


# Assessment of cardiac recovery in patients supported with venoarterial extracorporeal membrane oxygenation

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## Abstract

**Aims** Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is increasingly being used to support patients in cardiogenic shock (CS). Early determination of disposition is paramount, as longer durations of support have been associated with worse outcomes. We describe a stepwise, bedside weaning protocol to assess cardiopulmonary recovery during VA-ECMO.

**Methods and results** Over 1 year, we considered all patients on VA-ECMO for CS for the Weaning Protocol (WP) at our centre. During the WP, patients had invasive haemodynamic monitoring, echocardiography, and blood gas analysis while flow was reduced in 1 LPM decrements. Ultimately, the circuit was clamped for 30 min, and final measures were taken. Patients were described as having durable recovery (DR) if they were free of pharmacological and mechanical support at 30 days post-decannulation. Over 12 months, 34 patients had VA-ECMO for CS. Fourteen patients were eligible for the WP at 4–12 days. Ten patients tolerated full flow reduction and were successfully decannulated. Twenty-four per cent of the entire cohort demonstrated DR with no adverse events during the WP. Patients with DR had significantly higher ejection fraction, cardiac index, and smaller left ventricular size at lowest flow during the WP.

**Conclusions** We describe a safe, stepwise, bedside weaning protocol to assess cardiac recovery during VA-ECMO. Early identification of patients more likely to recover may improve outcomes during ECMO support.

**Keywords** VA-ECMO; Mechanical circulatory support; Cardiogenic shock; Cardiac recovery

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## Introduction

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is a short-term mechanical circulatory support (MCS) strategy frequently used in patients with refractory cardiogenic shock (CS). Strategic implementation of VA-ECMO may serve as a bridge to either recovery of cardiopulmonary function or transition to more durable therapies such as left ventricular assist device (LVAD) implantation or cardiac transplantation. Use of ECMO for CS has almost doubled over the past 4 years.<sup>1</sup> Early determination of disposition (bridge to recovery, transition to alternate MCS, or listing for urgent cardiac transplantation) during ECMO support is paramount, as

longer durations of VA-ECMO support have been shown to be associated with worse outcomes.<sup>2</sup>

Integral to determination of disposition is an assessment of cardiac and pulmonary function during VA-ECMO support. Unlike other forms of MCS, the ability to wean from VA-ECMO will depend on recovery of both cardiac and pulmonary function. Ideally, weaning protocols would assess each independently. There is limited prior literature describing weaning protocols to assess recovery during VA-ECMO. The various strategies described include echocardiographic assessment of cardiac function,<sup>3,4</sup> the ability to tolerate a volume challenge,<sup>5</sup> or reduction in vasopressor support<sup>6</sup> during reduced ECMO flow. A more recent report described a tech-

nique where pump speeds were adjusted to allow retrograde flow through the circuit to assess cardiac function.<sup>7</sup> Notably, none of these prior reports used invasive haemodynamics to aid in decision making.

We describe a formal, stepwise weaning protocol using haemodynamic and echocardiographic measures to assess cardiopulmonary function during VA-ECMO support.

## Methods

### Study population

In February of 2018, we instituted a formal, stepwise weaning protocol at our institution to assess cardiopulmonary recovery in patients with CS supported with VA-ECMO. All patients supported with VA-ECMO at our institution were considered for the Weaning Protocol (WP). Patients were deemed ineligible for the WP if they manifested any of following exclusion criteria: active sepsis, significant abnormalities on chest radiograph, high pressor requirement, uncontrolled arrhythmia, persistent significant elevation of lactate, or severe neurological injury. Over the subsequent 11 months, we initiated a prospective observational study to capture serial clinical, haemodynamic, and biomarker data in all patients supported with VA-ECMO at our centre and to capture data from the WP. The study was approved by the institutional review board.

### Demographics and clinical data collection

Demographic data were obtained from chart review at baseline. Key clinical and haemodynamic data and levels of vasopressor support were recorded at baseline (within 24 h of ECMO initiation) and daily during VA-ECMO support. The status of patients decannulated for recovery was assessed 30 days after ECMO discontinuation.

### Weaning Protocol

The WP was performed electively at the bedside in the cardiothoracic intensive care unit (*Figure 1*). Data from the WP were utilized by the clinical team to determine candidacy for ECMO decannulation to be performed at a later stage in the operating room. Each procedure required the participation of a multidisciplinary team including a cardiothoracic surgeon, heart failure cardiologist, intensivist, perfusionist, echocardiography technician, and nurse.

#### *Pre-Weaning Protocol preparation*

One to 2 days prior to the weaning study, fluid balance was optimized (diuretics were given to target central venous

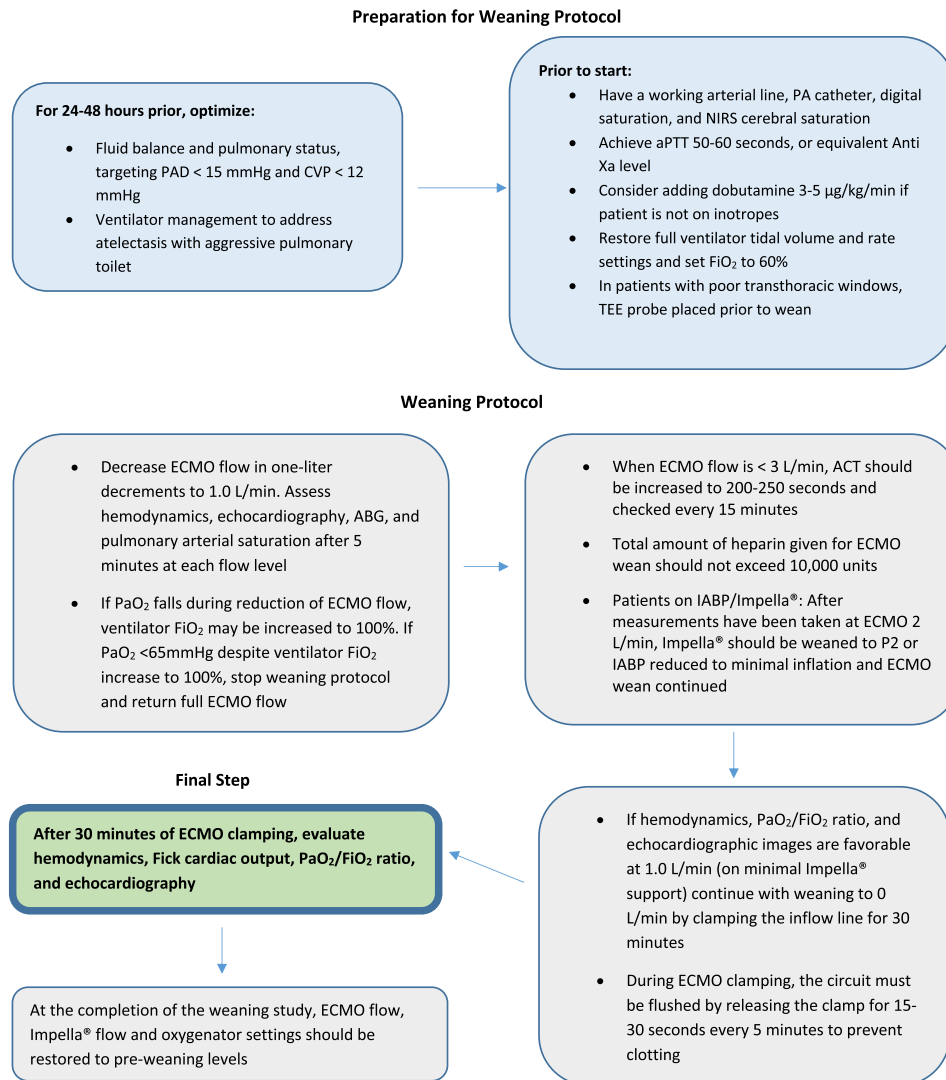
pressure < 12 mmHg and pulmonary artery diastolic pressure < 15 mmHg), and ventilator settings were adjusted to minimize atelectasis while performing aggressive pulmonary toilet.

Patients were required to have an arterial line (ideally right upper extremity), pulmonary artery catheter, and monitoring of cerebral tissue oxygenation using near-infrared spectroscopy (NIRS). In patients with suboptimal transthoracic images, transesophageal echocardiography was utilized. Heparin was dosed to achieve an activated partial thromboplastin time of 50–60 s prior to any decrease in ECMO flow, and patients were initiated on dobutamine 3–5 µg/kg/min if they were not already on inotropes.

#### *Weaning procedure*

Extracorporeal membrane oxygenation flow was decreased in 1 L decrements from full support to 1.0 L/min with measurements taken after 5 min at each stage. Haemodynamic, echocardiographic, pulmonary arterial and systemic blood gasses, NIRS, and inotrope score<sup>9</sup> were recorded at full support and at each stage. Echocardiographic images were acquired from the parasternal long, apical four-chamber and two-chamber views where windows permitted. Colour Doppler of the aortic, mitral, and tricuspid valve were acquired when possible. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method. Haemodynamic measures from the Swan-Ganz catheter included central venous pressures, pulmonary arterial pressure, pulmonary capillary wedge pressure (PCWP; when possible), and Fick calculation of cardiac output. If systemic oxygenation fell during reduction of ECMO flow, ventilator oxygenation was increased. The protocol was aborted if systemic PaO<sub>2</sub> fell below 65 mmHg despite these measures. When ECMO flow was below 3 L/min, activated clotting time was measured every 15 min and maintained at 200–250 s with intermittent heparin dosing. Any percutaneous mechanical support [intra-aortic balloon pump (IABP), Impella®] used for left ventricular (LV) venting was minimized when ECMO flow reached 2 L/min. If haemodynamics and echocardiographic images were favourable after 5 min at 1 L/min, clamping of the inflow line was initiated. During ECMO clamping, the circuit was flushed by releasing the clamp for 15–30 s every 5 min to prevent clotting. After 30 min of clamping, final data were recorded. At the completion of the weaning study, ECMO, Impella®/IABP, and ventilator settings were restored to pre-weaning settings. In the event that there was evidence for cardiac recovery in the absence of sufficient pulmonary recovery (PaO<sub>2</sub>/FiO<sub>2</sub> < 200), veno-venous ECMO was considered. There were no pre-specified haemodynamic or echocardiographic thresholds for ECMO decannulation. Rather, the totality of these data after 30 min of clamping was used by the clinical team to make the ultimate decision. Our ECMO

**Figure 1** Schematic outlining the Weaning Protocol. ABG, arterial blood gas; ACT, activated clotting time; aPTT, activated partial thromboplastin time; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation;  $\text{FiO}_2$ , fraction of inspired oxygen; IABP, intra-aortic balloon pump; NIRS, near-infrared spectroscopy; PA, pulmonary artery; PAD, pulmonary artery diastolic pressure;  $\text{PaO}_2$ , partial pressure of oxygen; TEE, transesophageal echocardiogram.



weaning policy stated, 'Patients who tolerate 30 minutes of clamping while maintaining hemodynamic stability could be considered for decannulation without the need for immediate transition to alternative MCS. Patients should be on no more than 5  $\mu\text{g}/\text{kg}/\text{min}$  of dobutamine or equivalent and no more than low doses of pressors. These measures are suggested as guidelines only and the decision for ECMO removal will be made by the team based upon the patient's overall clinical condition.' Patients undergoing ECMO decannulation were taken electively to the operating room.

### Post extracorporeal membrane oxygenation-decannulation follow-up

Key clinical and haemodynamic data were recorded 6 days post-decannulation in patients who underwent removal of ECMO for recovery. At 30 days post-decannulation, patient status was recorded as one of the following dispositions: no requirement for mechanical or pharmacological support, ongoing pharmacological support, ongoing temporary circulatory support, or durable LVAD.

## Data analysis

Patients were described as having durable recovery (DR) if they underwent ECMO removal and remained free of both pharmacological and mechanical support at 30 days post-decannulation. Data are presented as mean  $\pm$  SD for continuous and  $n$  (%) for categorical. Baseline data were compared between DR and no DR with Student's  $t$ -test or  $\chi^2$ /Fisher's exact as appropriate. Haemodynamic variables were tested in the WP cohort using the same tests. We further explored the relationship between DR and the absolute values of key clinical biomarkers (serum creatinine, serum lactate, and liver function tests) at baseline and 72 h (Student's  $t$ -test), as well as the relationship between DR and the changes in these biomarkers from baseline to 72 h of support ( $\chi^2$  tests). Analyses of the changes in biomarkers over time were limited to patients with paired data. All analysis was performed with SAS 9.4 (Cary, NC) with a  $P$ -value of 0.05 marking statistical significance.

## Results

### Baseline demographics

From February to December 2018, 34 patients ( $60 \pm 11$  years; 21 males and 13 females) with CS were supported with VA-ECMO, which represents our study cohort (Table 1).

Indications for ECMO included post-acute myocardial infarction shock (29%), post-cardiotomy shock (18%), and other causes (53%) (cardiac arrest, acute decompensated heart failure, arrhythmia, and primary cardiac graft failure). At baseline, the mean inotrope score was  $34.2 \pm 47.3$ . At the time of ECMO initiation, 41% of patients were undergoing resuscitation for ventricular tachycardia/ventricular fibrillation.

### Clinical course of study patients

#### Weaning Protocol

Fourteen patients (41%) underwent the WP after a mean duration of 7 days (range, 4–12) of ECMO support (Figure 2). Nine of these patients had concomitant support with an IABP or Impella® device for LV venting. Ten patients had successful WP, defined as haemodynamic stability at 30 min of full flow reduction. Nine of these 10 patients underwent full clamping and for the remaining patient, minimum flow was limited to 2 L/min due to anticoagulation concerns. No adverse events occurred during any of the weaning studies, and there was no evidence for clot formation in the circuit during clamping. All 10 patients with successful WP were safely decannulated at the recommendation of the clinical team and without the need for transition to alternate MCS. Seven patients with successful WP ultimately met criteria for DR and three did not (two LVAD implantation and one died of sepsis). Four patients failed the WP, becoming hypotensive prompting early termination of the protocol, and were not decannulated

**Table 1** Demographic characteristics

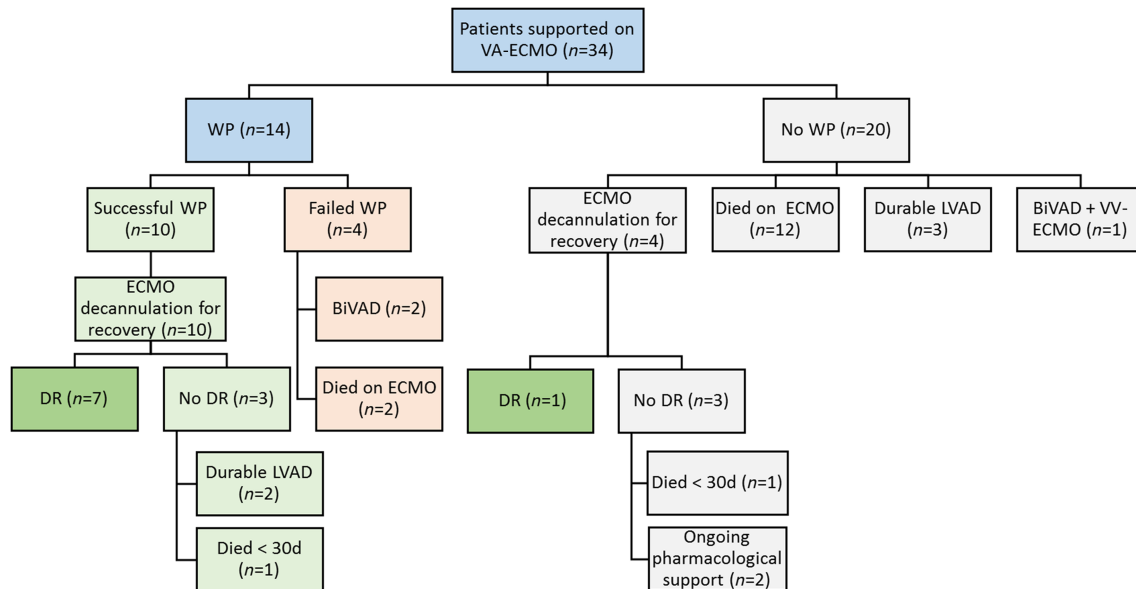
	DR	No DR	Total	$P$ -value
Number (%)	8 (23.5)	26 (76.5)	34 (100)	
Age, years	$63.3 \pm 9.8$	$59 \pm 11.5$	$60 \pm 11.1$	0.35
BSA, m <sup>2</sup>	$1.91 \pm 0.2$	$1.95 \pm 0.2$	$1.94 \pm 0.2$	0.62
Presentation to ECMO, days	$5.1 \pm 5.0$	$5.5 \pm 6.1$	$5.4 \pm 6.1$	0.9
Sex (%)				
Male	3 (14.3)	18 (85.7)	21	0.11
Female	5 (38.5)	8 (61.5)	13	
Cause of CS (%)				
Post-AMI shock	3 (30)	7 (70)	10	0.82
Post-cardiotomy shock	1 (16.7)	5 (83.3)	6	
Other <sup>a</sup>	4 (22.2)	14 (77.8)	18	
Status preceding ECMO				
VT/VF (%)	3 (21.4)	11 (78.6)	14	0.81
Receiving RRT (%)	0 (0)	6 (100)	6	0.30
Inotrope score <sup>b</sup>	$24.8 \pm 42.4$	$37.3 \pm 49.2$	$34.2 \pm 47.3$	0.52
Lactate, mmol/L	$7.1 \pm 5.0$	$5.7 \pm 4.7$	$6.1 \pm 5.2$	0.5
Past medical history (%)				
CAD	6 (23.1)	20 (76.9)	26	0.91
Chronic NICM	0 (0)	4 (100)	4	0.55
DM	3 (21.4)	11 (78.6)	14	0.99
CKD	1 (14.3)	6 (85.7)	7	0.99

AMI, acute myocardial infarction; BSA, body surface area; CAD, coronary artery disease; CKD, chronic kidney disease; CS, cardiogenic shock; DM, diabetes mellitus; DR, durable recovery; ECMO, extracorporeal membrane oxygenation; NICM, non-ischaemic cardiomyopathy; RRT, renal replacement therapy; VT/VF, ventricular tachycardia/ventricular fibrillation.

<sup>a</sup>Other causes of CS included cardiac arrest, acute decompensated heart failure, arrhythmia, and primary graft dysfunction.

<sup>b</sup>Inotrope score = dopamine ( $\times 1$ ) + dobutamine ( $\times 1$ ) + amrinone ( $\times 1$ ) + milrinone ( $\times 15$ ) + epinephrine ( $\times 100$ ) + norepinephrine ( $\times 100$ ) with each drug dosed in  $\mu\text{g}/\text{kg}/\text{min}$ .<sup>9</sup>

**Figure 2** Clinical outcomes 30 days after ECMO decannulation. Successful WP defined as haemodynamic stability after 30 min at lowest flow. BiVAD, biventricular assist device; DR, durable recovery; LVAD, left ventricular assist device; VA-ECMO, venoarterial extracorporeal membrane oxygenation; VV-ECMO, veno-venous extracorporeal membrane oxygenation; WP, Weaning Protocol.



(two temporary biventricular assist device and two died on ECMO).

#### Patients not undergoing Weaning Protocol

Nineteen patients (56%) met pre-specified exclusion criteria and did not undergo the WP. One additional patient did not undergo the WP because of surgical preference. Of these 20 patients, 12 died on ECMO and 4 were transitioned to alternate MCS. Four patients in the cohort were decannulated without undergoing the WP: one demonstrated DR, one died, and two required ongoing pharmacological support at the 30 day assessment.

#### Thirty-day and long-term follow-up post-decannulation for recovery

In a cohort of ECMO patients actively monitored for recovery, 24% (8 patients) met our pre-specified endpoint of DR. Of the patients who underwent the WP, 50% (7 patients) achieved DR and have remained clinically stable and free of mechanical and pharmacological support for 58–636 days, and all patients with DR survived to discharge. The eighth patient who met DR did not undergo the WP and required re-initiation of inotropic support at Day 49 and later died of multi-organ failure.

### Factors associated with durable recovery

#### Baseline demographics

There were no significant differences in baseline demographics between the DR and non-DR groups (Table 1). How-

ever, women tended to demonstrate DR more frequently than men (38% vs. 14%,  $P = 0.11$ ). Notably, the aetiology of CS was not a factor in a patient's likelihood to recover and one-fifth of patients placed on ECMO while being actively resuscitated ultimately met DR.

#### Change in clinical biomarkers at 72 h on extracorporeal membrane oxygenation support

We analysed the relationship between DR and the absolute values of key clinical biomarkers at baseline and 72 h, as well as the relationship between DR and the changes in these biomarkers from baseline to 72 h of support. There was a trend to a larger decrease in international normalized ratio (INR) at 72 h in the DR group as compared with the patients without DR ( $-21.2 \pm 16\%$  vs.  $8.1 \pm 59.7\%$ ;  $P = 0.216$ ), with 86% of DR patients and 67% of patients without DR showing a reduction in INR at 72 h. Lactate decreased in almost all patients in both groups; however, there was a trend towards a greater reduction in DR patients ( $-61.2 \pm 47.3\%$  vs.  $-24.8 \pm 128.9\%$ ;  $P = 0.474$ ). Notably, only two out of the eight (25%) DR patients were on renal replacement therapy (RRT) at 72 h as compared with 14 out of 26 (54%) non-DR patients. Creatinine was analysed in patients not on RRT at either time point. We found no relationship between improvement in creatinine and recovery. Similarly, we found no relationship between improvement in liver function tests and recovery.

#### Weaning Protocol data

Table 2 shows the haemodynamic measurements at lowest tolerated flow in the 14 patients undergoing the WP compar-



**Table 2** Haemodynamic and echocardiographic data at lowest tolerated extracorporeal membrane oxygenation flow

	DR (n = 7)	No DR (n = 7)	P-value
Day of WP (days of support)	6.6 ± 3.2	8.3 ± 1.4	0.121
Inotropes			
Inotrope score <sup>a</sup>	4.0 ± 2.1	3.3 ± 0.8	0.431
N =	6	7	
Tolerated 30 min clamping	6 <sup>b</sup>	3	
Patients with IABP/Impella®	4	5	
NIRS (rSO <sub>2</sub> )	72.3 ± 4.3	70.4 ± 4.1	0.412
HR (b.p.m.)	93.3 ± 16.4	104.4 ± 18.5	0.257
MAP (mmHg)	66.4 ± 6.3	57.9 ± 8.9	0.06
CVP (mmHg)	9.3 ± 0.8	9.3 ± 3.9	0.980
PAP systolic (mmHg)	37.8 ± 8.1	30.3 ± 9.0	0.128
PAP diastolic (mmHg)	13.8 ± 2.6	10.7 ± 4.5	0.136
PAP mean (mmHg)	24.6 ± 5.4	19.5 ± 6.1	0.122
CI (L/min/m <sup>2</sup> )	4.0 ± 0.8	2.7 ± 0.6	0.005
EF (%)	52.9 ± 22.7	20.7 ± 7.1	0.004
LVEDD (cm)	3.8 ± 0.6	5.3 ± 0.9	0.004

CI, Fick cardiac index; CVP, central venous pressure; DR, durable recovery; EF, ejection fraction; HR, heart rate; IABP, intra-aortic balloon pump; LVEDD, left ventricular end-diastolic diameter; MAP, mean arterial pressure; NIRS, near-infrared spectroscopy; PAP, pulmonary artery pressure; rSO<sub>2</sub>, regional oxygen saturation; WP, Weaning Protocol.

<sup>a</sup>Inotrope score.<sup>9</sup>

<sup>b</sup>The seventh patient's WP limited to 2 LPM due to anticoagulation concerns.

ing patients with DR to those without. Of note, reliable PCWP measurements could only be acquired in three patients and were therefore not included in the analysis. In the DR group, haemodynamics were measured after 30 min of clamping in six of the seven patients (remaining patient at 2 L/min). In the non-DR group, only three of the patients tolerated clamping such that the haemodynamic measurements shown may underestimate the differences between the groups (lowest tolerated flow in the four who did not was 1.0–2.1 LPM). At lowest flow, patients who ultimately demonstrated DR had significantly higher cardiac index (4.0 ± 0.8 vs. 2.7 ± 0.6 L/min/m<sup>2</sup>, *P* = 0.005), ejection fraction (52.9 ± 22.7% vs. 20.7 ± 7.1%, *P* = 0.004), and smaller left ventricular size (3.8 ± 0.6 vs. 5.3 ± 0.9 cm, *P* = 0.004) and tended to have higher blood pressure. All seven patients with DR tolerated 30 min of full flow reduction during the WP. Three patients in the non-DR group tolerated full flow reduction and safely underwent decannulation. Only patients who met at least two of the following haemodynamic/echocardiographic criteria went on to achieve DR: left ventricular end-diastolic diameter (LVEDD) ≤ 4.5 cm, cardiac index ≥ 3 L/min/m<sup>2</sup>, and LVEF ≥ 35%.

## Discussion

In this cohort of patients supported with VA-ECMO for CS, 41% could undergo the WP and there were no adverse events during weaning. All patients that could tolerate 30 min of full flow reduction were able to be safely decannulated for recovery. However, patients that failed the WP died on ECMO or required transition to alternate MCS. Furthermore, the single patient that underwent ECMO decannulation without first undergoing the WP failed to have long-term recovery. In

our population of VA-ECMO patients prospectively studied for recovery, our pre-specified endpoint of DR was met by 24% of all patients and 70% of those who had a successful WP. Importantly, all patients who had successful WP and met DR were stable in long-term follow-up.

Currently, there is little consensus regarding how to best assess recovery in patients supported with VA-ECMO that might help guide decision making for decannulation for recovery or transition to alternate MCS. Prior reports have based decision making upon echocardiographic measures at various degrees of reduction of ECMO support.<sup>5,6,10</sup> No prior reports have described the use of invasive haemodynamics to aid in decision making. Previous protocols were performed bedside, but full flow reduction (ECMO clamping) was completed only in the operating room.<sup>10,11</sup> In our protocol, ECMO clamping was performed bedside with haemodynamic and echocardiographic measures taken after 30 min. We believe that this approach allows the multidisciplinary team to make elective decisions about transitions of care prior to taking the patient to the operating room. Prior reports have used varying definitions for recovery including the ability to decannulate,<sup>4,5,7,12</sup> haemodynamic stability for 12 and 48 h post-decannulation,<sup>11,13</sup> and no further requirement for MCS within 30 days.<sup>8,10</sup> Despite our more stringent definition of DR (no requirement for mechanical or pharmacological support at 30 days), more than two-thirds of patients with successful WP met this endpoint. Existing series suggest that up to 50% of patients decannulated for recovery do not survive to hospital discharge.<sup>14,15</sup> In contrast, 90% of patients who underwent the WP and were decannulated ultimately survived to discharge.

We explored demographic, clinical, and biomarker metrics at the time of ECMO initiation, on support, and during the WP that might identify patients likely to demonstrate DR.

Neither baseline characteristics nor clinical response to support at 72 h could identify patients who went on to DR. During the WP, the ability to tolerate 30 min of lowest flow (successful WP) always predicted successful decannulation. Although we do not yet have a large enough study cohort to reliably predict who will then go on to achieve DR, haemodynamic and echocardiographic data during the WP revealed significant differences in key measures (cardiac index, LVEF, and LVEDD) between the DR and non-DR groups. A larger sample size may yield reliable predictors of DR.

This study is limited by its small sample size, but we feel it is a useful addition to the literature, as there are little prospective data available in this population. Less than half of the study cohort was eligible for the WP, and it is possible that patients who did not undergo the WP might have demonstrated cardiac recovery. However, patients excluded from the WP would not have been suitable for decannulation due to critical illness. We cannot conclude from this study that 30 min of clamping is required to assess suitability for decannulation. To draw this conclusion, we would have had to show that patients stable after 30 min at other low flow states then became unstable at 30 min of clamping. We did

not re-evaluate patients who failed the WP, and we cannot discount the possibility that cardiac function may have improved over long periods of support. Lastly, we do not report measures of right ventricular (RV) function in this study, although tricuspid annular plane systolic excursion was not helpful in our experience. Future studies with alternate measures may clarify the role of RV function in DR.

In conclusion, we describe a safe, bedside, stepwise weaning protocol to assess cardiac recovery during VA-ECMO. Early identification of patients more likely to recover may improve outcomes during ECMO support.

## Conflict of interest

There are no conflicts of interest for the present work.

## Funding

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## References

1. Extracorporeal Life Support Organization. ECLS Registry Report, International Summary. 2018. <https://www.else.org/Registry/Statistics.aspx> Accessed January 29, 2019.
2. Smith M, Vukomanovic A, Brodie D, Thiagarajan R, Rycus P, Buscher H. Duration of veno-arterial extracorporeal life support (VA ECMO) and outcome: an analysis of the Extracorporeal Life Support Organization (ELSO) registry. *Crit Care* 2017; **21**: 45.
3. Aissaoui N, El-banayosy A, Combes A. How to wean a patient from veno-arterial extracorporeal membrane oxygenation. *Intensive Care Med* 2015; **41**: 902–905.
4. Rousse N, Juthier F, Pinçon C, Hysi I, Banfi C, Robin E, Fayad G, Jegou B, Prat A, Vincentelli A. ECMO as a bridge to decision: recovery, VAD, or heart transplantation? *Int J Cardiol* 2015; **187**: 620–627.
5. Cavarocchi NC, Pitcher HT, Yang Q, Karbowski P, Miessau J, Hastings HM, Hirose H. Weaning of extracorporeal membrane oxygenation using continuous hemodynamic transesophageal echocardiography. *J Thorac Cardiovasc Surg* 2013; **146**: 1474–1479.
6. Pappalardo F, Pieri M, Arnaez Corada B, Ajello S, Melisurgo G, de Bonis M, Zangrillo A. Timing and strategy for weaning from venoarterial ECMO are complex issues. *J Cardiothorac Vasc Anesth* 2015; **29**: 906–911.
7. Ling L, Chan KM. Weaning adult patients with cardiogenic shock on veno-arterial extracorporeal membrane oxygenation by pump-controlled retrograde trial off. *Perfusion* 2018; **33**: 339–345.
8. Luyt CE, Landivier A, Leprince P, Bernard M, Pavie A, Chastre J, Combes A. Usefulness of cardiac biomarkers to predict cardiac recovery in patients on extracorporeal membrane oxygenation support for refractory cardiogenic shock. *J Crit Care* 2012; **27**: 524.e7–524.e14.
9. Kobashigawa J, Zuckermann A, Macdonald P, Leprince P, Esmailian F, Luu M, Mancini D, Patel J, Razi R, Reichenspurner H, Russell S, Segovia J, Smedira N, Stehlik J, Wagner F, Consensus Conference participants. Report from a consensus conference on primary graft dysfunction after cardiac transplantation. *J Heart Lung Transplant* 2014; **33**: 327–340.
10. Aissaoui N, Luyt CE, Leprince P, Trouillet JL, Léger P, Pavie A, Diebold B, Chastre J, Combes A. Predictors of successful extracorporeal membrane oxygenation (ECMO) weaning after assistance for refractory cardiogenic shock. *Intensive Care Med* 2011; **37**: 1738–1745.
11. Huang KC, Lin LY, Chen YS, Lai CH, Hwang JJ, Lin LC. Three-dimensional echocardiography-derived right ventricular ejection fraction correlates with success of decannulation and prognosis in patients stabilized by venoarterial extracorporeal life support. *J Am Soc Echocardiogr* 2018; **31**: 169–179.
12. Affronti A, Di Bella I, Carino D, Ragni T. Levosimendan may improve weaning outcomes in venoarterial ECMO patients. *ASAIO J* 2013; **59**: 554–557.
13. Sugiura A, Abe R, Nakayama T, Fujimoto Y, Himi T, Sano K, Oda S, Kobayashi Y, Kobayashi Y. Predictors of successful weaning from veno-arterial extracorporeal membrane oxygenation after coronary revascularization for acute myocardial infarction complicated by cardiac arrest: a retrospective multicenter study. *Shock* 2018; **51**: 690–697.
14. Aso S, Matsui H, Fushimi K, Yasunaga H. In-hospital mortality and successful weaning from venoarterial extracorporeal membrane oxygenation: analysis of 5,263 patients using a national inpatient database in Japan. *Crit Care* 2016; **20**: 80.
15. Ortuno S, Delmas C, Diehl JL, Bailleul C, Lancelot A, Naili M, Chollet B, Piracchio R, Aissaoui N. Weaning from veno-arterial extra-corporeal membrane oxygenation: which strategy to use? *Ann Cardiothorac Surg* 2019; **8**: E1–E8.