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Original Article

PERSUADE Survey—PERioperative AnestheSia and Intensive Care Management of Left VentricUlar Assist DevicE Implantation in Europe and the United States

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Objective: To comprehensively assess relevant institutional variations in anesthesia and intensive care management during left ventricular assist device (LVAD) implantation.
Design: The authors used a prospective data analysis.
Setting: This was an online survey.
Participants: Participants were from LVAD centers in Europe and the US.
Interventions: After investigating initial interest, 91 of 202 European and 93 of 195 US centers received a link to the survey targeting institutional organization and experience, perioperative hemodynamic monitoring, medical management, and postoperative intensive care aspects.
Measurements and Main Results: The survey was completed by 73 (36.1%) European and 60 (30.8%) US centers. Although most LVAD implantations were performed in university hospitals (>5 years of experience), significant differences were observed in the composition of the preoperative multidisciplinary team and provision of intraoperative care. No significant differences in monitoring or induction agents were observed. Propofol was used more often for maintenance in Europe ($p < 0.001$). The choice for inotropes changed significantly from

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preoperatively (more levosimendan in Europe) to intraoperatively (more use of epinephrine in both Europe and the US). The use of quantitative methods for defining right ventricular (RV) function was reported more often from European centers than from US centers ($p < 0.05$). Temporary mechanical circulatory support for the treatment of RV failure was more often used in Europe. Nitric oxide appeared to play a major role only intraoperatively. There were no significant differences in early postoperative complications reported from European versus US centers.
Conclusions: Although the perioperative practice of care for patients undergoing LVAD implantation differs in several aspects between Europe and the US, there were no perceived differences in early postoperative complications.

KeyWords: LVAD implantation; anesthesia; intensive care; survey; perioperative mangement; center differences

The number of patients with chronic heart failure is increasing worldwide,[1] and some do not respond well to conventional medical therapy. For these patients, heart transplantation is the gold standard treatment, providing great improvement in morbidity and mortality.[1] Unfortunately, the number of patients on waiting lists exceeds the number of available organs, and the mortality of wait-listed patients is high.[1] Due to organ shortage and strict criteria for eligibility as an organ recipient, implantation of durable mechanical circulatory support (DMCS) systems, such as left ventricular assist devices (LVADs), has become a reasonable option for bridging to transplantation or destination therapy.[1-3] The combination of an increasing incidence of heart failure, persistent organ shortage, and improved long-term outcomes with the newest LVAD generation likely has contributed to the growing number of implantations over the last decade.[4,5] In the US alone, there are approximately 2,400 implantations per year.[6,7]

Despite significant technologic improvements, implantation of DMCS devices still comes with a risk for multiple complications, particularly in the first 90 days after implantation.[6] The most serious complications are vasoplegia, right ventricular (RV) failure, pump thrombosis, gastrointestinal bleeding, stroke, and driveline infections.[6,8-10] Anesthesiologists, both in the operating room and in the intensive care setting, are inextricably involved in the care of these patients. Despite this, there are only a few international reports on anesthesia and intensive care management for LVAD implantation. Aside from a short intraoperative and immediate postoperative guideline published in 2013 by the International Society for Heart and Lung Transplantation,[11] there are no recently published detailed international guidelines concerning the perioperative management of these patients. Most centers have their own institutional protocols for LVAD implantation and postoperative management, presumably based on limited literature and institutional preferences.

To research the current state of perioperative anesthesia and intensive care for these patients, the perioperative anesthesia and intensive care management of ventricular assist device implantation (PERSUADE) survey was conducted. The PERSUADE survey explored real-world institutional practices for anesthesia and intensive care management of LVAD implantation. This survey differed from most practice surveys as it did not seek individual clinicians' responses or attitudes but rather an institutional representation of clinical practice. Comprehensively relevant variations in clinical practices in Europe and the US are compared and discussed.

Methods

The local ethics committee of the University Medical Center Utrecht, the Netherlands, confirmed that the Medical Research Involving Human Subjects Act did not apply to this study because no individual patient data were collected. Therefore, an official approval of this study by the local ethics committee in Utrecht, the Netherlands, was not required under the Medical Research Involving Human Subjects Act (METC: 19-613/c).

The survey was performed in collaboration with the European Association of Cardiothoracic Anaesthesiology and Intensive Care and the American Society for the Advancement of Transplant Anaesthesia. The survey questionnaire, composed by Nandor Marczin and Eric E.C. de Waal, was endorsed by the European Association of Cardiothoracic Anaesthesiology and Intensive Care on October 18, 2018. To assess the survey's intelligibility, a pilot of this questionnaire was sent to a cardiothoracic anesthesiologist working at the University Medical Center Utrecht, the Netherlands, who was not involved in the project.

The survey contained 36 questions in the following 4 major categories: (1) experience-related information, (2) perioperative hemodynamic monitoring, (3) perioperative medical management, and (4) postoperative intensive care management (Supplementary Appendix S1). The survey was distributed using the online survey tool LimeSurvey (LimeSurvey GmbH, Hamburg, Germany).

All European and US LVAD centers were identified. A representative of those centers was contacted by email with an invitation to select 1 responsible person per center to complete the survey: an anesthesiologist, a cardiothoracic surgeon, or an intensivist. Subsequently, all centers that had not responded to the initial invitation by phone were approached to enhance the number of participating centers. The responsible person per center willing to participate received a link to the survey, together with instructions for correctly completing the survey and a PDF with all questions, allowing them to discuss the questions with their entire team. Most importantly, the requirement to answer as a representative of the whole group was emphasized. Due to the coronavirus disease pandemic, the

authors asked to use 2019 as the reference year for every institution because the deadline for completing the survey was extended several times. Every participant was given sufficient time to complete the survey. Multiple reminders were sent to those who did not respond.

Statistical Analysis

All data were collected initially in LimeSurvey. Data were then imported from LimeSurvey into Microsoft Excel (version 16.74; Microsoft Corporation, Redmond, WA) and SPSS version 28 (IBM SPSS, Inc, Armonk, NY). Frequencies (%) were used to express the results of all centers that completed the survey. The main characteristics of the data were explored, and differences between European and US centers were evaluated. Finally, statistical analyses were performed in SPSS using Fisher's exact test. Significant differences between European and US centers were assessed.

Results

Institution-RelatedInformation

In total, 195 US and 202 European cardiac centers implanted LVADs. Of these, 93 US and 91 European LVAD centers were willing to participate and received a link to the survey. Finally, the survey was completed by 60 centers from 26 US states (response rate of 30.8%), and 73 centers from 23 European countries (response rate of 36.1%). Figure 1 and Table 1 provide information about the geographic distribution and the respective institutions.

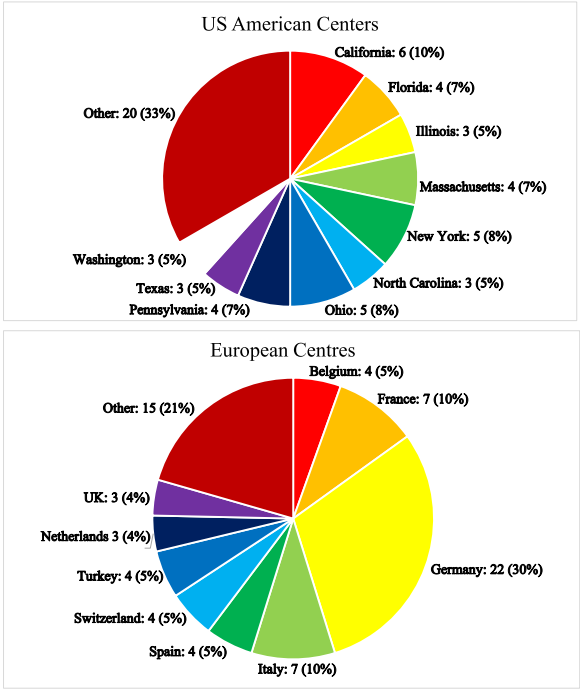

Fig 1. Geographic distribution of participating left ventricular assist devices centers.

In Europe, more cardiac anesthesiologists and intensivists were involved in the preoperative multidisciplinary team ($p < 0.01$ and $p = 0.04$, respectively). Also, a dedicated subset of cardiac anesthesia team members was involved more often in intraoperative care ($p < 0.01$). On average, more US centers implanted >10 LVADs annually ($p < 0.01$).

Perioperative Hemodynamic Monitoring

Beyond basic monitoring, pulmonary artery catheters, transesophageal echocardiography, near-infrared spectroscopy, and processed electroencephalogram monitoring were used most often intraoperatively. When a pulmonary artery catheter was used intraoperatively, most centers cannulated them after induction in the operating room.

Perioperative Medical Management

Anesthetic Management

The first choices of intravenous (IV) induction agents were propofol and etomidate in most centers in Europe and the US (propofol 42.5% *vs* 35.0%, respectively; etomidate 31.5% *vs* 46.7%, respectively; $p = 0.09$). However, the first choice of opioids was significantly different. Most European centers preferred sufentanil (53.4% *vs* 5.1% in the US), whereas US centers preferred fentanyl (94.9% *vs* 31.5% in Europe; $p < 0.01$). In the US, the most frequently used maintenance agent was isoflurane (80.0% *vs* 5.5% in Europe, $p < 0.01$). In Europe, the most commonly used agents were sevoflurane (69.9% *vs* 30.0% in the US, $p < 0.01$) and propofol (61.6% *vs* 15.0% in the US, $p < 0.01$).

Perioperative Medical Management: Preimplantation Inotropic Support

Norepinephrine and levosimendan were significantly more frequently prescribed preoperatively in European patients with end-stage heart failure than in US patients, who more often received phosphodiesterase inhibitors ($p < 0.001$). However, after induction of anesthesia, levosimendan administration in Europe decreased compared with that observed preoperatively, whereas epinephrine administration was higher in US patients ($p = 0.002$; Table 2).

RV Dysfunction

Combinations of hemodynamic parameters were used to define RV failure, such as central venous pressure (CVP)/pulmonary capillary wedge pressure ratio and pulmonary artery pulse pressure/right atrial pressure index (PAPi). In addition, the mean pulmonary artery pressure-CVP gradient was more commonly used in the US (55.0% *vs* 32.9%, $p = 0.01$). In contrast, the RV stroke work index (RVSWI) was more commonly used in Europe (28.8% *vs* 13.3%, $p < 0.05$).

The preferred echocardiographic indicators of RV failure were overall impression by "eyeballing" (Europe = 51, 69.9%; US = 52, 86.7%; $p = 0.02$), tricuspid annular plane systolic excursion <16 mm (Europe = 38, 52.1%; US = 39, 65.0%;

Table 1
Experience-related information

		Europe (n = 73)	United States (n = 60)	p Value
Institution	University hospital	55 (75.3%)	49 (81.7%)	
	Community hospital	4 (5.5%)	3 (5.0%)	0.68
	Specialized cardiothoracic center	14 (19.2%)	8 (13.3%)	
Provision of anesthesia	Only selected members of cardiac anesthesia team	42 (57.5%)	7 (11.7%)	< 0.01*
Members of preoperative multidisciplinary team	Cardiologists	71 (97.3%)	60 (100%)	0.50
	Cardiothoracic surgeons	72 (98.6%)	60 (100%)	1.00
	Cardiac anesthesiologists	56 (76.7%)	27 (45.0%)	< 0.01*
	Intensivists	38 (52.1%)	20 (33.3%)	0.04*
	LVAD technicians	33 (45.2%)	30 (50.0%)	0.61
	Other	10 (13.7%)	15 (25.0%)	0.08
Years of experience	2 to 5	2 (2.7%)	2 (3.3%)	0.72
	5 to 10	17 (23.3%)	13 (21.7%)	
	10 to 20	36 (49.3%)	25 (41.7%)	
	>20	18 (24.7%)	20 (33.3%)	
Total number of LVAD implantations in 2019	<10	23 (31.5%)	8 (13.3%)	< 0.01*
	10 to 20	31 (42.5%)	12 (20.0%)	
	20 to 40	13 (17.8%)	22 (36.7%)	
	<40	6 (8.2%)	18 (30.0%)	
Surgical approaches	Median sternotomy without bypass	6 (8.2%)	7 (11.7%)	0.57
	Median sternotomy with bypass	69 (94.5%)	58 (96.7%)	0.69
	Minimal invasive approach without bypass	9 (12.3%)	4 (6.7%)	0.38
	Minimal invasive approach with bypass	24 (32.9%)	26 (43.3%)	0.28
	Other	3 (4.1%)	1 (1.7%)	0.91
Department in charge of postoperative care	Department of anesthesiology	29 (39.7%)	14 (23.3%)	
	Department of (Cardio-)Thoracic Surgery	21 (28.8%)	19 (31.7%)	0.11
	Department of Critical Care Medicine	16 (21.9%)	14 (23.3%)	
	Other	7 (9.6%)	12 (20.0%)	

Abbreviations: LVAD, left ventricular assist devices.
* Statistically significant.

p = 0.16), RV end-diastolic diameter left ventricular end-diastolic diameter ratio (Europe = 27, 37.0%; US = 8, 13.3%; p < 0.01), constant bowing of the interatrial septum (Europe = 41, 56.2%; US = 42, 70.0%; p = 0.11), and dilated right-sided chambers (Europe = 39, 53.4%; US = 38, 63.3%; p = 0.29).

Pulmonary Hypertension

Approximately one-third of the centers in both Europe and the US took the transpulmonary gradient into consideration to differentiate between arterial and venous pulmonary

Table 2
Initial inotropic support

Primary inotropic support	Possible agents	Europe (n = 73)	United States (n = 60)	p Value
Primary institutional inotropic support on the ward/CCU BEFORE LVAD implantation	None	4 (5.5%)	0 (0%)	0.13
	Dopamine	4 (5.5%)	7 (11.7%)	0.22
	Norepinephrine	28 (38.4%)	6 (10.0%)	< 0.01*
	Dobutamine	44 (60.3%)	45 (75.0%)	0.10
	PDE3 inhibitors	27 (37.0%)	50 (83.3%)	< 0.01*
	Epinephrine	9 (12.3%)	15 (25.0%)	0.07
	Levosimendan	40 (54.8%)	0 (0%)	< 0.01*
	NO	2 (2.7%)	4 (6.7%)	0.41
Primary inotropic support BEFORE LVAD implantation AFTER induction of anesthesia	None	2 (2.7%)	0 (0%)	0.50
	Continuation of preoperative support	26 (35.6%)	26 (43.3%)	0.38
	Dopamine	3 (4.1%)	1 (1.7%)	0.63
	Norepinephrine	33 (45.2%)	20 (33.3%)	0.21
	Dobutamine	28 (38.4%)	20 (33.3%)	0.59
	PDE3 inhibitors	25 (34.2%)	21 (35.0%)	1.00
	Epinephrine	28 (38.4%)	40 (66.7%)	< 0.01*
	Levosimendan	13 (17.8%)	0 (0%)	< 0.01*
	NO	8 (11.0%)	3 (5.0%)	0.34

Abbreviations: CCU, coronary care unit; LVAD, left ventricular assist device; NO, nitric oxide; PDE3, phosphodiesterase 3.
* Statistically significant.

hypertension (PH) during LVAD implantation (p = 0.47). For both groups of centers, the main treatment strategy for intraoperative pulmonary arterial hypertension was inhaled nitric oxide and IV milrinone. In addition, inhaled epoprostenol was more commonly used in centers in the US (40.0% *vs* 1.4% in Europe, p ≤ 0.01). In contrast, inhaled iloprost was more commonly used in European centers (32.9% *vs* 0% in the US, p < 0.01).

Cardiopulmonary Bypass and Cardioprotective Management During Implantation

Almost all centers used cardiopulmonary bypass (CPB) during LVAD implantations (Europe = 64, 87.7%; US = 59, 98.3%; p = 0.14). In 60 centers in Europe (82.2%) and 53 centers in the US (88.3%), LVAD implantations were performed as a beating-heart procedure; the rest used cardioplegic arrest or fibrillating heart procedures, and the majority used normothermic temperature management during CPB (Europe = 64, 87.7%; US = 54, 90.0%). During CPB, the ventilation strategy in most centers was to either stop ventilation (Europe = 23, 31.5%; US = 32, 53.3%) or decrease the tidal volume and respiratory rate (Europe = 35, 47.9%; US = 23, 38.3%). Significantly more centers in the US routinely used hemofiltration during CPB (76.7% *vs* 24.7%, p ≤ 0.01). Targeted hemoglobin levels to come off CPB were significantly lower in US centers (86.6% aimed at 8.0 to 9.0 g/dl or <8.0 g/dl) than in European centers (53.4%, p < 0.01). Several parameters were used to define vasoplegia (Table 3). Only a few centers proposed norepinephrine dosages of more than 200-to-500 ng/kg/min or the simultaneous use of 2 or more vasopressors.

Table 3
Parameters used to define vasoplegia

	Europe (n = 73)	United States (n = 60)	p Value
Clinical feeling from attending physician	32 (43.8%)	37 (61.7%)	0.06
Norepinephrine > 100 ng/kg/min IV over several hours	42 (57.5%)	25 (41.7%)	0.08
Vasopressin > 1 U/h over several hours	24 (32.9%)	26 (43.3%)	0.28
MAP < 50 mm Hg over several hours	35 (47.9%)	38 (63.3%)	0.08
Cardiac index > 2.5 l/min/m^2	16 (21.9)	21 (35.0%)	0.12
SVR < 800 dynes·s·cm^{-5}	40 (54.8%)	41 (68.3%)	0.15
Other	5 (6.8%)	11 (18.3%)	0.04*

Abbreviations: IV, intravenous; MAP, mean arterial pressure; SVR, systemic vascular resistance.
* Statistically significant.

Weaning From CPB

Similarities and differences in diagnostic and therapeutic strategies during weaning from CPB are presented in Table 4.

Blood Conservation and Management of Perioperative Bleeding

In Europe, significantly more centers chose not to routinely correct the preoperative international normalized ratio (INR) than US centers (30.1% *vs* 11.7%, p < 0.01). Moreover, many centers (22 in Europe and 37 in the US) corrected the preoperative INR to 1.5 to 1.8. Although many centers chose to correct with vitamin K, 4-factor prothrombin complex concentrate was used more significantly in Europe than in the United States (60.3% *vs* 26.7%, p < 0.01). In addition, bridging with low-

Table 4
Diagnostic and therapeutic strategies during weaning from cardiopulmonary bypass

		Europe (n = 73)	United States (n = 60)	p Value
Primary diagnostic strategy to increase the LVAD rotations during weaning from cardiopulmonary bypass†	TEE evaluation of the RV volume	16 (21.9%)	11 (18.6%)	0.71
	TEE evaluation of the LV volume	10 (13.7%)	14 (23.7%)	
	Position interventricular septum	43 (58.9%)	31 (52.5%)	
	Cardiac output determined by the LVAD	2 (2.7%)	2 (3.4%)	
	CCO determined by pulmonary artery catheter	1 (1.4%)	1 (1.7%)	
	SvO_2 measured with pulmonary artery catheter	0 (0.0%)	0 (0%)	
	Assessment of tissue perfusion and microcirculation	1 (1.4%)	0 (0%)	
Primary therapeutic strategy if RV function worsens during weaning from bypass	Change inotropes	40 (54.8%)	52 (86.7%)	< 0.01*
	RVAD implantation	13 (17.8%)	5 (8.3%)	
	ECMO	10 (13.7%)	0 (0%)	
	Other (NO, Impella, combination of above, add inhaled epoprostenol)	10 (13.7%)	3 (5.0%)	
First-choice measurement to decide to give fluids to the patient after weaning from cardiopulmonary bypass	Echocardiographic measurements of preload			0.02*
	Trendelenburg	29 (39.7%)	20 (33.3%)	
	Pulmonary artery catheter measurements of preload (such CVP and Wedge)	2 (2.7%)	0 (0%)	
	LVAD measurements (cardiac output, pulsatility index events, adapted rpms)	4 (5.5%)	14 (23.3%)	
	Combination of above	5 (6.8%)	6 (10.0%)	
		33 (45.2%)	20 (33.3%)	

Abbreviations: CCO, continuous cardiac output; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; LV, left ventricle; LVAD, left ventricular assist device; NO, nitric oxide; RPMS, rotations per minute; RV, right ventricle; RVAD, right ventricular assist device; SvO_2, mixed venous oxygen saturation; TEE, transesophageal echocardiography.
* Statistically significant.
† Missing data: 1.

molecular-weight heparin or heparin was also used more often in Europe (32.9% *vs* 23.3%).

In Europe, there were more centers with a special transfusion protocol for patients with LVADs than in the United States (26.0% *vs* 11.7%, $p < 0.05$). Most of the centers routinely used cell savers as their first choice of blood salvage technique (93.2% in Europe *vs* 85.0% in the US, $p = 0.08$). The routine use of antifibrinolytic therapy differed significantly; that is, in Europe, almost all centers used tranexamic acid (94.5% *vs* 56.7% in the US, $p < 0.01$), whereas in the US, aminocaproic acid was commonly used (41.7% of US centers and 0.0% in Europe, $p \leq 0.01$).

The most frequently used coagulation strategy after weaning from CPB at both locations was to fully reverse heparin (82.2% *vs* 90.0%). Furthermore, fresh-frozen plasma, platelets, and 4-factor prothrombin complex concentrate are used in Europe and the US.

Postoperative Intensive Care Management

In two-thirds of intensive care units in centers in Europe and the US, the primary anticoagulation strategy when blood loss was controlled was heparin IV as a bridge to oral medication (93.2% in Europe, 76.7% in the US). Some centers in Europe (6.8%) and the US (23.3%; $p = 0.01$) preferred vitamin K antagonists instead of bridging with heparin IV.

Early Postoperative Complications

Early postoperative complications are presented in Table 5. There were no significant differences between the European and US cohorts regarding the most commonly reported postoperative complications.

Discussion

To the authors' knowledge, this was the first survey investigating clinical practices of perioperative care for LVAD implantation in European and US centers. The response rate was high, with 73 centers in Europe and 60 centers in the US. A very extensive list of questions was developed that covered several areas of care before, during, and the first days after LVAD implantation related to outcomes to compare current practice with the international literature. Institution-related information, perioperative monitoring, perioperative medical treatment, and postoperative intensive care aspects are discussed, respectively.

Table 5
Complications during the postoperative period

	Europe (n = 73)*	United States (n = 60)†	p Value
Vasoplegia, median (SD)	25.0 (26.3)	20.0 (22.0)	0.95
RV failure requiring mechanical circulatory support, median (SD)	10.0 (12.2)	10.0 (15.9)	0.22
Renal failure requiring RRT, median (SD)	18.8 (16.8)	18.3 (16.1)	0.91
Gastrointestinal bleeding, median (SD)	5.0 (8.7)	10.0 (8.6)	0.33

Abbreviations: RRT, renal-replacement therapy; RV, right ventricle.
* Missing data: 3.
† Missing data: 9.

Institution-Related Information

Although most LVAD implantations were performed in university hospitals, significant differences were observed in the composition of the preoperative multidisciplinary team and provision of intraoperative care. It is advocated that an advanced heart failure team should manage all patients potentially requiring DMCS (class I, level of evidence C),[12] consisting of cardiothoracic surgeons, intensive care specialists, cardiologists, perfusionists, long-term MCS coordinators, psychologists, and other allied healthcare professionals such as cardiothoracic anesthesiologists and geriatricians.[13,14] There were only a few centers in which nonphysician team members, such as psychologists or physiotherapists, were part of the evaluation team (13.7% in Europe and 25.0% in the US). However, a multidisciplinary team with special attention to preoperative optimization in the context of enhanced recovery after surgery may impact postoperative outcomes.[13,15] It is obvious that experience with the perioperative procedures of DMCS implantation has an impact on outcomes.[16] Experience is related to the number of procedures annually and the members of the whole team.

The majority of centers both in Europe and the US performed >10 LVAD implantations per year. In the US, most centers (88.3%) did not have a subset of members of the cardiac anesthesia team caring for these patients, whereas in Europe, more than half of the centers (57.5%) did. If only selected members of the cardiac anesthesia team provided care, they might have had more exposure to these procedures and, therefore, may have had increased experience.

Perioperative Hemodynamic Monitoring

Durable mechanical circulatory support implantation deserves adequate perioperative monitoring to rapidly detect, further prevent, and guide treatment of specific unwanted deteriorating physiologic parameters.[14] Besides basic hemodynamic monitoring (electrocardiogram, noninvasive blood pressure, peripheral oxygen saturation, and end-tidal CO_2), more advanced hemodynamic monitoring is necessary, such as invasive arterial blood pressure monitoring; whereas a pulmonary artery catheter is an essential tool in the perioperative assessment of LVAD recipients.[13,17] The currently available pulmonary artery catheter, used in most centers (>85%) on both continents, enables continuous cardiac output monitoring, central venous and pulmonary artery pressure monitoring, and continuous mixed venous oxygen saturation measurement. Central and mixed venous oxygen saturation help interpret the circulation, helping guide hemodynamic therapy.[18] Moreover, intraoperative near-infrared spectroscopy and processed electroencephalogram monitoring are used in more than half of the LVAD centers.

Perioperative Medical Management

The most important aspect when choosing the best agent for induction of anesthesia in end-stage heart failure patients is the reduction in orthosympathetic stress due to the use of anesthetic agents, necessitating a cautious approach for induction. Although Potapov et al.[13] did not recommend the use of propofol due to its cardiodepressive side effects, in this survey, propofol, and etomidate were more or less equally used in Europe and the US. Moreover, inotropic agents, such as a bolus and/or continuous infusions, starting at the induction of anesthesia, may help to counteract the loss of orthosympathic stress during anesthesia induction to prevent systemic hypotension.[19] In the maintenance of anesthesia, the most frequently used classic anesthetic agents are sevoflurane or isoflurane, propofol, and opioids such as sufentanil, fentanyl, and remifentanil. As isoflurane and fentanyl are inexpensive in the US, this may have been one of the main reasons for the difference in medication strategy.

Many patients with end-stage heart failure suffer from venous PH with or without RV failure. The main treatment options on the ward or coronary care unit include an inotropic agent, such as dobutamine, together with a vasoconstrictive agent (norepinephrine, epinephrine). Levosimendan and norepinephrine are used more often in Europe, whereas phosphodiesterase 3 (PDE3) inhibitors and epinephrine are used more often in the US. Although it was published that inhaled nitric oxide via face mask before induction of anesthesia in patients with class 2 or 3 PH (Dana Point classification) might be helpful to reduce PH,[20] this may be questionable in patients with severe left ventricular failure scheduled for LVAD implantation, as left ventricular end-diastolic pressures may further increase. The same is true for the preoperative use of levosimendan and PDE3 inhibitors in patients with end-stage heart failure with severely depressed LV function. It might be useful to investigate outcomes in these patients by comparing the preoperative use of levosimendan and/or PDE3 inhibitors with the use of dobutamine, as dobutamine serves as an inotropic agent without effects on pulmonary vascular resistance.

This survey demonstrated that there is a significant shift in the choice of inotropes before and after the induction of anesthesia. The loss in orthosympathetic tone and vasomotor tone may necessitate the use of norepinephrine and epinephrine after induction.[19] Moreover, the use of levosimendan in European centers decreased after induction, which might have been a consequence of a different preference of the cardiac anesthesiologist for inotropic agents used in the operating room. In addition, the use of levosimendan may decrease after induction to avoid associated hypotensive events due to the combined effects of loss of orthosympathetic tone, the use of anesthetic agents, the vasodilatory effects of levosimendan, the response of the inflammatory system to surgery, the use of extracorporeal circulation, and the use of blood products. Levosimendan has a long half-life, and its effect may continue for the next few hours. None of the US centers mentioned using levosimendan during LVAD implantation because it was not approved for use in the US.[21] Moreover, there is no or limited evidence for any beneficial effect of levosimendan in patients with LVADs.[22,23] The preoperative use of levosimendan may reduce the risk of RV failure without any significant effect on in-hospital, 30-day, and 5-year mortality.[24]

Only a few institutions (4.5%) in Europe and the US used inhaled nitric oxide preoperatively, and a few more used nitric oxide after induction of anesthesia (up to 8% of the centers). However, its use increased significantly for the intraoperative treatment of PH (82%), with or without concomitant use of other inhaled agents, such as milrinone and iloprost or IV milrinone.[25–28]

The incidence of RV failure after LVAD implantation ranges between 20 and 40%. Several clinical, hemodynamic, and echocardiographic parameters or calculated parameters are used to predict RV failure.[29,30] In the survey, the most frequently used hemodynamic parameters were CVP, mean pulmonary artery pressure-CVP gradient, CVP/pulmonary capillary wedge pressure ratio, and RVSWI, respectively, and, to a lesser extent, PAPi. A systematic review and meta-analysis from Bellavia et al., including 36 studies, showed that RVSWI, besides CVP, had the highest effect size in identifying patients at risk for RV failure after LVAD implantation.[31] It is interesting to note that only 28.8% of European centers and 13.3% of the US centers used RVSWI.

A newer parameter predicting RV failure after LVAD implantation, and hardly reported at the time of this investigation, is preoperative PAPi.[32] If the preoperative PAPi is too low (eg, <1.85), then inotropes could be used to improve PAPi, leading to an optimal PAPi. The change in PAPi (ΔPAPi) is then defined as the difference between the first measurement of PAPi and the optimal PAPi. Subsequently, initial PAPi, optimal PAPi, and ΔPAPi can then be used as predictors for RV failure after LVAD implantation.[33] The authors suggest combining CVP, RVSWI, and PAPi to identify patients at risk for RV failure during LVAD implantation, although these parameters are preload-dependent.

Echocardiographic prediction of RV failure after LVAD implantation is difficult, due to its triangular shape. Several studies have been published, and only scarce transthoracic and transesophageal echocardiographic parameters are statistically significant to predict postoperative RV failure, such as RV fractional area change and RV free wall longitudinal strain.[29-31] Of note, RV end-diastolic diameter-left ventricular end-diastolic diameter ratio was one of the echocardiographic measurements with the highest effect size in predicting RV failure and, therefore, might be used in daily practice.[31] In this study, eyeballing of the RV, bowing of the interatrial septum, tricuspid annular plane systolic excursion, and a dilated right atrium or RV were used most often, respectively, although the literature was inconclusive for most of these approaches. Very recently, it was reported that contrast-enhanced electrocardiogram-gated computed tomography angiography predicts pre-LVAD implantation postoperative RV failure.[34]

Despite optimization with inotropes, weaning from bypass may be difficult in terms of RV failure, and, in case of persistent RV failure, temporary MCS of the RV may be necessary. Investigating the different centers, changes in inotropes were

the most frequent first choice in the US (86.7%). In contrast, in Europe, a broader selection of treatment options was proposed besides changes in inotropes, including RV assist device implantation, extracorporeal membrane oxygenation, or other devices. Currently, several invasive treatment options are available, including venoarterial extracorporeal membrane oxygenation, temporary RV assist device with a single- (Biomedicus or Tandemlife) or double-lumen cannula (ProtekDuo Tandemlife), percutaneous Impella (Abiomed), and/or TandemHeart.[35] Importantly, it was reported recently that intraoperative RV MCS for patients with LVADs is associated with a better outcome than postoperative implantation.[36]

There is no study about the use of hemofiltration on CPB during LVAD implantation. Moreover, there is little information available on routine cardiac surgery. An observational single-center study in routine cardiac surgery patients suggested that hemofiltration can lead to hemoconcentration, elevated lactate levels, and increased inotropic support. The routine use of hemofiltration may have a wide range of negative effects and should be used cautiously. They advised the limited use of hemofiltration in patients with impaired renal function, positive fluid balance, and reduced response to diuretics, or in patients with a prolonged time on CPB for longer than 2 hours.[37] Although there is typically no cross-clamping of the aorta and no use of cardioplegic solutions, patients with end-stage heart failure may have a decompensated state with volume overload, and the use of peribypass hemofiltration may have a beneficial aspect on these patients. It is unclear why US LVAD centers used hemofiltration during bypass more often than European centers.

US centers seemed to have a more restrictive transfusion policy during weaning from CPB. Some small single-center studies investigated the outcome of adults undergoing LVAD implantation and transfusion. An association between early massive transfusion and adverse outcomes was reported.[38,39] Therefore, a more restricted transfusion protocol seems reasonable. However, the ideal hemoglobin target in patients with LVADs remains unclear and should be investigated in the future.

Postoperative Intensive Care Aspects

The most common early postoperative complications after LVAD implantation are vasoplegia, RV failure, acute kidney failure, and bleeding complications. Although many papers have been published about cardiac vasoplegia syndrome, a clear definition is lacking.[40,41] In the PERSUADE survey, the parameter mentioned most often in Europe was a norepinephrine continuous drip $\geq$100 ng/kg/min. In contrast, in the US, the most frequently used parameter was a systemic vascular resistance of $<$800 dynes·s·cm^{-5}. Vasopressin of $>$1 U/h was one of the options in the questionnaire, and was used in the definition of vasoplegia in Europe in 24 centers (32.9%) and the US in 26 centers (43.3%; p = 0.28). However, the use of vasopressin might be controversial, as vasopressin affects V1a and V2 receptors, introducing vasoconstrictive or vasodilatory effects, respectively. A CI of $>$2.5 L/min/m^2 was the least-mentioned parameter used in the definition of vasoplegia before other parameters, such as the need for multiple vasoconstrictors (1 center in Europe and 6 centers in the US). The incidence of vasoplegia after continuous-flow LVAD implantation mentioned in this study was around 20 to 25%. Several other studies reported the incidence of vasoplegia after continuous-flow LVAD implantation ranging between 8 and 60%, depending on the used definition, with subsequent worse outcomes.[8-10] To further refine and intensify research in this field, a uniform definition for cardiac surgery vasoplegia is deemed necessary.

About 12% of the patients with end-stage heart failure have various stages of acute kidney disease. The implantation of an LVAD affects the incidence of acute kidney failure, with some improving due to the improved circulation; whereas others initially or further deteriorate, necessitating renal-replacement therapy.[42] Moreover, the combination of preoperative RV dysfunction and renal failure has an impact on postoperative renal failure and mortality.[43]

The interaction between coagulation and anticoagulation plays an important role during and after LVAD implantation. Preoperatively, most patients were taking vitamin K antagonists (acenocoumarol, fenprocoumon, or warfarin). The authors observed a global difference in the correction of an increased INR before surgery. Moreover, antifibrinolytics were generally used (tranexamic acid in Europe and tranexamic acid or aminocaproic acid in the US). In general, postoperative heparin intavenous was started after several hours of hemostasis.[44]

Limitations

There were several limitations in this study. First, it cannot be fully guaranteed that the respondent filled in the institutional representation of the clinical practice rather than the individual clinician's response or attitudes. Second, the respondents were instructed to complete the survey with practice data from 2019 before the coronavirus disease pandemic, but it cannot be guaranteed that the respondents complied. Third, the number of questions in the questionnaire was restricted to obtain a response from respective centers as high as possible. This restriction meant that several anesthesia- and intensive care-related topics might have been underexposed, not mentioned, or included in this survey. However, this restriction might have had an effect on the response rate, as the response rate in the survey was much higher than that of a comparable survey performed in centers doing lung transplantations.[45]

In conclusion, although there are many papers published about several preoperative aspects, intraoperative monitoring, intraoperative medical management, and early postoperative intensive care aspects, there are many differences in the management of these patients during LVAD implantation in Europe compared with the US. Fortunately, there are no differences in early outcomes after LVAD implantation comparing both locations, although it is unclear what the specific effects of different treatment strategies are. Combining the

best of each continent and reviewing the literature more extensively might lead to further improvements in outcomes. Therefore, these findings confirmed the need for an international anesthesia- and intensive care-driven consensus to guide perioperative monitoring and pharmacologic support in LVAD implantation.

Declaration of Competing Interest

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2023.10.013.

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