Load Dependency of Right Ventricular Performance Is a Major Factor to be Considered in Decision Making Before Ventricular Assist Device Implantation

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Background—Left ventricular assist devices (LVADs) provide better outcome than biventricular devices, but it is a challenge to predict the impact of LV mechanical unloading on postoperative right ventricular (RV) function preoperatively. We assessed the load dependency in RV performance before and after LVAD implantation aiming to improve preoperative decision making.

Methods and Results—Laboratory, echocardiography, and right heart catheterization data collected from 205 patients before LVAD implantation were tested for relationship with postoperative RV function. Comparing patients with different time-course of RV function after LVAD implantation, we found significant differences (P < 0.01) in preoperative RV end-diastolic short-/long-axis and long-axis/length-area ratios, tricuspid annulus peak systolic velocity, RV peak longitudinal global systolic strain rate, systolic pressure gradient between RV and right atrium (∆P_{RV−RA}), tricuspid regurgitation velocity-time integral, and pulmonary arterial pressure between patients with and without postoperative RV failure. High predictive values for postoperative RV failure were found for end-diastolic short-/long-axis ratio ≥0.6, tricuspid annulus peak systolic velocity <8 cm/s, and peak systolic longitudinal strain rate <0.6 in patients with maximum ∆P_{RV−RA} <35 mmHg. These parameters also seemed predictive for RV failure in patients with tricuspid regurgitation grade >2 and pulmonary arterial pressure <50 mmHg. End-diastolic short-/long-axis ratio <0.6, tricuspid annulus peak systolic velocity ≥28 cm/s, and peak systolic longitudinal strain rate ≥0.6 in patients with maximum ∆P_{RV−RA} ≥35 mmHg showed high predictive values for postoperative freedom from RV failure. The RV load adaptation index seemed particularly predictive for RV function after LVAD implantation.

Conclusions—RV geometry and velocity of contraction before LVAD implantation become more predictive for postoperative RV function and can improve decision making before VAD implantation if preoperative RV pressure load and tricuspid regurgitation are also considered. (Circulation. 2013;128[suppl 1]:S14-S23.)

Key Words: echocardiography ▶ heart failure ▶ heart-assist device ▶ hemodynamics ▶ risk factors ▶ surgery ▶ ventricles

Given the lack of organs available for heart transplantation, lifesaving long-term mechanical circulatory support by implantation of ventricular assist devices (VADs) is today an established treatment for patients with end-stage heart failure (HF). VADs are primarily designed as a bridge to heart transplantation or as permanent therapy for those who cannot undergo heart transplantation, but in a limited number of patients VADs may become a bridge to cardiac recovery allowing successful VAD explantation. Candidate selection for long-term VAD therapy is complex, and the decision between left VAD (LVAD) and bi-VAD (BVAD) implantation involves a large number of criteria in addition to the evaluation of right ventricular (RV) function.1,2

LVADs are more reliable and safer for patients and also definitely provide a better quality of life than BVADs, but a relevant proportion of patients who undergo LVAD implantation develop severe RV failure that adversely affects the outcome, being associated with increased mortality.3–5 Analysis of international registry data has identified RV dysfunction requiring biventricular support as the most prominent risk factor for early mortality after VAD implantation, and there is definite proof that RV dysfunction negatively impacts the outcome after LVAD implantation.1,6–7 However, it remains a challenge to evaluate RV function and predict its time-course during LV support.

The determination of patients who are at greater risk for developing postoperative RV failure and its relative importance remain controversial and incompletely known.1,6 Because of its high load dependency, the RV function usually either remains unchanged or will even improve after...
reduction of pulmonary vascular resistance (PVR) subsequent to LVAD implantation, as long as the postoperative outcome is not impaired by irreversibly poor end-organ function, and LV unloading is properly optimized to avoid excessive interventricular septum shifting from right to left.7–10 RV failure after LVAD implantation seemed related to preoperative RV geometry and tricuspid regurgitation (TR), which are highly load-sensitive variables.8

The aim of this study was to assess the potentially misleading impact of load dependency in RV size, shape, and performance on the preoperative RV evaluation and predictability of the time-course of RV function after LVAD implantation, with the final goal to provide more information that can improve preoperative decision making between LVAD and BVAD implantation. We also aimed to identify the echocardiographic variables with the highest predictive value for postoperative RV function after LVAD implantation to provide additional data suitable for optimization of RV echocardiographic evaluation before VAD implantation.

Methods

Patients, Data Collection, and Study Design

After the promising results of a preliminary study on this topic that evaluated our patients who underwent VAD implantation before 2006, the present study focused on our patients who underwent VAD implantation after January 2006, when the evaluation of RV function was optimized by additional use of tissue Doppler and strain imaging. Thus, in the present evaluation, we included our adult patients who after that date received an LVAD designed either as a bridge to transplantation or as a permanent therapy. In addition, we included in the evaluation all patients who, during the same time period, were preoperatively considered suitable for LVAD implantation, but the intraoperative situation necessitated a decision change in favor of BVAD implantation. Patients who primarily received a BVAD in accordance with a preoperative decision were excluded from this study. We also excluded from the evaluation all patients with RV ejection fraction (RVEF) ≥50% (in the absence of TR grade ≥2) because a preoperative normal or borderline normal RVEF usually allows LVAD implantation without relevant risks for postoperative RV failure. The other exclusion criteria were atrial fibrillation, pacemaker dependency, tricuspid valve (TV) prosthesis, and age <18 years. Patients with atrial fibrillation were excluded because of the difficulty in reliably evaluating RV function in such patients, with permanent variations in preload and afterload generated by irregular RV filling. Patients on hemodialysis were also excluded because of their high variations in plasma volume with consequent variations in RV loading conditions and TR, which can both substantially impede reliable assessments of RV function. Also, patients with prosthetic TVs were excluded because these valves do not usually allow measurements of the pressure gradient between the RV and the right atrium (ΔP_{RV-RA}). Pacemaker dependency was also considered an exclusion criterion because pacemaker activation can induce echocardiographic findings with potentially misleading influence on the evaluation of RV function. Patients were also excluded if the image quality of preoperative standard echocardiography was deemed insufficient to perform analysis of RV function.

All patients received emergency VAD implantation because of life-threatening irreversible end-stage HF unresponsive to medical treatment, including continuous inotropic support.

The main goals of this retrospective evaluation of prospectively gathered information on preoperative RV size, geometry, and function, pulmonary hemodynamics, and TV function were as follows: (1) assessment of the potentially misleading impact which the load dependency of RV performance might have on decision making between LVAD and BVAD implantation, (2) identification of parameters with the highest predictive value for postoperative RV function after LVAD implantation, and (3) optimization of the evaluation of RV function by echocardiography.

Main outcome measures were RV function and freedom from right HF (RHF) after LVAD implantation. Postoperative RHF was defined by the need for the previously unplanned insertion of a right VAD after LVAD implantation or the necessity of both prolonged reduction of PVR by nitric oxide or iloprost inhalation (±oral sildenafil) and intravenous inotrope therapy for >10 consecutive days to increase the cardiac index (CI) >2 L/min per m².

To attain our goals, laboratory data, echocardiographic variables, and invasively obtained hemodynamic data were prospectively collected according to a well-established protocol in all patients who fulfilled the criteria for inclusion in this study. The study was approved by an institutional review committee, and the subjects gave informed consent.

Echocardiographic Assessment of Right Heart Function

Transthoracic echocardiography was a cornerstone for right heart assessment. An overview of transthoracic echocardiography variables, which were prospectively collected in all patients, is shown in Table 1. All preoperative transthoracic echocardiography data used in the study were obtained between 2 and 24 hours before surgery. Transthoracic echocardiography was performed according to the guidelines of the American Society of Echocardiography85 using GE Vivid 7 and Vivid E9 ultrasound machines. Strain analysis of the 2-dimensional (2D) echocardiography images was performed off-line with the aid of a customized software package (EchopAC, General Electric).

To assess the potential impact of the load dependency of RV performance on decision making in favor of either LVAD or BVAD
implmentation, we introduced several variables that were not evaluated in our previous studies. These new variables were TR velocity-time integral (VTI_{TR}), lateral tricuspid annulus peak systolic velocity (TAPSm), and RV peak global systolic longitudinal strain rate (PSsRrL) measured by CW-Doppler, tissue Doppler, and speckle-tracking derived 2D strain imaging, respectively. Although the wall motion and deformation velocity measures TAPSm and PSsRrL, respectively, provide useful information on RV function, which especially in patients with TR grade >2 might be superior to the functional data provided by RVEF, RV fractional area change (FAC), and tricuspid annulus peak systolic excursion, these velocity parameters are also load dependent. With increasing TR, even ΔP/Δt becomes less reliable for assessment of RV contractile function. It, therefore, remains a challenge to distinguish between 2 enlarged RVs with similarly impaired function but different in their potential for reverse remodeling and functional improvement after afterload reduction subsequent to mechanical unloading of the LV. If, for example, an afterload mismatch was the main cause for RV deterioration, there are logically more chances for RV improvement than in the case of RV deterioration caused by impaired contractility. With similar or even lesser changes in RV size and geometry including TV annulus dilation followed by TR, a strong RV can develop higher intraventricular pressures in response to an increase in PVR than an RV weakened by impaired contractile function. Thus, RV size, geometry, and systolic pressure, plus degree of TR, are essential variables for the evaluation of RV contractile function. However, being interrelated, these variables might become most useful in a combined evaluation.

Previously, we showed that the RV end-diastolic short-/long-axis ratio (S/L), also known as sphericity index, is useful for the prediction of RV function after LVAD implantation. However, the ratio between RV end-diastolic volume and long-axis length (L_{ED}) that includes both size and geometry might be more useful because 2 dilated ventricles with identical S/L ratios may have different RV end-diastolic volume/L_{ED} ratios. Because the RV end-diastolic volume correlates well with the more easily and reliably measurable RV end-diastolic area (A_{ED}), the 2 ratios, A_{ED}/L_{ED} and RV end-diastolic volume/L_{ED}, can be considered to be of similar value for RV evaluation. With progressive alteration of LV function, the RV systolic pressure will increase in response to the increasing PVR. However, 2 patients with identical RV systolic pressure values may have different alterations in RV size and geometry and also different degrees of TR secondary to TV annulus dilation. The RV with better adaptation to pressure load will show a higher ΔP/Δt, less dilation, and less TR. Taking all these pathophysiological and hemodynamic aspects into consideration, we aimed to combine pressure, size, and geometry to improve their predictive value for RV function after LVAD implantation. Replacing the pressure gradient ΔP_{RV−RA} by the TR velocity from which it was actually calculated (Bernoulli equation) and using VTI_{TR} instead of TR velocity, an RV load adaptation index (LAI_{RV}) can be obtained by dividing VTI_{TR} by A_{ED}/L_{ED}, as follows:

\[ \text{LAI}_{RV} = \frac{\text{VTI}_{TR}}{A_{ED}/L_{ED}} = \frac{\text{VTI}_{TR} (cm/s) \times L_{ED} (cm)}{A_{ED} (cm^2)} \]

In patients with impaired LV function, a small RV A_{ED} relative to the long-axis length (no altered size and geometry), despite a high VTI_{TR} (high pressure load), indicates good adaptation to load expressed by a high LAI_{RV}. On the contrary, large RV A_{ED} relative to the RV long-axis length in the presence of normal or low VTI_{TR} (ie, low LAI_{RV}) will be found in patients with impaired RV contractile function and excessive TR, indicating RV dilation, RA pressure increase, and inability to develop high RV systolic pressures.

The majority of the echocardiographic variables selected for our study, especially the right ventricle end-diastolic diameter, S/L and TAPSm, were reliably measurable in all evaluated patients. VTI_{TR} measurements, which are difficult in patients without relevant TR, were not problematic in our patient cohort where all patients had tricuspid regurgitant jets that allowed optimal CW Doppler recordings. This high prevalence of TR is explainable by the fact that the RVEF was reduced in all the evaluated patients and the vast majority (98%) had pulmonary venous hypertension (mean pulmonary pressure ≥25 mm Hg). More difficult were the RVEF, FAC, and 2D strain measurements in patients with poor image quality. However, with the exception of PSsRrL, all echocardiographic parameters selected for our study were measured in all patients. PSsRrL measurements were possible in 184 (89.8%) of the 205 evaluated patients. In 17 (10.6%) of the 160 patients without RVH after LVAD implantation and 4 (8.9%) of those with RVH after LVAD implantation, we were not able to provide sufficient image quality for PSsRrL calculation.

**Invasive Hemodynamic Measurements**

All patients underwent right heart catheterization as part of their preassess evaluation. Right heart catheterization protocol includes the measurement of right atrial, RV, and pulmonary artery pressure (systolic, diastolic, and mean), pulmonary capillary wedge pressure, and cardiac output, as well as the calculation of PVR and CI. Direct measurement of systemic arterial pressure with an arterial line was also performed in all patients as part of the preassess evaluation.

**Measurement of Blood Chemistry and Hematologic Variables**

The laboratory protocol includes various measurements with potential relevance for the prediction of patient outcome after LVAD implantation with respect to right heart function, were performed within a 24-hour window before device implantation. Of these variables, serum creatinine, blood urea nitrogen, bilirubin, hemoglobin, serum lactate dehydrogenase, alanine aminotransferase, serum Na^+, C-reactive protein, and T- and EL workers were included in the evaluation.

**Preoperative Device Selection**

In accordance with the results of our previous study on the preoperative prediction of postoperative RV function in patients who underwent LVAD implantation, since 2006 we have preferred to implant a BVAD or a total artificial heart in patients with irreversible TR grade >3 and usually also in those with TR grade <3 if RV dilation (end-diastolic diameter in the RV outflow tract >36 mm) and alteration of RV geometry (short-/long-axis ratio >0.6) plus impaired RV systolic function (RVEF<30%) coexist with normal or relatively reduced PVR.

**Statistics**

Statistical analysis was performed using SPSS 18.01 for Windows (SPSS Inc, Chicago, IL). Qualitative data are presented as numbers and percent and quantitative data as means and SD or as medians and quartiles for variables with more skewed distribution. For comparison between the 2 patient groups, Student t test, Mann–Whitney U test, or χ^2 test was used. Receiver operating characteristic curves (ROC) were used to evaluate the discriminatory value of different variables to test their prognostic accuracy in the prediction of freedom from RHF. Sensitivity, specificity, and predictive values calculated for selected parameters according to both prespecified cutoff points and optimal cutoff values obtained from ROC analysis were expressed as percentages and 95% confidence intervals. Univariable logistic regression was performed to calculate odds ratios and 95% confidence intervals for the occurrence of RHF, followed by a multivariable approach. NT-proBNP, lactate dehydrogenase, alanine aminotransferase, and C-reactive protein were subjected to natural log-transformation for logistic regression. The final model was chosen according to the Akaike information criterion. All reported tests are 2-sided and not adjusted for multiple comparisons. The significance threshold was set at 1%. Kaplan–Meier calculations were used to estimate the probability of postoperative survival in patients with and without RHF after LVAD implantation.

**Results**

Early postoperatively, of the 475 patients who received an LV mechanical support system during the study period, 45 (9.5%)
showed severe RV failure that necessitated additional mechanical support for the RV; another 19 (4.0%) developed RV failure that caused patient death or the necessity for prolonged (>10 days) inotropic support combined with pharmacological reduction of PVR. In >90% of those patients, RV failure already appeared during the first day after surgery. Only in 6 (9.4%) patients did postoperative RV failure become evident after the first postoperative day (between second and fourth day after surgery).

Table 2. Patient Characteristics and Selected Laboratory Data Before LVAD Implantation

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Evaluated Patients (n=205)</th>
<th>No Postoperative RVF (n=160)</th>
<th>Postoperative RVF (n=45)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>52 (31–68)</td>
<td>52 (31–68)</td>
<td>55 (39–66)</td>
<td>0.10</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>182/23</td>
<td>141/19</td>
<td>41/4</td>
<td>0.23</td>
</tr>
<tr>
<td>BMI</td>
<td>25.6 (19.3–34.8)</td>
<td>25.2 (19.3–33.4)</td>
<td>27.0 (20.5–34.8)</td>
<td>0.09</td>
</tr>
<tr>
<td>HF duration, mo</td>
<td>50 (1–98)</td>
<td>48 (1–98)</td>
<td>50 (1–88)</td>
<td>0.94</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy, %</td>
<td>41.5</td>
<td>40.6</td>
<td>44.4</td>
<td>0.65</td>
</tr>
<tr>
<td>IABP before surgery, n/%</td>
<td>18/8.8</td>
<td>13/8.1</td>
<td>5/11.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Preoperative ventilation, n/%</td>
<td>12/5.9</td>
<td>9/5.6</td>
<td>3/5.7</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Table 3. Echocardiographic and Invasive Hemodynamic Measurements Before LVAD Implantation

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Evaluated Patients (n=205)</th>
<th>No Postoperative RVF (n=160)</th>
<th>Postoperative RVF (n=45)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP mean, mmHg</td>
<td>31.0 (22–45)</td>
<td>32.0 (25–45)</td>
<td>28.0 (22–36)</td>
<td>0.02</td>
</tr>
<tr>
<td>CI, L/min per m² BSA</td>
<td>2.0 (1.3–2.9)</td>
<td>2.2 (1.5–2.9)</td>
<td>2.0 (1.3–2.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>CVP, mmHg</td>
<td>12.0 (7–21)</td>
<td>11.0 (7–20)</td>
<td>18.0 (13–21)</td>
<td>0.01</td>
</tr>
<tr>
<td>PCWP, mmHg</td>
<td>18.0 (14–25)</td>
<td>19.0 (15–25)</td>
<td>17.0 (14–20)</td>
<td>0.05</td>
</tr>
<tr>
<td>PVR, dyn·cm⁻⁵·s⁻¹</td>
<td>250.0 (175–535)</td>
<td>255.0 (180–535)</td>
<td>230.0 (175–355)</td>
<td>0.05</td>
</tr>
<tr>
<td>End-diastolic RVOT diameter, mm</td>
<td>33.0 (27–45)</td>
<td>33.0 (27–44)</td>
<td>36.0 (30–45)</td>
<td>0.03</td>
</tr>
<tr>
<td>Right ventricular S/Lo, %</td>
<td>0.55 (0.45–0.68)</td>
<td>0.54 (0.45–0.68)</td>
<td>0.62 (0.52–0.68)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Right ventricular FAC, %</td>
<td>25 (18–34)</td>
<td>25 (18–34)</td>
<td>23 (20–28)</td>
<td>0.07</td>
</tr>
<tr>
<td>RVEF, %</td>
<td>35 (25–48)</td>
<td>35 (25–48)</td>
<td>33 (28–40)</td>
<td>0.07</td>
</tr>
<tr>
<td>TAPSE, cm</td>
<td>1.40 (1.05–2.15)</td>
<td>1.43 (1.05–2.15)</td>
<td>1.35 (1.10–1.60)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TAPSm, cm/s</td>
<td>9.0 (4.7–11.8)</td>
<td>9.5 (6.8–11.8)</td>
<td>6.0 (4.7–8.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PSSrL, t/s</td>
<td>0.81 (0.4–1.0)</td>
<td>0.87 (0.58–1.0)</td>
<td>0.53 (0.4–0.79)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ΔP⁰−⁵⁰⁰−⁵⁰⁰, mmHg</td>
<td>40 (18–62)</td>
<td>42 (28–62)</td>
<td>28 (18–39)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PSSrL×ΔP⁰−⁵⁰⁰, t/mmHg/s</td>
<td>34.8 (7.6–52.5)</td>
<td>36.4 (18–52.5)</td>
<td>14 (7.6–3.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RV load adaptation index (LAIₚₚ)</td>
<td>20 (8–30)</td>
<td>22 (12–30)</td>
<td>10 (8–11)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TR grade &gt;2, n/ %</td>
<td>40/19.5</td>
<td>26/16.2</td>
<td>14/31.1</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

ALT indicates alanine aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CrP, C-reactive protein; Hb, hemoglobin; HF, heart failure; IABP, intra-aortic balloon pump; LDH, lactate dehydrogenase; LVAD, left ventricular assist device; NT-proBNP, N-terminal brain natriuretic peptide; and RVF, right ventricular failure.

*Statistically significant: P<0.01.

†Only 184 (89.8%) of the 205 evaluated patients had reliable PSSrL measurements that were eligible for inclusion in statistical calculations.

‡LAIₚₚ=VTI₀₉₀×L₀/L₀₉₀.

ΔP⁰−⁵⁰⁰−⁵⁰⁰ indicates pressure gradient between right ventricle and right atrium; PSSrL, peak systolic longitudinal strain rate; PVR, pulmonary vascular resistance; RVEF, right ventricular ejection fraction; RVF, right ventricular failure; RVOT, right ventricular outflow tract; S/Lo, end-diastolic short-/long-axis ratio; TAPSE, tricuspid annulus pressure systolic excursion; TAPSm, tricuspid lateral annulus peak systolic wall motion velocity; TR, tricuspid regurgitation; and VTI, velocity-time integral.

*Statistically significant: P<0.01.
Late appearance of life-threatening RV failure during LVAD support was rare. However, 3 patients without early RV failure after LVAD implantation died after the first postoperative year because of irreversible RV failure.

Because we focused this study on adults, patients who were <18 years at the time of surgery (n=33) were excluded. Of the 442 adults who underwent LVAD implantation during the study period, 159 were excluded because, in the absence of relevant TR, their RVEF was ≥50%. Another 42 patients were excluded because of atrial fibrillation, pacemaker dependency, renal insufficiency with hemodialysis, or prosthetic TV. Finally, 36 patients had to be excluded because their echocardiographic image quality was insufficient for analysis of RV function. Thus, finally only 205 (45 with and 160 without early postoperative RHF) patients were eligible for inclusion in the evaluation.

During the first 3 days after surgery, 66 (41.3%) of the 160 patients who remained free from postoperative RHF showed improvement in RV function, 72 (45%) revealed no changes in RV function compared with preoperative data, and only 22 (13.7%) showed mild-to-moderate alterations in RV size, geometry, and function, which, however, did not meet the criteria for RHF. The 3-year survival probability was 58.4% in this group. Of the 45 patients who developed postoperative RHF, only 8 patients (17.8%) were alive at the time of evaluation, and the 3-year survival probability in this group reached only 17.1%. In 6 patients who also required a right VAD after LVAD insertion, the unloading-promoted RV recovery allowed successful removal of the right VAD later.

**Comparison Between Patients With and Without Postoperative RV Failure**

Comparing the 2 patient groups with different time-course of RV function after LVAD implantation, we found no significant differences in patient age, sex, body surface area, body mass index, duration of HF before LVAD implantation, prevalence of coronary disease, prevalence of patients with intra-aortic balloon pumps before surgery, or prevalence of patients with preoperative ventilation (Table 2). There were, however, differences in certain blood chemistry variables and biomarkers, such as lactate dehydrogenase, creatinine, C-reactive protein, and NT-pro-BNP, which were significantly higher in the RV failure group (Table 2). Several preoperative echocardiographic and hemodynamic invasive measurements also showed significant differences between the 2 groups (Table 2 and Figure 1). Thus, patients who postoperatively developed RV failure had preoperatively significantly higher RV S/L_Ed, lower long-axis/length-area ratios (L/A_Ed), lower tricuspid annulus peak systolic excursion and TAPSm, lower RV PSSrL, lower VTI_Trv, and lower ΔP_{RV−RA}. Preoperative central venous pressure (CVP) and prevalence of TR grade >2 were also significantly higher in the RV failure group (Figure 2).

**Risk Factors for RV Failure After LVAD Implantation**

Univariable logistic regression revealed several echocardiographic, laboratory, and invasively measured hemodynamic variables as relevant risk factors for early appearance of RV failure after LVAD implantation (Table 4). Of these, high serum creatinine, TR grade >2, and high CVP seemed

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**Figure 1. A–F.** Preoperative distribution of selected variables in patient groups with and without right heart failure (RHF) after left ventricular assist device implantation. The differences between the 2 groups were statistically significant for all variables (P<0.001). RV indicates right ventricle.
particularly important in our evaluated patients. However, of all investigated variables, only the CVP and the mean pulmonary arterial pressure (PAP) were found to reach statistical significance in a multivariable analysis of predictors of HF, which identified only these 2 parameters as independent postoperative predictors of postoperative RV failure (odds ratio 6.2 for CVP increase and 0.5 for mean PAP decrease).

**Prediction of RV Function After LVAD Implantation**

Based on optimal cutoff values obtained from ROC analysis (Table 5), \( \Delta P_{RV-RA} \), TAPSm, and PSSrL revealed high predictive values (between 92% and 96%) for postoperative freedom from RV failure and partially also for the development of RV failure after LVAD implantation (between 70% and 95%). The combined variables PSSrL \( \times \Delta P_{RV-RA} \) showed optimal predictive value for RV function after LVAD implantation. Thus, PSSrL \( \times \Delta P_{RV-RA} \) and LAI, respectively, revealed 87% and 97% predictive values for freedom from RV failure after LVAD implantation and 83% and 97% predictive values for postoperative RV failure (Table 5). The ROC curves for prediction of RV function after LVAD implantation (Figure 3) show high values for the areas under the curves for \( S/L_{TD} \), TAPSm, PSSrL, PSSrL \( \times \Delta P_{RV-RA} \) and LAI (between 0.873 and 0.986), which indicate high ability of preoperative echocardiography to correctly classify patients with and without the potential for an RV failure–free outcome after LVAD implantation.

The 35 mm Hg cutoff value for \( \Delta P_{RV-RA} \) obtained from ROC curves allowed the separation of the evaluated patients into 2 groups, with different prevalence of patients with and without the ability to remain free from RV failure after LVAD implantation. Thus, in the group of 155 patients with preoperative \( \Delta P_{RV-RA} \geq 35 \) mm Hg, the prevalence of those with postoperative freedom from RV failure reached 95.5%, whereas in the group of 50 patients with \( \Delta P_{RV-RA} \leq 35 \) mm Hg the prevalence of those who developed RV failure after LVAD implantation was 76%. Evaluating the 2 patient groups separately, for patients with \( \Delta P_{RV-RA} > 35 \) mm Hg we found high predictive values for postoperative freedom from RV failure (between 96.7% and 97.3%) for \( S/L_{TD} \leq 0.57 \), TAPSm \( \geq 8 \) cm/s, PSSrL \( \leq 0.6/s \), PSSrL \( \times \Delta P_{RV-RA} \geq 24 \) mm Hg/s, and LAI \( > 14 \), whereas those with \( \Delta P_{RV-RA} \leq 35 \) mm Hg, \( S/L_{TD} \geq 0.57 \), TAPSm \( \leq 8 \) cm/s, PSSrL \( \geq 0.6/s \), PSSrL \( \times \Delta P_{RV-RA} \leq 24 \) mm Hg/s, and LAI \( \leq 14 \) showed reliably high predictive values for postoperative RV failure, ranging between 85.4% and 92.5% (Table 6). The ROC curves for prediction of RV function after LVAD implantation in patients with \( \Delta P_{RV-RA} > 35 \) mm Hg (Figure 4) showed high values for the areas under the curves (between 0.808 and 0.965) for \( S/L_{TD} \), TAPSm, PSSrL, PSSrL \( \times \Delta P_{RV-RA} \), and LAI, which indicate high ability of these variables to correctly classify patients with and without the potential for an RV failure–free outcome after LVAD implantation.

In the 40 patients with TR grade \( \geq 2 \) before LVAD implantation, those with systolic PAP \( > 50 \) mm Hg had a predictive value of 88.5% for freedom from RV failure, whereas those with systolic PAP \( \leq 50 \) mm Hg had a predictive value of 92.9% for RV failure.
failure after LV AD implantation. For patients with TR grade >2 and systolic PAP <50 mm Hg, TAPSm ≤8 cm/s, LAI ≤14, PSSrL ≤0.6/s, and PSSrL×ΔP RV−RA ≤24 mm Hg/s revealed predictive values of ≥92.9% for RV failure after LV AD implantation.

Discussion

Our results are in concordance with the main previous observations which revealed that patients with different time-course of RV function after LVAD implantation already show significant differences preoperatively not only in echocardiographic measures used for RV assessment but also in certain laboratory and invasively measured hemodynamic data.1,9–15 Thus, previous important studies on this topic showed that patients with severe RV failure after LVAD implantation usually have a lower preoperative CI, more elevated CVP, lower tricuspid annulus peak systolic excursion, higher bilirubin, higher aspartate and alanine aminotransferase, higher blood urea nitrogen, and higher serum creatinine levels.1,3,14–19 However, not all of these variables appeared in all studies as relevant risk factors that might be at least partially explained by differences between different centers with regard to their selection criteria for LVAD and BVAD implantation. Some investigating groups did not find, for example, elevated serum bilirubin levels to be a relevant risk factor for postoperative RV failure in their patients.9,18 Quantitative scoring systems for predicting the need for an additional RV support in patients with congestive HF also include one or the other above-mentioned risk factors, such as CI, serum creatinine, blood urea nitrogen, or serum bilirubin.1,16,17 In our previous study, patients with RV failure after LVAD implantation had preoperatively higher S/L ED ratios reflecting higher TV geometry alterations, lower CI, more pronounced TR, higher CVP values, and also higher NT-ProBNP and C-reactive protein values.9 These observations were confirmed by this study of a larger number of evaluated patients although we set the significance threshold at 1% to avoid possible severe inflation of type I error that might have resulted from selection of the most often used α=0.05 as the significance threshold. In addition to our previous observations, the present study revealed also significantly lower RV wall motion and deformation velocity values.

Table 5. Predictive Value of Preoperatively Measured Echocardiographic Variables for Postoperative RV Function in Patients Who Underwent LVAD Implantation

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cutoff*</th>
<th>Sensitivity % (CI)†</th>
<th>Specificity % (CI)†</th>
<th>NPV‡ % (CI)</th>
<th>PPV§ % (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/L ED</td>
<td>0.57</td>
<td>84 (72–93)</td>
<td>74 (70–76)</td>
<td>94 (90–94)</td>
<td>46 (40–52)</td>
</tr>
<tr>
<td>ΔP RV−RA</td>
<td>35 mm Hg</td>
<td>84 (73–92)</td>
<td>93 (89–95)</td>
<td>96 (92–98)</td>
<td>76 (66–83)</td>
</tr>
<tr>
<td>TAPSm</td>
<td>8 cm/s</td>
<td>84 (73–92)</td>
<td>90 (93–98)</td>
<td>95 (92–98)</td>
<td>70 (61–77)</td>
</tr>
<tr>
<td>PSSrL</td>
<td>0.6/s</td>
<td>80 (70–85)</td>
<td>98 (95–99)</td>
<td>92 (81–98)</td>
<td>95 (92–96)</td>
</tr>
<tr>
<td>PSSrL×ΔP RV−RA</td>
<td>24 mm Hg/s</td>
<td>89 (79–95)</td>
<td>96 (93–98)</td>
<td>87 (77–93)</td>
<td>97 (84–99)</td>
</tr>
<tr>
<td>LAI</td>
<td>14</td>
<td>91 (80–97)</td>
<td>95 (92–97)</td>
<td>97 (95–99)</td>
<td>83 (73–88)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; LAI, load adaptation index; LVAD, left ventricular assist device; NPV, negative predictive value; PPV, positive predictive value; ΔP RV−RA, pressure gradient between right ventricular and right atrium; PSSrL, peak systolic longitudinal strain rate; RV, right ventricular; S/L ED, end-diastolic short-/long-axis ratio; and TAPSm, tricuspid lateral annulus peak systolic wall motion velocity.

*Optimal cutoff derived from receiver-operating characteristic curve analysis.
†95% confidence interval.
‡Negative predictive value=prediction for freedom from RV failure.
§Positive predictive value=prediction for development of RV failure.

Figure 3. Receiver operating characteristic curves for prediction of right ventricular (RV) function after left ventricular assist device (LVAD) implantation. The high values for the areas under the curves that measure discrimination indicate a high ability of preoperative RV end-diastolic short-/long-axis ratio (S/L ED) and load adaptation index (LAI; A), as well as preoperative tricuspid lateral annulus peak systolic wall motion velocity (TAPSm), peak systolic longitudinal strain rate (PSSrL), and PSSrL×ΔP RV−RA; B) to correctly classify patients with and without RV stability after LVAD implantation.
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(reduced TAPSm and PSSrL, respectively) in patients with postoperative worsening in RV function. These velocity measures seemed able to allow a good distinction between patients with and without the potential to remain free from RV failure after LVAD implantation before surgery. Thus, at certain cutoff values derived from ROC analysis, TAPSm and PSSrL revealed high predictive values for postoperative freedom from RV failure. These results confirm both the importance of longitudinal shortening for RV systolic function and the superiority of velocity parameters for evaluation of systolic RV function. According to our experience, although RV wall motion velocity measurements by tissue Doppler are most reliable at the lateral tricuspid annulus, RV speckle-tracking derived regional 2D longitudinal strain rate measurements below the tricuspid annulus or in any other RV myocardial region are more difficult to perform because the segmental 2D strain rate curves are often altered by noisy signals. This limitation was overcome in our study by using the 2D global longitudinal strain rate curves. The global longitudinal strain rate, being the average value of all segmental strain rates, yields smooth curves that can be easily evaluated. The more recently introduced real-time 3-dimensional speckle tracking might be another useful tool for evaluation of global RV function and, at least theoretically, even more valuable than 2D speckle tracking. With further technical improvements and full validation, 3-dimensional speckle tracking strain may become the more valuable method for the assessment of myocardial function. Currently, however, 2D speckle tracking strain imaging seems to offer the most robust measurement of subclinical myocardial dysfunction.

The main goal of the present study was, however, to assess the impact of load dependency in RV size, shape, and performance on the preoperative RV evaluation and to detect variables with predictive value for a preoperative forecast of the RV function after LVAD implantation. It is well known that, in patients with LV failure, the high filling pressures induce an increase in PVR, and consequently, both pulmonary hypertension and accompanying right heart dysfunction are common features in end-stage disease. A recent perioperative transesophageal echocardiography study confirmed the supposition that mechanical LV unloading can induce acute reduction in both pulmonary capillary wedge pressure and PVR.

Table 6. Selected Variables for Prediction of Time-Course of RV Function After LVAD Implantation in Patients With Different ΔP_{RV-RA}*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cutoff†</th>
<th>No RV Failure in Group With ΔP_{RV-RA} &gt;35 mmHg‡</th>
<th>RV Failure in Group With ΔP_{RV-RA} ≤35 mmHg§</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/L axis ratio</td>
<td>0.57</td>
<td>97.3%</td>
<td>89.5%</td>
</tr>
<tr>
<td>TAPSm</td>
<td>8 cm/s</td>
<td>97.2%</td>
<td>85.4%</td>
</tr>
<tr>
<td>PSSrL</td>
<td>0.6/s</td>
<td>96.7%</td>
<td>89.7%</td>
</tr>
<tr>
<td>PSSrL×ΔP_{RV-RA}</td>
<td>24 mm/Hg/s</td>
<td>97.3%</td>
<td>90.0%</td>
</tr>
<tr>
<td>LAI</td>
<td>14</td>
<td>97.3%</td>
<td>92.5%</td>
</tr>
</tbody>
</table>

LAI indicates load adaptation index; LVAD, left ventricular assist device; PSSrL, peak systolic longitudinal strain rate; ΔP_{RV-RA}, pressure gradient between right ventricular and right atrium; RV, right ventricular; S/L, short-/long-axis; and TAPSm, tricuspid lateral annulus peak systolic wall motion velocity.
*Pressure gradient between right ventricle and right atrium.
†Optimal cutoff derived from receiver operating characteristic curve analysis.
‡Totally 155 patients (148 without and 7 with early postoperative RV failure).
§Totally 50 patients (38 with and 12 without early postoperative RV failure).

Figure 4. Receiver operating characteristic curves for prediction of freedom from right ventricular (RV) failure after left ventricular assist device (LVAD) implantation in patients with a preoperative pressure gradient between RV and RA (ΔP_{RV-RA}) >35 mmHg. The high values for the areas under the curves that measure discrimination indicate a high ability of preoperative RV end-diastolic short-/long-axis ratio (S/L_{ED}) and load adaptation index (LAI; A), as well as preoperative tricuspid lateral annulus peak systolic wall motion velocity (TAPSm), peak systolic longitudinal strain rate (PSSrL), and PSSrL×ΔP_{RV-RA} (B) to correctly classify patients with and without the potential for an RV failure–free outcome after LVAD implantation.
accompanied by acute improvement in RV geometry and function.\(^6\) It seems, therefore, essential to recognize preoperatively those RVs that still have the potential to recover after afterload reduction subsequent to the mechanical LV unloading. This is not possible without reliable data on RV afterload and preload.

In our present study, patients with and without RV failure after LVAD implantation had preoperatively different mean PAP and \(\Delta P_{\text{RV-RA}}\) values (\(P=0.02\) and \(P<0.01\), respectively), whereas FAC and RVEF were rather similar (\(P=0.07\) for both). The misleadingly relatively high preoperative RVEF and FAC values in patients who postoperatively developed RV failure are explainable mainly by the more pronounced TR and lower PVR found in this group. Thus, RVs with similar systolic function if expressed as RVEF or FAC can reveal postoperatively a totally different time-course in RV function, which seems closely related to their different ability to overcome the afterload increase. The majority of our patients who developed severe RV failure after LVAD implantation had preoperatively lower PAP and \(\Delta P_{\text{RV-RA}}\) values in comparison with those who showed stable or improved RV function after LVAD implantation, and high \(\Delta P_{\text{RV-RA}}\) values also seemed predictive for postoperative freedom from RV failure. In our study, of the 155 patients with \(\Delta P_{\text{RV-RA}} >35\) mm Hg, only 7 patients (4.5%) showed severe RV failure after LVAD implantation, whereas in the smaller group of 50 patients with \(\Delta P_{\text{RV-RA}} <35\) mm Hg, 38 (76%) were found to have RV failure after LVAD implantation. RV wall motion and deformation velocity measures (TAPsm and PSSrL, respectively), which are possibly less load dependent than the conventional echo measures used for RV assessment and the combined parameters that include either the deformation velocity and load (PSSrLx\(\Delta P_{\text{RV-RA}}\)) or the size, geometry, and load (LAI), showed the highest predictive values for postoperative freedom from RV failure. These results confirmed our hypothesis that \(\Delta P_{\text{RV-RA}}\) can be useful for the assessment of RV function in its relationship with load (afterload and preload) and that its combination with velocity of myocardial shortening or RV size and geometry might allow reliable preoperative predictions of RV function after afterload reduction by mechanical LV unloading. In this study, CVP and mean PAP were also found to reach statistical significance in a multivariable analysis of predictors of HF, identifying these 2 pressure parameters as independent preoperative predictors of postoperative RV failure. Low pulmonary artery pressure and intraoperative CVP were previously also found to be significant predictors of RHF after LVAD insertion.\(^1,3\) In our study, although the preoperative TAPsm, PSSrL, \(\Delta P_{\text{RV-RA}}\), PSSrLx\(\Delta P_{\text{RV-RA}}\), and the LAI seemed highly predictive for postoperative RV function, none of these variables reached statistical significance in a multivariate analysis. This might be explained by the fact that all these variables are interrelated each with another. Thus, \(\Delta P_{\text{RV-RA}}\) depends on PAP and CVP, TAPsm and PSSrL depend, like the PAP, on the PVR, and the LAI includes \(\Delta P_{\text{RV-RA}}\).

**Limitations**

Data were obtained from a single-center retrospective study of prospectively gathered information. Evaluating a highly selected and, therefore, relatively homogeneous patient cohort that included only patients who were preoperatively deemed to have the potential to remain free from RV failure after LVAD implantation, we found only a lower number of variables with highly significant differences between the groups with and without postoperative RV failure. Because our patient selection strategy produced a higher prevalence of postoperative freedom from RV failure, our positive predictive values are higher than they would be in a sample with lower prevalence of patients with postoperative freedom from RV failure. The modest statistical power because of the number of events (45/205) also makes it relatively difficult to judge properly all the results, and it also seems likely that the choice of optimal cutoff points and especially the high values of the corresponding performance characteristics (sensitivity, specificity negative predictive value, positive predictive value, and area under the curve) are overestimated. However, these limitations were unavoidable because a randomized study on this topic was, and will in the future, not possible because LVAD implantation cannot be performed in patients with preoperative severe RV failure that is deemed to be nonreversible by mechanical LV unloading.

**Conclusions**

RV geometry and velocity of contraction before LVAD implantation become more predictive for postoperative RV function if preoperative RV pressure load and RV preload (including TR) are also considered. RV geometry parameters, such as \(S/L_{\text{ED}}\) or \(L/A_{\text{ED}}\) ratios, as well as the wall motion and myocardial deformation velocity parameters TAPsm and PSSrL, respectively, in connection with either maximum \(\Delta P_{\text{RV-RA}}\) or VTITR (all easily measurable by echocardiography), seemed able to distinguish between patients with and without the potential to remain free from RV failure after LVAD implantation. Our data recommend especially the LAI and the parameter combination PSSrLx\(\Delta P_{\text{RV-RA}}\) as potentially useful tools for the improvement of decision making before VAD implantation.

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**Disclosures**

None.

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