Incidence and Implications of Left Ventricular Distention During Venoarterial Extracorporeal Membrane Oxygenation Support

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Left ventricular distention (LVD) during venoarterial extracorporeal membrane oxygenation (VA-ECMO) support is increasingly recognized but seldom reported in the literature. The current study defined LVD as not present (LVD–); subclinical (LVD+, evidence of pulmonary edema on chest radiograph AND pulmonary artery diastolic blood pressure greater than 25 mm Hg within the first 2 hours of intensive care unit admission); or clinical (LVD++, need for decompression of the left ventricle immediately following VA-ECMO initiation). Among 226 VA-ECMO device runs, 121 had sufficient data to define LVD retrospectively. Nine patients (7%) developed LVD++ requiring immediate decompression, and 27 patients (22%) met the definition of LVD+. Survival to discharge was similar among groups (LVD++: 44%, LVD+: 41%, LVD–: 44%). However, myocardial recovery appeared inversely related to the degree of LVD (LVD++: 11%, LVD+: 26%, LVD–: 40%). When death or transition to device was considered as a composite outcome, event-free survival was diminished in LVD++ and LVD+ patients compared with LVD–. Multivariable analysis identified cannulation of VA-ECMO during extracorporeal cardiopulmonary resuscitation (ECPR) as a risk factor for decompression (odds ratio [OR]: 3.64, confidence interval [CI]: 1.21–10.98; $p = 0.022$). Using a novel definition of LVD, the severity LVD was inversely related to the likelihood of myocardial recovery. Survival did not differ between groups. Extracorporeal cardiopulmonary resuscitation was associated with need for mechanical intervention. *ASAIO Journal* 2017; 63:257–265.

Key Words: mechanical circulatory support, ECMO, cardiogenic shock

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Submitted for consideration October 2016; accepted for publication in revised form February 2017.

Disclosures: Y.N. receives a consulting fee from Thoratec; A.R.G. receives honoraria from Abiomed.

Funded by Institutional resources.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML and PDF versions of this article on the journal's Web site (www.asaiojournal.com).

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DOI: 10.1097/MAT.0000000000000553

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is becoming an increasingly accepted means of providing cardiopulmonary support to the acutely failing heart.[1–5] In fact, use of percutaneous mechanical circulatory support devices, including VA-ECMO, has increased 1511% from 2007 to 2011.[6] As its use increases, incidence of the common complications of support, including significant bleeding, stroke, infection, acute kidney injury, and limb ischemia have become more widely characterized.[7] An additional, but nonetheless important, complication of VA-ECMO support that is increasingly recognized but continues to be underreported in the literature is left ventricular distention (LVD).[7] The already impaired left ventricle (LV) may be unable to eject blood against the afterload created by VA-ECMO blood flow, resulting in inadequate opening of the aortic valve. This may lead to significant stagnation of the blood within the LV, increasing the risk for LV thrombus formation.[8] Dilatation of the LV increases wall stress and myocardial oxygen demand, hindering the ability of the LV to recovery.[9,10] Increases in LV end-diastolic pressure can also contribute to pulmonary edema and potentiate ventricular arrhythmias. Despite various strategies of managing clinically significant LVD, there exists no universal definition to aid in its identification.[11–13] In addition, its clinical impact is poorly understood. We hypothesized that LVD is under recognized, and would negatively impact both survival and myocardial recovery. We propose a novel definition of LVD utilizing radiologic and hemodynamic parameters to retrospectively analyze its incidence and impact on outcomes of patients receiving VA-ECMO support for refractory cardiogenic shock (RCS).

Methods

This study was approved by our institutional review board. Informed consent was obtained when possible, for those unable to consent a waiver of consent was granted owing to the retrospective nature of the study.

Left Ventricular Distention Definition

The current study classifies patients into three primary clinical groups within the first 2 hours of VA-ECMO support: no LVD (LVD–), subclinical LVD (LVD+), and clinical LVD (LVD++). Subclinical LVD was defined as evidence of pulmonary edema on chest radiograph AND pulmonary artery diastolic blood pressure (PADBP) greater than 25 mm Hg within the first 2 hours of VA-ECMO support after intensive care unit (ICU) admission. Pulmonary artery diastolic blood pressure was used as a surrogate for left ventricular end diastolic

pressure (LVEDP). Clinical LVD was defined as the need for mechanical intervention to decompress the LV immediately after VA-ECMO initiation because of pulmonary edema, ventricular arrhythmia, or significant stagnation of blood within the LV. Those patients who were not immediately decompressed and who did not meet the definition for LVD+ were considered LVD−.

Patient Population

A total of 226 VA-ECMO device runs were executed during the study period from March 2007 to November 2014. Among these, 16 patients were excluded for having a percutaneous micro axial flow pump in place before VA-ECMO placement, which remained in place during VA-ECMO support. Among the remaining patients, 121 had sufficient hemodynamic, radiographic, and LVD interventional data to be included in the study population. To compare preoperative demographic, hemodynamic, and laboratory data, patients were classified by the above LVD definitions. Patients who required delayed decompression were included in the LVD+ and LVD− groups depending on whether they initially met the definition for subclinical or no LVD. For sensitivity analysis and to identify predictors of need for mechanical decompression, all patients who underwent decompression (LVD++ and those requiring delayed decompression) were compared with LVD+ and LVD− patients who did not require decompression.

Variables and Outcomes of Interest

Patient demographics and preoperative laboratory values were collected for all patients. Hemodynamic parameters were recorded from immediately before VA-ECMO cannulation, for the first 6 hours after ICU admission, and at 24 hours of support. Operative data including location of cannulation and details of cannula size and placement were included. The primary outcome was survival to discharge. Secondary outcomes included myocardial recovery, defined as decannulation from VA-ECMO and survival to discharge or to 30 days, and survival free of device exchange as bridge-to-decision or implantation of a durable ventricular assist device. Risk factors for need for decompression and mortality within 30 days were also analyzed.

Patient Management

Our algorithm for the initial evaluation of patients with RCS has been reported elsewhere.[14] Venoarterial extracorporeal membrane oxygenation is placed at the bedside, in the catheterization laboratory, or in the operating room. Our preferred approach is peripheral cannulation *via* the femoral artery and vein with 15 Fr and 23 Fr cannulas, respectively.[15] A distal perfusion cannula is inserted at the time of cannulation only if there is weak or absent Doppler signal in the ipsilateral lower extremity. Axillary arterial cannulation or central cannulation into the aorta and pulmonary artery are used in select cases. Whenever feasible, we use "partial flow" VA-ECMO support (extracorporeal blood flow of 3–4 L/min) in conjunction with aggressive inotropic support in an effort to preserve native myocardial contractility and ejection of the LV while maintaining total circulating systemic blood flow and end organ perfusion.[15] Aggressive diuresis is utilized in combination with continuous veno-venous hemodialysis (CVVHD) to manage patients' total circulating blood volume. Aortic valve opening as evidenced by pulsatility on a peripheral arterial line and by bedside echocardiography is maintained by titrating extracorporeal blood flow, vasopressors, and inotropes to mitigate complications associated with LVD. If clinically significant LVD is noted following cannulation (increasing PADBP, worsening oxygenation, fulminant pulmonary edema, refractory ventricular arrhythmia with enlarging left ventricular end diastolic diameter, or significant stagnation of blood within the LV), our institution favors percutaneous femoral placement of an Impella 2.5 or CP left ventricular assist device (LVAD; Abiomed, Danvers, MA) to aid in unloading the LV. Should LVD continue, the patient is evaluated for device exchange to a bridge-to-decision device with a ST-VAD.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation. Those variables that are non-normally distributed are recorded as median (interquartile range, IQR). Categorical data are presented as counts and percentages. One-way analysis of variance (ANOVA) and χ^2 tests were used to compare continuous and categorical variables, respectively, across groups. Kruskal–Wallis analysis was utilized in those variables that were non-normally distributed. To identify predictors of need for early or late decompression, univariable and multivariable logistic regression analysis was performed utilizing relevant clinical baseline variables. Significance was defined as $p < 0.05$. StataSE version 13 (StataCorp, LP College Station, TX) was utilized for analysis.

Results

A total of 121 device runs were included in the current study (**Figure 1**). Nine patients (7.4%) developed clinically significant LV distention requiring immediate decompression (LVD++), 27 patients (22.3%) met the definition for LVD+ based on initial chest radiograph and PADBP following VA-ECMO cannulation, and 85 patients neither required immediate intervention nor met the definition above (LVD−). Sensitivity analysis was performed to identify relevant clinical differences between those patients included in the current study and those excluded because of lack of hemodynamic data. Overall patient population and types of intervention required are summarized in **Figure 1**.

Baseline demographics and etiology of RCS are summarized in **Table 1**. There was no significant difference in age, gender, body mass index (BMI), or comorbid conditions across groups, except for a higher incidence of chronic obstructive pulmonary disease in the LVD+ group. Approximately, one-third of LVD++ patients experienced RCS after acute myocardial infarction (AMI), with subclinical LVD+ being present in more than 50% (n = 15, 55.6%) of postcardiotomy shock (PCS) patients. All patients who presented with RCS in the setting of acute decompensated heart failure (ADHF) and required mechanical decompression underwent delayed decompression.

Table 2 summarizes preoperative hemodynamic and laboratory data. Overall, 40% of patients were already being supported with an intraaortic balloon pump (IABP). Of particular

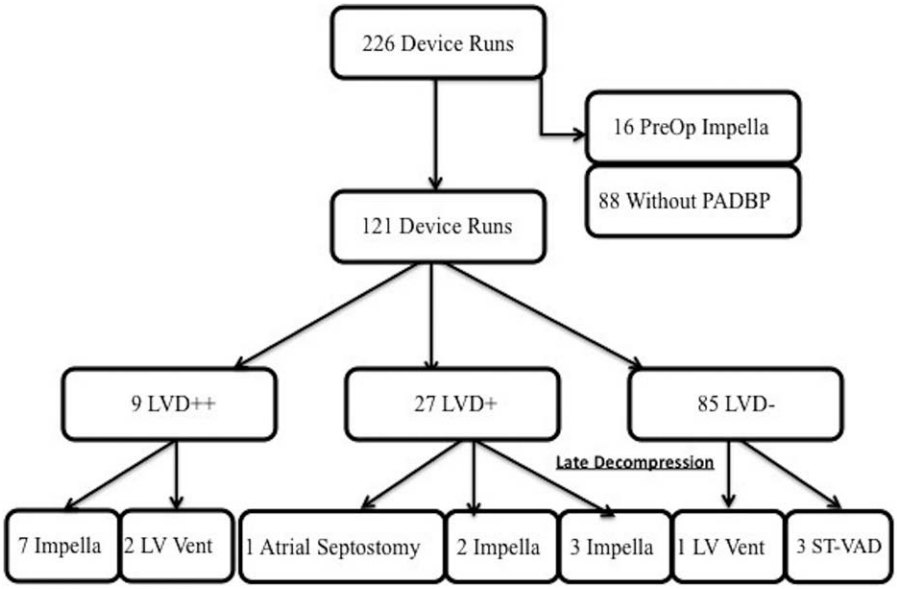

Figure 1. Patient and intervention selection algorithm. Among 226 device runs during the study period, 121 were included for analysis. Among these nine patients developed LVD++, 27 LVD+, and 85 had no evidence of LVD (LVD–). Among the LVD+ and LVD– group, 10 patients required delayed decompression. LVD, left ventricular distention.

significance, 66.7% of LVD++ patients were placed onto VA-ECMO as extracorporeal cardiopulmonary resuscitation (ECPR) in the setting of cardiac arrest. Extracorporeal cardiopulmonary resuscitation represented a significantly smaller proportion of the LVD+ and LVD– groups (11.1% LVD+, 19.3% LVD–; $p = 0.004$). Preoperative mean arterial pressure of the overall cohort was 62.55 ± 20.70 mm Hg and was significantly lower in LVD++ patients (51.44 ± 23.15 mm Hg), owing in part to the high prevalence of ECPR in that group. Laboratory values including hemoglobin, creatinine, and lactate did not differ significantly between LVD++, LVD+, and LVD– patients. Precannulation echocardiographic data were only available for a small subset of patients. Despite the small number of data points available, there was no difference in baseline LVEDD, mitral regurgitation, or aortic insufficiency. Notably all patients who required decompression had a significantly depressed ejection fraction (less than 30%), when compared with only half of LVD+ patients and 40% of LVD– patients.

The femoral artery (69.5%) was used more commonly for peripheral cannulation than the axillary artery (10.4%), with no patients in LVD++ group having undergone axillary arterial cannulation. Central cannulation was utilized in 23 patients. Initial extracorporeal blood flow was 3.61 ± 0.84 L/min overall, without significant differences between group. Need for immediate placement of distal perfusion cannula occurred in 33 patients (27.2%) and was not significantly more common among those who required early decompression (LVD++) (**Table 3**).

Differences in PADBP over time are summarized in **Figure 2**. It appears that those patients with LVD++, who by definition underwent decompression, achieved PADBPs similar to those who never had LVD. Pulmonary artery diastolic

Table 1. Demographics and Medical History

Characteristics	Overall	LVD++	LVD+	LVD–	*p*
Patients (n)	121	9	27	85	
Age (years); mean ± SD	56.41 ± 15.99	53.67 ± 14.53	59.93 ± 11.63	57.22 ± 16.18	0.527
Male; n (%)	94 (77.69)	6 (66.67)	21 (77.78)	67 (78.82)	0.707
BMI (kg/m^2)	28.46 ± 5.61	26.29 ± 3.47	28.23 ± 5.52	28.78 ± 5.82	0.439
CAD; n (%)	57 (47.11)	6 (66.67)	12 (44.44)	39 (45.88)	0.563
HLD; n (%)	55 (45.45)	5 (55.56)	11 (40.74)	39 (45.88)	0.685
HTN; n (%)	76 (63.33)	5 (62.50)	21 (77.78)	50 (58.82)	0.193
COPD; n (%)	11 (9.17)	0 (0.00)	7 (25.93)	4 (4.71)	0.006
DM; n (%)	35 (28.93)	4 (44.44)	10 (37.04)	21 (24.71)	0.242
Etiology of RCS					0.142
PCS	53 (43.80)	2 (22.22)	15 (55.56)	36 (42.35)	
AMI	26 (21.49)	3 (33.33)	4 (14.81)	19 (22.35)	
PGF	16 (13.22)	1 (11.11)	1 (3.70)	14 (16.47)	
ADHF	14 (11.57)	0 (0.00)	4 (14.81)	10 (11.67)	
Other	12 (9.92)	3 (33.33)	3 (11.11)	6 (7.06)	

ADHF, acute decompensated heart failure; AMI, acute myocardial infarction; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; LVD, left ventricular distention; PGF, primary graft failure; PCS, postcardiotomy shock; RCS, refractory cardiogenic shock.

Table 2. Preoperative Characteristics

Characteristics	Overall	LVD++	LVD+	LVD–	*p*
Patients (n)	121	9	27	85	
Hemodynamics					
IABP, n (%)	49 (40.83)	1 (11.11)	9 (34.62)	39 (45.88)	0.107
ECPR, n (%)	25 (21.01)	6 (66.67)	3 (11.11)	16 (19.28)	0.004
Heart rate (mean ± SD)	97.71 ± 24.23	94.00 ± 12.73	94.95 ± 21.62	99.12 ± 25.99	0.768
MAP (mm Hg) mean ± SD	62.55 ± 20.70	51.44 ± 23.15	70.43 ± 18.69	61.35 ± 20.37	0.044
Laboratory values					
Hemoglobin (mg/dl), mean ± SD	10.47 ± 2.20	11.10 ± 2.95	10.50 ± 1.86	10.39 ± 2.21	0.654
Creatinine (mg/dl) median (IQR)	1.5 (1.1–2.2)	1.2 (0.8–1.4)	1.8 (1.4–2.8)	1.5 (1.2–2.2)	0.362
Lactate (mg/dl) mean ± SD	6.94 ± 4.87	10.04 ± 4.60	7.16 ± 5.70	6.60 ± 4.56	0.313

AI, aortic insufficiency; ECPR, extracorporeal cardiopulmonary resuscitation; EF, ejection fraction; IABP, intraaortic balloon pump; LVD, left ventricular distention; LVEDD, left ventricular end diastolic diameter; MAP, mean arterial pressure; MR, mitral regurgitation.

blood pressure before intervention was unavailable in those who received decompression during the index procedure. We hypothesize that many of the patients who required immediate decompression developed LVD in the setting of an acute process, in which pulmonary edema can develop much more rapidly and without markedly elevated filling pressures. LVD+ patients had consistently higher PADBP values before cannulation, but these appeared to improve during the first 6 hours of VA-ECMO support and remained low at 24 hours.

A total of 10 patients (3 LVD+, 7 LVD–) required delayed decompression for LVD. Median time to intervention was 23.1 (21.3–30.5) hours. Etiologies for RCS in these patients included ADHF (n = 4, 28.6%), AMI (n = 3, 11.5%), and PCS (n = 2, 3.8%) and differed significantly among groups (p = 0.032). Among these patients, 30% (n = 3) received VA-ECMO during ECPR. Median PADBP in this group immediately before intervention was 21.88 ± 8.13 mm Hg (see Supplemental Figure, Supplemental Digital Content, http://links.lww.com/ASAIO/A141). Those who required delayed decompression did demonstrate higher initial flow compared with the LVD+ group who did not require decompression (3.65 ± 0.86 L/min *vs.* 3.45 ± 0.90 L/min). Echo data within the first 24 hours of support were available for six of the 10 patients who required delayed decompression. The mean LVEDD in these patients was 6.1 ± 1.3 cm (as compared with 5.6 ± 1.3 cm in the LVD+ group). Mean ejection fraction in these patients was 18.8% compared with 21.4% in those in the LVD+ group who did not require decompression. Flow index, defined as the average flow at 24, 48, and 72 hours while on support adjusted for body surface area, was higher in those requiring delayed decompression (2.4 ± 0.3 L/min/m^2) compared with the three groups displayed in **Table 3**. The characteristics of those who did and did not require delayed decompression within the LVD+ group are summarized in the Supplemental Table 1 (Supplemental Digital Content, http://links.lww.com/ASAIO/A142). The types of interventions utilized and the indications for decompression are summarized in **Figure 1**.

Primary and secondary outcomes are summarized in **Table 4** and **Figure 3**. Mean duration of VA-ECMO support was 4.11 ± 2.98 days, with a median hospital length of stay of 29 days, approximately half of which was spent in the ICU. The primary outcome, survival to discharge, was achieved by 43% (n = 52) of the overall cohort and did not differ significantly across groups. Only 20% of LVD++ patients who survived to discharge achieved myocardial recovery, while 60% of LVD+ and 80% of LVD– achieved this outcome. The remainder of patients in each group required initial device exchange to ST-VAD or long-term durable VAD. When freedom from death or device exchange was assessed as a composite end-point, LVD++ appeared to have the worst outcomes, followed by LVD+ and LVD– (p = 0.08; **Figure 4A**). In sensitivity analysis, when LVD++ patients (n = 9) were combined with those requiring delayed decompression (n = 10), this association was further strengthened (**Figure 4B**). Among patients who were decompressed, survival to discharge was 44.4% (4/9) in those decompressed early and 10.0% (1/10) in those who underwent delayed decompression.

When all preoperative characteristics were entered into univariable logistic regression analysis to identify predictors of need for decompression, etiology of RCS (p = 0.084) and ECPR (odds ratio [OR]: 4.73, confidence interval [CI]: 1.66–13.47, p = 0.004) were significantly associated with need for decompression (**Table 5**). When these two variables were entered into a multivariable model, only ECPR remained a risk factor for decompression (OR: 3.64, CI: 1.21–10.98; p = 0.022). Of note, need for decompression (OR: 0.50, CI: 0.18–1.37; p = 0.177)

Table 3. Cannulation Details

Characteristics	Overall	LVD++	LVD+	LVD–	*p*
Patients (n)	121	9	27	85	
Arterial cannulation, n(%)					0.303
Femoral	80 (69.57)	8 (88.89)	15 (65.22)	57 (68.67)	
Central	23 (20.00)	1 (11.11)	3 (13.04)	19 (22.89)	
Axillary	12 (10.43)	0 (0.00)	5 (21.74)	7 (8.43)	
Initial flow (L/min)	3.61 ± 0.84	3.67 ± 0.70	3.53 ± 0.92	3.62 ± 0.84	0.907
Flow index (L/min/m^2)	1.9 ± 0.5	1.7 ± 0.6	1.8 ± 0.5	1.9 ± 0.5	0.328

LVD, left ventricular distention.

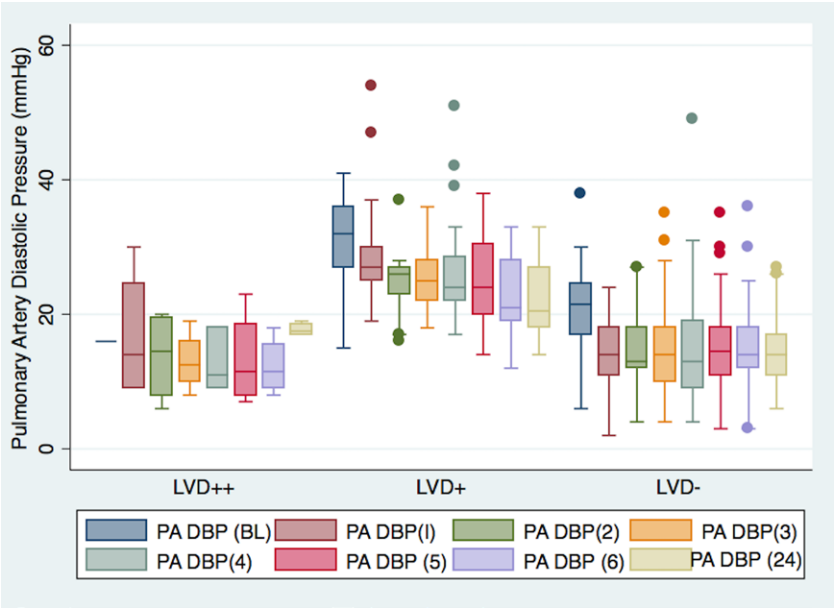

Figure 2. Pulmonary artery diastolic pressure *versus* time on VA-ECMO support. Pulmonary artery diastolic pressures displayed at time points: immediately before VA-ECMO cannulation, after the first 6 hours of support, and at 24 hours after support initiation among those with LVD++, LVD+, and LVD−. LVD, left ventricular distention; VA-ECMO, venoarterial extracorporeal membrane oxygenation. full color online

and initial PADBP (OR: 0.97, CI: 0.92–1.01; $p = 0.138$) were not independently associated with 30 day survival.

Discussion

The current study highlights the development of LVD as a potential complication of VA-ECMO support. It is the first to propose a definition based upon clinical, hemodynamic, and radiographic criteria allowing for quantitative evaluation of the impact of both clinical and subclinical LVD on outcomes. There are several clinically relevant findings noted in this cohort study. Clinically significant LVD requiring decompression occurred in 16% of device runs. An additional 20% of patients had hemodynamic and radiographic evidence of LVD that was not severe enough to require decompression. The ability of the patient to recover native cardiac function was inversely associated with the degree of LVD. In addition, freedom from the composite outcome of death or device exchange was impaired in patients with clinical and subclinical LVD, although survival to discharge alone appeared to be unaffected. Finally, ECPR was a clinically significant predictor of need for decompression.

Rationale of Our Definition of Left Ventricular Distention

In generating the categories of LVD utilized in the current study, we felt it was important to create a definition, which would easily capture two types of patients: those patients who required immediate decompression and those who might have similar physiology, but to a less severe degree. Thus, we first chose to identify clinically significant LVD requiring immediate invasive intervention, hypothesizing that these patients would display the most severe form of LVD physiology. LVD+ was defined by a PADBP of greater than 25 mm Hg in the first 2 hours after ICU admission for VA-ECMO cannulation with evidence of pulmonary edema on chest radiograph. In principle, LVD should be defined by LVEDP alone, which would represent the gold standard of diagnosis and identification. The next best surrogate measure would be pulmonary capillary wedge pressure (PCWP). However, PCWP was not routinely recorded in the period immediately following VA-ECMO initiation. Thus, PADBP was chosen as the most readily available surrogate for LVEDP. We chose a cutoff of 25 mm Hg based on the expectation that PADBP would be slightly elevated in comparison to PCWP, and based, in part, on the inclusion criteria of the Should We Emergenctly Revascularize Occluded Coronaries

Table 4. Outcomes

Characteristics	Overall	LVD++	LVD+	LVD−	*p*
Patients (n)	121	9	27	85	
Length of support	4.11 ± 2.98	3.19 ± 3.62	4.05 ± 3.78	4.22 ± 2.63	0.612
Hospital stay	29 (10–48)	33 (20–43)	28 (6–34)	30 (12–49)	0.335
ICU stay	15 (8–31)	12 (3–43)	14 (5–19)	15 (8–34)	0.326
Survival to discharge	52 (42.98)	4 (44.44)	11 (40.74)	37 (43.53)	0.953
Myocardial recovery	42 (34.71)	1 (11.11)	7 (25.93)	34 (40.00)	0.152
Transition to VAD	33 (27.27)	3 (33.33)	8 (29.63)	22 (25.88)	0.837
30 day survival	62 (51.24)	4 (44.44)	12 (44.44)	46 (54.12)	0.656

Results are reported as mean ± SD, median (IQR), or n (%).
ICU, intensive care unit; LVD, left ventricular distention; VAD, ventricular assist device.

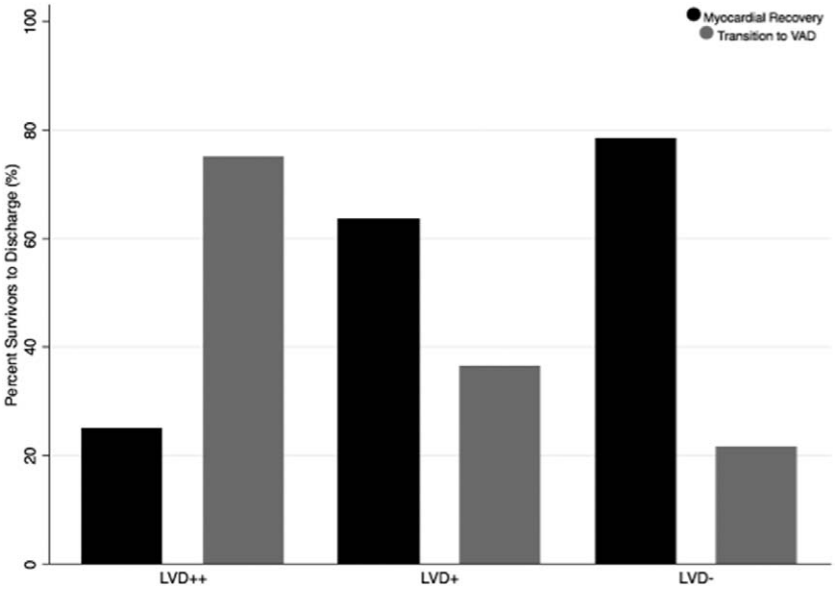

Figure 3. Myocardial recovery and device exchange by LVD severity. Among survivors to discharge, the proportion of patients in each group (LVD++, LVD+, LVD–) who achieved myocardial recovery or required device exchange to a short-term surgical ventricular assist device or to a durable long-term ventricular assist device. LVD, left ventricular distention. full color online

for Cardiogenic Shock (SHOCK) trial—which included a PCWP > 15 mm Hg.[16] Finally, we chose to include evidence of pulmonary edema on chest radiograph to prevent inclusion of those patients with isolated intrinsic pulmonary vascular processes and without elevated left-sided filling pressures. Because of the retrospective nature of the study, echocardiographic data were not utilized, as formal, objective reports were often unavailable when point of care testing was performed.

Incidence of Left Ventricular Distention

Left ventricular distention during VA-ECMO support has not been well reported[7,17] and is often difficult to compare across studies because of lack of a universally accepted definition. Schwarz *et al.*[18] reported a 10.9% incidence of LVD in their series of 46 patients, defined as LV distention resulting in pulmonary edema. Other published series, both adult and pediatric, report incidences between 12% and 68%.[19–21] In the current study, we found the incidence of LVD++ to be 7%, with an additional 8% requiring delayed decompression. After including those who met hemodynamic and radiographic criteria for LVD but did not necessitate decompression, a total of 35% of patients demonstrated some degree of LVD. Given that in our series, one in every five patients was undergoing cardiopulmonary resuscitation, and that cannulation during ECPR was found to be a risk factor of need for decompression, the incidence of clinical LVD may have been considerably lower if those patients had been excluded from the current analysis.

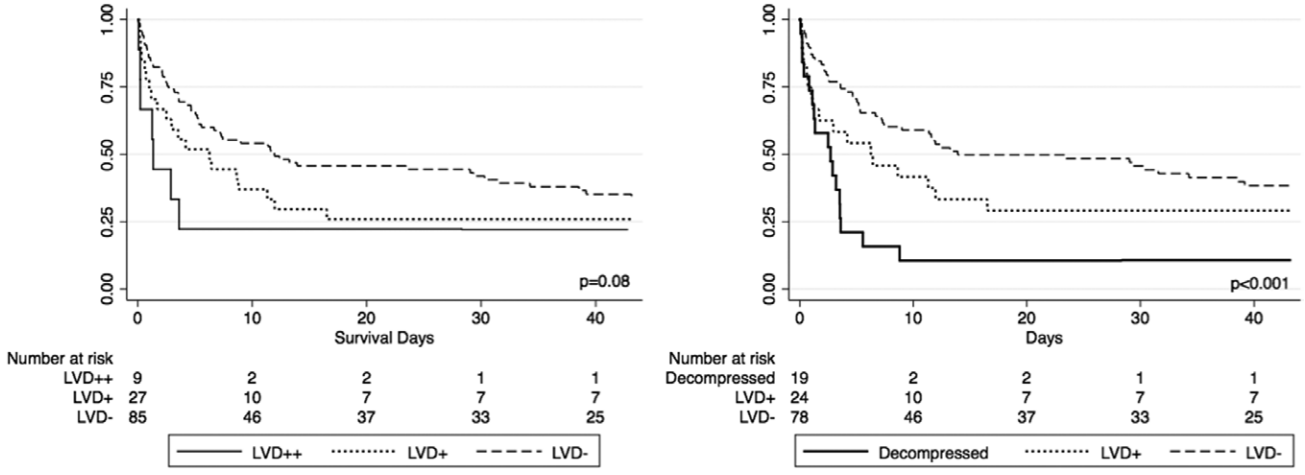

Figure 4. A: Freedom from death or device exchange among LVD++, LVD+, and LVD–. Kaplan-Meier analysis of freedom from death or device exchange among LVD++, LVD+, and LVD– patients. **B**: Freedom from death or device exchange among those decompressed, LVD+, and LVD–. Kaplan–Meier analysis of freedom from death or device exchange among all patient requiring decompression (LVD++ as well as those requiring late decompression) *versus* LVD+ and LVD– patients who did not require decompression. LVD, left ventricular distention. full color online

Table 5. Predictors of Need for Decompression (Early or Late)

	Univariate Analysis		Multivariate Analysis	
Variable	OR (95% CI)	*p*	OR (95% CI)	*p*
Age	0.99 (0.96–1.03)	0.770		
Male gender	1.09 (0.33–3.61)	0.886		
BMI > 30	0.75 (0.26–2.12)	0.582		
CAD	2.17 (0.79–5.97)	0.133		
HLD	1.10 (0.41–2.92)	0.855		
HTN	0.68 (0.25–1.88)	0.459		
Etiology		0.084		0.225
PCS	Reference		Reference	
ADHF	4.9 (1.05–22.94)		3.94 (0.80–19.40)	
PGD	0.82 (0.08–7.89)		0.70 (0.07–6.97)	
AMI	3.68 (0.94–14.43)		3.07 (0.75–12.65)	
Other	6.13 (1.27–29.58)		4.16 (0.80–21.67)	
IABP	1.06 (0.39–2.87)	0.902		
ECPR	4.73 (1.66–13.47)	0.004	3.64 (1.21–10.98)	0.022
MAP < 65	1.24 (0.37–4.19)	0.724		
Hgb < 8	1.38 (0.27–7.08)	0.698		
Creatinine > 2	1.10 (0.36–3.36)	0.867		
Lactate > 3	1.58 (0.58–4.35)	0.371		

ADHF, acute decompensated heart failure; AMI, acute myocardial infarction; BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; ECPR, extracorporeal cardiopulmonary resuscitation; Hgb, hemoglobin; HLD, hyperlipidemia; HTN, hypertension; IABP, intraaortic balloon pump; MAP; mean arterial pressure; OR, odds ratio; PCS, postcardiotomy shock; PGD, primary graft dysfunction.

Mechanism and Risk Factors of Left Ventricular Distention

Although VA-ECMO offers critical systemic circulatory support (increased arterial pressure, increased circulatory output) in patients with RCS, its physiology may prevent complete unloading of the LV.[22] This is primarily due to persistent preload and increased afterload, which results in increased myocardial oxygen demands and, importantly, an increase in the overall mechanical work performed by the heart, particularly as VA-ECMO blood flow increases.[10,23] Left ventricular distention is ultimately a product of severe LV dysfunction, which can occur in both the acutely and chronically failing heart. In the case of chronic heart failure, functional mitral regurgitation from chronic annular dilatation can provide some relief by decompressing the LV, but can also lead to elevated left atrial pressures resulting in significant pulmonary edema and worsening oxygenation.[9] In the case of acute heart failure, such as following an acute ischemic event or myocarditis, lack of functional mitral regurgitation may contribute to significant increases in intraventricular pressures and LV wall stress, resulting in increased workload and decreased diastolic coronary perfusion, further impairing the ability of the heart to recover.[24] In fact, in the pediatric population, it has been suggested that early elective LV decompression might reduce the duration of VA-ECMO support.[25]

We identified ECPR as a risk factor for decompression. We believe this phenomenon is likely an effect of severe LV dysfunction because of myocardial stunning after cardiopulmonary resuscitation superimposed on an already abnormal or weakened myocardium. Even with inotropic support, placement of VA-ECMO in this setting likely generates enough afterload to prevent continued LV ejection, contributing to the development of acute pulmonary edema.

Prevention and Management of Left Ventricular Distention

Over time, there have been multiple proposed strategies to ameliorate clinically significant LVD, although current American College of Cardiology (ACC), American Heart Association (AHA), and European Society of Cardiology (ESC) guidelines do not specifically address VA-ECMO management strategies.[26,27] It has become more widely accepted that a "partial flow approach" in combination with high doses of inotropes improves LV contractility and reduces afterload during VA-ECMO support.[15,17] In general, however, it is also accepted that some degree of LVD will occur simply because of mechanical circulatory support physiology.[23] Previously reported strategies for the management of clinically significant LVD include balloon atrial septostomy[12] and mechanical LV venting.[28,29] We previously reported one of the first applications of an Impella device in this setting, and this strategy remains our preference.[13] More recently, we are employing an external ventricular assist device to the VA-ECMO circuit *via* LV cannulation as a means of LV decompression.[30] However, the importance of appropriate monitoring and conservative management cannot be over-emphasized. Invasive hemodynamic monitoring with pulmonary artery catheters and right radial arterial catheters is our routine. The pulmonary artery catheter provides hemodynamic information on LV loading conditions, and pulsatility on the right radial arterial line assures ejection from the LV. An echocardiogram is performed shortly after ECMO initiation, whenever weaning is attempted, and on an as needed basis. Overall, our goal in management is to optimize systemic circulatory support impairment in LV contractility created by VA-ECMO by adjusting inotropic support and flows. In fact, the analysis of our LVD+ group showed the improvement in PADBP over time.

Currently, we do not prophylactically decompress high-risk individuals or those who fall into the subclinical LVD+ group. Data from the current study, however, do raise the question of whether earlier intervention, or even prophylactic intervention, could provide clinical benefit. In the future, randomized control trials in high-risk individuals are needed to address the possible benefit of early decompression, particularly as it relates to myocardial recovery.

Outcomes of Left Ventricular Distention

Overall survival to discharge was 43% and was not significantly different among groups. Among survivors, increasing degree of LVD conferred high rates of need for device transition and lower likelihood of achieving myocardial recovery (**Figure 3**). When a composite outcome of death or device transition was utilized, LVD++ and LVD+ displayed lower rates of event-free survival in the first 30 days following VA-ECMO cannulation (**Figure 4A**). This trend was exaggerated when those who required any type of decompression (LVD++ and delayed decompression) were compared with nondecompressed LVD+ and LVD− (**Figure 4B**). It is unclear whether this is directly related to LVD physiology or whether the development of LVD is merely a surrogate for the most severe myocardial dysfunction, which predisposes the patient to the development of RCS and subsequent multisystem organ dysfunction. This finding could also reflect the large proportion of ECPR patients, who have been shown to have poor outcomes, independent of LVD physiology.[31]

Although it makes sense that LVD would negatively impact the ability of the native heart to recover, no previous studies have demonstrated this observation. The current study suggests that an increasing degree of LVD results in decreased likelihood of myocardial recovery, both among all patients (**Table 4**) and among those who survived to discharge (**Figure 3**). Although there was a trend toward significance in the initial analysis, a sensitivity analysis comparing those decompressed (early or late) with nondecompressed LVD+ and LVD− demonstrated significant differences in myocardial recovery (decompressed: 5%, LVD+: 29%, LVD−: 44%; $p = 0.003$) and device exchange (decompressed: 53%, LVD+: 29%, LVD−: 21%; $p = 0.022$). In addition, it is important to note that the potential for myocardial recovery was lower in those with clinical LVD despite intervention, which may suggest the need for earlier, more aggressive unloading in those with significant risk factors.

Limitations

Because of the retrospective nature of the study, many important data points, including echocardiographic findings immediately before intervention for LVD, were unable to be obtained. This prevented us from correlating hemodynamic measurements (PADBP) to LV dimensions, contractility, or aortic valve opening. We were also unable to assess degree of mitral regurgitation in order to quantify its impact on LVD. In addition, many of our conclusions are limited by sample size and the fact that many patients were excluded from our analysis owing missing hemodynamics measurements. Those patients who were excluded did demonstrate some differences in population characteristics in comparison to those included (*e.g.,* gender, IABP use, ECPR prevalence), which could limit generalizability of results. Gold standard measurements of left-sided filling pressures (LVEDP, PCWP) were not available, and thus utilizing PADBP as a surrogate may introduce some error. Our definition chose an absolute cutoff for PADBP rather than a delta pressure, which could have a greater degree of clinical significance. We also incorporated the need for mechanical decompression into our definition, although we recognize that no defined set of criteria exist to determine the need for mechanical decompression. Finally, the limitations of retrospective analysis are inherent in the current study.

Conclusion

Clinical and subclinical LVD, as outlined by our novel definition, are likely under recognized in the VA-ECMO population. The ability of the heart to recover native function appears to be impaired in those patients who require decompression or have subclinical LVD, although overall survival to discharge is not significantly affected. Those patients with RCS in the setting of AMI may be at higher risk for the need for early decompression, while those with ADHF are at particularly high risk for delayed decompression. ECPR-associated VA-ECMO cannulation was identified as a significant risk factor for the need for decompression.

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