Flow Manipulation and the Association with Myocardial Systolic Function During Extracorporeal Life Support

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Abstract

Background:

Peripheral veno-arterial extracorporeal membrane oxygenation (V-A ECMO) is used to support circulatory failure refractory to conventional therapy. However, data on the heart-ECMO interaction at different levels of ECMO blood flow during the immediate period after ECMO initiation are sparse. We evaluated the effects of varying ECMO blood flow rate on left ventricular systolic function.

Methods:

Adult patients who were supported by peripheral V-A ECMO in a tertiary referral center were recruited. Serial hemodynamic and cardiac performance parameters were measured by transthoracic echocardiogram within the first 48 hours after implementation of V-A ECMO. Measurements at 100%, 120%, and 50% of target blood flow (TBF) were compared.

Results:

A total of 45 patients were included, 32 (71.1%) were male, and the median age was 57 (50-64) years. The main indications for V-A ECMO were myocardial infarction 25 (55.6%) and myocarditis 6 (13.3%). With a decrease in extracorporeal blood flow from 100% to 50% of TBF, mean arterial pressure dropped from 75 ± 18 to 67 ± 20 mmHg ($p < 0.001$), but stroke volume increased from 15 (8-25) to 21 (13-34) mL ($p < 0.001$), and cardiac index increased from 0.8 (0.5-1.3) to 1.2 (0.7-1.7) L/min/m² ($p < 0.001$). All indices of left ventricular contractility improved at 50% compared with 100% TBF: the global longitudinal strain improved from -2.8 (-5.4-0) to -4.7 (-8.2- -1.1)% ($p < 0.001$); left ventricular ejection fraction increased from 16.8 (10.0-28.5) to 28.2 (18.0-35.5)% ($p < 0.001$); and left ventricular outflow tract velocity time integral increased from 4.7 (2.7-7.8) to 7.7 (3.9-11.3) cm ($p < 0.001$). The addition of echocardiographic parameters improved the discrimination of the SAVE score in predicting hospital mortality (AUROC 0.71 vs 0.58).

Conclusions:

In the initial period of V-A ECMO support, left ventricular systolic function quantified bedside echocardiography was inversely related to ECMO blood flow rate. The heart-ECMO interaction should be considered when determining goals of ECMO flow after initiation.

Background

The use of veno-arterial extracorporeal membrane oxygenation (V-A ECMO) as a form of temporary mechanical circulatory support has increased exponentially over the past decade [1]. Due to its relative ease of setting up, peripheral V-A ECMO has become a readily available option to facilitate resuscitation at the bedside. A recent randomized controlled trial found that early ECMO-facilitated resuscitation for patients with out-of-hospital cardiac arrest significantly improved survival to hospital discharge [2].

In the peripheral configuration of V-A ECMO, oxygenated blood from the ECMO circuit returns to the arterial system in a “retrograde” manner from cannulas sited in peripheral vasculature, most commonly the femoral

artery. This returning blood flow may increase the left ventricular (LV) afterload, leading to increase in LV wall stress and myocardial oxygen demand, a condition that may be deleterious to the recovery of an acutely-injured heart [3]. Although this phenomenon has been postulated, the magnitude of changes in LV performance parameters in response to different levels of ECMO blood flow during the early period after initiation have not been well-delineated in prospective cohorts, and the lack of such fundamental physiological data regarding the heart-ECMO interaction may be partially accountable for the difficulty in establishing recommendations for target flow rates.

In this prospective observational study, we examined hemodynamic data and echocardiographic parameters of LV function in response to different levels of ECMO blood flow during acute cardiogenic shock. We hypothesized that LV systolic function is inversely related to the ECMO blood flow rate during the initial period of peripheral V-A ECMO support.

Material And Methods

Study Population

This was a single-center prospective observational study including all adult patients (≥ 18 years old) with acute cardiogenic shock who were admitted between April 2019 and June 2021, and were treated with peripheral V-A ECMO in the intensive care unit (ICU) of Queen Mary Hospital in Hong Kong.

Patients were excluded if they met one of the following criteria: (1) clinically unstable hemodynamics including unstable or poor ECMO blood flow which precludes ECMO flow adjustment; (2) presence of pathological intracardiac shunt, for example, ventricular septal defect; (3) presence of iatrogenic shunt, for example, left ventricular vent; (4) echocardiographic image quality unsatisfactory for data processing; or (5) absence of patient or surrogate consent. This study was approved by the Institutional Review Board of the University of Hong Kong/ Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) (IRB Reference Number: UW 17-449). Informed consent was obtained from all participants or their surrogates if the fitness to consent was impaired.

Material, Equipment and Procedures

Transthoracic echocardiogram (TTE) examinations were performed as soon as practicable within the first 48 hours after initiation of V-A ECMO support by one of 3 physicians trained in detailed cardiac echocardiography, using a commercially available system (General Electric Healthcare Vivid q cardiovascular ultrasound system). Two-dimensional sequences with three beats were obtained using a 3.5 MHz ultrasound transducer probe at a frame rate of 50 frames/sec and stored digitally in Digital Imaging and Communications in Medicine (DICOM) format. Standard echocardiographic measurements were obtained according to current recommendations [4], and repeated with ECMO flow settings at 100%, 120%, and 50% target blood flow (TBF) (defined as 50-80 ml/kg ideal body weight/min) [5, 6]. At each ECMO blood flow setting, echocardiographic measurements were taken after 5 minutes of flow adjustment to allow equilibration. Measurements were abandoned and further flow adjustment not attempted if the patient developed clinically significant acute deterioration in hemodynamics. To minimize effects of

pharmacologically-induced alterations in systemic vascular resistance, the titration of vasopressor administration during ECMO flow adjustment was not recommended.

LV systolic function assessment included left ventricular ejection fraction (LVEF), fractional shortening (FS), left ventricular outflow tract (LVOT) velocity-time integral (VTI), left ventricular index of myocardial performance (LIMP), and peak systolic tissue velocity (s') at the mitral annulus measured by pulsed-wave Doppler. LVEF was measured using both the linear (Teichholz formula) and biplane Simpson methods. Myocardial strain for each of the cardiac segments were measured by two-dimensional speckle tracking echocardiography in longitudinal 3-chamber, 4-chamber and 2-chamber planes. The LV global longitudinal strain (GLS) was obtained by averaging segmental strain values. All echocardiographic measurements were analyzed offline by a single investigator blinded to clinical data and subsequent analyses. Detailed definitions of these measurements are shown in Additional file 1.

Hemodynamic data were measured by continuous invasive measurement of arterial pressure and by parameters obtained during transthoracic echocardiography according to current recommendations [7].

Outcomes

The primary outcome was the LV systolic function measured by GLS. Secondary outcomes were other measures of LV systolic function, including LVEF using modified Simpson's rule, LVOT VTI, LIMP, and s' at the lateral and septal mitral annular level.

Statistical Analysis

Primary Analysis

All analyses were performed with prespecified endpoints and statistical methods. Data were expressed either as mean $\pm$ standard deviation or median with interquartile ranges for continuous variables, and frequencies with percentages for categorical variables. Comparisons between LV parameters at different ECMO flow rates were made using paired t-tests or Wilcoxon signed-rank tests.

Secondary Analysis

We examined whether data gathered early after ECMO implantation is useful to predict eventual clinical outcomes. The performance of 2 different models were assessed – Model 1 was the Survival After Veno-arterial ECMO (SAVE) score [8]; Model 2 was the SAVE score together with echocardiographic parameters of LV systolic function obtained at 100% TBF, including LVEF measured by the biplane method, LVOT VTI, average s' at the mitral annulus, and LV GLS. The utility of these models to predict hospital mortality and successful weaning from V-A ECMO were examined. Model calibration and discrimination were examined by the Hosmer-Lemeshow test and the area under receiving operating characteristic (AUROC) curve.

Sensitivity Analysis

It is possible that the concurrent use of intra-aortic balloon pump (IABP) affects echocardiographic parameters of LV function, therefore, a subgroup analysis excluding patients on IABP during ECMO was performed.

Data management and statistical analyses were performed in Stata, version 13 (StataCorp LP). Bonferroni correction was used to adjust for multiple comparisons, and a two-tailed P value of less than 0.025 was considered statistically significant.

Results

Study Population

From 1st April 2019 to 30th June 2021, 76 adult patients who were admitted to the ICU with a diagnosis of cardiogenic shock requiring V-A ECMO support were identified (Figure 1). After excluding 18 patients with unstable hemodynamics and could not tolerate ECMO flow adjustment, 3 patients who had LV venting, 2 patients requiring urgent cardiectomy, 1 patient with ventricular septal defect, 3 patients who had unsatisfactory echocardiographic image quality, and 4 patients who did not give informed consent, the final patient cohort consisted of 45 patients.

The median age of the study population was 57 (50-64) years and there were 32 (71.1%) males. The most common indications of V-A ECMO were acute coronary syndrome (25, 55.6%) and myocarditis (6, 13.3%). Baseline characteristics are summarized in Table 1. A total of 32 (71.1%) patients received V-A ECMO during extracorporeal cardiopulmonary resuscitation (ECPR), these patients are summarized in Additional file 2.

On day 1 of ECMO support, the worst mean arterial pressure (MAP) was 61 (47-82) mmHg and the highest heart rate were 114 (95-127) bpm. The vasoactive inotropic score was 21.7 (6.3-48.7), and the worst lactate level was 11.7 ± 6.0 mmol/L. The mean APACHE IV score was 123.0 ± 29.0 . Clinical parameters are summarized in Additional file 3.

Clinical Outcomes

The median duration on V-A ECMO was 134.3 (76.6-189.6) hours. There were 23 (51.1%) patients who were able to be weaned off ECMO. The median length of stay in ICU was 7.3 (5.1-13.0) days, with 21 (46.7%) patients surviving the ICU stay and 20 (44.4%) patients surviving the hospital stay. 2 (4.4%) patients had IABP inserted prior to V-A ECMO, and 4 (8.9%) patients required IABP insertion after ECMO was initiated. 19 (42.2%) patients required renal replacement therapy, and 42 (93.3%) patients required invasive mechanical ventilation. 2 (4.4%) patients had ischemic limb requiring fasciotomy, and 3 (6.7%) patients suffered from ischemic stroke. Major bleeding was defined according to ELSO definitions [9], and encountered in 10 (22.2%) patients. The clinical outcomes are summarized in Additional file 4.

Hemodynamic Data

There were significant differences in hemodynamic parameters with ECMO blood flows at 50% compared with 100% and 120% TBF. The MAP was significantly lower at 50% compared with 100% TBF, and at 50% compared with 120% TBF (67 ± 20 vs 75 ± 18 mmHg, $p < 0.001$; 67 ± 20 vs 78 ± 18 mmHg, $p < 0.001$; respectively). Having ECMO blood flow at 50% TBF when compared with 100% TBF and 120% TBF was associated with higher stroke volume (SV) [21 (13-34) vs 15 (8-25) mL, $p < 0.001$; 21 (13-34) vs 12 (6-22) mL, $p < 0.001$], and

higher cardiac index (CI) [1.2 (0.7-1.7) vs 0.8 (0.5-1.3) L/min/m², p<0.001; 1.2 (0.7-1.7) vs 0.5 (0.3-1.4) L/min/m², p<0.001], respectively.

Left Ventricular Systolic Function Measurements

TTE were performed on a mean 1.1 ± 0.7 days after initiation of ECMO. The LV systolic function was significantly better across all echocardiographic measurements at 50% TBF compared with 100% TBF, and at 50% TBF compared with 120% TBF. These included the LVEF measured by the biplane method [28.2 (18.0-35.5) vs 16.8 (10.0-28.5)%, p<0.001; 28.2 (18.0-35.5) vs 13.1 (8.3-26.3)%, p<0.001], FS [10.9 (6.7-15.7) vs 6.2 (3.3-10.9)%, p<0.001; 10.9 (6.7-15.7) vs 5.2 (2.4-9.3)%, p<0.001], LIMP [1.1 (0.8-1.6) vs 1.6 (1.1-2.3), p<0.001; 1.1 (0.8-1.6) vs 1.7 (1.2-2.3), p<0.001], LVOT VTI [7.7 (3.9-11.3) vs 4.7 (2.7-7.8) cm, p<0.001; 7.7 (3.9-11.3) vs 3.5 (1.9-7.8) cm, p<0.001], and s' measured at the medial [0.04 (0.03-0.06) vs 0.03 (0.03-0.05) m/s, p=0.003; 0.04 (0.03-0.06) vs 0.03 (0.03-0.04) m/s, p<0.001] and lateral mitral annulus [0.05 (0.03-0.06) vs 0.04 (0.03-0.06) m/s, p=0.054; 0.05 (0.03-0.06) vs 0.04 (0.03-0.05) m/s, p=0.003]. Detailed echocardiographic data at different levels of ECMO blood flows are shown in Table 2, and stratified by hospital mortality in Additional file 5. Spaghetti plots for various measures of LV function against ECMO TBF are shown in Figure 2.

Myocardial Strain Measurements

The myocardial systolic function measured by LV GLS was significantly better at 50% TBF compared with 100% TBF and 120% TBF, respectively [-4.7 (-8.2- -1.1) vs -2.8 (-5.4-0) %, p<0.001; -4.7 (-8.2- -1.1) vs 0 (-4.8-0) %, p<0.001]. Similarly, there were significant differences in segmental strain values obtained at the LV longitudinal 3-chamber, 2-chamber, and 4-chamber views when ECMO blood flow was titrated.

Prediction of Clinical Outcomes

The performance of 2 clinical models including data gathered early after ECMO implantation to predict eventual hospital mortality and successful weaning from V-A ECMO were examined. Model 2 which included the SAVE score and echocardiographic parameters of LV systolic function obtained at 100% TBF had better discriminatory value compared with SAVE score only in predicting the hospital mortality (AUROC 0.71, 95% CI 0.56-0.87 vs 0.58, 95% CI 0.40-0.76; respectively) and successful weaning from V-A ECMO (AUROC 0.67, 95% CI 0.51-0.83 vs 0.55, 95% CI 0.38-0.73; respectively) (Figure 3).

The AUROC curves for Model 2 measured at different levels of ECMO blood flow were compared. Variables obtained at 100% TBF compared with 50% and 120% TBF had the best discrimination for hospital mortality (AUROC 0.71, 95% CI 0.56-0.87 vs. 0.67, 95% CI 0.51-0.83 vs 0.63, 95% CI 0.46-0.80; respectively) and successful weaning from V-A ECMO (AUROC 0.67, 95% CI 0.51-0.83 vs 0.61, 95% CI 0.45-0.78 vs 0.63, 95% CI 0.46-0.80; respectively) (Figure 4). Hosmer-Lemeshow tests suggested that the models were well-calibrated (p > 0.05 for all).

Sensitivity Analysis

6 (13.3%) patients who had IABP during ECMO were excluded from the subgroup analysis. All indices of LV systolic function were significantly better at 50% TBF were compared with 100% TBF and 120% TBF,

respectively (Table 3).

Discussion

In a large prospective cohort of patients on V-A ECMO, we provided robust echocardiographic evidence of the afterload effect of peripheral V-A ECMO support during the acute phase of myocardial injury. Across all measures of LV function, increasing ECMO blood flow was associated with significantly decreased LV systolic function. These physiological data are fundamental to understanding the heart-ECMO interaction, guiding titration of ECMO blood flow, and optimizing cardiac recovery. We also showed that incorporation of echocardiographic measurements improved the predictive ability of commonly used risk scores such as the SAVE score, highlighting the importance of a multidimensional assessment of patients on ECMO.

The prevalent beliefs about hemodynamics during peripheral V-A ECMO include a decrease in the SV and cardiac output due to reduction in native cardiopulmonary circulation and an increase in the LV afterload [10]. Depending on the competing effects on decreasing preload and increasing afterload, the LV chamber size and systolic function may be variable. In a pilot study including 22 patients by Aissaoui et al., it was shown that the LVEF, VTI, and LV strain were all load dependent [11]. The authors found that tissue Doppler velocities were more useful than LV strain for characterizing the LV function, but broad generalization of the study findings are limited by the cohort having included both central and peripheral V-A ECMO configurations. Our cohort included a homogenous group of patients supported on peripheral V-A ECMO, who, by nature of the retrograde return of blood flow in the descending aorta, are particularly sensitive to load variations induced by changes in ECMO flow settings. All measures of LV systolic function were better with the ECMO blood flow set at 50% of target, including increase in LV GLS, increase in LVEF, increase in LVOT VTI, and increase in s' at the mitral annulus.

The optimization of ECMO blood flow for the heterogeneous conditions necessitating V-A ECMO is a complex issue, with sparse evidence for specific targets in published literature. Considering that initial ECMO set up is largely titrated to a target flow, this “ECMO dose” should be better delineated. While a general target ECMO flow of 50-80 mL/kg/min have been proposed [5, 6], others have emphasized targeting mean arterial pressure or venous oxygen saturation to ensure adequate oxygen delivery [12, 13]. There are increasing data to suggest improved outcomes after concurrent LV unloading during V-A ECMO [14], with marked reduction of the pulmonary venous pressure, potentially reducing the degree of pulmonary edema and limiting myocardial infarct size [3]. However, few studies have provided direct echocardiographic evidence of depressed LV systolic function that were correlated with higher ECMO flows in a dose-dependent manner. Whether “permissively low” ECMO blood flows should be targeted after ECMO implantation in return for better LV systolic function deserves careful consideration, taking into account other physiological effects of ECMO at lower flows such as increased hemolysis in the centrifugal pump [15].

We highlighted that quantitative echocardiography in the management of patients requiring V-A ECMO extends beyond assessment of myocardial function at stably maintained ECMO flows [16]. Recent data have emerged that dynamic indices such as improvement in tissue Doppler velocities predict ECMO weanability [17]. The interplay between LV performance metrics and different levels of ECMO blood flow needs to be mapped out for the individual patient, and repeated profiling should be attempted throughout the course of

ECMO support. While most conventional measures of LV systolic function could be used in patients with V-A ECMO, myocardial strain has emerged as a relatively load-independent measurement that is more reproducible than LVEF, even when performed by less-experienced operators [18]. These properties make strain imaging an attractive tool for repeated assessment at the point-of-care and should be considered by all ECMO providers [19].

The SAVE score is one of the most widely accepted risk prediction models to estimate hospital survival for patients on V-A ECMO [8]. However, it performed modestly in our cohort, possibly due to the significant proportion of patients who had received ECMO during ECPR, who were not considered in the original development of the SAVE score. ECPR-specific scores have since been published [20], but their widespread adoption is limited by the lack of external validation. We showed that by incorporating echocardiographic derivatives of LV function, the performance of the SAVE score could be improved, with a possibility to be broadly applicable to all V-A ECMO patients, regardless of ECPR status. This should be a future priority for collaborative international multicenter studies.

One of the limitations of this study is its single-centered design, with possible systemic biases in patient selection and management. However, the inclusion criteria were not restrictive, and this is one of the larger V-A ECMO cohorts with detailed echocardiographic documentation of the heart-ECMO interaction at various flow rates. Second, patients who were hemodynamically unstable during the first 48 hours and patients who had LV venting had to be excluded by nature of the study design, potentially limiting the application of the study findings to these patients. Third, other aspects of patient management, including the use of inotropes and titration of positive end-expiratory pressure were not protocolized, possibly introducing confounding effects on variable preload and afterload.

Conclusions

We provided hemodynamic and echocardiographic data to demonstrate the inverse effects of ECMO blood flow on LV systolic function in a dose-dependent manner. These physiological data highlight the significance of determining goals of ECMO flow after initiation. The incorporation of echocardiographic parameters to established risk scores in a multidimensional assessment may improve the prediction of important clinical outcomes.

Abbreviations

APACHE	Acute Physiology and Chronic Health Evaluation
AUROC	Area under the receiver operating characteristic
CI	Cardiac index
CPI	Cardiac Power Index
ECPR	Extracorporeal cardiopulmonary resuscitation
FS	Fractional shortening
GLS	Global longitudinal strain
IABP	intra-aortic balloon pump
ICU	Intensive care unit
LV	Left ventricular
LVEF	Left ventricular ejection fraction
LVOT	Left ventricular outflow tract
LIMP	Left ventricular index of myocardial performance
MAP	Mean arterial pressure
S'	Peak systolic tissue velocity at mitral annulus
SAVE	Survival after veno-arterial ECMO
SV	Stroke volume
TBF	Target blood flow
TTE	Transthoracic echocardiography
V-A ECMO	Veno-arterial extracorporeal membrane oxygenation
VF	Ventricular fibrillation
VT	Ventricular tachycardia
VTI	Velocity time integral

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Institutional Review Board of the University of Hong Kong/ Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) (IRB Reference Number: UW 17-449). Informed consent was obtained from all participants or their surrogates if the fitness to consent was impaired.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

PYN, TSM and WCS participated in the conception and design of the study. PYN, TSM, ASW and WCS participated in data acquisition. AI, SF and ACL helped with the data management and analysis. PYN and TSKM drafted the manuscript. All authors revised and approved the final manuscript, and are accountable for the accuracy and integrity of the work.

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Tables

Table 1. Baseline characteristics of the patient population

	N=45
Demographics	
Age	57 (50-64)
Sex - male	32 (71.1%)
Mean body mass index	25.3 ± 4.0
Mean body surface area	1.8 ± 0.2
Hospital stay before ECMO initiation, hours	0.6 (0-23.6)
Co-morbidities	
Active smoker	15 (33.3%)
Hypertension	14 (31.1%)
Hypercholesterolemia	12 (26.7%)
Diabetes mellitus	10 (22.2%)
Ischemic heart disease	6 (13.3%)
Arrhythmia	7 (15.6%)
Congestive heart failure	5 (11.1%)
Valvular heart disease	1 (2.2%)
Cardiomyopathy	2 (4.4%)
Obstructive sleep apnea	1 (2.2%)
Ischemic stroke	1 (2.2%)
Intracerebral hemorrhage	2 (4.4%)
Indications for V-A ECMO	
Acute coronary syndrome	25 (55.6%)
Myocarditis	6 (13.3%)
Malignant arrhythmia	4 (8.9%)
Endocrine-related heart failure	3 (6.7%)
Decompensated heart failure	4 (8.9%)
Clinical Scores	
APACHE IV score	123.0 ± 29.0
APACHE II score	31.8 ± 8.2
SAVE score	-4.6 ± 4.5
Vasoactive Inotropic Score ^a	21.7 (6.3-48.7)

All data are presented as frequency with percentages or mean ± standard deviation, or median with interquartile range (IQR) unless specified.

^a The Vasoactive Inotropic Score was calculated as: Dopamine dose ($\mu\text{g/kg/min}$) + Dobutamine dose ($\mu\text{g/kg/min}$) + $100 \times$ Adrenaline dose ($\mu\text{g/kg/min}$) + $10 \times$ Milrinone dose ($\mu\text{g/kg/min}$) + $10\,000 \times$ Vasopressin dose (unit/kg/min) + $100 \times$ Noradrenaline dose ($\mu\text{g/kg/min}$).

Abbreviations: APACHE II score: acute physiology and chronic health evaluation II score; APACHE IV score: acute physiology and chronic health evaluation IV score; SAVE: Survival after Veno-Arterial ECMO score; V-A ECMO: veno-arterial extracorporeal membrane oxygenation.

Table 2. Comparison of Echo Findings at Different Levels of ECMO Target Blood Flow

ECMO Target Blood Flow					
	100%	120%	50%	P value for 100% and 50%	P value for 120% and 50%
Left ventricle size					
LVIDd, cm	4.3 (3.6-4.8)	4.1 (3.5-4.8)	4.0 (3.3-4.8)	0.009	0.25
LVIDs, cm	4.0 (3.3-4.6)	3.7 (3.1-4.7)	3.5 (2.8-4.2)	<0.001	<0.001
LVEDV, mL	70.0 (44.4-113.7)	59.6 (44.2-109.4)	78.0 (41.0-108.7)	0.98	0.92
LVESV, mL	55.2 (29.6-88.9)	54.9 (32.0-94.7)	51.4 (26.3-92.2)	0.040	0.009
Left ventricular systolic function					
LVEF, %					
- Linear method	14.1 (7.8-24.5)	12.1 (5.3-20.9)	22.9 (14.8-34.1)	<0.001	<0.001
- Biplane	16.8 (10.0-28.5)	13.1 (8.3-26.3)	28.2 (18.0-35.5)	<0.001	<0.001
FS, %	6.2 (3.3-10.9)	5.2 (2.4-9.3)	10.9 (6.7-15.7)	<0.001	<0.001
LIMP	1.6 (1.1-2.3)	1.7 (1.2-2.3)	1.1 (0.8-1.6)	<0.001	<0.001
LVOT VTI, cm	4.7 (2.7-7.8)	3.5 (1.9-7.8)	7.7 (3.9-11.3)	<0.001	<0.001
s' - medial mitral annulus, m/s	0.03 (0.03-0.05)	0.03 (0.03-0.04)	0.04 (0.03-0.06)	0.003	<0.001
lateral mitral annulus, m/s	0.04 (0.03-0.06)	0.04 (0.03-0.05)	0.05 (0.03-0.06)	0.054	0.003
Left ventricular diastolic function					
E/A (if patient is in SR)	0.8 (0.6-1.0)	0.8 (0.6-1.1)	0.9 (0.6-1.1)	0.31	0.47
e' - medial, m/s	0.03 (0.02-0.04)	0.03 (0.02-0.04)	0.03 (0.02-0.05)	0.028	0.001
lateral, m/s	0.03 (0.03-0.05)	0.03 (0.02-0.04)	0.04 (0.03-0.05)	0.65	<0.001
E/e'- mean	11.9 (8.4-18.3)	11.2 (7.6-18.5)	11.1 (7.7-17.0)	0.94	0.76

Hemodynamic parameters					
SBP, mmHg	92 (77-105)	100 (82-112)	85 (71-107)	0.041	<0.001
DBP, mmHg	74±17	71±17	60±16	<0.001	<0.001
MAP, mmHg	75±18	78±18	67±20	<0.001	<0.001
HR, bpm	93±19	91±19	94±19	0.68	0.072
Stroke volume, mL	15 (8-25)	12 (6-22)	21 (13-34)	<0.001	<0.001
Cardiac output, L/min	1.3 (0.8-2.2)	1.0 (0.5-2.3)	2.0 (1.2-3.1)	<0.001	<0.001
Cardiac index, L/min/m²	0.8 (0.5-1.3)	0.5 (0.3-1.4)	1.2 (0.7-1.7)	<0.001	<0.001
CPO, Watts	0.2 (0.1-0.4)	0.2 (0.1-0.4)	0.3 (0.2-0.5)	<0.001	<0.001
CPI, Watts/m²	0.1 (0.1-0.2)	0.1 (0-0.2)	0.2 (0.1-0.3)	<0.001	<0.001
Strain values, %					
Global longitudinal strain	-2.8 (-5.4-0)	0 (-4.8-0)	-4.7 (-8.2-1.1)	<0.001	<0.001
Longitudinal 3-chamber strain	-3.5 (-6.2-0)	0 (-5.5-0)	-4.8 (-8.5-0)	0.011	<0.001
Longitudinal 2-chamber strain	-3.5 (-6.0-0)	0 (-3.8-0)	-4.5 (-8.7-0)	<0.001	<0.001
Longitudinal 4-chamber strain	0 (-5.2-0)	0 (-5.0-0)	-3.7 (-7.2-0)	0.044	<0.001

Abbreviations: CPI: cardiac power index; CPO: cardiac power output; DBP: diastolic blood pressure; e': early diastolic tissue velocity at mitral annulus; E/A: early to late diastolic transmitral flow velocity; E/e': early diastolic transmitral flow velocity to e'; ECMO: extracorporeal membrane oxygenation; FS: fractional shortening; HR: heart rate; LIMP: left ventricular index of myocardial performance; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; LVIDd: left ventricular internal diameter in diastole; LVIDs: left ventricular internal diameter in systole; LVOT: left ventricular outflow trace; MAP: mean arterial pressure; s': peak systolic tissue velocity at mitral annulus; SBP: systolic blood pressure; VTI: velocity time integral.

Table 3. Sensitivity Analysis

ECMO Target Blood Flow N=39					
	100%	120%	50%	P value for 100% and 50%	P value for 120% and 50%
Left ventricular systolic function					
LVEF, %					
- Biplane	16.8 (10.0- 28.5)	12.9 (8.3- 26.3)	28.2 (17.6- 35.8)	<i><0.001</i>	<i><0.001</i>
FS, %	6.3 (3.2- 10.9)	5.3 (2.2- 9.3)	10.5 (6.1- 15.7)	<i><0.001</i>	<i><0.001</i>
LIMP	1.6 (1.0- 2.0)	1.5 (1.1- 2.3)	1.1 (0.8- 1.5)	<i><0.001</i>	<i><0.001</i>
LVOT VTI, cm	4.9 (2.7- 8.5)	4.4 (2.0- 8.2)	8.1 (3.9- 11.7)	<i><0.001</i>	<i><0.001</i>
s' - medial mitral annulus, m/s	0.03 (0.03- 0.05)	0.03 (0.02- 0.04)	0.04 (0.03- 0.06)	<i>0.002</i>	<i><0.001</i>
lateral mitral annulus, m/s	0.04 (0.03- 0.06)	0.04 (0.03- 0.05)	0.05 (0.03- 0.06)	<i>0.024</i>	<i>0.005</i>

Abbreviations: ECMO: extracorporeal membrane oxygenation; FS: fractional shortening; LIMP: left ventricular index of myocardial performance; LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow trace; s': peak systolic tissue velocity at mitral annulus; VTI: velocity time integral.

Figures

Figure 1

Flow Diagram of the Study

A total of 76 adult patients were admitted to the intensive care unit with a diagnosis of cardiogenic shock requiring V-A ECMO support between 1st April 2019 and 30th June 2021. After excluding 30 patients, the final patient cohort consisted of 46 patients.

ICU: intensive care unit; LV: left ventricular; OT: operation; V-A ECMO: veno-arterial extracorporeal membrane oxygenation.

Figure 2

Spaghetti Plots for Various Measures of Left Ventricular Function against ECMO Target Blood Flow

The plots of LVEF (left ventricular ejection fraction; top left), FS (fractional shortening; top middle), LIMP (left ventricular index of myocardial performance; top right), LVOT VTI (left ventricular outflow tract velocity time integral; bottom left), s' (peak systolic tissue velocities measured at medial mitral annulus; bottom middle), and LV GLS (left ventricular global longitudinal strain; bottom right) against ECMO target blood flow of 50%, 100%, and 120% ($n=45$). Each blue line represents an individual participant. The line of best fit for each plot is shown in red.

Figure 3

Receiving Operating Characteristic Curves to Predict Hospital Mortality and Weaning Off ECMO

The receiving operative characteristic curves using Model 1 (SAVE score) (red), and Model 2 (SAVE score and echocardiographic parameters of left ventricular systolic function obtained at 100% ECMO target blood flow) (blue) to predict hospital mortality (Panel A) and successful weaning from V-A ECMO (Panel B). Model 2 had the best discriminative ability with the area under receiving operating characteristic curves of 0.71 (95% CI 0.56 – 0.87) and 0.67 (95% CI 0.51 – 0.83), respectively.

Figure 4

Receiving Operating Characteristic Curves of Model 2 at Different Levels of ECMO Blood Flow to Predict Hospital Mortality and Weaning Off ECMO

The receiving operative characteristic curves using Model 2 at 100% (red), 120% (blue) and 50% (orange) ECMO target blood flow to predict hospital mortality (Panel A) and successful weaning from V-A ECMO (Panel B). Variables obtained at 100% ECMO TBF had the best discriminative ability with the area under receiving operating characteristic curves of 0.71 and 0.67, respectively.

TBF: target blood flow; V-A ECMO: veno-arterial extracorporeal membrane oxygenation.

Supplementary Files

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