Cardiovasc Surg Int 2022;9(3):168-175
http://dx.doi.org/DOI: 10.5606/e-cvsi.2022.1349
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Defining early right ventricular failure during left ventricular assist device implantation: Retrospective analysis of intraoperative management

Mustafa Şimşek[1], Müge Taşdemir Mete[2]

[1]Department of Anesthesiology and Reanimation, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Türkiye
[2]Department of Cardiovascular Surgery, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Türkiye

Received: May 18, 2022 ***Accepted:*** August 08, 2022 ***Published online:*** October 14, 2022

ABSTRACT

Objectives: In this study, we aimed to share the intraoperative anesthesia management of left ventricular assist device (LVAD) implantation and our approach to right ventricular failure (RVF) that developed in this process, and our results.

Patients and methods: A total of 82 patients (71 males, 11 females; mean age: 49.4±9.4 years; range, 18 to 71 years) who underwent LVAD implantation between February 2013 and June 2020 were included in the retrospective study. Preoperative echocardiography, cardiac catheterization findings, and intraoperative records were reviewed. In light of the preoperative hemodynamic, echocardiographic, and preoperative echocardiographic findings of the patients, RVF levels were preoperatively determined, and a medical and mechanical support therapy algorithm for RVF was created. The postoperative outcomes were evaluated within the framework of this algorithm.

Results: The mean preoperative left ventricular ejection fraction was 19.6%, and the mean right ventricular ejection fraction was 37.4%. According to our algorithm, eight (9.7%) patients developed severe, 12 (14.6%) moderate, and 48 (58.5%) mild RVF. No RVF was present in 14 (17.2%) patients. The vasoactive inotrope score was 25.7±1.3 in the advanced RVF group and compatible with the severity of RVF. Extracorporeal membrane oxygenation use was required in three (37.5%) patients who had severe RVF. Right ventricular assist device was implanted in one of the three patients with extracorporeal membrane oxygenation due to advanced RVF in the postoperative period. Mortality was observed in two (25%) patients in the advanced group, one (8.3%) in the moderate, three (6.25%) in the mild, and two (14%) in the normal RVF group.

Conclusion: A standardized method for defining the RVF severity and a well-defined treatment protocol according to its degree of severity is lacking. Considering hemodynamic and echocardiographic data, grading of RVF in patients is vital for determining the treatment protocol. Treatment for RVF should be converted into standard universal algorithms.

Keywords: Assist device, heart failure, left ventricle, right ventricle.

Left ventricular assist devices (LVADs) are increasingly used in advanced heart failure to provide adequate organ perfusion and improve quality of life. Perioperative management of LVAD implantation requires a multidisciplinary approach. In the presence of right ventricular failure (RVF), it is necessary to determine the degree of failure, start right inotropic therapy on time, and use short-term mechanical support systems if sufficient flow cannot be achieved.[1]

The incidence of RVF after LVAD implantation ranges from 5 to 44%.[2] Female sex, INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) level 1, preoperative end-organ disorder, preoperative RVF, high pulmonary vascular resistance (PVR), nonischemic cardiomyopathy as etiology, history of a previous cardiac operation, and severe tricuspid insufficiency have been described as risk factors for the development of RVF after LVAD.[3] Right ventricular failure may develop immediately after LVAD implantation, during the early intensive care period, or late during follow-up after discharge.[4] Right ventricular failure in the operative or early postoperative period after implantation carries a significant mortality risk.[3]

Corresponding author: Mustafa Şimşek, MD. Dr. Siyami Ersek Göğüs Kalp ve Damar Cerrahisi Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, 34668 Üsküdar, İstanbul, Türkiye.
Tel: +90 505 - 778 99 80 e-mail: mustafasimsek73@gmail.com

Citation:
Şimşek M, Taşdemir Mete M. Defining early right ventricular failure during left ventricular assist device implantation: Retrospective analysis of intraoperative management. Cardiovasc Surg Int 2022;9(3):168-175.

Management of RVF in LVAD implantation is challenging and there is no generally accepted common RVF definition.[5] In the studies performed, the definition of severe RVF is given on the basis of mechanical treatment and inotrope necessity. There are different clinical practices for managing intraoperative RVF, focusing on medication and mechanical support but not discussing a stepwise management protocol according to the degree of severity of RVF.

In this study, we aimed to present our algorithm for defining RVF, the management approach for RVF after LVAD implantation.

PATIENTS AND METHODS

Eighty-two patients (71 males, 11 females; mean age: 49.4±9.4 years; range, 18 to 71 years) who underwent LVAD implantation due to end-stage heart failure at the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital between February 2013 and June 2020 were included in the retrospective study. The patients were evaluated by the advanced heart failure team per the protocol. Patients who underwent biventricular assist device (BIVAD) or total artificial heart (TAH) implantations were excluded. All patients received the standard preoperative management and treatment protocols decided by the advanced heart failure team. For the management of RVF, the algorithm defined by the team was applied. Preoperative demographic data, preoperative echocardiography, intraoperative cardiac catheterization findings, and intraoperative data were recorded.

None of the patients had mitral, tricuspid, or aortic stenosis of any degree. Patients with moderate or severe aortic regurgitation were not included in the LVAD program. Commonly, patients in the LVAD program have moderate to severe mitral regurgitation due to cardiomyopathy. As a routine approach, neither repair nor replacement of the mitral valve is performed during LVAD surgery as the LVAD unloads the left ventricle effectively. For tricuspid regurgitation tricuspid annuloplasty is performed only in the presence of severe regurgitation.

Standard open heart surgery monitoring was performed in each patient. A pulmonary artery catheter was used for mixed venous saturation, central venous pressure (CVP), and pulmonary arterial pressure measurement. External defibrillator pads were placed before anesthesia induction. After preoxygenation, anesthesia induction was ensured with midazolam (0.1 mg/kg), fentanyl (1-2 mg/kg), and rocuronium (1 mg/kg); anesthesia was maintained with volatile anesthetics (sevoflurane), fentanyl, and a propofol infusion. A transesophageal echocardiogram (TEE) probe (Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway) was placed in all patients after intubation.

All operations were carried out with standard median sternotomy. Before cannulation, 300 IU/kg of heparin was administered. Arterial cannulation was performed using the ascending aorta or, in redo cases, the femoral artery. Venous cannulation was performed with the bicaval (in patients who will undergo tricuspid valve intervention) or two stage single atrial venous cannula technique. Cardiopulmonary bypass was initiated with an activated clotting time >400 sec. Left ventricular assist device implantations were performed on a normothermic beating heart.

A comprehensive perioperative TEE examination was performed in all patients undergoing LVAD implantation. The correct placement of the inflow cannula, toward the mitral valve and away from the

Table 1
Intraoperative TEE evaluation parameters before and after LVAD implantation and after weaning

Before LVAD implantation
Atrium and ventricle dimensions
Valvular functions
Ejection fraction
ASD, PFO
TAPSE
Intracardiac thrombus
Apical inflow cannulation location *vs.* mitral valve position
After LVAD implantation and before/after weaning
Apical inflow cannulation location *vs.* mitral valve position
Outflow and ascending aorta evaluation
Deairing
Interventricular septum position and shift
Ventricular contraction evaluation
Valvular functions
Flow and ventricular unloading

TEE: Transesophageal echocardiogram; LVAD: Left ventricular assist device; ASD: Atrial septal defect; PFO: Patent foramen ovale; TAPSE: Tricuspid annular plane systolic excursion.

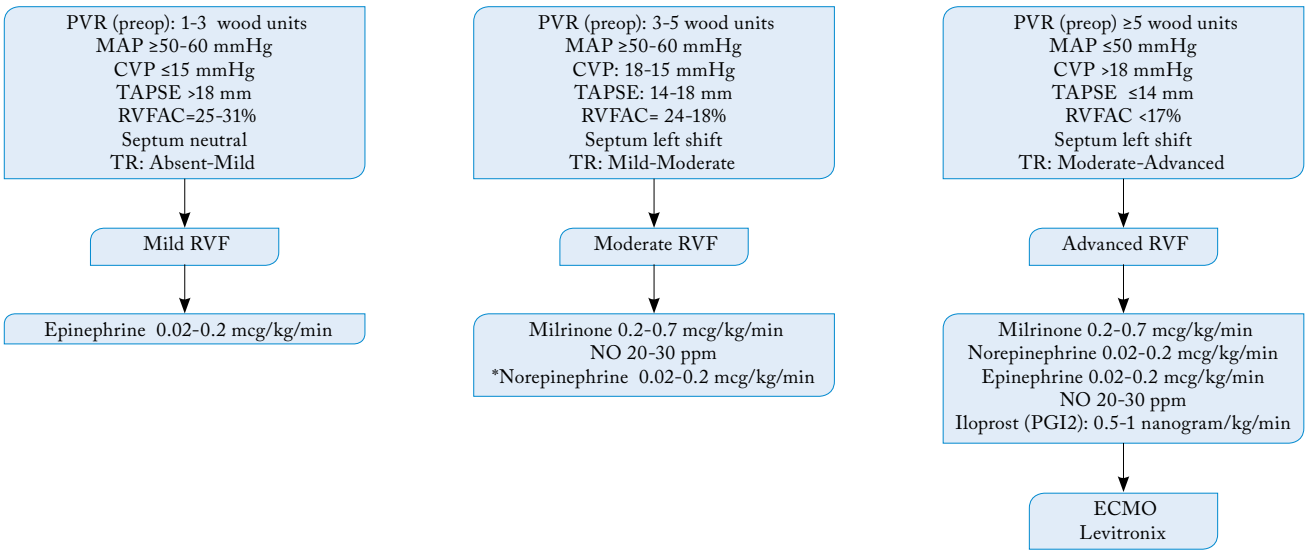

Figure 1. Right ventricular failure identification and management algorithm used in the intraoperative period.

RVF: Right ventricular failure; MAP: Mean arterial pressure; CVP: Central venous pressure; TAPSE: Tricuspid annular plane systolic excursion; RVFAC: Right ventricular fractional area change; TR: Tricuspid regurgitation; RVF: Right ventricular failure; ECMO: Extracorporeal membrane oxygenation; * If MAP ≤50 mmHg when milrinone was started, norepinephrine was added to the treatment.

ventricular septum, was assessed with intraoperative TEE. Our targets for TEE evaluation are given in Table 1.

The arterial blood gas parameters (pH, PCO_2 [partial pressure of carbon dioxide], PO_2 [partial pressure of oxygen], lactate, blood glucose, HCO_3, sodium, potassium, calcium, and chlorine) and hemodynamic parameters (heart rate [HR], mean arterial pressure [MAP], CVP, SPO_2 [peripheral capillary oxygen saturation]) were optimized before weaning off from cardiopulmonary bypass (CPB) and switching to full support by the LVAD device. Under optimal conditions (36-37˚C, HR: 80-100/min, mixed venous oxygen saturation ≥70%, arterial pH: 7.35-7.45, PO_2 and PCO_2 within normal limits, Hct [hematocrit]: 25-30%, potassium: 4.0-5.0 mEq/L, MAP ≥50 mmHg, CVP: 8-12 mmHg), CPB was terminated and LVAD was adjusted with adequate flow. Inotrope and pulmonary vasodilator therapy were initiated according to the RVF protocol. In Figure 1, the algorithm for the inotropic support and pulmonary vasodilator therapy used for weaning intraoperatively after LVAD implantation is displayed. The grade of the RVF was defined according to the group in which the majority of the criteria were matching (the group in which three or more criteria met among the seven parameters).

The vasoactive inotrope score (VIS) that reflects the sum of the inotropes were calculated for each patient after completion of LVAD implantation in the operating room. Vasoactive inotrope scores of patients on inotropes was calculated using the formula: dopamine dose (μg/kg/min)+dobutamine dose (μg/kg/min) + 100 × epinephrine (μg/kg/min) + 10 × milrinone dose (μg/kg/min) + 10000 × vasopressin doses (unit/kg/min) + 100 × norepinephrine doses (μg/kg/min).

Additional mechanical support was considered in patients with advanced RVF refractory to medical treatment. After CPB was terminated, the activated clotting time was neutralized with a heparin-protamine ratio of 1:1. After decannulation, bleeding control was achieved, and the sternum was closed. The patients were followed in the intensive care unit.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 28.0.1 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed as mean ± standard deviation, median (min-max), or number and frequency. The groups were compared using the chi-square and Kruskal-Wallis tests. A p value <0.05 was considered statistically significant.

RESULTS

The mean preoperative left ventricular ejection fraction was 19.6±4.6%, and the mean right ventricular ejection fraction was 37.4±9.7%. Preoperative mechanical support was necessary in 15 patients: left ventricular Levitronix Centri Mag (Levitronix LLC, Waltham, MA, USA) in seven (8.53%) patients, Venoarterial ECMO (Sorin Group STOCKERT SCPC, Munich, Germany) in four (4.87%) patients, and IABP (Datascope System 98 Datascope Corp., Fairfield, CT, USA) in four (4.87%) patients. Twenty-nine (35.3%) patients were on inotropes preoperatively, and nine (10.97%) patients were on mechanical ventilation before the operation. The mean preoperative tricuspid annular plane systolic excursion (TAPSE), pulmonary vascular resistans

Table 2
Demographic data (n=82)

	n	%	Mean±SD	Mean	Min-Max
Sex					
Female	11	13.4			
Male	71	86.6			
Mean age (year)			49.4±9.4		18-71
Diabetes mellitus	26	31.7			
Hypertension	31	37.8			
Body mass index (kg/m^2)			27.1±5.2		
Etiology of heart failure					
Dilated cardiomyopathy	42	51.21			
Ischemic cardiomyopathy	40	48.78			
INTERMACS Classification					
INTERMACS 1	7	8.53			
INTERMACS 2	8	9.75			
INTERMACS 3	14	17.07			
INTERMACS 4	38	46.34			
INTERMACS 5	15	18.29			
ECMO	4	4.87			
Levitronix	7	8.53			
IABP	4	4.87			
Preoperative hemodynamic					
Preoperative inotrope support	29	35.36			
Preoperative TAPSE (mm)				16.5	25-7
Preoperative PVR (WU)*				3.13	8-1
Preoperative CI (L/min/m^2)				1.195	2.4-0.95
Preoperative PCWP (mmHg)				17.90	41-10
Preoperative LVEF		19.6			
Preoperative RVEF	16	37.4			

ECMO: Extracorporeal membrane oxygenation; TAPSE: Tricuspid annular plane systolic excursion; PVR: Pulmonary vascular resistance; WU: Wood unit; CI: Cardiac index; PCWP: Pulmonary capillary wedge pressure; LVEF: Left ventricular ejection fraction; RVEF: Right ventricular ejection fraction.

(PVR), cardiac index (CI) and pulmonary capillary wedge pressure (PCWP) were 16.5 (7-25), 3.13 (1-8) wood units, 1.195 (0.95-2.4) L/min/m^2, and 17.90 (10-410) mmHg, respectively (Table 2).

Only two patients had severe tricuspid regurgitation before the operation, and concomitant tricuspid annuloplasty was performed. Both patients were in the severe RVF group. HeartMate II (HMII; St. Jude Medical, Inc. [Thoratec Corporation], Pleasanton, CA) was implanted in 31 patients (37.80%), Heartmate III (HMIII; St. Jude) Medical, Inc. [Thoratec Corporation], Pleasanton, CA) in 27 patients (32.92%), and Heartware HVAD Ventricular Assist System (HeartWare, Framingham, MA) in 24 patients (29.26%). Wood unit. According to our algorithm, eight (9.7%) patients developed severe, 12 (14.6%) moderate, and 48 (58.5) mild RVF. No signs of RVF were detected in 14 (17.2%) patients. Inotrope and vasodilator therapy were started according to this RVF classification. Among the seven patients who underwent surgery at the INTERMACS level 1, three patients developed severe, two patients moderate, and two patients mild RVF. Among all patients, the mean VIS values were 25.7±1.3 in the eight patients with advanced RVF, 19.5±1.5 in the 12 patients with moderate RVF, and 10.8±1.6 in the 48 patients with mild RVF. In 14 patients without RVF, the mean VIS was 3.6±1.1.

The mean duration of inotrope requirement was longer in patients with advanced RVF. Postoperative venoarterial extracorporeal membrane oxygenation (ECMO) was used in all patients who developed advanced RVF. The mean intubation time, renal replacement therapy requirement, and bleeding revision rates were higher in patients with advanced RVF (Table 3). As the degree of RVF increased, the INTERMACS level, need for inotropes, VIS value, need for ECMO and renal replacement therapy, and prolonged intubation time were found to be higher ($p<0.05$).

Although the overall patient number in the study was 82, the number of patients and morbidities were not sufficient to make a comparative analysis of each group. Instead, the study aimed to share our criteria for RVF after LVAD implantation as a contribution to further studies. A right ventricular assist device (RVAD) was implanted in the first postoperative week in one of the three patients who could not be weaned off the required support with an ECMO due to advanced RVF in the postoperative

Table 3
Patient profiles according to the degree of perioperative RVF after implantation

	Advanced RVF (n=8)			Moderate RVF (n=12)			Mild RVF (n=48)			Normal RV (n=14)		
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD
INTERMACS I	3	37.5		2	16.6		2	4.1		0	0	
Preoperative mechanical support	4	50		4	33.3		6	12.5		1	7.1	
Preoperative inotrope support	8	100		12	100		6	12.5		3	21.4	
Postoperative inotrope requirement (days)			9.8±2.8			6.6±1.4			4.4±1.2			1.7±0.9
VIS average (per patient)			25.7±1.3			19.5 ±1.5			10.8±1.6			3.6±1.1
Postoperative ECMO use	3	37.5		0	0		0			0	0	
Renal replacement therapy	3	37.5		1	8.3		0			0	0	
Intubation (days)			6±1.8			3.2±1.2			1.6±0.7			1.1±0.4
Reoperation for bleeding	2	25		0	0		2	4.1		0	0	
Mortality	2	25		1	8.3		3	6.25		2	14.2	

RVF: Right ventricular failure; RV: Right ventricul; VIS: Vasoactive inotrope score; ECMO: Extracorporeal membrane oxygenation.

period. Two patients with advanced RVF died due to prolonged intubation, infection, and sepsis. Two patients with normal right ventricular function died due to a major cerebrovascular event.

DISCUSSION

In LVAD patients, a postoperative process that will provide adequate LVAD flow and tissue perfusion can be ensured with careful intraoperative anesthesia management, and patient hemodynamics will be less affected by the underlying pulmonary and right ventricular dysfunction.[6,7] The first step in patient management during anesthesia preparations is advanced hemodynamic monitoring. In patients with advanced heart failure, a decrease in left ventricular preload or an increase in left ventricular afterload can cause rapid hemodynamic decompensation.[8] These patients require large amounts of circulating catecholamines to maintain vasoconstriction.[9,10] Suppression of the sympathetic system during induction or maintenance of anesthesia may cause severe decompensation in this patient group.[11-13] In patients undergoing LVAD implantation, TEE is a useful diagnostic and monitoring tool that provides insight into the position of the access cannula, ventricular contraction, filling pressures, and valve functions.[14-16] In our patient series, all patients underwent perioperative a TEE examination.

Evaluation of right ventricular functions is of particular importance.[17] Right ventricular function is affected by preload, PVR, and contractility. Upon initialization of the LVAD device, right ventricular preload increases, and left ventricular afterload can be optimized by adjusting the device flow. After the LVAD is implanted, the ventricular septum should be in a neutral to left position with the left ventricle moderately decompressed. Insufficient left ventricle decompression causes rightward septal shift and a decrease in LVAD flow, while excessive ventricular decompression causes the septum to deviate to the left and the device to suction, compromising the contractility of the right ventricle.

The interventricular septum may deviate to the left, impairing the septal contribution to right ventricular contraction and causing RVF. When RVF develops, it will increase left ventricular failure due to the septal compound system.[18] Therefore, visual control with TEE gains importance during the termination of CPB to assess the need for fluid and inotropic support during the incremental raising of the LVAD flow. The presence and degree of RVF can be successfully defined with monitoring and TEE examination.

Although various definitions of RVF and risk scoring systems have been defined, there is no standard accepted classification that guides treatment algorithms.[19] Existing definitions are generally based on the treatment of RVF. High dose and duration (more than two weeks) inotropic support RVAD, ECMO, and long-term use (two to 14 days) of inhaled nitric oxide are indicated as RVF treatment.[20-22]

Clinical differences are common in the detection and management of intraoperative RVF. Although the general strategies are known, the literature on treatment combinations, timing, and doses is limited. In our algorithm, patients were classified as mild, moderate, and advanced RVF by evaluating postoperative hemodynamic parameters (MAP, CVP, and PCWP), echocardiographic parameters (TAPSE, right ventricular fractional area change [RVFAC], interventricular septum position, and tricuspid valve function) and preoperative echocardiographic findings. Patients were managed according to this evaluation of RVF. The main purpose of the treatment algorithm was to optimize preload, afterload, and contractility using pulmonary vasodilators and inotropes. The requirement of inotropes or mechanical support was determined according to these parameters.

Inotropes, such as milrinone, or pulmonary vasodilators, such as nitric oxide and iloprost (PGI2 analogue), support the right ventricle by reducing afterload and optimizing preload.[23] Inhaled nitric oxide can produce a 43% reduction in PVR and decrease transpulmonary gradient (TPG).[24] In our patients, 20-30 ppm nitric oxide was used in 38 (46.34%) patients. In addition, hypoxia, hypercarbia, and acidosis should be avoided to minimize PVR.[18] Right ventricular failure after LVAD is encountered in 5 to 44% of operated patients across studies that use varying definitions of RVF.[25] Advanced RVF was detected in three (3.6%) of our patients, moderate RVF in 12 (14.6%) patients, and mild RVF in 48 (58.5%) patients. Due to varying definitions of RVF, no comparison with other studies could be made in this respect. The vasoactive inotropic scoring system is an objective indicator of inotrope therapy. Many studies have shown a correlation between high VIS values and poor outcomes.

Albeit, cut-off values for VIS vary greatly between studies.[26] In a study conducted in adult cardiac surgery patients, one-year mortality was higher in patients with a VIS ≥30.[27] In a study on the prognostic value of VIS after LVAD implantation,[28] high postoperative VIS (≥20) was associated with adverse in-hospital outcomes and was a good predictor of in-hospital mortality. In our study, the mean VIS value was 25.7±1.3 in patients with advanced RVF, 19.5±1.5 in moderate RVF, 10.8±1.6 in mild RVF, and 3.6±1.1 in patients without any RVF. Both RVF and mortality are more frequent with high VIS values. The necessity of using RVAD after LVAD is reported as 2.6%.[29] In The European Association For Cardio Thoracic Surgery, (EACTS) expert opinion statement, it was revealed that RVAD was required at a rate of 6 to 28% in patients using LVAD.[30] In our series, RVAD was used in one (5%) of 20 patients with moderate and severe RVF. Two patients with advanced RVF could not be weaned from RVF, and RVAD, which is the next treatment step, could not be used due to sepsis and multi-organ failure. Right ventricular failure after LVAD implantation is associated with high mortality and morbidity.[22] The RVF development rate is 9 to 42% after LVAD implantation,[22] and the mortality rate is stated to be 8%.[30] In our patient series, the mortality rate was 25% in patients with advanced RVF and 8.3% in patients with moderate RVF. When RVF is excluded from grouping, mortality is 9.7% in all patients.

The limitations of this study include its retrospective data collection and the relatively limited number of cases. Due to the limited number of patients with different grades of RVF, a statistically significant comparison was challenging. However, we believe it is important that the same treatment algorithm is applied to all patients, and thus we aimed to share our intraoperative patient management to form a basis for prospective studies.

In conclusion, intraoperative management during LVAD implantation requires a multidisciplinary approach and is crucial in the presence of RVF. A standardized method for defining the RVF severity and a well-defined treatment protocol according to its degree of severity is lacking. Defining the degree of RVF is essential to provide optimal treatment. We suggest our definitive criteria for evaluating mild, moderate, and severe RVF after LVAD implantation, which is helpful for a stepwise approach to management. The clinical criteria proposed here can be helpful for future studies aiming at a universal algorithm for defining the management of RVF after LVAD implantation.

Ethics Committee Approval: The study protocol was approved by the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (Date/no: 08-03-2021/E-28001928-604.01.01). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

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

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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