ORIGINAL ARTICLE

Impact of a surgical approach for implantation of durable left ventricular assist devices in patients on extracorporeal life support

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Abstract

Background: The aim of this study was to evaluate the impact of the surgical approach on the postoperative outcome in patients who underwent left ventricular

Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; CRP, C-reactive protein; ECLS, extracorporeal life support; EUROMACS, European Registry for Patients with Mechanical Circulatory Support; FFP, fresh frozen plasma; FS, full sternotomy; HLM, heart-lung machine; HTx, heart transplantation; ICM, ischaemic cardiomyopathy; ICU, intensive care unit; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; IQR, interquartile range; LIS, less invasive surgery; LVAD, left ventricular assist device; MCS, mechanical circulatory support; OR, odds ratio; RV, right ventricle; RVF, right ventricular failure; *SD*, standard deviation; SHR, subdistribution hazard ratio; VAD, ventricular assist device; va-ECLS, veno-arterial extracorporeal life support.

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assist device (LVAD) implantation after having received veno-arterial extracorporeal life support (va-ECLS) using data from a European registry (ECLS-VAD). Five hundred and thirty-one patients were included.

Methods: A propensity score-adjusted outcome analysis was performed, resulting in 324 patients in the full sternotomy (FS) group and 39 in the less invasive surgery (LIS) group. **Results:** The surgery lasted in median 236 min in the FS group versus 263 min in the LIS group (p = 0.289). The median chest tube output during the first 24 h was similar in both groups. Patients who underwent implantation with an FS required more blood products during the first 24 postoperative hours (median 16 vs. 12, p = 0.033). The incidence of revision due to bleeding was also higher (35.5 vs. 15.4%, p = 0.016). A temporary postoperative right ventricular assist device was necessary in 45.1 (FS) versus 23.1% (LIS) of patients, respectively (p = 0.067). No stroke occurred in the LIS group during the first 30 days after surgery (7.4% in the FS group). The incidence of stroke and of renal, hepatic, and respiratory failure during the follow-up was similar in both groups. The 30-day and one-year survival were similar in both groups. **Conclusion:** LIS for implantation of a durable LVAD in patients on va-ECLS implanted for cardiogenic shock is associated with less revision due to bleeding, less administration of blood products and absence of perioperative stroke, with no impact on survival.

KEYWORDS

bleeding, ECLS, minimally invasive approach, outcome, sternotomy, VAD

1 | INTRODUCTION

Continuous-flow left ventricular assist devices (LVADs) are a standard treatment of patients with severe end-stage heart failure,¹ even in extremis for patients on temporary circulatory support. Implantation of durable LVADs in patients on veno-arterial extracorporeal life support (va-ECLS) is a challenging scenario associated with a high mortality rate,²⁻⁴ and all efforts should be put in place to decrease perioperative morbidity and mortality. For several years, the routine approach for LVAD implantation has involved a full sternotomy on cardiopulmonary bypass. However, less invasive surgical techniques, including a sternumsparing approach⁵ or partial sternotomy, employing ECLS for circulatory support during implantation or even off-pump or a combination thereof,^{5,6} are becoming increasingly popular¹ as they appear to be associated with a reduction in surgical traumas, blood loss, and hospital stays.^{5,7} Additionally, preserving the retrosternal part of the pericardium around the right ventricle (RV) during less invasive surgery (LIS; e.g., left anterior thoracotomy combined with right anterior thoracotomy or partial upper sternotomy) may help prevent postoperative right ventricular failure (RVF). Thus, avoiding a full sternotomy in critically ill patients would be beneficial. However, the impact of a full sternotomy versus LIS with a sternotomy-sparing or partial sternotomy approach remains unclear.

Understanding the challenges and the impact on outcomes in a large "real-world" cohort of patients is paramount. To analyze the impact of a surgical approach (full sternotomy vs. LIS) on the outcome in critically ill patients who underwent LVAD implantation on va-ECLS based on data from the largest European registry, we created a model where all patients in the full sternotomy group would be potential candidates for LIS, and assumed that the decision was based solely on the surgeon's preference.

2 | METHODS

2.1 | Patient population

The ECLS-VAD registry is a multicentre retrospective study that gathered data on consecutive patients who underwent implantation of durable mechanical circulatory support (MCS) devices after va-ECLS between January 2010 and August 2018 in eleven high-volume European centres.⁸ Patients who underwent durable MCS implantation after va-ECLS support were eligible to participate. At all institutions the main goal after va-ECLS implantation was to wean the patient off mechanical support. Patients who did not meet weaning criteria were considered for durable MCS after an adequate neurological evaluation. All va-ECLS implantations were performed as emergency procedures; patients with postcardiotomy heart failure were also included in the register. The data collection and retrospective analysis were performed after obtaining approval from the institutional review board of each participating center. Internally validated preoperative, intraoperative, and postoperative data were collected from hospital charts from a total of 531 patients. The Interagency Registry for Mechanically Assisted

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Circulatory Support (INTERMACS) definitions of complications were applied in the database.

For the presented study patients who received

- 1. a total artificial heart (n = 19),
- 2. pulsatile devices (implantable, n = 2 and paracorporeal, n = 5),
- concomitant intracardiac procedures (valve surgery, closure of septal defects or patent foramen ovale, thrombectomy, aneurysmectomy, and similar, n = 116), and
- ECLS for postcardiotomy heart failure or patients with central cannulation (n = 69)

were excluded from the analysis.

The remaining 363 patients were divided into an FS group (full median sternotomy, n = 324) and a LIS group (patients in whom the apex was approached through left thoracotomy and the ascending aorta through right thoracotomy or through partial sternotomy, n = 39); all of them had been on peripheral va-ECLS and received a durable continues-flow LVAD.

The main endpoint was survival; postoperative bleeding, the need for blood products and surgical re-exploration as well as complications and end organ dysfunction/failure including RVF, stroke, and infections were also analyzed.

Patient follow-up was completed as of June 1st, 2020.

3 | SURGICAL PROCEDURES

The LVAD implantation, postoperative blood product, and factor administration were performed according to institutional protocols which vary between the participating institutions. LIS was performed using left anterior sternotomy to access the apex combined with upper partial sternotomy or right anterior thoracotomy to access the ascending aorta. 20.1% of the patients had a history of cardiac surgery (years or months before index hospitalization). These patients were included in the analysis. In case of severe RVF during the LVAD implantation, temporary RV support was established using a directly cannulated right ventricular assist device (RVAD) in patients with FS approach, with anastomosis of the 10 mm graft to the pulmonary artery and tunnel to the outside allowing for venous drainage from the femoral vein, and a peripheral va-ECLS in patients with LIS approach. In case of postoperative RVF, a percutaneous RVAD was employed, with one cannula inserted into the pulmonary artery and venous drainage from the right atrium through the femoral vein. According to institutional protocols, anticoagulation was commenced in the ICU as soon as bleeding had subsided (chest tube output and need for blood products).

4 | STATISTICAL ANALYSIS

Continuous variables are summarized as mean and standard deviation (*SD*), or as median and interquartile range [IQR] in the case of skewed data. For categorical variables, numbers and percentages are presented. Patient groups were compared using Student's t-test for normally distributed continuous data, and the Mann-Whitney *U* test for non-normally distributed continuous data. For categorical data, χ^2 tests with Yates' continuity correction was used. Survival was evaluated using Kaplan-Meier estimates censoring for transplantation, weaning, and ongoing support. To account for imbalances in the LIS and the FS group, a propensity score was calculated with age, ICM, INTERMACS level, gender, previous cardiac surgery, BMI > 30, peripheral artery disease, CPR, log(CRP), log(BUN), log(MELD-XI score), renal replacement therapy, CPB use for implantation, and preoperative administration of adrenaline and noradrenaline. The influence of LIS on survival (30 days and 1 year) and on postoperative complications was calculated with logistic regression adjusting for the propensity score.

Competing risk analyses were used to evaluate the incidence of first stroke, infection, bleeding, and pump thrombosis with death, heart transplantation, and LVAD weaning as competing outcomes. For these outcomes, subdistribution hazard ratios (SHRs) were calculated using the Fine-Gray model with the propensity score as a covariate.⁹ The influence of LIS on survival was estimated in a Cox regression adjusting for the propensity score. *E* values for the point estimator and the confidence limit nearest to nil were calculated to assess the impact of unmeasured confounding on a risk ratio scale, with high *E* values indicating a robust treatment-outcome association.¹⁰ We assumed a *p* value of <0.05 as the threshold for statistical significance. The analysis was explorative in nature. R software, version 3.5.2 was used for statistical analyses.

5 | RESULTS

5.1 | Patient characteristics

LIS was performed in 6 of 11 study centers, with the proportion varying between 3% and 46% within the center.

The preoperative baseline data of both groups are presented in Table 1.

5.2 | Outcome

5.2.1 | Intraoperative outcomes

The vast majority of patients received an implantable continuous-flow LVAD (FS vs. LIS; HeartWare HVAD (Medtronic, 73.5% vs. 89.7%), HeartMate II (Abbott, 15.7% vs. 2.6%) and HeartMate3 (Abbott, 7.6% vs. 7.7%) without differences between groups (p = .084). The duration of surgery was similar in both groups (Table 2).

5.3 | Postoperative outcomes

Postoperative outcomes are shown in Table 2. The chest tube output during the first 24 h was similar in both groups. The incidence of

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TABLE 1 Preoperative characteristics in non-adjusted cohort	Parameter	FS = 324	LIS = 39	p value	SMD
	Preoperative characteristics				
	Age (years, mean (SD))	52.66 (11.30)	52.45 (11.30)	0.913	0.019
	Male (n, %)	263 (81.2)	33 (84.6)	0.76	0.092
	BMI (kg/m², mean (SD))	26.54 (5.40)	25.41 (3.44)	0.202	0.25
	Diagnosis ICM (n, %)	178 (54.9)	18 (46.2)	0.384	0.176
	Type II diabetes mellitus (n, %)	79 (24.8)	9 (28.1)	0.683	0.031
	Peripheral artery disease (n, %)	16 (5.0)	3 (7.7)	0.731	0.138
	Atrial fibrillation (n, %)	89 (27.6)	10 (25.6)	0.950	0.09
	INTERMACS level 1 (n, %)	261 (82.6)	27 (69.2)	0.150	0.203
	Renal replacement therapy (n, %)	106 (33.7)	3 (7.7)	0.002	0.725
	Redo cardiac surgery (n, %)	62 (19.1)	11 (28.2)	0.261	0.215
	Noradrenaline (n, %)	217 (67.0)	22 (56.4)	0.256	0.219
	Adrenaline (n, %)	198 (61.1)	14 (35.9)	0.004	0.521
	Milrinone (n, %)	133 (41.0)	9 (23.1)	0.046	0.392
	CPR (n, %)	113 (34.9)	4 (10.3)	0.003	0.616
	IABP therapy (n, %)	80 (24.8)	6 (15.4)	0.271	0.249
	ECLS duration (days, median [IQR])	5.00 [2.00, 9.00]	4.00 [3.00, 6.50]	0.268	0.181
	LVAD system (n, %)			0.084	0.553
	HeartWare HVAD®	238 (73.5)	35 (89.7)		
	HeartMate II	51 (15.7)	1 (2.6)		
	HeartMate III	25 (7.6)	3 (7.7)		
	Other	10 (3.1)	0 (0.0)		
	CPB use for implantation (n, %)	168 (51.9)	11 (28.2)	0.009	0.497
	Preoperative laboratory parameters				
	Platelets ×10 ³ (mean (SD))	102.24 (73.36)	118.74 (85.05)	0.193	0.208
	Haemoglobin (g/dl, mean (SD))	9.77 (1.64)	9.94 (1.47)	0.539	0.109
	WBC (mean (SD))	12.23 (4.97)	12.15 (6.05)	0.926	0.014
	Lactate (mmol/L, median [IQR])	1.11 [0.70, 1.70]	0.87 [0.70, 1.30]	0.22	0.181
	Creatinine (mg/dl, median [IQR])	1.20 [0.83, 1.94]	1.08 [0.81, 1.50]	0.138	0.163
	Bilirubin (median [IQR])	1.78 [0.99, 3.92]	1.73 [1.13, 3.40]	0.838	0.195
	AST (U/L, median [IQR])	93.00 [47.00, 248.25]	98.00 [61.10, 226.50]	0.659	0.12
	ALT (U/L, median [IQR])	67.00 [27.50, 163.00]	171.00 [54.00, 777.50]	0.011	0.34
	BUN (mg/dl, median [IQR])	60.00 [35.00, 88.59]	50.50 [32.70, 72.19]	0.066	0.252
	pH (g/dl, median [IQR])	7.40 [7.32, 7.47]	7.40 [7.37, 7.46]	0.689	0.178
	CRP (mg/dl, median [IQR])	13.55 [6.94, 25.00]	8.74 [3.95, 12.70]	0.001	0.48
	INR (median [IQR])	1.30 [1.13, 1.60]	1.30 [1.20, 1.65]	0.428	0.029
	aPTT (median [IQR])	49.75 [42.2, 60.32]	56.0 [44.9, 77.5]	0.036	0.443
	MELD XI score (median [IQR])	21.00 [12.00, 28.25]	14.00 [11.00, 21.50]	0.014	0.505

Abbreviations: aPTT, activated partial thromboplastin time; AST, aspartate transaminase; ALT, alanine transaminase; BMI, body mass index; CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; CRP, C-reactive protein; ECLS, extracorporeal life support; IABP, intra-aortic balloon pump; ICM, ischaemic cardiomyopathy; INR, international normalized ratio; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; IQR, interquartile range; LIS, less invasive surgery; LVAD, left ventricular assist device; MELD-XI score, Model for End-stage Liver Disease Excluding INR; SD, standard deviation; SMD, standardized mean distance; WBC, white blood cell count.

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TABLE 2 Adjusted intraoperative and postoperative results

Parameter	FS	LIS	Propensity score-adjusted coefficients or risks (95% CI)	Adiusted p value
Intraoperative				
Surgery duration (min, median [IQR])	236 [190, 300]	263 [190, 300]	3.69 (-36.9, 28.8)	0.824
Postoperative complications				
Drainage in 24 h (ml, median [IQR])	1090 [700, 1930]	650 [466, 1230]	360 (-229.00, 847.11)	0.261
FFP (units, first 24 h after surgery; median [IQR])	5 [0, 9]	3 [2, 6]	2,15 (-0.31, 4.60)	0.087
PRBC (units, first 24 h after surgery; median [IQR])	8 [4, 11]	5 [3, 8]	1.66 (-0.51, 0.22)	0.121
Platelets (units, first 24 h after surgery; median [IQR])	3 [2, 5]	2 [0,4]	1.39 (0.27, 2.50)	0.015
Total blood products in first 24 h after surgery median [IQR]	16 [9, 24]	12 [7, 15]	5.2 (1.22, 9,98)	0.033
Revision due to bleeding (n, %)	115 (35.5)	6 (15.4)	OR: 3.4 (1.25, 9.26)	0.016
RVAD implantation (n, %)	146 (45.1)	9 (23.1)	OR: 2.23 (0.97, 5.54)	0.067
Renal replacement therapy (n, %)	197 (60.5)	15 (38.5)	OR: 1.97 (0.91, 4.27)	0.087
Renal failure (n, %)	112 (47.1)	14 (40.0)	OR: 1.46 (0.64, 3.32)	0.387
Hepatic failure (n, %)	81 (34.3)	8 (22.9)	OR: 1.45 (0.40, 15.37)	0.333
Respiratory failure (n, %)	151 (64.0)	17 (48.6)	OR: 1.68 (0.75, 3.79)	0.214
GI bleeding (n, %)	40 (12.3)	8 (20.5)	SHR: 0.56 (0.23, 1.46)	0.252
Driveline infection (n, %)	63 (19.4)	11 (28.2)	SHR: 1.11 (0.52, 2.37)	0.800
Pump thrombosis (n, %)	31 (9.6)	2 (5.1)	SHR: 1.76 (0.45, 6.83)	0.410
Stroke during first 30 days after LVAD implantation (<i>n</i> , %)	24 (7.4)	0	n/a	n/a
Ischaemic	12	0		
Haemorrhagic	11	0		
Unknown	1	0		
Stroke (n, %)	69 (21.3)	10 (25.6)	SHR: 1.07 (0.52,2.19)	0.851
Ischaemic	33	5		
Haemorrhagic	36	5		
Disabling	29	4		
Non-disabling	13	6		
Unknown	27	0		
Outcome				
30-day survival (%)	75.2	94.9	OR: 0.26 (0.06, 1.17)	0.079
1-year survival (%)	54.0	71.8	OR: 0.55 (0.24, 1.25)	0.156
Follow-up time (years, median [IQR])	0.73 [0.07, 2.55]	1.55 [0.63, 3.87]	HR ^a : 0.58 (0.33, 1.03)	0.063
HTx (n, %)	64 (19.8)	14 (35.9)	SHR: 1.57 (0.82,3.04),	0.180

Abbreviations: CI, confidence interval; FFP, fresh frozen plasma; FS, full sternotomy; GI bleeding, gastrointestinal bleeding; HR, hazard ratio; HTx, heart transplantation; IQR, interquartile range; LIS, less invasive surgery; n/a, not applicable; OR, odds ratio; PRBC, packed red blood cells; RVAD, right ventricular assist device; SHR, subdistribution hazard ratio.

^aHR for overall survival.

revision due to bleeding was higher in the FS group (35.5 vs. 15.4%, resp., adjusted p = 0.016, *E* value: 6.2 and 1.8 for lower Cl). Patients who underwent implantation via an FS required more blood products in first 24 h after surgery (median [IQR] 16 [9, 24] vs. 12 [7, 15], adjusted p = 0.033, *E* value: 9.8 and 1.7 for lower Cl).

A temporary RVAD was necessary in 45.1 versus 23.1% of patients in the FS or the LIS group, respectively (AOR: 2.23 95% CI [0.97, 5.54], adjusted p = 0.067). The incidence of postoperative

stroke, renal, hepatic, and respiratory failure was similar in both groups.

The 30-day survival was 75.2% in the full sternotomy group versus 94.9% in the LIS group (AOR: 0.26 95%CI [0.06, 1.17], adjusted p = 0.079, E value: 7.2 and 1 for upper CI); the 1-year survival was 54.0 (FS) versus 71.8% (LIS), respectively (AOR: 0.55 95%CI [0.24, 1.25], adjusted p = 0.156)

(Figure 1). Causes of death in both groups are presented in Table 3.



FIGURE 1 Adjusted results of the Kaplan-Meier analysis for survival in both groups. Patients were censored for death, HTx, and pump removal for recovery

6 | DISCUSSION

This large-scale, multi-centre "real-world" study of patients undergoing LVAD implantation while on va-ECLS for cardiogenic shock demonstrates a similar clinical outcome and survival of up to 2 years for patients implanted using the FS or LIS approach.

In our study, patients who underwent concomitant intracardiac procedures and who were supported with central ECLS for postcardiotomy syndrome were excluded from the analysis. This approach creates a model where all patients in the full sternotomy group would be potential candidates for LIS. However, because LIS was developed and clinically applied after the first patient was enrolled in the ECMO/VAD Register in 2010,¹¹ only 10% of potential candidates for LIS actually underwent LIS, mainly after 2014. These patients probably represent a strictly selected cohort with an assumed good right

TABLE 3 Causes of death

Cause of death	Full sternotomy	LIS
MODS (n, %)	69 (41.1)	5 (35.7)
Septic shock (n, %)	35 (20.8)	5 (35.7)
Stroke (n, %)	30 (17.9)	2 (14.3)
Heart failure (n, %)	6 (3.6)	0
Hemorrhagic shock (n, %)	5 (3.0)	0
Respiratory failure (n, %)	5 (3.0)	1 (7.1)
Other (n, %)	18 (10.7)	1 (7.1)

Abbreviations: LIS, less invasive surgery; MODS, multiple organ dysfunction syndrome.

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ventricular function. However, evaluating the RV function in patients on ECLS is very difficult, since the RV is unloaded and blood flow through the lungs is low. Therefore, the RV function post-LVAD implantation cannot be predicted accurately with the current armamentarium, and preoperative RV parameters were not included in the propensity score. In this situation the surgeon's subjective judgment may play a decisive role and may affect the decision for a specific surgical technique and therefore the degree of bias in the study presented here. The LIS approach was performed in six out of eleven institutions. We assume that the choice of surgical approach in our study was based on the surgeon's experience, with the aim to perform the best surgery in each particular case. Despite the fact that FS patients were sicker (more preoperative CPR, renal replacement treatment, higher CRP and MELD-XI score, more inotropic support) and more often underwent surgery on CPB, an adjustment of the results based on accurate propensity scoring for important preoperative confounders enables a reliable comparison of the impact of different surgical approaches on the outcome.

In our study, the incidence of postoperative temporary RV support was higher than in general LVAD populations (INTERMACS report,¹² EUROMACS report¹³). However, it was similar to that reported for patients with need for preoperative ECLS.² In fact, the need for preoperative ECLS is the second strongest risk factor, after INTERAMCS level 1, for postoperative need for temporary RVAD support, as shown in a recent INTERMACS analysis.¹⁴ Although postoperative temporary RV support was necessary in the FS group almost twice as often as in the LIS group (45.1% vs. 23.1%), the difference between both groups did not reach statistical significance. However, it is possible that our study cohort might lack the power to show a significant difference; future studies with larger patient populations for LIS could potentially show an association of LIS approaches with lower risk for postoperative need for temporary RV support.

The impact of the surgical approach is more prominent during first days after surgery. Despite the fact that the incidence of stroke in our population was similar between the groups, with an equal distribution between strokes of ischaemic and haemorrhagic aetiology, no strokes were observed in the LIS group during the first 30 days after LVAD implantation.

The volume of chest tube loss in the first 24 h was similar in both groups. However, the consequences, i.e. more revisions and more blood products—especially platelet units administered in the FS group—suggest that "more bleeding" occurred. Postoperative bleeding and re-exploration have a detrimental effect on the outcome after cardiac surgery,¹⁵⁻¹⁷ including possible excessive procoagulation. Other factors which may explain the higher perioperative stroke rate may include mobilization of left atrial or ventricular thrombi that were not detected preoperatively, with subsequent embolization during elevation of the heart to gain access to the apex in the full sternotomy group. We believe that a combination of more re-exploration due to bleeding, possible excessive procoagulation and a greater use of

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blood products and elevation of the heart during LVAD implantation through FS may have led to perioperative strokes in the FS group.

Based on the fact that the total blood product use and incidence of revision due to bleeding were significantly higher in the FS group, one may assume that the overall cost may have been higher in the FS group. Unfortunately, our registry contains no data on the duration of hospitalization and ICU stay.

The LIS approach is associated with fewer or no adhesions behind the sternum, thus facilitating sternotomy for later HTx. However, opening and placing the pump into the left pleural space causes severe adhesions, despite or even because of the use of surgical membranes, which may have a detrimental effect during reoperation (pump exchange, removal for recovery or HTx). Follow-up studies should investigate the impact of the various surgical approaches on the late postoperative course, especially after HTx. The partial preservation of pericardial integrity is a subject of ongoing discussion regarding postoperative RV function.⁷ In our study the incidence of postoperative temporary RV support did not differ between the groups. Therefore, our findings suggest that LIS does not reduce the risk for RV failure after LVAD implantation in va-ECLS patients.

Patients who were previously on va-ECLS due to cardiogenic shock are sicker, many of them have undergone cardiopulmonary resuscitation, have been on a ventilator due to respiratory dysfunction and exhibit some degree of RV dysfunction²; most importantly, a severe disturbance of coagulation (Table 1) related to ECLS is always present.^{2,4} Therefore, the transfer of our results to less sick patients without the need for hemodynamic stabilization and recovery from severe cardiogenic shock on ECLS before LVAD implantation should be done with caution, and prospective randomized studies in both populations are required.

7 | LIMITATIONS

This was a retrospective and non-randomized study. Due to the multicentre nature of the study, surgical techniques and perioperative decisions may differ between centres and may to some degree influence the study results. However, the propensity score adjustment eliminates the majority of such effects. Nevertheless, a coincidental relationship between stroke and mortality in our study cannot be excluded.

It should also be noted that our study cohort might lack the power to show a significant difference in outcome due to the small population in the LIS group. Future randomized, controlled studies are warranted.

8 | CONCLUSION

The intermediate-term survival is comparable between both groups. A less invasive surgical approach for LVAD implantation directly from va-ECLS is safe and is associated with a lower incidence of re-exploration due to bleeding, fewer blood products administered immediately after surgery and absence of perioperative stroke compared to FS. Future randomized, controlled studies are warranted.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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