Journal of the American Heart Association

ORIGINAL RESEARCH

Use of Percutaneous Atrioseptotosmy for Left Heart Decompression During Veno-Arterial Extracorporeal Membrane Oxygenation Support: An Observational Study

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BACKGROUND: Left ventricular overload is frequent under veno-arterial extracorporeal membrane oxygenation, which is associated with a worsening of the prognosis of these patients. Several left heart decompression (LHD) techniques exist. However, there is no consensus on their timing and type. We aimed to describe characteristics and outcomes of patients undergoing LHD and to compare percutaneous atrioseptostomy (PA) to other LHD techniques.

METHODS AND RESULTS: Retrospective analysis was conducted of consecutive and prospectively collected patients supported by veno-arterial extracorporeal membrane oxygenation for refractory cardiac arrest or cardiogenic shock between January 2015 and April 2018, with a 90-day follow-up in our tertiary center. Patients were divided according to the presence of LHD, and then according to its type (PA versus others). Thirty-nine percent (n=63) of our patients (n=163) required an LHD. Patients with LHD had lower left ventricular ejection fraction, more ischemic cardiomyopathy, and no drug intoxication-associated cardiogenic shock. PA was frequently used for LHD (41% of first-line and 57% of second-line LHD). PA appears safe and fast to realize (6.3 [interquartile range, 5.8–10] minutes) under fluoroscopic and echocardiographic guidance, with no acute complications. PA was associated with fewer neurological complications (12% versus 38%, P=0.02), no need to insert a second LHD (0% versus 19%, P=0.04), and higher 90-day survival compared with other techniques (42% versus 19%, log-rank test P=0.02), despite more sepsis (96% versus 73%, P=0.02) and blood transfusions (13.5% versus 7%, P=0.01). Multivariate analysis confirms the association between PA and 90-day survival (hazard ratio, 2.53 [1.18–5.45], P=0.019).

CONCLUSIONS: LHD was frequently used for patients supported with veno-arterial extracorporeal membrane oxygenation, especially in cases of ischemic cardiomyopathy and low left ventricular ejection fraction. PA seems to be a safe and efficient LHD technique associated with greater mid-term survival justifying the pursuit of research on this topic.

Key Words: atrioseptostomy ■ cardiogenic shock ■ left heart decompression ■ left ventricular venting ■ veno-arterial extracorporeal membrane oxygenation

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has been increasingly used as a rescue therapy in cases of refractory cardiogenic shock (RCS) and refractory cardiac arrest (RCA) regardless of their causes.[1] Recent technical advances have allowed wide use in the intensive care and cardiology

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Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.024642

For Sources of Funding and Disclosures, see page 12.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Although up to 40% of patients supported by veno-arterial extracorporeal membrane oxygenation need left heart decompression, no consensus exists on the most efficient type, the optimal strategy, and timing of realization.
- Percutaneous atrioseptostomy emerges as a rapid (<10 minutes), safe, and efficient technique to prevent and/or cure left heart overload associated with veno-arterial extracorporeal membrane oxygenation.
- Percutaneous atrioseptostomy was associated with fewer neurological complications, no need for second-line left heart decompression, and higher 90-day survival compared with other left heart decompression techniques.

What Are the Clinical Implications?

- Future research is needed to establish the precise timing of implantation and type of left heart decompression to use, based on safety, cost, and efficacy criteria (hemodynamic and prognostic effects).

Nonstandard Abbreviations and Acronyms

AFP	axial flow pump
IABP	intra-aortic balloon pump
LHD	left heart decompression
PA	percutaneous atrioseptostomy
RCA	refractory cardiac arrest
RCS	refractory cardiogenic shock

community, although to date, no randomized trials support its use, which explains the low level of recommendation in American or European guidelines (class of recommandation IIb level of evidence C).[2,3]

VA-ECMO provides temporary circulatory support and oxygenation that should allow correction of multiorgan failure, possible myocardial recovery, or bridge to an end-stage heart failure project (durable mechanical circulatory support or heart transplantation).[3] However, VA-ECMO support is still associated with a high rate of complications,[4] and the effect on outcome is debated with a persistently high short-term mortality (40%–60%).[5] In a relevant proportion of patients, the retrograde aortic VA-ECMO flow is associated with increase in left ventricular (LV) afterload, insufficient LV unloading, severe pulmonary congestion, and potential intracardiac thrombosis, thereby altering prognosis.[6] The deleterious effect of retrograde aortic flow seems all the more marked when patients present with a predominant LV failure, with a 2.2-fold increase in short-term mortality.[7]

To solve this crucial issue, in addition to a strategy of running extracorporeal membrane oxygenation at the lowest possible flow rates and/or inotrope infusion, numerous left heart decompression (LHD) techniques have been described. These include association with an intra-aortic balloon pump (IABP) or a transaortic axial flow pump (AFP), or a centrifugal pump with a transseptal inflow cannula, or adjunction of a surgical LV venting cannula connected to the venous circuit of the VA-ECMO (via a transapical or arterial access). Furthermore, the creation of a right-to-left shunt through percutaneous atrioseptostomy (PA) or even the centralization of the extracorporeal membrane oxygenation with direct cannulation of cardiac cavities are also used by some teams.[8]

At this time, however, there is no consensus on the clinical and temporal criteria to justify LV unloading, and no technique has demonstrated superiority in relation to others.[9] In this context, the 2 aims of this study were (1) to evaluate the 90-day outcomes of patients who have undergone VA-ECMO with or without associated LHD and (2) to compare outcomes of patients with LHD between PA and other types of LHD.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Population

This study was based on a retrospective analysis of additional data from patients consecutively included in a prospective registry of all patients who received VA-ECMO support for RCS or RCA in our multidisciplinary intensive care unit (Rangueil University Hospital, Toulouse, France) during a 3-year period (2015–2018). Following cardiotomy RCS or RCA, patients aged <18 years and adult patients subject to protective measures were excluded. Details on the indications, contraindications, and management of extracorporeal membrane oxygenation as well as techniques for performing left ventricular decompression are available in Data S1.

VA-ECMO Indications and Management

VA-ECMO indications and management were based on our local protocol and available guidelines through a multidisciplinary team including cardiologists, intensivists, and cardiac surgeons.

VA-ECMO was initiated using a femoral approach with a modified Seldinger technique with addition of a

systematic ipsilateral superficial femoral artery reperfusion. Flow was adjusted to target mean arterial pressure ≥65 mm Hg. Inotrope support with dobutamine could be continued to maintain aortic valve opening. Anticoagulation was systematically started by intravenous unfractionated heparin (anti-Xa level target 0.2 to 0.4 IU/mL). VA-ECMO weaning was based on a set of clinical–biological and ultrasound criteria assessed by daily weaning trial.

LHD Indications and Techniques

The need for LHD and selection of the type of LHD were assessed by our local team. In case of refractory and critical pulmonary congestion, a curative LHD was introduced. In cases of severely depressed left ventricular ejection fraction (LVEF), low differential arterial pressure (<5–10 mm Hg), major distention of the left ventricle, or absence of aortic valve opening, a preventive LHD was considered.

Timing and type of LHD was left at the discretion of the cardiogenic shock heart team. Different types of LHD were used in our series depending on the implantation site of the VA-ECMO, availability of materials, and medical–surgical skills: an IABP, an AFP, a surgical LHD connected to the venous circuit of the VA-ECMO, or a PA.

For PA, a left–right shunt through perforation of the interatrial septum after femoral vein catheterization was created. It was performed under fluoroscopic guidance in the hemodynamical or electrophysiological laboratories, under transesophageal echocardiography when needed. After femoral venous catheterization, transseptal puncture was performed according to the usual techniques[10] with a SLO sheath (St. Jude Medical) and Brokenbrough needle, under common fluoroscopic landmarks and/or pressure monitoring. Of note, transseptal puncture was sometimes especially difficult in this situation, because of the presence of the extracorporeal membrane oxygenation venous canula, anticoagulation, and dilated/distorted cardiac anatomy. Then, an aortic valvuloplasty balloon (10–18 mm diameter) was mounted over a 0.32-mm guidewire positioned in the left superior pulmonary vein. The sheath was then removed into the right atrium, and the balloon was inflated through the transseptal puncture over the wire to create an interatrial communication and thus maintain a significant left–right shunt.[11]

Data Collection

Whole data had been prospectively collected from medical records and clinical information management systems. The first section included all general patient data (sex, age, body mass index, cardiovascular risk factors, medical history, previous treatments, VA-ECMO indication, RCS or RCA cause, SAPS2 [Simplified Acute Physiology Score 2], SOFA [Sequential Organ Failure Assessment], and ENCOURAGE [Prediction of Cardiogenic shock Outcome for AMI patients salvaGed by VA-ECMO] severity scores), clinical and paraclinical status as treatments at VA-ECMO insertion, initial patient's project (bridge to transplantation and/or durable mechanical circulatory support and/or recovery), complications and outcomes while in the intensive care unit and hospital, and 90-day follow-up. The second part included specific data on LHD such as preventive or curative indication, type and methods of implantation, evolution of clinical and paraclinical parameters at H0, H24 and H48 post LHD implantation, and associated complications (bleedings, intracardiac thrombi or systemic embolisms, sepsis, neurological disorders, need for surgical revision, and need for renal replacement therapy).

Ethics and Regulations

This study's protocol was submitted and approved by the institutional review board of the Toulouse University Hospital (number 11–0214) after declaration of the registry to the National Commission on Informatics and Liberty, and follows the Declaration of Helsinki. As an observational study, patients' consent was not required.

Statistical Analysis

Distribution of values was assessed with the Shapiro-Wilk test. Results were expressed in median and interquartile range for the quantitative variables and in number and percentage for the qualitative variables.

The study population was separated into 2 groups based on whether or not an LHD was used. In a second step, the population of patients who had received an LHD was specifically analyzed, with comparison between patients having undergone PA and patients receiving another type of LHD. Groups were compared using the nonparametrical Mann-Whitney *U* test for continuous variables and χ^2 test or Fisher exact test (used when n<5 in >20% of cells) for qualitative variables as suitable.

In the LHD group, time-evolution of parameters for the 48 hours following LHD was assessed by Friedman test for continuous variables and a Mantel-Haenszel χ^2 test for qualitative variables.

Survival rates were analyzed using the Kaplan-Meier method and compared with the log-rank test between groups. To determine independent predictors of 90-day mortality and confirm the association between PA and prognosis, 2 different multivariable Cox proportional hazard model analyses were conducted, including variables available at the time of LHD performance. Model 1 included body mass index, tachycardia-induced cardiomyopathy, prior cardiac arrest, and PA. Model 2 included recent myocardial

infarction, time under mechanical ventilation before LHD, curative indication of LHD, and PA.

Finally, a second survival analysis was performed on the basis of a composite end point combining death–heart transplantation or left ventricular assist device at 90 days between patients with PA and patients with others type of LHD.

A 2-sided *P* value <0.05 was considered statistically significant. Statistical analysis was performed using MedCalc statistical software (Mariakerke, Belgium) and the free software R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

General Population

During a 3-year period, 163 consecutive patients who underwent VA-ECMO were prospectively and consecutively included. Characteristics of the population are summarized in Table S1. Patients had a mean age of 55 years (IQR, 42–61 years) and were predominantly men (n=113, 69%). Patients presented with hemodynamic instability despite a high level of vasopressors and inotropes (noradrenaline 58%, dobutamine 37%, and/or adrenaline 65%). Associated multiorgan failure was severe (SAPS2 68.5, SOFA 11, and ENCOURAGE 22).

Sixty-three patients (39%) required 1 (n=56) or 2 (n=7) LHD procedures. Table S1 compares patients with and without LHD. VA-ECMO was initiated in nearly two-thirds of cases for RCS (n=42, 67%) and preferentially by femoro-femoral cannulation (n=148, 90.8%) without difference between groups. Groups were comparable at VA-ECMO initiation, except for a lower LVEF (10% versus 10%, *P*=0.009) and a lower percentage of bilateral mydriasis (12.7% versus 29.8%, *P*=0.018) in the LHD group. Likewise, a history of ischemic cardiomyopathy (51% versus 29%, *P*=0.053) and an RCS secondary to myocardial infarction (44.6% versus 16%, *P*≤0.001) were more frequent in the LHD group, whereas no drug overdose-associated RCS needed LHD placement.

LHD Population

Table 1 and Figure 1 describe the specific characteristics of the LHD group. For over half (52%) of the population, LHD was introduced early after VA-ECMO implantation (on the same day).

In 56 (89%) patients, a single LHD was necessary, and among those patients, LHD was performed for preventive grounds in 60% (n=38). IABP and PA were the preferentially used LHD techniques (43% and 41%, respectively), followed by AFP (n=8, 13%) and surgical discharges (n=2, 3%). In the 7 (11%) patients requiring a second LHD, PA was performed in 4 (57.1%), and no IABP was inserted. The average time until insertion of this second LV discharge was 1 day [IQR, 1–3.5].

In-Hospital and 90-Day Outcomes

During the first 48 hours after LHD insertion, we observed a significant pH and lactate clearance (Table S2). However, LHD was also associated with a significant decrease in hemoglobin and platelets (11.6 to9.1 g/dL, *P*<0.001 and 140 to 93 G/L, *P*<0.001 between H0 and H48, respectively, for hemoglobin and platelets), as well as with a significant increase in total bilirubin (13.2 to 24.5 mmol/L, *P*<0.001), suggesting hemolysis and/or blood loss because it is associated with a higher consumption of blood products. No significant differences were found in terms of neurological complications, sepsis, renal replacement therapy, or surgical revision of the insertion site. Duration of intensive care unit stay was longer in the LHD group (28 versus 13 days; *P*<0.007), without a difference in the total duration of hospitalization (35 versus 41 days, *P*=0.251).

No difference between groups was observed in rates of successful VA-ECMO weaning, bridge to left ventricular assist device or transplantation, and mortality at 90 days (Figure 1). There was no difference in terms of 90-day survival (Figure S1), but a trend to better survival for patients without LHD or with PA versus others type of LHD was noted (*P*=0.053) (Figure 2). The most frequent cause of death was multiple organ failure in 39%, without a difference between groups. No difference was found in terms of survival between patients with LHD according to curative or preventive indication (34% versus 12%; *P*=0.252) (Figure S2).

Comparison of Atrioseptostomy and Other Types of LHD

The methods for performing PA are summarized in Table 2. Echocardiography demonstrated a large left-to-right atrial shunting in all patients (Figure 3). Invasive left atrial pressure monitoring was available for only 8 patients, with PA showing an initial elevation with a significant decrease after the procedure (23.5 versus 14.5 mm Hg, respectively; *P*=0.014). No acute complication occurred. Correction of pulmonary fluid retention was achieved in all patients, with an acutely oxygen saturation improvement in a few minutes and a normalization of pulmonary chest radiography in a few hours to a few days (data not shown).

Table 1 compares the characteristics of patients with PA versus those with other LHD techniques. No significant difference was observed between the 2 groups, especially in terms of LHD indication (curative or preventive), except for higher body mass index (25

Table 1. Description of the Population With LHD and Comparison Between Patients With Atrioseptostomy Versus Other Types of Left Ventricle Venting

	Non-LHD population, n=100	Total population with LHD, n=63	Atrioseptostomy, n=26 (41%)	Other LHD, n=37 (59%)	*P* value, PA versus other LHD
Demographic data					
Men	65 (65%)	48 (76%)*	22 (85%)	26 (70%)	0.238
Age, y	52 (36 to 62)	57 (47 to 60)†	56 (46 to 57)	58 (50 to 61)	0.168
BMI, kg/m^2	25.3 (22 to 29)	26.6 (24 to 30)	28.1 (26.4 to 31.2)	25 (22.2 to 26.9)	0.002
Underlying heart disease					
Ischemic	29 (29%)	32 (51%)	16 (62%)	16 (43%)	0.156
Dilated	11 (11%)	9 (14%)	6 (23%)	3 (8%)	0.144
Hypertrophic	10 (10%)	2 (3%)	1 (4%)	1 (3%)	1.000
Valvular	8 (8%)	3 (5%)	1 (4%)	2 (5%)	1.000
Tachycardia-induced cardiomyopathy	9 (9%)	8 (13%)	6 (23%)	2 (5%)	0.056
None	32 (32%)	18 (29%)	6 (23%)	12 (32%)	0.573
Cardiovascular risk factors					
Hypertension	32 (32%)	22 (36%)	6 (23%)	16 (43%)	0.109
Diabetes	15 (15%)	9 (14%)	5 (19%)	4 (11%)	0.469
Smoking	49 (49%)	38 (60%)	11 (42%)	27 (73%)	0.016
Dyslipidemia	23 (23%)	17 (27%)	7 (27%)	10 (27%)	1.000
Indication for VA-ECMO					
RCS/RCA	68 (68%)/32 (32%)	42 (67%)/21 (33%)	18 (69%)/8 (31%)	24 (65%)/13 (35%)	0.719
Cause of the RCS					
End-stage heart failure	10 (10%)	8 (13%)	5 (19%)	3 (8%)	0.257
Recent myocardial infarction	16 (16%)	28 (44%)	8 (31%)	20 (54%)	0.077
Electrical storm	13 (13%)	9 (14%)	5 (19%)	4 (11%)	0.472
Other, pulmonary embolism, ARDS	15 (15%)	7 (11%)	3 (12%)	4 (11%)	1.000
RCA before initiation of VA-ECMO					
Prior cardiac arrest	56 (56%)	37 (59%)	12 (46%)	25 (68%)	0.092
Out-of-hospital RCA	25 (25%)	11 (17%)	3 (12%)	8 (22%)	0.502
No flow >5 min	6/51 (12%)	3/36 (8%)‡	1 /11 (9%)	2 /25 (8%)	1.000
Bilateral mydriasis at initiation	28/94 (30%)	7/55 (13%)	3/25 (12%)	4/30 (13%)	1.000
Severity score at initiation					
ENCOURAGE	21 (14 to 27)	23 (17 to 28)	18.5 (14.8 to 23.5)	23 (15 to 28)	0.391
SOFA	12 (9 to 13)	10 (9 to 12)	9.5 (7.5 to 12)	11 (9 to 12)	0.289
SAPS2	68 (54 to 78)	70 (57 to 80)	71.5 (57.5 to 79.5)	66 (53 to 79)	0.679
Therapeutics used before initiation					
Noradrenaline	62 (62%)	32 (51%)	13 (50%)	19 (51%)	0.917
Adrenaline	60/98 (61%)	44 (70%)	16 (62%)	28 (76%)	0.257
Dobutamine	32 (32%)	28 (44%)	11 (42%)	17 (46%)	0.798
Mechanical ventilation	94 (94%)	55 (87%)	20 (77%)	35 (95%)	0.059
Clinical and biological data at initiation of VA-ECMO					
HR, bpm	57 (0 to 115)	90 (0 to 110)	91.5 (0 to 111.5)	90 (0 to 110)	0.711
MAP, mm Hg	50 (0 to 65)	55 (0 to 70)	60 (0 to 70)	50 (0 to 72)	0.987
LVEF, %	10 (5 to 25)	10 (5 to 15)	7.5 (5 to 15)	10 (5 to 13.8)	0.525
Arterial blood pH	7.19 (7.03 to 7.35)	7.22 (7.1 to 7.33)	7.24 (7.06 to 7.33)	7.21 (7.05 to 7.3)	0.525
PaO_2, mm Hg	113 (77 to 255)	105 (72.7 to 279)	111 (75 to 246)	104 (78.7 to 289)	0.994

(*Continued*)

Table 1. Continued

	Non-LHD population, n=100	Total population with LHD, n=63	Atrioseptostomy, n=26 (41%)	Other LHD, n=37 (59%)	*P* value, PA versus other LHD
$PaCO_2$, mm Hg	39.2 (30.9 to 50.3)	40 (29 to 47)	39 (28.7 to 44.1)	40 (29.4 to 48.2)	0.433
Lactatemia, mmol/L	6.7 (3.8 to 14)	8.3 (3 to 14.9)	4.65 (2.4 to 13.6)	8.5 (3.8 to 16)	0.275
Serum creatinine, µmol/L	138 (103 to 177)	127.5 (103 to 164)	128 (108 to 168)	130.5 (101.5 to 160.3)	0.884
ASAT, IU/L	184 (79 to 612)	229 (47 to 647)	86.5 (45.3 to 415.8)	437 (57 to 736)	0.178
ALAT, IU/L	105 (48 to 403)	112 (57 to 338)	66.5 (37 to 344.8)	162 (63 to 317.5)	0.364
PT, %	52.5 (40 to 69)	55 (36 to 71)	57 (48.3 to 71.8)	53 (34 to 68.3)	0.293
Hemoglobin, g/dL	12.3 (10.2 to 14)	12.6 (10.1 to 15.2)	14.1 (10.8 to 15.8)	12.2 (10.1 to 15)	0.205
Delay between VA-ECMO and LHD		0 (0 to 1)	1 (0 to 2.75)	0 (0 to 1)	0.041
Indication first discharge					
Curative/preventive	…	25 (40%)/38 (60%)	14 (54%)/12 (46%)	11 (30%)/26 (70%)	0.054
Discharge efficiency					
Lactate relative variation at H24	…	−0.29 (−0.53 to 0.38)	−0.2 (−0.52 to 0.84)	−0.29 (−0.51 to 0.22)	0.499
Lactate relative variation at H48	…	−0.33 (−0.7 to 0.13)	−0.24 (−0.73 to 0.41)	−0.49 (−0.67 to −0.02)	0.401
LHD-associated hemolysis					
Platelets relative variation at H48	…	−0.33 (−0.56 to −0.16)	−0.23 (−0.38 to −0.12)	−0.53 (−0.59 to −0.38)	0.009
Bilirubin relative variation at H48	…	0.79 (0.28 to 169)	0.76 (0.26 to 1.35)	1.1 (0.5 to 2.8)	0.547
LHD associated complications					
Surgical revision of the insertion site	…	7 (11%)	5 (19%)	2 (5%)	0.110
Tamponade	…	8 (13%)	4 (15%)	4 (11%)	0.707
Limb ischemia	…	9 (14%)	3 (12%)	6 (16%)	0.725
RRT	29 (29%)	27 (43%)	11 (42%)	16 (43%)	0.942
LV thrombus	7 (7%)	6 (10%)	5 (19%)	1 (3%)	0.073
RV thrombus	…	2 (3%)	2 (8%)	0 (0%)	0.166
Neurological complications	23 (23%)	17 (27%)	3 (12%)	14 (38%)	0.024
Sepsis	70 (70%)	52 (83%)	25 (96%)	27 (73%)	0.020
Need for a second LHD		7 (11%)	0 (0%)	7 (19%)	0.035
Blood product transfusions during hospitalization					
pRBCs	6 (2 to 11)	10 (5 to 17)	13.5 (9 to 19.5)	7 (4 to 13)	0.014
Fresh frozen plasma	0.5 (0 to 6)	3 (0 to 6)	3.5 (0 to 6)	3 (0 to 6)	0.848
Platelet concentrates	1 (0 to 7)	3 (0 to 12)	5.5 (1 to 14.5)	2 (0 to 11)	0.1367
Evolution					
Length of ICU stay, d	13 (9 to 21)	28 (15 to 40)	31 (22.5 to 41.5)	15 (12.5 to 24.5)	0.093
Length of hospital stay, d	35 (21 to 51)	41 (29 to 58)	50.5 (38 to 57.8)	32 (18 to 34)	0.178
Duration of VA-ECMO, d	5 (3 to 7)	10 (6.3 to 16)	13 (10 to 25)	8 (5.5 to 12.5)	0.008
VA-ECMO weaning	54 (54%)	34 (54%)	15 (58%)	19 (51%)	0.622
Transplant or chronic assistance at M3	9/98 (9%)	6/62 (10%)	5/25 (20%)	1 (3%)	0.035
Death at 90 d	56 (56%)	45 (71%)	15 (58%)	30 (81%)	0.045
Cause of death					
Cardiological	…	3 (7%)	1 (7%)	2 (7%)	0.054

(*Continued*)

Table 1. Continued

	Non-LHD population, n=100	Total population with LHD, n=63	Atrioseptostomy, n=26 (41%)	Other LHD, n=37 (59%)	*P* value, PA versus other LHD
Neurological	…	3 (7%)	0 (0%)	3 (10%)	
Multiorgan failure	…	25 (56%)	7 (47%)	18 (47%)	
Absence of recovery and project	…	5 (11%)	4 (27%)	1 (3%)	
Hemorrhage	…	1 (2%)	0 (0%)	1 (3%)	
Sepsis	…	2 (4%)	2 (13%)	0 (0%)	
Other/not found	…	6 (13%)	1 (7%)	5 (17%)	

ALAT indicates alanine aminotransferase; ARDS, acute respiratory distress syndrome; ASAT, aspartate aminotransferase; BMI, body mass index; ENCOURAGE, Prediction of Cardiogenic shock Outcome for AMI patients salvaGed by VA-ECMO; H, time in hours post LHD implantation; HR, heart rate; ICU, intensive care unit; LHD, left heart decompression; LV, left ventricle; LVEF, left ventricular ejection fraction; M3, 3 months; MAP, mean arterial pressure; PA, percutaneous atrioseptostomy; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; pRBCs, packed red blood cells; PT, prothrombin time; RCA, refractory cardiac arrest; RCS, refractory cardiogenic shock; RRT, renal replacement therapy; RV, right ventricle; SAPS2, Simplified Acute Physiology Score 2; SOFA, Sequential Organ Failure Assessment; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

*Copied result N (%), N being the number of cases and (%) the ratio of cases over the total number expressed as a percentage.

†Copied result M (25–75), M being the median and 25–75 the interquartile range.

‡When data are missing, the case/total ratio is indicated before the percentage.

versus 28.1 kg/m^2; *P*=0.02) and fewer smokers (42% versus 73%, *P*=0.01) in the PA subgroup. However, PA was realized later (1 [IQR, 0–2.75] versus 0 [IQR, 0–1] days; *P*=0.041).

LHD-associated complications significantly differed between groups, with fewer neurological complications (12% versus 38%; *P*=0.024), lower platelet count variations at 48 hours (−0.23 [IQR, −0.38 to −0.12] versus −0.53 [IQR, −0.59 to −0.38]; *P*=0.009), and no recourse to a second LHD (0% versus 19%; *P*=0.035) in the PA group, whereas more sepsis (96% versus 73%; *P*=0.020) and packed red blood cell transfusions (13.5% versus 7%; *P*=0.014) happened in this group.

PA was associated with a significantly higher 90-day survival compared with other LHD techniques (42% versus 19%; *P*=0.011*)* (graphical abstract). Moreover, PA is associated with a nonsignificant trend to higher

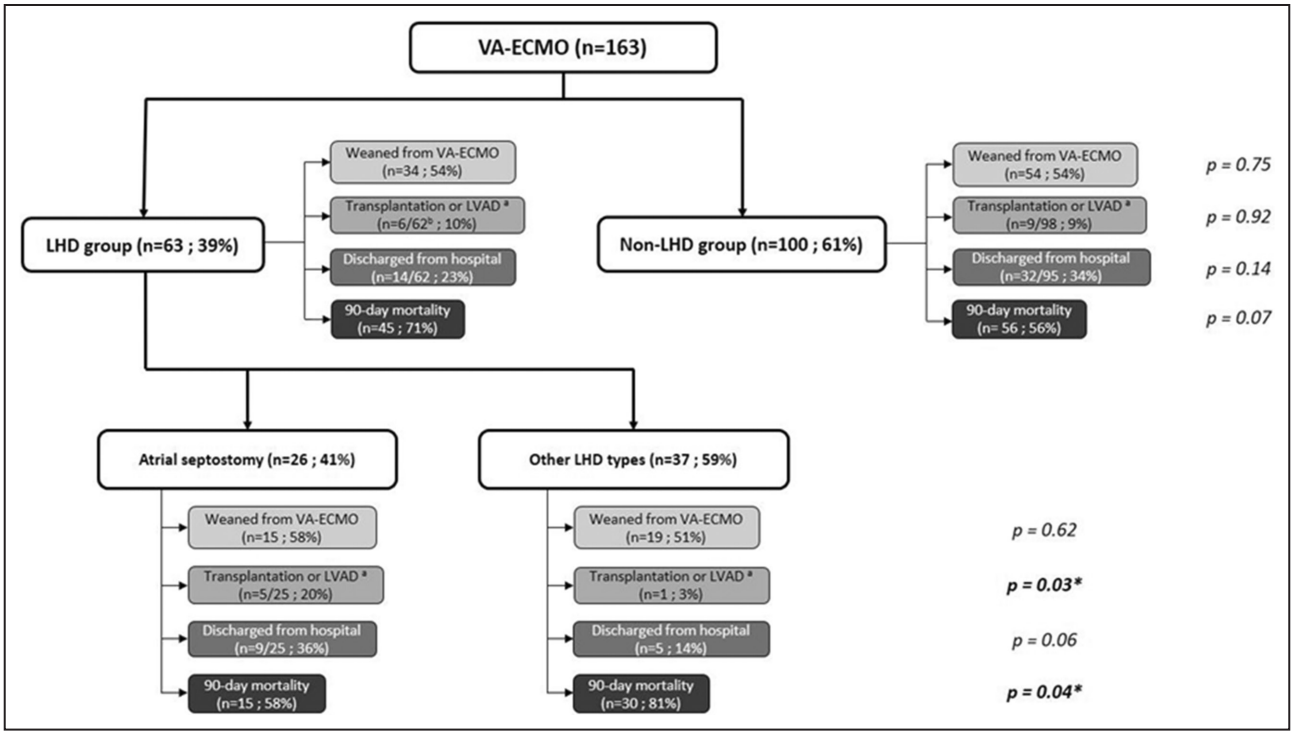

Figure 1. Flowchart.

[a]At 90 days. [b]In case of missing data, the ratio of cases over the total number is indicated before the percentage. LHD indicates left heart decompression; LVAD, left ventricular assist device; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

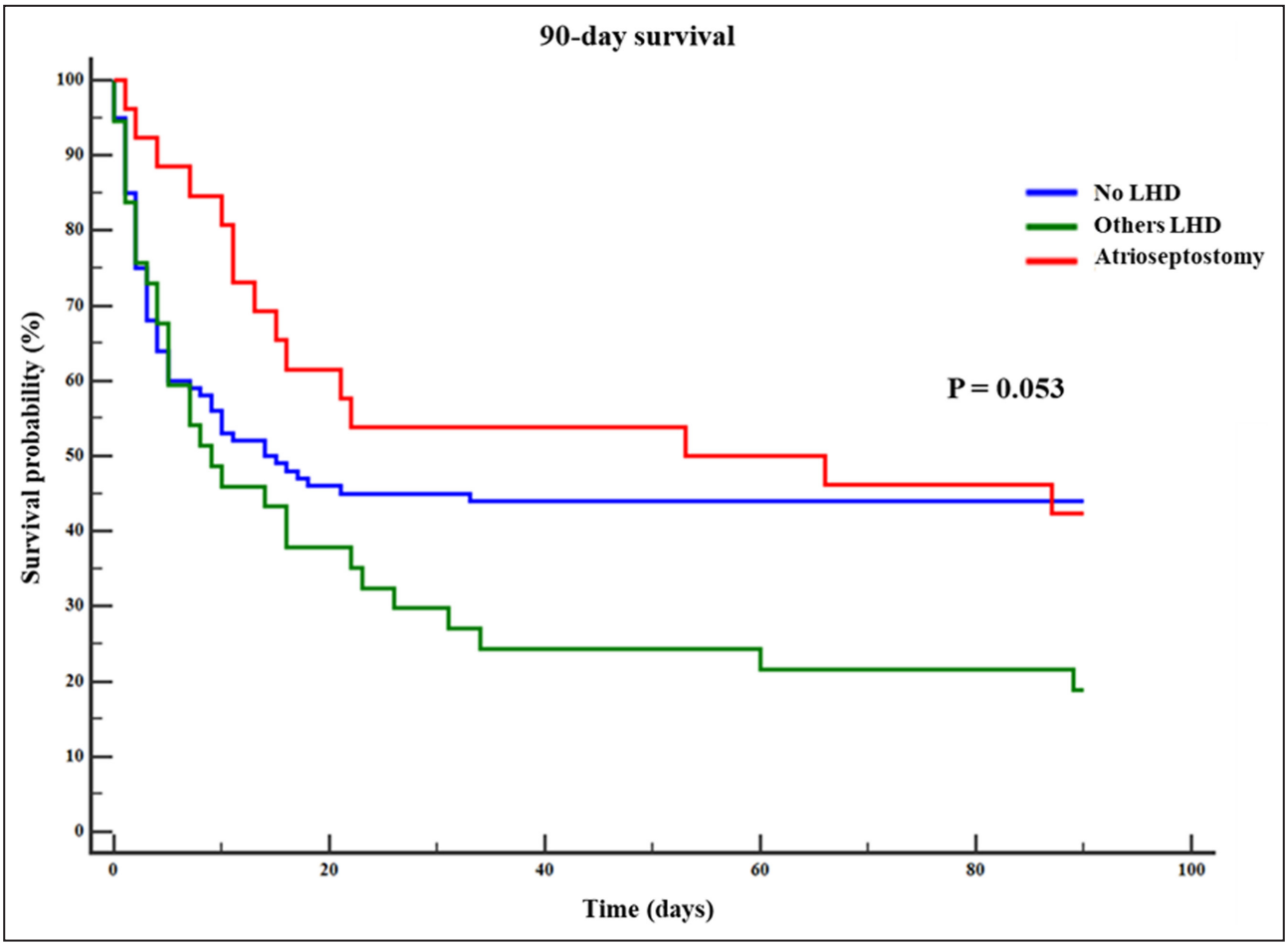

Figure 2. Kaplan-Meier curves describing 90-day survival of patients who underwent veno-arterial extracorporeal membrane oxygenation (VA-ECMO) without left heart decompression (LHD) (blue) and discharged by atrioseptostomy (red) versus other discharges (green).

The other discharges were represented by an intra-aortic balloon pump and/or a microaxial flow pump, and/or a LHD surgical technique (addition of a left intraventricular cannula to the VA-ECMO venous circuit through a transvalvular aortic cannula through a subclavian artery or axillary artery, or directly through the left ventricle by transapical thoracotomy or sternotomy). *P* value is unadjusted.

survival without a ventricular assist device or transplantation at 90 days (*P*=0.069) (Figure 4).

Factors related to 90-day mortality are reported in Table S3 and Table S4. PA was independently associated with a higher 90-day survival (hazard ratio [HR], 2.53 [1.17–5.45]; *P*=0.019 in Model 1 and HR, 1.99 [1.03–3.85]; *P*=0.041 in Model 2).

At 90 days follow-up, for surviving patients after extracorporeal membrane oxygenation withdrawal and without a left ventricular assist device or heart transplantation, significant left-to-right atrial shunting was present in only 1 out of 6 (17%) and spontaneously disappeared at 6 months.

DISCUSSION

In this large monocentric series of 163 patients who underwent VA-ECMO supported for RCS or RCA, 39% required LHD (60% on preventive and 40% on curative grounds). LHD was more frequently used in cases of acute or chronic ischemic cardiomyopathy and in cases of lower LVEF. LHD was associated with more bleeding and longer duration of intensive care unit stay but not with difference in 90-day survival. PA was the most used LHD technique in our series, corresponding to 41% of first-line and 57% of second-line LHD. It was associated with fewer neurological complications, no need to insert a second-line LHD, and a 1.4-fold higher 90-day survival compared with other LHD techniques, despite more sepsis and more red blood cell transfusions.

In our classic population of patients who underwent VA-ECMO, despite more previous cardiac arrest (51.7% versus 44.5%) and a lower LVEF (10% versus 29.8%) at VA-ECMO initiation,[12] our population's prognosis was consistent with the literature, with 54% weaned (versus

Table 2. Methods of Performing the Percutaneous Balloon Atrioseptostomy

Atrioseptostomy, n=26	
Implantation site	
Catheterization laboratory	23 (89%)*
Electrophysiology laboratory	2 (8%)
Operating room	1 (4%)
Guiding technique	
Radiograph	24/24 (100%)
TTE	2/24 (8%)
TEE	7/24 (29%)
Balloon size	
10 mm	1/22 (5%)
14 mm	1/22 (5%)
15 mm	16/22 (73%)
18 mm	4/22 (18%)
Radiography time, min	6.3 (5.8–10)†,‡
Total duration of the procedure, min	37.5 (31.8–49.3)‡
Left atrial pressure, mm Hg, n=8	
Before PA	23.5 (19.8–26.3)†
After PA	14.5 (14–16.3)†

PA, percutaneous atrioseptostomy; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography.

*Copied result n/N (%), n being the number of cases, N the total number, and (%) the ratio of cases over the total number expressed as a percentage.

†Copied result M (25–75), M being the median and 25–75 the interquartile range.

‡Patients for whom another procedure was performed at the same time as the atrioseptostomy were not included in these results.

56% in the Extracorporeal Life Support Organization registry[4]) and 62% deaths at 3 months (versus 60% in a recent extensive meta-analysis[12]).

At this time, there is no consensus or recommendation on the most efficient LHD technique,[8] the optimal strategy (preventive or curative),[13] or the best implantation timing (before, during, after initiation of VA-ECMO).[12,14] Although our percentage of patients with LHD approaches that of a recent large meta-analysis[12] (39% versus 42%), IABP was almost exclusively used (92%), far ahead other LHD techniques. Interestingly, PA was not mentioned. In our cohort, IABP and PA were the preferential LHD techniques used (43% and 41% of first-line LHD, respectively), followed by AFP (13%), whereas surgical discharges were exceptional (3%), likely because of the noninclusion of patients with postcardiotomy shock. LHD was more frequently used in cases of RCS/RCA following myocardial infarction as previously described,[12] but also more frequently in case of previous severe ischemic cardiomyopathy and severe LVEF alteration. It is in these patients, whose residual left cardiac function is more precarious, that LV overload, brought on by VA-ECMO, may entail the greatest risk of pulmonary edema and LV or aortic root thrombosis, thereby worsening their prognosis.[7,15] We did not find any difference in terms of VA-ECMO weaning or mid-term outcomes between LHD and non-LHD groups, contrary to a recent meta-analysis[14] suggesting that LV unloading may be associated with more VA-ECMO weaning and lower short-term mortality in cases of early LHD implantation (<12 hours after VA-ECMO initiation). Furthermore, we did not find a mortality difference between curative and preventive LHD contrary to a previous report.[13] However, comparing these results remains elusive, because the type of LHD and definitions used for preventive/curative LHD are not standardized.[8]

Interestingly, we found a significant and independent association between PA use and 90-day survival compared with other LHD techniques when results were adjusted for body mass index, RCS cause (recent myocardial infarction or tachycardia-induced cardiomyopathy), prior cardiac arrest, or time under mechanical ventilation at LHD realization. The nonsignificant association found between the PA and 90-day survival (versus other LHD techniques and patients not decompressed, P=0.053) or between the PA and 90-day survival without a ventricular assist device or transplant at 90 days (versus other LHD techniques, P=0.0692), tends to confirm the potential beneficial effect of the PA. However, the small sample size limits the inclusion of more potential confounding factors in the multivariate analysis and precludes a definite conclusion.

LHD-associated complications are frequent, but depend on LHD type, expertise, and skills. Hemolysis is a well-documented side effect for AFP[16] and IABP,[17] but surprisingly seemed also associated with PA, even if thrombocytopenia is less profound. Previous pediatric series[11] reported potentially severe complications during a PA procedure in 9.4% of patients (pericardial effusion, supraventricular and ventricular arrhythmias), which were not found in our series. However, we report more transfusions and sepsis in our PA population, without obvious explanations. Interestingly, although there was a trend toward more LV thrombus, PA was associated with >3 times fewer neurological complications.

Thanks to a trained team, PA emerged as a quick and safe procedure, with a median radiograph time of 6.3 minutes (versus 13.8 minutes in previous series[11]) and a median total procedure time of 37.5 minutes. However, to perform PA safely, an interventional cardiologist trained in percutaneous rhythmological (transcatheter ablation of atrial fibrillation or ventricular tachycardia) or cardiac structural (transcatheter mitral valve repair, for example) interventions is necessary. Experience with transseptal puncture is mandatory, because the venous cannula of the VA-ECMO system can complicate its realization. Multimodality imaging by fluoroscopy and transesophageal echocardiography can help guide the interventional cardiologist. In some cases, a decrease in

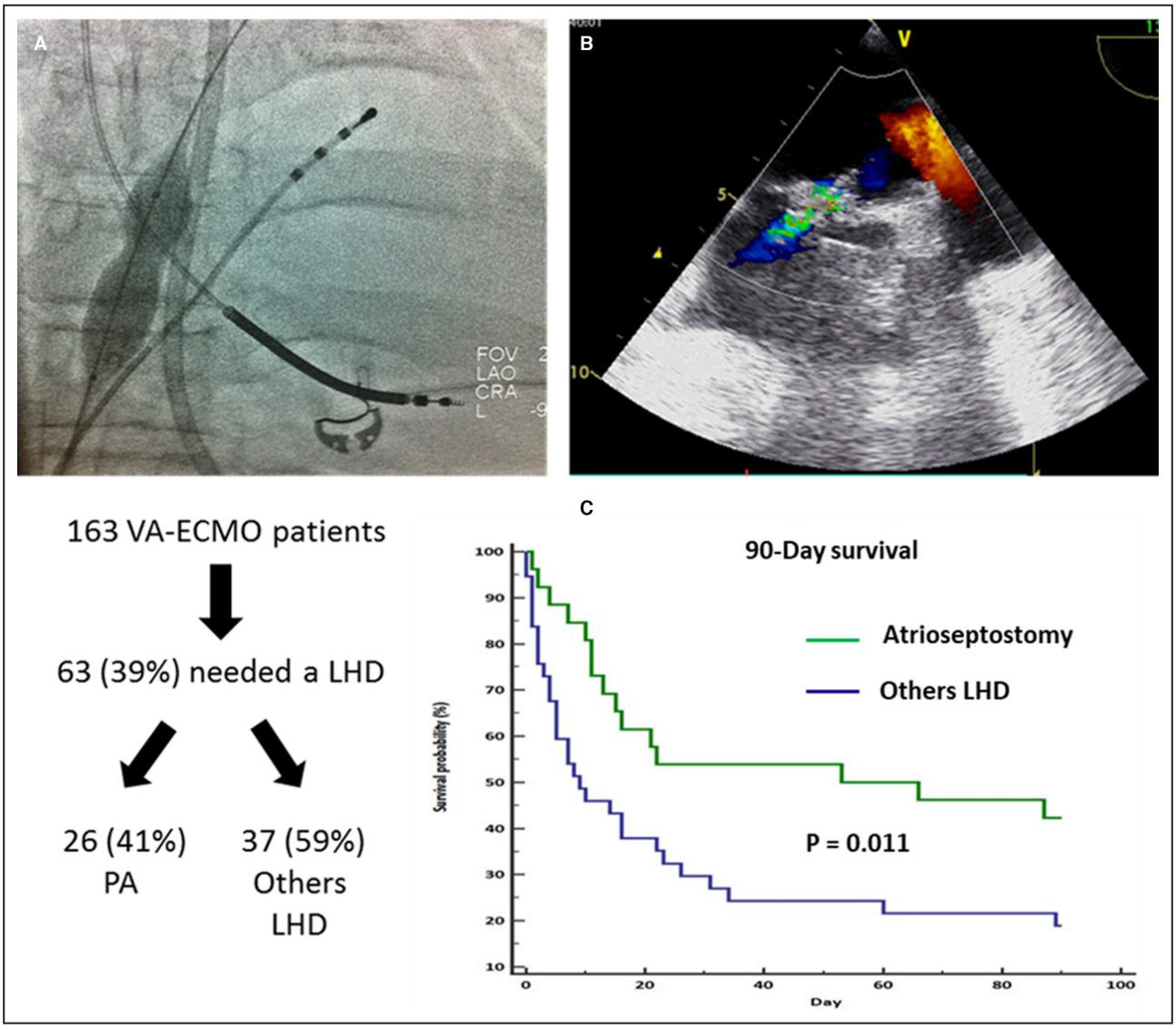

Figure 3. Central illustration.
Percutaneous balloon atrioseptostomy realization under fluoroscopic (**A**) and Doppler color transesophageal echocardiography guidance (**B**). Kaplan-Meier curves describing 90-day survival for patients who underwent veno-arterial extracorporeal membrane oxygenation (VA-ECMO) discharged by atrioseptostomy (green) versus other discharges (blue) (**C**). *P* value is unadjusted. LHD indicates left heart decompression; and PA, percutaneous atrioseptostomy.

the VA-ECMO flow facilitating the reloading of the right atrium is necessary to allow the delivery of the material and the creation of the interatrial shunt.

The mid-term persistence of interatrial shunting following PA may expose to a theoretical risk of ischemic cerebrovascular accident and dilation of the right heart cavities. However, a mid-term spontaneous closure was previously described in 20% of the patients,[18] and after 4 years of follow-up, no increased risk of stroke was found in a large congenital pediatric population.[19] Only 1 persistent atrioseptostomy was found at 3 months and disappeared at 6 months in our series. In case of interatrial shunting persistence, a close cardiological follow-up may be proposed to allow a potential percutaneous closure in rare symptomatic case.

Limitations

This study was a retrospective observational analysis that comes from a prospective registry, limiting definite conclusions. This was a monocentric series with a highly heterogeneous population in terms of VA-ECMO and LHD indications, reflecting our local habits, and extrapolating these results to other groups and settings should remain prudent. The lack of consensus or recommendations in terms of indication, type of LHD, and timing (preventive versus curative) reinforce

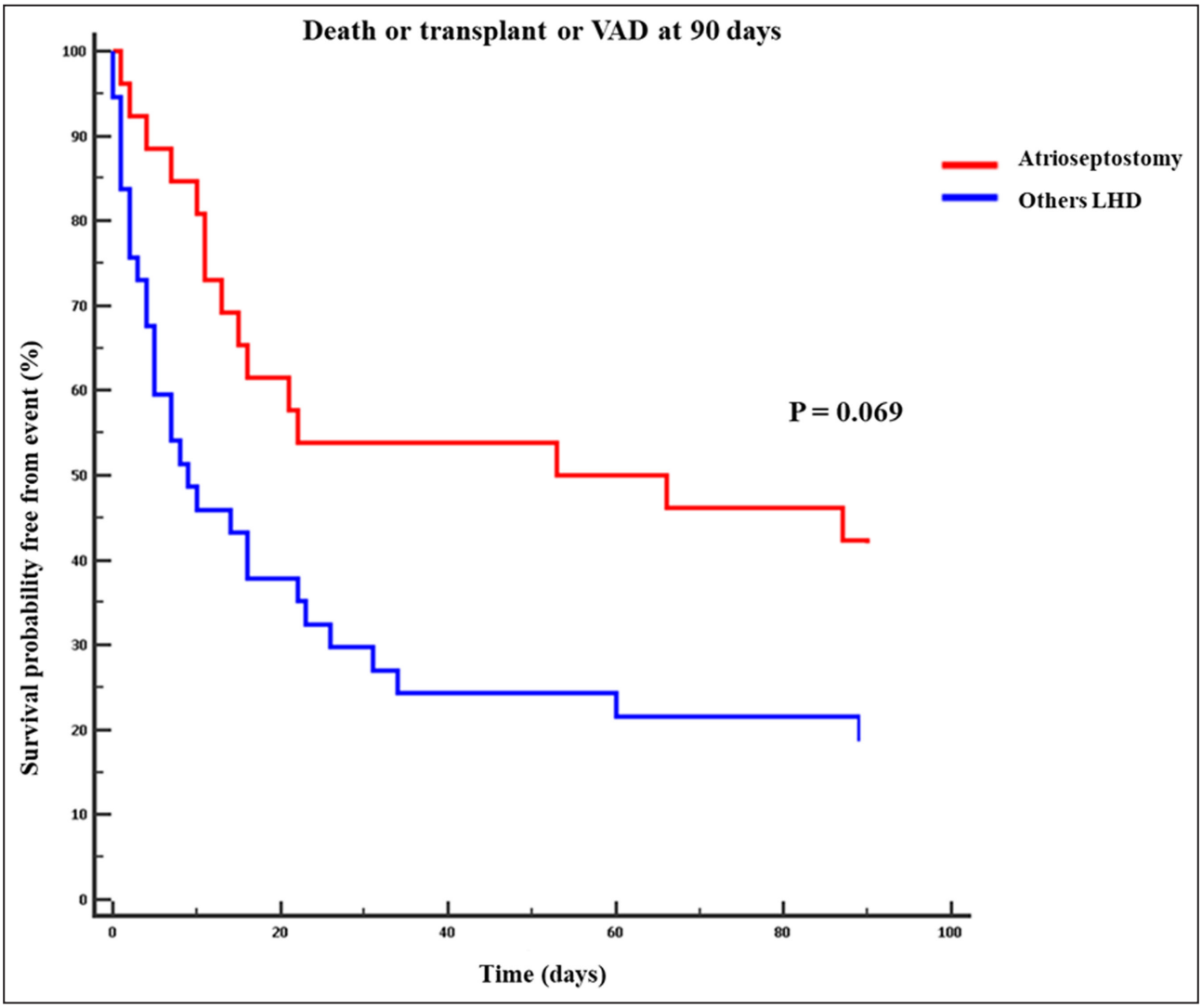

Figure 4. Kaplan-Meier curves describing survival free from ventricular assist device (VAD) or transplant at 90 days according to the type of left heart decompression (LHD): percutaneous atrioseptostomy (red) and others type of left heart decompression (blue).

The other discharges were represented by an intra-aortic balloon pump and/or a microaxial flow pump, and/or an LHD surgical technique (addition of a left intraventricular cannula to the veno-arterial extracorporeal membrane oxygenation venous circuit through a transvalvular aortic cannula through a subclavian artery or axillary artery, or directly through the left ventricle by transapical thoracotomy or sternotomy). *P* value is unadjusted.

the central effect to which we must add local expertise, which likely limits procedure times and complications. A dedicated randomized trial comparing VA-ECMO support with versus without LV unloading in patients with RCS and RCA would be needed, but difficult to achieve. Subanalysis of ongoing prospective randomized studies studying VA-ECMO in severe cardiogenic shock (EURO-SHOCK [Testing the Value of Novel Strategy and Its Cost Efficacy in Order to Improve the Poor Outcomes in Cardiogenic Shock] [NCT03813134], ANCHOR [Assessment of ECMO in Acute Myocardial Infarction Cardiogenic Shock] [NCT04184635], and ECLS-SHOCK [Extracorporeal Life Support in Cardiogenic Shock] [NCT03637205]) may give some clues. A multicentric observational analysis on a more extensive population could allow collecting similar patients based on severity level, cause of shock, LHD type, and implantation time, and to draw more solid conclusions on the potential interest of one type of discharge in relation to another. Finally, the relatively low cost of atrioseptostomy is also an element to be considered when choosing LHD in limited health care systems, even if it was not studied in this series.

CONCLUSIONS

In this large monocentric observational series of refractory cardiogenic shock and cardiac arrest supported by VA-ECMO, LHD was required in almost 40% of the cases. It was notably used in cases of acute or chronic ischemic cardiomyopathy and in case of low LVEF. Percutaneous balloon atrioseptostomy seems to be a fast, safe, and efficient LHD technique, associated with greater mid-term survival. Further multicenter studies are needed to confirm these results.

ARTICLE INFORMATION

Received November 9, 2021; accepted June 28, 2022.

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Acknowledgments

The authors thank the resuscitation, cardiology, and cardiac surgery teams involved in the care of these patients. The authors convey special thanks to L. Bru, L. Regis, and Dr Pichon, who helped us greatly in collecting and analyzing the data necessary for this work.

Sources of Funding

This research received no external funding.

Disclosures

None.

Supplemental Material

Data S1
Tables S1–S4
Figures S1–S2

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SUPPLEMENTAL MATERIAL

Data S1. Supplemental Methods

VA-ECMO management protocol

VA-ECMO indications and management were based on our local protocol and available guidelines through a multidisciplinary team including cardiologists, intensivists, and cardiac surgeons. Briefly, VA-ECMO was discussed for RCS defined by persisting mismatch between oxygen supplies and tissue needs due to a pump dysfunction despite inotrope and/or vasopressor perfusion. In case of RCA, VA-ECMO implantation was discussed only for selected patients (≤ 70 yo, witnessed cardiac arrest, BMI < 40 kg/m², end-tidal CO2 > 10 mmHg, pH level > 6.9 and lactatemia < 25 mmol/L at ICU arrival). Contra-indications to VA-ECMO were common: age > 80 years; anticoagulation contraindication; severe peripheral artery disease; significant aortic regurgitation; life expectancy less than 5 years due to associated chronic or acute illness and severe post anoxic coma. Anticipated directives were also taken into consideration.

VA-ECMO was initiated under general anesthesia by femoral approach thanks to a modified Seldinger technique. The circuit used includes a venous inflow cannula (23 to 29 Fr) inserted up to the inferior vena cava - right atrium junction, a SORIN® centrifuge pump with a D905® oxygenator (or a MAQUET® centrifuge pump with a QUADROX® oxygenator), and an arterial outflow cannula (19 to 21 Fr) inserted up to the common iliac artery with systemic insertion of a reperfusion cannula (7 Fr) for the ipsilateral superficial femoral artery. The initial output is adjusted to the theoretical cardiac output (70/mL/kg/min) then to a target MAP ≥ 65 mmHg (after volume loading and vasopressors, if necessary). Inotrope support with dobutamine could be continued to maintain an aortic valve opening. Curative anticoagulation was started by intravenous unfractionated heparin for a target anti-Xa level between 0.2 and 0.4 IU/mL. The decision to wean the patient from VA-ECMO depends on a set of clinic-biological and ultrasound criteria assessed by daily weaning trial at a minimum VA-ECMO output of 1.5-2 L/min.

Characteristics of left heart decompression used (9)

The IABP (AutoCAT 2 Wave TELEFLEX®) is implanted in the descending aorta then connected to an electrocardiogram in order to inflate the balloon with helium during protodiastole and deflate it during telediastole, thereby reducing the LV afterload while increasing diastolic blood pressure (DBP) and thus coronary and cerebral perfusion.

The micro-axial flow pump Impella (Abiomed, Danvers, MA, USA) is a catheter-based LV assist device which is inserted into the LV cavity via arterial access (axillary or subclavian acess in case of Impella 5.0, and femoral access in case of Impella CP). From that position, it actively drains blood from the LV and propels it into the proximal ascending aorta, thereby decreasing LV preload and increasing cardiac output.

Percutaneous atrioseptostomy (PA) involves creating a left-right shunt through perforation of the interatrial septum after femoral vein catheterization. PA was performed under fluoroscopic guidance in the hemodynamical or electrophysiological laboratories, with the help of trans-oesophageal echocardiography when needed. After femoral venous catheterization, transseptal puncture was performed according to usual techniques (10) with a SLO sheath (St Jude Medical ™) and Brokenbrough needle, under common fluoroscopic landmarks and/or pressure monitoring. Of note that transseptal puncture was sometimes especially tricky in this situation, due to the presence of the ECMO venous canula, anticoagulation and dilated/distorted cardiac anatomy. Then an aortic valvuloplasty balloon (diameter 10 to 18 mm) was mounted over a 0.32 mm guidewire positioned in the left superior pulmonary vein. The sheath was then removed into the right atrium and the balloon was inflated at the level of the transseptal puncture in order to create an inter-atrial communication and thus maintain a significant left-right shunt (11).

The surgical decompression is the addition of a left intraventricular cannula to the venous circuit of the VA-ECMO by surgical approach: a transvalvular aortic cannula by a subclavian artery or axillary approaches , or directly through the LV by transapical thoracotomy or sternotomy.

The different LHD techniques were implemented and checked under x-ray and/or ultrasound guidance (transesophageal echo (TEE) or transthoracic echo (TTE)).

Table S1. Comparison of characteristics of cardiogenic shock or refractory cardiac arrest VA-ECMO patients with vs without left heart decompression

	General population n=163	Non-LHD group n=100 (61%)	LHD group n=63 (39%)	*p-value*
Demographic data				
Male	113 (69%)*	65 (65%)	48 (76%)	*0.133*
Age (years)	55 (42 – 61) †	52 (36 – 62)	57 (47 – 60)	*0.091*
BMI (kg/m²)	25.9 (22.8 – 29.4)	25.3 (22 – 29)	26.6 (24 – 30)	*0.071*
Previous known heart disease				
Ischemic	61 (37%)	29 (29%)	32 (51%)	*0.053*
Dilated	20 (12%)	11 (11%)	9 (14%)	*0.535*
Hypertrophic	12 (7%)	10 (10%)	2 (3%)	*0.105*
Valvular	11 (7%)	8 (8%)	3 (5%)	*0.424*
Tachycardia induced cardiomyopathy	17 (10%)	9 (9%)	8 (13%)	*0.453*
None	50 (31%)	32 (32%)	18 (29%)	*0.645*
Cardiovascular risk factors				
Hypertension	54 (33%)	32 (32%)	22 (36%)	*0.648*
Diabetes	24 (15%)	15 (15%)	9 (14%)	*0.901*
Smoking	87 (53%)	49 (49%)	38 (60%)	*0.160*
Dyslipidemia	40 (25%)	23 (23%)	17 (27%)	*0.527*
Indication for VA-ECMO				
RCS / RCA	110 (68%) / 53 (32%)	68 (68%) / 32 (32%)	42 (67%) / 21 (33%)	*0.269*
Etiology of the RCS				
End-stage heart failure	18 (11%)	10 (10%)	8 (13%)	*0.799*
Recent myocardial infarction	44 (27%)	16 (16%)	28 (44%)	***<0.001***
Drug overdose	13 (8%)	13 (13%)	0 (0%)	***0.002***
Electrical storm	24 (15%)	15 (15%)	9 (14%)	*0.999*
Other (pulmonary embolism, ARDS, etc.)	31 (19%)	24 (24%)	7 (11%)	*0.069*

Severity score at initiation				
ENCOURAGE	22 (14.2 – 27.8)	21 (14 – 27)	23 (17 – 28)	*0.425*
SOFA	11 (9 – 13)	12 (9 – 13)	10 (9 – 12)	*0.192*
SAPS2	68.5 (55 – 79)	68 (54 – 78)	70 (57 – 80)	*0.571*
Therapeutics at initiation				
Noradrenaline	94 (58%)	62 (62%)	32 (51%)	*0.144*
Adrenaline	104/161 (65%) ‡	60/98 (61%)	44 (70%)	*0.245*
Dobutamine	60 (37%)	32 (32%)	28 (44%)	*0.135*
RRT	7 (4%)	7 (7%)	0 (0%)	*0.146*
Mechanical ventilation	149 (91%)	94 (94%)	55 (87%)	*0.132*
RCA before initiation of VA-ECMO				
Prior cardiac arrest	93 (57%)	56 (56%)	37 (59%)	*0.747*
Out-of-hospital RCA	36 (22%)	25 (25%)	11 (17%)	*0.342*
No flow > 5 min	9/87 (10%)	6/51 (12%)	3/36 (8%)	*0.727*
Bilateral mydriasis at initiation	35/149 (23%)	28/94 (30%)	7/55 (13%)	***0.018***
Clinical and biological data at initiation of VA-ECMO				
HR (bpm)	73.5 (0 – 111)	57 (0 – 115)	90 (0 – 110)	*0.627*
MAP (mmHg)	50 (0 – 67)	50 (0 – 65)	55 (0 – 70)	*0.383*
LVEF (%)	10 (5 – 20)	10 (5 – 25)	10 (5 – 15)	***0.009***
Arterial blood pH	7.21 (7.05 – 7.35)	7.19 (7.03 - 7.35)	7.22 (7.1- 7.33)	*0.815*
PaO2 (mmHg)	108 (74.7 – 267.5)	113 (77 – 255)	105 (72.7 – 279)	*0.947*
PaCO2 (mmHg)	39.6 (30 – 49)	39.2 (30.9 – 50.3)	40 (29 – 47)	*0.593*
Lactatemia (mmol/L)	7.1 (3.2 – 14.3)	6.7 (3.8 – 14)	8.3 (3 - 14.9)	*0.903*
Serum creatinine (µmol/L)	135 (103 – 171.5)	138 (103 - 177)	127.5 (103 – 164)	*0.648*
ASAT (IU/L)	184 (62.5 – 611.5)	184 (79 – 612)	229 (47 – 647)	*0.935*
ALAT (IU/L)	107.5 (56 – 370.5)	105 (48 – 403)	112 (57 – 338)	*0.877*

PT (%)	55 (39 – 69)	52.5 (40 – 69)	55 (36 – 71)	*0.977*
Hemoglobin (g/dL)	12.5 (10.1 – 15.0)	12.3 (10.2 – 14)	12.6 (10.1 - 15.2)	*0.508*
Blood product transfusions during hospitalization				
pRBCs	8 (3 -13)	6 (2 – 11)	10 (5 – 17)	***<0.001***
Fresh frozen plasma	2 (0 – 6)	0.5 (0 – 6)	3 (0 – 6)	*0.063*
Platelet concentrates	1 (0 – 8)	1 (0 – 7)	3 (0 – 12)	***0.006***
Complications				
Neurological complications	40 (25%)	23 (23%)	17 (27%)	*0.583*
Sepsis	122 (75%)	70 (70%)	52 (83%)	*0.181*
RRT	56 (34%)	29 (29%)	27 (43%)	*0.094*
LV thrombus	13 (8%)	7 (7%)	6 (10%)	*0.768*
Evolution				
Duration of ICU stay (days)	16.5 (11 – 28)	13 (9 – 21)	28 (15 – 40)	***0.007***
Length of hospital stay (days)	36.5 (23.3 – 53.3)	35 (21 – 51)	41 (29 – 58)	*0.251*
Duration of VA-ECMO (days)	6 (4 - 10)	5 (3 – 7)	10 (6.3 – 16)	***<0.001***
Weaning VA-ECMO	88 (54%)	54 (54%)	34 (54%)	*0.9969*
Transplant or chronic assistance at 3 months	15/160 (9%)	9/98 (9%)	6/62 (10%)	*0.921*
Death at D90	101 (62%)	56 (56%)	45 (71%)	*0.066*

*Copied result N (%), N being the number of cases and (%) the ratio of cases over the total number, expressed as a percentage

† Copied result M (25 – 75P), M being the median and 25 – 75P the interquartile range ‡ When data are missing, the case/total ratio is indicated before the percentage ()

ALAT: alanin aminotransferase; ASAT: aspartate aminotransferase; ARDS: acute respiratory distress syndrome; bpm: beats per minute; BMI: body mass index; D: day; HR: heart rate; ICU: intensive care unit; LHD: left heart decompression; LV: left ventricle; LVEF: left ventricular ejection fraction; MAP: mean arterial pressure; pRBCs: packed red blood cells; PACO2: partial pressure of carbon dioxide; PaO2: partial pressure of oxygen; PT: prothrombin time; RCA: refractory cardiac arrest; RCS: refractory cardiogenic shock; RRT: renal replacement therapy; SAPS2: simplified acute physiology score 2; SOFA: sequential organ failure assessment; VA-ECMO: veno-arterial extracorporeal membrane oxygenation

Table S2. Progression of the variables of interest during the first 48 hours after introduction of the left heart decompression

	Total LHD population (n=63)			Atrioseptostomy (n=26)			Other LHD (n=37)		
	M(25-75p)	Friedman test p	p<0.05 between variables	M(25-75p)	Friedman test p	p<0.05 between variables	M(25-75p)	Friedman test p	p<0.05 between variables
				Lactatemia (mmol/L)					
H0*	4.5 (1.7-8.8)†		(H48)	3.0 (1.7 – 9.7)		NA‡	6.5 (3.5 – 11.9)		(H48)
H24	3.2 (1.7-4.9)	***0.012***	(H48)	2.8 (2 – 4.4)	*0.103*	NA	3.8 (1.7 – 6.0)	***0.017***	NS§
H48	2.1 (1.5-3.5)		(H0) (H24)	1.9 (1.5 – 2.8)		NA	2.1 (1.5 – 4.3)		(H0)
				Arterial blood pH					
H0	7.31 (7.23 - 7.430)		(H24) (H48)	7.31 (7.23 – 7.43)		(H48)	7.23 (7.12 – 7.34)		(H24) (H48)
H24	7.38 (7.34 - 7.440)	***<0.001***	(H0)	7.37 (7.34 – 7.44)	***0.029***	NS	7.38 (7.29 – 7.42)	***0.011***	(H0)
H48	7.43 (7.35 - 7.475)		(H0)	7.44 (7.38 – 7.48)		(H0)	7.42 (7.36 – 7.47)		(H0)
				Total bilirubin (mmol/L)					
H0	13.2 (6.5 - 23.8)		(H24) (H48)	18.2 (11.8 – 34.6)		(H48)	14.3 (6.5 – 20.9)		(H24) (H48)
H24	18.2 (12.7 - 35.1)	***<0.001***	(H0) (H48)	23.9 (13 – 50.2)	***<0.001***	NS	26.1 (14.5 – 36.1)	***<0.001***	(H24)
H48	24.5 (15.5 - 57.8)		(H0) (H24)	57.8 (21.8 – 89)		(H0)	32.4 (21.5 – 45)		(H48)
				Hemoglobin (g/dL)					
H0	11.6 (9.7 – 14)	***<0.001***	(H24) (H48)	10.8 (9.2 – 12.8)	***0.006***	(H24) (H48)	12.4 (10.8 – 14.9)	***<0.001***	(H24) (H48)
H24	10 (8.6 – 11)		(H0)	10.0 (8.7 – 11.0)		(H0)	9.9 (8.5 – 11.7)		(H0)

			(H48)						(H48)
H48	9.1 (8.2 - 10.2)		(H0) (H24)	9.0 (8.6 – 10.3)		(H0)	9.4 (8.1 – 10.2)		(H0) (H24)
Platelets (G/L)									
H0	140 (107 – 219)		(H24) (H48)	121 (98 – 79)		(H48)	217 (155 - 335)		(H24) (H48)
H24	108 (75 – 171)	***<0.001***	(H0) (H48)	103 (71 – 171)	***0.004***	NS	116 (82 – 63)	***<0.001***	(H0) (H48)
H48	93 (76 – 119)		(H0) (H24)	93 (85 - 121)		(H0)	94 (73 – 115)		(H0) (H24)
Serum creatinine (µmol/L)									
H0	122 (91 – 161)		NA	124 (78 – 168)		NA	124 (99 – 159)		NA
H24	144 (87 – 201)	0.626	NA	153 (99 – 205)	0.781	NA	137 (87 – 205)	0.715	NA
H48	131 (97 – 225)		NA	129 (108 - 216)		NA	131 (87 – 259)		NA
Diuresis during the last 24 hours									
H0	1350 (275-2400)		(H24)	1350 (720 – 2455)		NA	413 (65 – 1495)		NA
H24	1700 (809-2740)	***0.027***	(H0) (H48)	1540 (848 – 2425)	*0.277*	NA	1835 (615 – 2893)	**0.047**‖	NA
H48	1308 (968-1850)		(H24)	1355 (998 – 2413)		NA	1550 (1005 – 2366)		NA

***** H0; H24; H48: data at the time of LHD introduction; 24 hours after; 48 hours after

† Copied result M (25 – 75P), M being the median and 25 – 75P the interquartile range

‡ NA: not applicable

§ NS: non-significant

‖ Significant Friedman test but multiple comparisons of non-significant pairs

Table S3. Characteristics that affect 90-day mortality for VA-ECMO patients with left heart decompression based on multivariable Cox proportional-hazard model 1

Covariate	Exp(b)*	95% CI of Exp(b)	p-value
Percutaneous atrioseptostomy (vs others LHD)	**2.53**	**1.17 to 5.45**	**0.019**
Prior cardiac arrest	0.80	0.42 to 1.53	0.504
Tachycardia induced cardiomyopathy	1.50	0.50 to 4.44	0.469
BMI (kg/m^2)	1.01	0.95 to 1.08	0.781

BMI, body mass index; CI confidence interval; LHD, left heart decompression

*For a continuous covariate, Exp(b) is the increase of the hazard ratio for 1 unit change of the continuous variable. Note that when b is negative, then Exp(b) is less than 1 and Exp(b) is the decrease of the hazard ratio for 1 unit change of the continuous variable. For a dichotomous covariate, Exp(b) is the hazard ratio.)

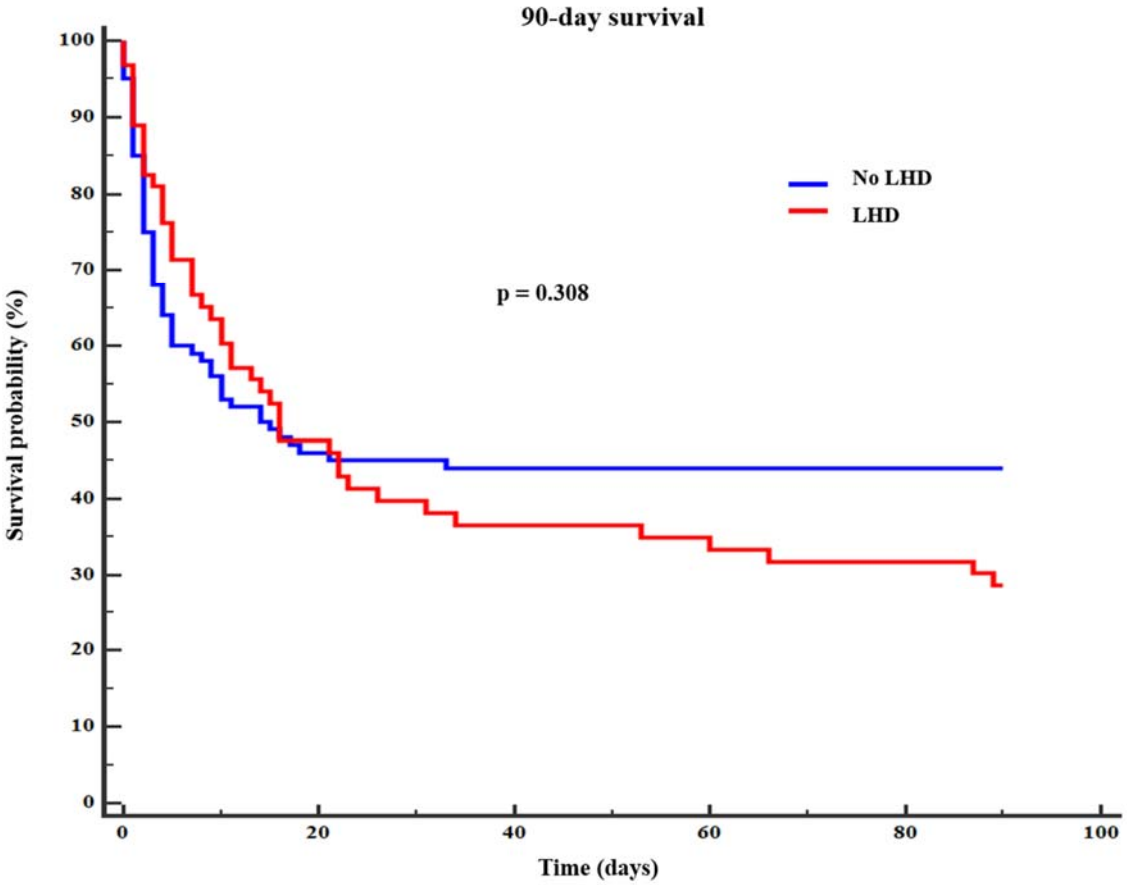
Table S4. Characteristics that affect 90-day mortality for VA-ECMO patients with left heart decompression based on multivariable Cox proportional-hazard model 2

Covariate	Exp(b)	95% CI of Exp(b)	p-value
Percutaneous atrioseptostomy (vs others LHD)	**1.99**	**1.03 to 3.85**	**0.041**
Time under MV before LHD performance (days)	0.99	0.61 to 1.61	0.982
Recent myocardial_infarction	1.16	0.63 to 2.16	0.637
Curative LHD indication (vs prophylactic)	1.05	0.55 to 2.04	0.876

CI confidence interval; LHD, left heart decompression; MV, mechanical ventilation

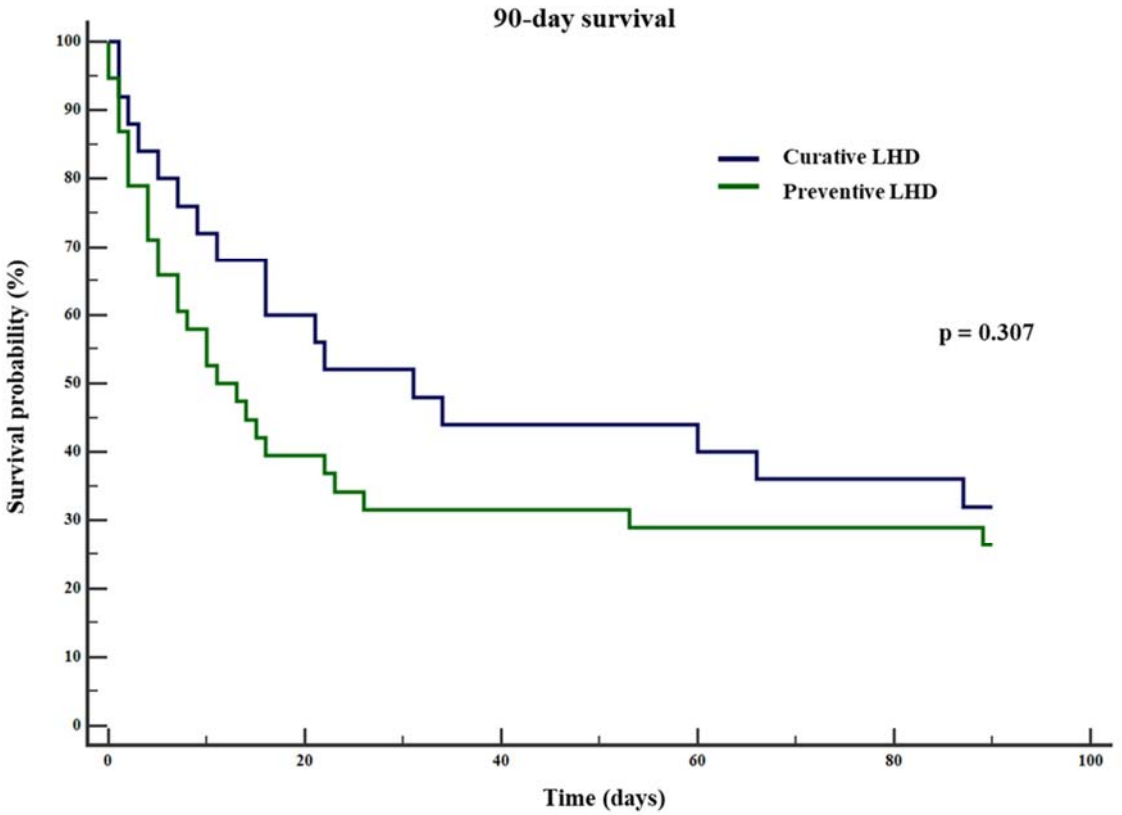
*****For a continuous covariate, Exp(b) is the increase of the hazard ratio for 1 unit change of the continuous variable. Note that when b is negative, then Exp(b) is less than 1 and Exp(b) is the decrease of the hazard ratio for 1 unit change of the continuous variable. For a dichotomous covariate, Exp(b) is the hazard ratio.)

Figure S1. Kaplan-Meier curves describing 90-day survival for patients on VA-ECMO for cardiogenic shock or refractory cardiac arrest with (red) vs without (blue) left heart decompression



Decompressed patients associated each patient one or more left heart decompression technic used during VA-ECMO support.Time is provided in days. “p-value” is unadjusted. LHD, left heart decompression.

Figure S2. Kaplan-Meier curves describing survival at 90-day for patients on VA-ECMO according to curative (blue) vs prophylactic (green) left heart decompression indication for decompressed patients



In case of refractory and critical pulmonary congestion, a "curative" LHD was introduced. In case of severely depressed left ventricular ejection fraction (LVEF), low differential arterial pressure (<5-10 mmHg), major distention of the left ventricle, or absence of aortic valve opening, a "preventive" LHD was considered. Time is provided in days. "p-value" is unadjusted. LHD, left heart decompression.