 (0.4-3.2)		
Decompensated chronic HF	2.1 (0.5-7.5)		
Myocarditis	0.7 (0.06-7.5)		
VT	0.7 (0.1-4.0)		
ECMO configuration		.5	
Peripheral	Reference		
Central	1.6 (0.5-5.4)		
Duration of ECMO support	1.07 (1.0-1.2)	.04	1.1 (1.0-1.21)
Creatinine at ECMO placement	1.5 (1.01-2.1)	.02	
PaO2 at ECMO weaning	1.01 (1.0-1.01)	.06	1.004 (1.0-1.008)
Pulmonary artery pressure at ECMO weaning	1.05 (1.0-1.11)	.05	
LVEF at ECMO weaning <45%	4.6 (1.0-22.1)	.03	
Severe RV dysfunction at ECMO weaning	2.8 (0.8-10.4)	.1	
Severe TR at ECMO weaning	6.7 (0.6-68.9)	.07	
Any degree of MR at ECMO weaning	3.8 (1.1-12.7)	.02	

AIC, Akaike information criterion; *OR*, odds ratio; *CI*, confidence interval; *BMI*, body mass index; *DM*, diabetes mellitus; *MI*, myocardial infarction; *ECMO*, extracorporeal membrane oxygenation; *HF*, heart failure; *VT*, ventricular tachycardia; *PaO2*, partial pressure of oxygen; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle; *TR*, tricuspid regurgitation; *MR*, mitral regurgitation. *The multivariate model had an area under the curve of 90.4% (95% CI, 83.9-96.9) and an unbiased estimate of out-of-sample accuracy of 85% based on leave-1-out cross-validation.

decision to convert to VV-ECMO should probably be considered more liberally in the presence of moderate-to-severe pulmonary dysfunction or modest radiologic improvement at the time of VA-ECMO weaning.

Transesophageal echocardiography is a crucial part of current weaning trials and allows for assessment of cardiac function recovery and residual valvular abnormalities.[11] A few studies have reported how ECMO support affects LV and right ventricle (RV) function and how heart and valve function at the time of weaning can affect patients' outcomes.[12,15] Pappalardo and colleagues[12] observed higher mortality in patients with persistent RV failure. Aissaoui and colleagues[15] showed that patients who failed a weaning trial had a significantly lower aortic velocity time integral, LVEF, pulse pressure, and lateral mitral annulus peak systolic velocity. They observed a 100% weaning rate in patients with an aortic velocity time integral 10 cm or greater and LVEF greater than 20% to 25%. In our series, we reviewed the most relevant echocardiographic parameters used by general practitioners to decide ECMO weaning, including LVEF, right ventricular ejection fraction, and the presence or absence of valvular abnormalities. We observed an important overall improvement in LVEF, but a more modest improvement in the RV function between ECMO placement and after ECMO removal. We also observed that any grade of residual mitral regurgitation after weaning from support was associated with higher in-hospital mortality, at least in the univariate analysis. The presence of severe LV dysfunction (<30%) was significantly associated with lower survival after weaning.

The functional analysis at midterm follow-up showed that acceptable quality of life was achieved in more than 70% of patients (NYHA class I and II), providing insight into long-term survival free from HF in patients who were successfully weaned from ECMO support (Figure 3). However, in this snapshot, approximately 20% of patients had moderate or greater mitral regurgitation and 30% reported NYHA functional class III or IV at the time of follow-up. A high

TABLE 5. Baseline characteristics of patients weaned and discharged with no support versus patients who failed weaning and underwent heart replacement therapy

Characteristic	Successfully weaned (n = 92)	Failed weaning and underwent HRT (n = 43)	*P* value
Male sex, n (%)	64 (69.6%)	31 (72.1%)	.84
Age, y (range)	61.4 (18.3-83.0)	52.4 (18.7-69.7)	.01
BMI, kg/m^2 (range)	28.3 (18.3-56.5)	26.5 (20.9-38.3)	.25
Diabetes, n (%)	34 (37.0%)	22 (51.2%)	.14
CKD, n (%)	26 (28.3%)	8 (18.6%)	.29
CAD, n (%)	69 (75.0%)	17 (39.5%)	<.01
Previous MI, n (%)	39 (42.4%)	13 (30.2%)	.19
Previous cardiac surgery, n (%)	35 (38.0%)	5 (11.6%)	<.01
VA-ECMO indication, n (%)			.40
Acute MI	34 (37.0%)	9 (20.9%)	
Postcardiotomy	31 (33.7%)	19 (44.2%)	
Decompensated chronic HF	14 (15.2%)	10 (23.3%)	
VT	8 (8.7%)	3 (7.0%)	
Myocarditis	4 (4.3%)	2 (4.6%)	
Takotsubo	1 (1.1%)	0 (0.0%)	
VA-ECMO configuration, n (%)			.81
Peripheral	77 (83.7%)	35 (81.4%)	
Central	15 (16.3%)	8 (18.6%)	
Duration of ECMO support, d (range)	5.0 (1-45.0)	6.0 (1-54.0)	.48
LVEF, %	21.2% ± 16.8%	17.6% ± 9.7%	.68
RV dysfunction, n (%)	n = 56	n = 33	.04
None	14 (25.0%)	2 (6.1%)	
Mild	17 (30.4%)	6 (18.2%)	
Moderate	15 (26.8%)	9 (27.3%)	
Severe	10 (17.8%)	16 (48.4%)	

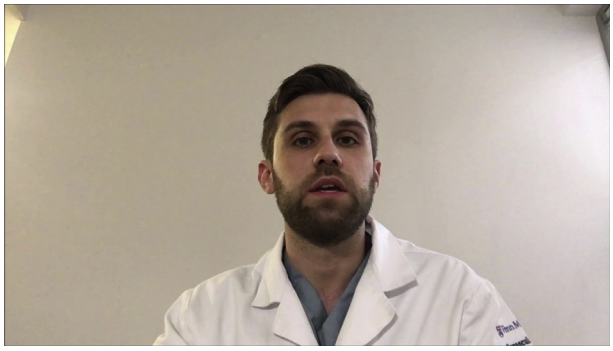
HRT, Heart replacement therapy; *BMI*, body mass index; *CKD*, chronic kidney disease; *CAD*, coronary artery disease; *MI*, myocardial infarction; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *HF*, heart failure; *VT*, ventricular tachycardia; *ECMO*, extracorporeal membrane oxygenation; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle.

readmission rate to the hospital due to cardiac conditions was also observed, suggesting the need for close monitoring.

When cardiac function is not improving, ECMO support can be used as a bridge to ventricular assist device placement or heart transplant safely and effectively in selected patients with acceptable midterm quality of life.[26-28] Garan and colleagues,[21] in a recent retrospective study including only patients with acute MI supported with VA-ECMO, did not find any statistically significant difference in short-term survival between patients weaned and discharged without HRT and patients who failed weaning and who underwent HRT. We found a significant difference in midterm survival between these 2 groups, favoring the use of HRT over nonselective ECMO weaning, which suggests that some patients who are weaned from ECMO may have compromised mid- and long-term outcomes and should be considered for HRT if they are suitable candidates. In our study, the decrease in patient survival from ECMO weaning to discharge is an important signal that requires further analysis in an attempt to improve patient outcomes.

Study Limitations

This study has several limitations. First, its retrospective nature carries evident limitations common to most single-center, observational studies, including the possibility of selection bias. Second, the relatively small number of



VIDEO 1. Dr Federico Sertic explaining the key points of this study. Video available at: https://www.jtcvs.org/article/S0022-5223(19)37089-8/fulltext.

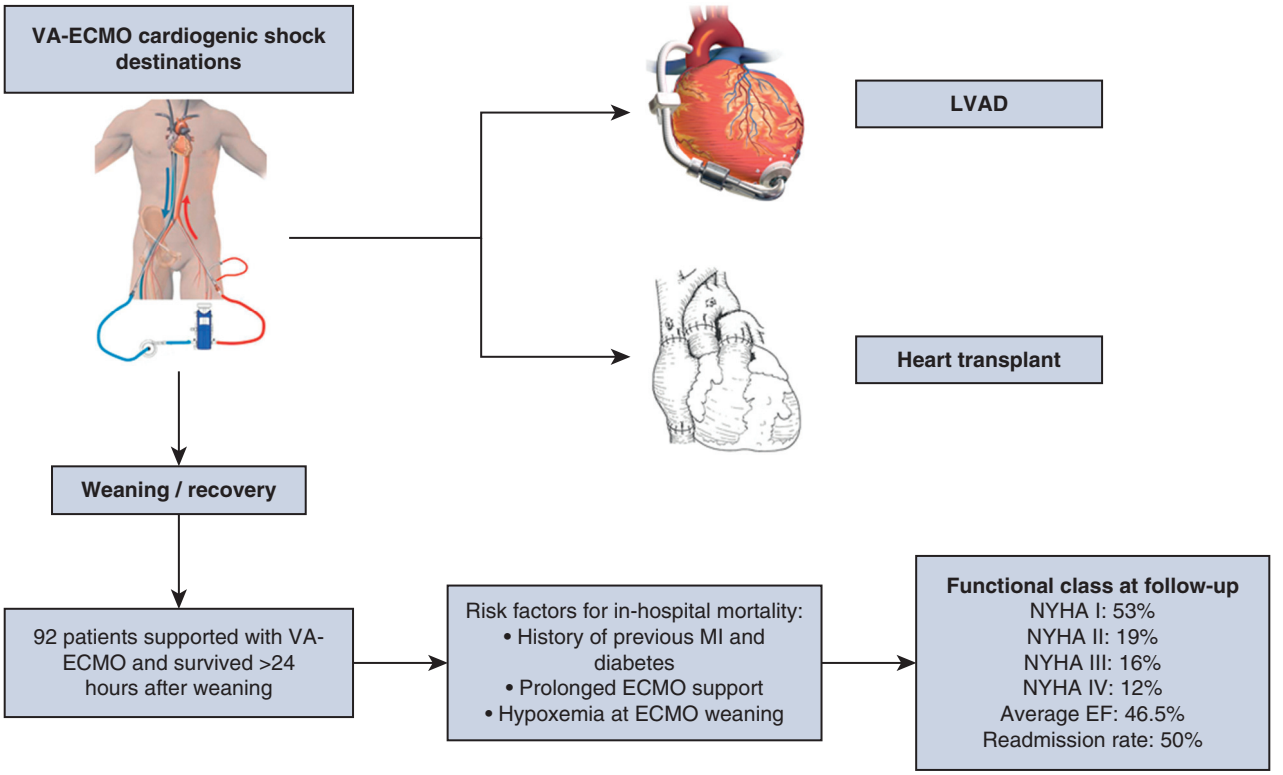


FIGURE 3. VA-ECMO destinations. *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation; *LVAD*, left ventricular assist device; *MI*, myocardial infarction; *NYHA*, New York Heart Association; *EF*, ejection fraction.

patients included in this series could affect the significance of the results. This is most notable in the results involving echocardiographic parameters at weaning and follow-up for which reports and imaging were lost because of changes in electronic medical records. Finally, the difference between patients who were treated with HRT after ECMO and those who were weaned requires further analysis. The analysis of these patients was limited and was not the primary objective of this study, but we included these data because they provide a valuable perspective of options available when considering ECMO weaning.

CONCLUSIONS

ECMO can be safely weaned in well-selected patients who have CS with acceptable midterm functional status. A group of these patients will still be subjected to in-hospital mortality despite successful separation from support. Previous MI, DM, prolonged ECMO support, and pulmonary dysfunction are independent predictors for in-hospital mortality after weaning from support. Patients with these characteristics should be considered for other heart replacement options. Other factors, including ejection fraction and valve regurgitation at the time of weaning, may affect patients' outcomes and should be investigated in future studies.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Saturday_May4/206BD/206BD/S11%20-%20Post%20Cardiotomy%20Shock%20Essentials/S11_7_webcast_110224915.mp4.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

References

1. McCarthy FH, McDermott KM, Kini V, Gutsche JT, Wald JW, Xie D, et al. Trends in U.S. extracorporeal membrane oxygenation use and outcomes: 2002-2012. *Semin Thorac Cardiovasc Surg*. 2015;27:81-8.
2. Chen J-S, Ko W-J, Yu H-Y, Lai LP, Huang SC, Chi NH, 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;34:950-7.
3. Schwarz B, Mair P, Margreiter J, Pomaroli A, Hoermann C, Bonatti J, et al. Experience with percutaneous venoarterial cardiopulmonary bypass for emergency circulatory support. *Crit Care Med*. 2003;31:758-64.

4. Pages ON, Aubert S, Combes A, Luyt CE, Pavie A, Leger P, et al. Paracorporeal pulsatile biventricular assist device versus extracorporal membrane oxygenation-extracorporal life support in adult fulminant myocarditis. *J Thorac Cardiovasc Surg*. 2009;137:194-7.
5. Rubino A, Costanzo D, Stanszus D, Valchanov K, Jenkins D, Sertic F, et al. Central veno-arterial extracorporeal membrane oxygenation (C-VA-ECMO) after cardiothoracic surgery: a single-center experience. *J Cardiothorac Vasc Anesth*. 2018;32:1169-74.
6. Chen Y-S, Lin J-W, Yu H-Y, Ko WJ, Jerng JS, Chang WT, et al. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. *Lancet*. 2008;372:554-61.
7. Pagani FD, Aaronson KD, Dyke DB, Wright S, Swaniker F, Bartlett RH. Assessment of an extracorporeal life support to LVAD bridge to heart transplant strategy. *Ann Thorac Surg*. 2000;70:1977-85.
8. Rousse N, Juthier F, Pinçon C, Hysi I, Banfi C, Robin E, et al. ECMO as a bridge to decision: recovery, VAD, or heart transplantation? *Int J Cardiol*. 2015;187:620-7.
9. Fukuhara S, Takeda K, Kurlansky PA, Naka Y, Takayama H. Extracorporeal membrane oxygenation as a direct bridge to heart transplantation in adults. *J Thorac Cardiovasc Surg*. 2018;155:1607-18.e6.
10. ECMO. Extra Corporal Life Support Registry Report. Ann Arbor, Michigan. Available at: https://www.elso.org/Portals/0/Files/Reports/2018/International%20Summary%20January%202018%20First%20Page.pdf. Accessed December 14, 2018.
11. Cavarocchi NC, Pitcher HT, Yang Q, Karbowski P, Miessau J, Hastings HM, et al. Weaning of extracorporeal membrane oxygenation using continuous hemodynamic transesophageal echocardiography. *J Thorac Cardiovasc Surg*. 2013;146:1474-9.
12. Pappalardo F, Pieri M, Arnaez Corada B, Ajello S, Melisurgo G, De Bonis M, et al. Timing and strategy for weaning from venoarterial ECMO are complex issues. *J Cardiothorac Vasc Anesthes*. 2015;29:906-11.
13. Platts DG, Sedgwick JF, Burstow DJ, Mullany DV, Fraser JF. The role of echocardiography in the management of patients supported by extracorporeal membrane oxygenation. *J Am Soc Echocardiogr*. 2012;25:131-41.
14. Santise G, Panarello G, Ruperto C, Turrisi M, Pilato G, Giunta A, et al. Extracorporeal membrane oxygenation for graft failure after heart transplantation: a multidisciplinary approach to maximize weaning rate. *Int J Artif Organs*. 2014;37:706-14.
15. Aissaoui N, Luyt C-E, Leprince P, Trouillet JL, Leger P, Pavie A, et al. Predictors of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock. *Intensive Care Med*. 2011;37:1738-45.
16. Aissaoui N, El-Banayosy A, Combes A. How to wean a patient from veno-arterial extracorporeal membrane oxygenation. *Intensive Care Med*. 2015;41:902-5.
17. Chang W-W, Tsai F-C, Tsai T-Y, Chang CH, Jenq CC, Chang MY, et al. Predictors of mortality in patients successfully weaned from extracorporeal membrane oxygenation. *PLoS One*. 2012;7:e42687.
18. García-Gigorro R, Renes-Carreño E, Pérez-Vela JL, Marin-Mateos H, Gutierrez J, Corres-Peiretti MA, et al. Mechanical support with venoarterial extracorporeal membrane oxygenation (ECMO-VA): short-term and long-term prognosis after a successful weaning. *Med Intensiva*. 2017;41:513-22.
19. Criteria Committee, New York Heart Association, Inc. *Diseases of the Heart and Blood Vessels. Nomenclature and Criteria for Diagnosis*. 6th ed. Boston, MA: Little, Brown and Co; 1964. 114.
20. Vallabhajosyula P, Kramer M, Lazar S, McCarthy F, Rame E, Wald J, et al. Lower-extremity complications with femoral extracorporeal life support. *J Thorac Cardiovasc Surg*. 2016;151:1738-44.
21. Garan AR, Eckhardt C, Takeda K, Topkara VK, Clerkin K, Fried J, et al. Predictors of survival and ability to wean from short-term mechanical circulatory support device following acute myocardial infarction complicated by cardiogenic shock. *Eur Heart J*. 2018;7:755-65.
22. Schmidt M, Zogheib E, Rozé H, Repesse X, Lebreton G, Luyt CE, et al. The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Intensive Care Med*. 2013;39:1704-13.
23. Li C-L, Wang H, Jia M, Ma N, Meng X, Hou X-T. The early dynamic behavior of lactate is linked to mortality in postcardiotomy patients with extracorporeal membrane oxygenation support: a retrospective observational study. *J Thorac Cardiovasc Surg*. 2015;149:1445-50.
24. Boulate D, Luyt C-E, Pozzi M, et al. Acute lung injury after mechanical circulatory support implantation in patients on extracorporeal life support: an unrecognized problem. *Eur J Cardiothorac Surg*. 2013;44:544-50.
25. Pappalardo F, Schulte C, Pieri M, Schrage B, Contri R, Soeffker G, et al. Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. *Eur J Heart Fail*. 2017;19:404-12.
26. Scherer M, Moritz A, Martens S. The use of extracorporeal membrane oxygenation in patients with therapy refractory cardiogenic shock as a bridge to implantable left ventricular assist device and perioperative right heart support. *J Artif Organs*. 2009;12:160-5.
27. Marasco SF, Lo C, Murphy D, Summerhayes R, Quayle M, Zimmet A, et al. Extracorporeal life support bridge to ventricular assist device: the double bridge strategy. *Artif Organs*. 2016;40:100-6.
28. Unai S, Yamane K, Tanaka D, Cook G, Hirose H, Cavarocchi NC, et al. Quality of life and mid-term survival of patients bridged with extracorporeal membrane oxygenation to left ventricular assist device. *ASAIO J*. 2017;63:273-8.

Key Words: extracorporeal membrane oxygenation, cardiogenic shock, in-hospital mortality

Discussion

Dr Amit A. Pawale *(New York, NY)*. You described the independent predictors of in-hospital mortality after weaning from VA-ECMO and their midterm survival. What proportion of patients who died within 24 hours were excluded as ''terminally weaned'' or in your article as a poor decision?

Dr Federico Sertic *(Philadelphia, Pa)*. There were 28 patients who died within 24 hours after weaning.

Dr Pawale. You mentioned prolonged ECMO support as a cause of mortality. Was it a linear trend in mortality with duration of support or was there a day after which the mortality went up suddenly?

Dr Sertic. We identified a linear correlation with an inflection point at 13.5 days associated with 80% in-hospital mortality.

Dr Pawale. So, 13.5 days on support?

Dr Sertic. On support, yes.

Dr Pawale. In your 3-year follow-up of all the patients who were weaned from VA-ECMO, did any of these patients get an LVAD or a transplant during these 3 years?

Dr Sertic. None of the patients underwent LVAD or heart transplant during subsequent admissions at our institution. For some of the patients, referred from out of the region, this information was not available.

Dr Pawale. At the wean from the ECMO, in what proportion of patients did you use adjuncts like a balloon pump, leaving the Impella in or using VV-ECMO for your pulmonary dysfunction patients?

Dr Sertic. Approximately 25% of the patients had an intra-aortic balloon pump to assist weaning; 5 patients were transitioned from VA to VV-ECMO, and we supported 5 patients with the Impella along with ECMO. We usually removed

the ECMO leaving the Impella in, and then we assessed for myocardial recovery. If the heart did not recover within a few days (2-3), we moved to long-term mechanical support.

Dr Mark S. Slaughter *(Louisville, Ky)*. You say ejection fraction (EF) at the time of weaning. It sounds as though it's a heterogeneous type of support, though. So if some are on a balloon pump and ECMO, some are on Impella and ECMO, some are on multiple inotropes and ECMO, was there any standardization or you just picked a day and that was the day of weaning as opposed to they are on 4 liters of ECMO, perhaps we can get the Impella out, they are down to 1 inotrope, now because they are EF, or you picked a day, because otherwise it seems arbitrary.

Dr Sertic. We chose the EF when a patient was deemed weanable after a successful weaning trial with transesophageal echocardiography assessment. The patient was then electively decannulated the following day in the operating room.

Dr Slaughter. If we are going to take ECMO out, we tend to wean it down over 5 days, and we get them down to about a liter and leave them at a liter for about 24 hours and then assess their ventricular function before we would ever take it out.

Dr Marc Ruel *(Ottawa, Ontario, Canada)*. You have a component in your article of successful weaning from ECMO; I think there were 90 such patients or so. You also reported patients who were discharged from hospital, which was a smaller number. Therefore, what is your definition of successful weaning from ECMO?

Dr Sertic. That's the main reason why we decided to do this study. The discrepancy between weaned and discharged patients. We wanted studies in the literature that have considered weaning successful if a patient is alive for more than 30 days and other studies if a patient is alive for more than 48 hours after weaning, which may be arbitrary. Therefore, we wanted to go into more depth and understand which factors need to be considered to achieve a successful weaning to try and reduce the gap between weaned and discharged patients, and discern when to consider other heart replacement options.

Dr Christian Bermudez *(Pittsburgh, Pa)*. I am Christian Bermudez, the principal investigator of this study. I want to make a few comments regarding the weaning process and why we did this study.

A number of reports have been done regarding outcomes of ECMO, but we don't understand clearly what parameters should be used to have a safe and effective ECMO weaning. The effects of EF or valvular abnormalities at the time of weaning are poorly understood. Weaning could be done in a slow fashion as you do. We do it in a more rapid fashion. We do serial echos, we lower the flow for a few minutes, for 20 minutes, up to 1 liter, and when we see that we have stable hemodynamics with a relatively acceptable EF (~25%-30%), then we decide to take the patient back to the operating room to do the weaning, ideally without mechanical support. The cases that we have weaned with the Impella were because they already had the Impella in place. We don't add the Impella after weaning because that patient may require long-term support. We consider that a failed weaning.

So we looked at the EF. We were concerned about the minimum EF needed to safely wean. As you see, in some you have below 30%. It's a complex process. On top of that, if you have mitral regurgitation with severe tricuspid regurgitation, you already see a trend toward poorer outcomes.

We excluded patients who died within 24 hours, because we wanted to exclude the patients who were terminally weaned. Sometimes patients are not candidates for advanced therapies. In those cases, when advanced options are not possible, frequently you just take the ECMO out and pray. We wanted to exclude those patients from the study. We wanted to see who survived at least 24 hours even though the definition of success has been 30 days, which I consider arbitrary. We probably should consider patient success when a patient goes home.

So this is an area that requires further analysis. How do we do it better? What do we consider successful weaning? When is it time to go to long-term device instead of trying multiple short-term options including Impellas, TandemHeart, and balloons, which in our experience has been associated with modest outcomes. We have experienced that a combination of multiple short-term devices can be done, but in general is not a great option and has led to poor outcomes. We consider that if they are not weanable from ECMO, a rapid VAD evaluation should be performed, and the patient should be bridged to a long-term device as soon as possible. As you see, the outcomes reflect that.

Dr Slaughter. I may have misunderstood your analysis, but I got the impression that ECMO was a risk factor for death or was it duration of support?

Dr Sertic. A risk factor for mortality was the prolonged duration of ECMO support.

Dr Slaughter. So the idea is if they are not better in about 2 weeks, then the answer is they are not going to get myocardial recovery or nothing?

Dr Sertic. Yes, correct.

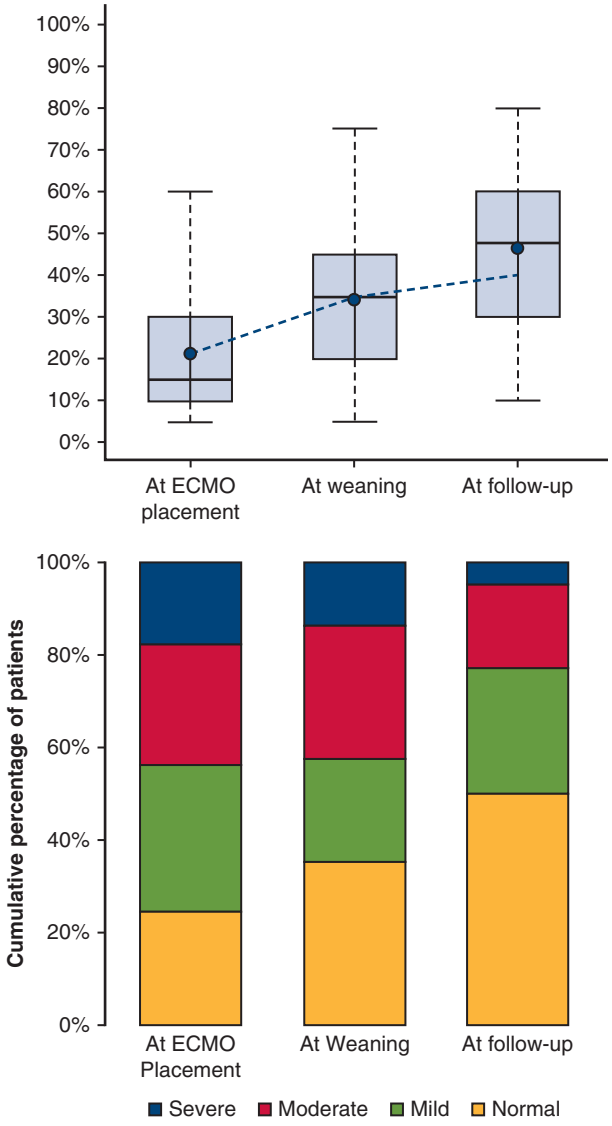


FIGURE E1. *Top*: Trajectory of cardiac functional recovery as indicated by LVEF in patients who were successfully weaned from VA-ECMO after CS, completed echocardiographic follow-up, and had echocardiographic data available at 3 time points (n = 22) ($P < .01$). *Bottom*: Improved and sustained RV function recovery in patients who were successfully weaned from VA-ECMO after CS, completed echocardiographic follow-up, and had echocardiographic data available at 3 time points (n = 22) ($P = .03$). *ECMO*, Extracorporeal membrane oxygenation.

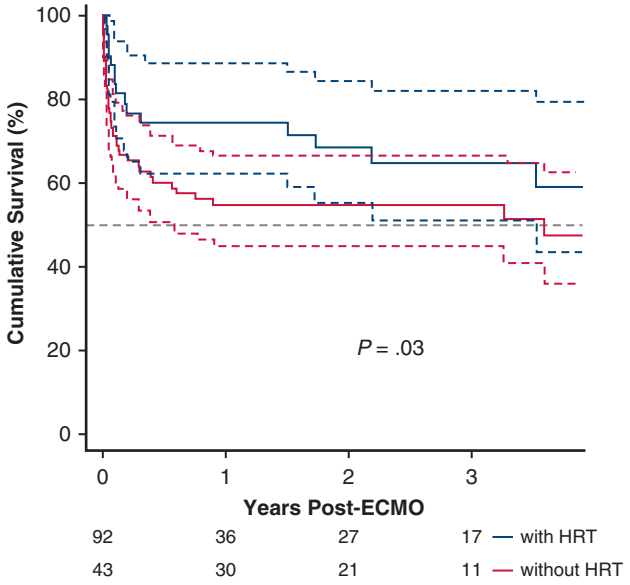


FIGURE E2. Kaplan–Meier curve comparing survival at midterm follow-up between patients who were successfully weaned from VA-ECMO after CS (n = 92) (*red line*) and patients who failed weaning from VA-ECMO and underwent HRT (LVAD/Htx) (n = 43) (*light blue line*) ($P = .03$). *HRT*, Heart replacement therapy; *ECMO*, extracorporeal membrane oxygenation.

ADULT

TABLE E1. Overall extracorporeal membrane oxygenation weaning: Successful wean versus terminal wean

Characteristic	Successfully weaned (n = 92)	Terminally weaned (n = 28)	*P* value
Sex			.38
Male	64 (69.6%)	24 (85.7%)	–
Female	28 (30.4%)	4 (14.3%)	–
Age, y (range)	61.4 (18.3-83.0)	64.0 (30.0-80.0)	.33
BMI, kg/m^2 (range)	28.3 (18.3-56.5)	32.9 (23.9-48.0)	.01
Diabetes, n (%)	34 (37.0%)	9 (32.1%)	.82
CKD, n (%)	26 (28.3%)	12 (42.8%)	.17
CAD, n (%)	69 (75.0%)	13 (46.4%)	.01
Previous MI, n (%)	39 (42.4%)	10 (35.7%)	.66
Previous cardiac surgery, n (%)	35 (38.0%)	8 (28.5%)	.50
VA-ECMO indication, n (%)			.92
Acute MI	34 (37.0%)	8 (28.5%)	
Postcardiotomy	31 (33.7%)	11 (39.3%)	
Decompensated chronic HF	14 (15.2%)	6 (21.4%)	
VT	8 (8.7%)	2 (7.1%)	
Myocarditis	4 (4.3%)	1 (3.7%)	
Takotsubo	1 (1.1%)	0 (0.0%)	
VA-ECMO configuration, n (%)			.40
Peripheral	77 (83.7%)	21 (75.0%)	
Central	15 (16.3%)	7 (25.0%)	
LV unloading, n (%)	16 (17.4%)	3 (10.7%)	.06
Surgical vent	11	0	
Impella	5	3	
Duration of ECMO support, d (range)	5.0 (1-45.0)	4.0 (1-16.0)	.56
LVEF at placement, %	21.2% ± 16.8%	18.3% ± 11.2%	.76
RV dysfunction at placement, n (%)			.06
None	14 (25%)	2 (8.7%)	
Mild	17 (30.4%)	4 (17.4%)	
Moderate	15 (26.8%)	7 (25.0%)	
Severe impairment	10 (17.8%)	10 (48.9%)	
LVEF at weaning/death, %	33.9% ± 17.9%	18.4% ± 15.6%	<.01
RV dysfunction at weaning/death, n (%)			<.01
None	23 (30.7%)	0 (0.0%)	
Mild	18 (24.0%)	5 (23.8%)	
Moderate	23 (30.7%)	4 (19.0%)	
Severe	11 (14.6%)	12 (57.2%)	
Lactate at placement	3.0 (0.3, 17.0)	8.2 (2.0, 22.0)	<.01
Lactate at weaning/death	1.1 (0.3, 10.4)	2.5 (1.0, 16.0)	<.01
Complications, n (%)			
AKI requiring dialysis	25 (27.2%)	17 (60.7%)	<.01
Bleeding requiring transfusion	21 (22.8%)	19 (67.8%)	<.01
Stroke	7 (7.6%)	8 (28.6%)	<.01
SSI	16 (17.4%)	2 (7.1%)	.24
Pneumonia	25 (27.2%)	7 (25%)	1.00
Mesenteric ischemia	2 (2.2%)	5 (17.8%)	<.01
Limb ischemia requiring fasciotomy	1 (1.1%)	3 (10.7%)	.04
DVT	15 (15.2%)	0 (0.0%)	.02
PEG	9 (9.8%)	0 (0.0%)	.11
Tracheostomy	34 (36.9%)	0 (0.0%)	<.01

(Continued)

TABLE E1. Continued

Characteristic	Successfully weaned (n = 92)	Terminally weaned (n = 28)	*P* value
ICU stay	17 d (3-125)	6 d (1-24)	<.01
Hospital stay	24 d (3-126)	7 d (2-24)	<.01

BMI, Body mass index; *CKD*, chronic kidney disease; *CAD*, coronary artery disease; *MI*, myocardial infarction; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *HF*, heart failure; *VT*, ventricular tachycardia; *LV*, left ventricle; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle; *AKI*, acute kidney injury; *SSI*, surgical site infection; *DVT*, deep vein thrombosis; *PEG*, percutaneous gastrostomy; *ICU*, intensive care unit.

TABLE E2. Echocardiographic data at extracorporeal membrane oxygenation placement, extracorporeal membrane oxygenation weaning, and before discharge or death

Echocardiographic measure	At ECMO placement	At ECMO weaning	*P* value
LVEF	(n = 75) 21.2% ± 16.8%	(n = 75)* 33.9% ± 17.9%	<.01
RV dysfunction	(n = 56)	(n = 75)	.52
None	14 (25.0%)	23 (30.7%)	
Mild	17 (30.4%)	18 (24.0%)	
Moderate	15 (26.8%)	23 (30.7%)	
Severe	10 (17.8%)	11 (14.6%)	
Mitral regurgitation	(n = 52)	(n = 75)	<.01
None	26 (50%)	40 (53.4%)	
Mild	12 (23.1%)	24 (32.0%)	
Moderate	12 (23.1%)	10 (13.3%)	
Severe	2 (3.8%)	1 (1.3%)	
Tricuspid regurgitation	(n = 49)	(n = 69)	<.01
None	23 (46.9%)	37 (53.6%)	
Mild	14 (28.6%)	24 (34.8%)	
Moderate	10 (20.4%)	4 (5.8%)	
Severe	2 (4.1%)	4 (5.8%)	

ECMO, Extracorporeal membrane oxygenation; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle. *Data were analyzed on the basis of availability at both time points.