


# Right heart failure with left ventricular assist devices: Preoperative, perioperative and postoperative management strategies. A clinical consensus statement of the Heart Failure Association (HFA) of the ESC

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Right heart failure (RHF) following implantation of a left ventricular assist device (LVAD) is a common and potentially serious condition with a wide spectrum of clinical presentations with an unfavourable effect on patient outcomes. Clinical scores that predict the occurrence of right ventricular (RV) failure have included multiple clinical, biochemical, imaging and haemodynamic parameters. However, unless the right ventricle is overtly dysfunctional with end-organ involvement, prediction of RHF post-LVAD implantation is, in most cases, difficult and inaccurate. For these reasons optimization of RV function in every patient is a reasonable practice aiming at preparing the right ventricle for a new and challenging haemodynamic environment after LVAD implantation. To this end, the institution of diuretics, inotropes and even temporary mechanical circulatory support may improve RV function, thereby preparing it for a better adaptation post-LVAD implantation. Furthermore, meticulous management of patients during the perioperative and immediate postoperative period should facilitate identification of RV failure refractory to medication. When RHF occurs late during chronic LVAD support, this is associated with worse long-term outcomes. Careful monitoring of RV function and characterization of the origination deficit should therefore continue throughout the patient's entire follow-up. Despite the useful information provided by the echocardiogram with respect to RV function, right heart catheterization frequently offers additional support for the assessment and optimization of RV function in LVAD-supported patients. In any patient candidate for LVAD therapy, evaluation and treatment of RV function and failure should be assessed in a multidimensional and multidisciplinary manner.

## Keywords

Right heart failure • Left ventricular assist device • Optimization of right ventricular function

## Introduction

Right heart failure (RHF) following implantation of a left ventricular assist device (LVAD) is relatively common. It ranges from 10–40%, including the immediate and long-term post-LVAD implantation period<sup>1,2</sup> and is associated with increased morbidity and mortality.<sup>3,4</sup> Some risk factors for post-LVAD implantation right ventricular (RV) failure are modifiable; thus every effort should be exerted to identify them and optimize RV function prior to LVAD implantation. Although technically feasible, implanting durable biventricular mechanical circulatory support devices to overcome significant RV failure significantly increases the risk of both short- and long-term complications, impairs quality of life, and is more complex to manage than LVAD therapy alone.<sup>5</sup> Therefore, maximal efforts to improve and optimize RV function before LVAD implantation is the preferred initial approach for many LVAD implanting centres and continues throughout the time the patient is under LVAD support.

## Pathophysiology of right heart failure following left ventricular assist device implantation

The aetiology of RHF following LVAD implantation is multifactorial and begins with a preoperatively impaired right ventricle which is then influenced by the changing physiology attributed to LVAD support in several ways<sup>6</sup>:

1. The LVAD increases systemic flow and consequently increases RV preload. Although in normal conditions the right ventricle can tolerate significant volume changes, the sudden increase in RV preload post-LVAD implantation might not be easily tolerated by a dysfunctional and vulnerable ventricle. This may

be exacerbated by the extra administered volume of fluids and blood products during the implantation and is worsened by systemic inflammation due to surgical stress.

2. Unloading of the left ventricle by the LVAD with a transapical flow (rather than transaortic) causes mechanical dyssynchrony of the interventricular septum, altering the geometry and the volume of the RV cavity, changing the coaptation points in the tricuspid valve apparatus and disrupting ventricular interdependence (coupling) with consequent alteration in RV function.

Additional factors that may impair RV function postoperatively are cardiopulmonary bypass (CPB)-related myocardial stunning, vasoplegia and altered myocardial coronary perfusion. Other characteristics that impede ventricular coupling include loss of pericardial restraint and altered mechanics of cardiac twist.<sup>7</sup> Although the LVAD, immediately upon its activation, effectively reduces left ventricular (LV) preload and pulmonary venous pressures, eventually resulting in the reduction of pulmonary arterial pressures supporting the RV function by reducing its afterload, the elevated pulmonary vascular resistance (PVR) can persist for weeks to months following LVAD implantation, thus delaying the positive effect of the LVAD on RV function.<sup>8,9</sup> Furthermore, while LVAD provides this apparent benefit to the RV function by unloading the left ventricle,<sup>10,11</sup> it has been shown that following an LVAD implantation, the right ventricle reveals a maladaptation to afterload and appears more afterload-sensitive.<sup>12</sup> However, the progressive, even months post-LVAD implantation, reduction in RV afterload results in improvements in RV function.<sup>12</sup>

Interestingly, in 5-year outcomes of LVAD therapy as recently reported from the MOMENTUM 3 trial, heart failure is now the leading cause of late deaths reflecting its importance and changing epidemiology as haemocompatibility-related deaths have become less frequent with better devices.<sup>13</sup>

## Definition/classification of right heart failure

Right heart failure following LVAD implantation is not an all or nothing phenomenon, but rather a spectrum of manifestations and consequences<sup>14</sup> ranging from a post-LVAD implantation failing right ventricle clinically responsive to diuretics, inotropes, and inhaled nitric oxide (iNO), to severe RV failure needing a temporary RV mechanical circulatory support. The reported incidence of RHF post-LVAD implantation ranges from 10–40%<sup>3,15</sup> with the variation being attributed, at least partially, to the various definitions of post-LVAD RHF, suggesting the need for a standardized definition. In the MOMENTUM trial and in the fully magnetically levitated group, 29.8%,<sup>16</sup> 27.9%<sup>17</sup> and 29.9%<sup>13</sup> encountered RHF at 6 months, 2 and 5 years post-LVAD implantation, respectively. In the recently published consensus document from the International Society for Heart and Lung Transplantation, though the criteria from the original definition have been retained, a conscious decision to register the event as RHF is required.<sup>18</sup> This will contribute to the uniformity of data reported from clinical trials.<sup>18</sup> The updated definition of post-LVAD implantation RV failure is shown on Table 1. Similarly, it has been suggested that the term ‘right heart failure’ be abandoned in favour of ‘heart failure’ in the late phase after LVAD implantation since such categorization discourages early identification of haemodynamic aberrancies which, if addressed at origination, could prevent subsequent development of RHF (which is generally an end result).<sup>19</sup>

## Prediction of right heart failure following left ventricular assist device implantation

The detrimental consequences of RHF following LVAD implantation have driven the field, from the early LVAD era to identify prognostic markers for post-LVAD implantation RHF. Several indices of RV function originating mainly from echocardiography and right heart catheterization, along with biochemical parameters, have been identified and have subsequently been tested for validation.

## Role of clinical assessment and medical history

When considering LVAD implantation, it is important to first evaluate the patient’s medical history. Long-standing distended jugular veins and peripheral oedema are indicators of RHF, which requires special attention and potential optimization before proceeding with the procedure. Potapov *et al.*<sup>20</sup> reported that visible ascites and discoloration of the skin of the legs secondary to hemosiderosis already progressing above the knees is supportive of long-standing RHF with very poor changes of reversibility. These clinical findings make the option of biventricular mechanical support inevitable. Both ischaemic and non-ischaemic cardiomyopathy can affect RV function by the underlying primary cardiomyopathic process and by

increasing the RV afterload. The long-term impact of these diseases on RV function following LVAD implantation is unclear.

A recent study showed that approximately 43% of ambulatory patients with newly diagnosed heart failure with reduced ejection fraction (HFrEF) have RV dysfunction.<sup>21</sup> While some patients showed improvement in RV function over time, others required an up-titration of heart failure medication during follow-up. However, there is a lack of longitudinal data on RV function in patients with HFrEF.

## Role of echocardiography

Echocardiography is the easiest diagnostic modality to perform and to repeat. It can provide insight on RV morphology and function and associated structural or functional abnormalities that may lead to the development of RHF. Presence of patent foramen ovale indicates its closure at the time of LVAD implantation. Identification of moderate to severe tricuspid regurgitation (TR) before LVAD implantation could indicate correction of the valve disease, though data are not clear.<sup>22,23</sup> Additionally, presence of moderate aortic valve regurgitation prompts surgical correction.<sup>24</sup>

Several echocardiographic parameters have been tested in clinical trials for their prognostication of RHF following LVAD implantation (Table 2).<sup>15,25–32</sup> Tricuspid annular plane systolic excursion (TAPSE) was found to have no prognostic value.<sup>15,25</sup> Peak systolic velocity of the tricuspid annulus by pulsed-wave tissue Doppler imaging has been observed to provide prognostic information for RHF post-LVAD implantation, with cut-off values ranging from 8.0 to 8.8 cm/s, though data are conflicting.<sup>26,27</sup> The degree of RV dilatation resulting from chronic volume and pressure overload has been evaluated as a predictor for RV failure post-LVAD implantation. However, this entity is dependent on volume loading of the right ventricle. A RV to LV end-diastolic basal diameter ratio (RV/LV ratio) >0.72 as a surrogate for disproportionate RV remodelling, has been shown to predict RV failure.<sup>28</sup> However, this finding has not been confirmed by others.<sup>15,25</sup> In the study by Raina *et al.*,<sup>15</sup> impaired RV fractional area change was associated with RHF post-LVAD implantation, although not confirmed by Kato *et al.*<sup>27</sup> RV volumes measured by three-dimensional (3D) echocardiography were also found to be predictive of RV failure following LVAD implantation, while the RV ejection fraction was not.<sup>30</sup>

Free wall RV longitudinal strain (RVLS) has been tested and was found to provide prognostic information for RHF following LVAD implantation as reported by Cameli *et al.*<sup>32</sup> suggesting that low RVLS values predicted the occurrence of RV failure following LVAD surgery. Interestingly, in this study, among those patients who improved their RVLS in response to intra-aortic balloon pump (IABP) support, none developed RV failure post-LVAD implantation. RVLS rate has also been identified as a useful tool in predicting RV failure post-LVAD implantation in the study by Dandel *et al.*<sup>26</sup> Patients with moderately increased RV end-diastolic volume index shown in 3D echocardiography were found to carry a higher risk of RHF post-LVAD implantation while, surprising enough, severe RV dilatation was found to be protective.<sup>31</sup>

The presence of at least moderate TR makes the assessment of the RV function more complex. However, considering the

**Table 1 Updated definition of right ventricular failure following left ventricular assist device implantation****Right heart failure****Early acute right heart failure**

- Need for implantation of a temporary or durable RVAD (including ECMO) concomitant with LVAD implantation (RVAD implanted before the patient leaving the operating room).

**Early post-implant right heart failure**

- Need for implantation of a temporary or durable RVAD (including ECMO) within 30 days following LVAD implantation for any duration of time; or,
- Failure to wean from inotropic or vasopressor support or inhaled nitric oxide within 14 days following LVAD implantation or having to initiate this support within 30 days of implant for a duration of at least 14 days.
  - The primary diagnosis of right heart failure is made by the presence of at least two of the following clinical findings:
    - Ascites
    - Functionally limiting peripheral oedema (>2+)
    - Elevated estimated jugular venous pressure at least halfway up the neck in an upright patient
    - Elevated measured CVP or right atrial pressure ( $\geq 16$  mmHg)
  - Or is associated with at least one of the following manifestations:
    - Renal failure with serum creatinine  $>2 \times$  baseline values.
    - Liver injury with an elevation of at least  $2 \times$  upper limit normal in AST/ALT or total bilirubin  $>2.0$
    - $SvO_2 < 50\%$
    - Cardiac index  $< 2.2$  L/min/m<sup>2</sup>
    - Reduction in pump flow of  $>30\%$  from the previous baseline in the absence of mechanical causes such as cardiac tamponade or tension pneumothorax
    - Elevated lactate  $>3.0$  mmol/L.
- Death occurring in patients within 14 days of LVAD implant who have not received an RVAD but who remain on inotropes or vasopressors at the time of death and meet criteria for the diagnosis of right heart failure on the basis of the above clinical findings (two criteria) or manifestations (one criterion) will be considered to have early post-implant right heart failure at the time of death. The contribution of early post-implant right heart failure to death (primary or secondary) will be made by the clinical care team.
- For pediatric patients, the diagnostic criteria above may be modified as follows:
  - Primary diagnosis of right heart failure based on at least two of the following clinical findings:
    - Ascites
    - Significant peripheral oedema (+2)
    - Elevated jugular venous pressure (visible in an upright patient) or hepatomegaly (3+ cm below costal margin)
    - Elevated CVP or right atrial pressure:
      - For age 10–18 years: CVP  $>14$  mmHg
      - For age 5–10 years: CVP  $>12$  mmHg
      - For age  $<5$  years: CVP  $>10$  mmHg.
  - Or at least one of the following manifestations:
    - Renal failure indicated by serum creatinine  $1.5 \times$  above baseline
    - Liver injury with an elevation of AST, ALT or total bilirubin of  $2 \times$  upper normal
    - Decrease in pump flow of 30% from a recent baseline in the absence of tamponade
    - Need to decrease the pump rate by 20% or more from a recent baseline owing to the poor filling of LVAD in a pulsatile system
    - Cardiac index  $< 2.2$  L/min/m<sup>2</sup>.

progressive development of TR in patients with chronic heart failure, the presence of severe TR on top of a dysfunctioning right ventricle makes the implantation of an LVAD in a patient who needs it a big challenge. Repair of more than moderate to severe TR is considered an accepted approach at the time of LVAD implantation.<sup>33–35</sup>

However, we are still lacking the gold standard echocardiographic parameter and cut-off point values for the assessment of RV function. This is because all these parameters, including those

haemodynamically derived, are volatile depending on preload and afterload conditions. Overall, echocardiographic parameters that predict occurrence of RV failure post-LVAD largely include markers that represent a larger than normal, volume overloaded right ventricle, especially in relation to the severity of LV failure. *Figure 1* provides a suggested diagnostic strategy based on the considered echocardiography parameters of RV function for the candidate for LVAD implantation.

**Table 1 (Continued)****Late right heart failure**

- Need for implantation of an RVAD (including ECMO) more than 30 days after an LVAD implantation. This may occur within the index hospitalization for LVAD implant or during subsequent rehospitalization for any diagnosis which resulted in a need for temporary or permanent right-sided mechanical assist devices.
- Hospitalization that occurs more than 30 days post-implant and which requires intravenous diuretics or inotropic support for at least 72 h and is associated with:
  - Diagnosis of right heart failure is made by the presence of at least two of the following clinical findings:
    - Ascites
    - Functionally limiting peripheral oedema (>2+)
    - Elevated estimated jugular venous pressure at least halfway up the neck in an upright patient
    - Elevated measured CVP (>16 mmHg).
  - Or which is associated with at least one of the following manifestations:
    - Renal failure with serum creatinine >2× baseline value
    - Liver injury with an elevation of at least 2× upper limit normal in AST/ALT or total bilirubin >2.0
    - A reduction in pump flow of >30% from the previous baseline in the absence of tamponade
    - SvO<sub>2</sub> <50%
    - Cardiac index <2.2 L/min/m<sup>2</sup>
    - Elevated lactate >3.0 mmol/L.
- For pediatric patients, the criteria should be modified as follows:
  - Requirement for intravenous diuretics or inotropic support of at least 72 h to treat right heart failure that was not present continuously since implantation (must have been without intravenous diuretics and inotropic support for at least 7 consecutive days at some time following implantation of LVAD)
    - Diagnosis of right heart failure must be based on at least two of the following clinical findings
      - Ascites
      - Significant peripheral oedema (+2)
      - Elevated JVP (visible in the upright patient) or hepatomegaly (3+ cm below costal margin)
      - Elevated CVP or right atrial pressure:
        - For age 10–18 years: CVP >14 mmHg
        - For age 5–10 years: CVP >12 mmHg
        - For age <5 years: CVP >10 mmHg.
    - Or at least one of the following manifestations
      - Renal failure indicated by serum creatinine 1.5× above baseline
      - Liver injury with elevation of AST, ALT or total bilirubin of 2× upper normal
      - Decrease in pump flow of 30% from a recent baseline in the absence of tamponade
      - Need to decrease pump rate by 20% or more from a recent baseline because of poor filling of LVAD in a pulsatile system
      - Cardiac index <2.2 L/min/m<sup>2</sup>.

**The association of the right heart failure event should be classified as:**

**Patient-related** (e.g. pre-implant right heart failure, volume overload secondary to non-adherence with medical management, severe aortic regurgitation, cardiorenal syndrome, arrhythmia induced, pulmonary disease, elevated pulmonary vascular resistance).

**Management-related** (e.g. related to implant surgery, volume overload, inotropic agent withdrawal).

**Device-related** (e.g. associated with pump malfunction, outflow graft compromise).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; RVAD, right ventricular assist device; SvO<sub>2</sub>, mixed venous oxygen saturation.

## Role of invasive haemodynamics

Right heart catheterization before LVAD implantation constitutes a standard diagnostic procedure for the evaluation of RV function. Right heart catheterization should be performed in patients that are euvolaemic and by a trained operator. Increased right atrial pressure (RAP) (>15 mmHg) indicating increased RV preload has been identified by several studies as a prognostic marker for RV failure following LVAD implantation.<sup>26,36–38</sup> Low mean pulmonary artery pressure (PAP) concomitant with impaired RV

systolic function, as well as increased PVR [(mean PAP – mean pulmonary capillary wedge pressure [PCWP])/cardiac output] have all been reported as potential predictors for RV failure post-LVAD implantation.<sup>39,40</sup> Other parameters, derived from right heart catheterization such as RV stroke work index (RVSWi) of >300 mmHg × ml/m<sup>2</sup><sup>39</sup> preoperatively minimizes the risk for RV assist device (RVAD) perioperatively. Subsequent studies reported the prognostic role of the impaired RVSWi parameter as a predictor for RHF post-LVAD implantation.<sup>38,40–42</sup>

**Table 2** Echocardiographic right ventricular parameters to predict right ventricular failure following left ventricular assist device implantation

RV function echocardiographic parameter	Cut-off value for predicting RV failure	Sensitivity (%)	Specificity (%)
TAPSE			
Grant et al. <sup>25</sup>	No predictive value	–	–
Raina et al. <sup>15</sup>	No predictive value	–	–
Peak systolic tricuspid annular velocity by pulsed-wave tissue Doppler			
Dandel et al. <sup>26</sup>	8 cm/s	84	90
Kato et al. <sup>27</sup>	4.4 cm/s	87	68
RV/LV ratio			
Kukucka et al. <sup>28</sup>	>0.72	0.80	0.74
Potapov et al. <sup>29</sup>			
Grant et al. <sup>25</sup>	No predictive value		
Raina et al. <sup>15</sup>	No predictive value		
RV fractional area change			
Raina et al. <sup>15</sup>	<31%	82	52
Kato et al. <sup>27</sup>	No predictive value		
RV ejection fraction			
Kiernan et al. <sup>30</sup>	No predictive value		
RV end-diastolic volume index			
Kiernan et al. <sup>30</sup>	>61 ml/m <sup>2</sup>	92	79
Otten et al. <sup>31</sup>	<84 ml/m <sup>2</sup>	NR	NR
RV end-systolic volume			
Kiernan et al. <sup>30</sup>	>47 ml/m <sup>2</sup>	83	93
RV free wall longitudinal strain			
Cameli et al. <sup>32</sup>	NR	NR	NR
RV longitudinal strain rate			
Cameli et al. <sup>30</sup>	NR	NR	NR
Dandel et al. <sup>26</sup>	<0.6/s	80	98
RV volume index			
Otten et al. <sup>31</sup>			

NR, not reported; RV, right ventricular; RV/LV, right ventricle to left ventricle end-diastolic basal diameter; TAPSE, tricuspid annular plane systolic excursion.

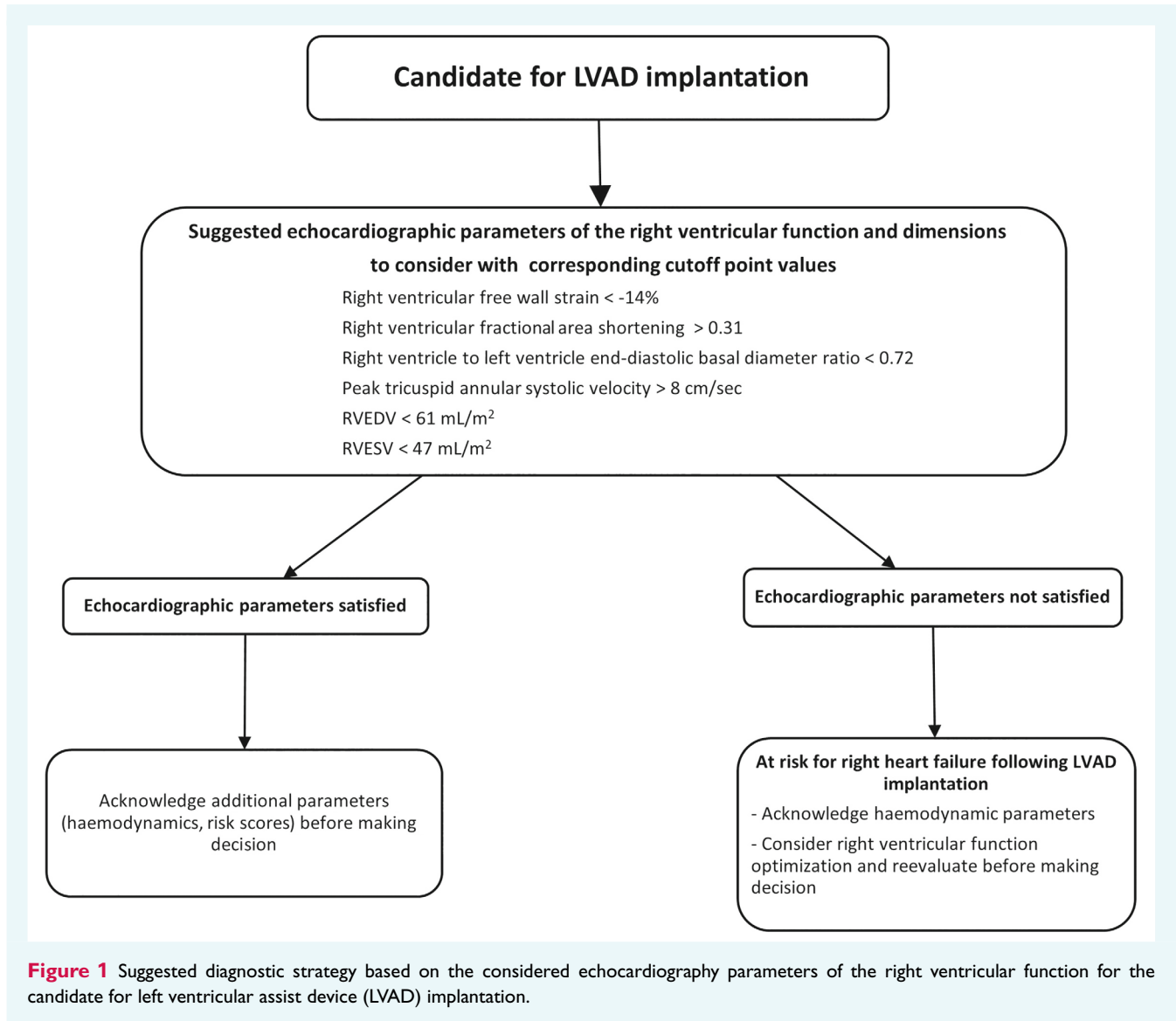
In addition, RAP/PCWP >0.63<sup>38,43–45</sup> and pulmonary artery pulsatility index (PAPi) [(pulmonary systolic artery pressure – pulmonary diastolic artery pressure)/RAP] <1.85<sup>38</sup> have, more recently, suggested an increased risk for RHF following LVAD implantation.<sup>46</sup> An improved PAPi, following the administration of diuretics, inotropes or even the placement of temporary mechanical circulatory support devices with the intention of optimizing a dysfunctional right ventricle before LVAD implantation, identifies a group of patients at lower risk for post-LVAD RHF. These changes on PAPi possibly reflect the dynamic RV contractile reserve.<sup>47</sup> The HeartMate 3 risk score that incorporates several clinical characteristics includes a RAP/PCWP ratio of >0.60 as a predictor for post-LVAD implant mortality.<sup>48</sup> Table 3 summarizes the haemodynamic parameters found to predict RHF post-LVAD implantation.<sup>26,30,37,39,40,42–46,49</sup> Figure 2 provides a suggested diagnostic strategy based on the considered haemodynamic parameters of RV function for the candidate for LVAD implantation.

Challenging cases for the evaluation of RV function are the special loading conditions to the heart posed by venoarterial extracorporeal membrane oxygenation (VA-ECMO) implantation or a temporary RVAD (surgically implanted CentriMag, Protek Duo cannula, Impella). Evaluation of the right ventricle by decreasing

the VA-ECMO or temporary RVAD support and increasing so RV preload are interventions that can potentially contribute to a better evaluation of RV function.

### Other prognosticators for right ventricular failure post-left ventricular assist device implantation

Abnormal biochemical values have been found to be predictors of RHF following LVAD implantation. Serum creatinine values >1.9–2.0 mg/dl were associated with increased risk for RV failure.<sup>42,50</sup> Similar findings have been reported for total bilirubin >2.0 mg/dl.<sup>42</sup> These biochemical values likely reflect presence of RHF-related end-organ dysfunction that may or may not be fully reversible after LVAD implantation, thereby complicating postoperative management. Additionally, a meta-analysis has identified that those of the patients that at the time of LVAD implantation were on continuous renal replacement therapy or on a ventilator were at higher risk for RV failure.<sup>36</sup> Furthermore, a pro-inflammatory milieu at the time of LVAD implantation has been found to increase the risk for RHF later.<sup>51</sup>



## Risk scores for the prediction of right ventricular failure post-left ventricular assist device implantation

Although many risk factors have been suggested for the prediction of RHF following LVAD implantation, there is no single index that can predict with sufficient accuracy the occurrence of RHF. For this reason, risk scoring systems have been proposed aiming to combine different types of variables and improve the prognostication (Table 4).<sup>37,42,50,52–55</sup> Many of these scores were generated from studies with relatively small numbers of patients and some included only patients with pulsatile LVADs. Some of the risk scores for the development of RHF post-LVAD implantation are the Michigan, Penn RVAD, CRITT, Utah, EUROMACS and recent STOP-RVF score. In any case, most of those scores have performed relatively poorly when validated and their clinical use is unclear.

## Interventions aiming at optimizing right ventricular function before left ventricular assist device implantation

Following LVAD implantation, the left ventricle undergoes remarkable unloading while, on the other hand, the right ventricle is obliged to adapt to the new haemodynamic conditions. Acknowledging that the new haemodynamic status is causing additional RV preload – even though there is a beneficial reduction in RV afterload –, efforts to optimize its function before LVAD implantation could make this adaptation safer. However, it worth mentioning that post-LVAD implantation effects on RV function are both supportive and detrimental and that the harming effects present immediately post-surgery whereas the beneficial effects occur over a period of weeks to months. Many parameters

**Table 3** Haemodynamic parameters to predict right ventricular failure following left ventricular assist device implantation

Haemodynamic parameter	n	Main findings
Right atrial pressure		
Dandel et al. <sup>26</sup>	205	CVP was higher in patients undergoing LVAD and postoperative RV failure compared to those without RV failure (18 vs. 11 mmHg, $p=0.01$ )
Drakos et al. <sup>37</sup>	175	Patients following LVAD that revealed RV failure had higher CVP preoperatively ( $>11.6 \pm 6.2$ vs. $9.5 \pm 5.1$ mmHg, $p=0.023$ )
Mean pulmonary artery pressure		
Fukamachi et al. <sup>39</sup>	100	Mean pulmonary artery pressure was lower in those patients that following LVAD needed RVAD vs. those that did not ( $31 \pm 5$ vs. $38 \pm 10$ mmHg, $p=0.015$ )
Ochiai et al. <sup>40</sup>	245	Mean pulmonary artery pressure was lower in those patients that following LVAD needed RVAD vs. those that did not ( $33 \pm 7$ vs. $37 \pm 9$ mmHg, $p=0.041$ )
RVSWi		
Fukamachi et al. <sup>39</sup>	100	RVSWi was lower in those patients that following LVAD needed RVAD vs. those that did not ( $151 \pm 75$ vs. $368 \pm 245$ mmHg $\times$ ml/m <sup>2</sup> , $p=0.011$ ). If preoperative RVSWi was $>300$ mmHg $\times$ ml/m <sup>2</sup> , none of the patients required RVAD support
Matthews et al. <sup>42</sup>	197	RVSWi $\leq 450$ mmHg $\times$ ml/m <sup>2</sup> had an OR 2.32 (95% CI 1.24–4.32) for RV failure following LVAD implantation
Ochiai et al. <sup>40</sup>	245	RVSWi $285 \pm 196$ mmHg $\times$ ml/m <sup>2</sup>
Kiernan et al. <sup>30</sup>	26	RVSWi was lower in those patients that following LVAD developed RV failure vs. those that did not ( $151 \pm 75$ vs. $368 \pm 245$ mmHg $\times$ ml/m <sup>2</sup> , $p=0.011$ )
CVP/PCWP		
Morine et al. <sup>43</sup>	132	RAP/PCWP ratio was higher in those LVAD patients that revealed RV failure compared to those that did not ( $0.69 \pm 0.19$ vs. $0.45 \pm 0.16$ , $p < 0.01$ )
Nitta et al. <sup>44</sup>	70	Patients with preoperative CVP/PCWP $>0.8$ had an OR 15.0 (95% CI 3.8–59.6) for RVAD support post-LVAD implantation
Shiga et al. <sup>45</sup>		A preoperative CVP/PCWP ratio $\geq 0.5$ was associated with an OR 11.39 (95% CI 1.164–111.4) for RVAD support post-LVAD implantation
PAPi		
Lim and Gustafsson <sup>46</sup>	85	In patients undergoing LVAD implantation, PAPi was lower in those that required RVAD compared to those that did not ( $1.7 \pm 0.3$ vs. $3.6 \pm 0.3$ , $p < 0.005$ )
Morine et al. <sup>43</sup>	132	PAPi was lower in patients with vs. without post-LVAD implantation RV failure ( $1.32 \pm 0.46$ vs. $2.77 \pm 1.16$ , $p < 0.001$ )
Raymer et al. <sup>49</sup>	216	The group of patients with LVAD that revealed severe RV failure postoperatively compared to those that did not, had significantly lower PAPi ( $2.47 \pm 2.03$ vs. $1.77 \pm 1.22$ , $p=0.001$ )

CI, confidence interval; CVP, central venous pressure; LVAD, left ventricular assist device; OR, odds ratio; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RV, right ventricular; RVAD, right ventricular assist device; RVSWi, right ventricular stroke work index.

reflecting RV function are potentially eligible for optimization, though there are no randomized studies in the literature to test the efficacy of this strategy. Subsequently, studies to define the target index of RV function for optimization before LVAD implantation are needed. The field becomes more complicated considering that all these echocardiographic and haemodynamic surrogate markers of RV function are volatile, depending not only on the intrinsic RV contractility but also on the preload, afterload and the inotropic support the right ventricle receives. Despite all these limitations, many centres adopt the strategy of the pre-LVAD RV optimization, particularly in patients with borderline, marginally functioning right ventricles. The optimization

can be achieved medically and/or by the application of temporary mechanical circulatory support.

### Optimization of right ventricular preload

Elevated central venous pressure (CVP) usually corresponds to increased morbidity and mortality in cardiac surgery, including perioperative mortality, heightened risk of acute kidney injury, and an elevated likelihood of right cardiac decompensation, even in the absence of prolonged overload. The control and optimization of blood volume are essential components of anaesthetic recommendations in cardiac surgery. Prolonged exposure of the right ventricle to increased preload leads to impaired RV systolic function with

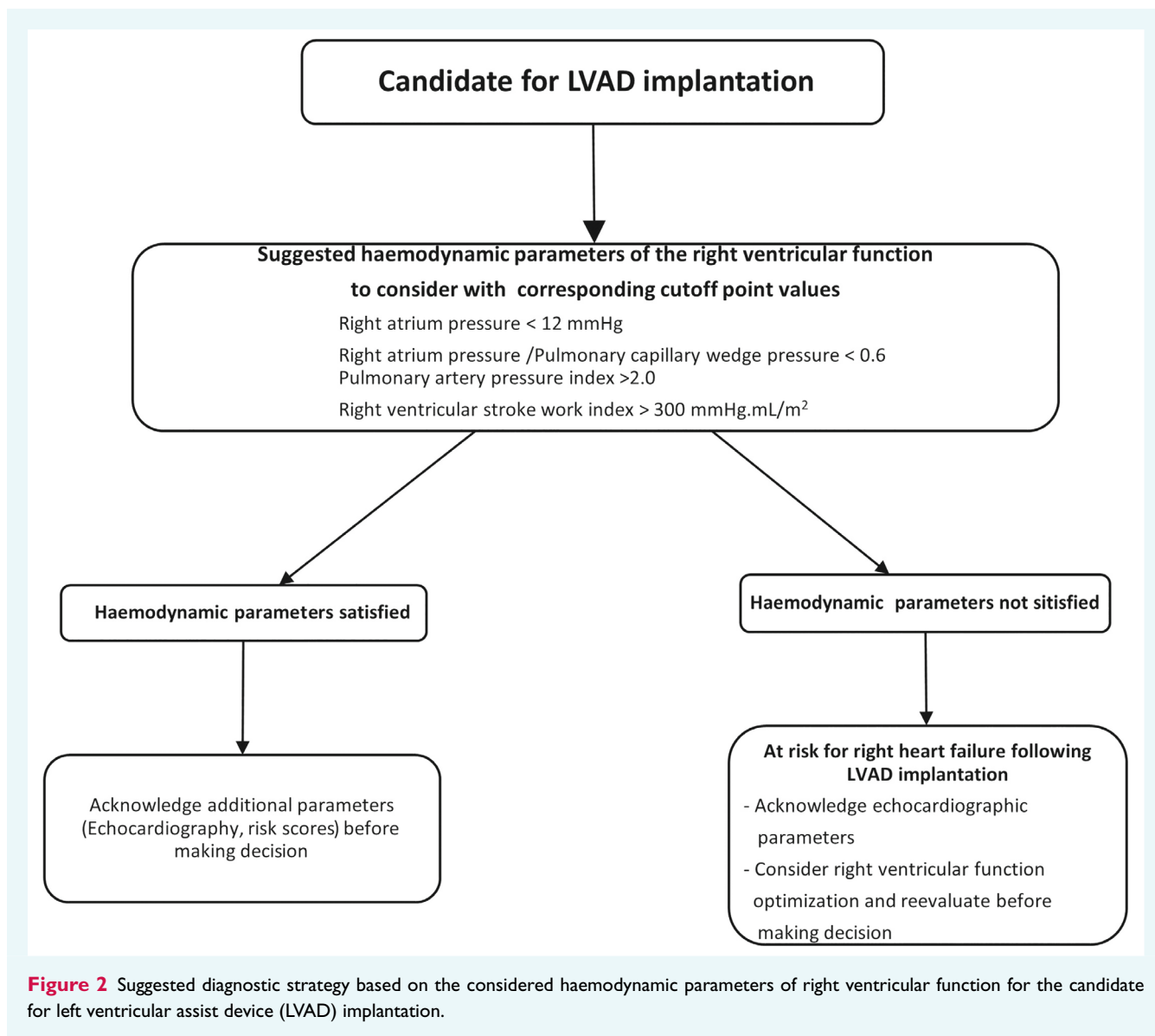


**Table 4** Risk scores for right ventricular failure following left ventricular assist device implantation

Score	Type of LVAD	Predictors for RV failure	Definition of RV failure	Discrimination/ C statistic, median (range) <sup>52</sup>
Matthews' score (n = 197) <sup>42</sup>	<ul style="list-style-type: none"> <li>86% pulsatile LVADs</li> <li>14% CF- LVADs</li> </ul>	<ul style="list-style-type: none"> <li>Vasopressor requirement</li> <li>AST <math>\geq 80</math> IU/L</li> <li>Bilirubin <math>\geq 2.0</math> mg/dl</li> <li>Creatinine <math>\geq 2.3</math> mg/dl</li> </ul>	<ul style="list-style-type: none"> <li>Intravenous inotrope support for 14 days</li> <li>Inhaled nitric oxide for <math>\geq 48</math> h</li> <li>Right-sided circulatory support (ECMO or RVAD)</li> <li>Or hospital discharge with an intravenous inotrope</li> </ul>	0.73 (0.65–0.81)
Fitzpatrick's (Penn RVAD score) (n = 226) <sup>50</sup>	<ul style="list-style-type: none"> <li>98% pulsatile LVADs</li> <li>2% CF-LVADs</li> </ul>	<ul style="list-style-type: none"> <li>Cardiac index <math>\leq 2.2</math> L/min/m<sup>2</sup></li> <li>RVSWi<sup>a</sup> <math>&lt; 300</math> mmHg <math>\times</math> ml/m<sup>2</sup></li> <li>Severe preoperative RV dysfunction</li> <li>Preoperative creatinine <math>\geq 1.9</math> mg/dl</li> <li>Previous cardiac surgery</li> <li>Systolic blood pressure <math>\leq 96</math> mmHg</li> </ul>	<ul style="list-style-type: none"> <li>Physician's decision to implant RVAD</li> </ul>	NR
Atluri's (CRITT) score (n = 218) <sup>53</sup>	<ul style="list-style-type: none"> <li>59% pulsatile LVADs</li> <li>41% CF-LVADs</li> </ul>	<ul style="list-style-type: none"> <li>CVP <math>&gt; 15</math> mmHg</li> <li>Severe RV dysfunction</li> <li>Preoperative intubation</li> <li>Severe tricuspid regurgitation</li> <li>Heart rate <math>&gt; 100</math> bpm</li> </ul>	<ul style="list-style-type: none"> <li>Decision to implant a BiVAD was made collectively by the heart failure team</li> </ul>	0.63 (0.60–0.74)
EUROMACS (n = 2000) <sup>54</sup>	<ul style="list-style-type: none"> <li>100% CF-LVADs</li> </ul>	<ul style="list-style-type: none"> <li>RAP/PCWP <math>&gt; 0.54</math></li> <li>Haemoglobin <math>\leq 10</math> g/dl</li> <li>Multiple intravenous inotropes</li> <li>INTERMACS class 1–3</li> <li>Severe RV dysfunction</li> </ul>	<ul style="list-style-type: none"> <li>Short- or long-term right-sided circulatory support, continuous inotropic support for <math>\geq 14</math> days</li> <li>Or nitric oxide ventilation for <math>\geq 48</math> h</li> </ul>	0.65 (0.63–0.67)
Drakos' (Utah score) (n = 175) <sup>37</sup>	<ul style="list-style-type: none"> <li>85% pulsatile LVADs</li> <li>15% CF-LVADs</li> </ul>	<ul style="list-style-type: none"> <li>Preoperative IABP</li> <li>Increased pulmonary vascular resistance</li> <li>LVAD destination therapy</li> </ul>	<ul style="list-style-type: none"> <li>RVAD implantation</li> <li>Inhaled nitric oxide for <math>&gt; 48</math> h</li> <li>Intravenous inotrope therapy for 14 consecutive days</li> </ul>	0.55 (0.47–0.59)
STOP-RVF risk calculator <sup>55</sup>	<ul style="list-style-type: none"> <li>100% CF LVADs</li> </ul>	<p>The calculator evaluated the following parameters:</p> <ul style="list-style-type: none"> <li>NICM</li> <li>IABP, Impella/venoarterial ECMO</li> <li>LVAD configuration</li> <li>INTERMACS profiles 1–2</li> <li>RAP/PCWP</li> <li>Use of ACEIs</li> <li>Platelet count</li> <li>Serum sodium</li> <li>Serum albumin</li> <li>Serum creatinine</li> </ul> <p>Online score <a href="https://cvrti.utah.edu/drakos/Site/tools.html">https://cvrti.utah.edu/drakos/Site/tools.html</a></p>	<ul style="list-style-type: none"> <li>RV failure was defined as the need for inotrope therapy for <math>&gt; 14</math> days and/or right-sided circulatory support (surgically or percutaneous-implanted MCS) within 30 days postoperatively</li> </ul>	0.75 (0.71–0.79)

ACEI, angiotensin-converting enzyme inhibitor; AST, aspartate aminotransferase; BiVAD, biventricular assist device; CF, continuous-flow; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; MCS, mechanical circulatory support; NICM, non-ischaemic cardiomyopathy; NR, not reported; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RV, right ventricular; RVAD, right ventricular assist device; RVSWi, right ventricular stroke work index.

<sup>a</sup>RVSWi is calculated from either one of the two formulas:  $RVSWi = (mPAP - mRAP) \times SVi \times 0.0136$  [normal range: 4–12 g/m/beat/m<sup>2</sup> (g/m<sup>2</sup>)]; or  $RVSWi = (mPAP - mRAP) \times SVi$  (normal range: 300–900 mmHg  $\times$  ml/m<sup>2</sup>).



experimental data suggesting an effect similar to the left ventricle with respect to up-regulation of stress and metabolic markers.<sup>56</sup> Increased CVP, namely CVP >12 mmHg,<sup>37,42,53</sup> indicate the need for decongestion before LVAD implantation. Close monitoring of CVP before LVAD implantation is needed.

### Optimization of right ventricular afterload

Right ventricular function is more sensitive to increased afterload compared to the left ventricle. The reduction of pulmonary pressures pre-LVAD implantation seems to offer some benefit, at least for RV function evaluation.<sup>57</sup> Reduction of LV filling pressures by optimizing LV function, even temporarily, before LVAD implantation, can reduce the pressures transmitted back from the left atrium to the pulmonary vascular bed subsequently

reducing the RV afterload. A right heart catheterization-guided reduction of PCWP using inotropes and diuretics could be very helpful.<sup>57</sup> Few studies have described the systematic administration of inotropes aiming at haemodynamic optimization of the non-inotrope-dependent patient undergoing LVAD implantation and compared their findings with registry data, showing no benefit. More data through randomized studies are needed to clarify the role of this strategy.<sup>58–61</sup> Additionally, the preoperative phosphodiesterase-5 inhibitor (PDE5i) use was associated with a higher incidence of prolonged inotropic support after LVAD implantation, resulting in an increased incidence of severe early RHF.<sup>62</sup> As previously indicated, the RAP/PCWP ratio, which is predictive of post-LVAD implant mortality with the HeartMate 3 pump, could be modified preoperatively. Whether such interventions result in a more favourable prognosis requires conduct of systematic studies.<sup>48</sup>

## Temporary mechanical circulatory support for right ventricular optimization: Intra-aortic balloon pump

Despite the lack of randomized controlled trials and the controversies regarding its use, IABP is a very widely used<sup>63</sup> and simple temporary mechanical circulatory support system that may haemodynamically stabilize the decompensated patients with advanced heart failure.<sup>64</sup> In a small case series of patients with advanced biventricular failure, Ntalianis *et al.*<sup>65</sup> reported that IABP, using the femoral approach for IABP implantation, improved parameters reflecting RV function (RVSWi, RAP, TAPSE and PAP). In this study, none of the patients that were subsequently supported with an LVAD developed RV failure. Tanaka *et al.*,<sup>66</sup> using the subclavian approach for IABP placement, found that IABP improved RV function in patients with chronic heart failure presenting with acute decompensation. Placement of IABP in patients with INTERMACS profile 2 was found to decrease RAP, PCWP, and PAP.<sup>66–68</sup> In another study, IABP supported patients compared to those with no IABP support had shorter postoperative intensive care unit (ICU) stay, and better haemodynamics following LVAD implantation.<sup>41</sup> A report from the INTERMACS registry showed that patients on pre-LVAD IABP support, despite being at more advanced heart failure stage including worse RV function, had the same post-LVAD outcomes as compared with the less severe heart failure patients not in the need for pre-LVAD implantation IABP support. This result suggests that IABP may mitigate the risk of early postoperative adverse outcomes, including RHF.<sup>69</sup> Furthermore, it has been found that the less the RV free wall is fibrotic, the more likely the IABP to improve RV function in patients undergoing LVAD implantation.<sup>70</sup> Randomized trials are needed to clarify the role of IABP for the haemodynamic optimization of patients undergoing LVAD implantation.

## Right ventricular function optimization following left ventricular assist device implantation for the prevention and management of early acute and early post-implant right heart failure

### General measures – medical therapy

#### Early acute right heart failure: Prevention and management

Minimizing perioperative blood loss eliminates the need for blood transfusion and the resultant increase in RV preload. Furthermore, volume resuscitation using blood products can induce lung injury, increasing PVR and, therefore, RV afterload.<sup>71</sup> During the implantation and following initialization of LVAD therapy, efforts should be focused on gradually weaning from CPB. Dobutamine and milrinone, combined with noradrenaline – if required due to

hypotension –, can provide substantial inotropic support to the right ventricle. For those cases with pre-LVAD implantation elevated PVR, administration of iNO decreases the RV afterload. Minimizing the time of CPB will decrease the ischaemic time and facilitate RV recovery. Meticulous de-airing using transesophageal echocardiography (TEE) guidance minimizes air embolization. Methods to decrease the RV afterload include the administration, before patient's weaning from CPB, of iNO until 48 h after separation of the CPB and extubation.<sup>72</sup>

#### Early post-implant right heart failure: Prevention and management

Following patient's extubation, the administration of PDE5i takes over.<sup>73</sup> However, iNO was not found to reduce the incidence of RV failure following LVAD implantation<sup>72</sup> and similarly the administration of PDE5i.<sup>73</sup> Further studies are needed to define the role of iNO and that of PDE5i in the early post-LVAD implantation period.

In a marginally functioning right ventricle, immediately following LVAD implantation, maximal systemic flows should be avoided. Increase in LVAD speed, recorded as revolutions per minute (RPM), should be performed gradually, aiming, in parallel, at a progressive weaning from CPB, that will facilitate the adaptation of the right ventricle to the new haemodynamic conditions. Guidance for the LVAD optimal RPM setting can be supported by TEE and invasive haemodynamic parameters. The presence of a dilated left ventricle, an opening of aortic valve at every cardiac cycle and an increase in mitral regurgitation indicate the need for additional LV unloading by increasing the RPM. Avoidance of excessive LV unloading is crucial to the optimal RV performance. In case of excessive LV unloading, suction events can trigger arrhythmias that will further deteriorate RV function. Leftward shifting of the interventricular septum will result in changes in RV geometry increasing RV dimensions, aggravating TR resulting in increased both RV preload and afterload, also impairing RV contractility. Vasopressors should be administered as needed aiming at a mean blood pressure >60–65 mmHg and <80 mmHg.<sup>74</sup> Following patient's transfer to the ICU, the above general principles also apply. The team caring for the patient with LVAD should aim for an RAP 10–12 mmHg. Peri- and postoperative monitoring with a Swan–Ganz catheter can be very helpful, especially for those patients that develop signs of haemodynamic instability. In the first postoperative hours at the surgical ICU, repeated transthoracic echocardiography can help with RPM optimization aiming at the best combined forward flow and RV function. Weaning off first iNO, subsequently slow weaning off inotropes and optimizing diuretic therapy, especially for borderline functioning right ventricles, can potentially minimize the events of deteriorating right ventricle.

### Temporary right ventricular mechanical circulatory support for the early acute and early right heart failure post-left ventricular assist device implantation

Temporary RV mechanical circulatory support is needed for those cases where the patient, following LVAD implantation, develops

profound RV failure that is not responding adequately to medical interventions and/or LVAD RPM optimization. In the operating room – early acute RHF – refractory RHF will manifest as unsuccessful CPB weaning. However, refractory to management RV failure in need for temporary RVAD can also develop later as an early post-implant RHF. A common scenario in that case is the progressive increase in RAP, decrease in LVAD flows and impairment in renal function, secondary to the kidney congestion because of RV failure.

Both for early acute RHF and early post-implant RHF, temporary RV mechanical circulatory support aims to stabilize the patient, unload the right ventricle and provide time for recovery of RV function. The main types of temporary RV mechanical circulatory support devices are shown in Table 5.<sup>75–78</sup>

Finding the appropriate timing for the implantation of the temporary RVAD is critical. Apparently, for those patients with early acute RHF and early post-implant RHF that present with profound RV dysfunction, the decision to implant a temporary RVAD is inevitable. However, post-LVAD RV dysfunction has a spectrum of severity that makes the timing for RVAD implantation far from being a straightforward decision. Previous studies suggested that a strategy for planned compared to non-planned temporary RVAD implantation has better outcomes, given that among patients who developed early acute RHF after LVAD insertion, only half could be weaned from the temporary RVAD support. The unweaned group was associated with a very low 6-month actuarial survival rate.<sup>79</sup> However, even in equivocal cases, planned temporary RVAD seems to result in better outcomes compared to delayed RVAD implantation.<sup>80</sup> Concurrent biventricular assist device implantation, instead of sequential, is associated with better outcome with annual survival rates reaching 56%.<sup>81</sup> Even though the planned RVAD implantation makes surgery and patient follow-up more complex, this seems to be counterbalanced by less mechanical ventilation time,

shorter ICU course, and, based on small studies, better survival rates. Although there are some small observational studies,<sup>82</sup> there have been no randomized studies comparing the percutaneous versus the surgical approach for temporary RVAD.

There are cases of patients with advanced heart failure in need for LVAD implantation that require temporary mechanical circulatory support with VA-ECMO implantation for stabilization. Furthermore, ECMO support can be used in patients already implanted with an LVAD for the support of the failing right ventricle. The advantage of ECMO is that it can substantially reduce the preload of the failing right ventricle. However, ECMO is the temporary device of mechanical circulatory support that can increase LV afterload and subsequently PAP, impairing RV systolic function.<sup>83</sup> The same physiology occurs for patients with LVAD both with early acute and early post-implant RHF under ECMO support.<sup>77,84</sup> The increased afterload is still an issue for the LVAD and should be carefully considered. However, ECMO is widely available and easily inserted.

### Weaning off a temporary right ventricular assist device/venoarterial extracorporeal membrane oxygenation

Next important step for the LVAD-supported patient on a temporary RVAD/VA-ECMO is the weaning timing and process. The procedure should take place slowly, providing the necessary time for the right ventricle to adapt. In order to proceed, the patient should be haemodynamically stable, on minimal doses of inotropes and vasopressors. The temporary RVAD support should be progressively reduced to the minimum per device accepted flow, acknowledging that haemodynamic measurements provided by the Swan–Ganz catheter can be challenging when Impella or an out-flow graft is in place in the pulmonary artery. An increase in RAP

**Table 5** Most used temporary right ventricular assist device

Type of device	CentriMag <sup>75</sup>	Protek Duo cannula <sup>76</sup>	VA-ECMO <sup>77</sup>	Impella RP <sup>78</sup>
Short description	Radial centrifugal pump that has been approved for use up to 30 days. Its inflow cannula lies in the right atrium or jugular/femoral vein and its outflow cannula in the main pulmonary artery, bypassing so the failing right ventricle. It allows the decannulation without chest opening. If needed, CentriMag is able to add in an oxygenator (RVAD ECMO oxygenator).	The cannula is placed percutaneously in the jugular vein and is advanced to the pulmonary artery. It has drainage holes in the right atrium and returns the blood in the pulmonary artery. It can be placed in the cath lab. It is connected to a pump and has the potential also to be connected to an oxygenator (RVAD ECMO configuration).	The circuit consist of an inflow cannula that can be placed in the femoral vein, a pump, an oxygenator and an outflow cannula that commonly is placed in the femoral artery or in the subclavian artery that returns the blood oxygenated.	Impella RP is a percutaneous placed micro-axial pump. It is advanced via the femoral or subclavian vein and traverses the tricuspid and pulmonic valves, in a way that the inflow part of the device is sitting in the right atrium and the outflow in the pulmonary artery. It has been tested in patients with RV failure post-LVAD implantation. It has been reported 70% survival rates to discharge for patients that needed temporary RVAD following LVAD implantation.

ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; RV, right ventricular; RVAD, right ventricular assist device; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

>15 mmHg while at the same time PCWP is <15 mmHg with low LVAD flows reveals a not yet recovered right ventricle. In that case, the patient should have a delayed second weaning off attempt or could have a higher priority for emergent heart transplantation and/or for implantation of a permanent RVAD. Protocols for temporary RVAD removal have been reported.<sup>77,78,82</sup> Echocardiography during the weaning off process can provide additional information on the potential of the right ventricle to adapt to the new haemodynamic conditions. The short axis is the preferred view for the visualization of the septum position. A flat septum indicates increased RV preload or inadequate RPM speed optimization.

## Prevention and management of late right heart failure following left ventricular assist device implantation

Appropriate general measures for long-term management of patients with an LVAD should be implemented as previously described.<sup>85–88</sup> RHF following LVAD implantation may occur not only in the early post-LVAD implantation period. RHF can persist or occur as a *de novo* event weeks, months, or even years following LVAD implantation.<sup>89,90</sup> An INTERMACS database analysis revealed progressive decline in the prevalence of RHF from 1 to 6 months post-LVAD implantation. The later the RHF presents, the higher the chance it represents a persistent, rather than a transient, abnormality. This makes potentially the 6 months post-LVAD implantation a time point that provides prognostic implications for the patient with late RHF.<sup>89</sup> The progression of the underlying cause of cardiac dysfunction has a major role, more evident in patients with dilated cardiomyopathy. The rate of late onset RHF has been found to be around 10–20%.<sup>91,92</sup> The new haemodynamic conditions arising from the LVAD function are additional parameters that can adversely affect RV function, especially for cases with marginal RV function. These observations demand special attention acknowledging that more than 50% of LVAD implantations are for destination therapy. There is no uniform definition of late post-LVAD implantation RV failure. Small series have defined RHF as the presence of RVSWi <300 mmHg × ml/m<sup>2</sup> at any pump speed.<sup>93</sup> The progress of the underlying disease of heart failure and the inadequate or excessive LV unloading can impair RV systolic function and loading conditions leading to the occurrence of late RHF.

Takeda *et al.*<sup>94</sup> defined late RHF as a condition requiring rehospitalization, after the index hospital discharge, and medical or surgical treatments, including strengthening of diuretics, inotropic support and RVAD implantation. It occurred in 11% of patients at a median of 141 days after LVAD implantation. Survival at 2 years was significantly worse in patients who developed late RHF (60% vs. 85%,  $p=0.016$ ). In addition, another study demonstrated reduced exercise capacity in patients with late RHF as indicated by a lower maximal workload and peak oxygen consumption 6 months postoperatively.<sup>95</sup>

Vidula and colleagues have described hospitalizations in HeartMate 3 LVAD implanted patients, and first rehospitalization (after

the index stay) caused by heart failure-related event versus other causes was associated with reduced survival (hazard ratio 2.2, 95% confidence interval 1.3–3.9;  $p=0.0014$ ). Male sex, non-White race, presence of cardiac resynchronization therapy/implantable cardioverter-defibrillator, obesity, higher RAP, smaller LV size, longer duration of index hospitalization, and lower estimated glomerular filtration rate at index discharge predicted heart failure hospitalizations.<sup>96</sup>

## Long-term medical therapy to support the right ventricle for patients with a left ventricular assist device

Although there are no randomized studies for the role of heart failure guideline-directed medical therapies (GDMT) for patients under LVAD support, retrospective studies describe better outcomes for patients that are on medications recommended by the heart failure guidelines.<sup>92</sup> To this direction a study provided clinical and histopathological evidence that adjuvant GDMT was associated with additional favourable effects that extended beyond the beneficial effects attributed to LVAD-induced unloading alone.<sup>97</sup> However, in cases of RHF following LVAD implantation, beta-blockers maybe down-titrated or even hold. A recent study in stable LVAD patients with elevated RAP and RV dysfunction showed that oral administration of milrinone increased the RVSWi.<sup>98,99</sup> Future studies will define the outcomes of these novel therapeutic strategies.

For patients with increased PAP post-LVAD implantation, the role of PDE5i administration is under investigation. Studies have shown that the administration of (oral) PDE5i after LVAD surgery, aiming to reduce PVR as well as the modification of anticoagulation, has been associated with increased bleeding rates,<sup>73</sup> while others have found fewer ischaemic strokes and improved survival.<sup>100</sup> In a randomized study, macinentan was administered in patients within 90 days following LVAD implantation to those patients that had elevated mean PAP despite reduced PCWP. It was found to effectively reduce PAP.<sup>101</sup> For these reasons prospective randomized studies are needed to clarify the role of PDE5i, especially in patients with elevated PVR on LVAD support and their impact on RV function and exercise capacity. Until more data are available, all patients on LVAD support should adhere to GDMT.<sup>102</sup>

## Role of imaging

Repeated echocardiograms at pre-determined intervals following LVAD implantation are indicated to optimize LVAD function by setting the most appropriate LVAD speed to minimize patient symptom. An LVAD surveillance echo exam should be considered at 1, 3, 6, and 12 months post-implantation and every 6 to 12 months thereafter.<sup>24</sup> Echocardiography can provide valuable information regarding the volume status of the patient as well as an estimation of PAP. Additionally, echocardiography can provide an indirect evaluation for the degree of LV unloading (Table 6).

For this purpose, LVAD speed optimization should take place at regular intervals, especially in cases where the right ventricle is functioning marginally. Avoiding excessive LV unloading could

**Table 6** Echocardiographic parameters for the optimization of right ventricular function in patients under left ventricular assist device support

Parameter	Finding	Potential explanation
Inferior vena cava	Dilated with minimal respiratory variation	<ul style="list-style-type: none"> <li>• Volume overload</li> <li>• RV failure</li> <li>• Excessive LV unloading</li> </ul>
RV dimension	Dilated	<ul style="list-style-type: none"> <li>• Excessive LV unloading</li> <li>• RV failure</li> <li>• Volume overload</li> </ul>
Tricuspid regurgitation	Moderate to severe tricuspid regurgitation	<ul style="list-style-type: none"> <li>• Excessive LV unloading</li> <li>• RV failure</li> <li>• Volume overload</li> </ul>
RV free wall strain	Decreased	<ul style="list-style-type: none"> <li>• RV failure</li> </ul>
Lung ultrasonography	Presence of B-lines	<ul style="list-style-type: none"> <li>• Lung congestion</li> </ul>
Position of the septum	Moved to the left	<ul style="list-style-type: none"> <li>• Excessive LV unloading</li> <li>• RV failure</li> <li>• During diastole: severe tricuspid regurgitation</li> <li>• During systole: pulmonary hypertension</li> </ul>
	Moved to the right	<ul style="list-style-type: none"> <li>• Insufficient LV unloading</li> </ul>
	In the middle	<ul style="list-style-type: none"> <li>• Appropriate LV unloading</li> </ul>
<b>Aortic valve opening</b>	Opens on every cardiac cycle	<ul style="list-style-type: none"> <li>• Insufficient LV unloading</li> <li>• LV function improved</li> </ul>
	Opens intermittently	<ul style="list-style-type: none"> <li>• Suggestive of satisfactory LV unloading</li> </ul>

LV, left ventricular; RV, right ventricular.

reduce RV preload. Furthermore, this could prevent morphologic changes of the right ventricle and the resultant increase in both RV preload and afterload. In any case, these interventions in modifications of the LVAD parameters should take place as long as they do not worsen patient symptoms.

### Role of right heart catheterization

In case of suboptimal acoustic windows or inconclusive echocardiographic exams, right heart catheterization and optimization of the LVAD speed in the catheterization laboratory could be a useful option that provides additional guidance for the optimization of RV function. Ideally, this should be done under echo guidance, by combining echocardiographic and invasive haemodynamic ramp study<sup>103</sup> described below. A more comprehensive understanding of the RV and LV response to the changing LVAD RPMs may be achieved suggesting the optimal LVAD speed (Table 7). A ramp

study aims to evaluate various LV parameters and RV function in relation to serial pump speeds for the minimization of patient symptoms acknowledging at the same time the achievement of optimal RV unloading. Estimated PAP sensors could potentially be helpful in the management of patients in the post-LVAD period aiming to optimize the RPM of the device and reduce the occurrence of RHF.<sup>104</sup>

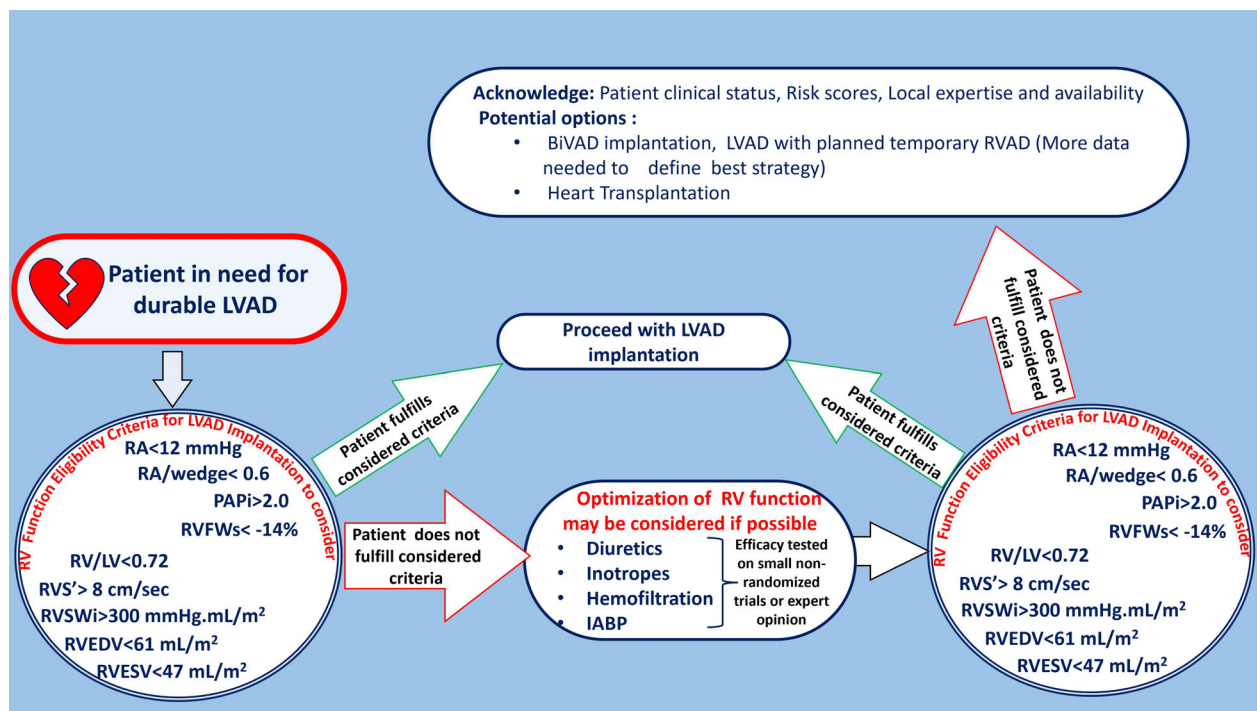
### Conclusion and take home messages (Figure 3)

- Right heart failure post-LVAD implantation is a persisting issue despite the rapid development of the technology of durable mechanical circulatory support for the left ventricle.
- Careful structural and functional assessment of the right ventricle before LVAD implantation using mainly echocardiography

**Table 7** Right heart catheterization haemodynamic parameters for the optimization of right ventricular function in patients under left ventricular assist device support

RAP >12 mmHg	Mean PAP >25 mmHg	PCWP >16 mmHg	Potential explanation and action to take
Yes	Yes	Yes	Volume overload: increase diuresis and RPM, inotropes as needed
Yes	No	No	RV failure: decrease RPM if possible
No	Yes	Yes	Inadequate LV unloading: increase RPM
No	Yes	No	Consider the administration of phosphodiesterase inhibitors aiming at the reduction of pulmonary vascular resistance and decrease of RV afterload

PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RPM, revolutions per minute; RV, right ventricular.



**Figure 3** Right ventricular function assessment and potential strategies for the patient in need for durable left ventricular assist device (LVAD) implantation. BiVAD, biventricular assist device; IABP, intra-aortic balloon counterpulsation; LV, left ventricle; PAPI, pulmonary artery pulsatility index; RA, right atrial pressure; RV, right ventricle; RVAD, right ventricular assist device; RVEDV, right ventricular end-diastolic volume; RVESV, right ventricular end-systolic volume; RVFWs, right ventricular free wall strain; RVSWi, right ventricular stroke work index.

and right heart catheterization can provide prognostic information for the ability of the right ventricle to adapt to the new, post-LVAD implantation, haemodynamic conditions. The assessment should include the comprehensive patient clinical state, including the need for inotropic support or short-term mechanical support as well as the renal and hepatic function.

- Although there is no specific surrogate prognostic marker for the occurrence of RHF following LVAD implantation, the combined assessment of multiple (haemodynamic, echocardiographic and biochemical) markers provides better prognostication.

- The patient that reveals multiple impaired markers of RV dysfunction preoperatively, could be considered for RV function optimization with medical and mechanical therapies. In case the patient reveals no signs of RV function improvement despite all the attempts for RV optimization, the patient is at increased risk for developing RV failure post-LVAD implantation and planned temporary biventricular circulatory support might be contemplated from the very beginning. For patients that reveal signs of severe RV dysfunction following LVAD implantation, a temporary RVAD implantation could be considered perioperatively or immediately postoperatively.

- Weaning off a temporary RVAD should take place under haemodynamic and echocardiographic monitoring.
- Right ventricular function evaluation and management should be done regularly for patients discharged home on LVAD support, for prompt detection of late RV failure.

## Gaps in knowledge and future perspectives

- Prospective randomized trials are needed aiming to phenotype various haemodynamic aberrancies leading to RV failure syndromes in patients undergoing LVAD implantation.
- Further studies are needed aiming to identify the role and the best strategy for RV optimization.
- In marginally functioning right ventricles before LVAD implantation, studies are needed to define whether a planned temporary RVAD or a planned durable RVAD provide the best outcome.
- The effects and potential benefits of assuring heart failure medications on top of LVAD therapy deserve to be investigated in prospective randomized trials.

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