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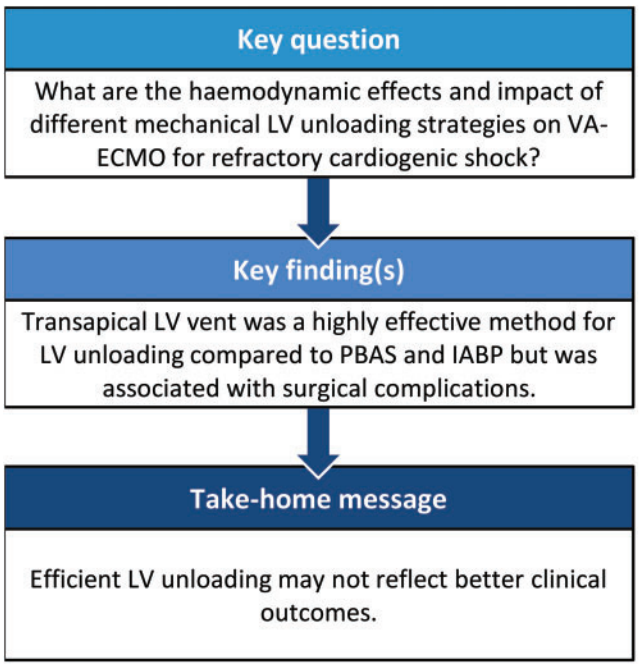
Comparison of left ventricular unloading strategies on venoarterial extracorporeal life support

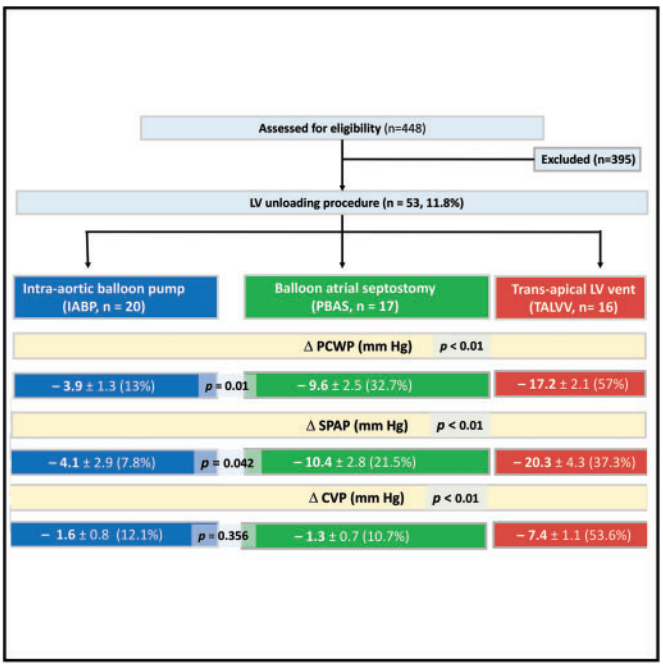
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Abstract

OBJECTIVES: Our goal was to compare the haemodynamic effects of different mechanical left ventricular (LV) unloading strategies and clinical outcomes in patients with refractory cardiogenic shock supported with venoarterial extracorporeal membrane oxygenation (VA-ECMO).

METHODS: A total of 448 patients supported with VA-ECMO for refractory cardiogenic shock between 1 March 2015 and 31 January 2020 were included and analysed in a single-centre, retrospective case–control study. Fifty-three patients (11.8%) on VA-ECMO required LV unloading. Percutaneous balloon atrial septostomy (PBAS), intra-aortic balloon pump (IABP) and transapical LV vent (TALVV) strategies were compared with regards to the composite rate of death, procedure-related complications and neurological complications. The secondary outcomes were reduced pulmonary capillary wedge pressure, pulmonary artery pressure, central venous pressure, left atrial diameter and resolution of pulmonary oedema on a chest X-ray within 48 h.

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RESULTS: No death related to the LV unloading procedure was detected. Reduction in pulmonary capillary wedge pressure was highest with the TALVV technique (17.2 ± 2.1 mmHg; $P < 0.001$) and was higher in the PBAS than in the IABP group; the difference was significant (9.6 ± 2.5 and 3.9 ± 1.3, respectively; $P = 0.001$). Reduction in central venous pressure with TALVV was highest with the other procedures (7.4 ± 1.1 mmHg; $P < 0.001$). However, procedure-related complications were significantly higher with TALVV compared to the PBAS and IABP groups (50% vs 17.6% and 10%, respectively; $P = 0.015$). We observed no significant differences in mortality or neurological complications between the groups.

CONCLUSIONS: Our results suggest that TALVV was the most effective method for LV unloading compared with PBAS and IABP for VA-ECMO support but was associated with complications. Efficient LV unloading may not improve survival.

Keywords: Venoarterial extracorporeal membrane oxygenation • Left ventricular unloading • Percutaneous balloon atrial septostomy • Transapical left ventricular vent

ABBREVIATIONS

IABP	Intra-aortic balloon pump
ICU	Intensive care unit
LA	Left atrial
LV	Left ventricle
PCWP	Pulmonary capillary wedge pressure
PBAS	Percutaneous balloon atrial septostomy
RCS	Refractory cardiogenic shock
TOE	Transoesophageal echocardiography
VA-ECMO	Venoarterial extracorporeal membrane oxygenation
TALVV	Transapical left ventricular vent

INTRODUCTION

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) provides immediate bedside cardiopulmonary and circulatory support for refractory cardiogenic shock (RCS) [1–3]. Because clinical indications are expanding, VA-ECMO provides a rescue option for bridging patients to decision and to long-term definitive therapies such as implantable circulatory support, a transplant or, rarely, recovery of native cardiac function [3–5]. However, VA-ECMO support is only temporary; it is limited to days or weeks with potentially adverse effects on the left heart [6, 7].

In patients with poor cardiac reserve, increased left ventricular (LV) afterload, wall stress and myocardial oxygen consumption may lead to LV distension and acute lung injury [6]. Residual flow through the pulmonary circuit, bronchial circulation to the left atrium, coronary circulation and Thebesian drainage may all contribute to LV overload [4]. Furthermore, circulatory stagnation within the left ventricle, left atrium or aortic root may result in intracardiac or aortic root thrombus formation. The incidence of LV distention requiring unloading in VA-ECMO-supported cases has been reported to be 20–30% [8, 9].

LV overload in patients with VA-ECMO support can be diagnosed with worsening pulmonary oedema, elevated pulmonary arterial diastolic pressure greater than 25 mmHg, echocardiographic evidence of LV distention, LV/left atrial (LA) thrombosis and refractory ventricular arrhythmias [8]. Although different techniques have been described for treating LV decompression in patients with VA-ECMO support [7], evidence for ideal solutions in guidelines is missing. The most commonly used method is the intra-aortic balloon pump (IABP), which restores pulsatility and decreases LV afterload during VA-ECMO [10, 11]. Other effective strategies for LV unloading include transapical LV venting (TALVV) [9, 12], transaortic LV venting [13, 14], left atrial decompression by minithoracotomy [15] and percutaneous or surgical pulmonary artery venting [16, 17]. Use of an axial flow catheter, namely the Abiomed Impella® (Abiomed, Danvers, MA, USA), and left atrial to femoral artery bypass, Tandem Heart™ (Tandem Life, Pittsburgh, PA, USA) devices are not available in our institution. Emerging transcatheter techniques are percutaneous transseptal cannula placement [18, 19] and left atrial decompression by percutaneous blade or balloon atrial septostomy (PBAS) [20–23].

In this single-centre study, our goal was to compare the efficiency of LV unloading and outcomes of different LV decompression strategies, namely PBAS, IABP and TALVV for left heart decompression in patients with RCS supported by VA-ECMO.

PATIENTS AND METHODS

Setting

The institutional ethics committee of the Ankara University School of Medicine approved this study (2020/I5-319-20). Before the procedures, patients were informed about procedural risks and therapeutic benefits. Written informed consent was obtained from all patients or their relatives. Our research was conducted according to the ethical principles of the World Medical Association Declaration of Helsinki.

Study population and protocol

A total of 448 adult patients supported with VA-ECMO for RCS between 01 March 2015 and 31 January 2020 were analysed in this single-centre retrospective case-control study. We identified 53 patients (11.8%) who had an LV unloading procedure during the VA-ECMO run. However, 395 patients did not require an LV unloading procedure during VA-ECMO support. The study flow diagram is demonstrated in Fig. 1. Patients who were treated with VA-ECMO for isolated right ventricular failure and temporary biventricular assist devices were excluded from the analysis.

Among the 53 patients who required the LV decompression procedure, 17 patients (32.1%) had the PBAS procedure, 20 patients (37.7%) had IABP support and 16 patients (30.2%) had the TALVV procedure.

The primary end-points were the composite rate of death, procedure-related complications and neurological outcomes with 3 different decompression strategies, namely PBAS, IABP and TALVV. The secondary end-points were delta change in pulmonary capillary wedge pressure (PCWP), systolic pulmonary artery pressure, central venous pressure, left atrial diameter and the

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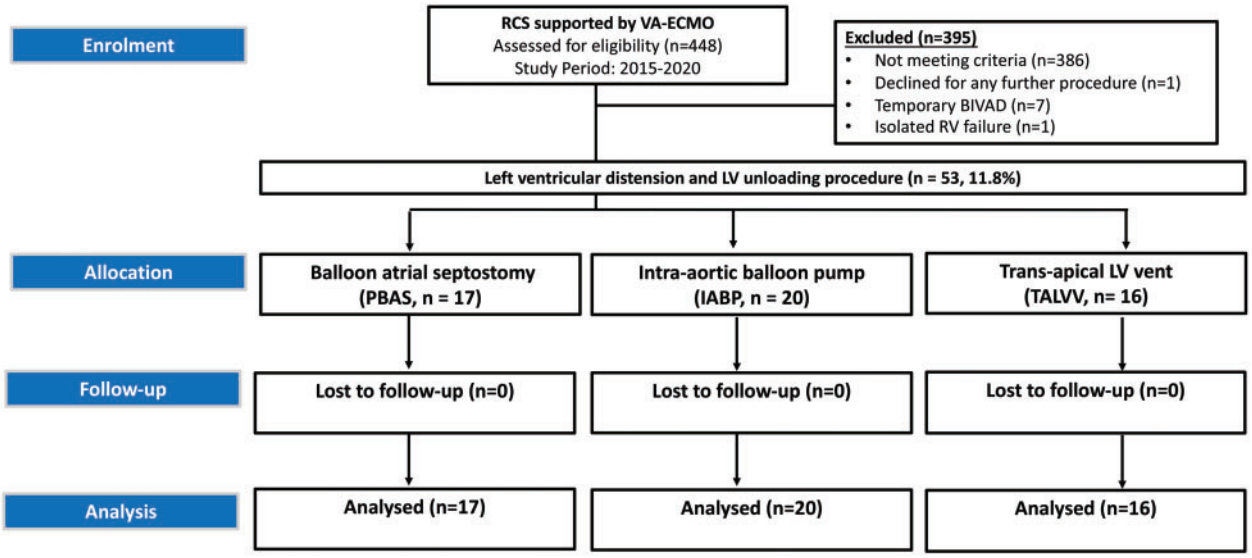


Figure 1: Overview of study flow diagram. BIVAD: biventricular assist device; LV: left ventricle; RCS: refractory cardiogenic shock; RV: right ventricle; VA-ECMO: venoarterial extracorporeal membrane oxygenation.

resolution of pulmonary oedema on a chest X-ray within 48 h. The resolution of pulmonary oedema on the chest X-ray was followed daily. We compared all the chest X-rays of patients who underwent 3 different LV unloading procedures at 48 h for standardization.

Venoarterial extracorporeal membrane oxygenation

The ECMO circuit used in this study was a continuous flow centrifugal pump (Jostra Rotaflow; Maquet Cardiopulmonary, Rastatt, Germany), an oxygenator (Jostra Quadrox; Maquet Cardiopulmonary) and a heat exchanger. We assessed biventricular filling and function, the interventricular septum position, the aortic valve opening, valvular regurgitation, intra-cardiac or aortic thrombus formation, pericardial effusion and cannula position by daily echocardiographic monitoring.

We used unfractionated heparin 50–100 units/kg bolus and heparin infusion 20–50 units/kg/h for anticoagulation. Activated clotting times were measured every 6 h with a target activated clotting time of 160–200 s (Medtronic ACT Plus^{TM}, Minneapolis, MN, USA). Activated partial thromboplastin time was measured twice daily with a goal of 50–60 s. The same protocol was applied for patients who had the LV unloading procedure. We also assessed antifactor Xa, platelet count, prothrombin time/international normalized ratio, fibrinogen and D-dimer when needed.

Timing and selection for left ventricular decompression methods

The multidisciplinary heart transplant team set the timing and type of the LV decompression procedure to initiate LV unloading as early as possible under Swan-Ganz catheterization, echocardiography and chest X-ray findings. LV unloading was considered in patients with evidence of pulmonary oedema on a chest radiogram, increased pulmonary artery diastolic blood pressure (>25 mmHg) or increased PCWP >20 mmHg on VA-ECMO support, inadequate response to increasing doses of inotropes and impaired aortic valve opening for every beat on echocardiography. Before the final decision, we made every effort to reduce LV loading, including reducing ECMO flow rates, increasing inotropic support and initiating vasodilators while maintaining sufficient mean arterial pressure. Our clinical criteria for choosing the type of LV venting were formed according to the clinical status of the patient to minimize the risk of potential complications. IABP was often the first line of LV unloading utilized for patients with post-infarction cardiogenic shock. However, IABP was avoided in patients with peripheral arterial disease. We often preferred PBAS or TALVV techniques in patients with decompensated chronic heart failure. In patients with LV thrombus and in redo cases, PBAS was the first line of the LV unloading method.

Percutaneous balloon atrial septostomy

The PBAS procedure was performed in the cardiac catheterization laboratory. After femoral vein access, the transseptal puncture was performed with a Brockenbrough needle under biplane fluoroscopy and transoesophageal echocardiography (TOE) guidance. Then, the balloon catheter was advanced into the right atrium and positioned in the left atrium. The balloon was quickly inflated with 3–4 ml of dilute radiopaque solution, locked and then sharply withdrawn into the right atrium down to the junction of the inferior caval vein. The catheter was then advanced into the right atrium body, so as not to obstruct inferior caval return, and then deflated rapidly. This manoeuver might be repeated 2–3 times. Finally, the catheter was removed, and left atrial decompression, the interatrial communication dimension and the absence of complications (pericardial haemorrhage, cardiac injury) were verified via TOE. The efficiency of the septostomy was evaluated with post-procedural measurement of PCWP, pulmonary artery diastolic pressure, a postero-anterior chest X-ray and evaluation of the LV dimensions and aortic valve opening on echocardiography.

Intra-aortic balloon pump support

IABP (Maquet Cardiopulmonary) implantation was performed in our hybrid operating room or at the bedside in the intensive

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care unit (ICU). With the patient under the local anaesthesia, the balloon catheter was placed using the Seldinger technique via a femoral artery. The location of the IABP with its tip lying distal to the left subclavian artery and the proximal portion ending above the origin of renal arteries is considered the 'safe zone'; the position was confirmed by fluoroscopy.

Transapical left ventricular venting

The TALVV procedure was performed in the operating room via a left anterolateral minithoracotomy. In patients with post-cardiotomy RCS, a pre-existing sternotomy was reopened. The cardiac apex on the chest surface was marked using TOE. A mini-thoracotomy was usually performed at the 5th or 6th intercostal space. After the pericardium was opened, the apex of the left ventricle was exposed using pericardial slings. We placed 2 purse-string sutures of 3–0 polypropylene, oriented at 90°, at the LV apex cannulation site for haemostasis. Using the Seldinger technique, a high-flow 19- to 21-Fr arterial cannula was placed over the wire into the left ventricle. After confirmation with TOE, the cannula was fixed with pledgeted purse-string sutures and connected via a Y connector to the venous access line of the ECMO circuit. Decompression of the left ventricle and optimal flow regulation were arranged by tightening or loosening the venous occluder device on the TALVV arm, which was placed proximally to the flow sensor. The average flow over the venting cannula was approximately 600–1800 ml. The aortic valve opening was monitored daily by transthoracic echocardiography.

Haemodynamic evaluation

For standardization of the baseline haemodynamic evaluation using a Swan-Ganz catheter, we set the ECMO flows where the aortic valve opening could be detected on the arterial pulse pressure tracing or M-mode echocardiography. Haemodynamic parameters were reassessed 24 h after the decompression procedure. Our ECMO weaning protocol was described in detail previously [24].

Statistical analyses

Statistical analyses were performed using SPSS version 25.0 (IBM SPSS Statistics, Chicago, IL, USA). Continuous variables are expressed as mean with standard deviation unless otherwise specified, and categorical variables are expressed as numbers and percentages. The distribution of continuously measured variables was tested with the Shapiro–Wilk test. We first compared data from baseline characteristics (Table 1) using the traditional

Table 1: Venoarterial extracorporeal membrane oxygenation patient characteristics, other clinical variables and laboratory findings, per left ventricular unloading group

Baseline characteristics	VA-ECMO + IABP (*n* = 20)	VA-ECMO + PBAS (*n* = 17)	VA-ECMO + TALVV (*n* = 16)	*P*-value
Age (years), mean ± SD	57.3 ± 8.5	54.9 ± 16.0	56.1 ± 8.0	0.751
Male gender, *n* (%)	12 (60)	10 (58.8)	10 (62.5)	0.976
Body surface area (kg/m^2), mean ± SD	1.85 ± 0.1	1.86 ± 0.1	1.86 ± 0.1	0.909
Body mass index (kg/m^2), mean ± SD	25.1 ± 2.3	25.3 ± 2.9	25.6 ± 2.4	0.862
Hypertension, *n* (%)	9 (45)	8 (47)	8 (50)	0.956
Diabetes, *n* (%)	6 (30)	5 (29.4)	5 (31.2)	0.993
Hyperlipidaemia, *n* (%)	8 (40)	7 (41.1)	6 (37.5)	0.976
History of peripheral vascular disease, *n* (%)	2 (10)	2 (11.7)	2 (12.5)	0.970
History of cardiac arrest, *n* (%)	1 (5)	1 (5.8)	1 (6.2)	0.986
Previous hospital admission for heart failure, *n* (%)	5 (25)	4 (25.1)	4 (25)	0.993
Previous implantable defibrillator, *n* (%)	4 (20)	3 (17.6)	3 (18.7)	0.983
Cardiac resynchronization therapy, *n* (%)	4 (20)	4 (25.1)	4 (25)	0.933
Previous stroke, *n* (%)	1 (5)	1 (5.8)	1 (6.2)	0.986
Current tobacco use, *n* (%)	7 (35)	6 (35.2)	5 (31.2)	0.963
COPD, *n* (%)	5 (25)	4 (25.1)	4 (25)	0.993
Hgb (g/dl), mean ± SD	11.1 ± 0.8	10.9 ± 0.7	11 ± 0.7	0.754
Platelet count ($\times 10^9$/l), mean ± SD	111.7 ± 15.9	109.5 ± 13.3	105.1 ± 14.6	0.413
Serum creatinine level (mg/dl), mean ± SD	1.7 ± 1.2	1.7 ± 1.3	1.7 ± 1.4	0.790
Renal failure, *n* (%)	2 (10)	2 (11.7)	2 (12.5)	0.970
LVEF (%), median (IQR)	20 (20–25)	20 (20–25)	20 (20–30)	0.836
Previous IABP support, *n* (%)	5 (25)	4 (23.5)	4 (25)	0.993
Multiorgan failure, *n* (%)	6 (30)	5 (29.4)	4 (25)	0.940
pH at VA-ECMO before LV unloading, U, mean ± SD	7.38 ± 0.11	7.37 ± 0.09	7.36 ± 0.10	0.557
Lactate at VA-ECMO before LV unloading, mg/dl, mean ± SD	6.1 ± 2.6	5.9 ± 2.5	6.3 ± 2.56	0.905
Mean arterial pressure at VA-ECMO (mmHg), mean ± SD	57.9 ± 8.2	57.3 ± 8.1	57.1 ± 8.7	0.956
Arterial access for VA-ECMO				0.868
Femoral artery, *n* (%)	16 (80)	14 (82.4)	12 (75)	
Axillary artery, *n* (%)	4 (20)	3 (17.6)	4 (25)	
Venous access for VA-ECMO				
Femoral vein, *n* (%)	20 (100)	17 (100)	16 (100)	

Data are presented as *n* (%) or mean ± SD and median with interquartile range.

COPD: chronic obstructive pulmonary disease; Hgb: haemoglobin; IABP: intra-aortic balloon pump; IQR: interquartile range; LV: left ventricular; LVEF: left ventricular ejection fraction; PBAS: percutaneous balloon atrial septostomy; SD: standard deviation; TALVV: transapical left ventricular vent; VA-ECMO: venoarterial extracorporeal membrane oxygenation.

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Table 2: Indications for venoarterial extracorporeal membrane oxygenation support for patients with refractory cardiogenic shock, per left ventricular unloading group

Indication	Only VA-ECMO ($n = 448$)	VA-ECMO + IABP ($n = 20$)	VA-ECMO + PBAS ($n = 17$)	VA-ECMO + TALVV ($n = 16$)	*P*-value
Acute myocardial infarction, *n* (%)	63 (14.1)	3 (15)	2 (11.7)	2 (12.5)	0.954
Decompensated chronic heart failure*, *n* (%)	148 (33.1)	7 (35)	6 (35.2)	6 (37.5)	0.986
Post-cardiotomy heart failure, *n* (%)	126 (28.1)	5 (25)	5 (29.4)	4 (25)	0.944
Tx-PGF, *n* (%)	6 (1.3)	1 (5)	0 (0)	0 (0)	0.431
Fulminant myocarditis, *n* (%)	9 (2.0)	1 (5)	1 (5.8)	1 (6.2)	0.986
Post LVAD right heart failure, *n* (%)	9 (2.0)	1 (5)	1 (5.8)	(0)	0.632
Sepsis-associated cardiomyopathy, *n* (%)	28 (6.2)	1 (5)	1 (5.8)	1 (6.2)	0.986
Pulmonary hypertension with right heart failure, *n* (%)	15 (3.3)	0 (0)	0 (0)	0 (0)	
Pulmonary embolism, *n* (%)	26 (5.8)	0 (0)	0 (0)	0 (0)	
Intractable arrhythmias, *n* (%)	6 (1.3)	1 (5)	1 (5.8)	2 (12.5)	0.665
ECPR, *n* (%)	12 (2.7)	0 (0)	0 (0)	0 (0)	

Data are presented as *n* (%) or mean ± SD.

ECPR: extracorporeal cardiopulmonary resuscitation; IABP: intra-aortic balloon pump; LVAD: left ventricular assist device; PBAS: percutaneous balloon atrial septostomy; SD: standard deviation; TALVV: transapical left ventricular vent; Tx-PGF: post-transplant primary graft failure; VA-ECMO: venoarterial extracorporeal membrane oxygenation.

Table 3: Haemodynamics during venoarterial extracorporeal membrane oxygenation support for refractory cardiogenic shock and after 3 different left decompression methods per left ventricular unloading group

Variables		VA-ECMO + IABP ($n = 20$)	VA-ECMO + PBAS ($n = 17$)	VA-ECMO + TALVV ($n = 16$)	*P*-value
VA-ECMO run (days), median (IQR)		16 (14–20)	16 (11–23.5)	16 (14–22.5)	0.962
Mean duration from VA-ECMO to LV unloading (h), mean ± SD		13.9 ± 3.6	46.1 ± 3.6	52.1 ± 4.9	<0.001
VA-ECMO output expressed as CI (l/min/m^2)		2.1 ± 0.2	2.2 ± 0.3	2.1 ± 0.3	0.485
Measurements					
Preintervention	PCWP (mmHg)	29.1 ± 2.5	29.3 ± 2.5	30.2 ± 2.8	0.431
	SPAP (mmHg)	52.3 ± 9.1	48.4 ± 9.4	54.4 ± 6.8	0.137
	LA diameter (mm)	56.6 ± 4.5	56.0 ± 7.2	56.9 ± 4.3	0.879
	CVP (mmHg)	13.2 ± 2.3	12.1 ± 2.1	13.8 ± 2.5	0.116
(Δ) change	PCWP (mmHg)	-3.9 ± 1.3	-9.6 ± 2.5[b]	-17.2 ± 2.1[a]	<0.001
	SPAP (mmHg)	-4.1 ± 2.9	-10.4 ± 2.8[b]	-20.3 ± 4.3[a]	<0.001
	LA diameter (mm)	-2.9 ± 1.1	-5.1 ± 1.1[b]	-14.8 ± 3.2[a]	<0.001
	CVP (mmHg)	-1.6 ± 0.8	-1.3 ± 0.7[b]	-7.4 ± 1.1[a]	<0.001

Data are presented as I (%) or mean ± SD and median with interquartile range.

[a]Reduction in PCWP, SPAP, LA diameter and CVP was significantly higher in the TALVV group compared to the PBAS and IABP groups.

[b]The PBAS technique was more effective than the IABP strategies in terms of reduction in PCWP ($P = 0.001$), SPAP ($P = 0.042$) and LA diameter ($P = 0.003$). There was no significant difference between PBAS and IABP in reducing CVP ($P = 0.356$).

Δ: change; CI: cardiac index; CVP: central venous pressure; IABP: intra-aortic balloon pump; IQR: interquartile range; LA: left atrial; LV: left ventricular; PBAS: percutaneous balloon atrial septostomy; PCWP: pulmonary capillary wedge pressure; SD: standard deviation; SPAP: systolic pulmonary artery pressure; TALVV: transapical left ventricular vent.

χ^2analysis. A comparison of means was performed using a one-way analysis of variance with *post hoc* Tukey honest significance difference or the Games–Howell multiple comparison test to adjust for pairwise mean comparisons between PBAS and IABP and LV vent groups. Dichotomous outcome comparisons between groups were conducted using Pearson's χ^2or Fisher's exact test when appropriate. Statistical significance was considered to be at the $P < 0.05$ level.

RESULTS

In this single-centre cohort of patients with RCS on VA-ECMO ($n = 448$) support, we identified 53 patients (11.8%) who had developed left ventricular distension and required an LV unloading procedure. Overall, the mean age of patients with VA-ECMO support was 55.8 ± 12.4; 276 (61.6%) were men. The mean pre-VA-ECMO left ventricular ejection fraction was 25.1 ± 4.8%. The median ECMO duration was 16 (interquartile range, 9–21) days. There were no significant differences in baseline characteristics between patients who underwent 3 different LV decompression strategies (Table 1). There was no conversion between the LV decompression methods and no unloading procedure-related deaths in this study cohort.

Decompensated chronic heart failure ($n = 148$, 33.1%) was the leading cause of RCS. As reported in Table 2, there were no significant differences between the 3 LV decompression groups in terms of RCS aetiology.

However, after LV unloading procedures, we noted a clinical and statistically significant difference between the PBAS, IABP and TALVV groups (Table 3). Reduction in PCWP was highest with the TALVV technique (17.2 ± 2.1 mmHg; $P < 0.001$) and was

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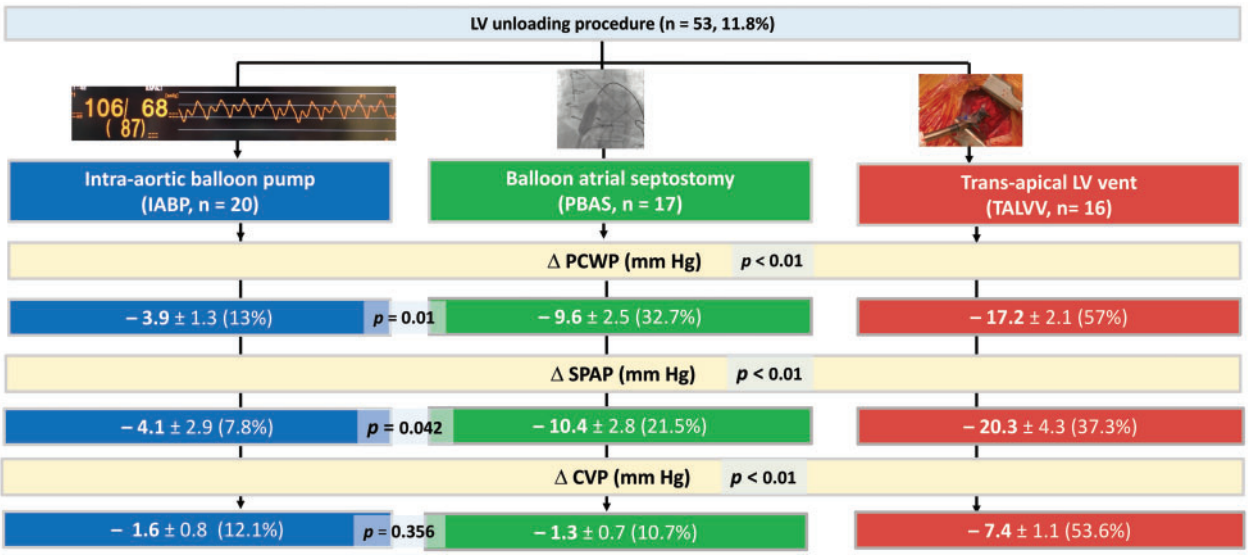


Figure 2: Haemodynamic changes after 3 different left ventricular unloading strategies. CVP: central venous pressure; LV: left ventricle; PCWP: pulmonary capillary wedge pressure; SPAP: systolic pulmonary artery pressure.

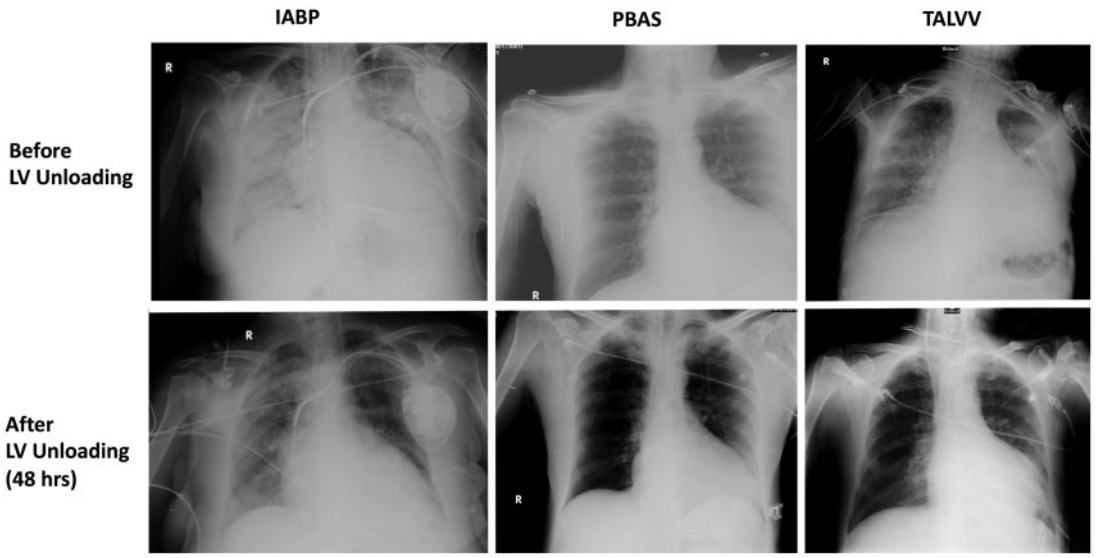


Figure 3: Chest X-ray illustrations of the resolution of pulmonary oedema before and 48 h after LV unloading procedures. IABP: intra-aortic balloon pump; LV: left ventricle; PBAS: percutaneous balloon atrial septostomy; TALVV: transapical left ventricular vent.

higher in the PBAS than in the IABP group; this difference was significant (9.6 ± 2.5 and 3.9 ± 1.3, respectively; $P = 0.001$) (Fig. 2). The TALVV technique was more effective than the PBAS and IABP strategies (20.3 ± 4.3 mmHg; $P < 0.001$) in reducing pulmonary arterial pressure. Similarly, reduction in the LA diameter and central venous pressure was highest with the TALVV technique (14.8 ± 3.2 mm and 7.4 ± 1.1 mmHg, respectively; $P < 0.001$).

A chest X-ray evaluation 48 h after the LV unloading procedure revealed significant resolution of pulmonary oedema with all techniques (Fig. 3). However, TALVV was the most effective method for LV unloading compared to PBAS and IABP. The TALVV group was also associated with significant complications, including bleeding at the access site ($n = 3$, 18.8%), thrombosis of the cannula ($n = 1$, 6.3%), ventricular arrhythmias ($n = 2$, 12.5%) and malposition of the cannula ($n = 2$, 12.5%) (Table 4). There was no significant difference among the groups regarding neurological complications. In addition, patient care and mobilization in the ICU were challenging in the TALVV group. Overall, there were no significant differences in the duration of VA-ECMO support, ICU stay and hospital stay among the groups. Nine (52.9%) patients in the PBAS group were weaned from VA-ECMO support, whereas 7 (43.7%) patients in the TALVV group and 11 (55%) patients in the IABP group ($P = 0.783$) were weaned.

DISCUSSION

This case–control study shows that in patients with VA-ECMO for RCS, about 12% of the patients develop LV distension and pulmonary oedema. However, no randomized controlled clinical trials have reported the optimal management strategy for LV unloading in patients on VA-ECMO support. Furthermore, a recent systematic review and meta-analysis on LV unloading with VA-ECMO by Kowalewski *et al.* [25] pointed out certain

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Table 4: Clinical outcomes, per left ventricular unloading group

Outcomes	VA-ECMO + IABP ($n = 20$)	VA-ECMO + PBAS ($n = 17$)	VA-ECMO + TALVV ($n = 16$)	*P*-value
Successful weaning from VA-ECMO, *n* (%)	11 (55)	9 (52.9)	7 (43.7)	0.783
Post-ECMO mechanical ventilation (days), mean ± SD	2.0 ± 0.4	1.9 ± 0.3	2.1 ± 0.3	0.381
Days in ICU, mean ± SD	16.2 ± 3.9	15.8 ± 4.3	17.4 ± 5.9	0.428
Days in hospital, mean ± SD	28.7 ± 4.6	28.2 ± 5.2	30.5 ± 4.4	0.360
Bridged to LVAD or heart transplantation	8 (40)	6 (35.3)	4 (25)	0.633
Complications related to LV unloading procedure, *n* (%)	2 (10)	3 (17.6)	8 (50)	
Access site bleeding, *n* (%)	0	1 (5.9)	3 (18.8)	
Thrombosis of cannulae/balloon, *n* (%)	0	0	1 (6.3)	
Cannulae/balloon malposition, *n* (%)	1 (5)	0	2 (12.5)	
Ventricular arrhythmias, *n* (%)	0	1 (5.9)	2 (12.5)	
Vascular complications, *n* (%)	1 (5)	0	0	
Aortic dissection, *n* (%)	0	0	0	
Pericardial tamponade, *n* (%)	0	1	0	
Neurological complications	0	1	2	
Intracranial haemorrhage, *n* (%)	0	0	1 (6.3)	
Acute ischaemic stroke, *n* (%)	0	1 (5.9)	1 (6.3)	
Seizure, *n* (%)	0	0	0	
Survival				
ICU deaths, *n* (%)	8 (40)	7 (41.2)	7 (43.8)	0.974
In-hospital deaths, *n* (%)	9 (45)	8 (47.1)	9 (56.3)	0.783
Cause of death				
Sepsis, *n* (%)	1 (5)	1 (5.9)	1 (6.3)	0.985
Multiorgan failure, *n* (%)	7 (35)	6 (35.3)	6 (37.5)	0.986
Cerebrovascular event, *n* (%)	1 (5)	1 (5.9)	2 (12.5)	0.664

Data are presented as *n* (%) or mean ± SD and median with interquartile range.

IABP: intra-aortic balloon pump; ICU: intensive care unit; LV: left ventricular; LVAD: left ventricular assist device; PBAS: percutaneous balloon atrial septostomy; SD: standard deviation; TALVV: transapical left ventricular vent; VA-ECMO: venoarterial extracorporeal membrane oxygenation.

methodological flaws in previously published data. VA-ECMO induces reverse aortic flow and leads to an increase in LV afterload. Myocardial oxygen demand and supply mismatch may worsen after VA-ECMO support. These phenomena can be associated with pulmonary oedema, poor outcomes and high mortality.

Initial management strategies for LV distension and pulmonary oedema in patients on VA-ECMO include reducing ECMO flow and medical therapies, including inotropic support, diuresis or ultrafiltration and fluid restriction. However, unless the left heart is vented or unloaded, these deleterious effects of VA-ECMO may compromise myocardial recovery and may prolong lung injury [4]. Effective left heart decompression can minimize ventricular distension, decrease end-diastolic pressures, increase subendocardial perfusion, resolve pulmonary oedema and allow myocardial recovery. The advantages of LV/LA decompression theoretically depend on 2 mechanisms. First, the reduction of LA pressure promotes early lung recovery. Second, ameliorated LV wall stress improves subendocardial perfusion, decreases myocardial oxygen consumption and, as a result, provides LV functional recovery [19]. So far, there is no consensus concerning the type and timing of left heart unloading on VA-ECMO. However, studies generally conclude that earlier LA decompression may result from a rapid weaning process and reduced complication risks related to prolonged VA-ECMO support. LV decompression can be successfully provided via various percutaneous methods, such as placement of IABP [10], transaortic LV venting [13, 14], percutaneous transseptal cannula placement [18, 19] and LA decompression by PBAS [20–23].

IABP typically increases coronary perfusion by increasing aortic diastolic pressures and reduces the LV afterload [4, 10]. Volume shifting of approximately 40 ml per beat by the IABP increases LV stroke volume and cardiac output by up to 1 l/min [7]. However, it reduces systolic blood pressure and provides an unreliable degree of LV unloading associated with slightly reduced LV preload [4]. As noted in our study, IABP causes a mild reduction in PCWP by an average of ≈3 to 4 mmHg [10].

PBAS is also a straightforward, feasible method for LV unloading compared to surgical LV decompression strategies. Published data describing the use of PBAS for left heart unloading are still limited. In our study, PBAS was the preferred method in high-risk patients due to its ease of application and the low risk of complications. Some case series have demonstrated its influence on LA decompression and LV functional recovery or survival. Aiyagari *et al.* [19] reported the results of 7 patients with reasonable LV decompression at a median time of 11 h after VA-ECMO implantation. In this study, 57% of patients were decannulated and survived. Kotani *et al.* [26] described a cohort, including 23 paediatric patients with VA-ECMO, who required LV decompression; 70% of these patients were successfully weaned from ECMO support. They showed that the early timing of the LV decompression method facilitates the VA-ECMO weaning process. On the contrary, Hacking *et al.* [12] were not able to prove the beneficial effects on survival of elective LV decompression at the initiation of VA-ECMO.

Surgical strategies for LV unloading include TALVV through a left anterior minithoracotomy [12], left atrial decompression by minithoracotomy [15] and surgical pulmonary artery venting [16, 17]. TALVV was the most efficient LV unloading method in our study compared to IABP and PBAS. However, as detected in this study, surgical techniques for LV unloading may have life-threatening complications, including bleeding, haemolysis and

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increased risk of infection. We also noted cannula malposition, thrombosis and ventricular arrhythmias. Some technical considerations may minimize the early complications of TALVV. In our experience, both transthoracic and TOE guidance, use of the Seldinger technique, identification of an LV apical 'dimple' for future potential left ventricular assist device implantation and appropriately positioned purse-string sutures are critical for a safe TALVV technique.

Limitations

This study has some limitations. First, defining the necessity of LV unloading is not standardized globally. Second, our study has a small sample size, and the research is a retrospective, case-control study. Selection bias is unavoidable if the selection of different treatment modalities is decided by the heart transplant team and may impact the clinical outcomes. However, our study was not designed to investigate the superiority of any decompression procedure. Rather, the goal was to evaluate the haemodynamic effects of different decompression strategies in a VA-ECMO setting and share procedure-related complications. Furthermore, the TandemHeart™ and Impella are other effective percutaneous options for decompression of the left chambers, but these options are unavailable in our country. We propose adopting a universal definition for the indications for LV unloading in patients with VA-ECMO, and then we may compare unloading strategies in a randomized controlled trial.

CONCLUSIONS

In this patient cohort, 12% of patients with VA-ECMO for RCS required an LV decompression procedure. In terms of the haemodynamic effects of LV unloading, TALVV was the most effective method when compared to PBAS and IABP. However, TALVV was associated with significant surgical complications. Future technical advances may minimize procedure-related complications. Currently, efficient transapical LV unloading did not result in better clinical outcomes. These results need to be confirmed in a large prospective randomized trial.

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Authors contributions

Ali İhsan Hasde: Conceptualization; Data curation; Methodology; Formal analysis; Investigation; Writing—original draft. **Mehmet Cahit Sarıcaoğlu:** Investigation; Methodology; Validation; Formal analysis. **Nur Dikmen Yaman:** Data curation; Methodology; Formal analysis; Writing—original draft. **Çağdaş Baran:** Conceptualization; Validation; **Evren Özçınar:** Validation; Resources; Supervision. **Mehmet Çakıcı:** Project administration; Validation; Visualization; Writing—original draft. **Mustafa Bahadır İnan:** Conceptualization; Methodology; Project administration; Formal analysis. **Ahmet Ruchan Akar:** Conceptualization; Project administration; Resources; Supervision; Validation; Writing—review & editing.

Reviewer information

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