Right ventricular failure after left ventricular assist device insertion: preoperative risk factors

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1. Introduction

Left ventricular assist device (LVAD) support has been used as a bridge to heart transplant and as an alternative to heart transplantation [1–3]. There are several potential complications during LVAD support including right ventricular (RV) failure, bleeding, air embolism, multiorgan failure, thromboembolism, infection and device failure. The ability of the RV to provide sufficient output to fill the LVAD is the major determinant of the correct LVAD functioning and the patients’ survival. The RV failure will develop in approximately 25% of patients receiving LVAD support [4–6]. The major concern on weaning from cardiopulmonary bypass is that RV failure usually occurs at variable degrees and that these patients are invariably in a state of vasodilatory shock [7,8]. Abnormalities of RV function have been attributed to primary abnormalities of the RV myocardium, excessive load imposed on the RV, or obstruction to RV inflow. Recent studies have also suggested that left ventricular (LV) function may significantly affect RV function. This ventricular interdependence is defined as the forces that are transmitted from one ventricle to the other through the myocardium and pericardium, independent from neural, humoral, or circulatory effects. Ventricular interdependence is a consequence of the close anatomic association between the ventricles. The evidence of diastolic ventricular interaction has been observed in postmortem and in isolated heart preparation: the volume/pressure in one ventricle can directly influence the ones in the other ventricle. Many studies [9] showed a systolic ventricular interdependence: right ventricular systolic pressure and pulmonary artery blood flow present both RV and LV components. The LVAD support induces the LV unloading and a decreasing afterload, increasing compliance and decreasing contractility of RV. With full LVAD support LV end-diastolic volume decreases, while right RV end-diastolic volume increases with a significant leftward septal shift. Global RV contractility is impaired with leftward septal shifting, but RV myocardial efficiency is maintained through a decrease in RV afterload and an increase in RV preload. In preexisting pathologic condition the RV response is qualitatively the same, but the decrease in LV systolic function decreases LV assistance to RV function.

The aim of this study is to identify preoperative risk factors for RV failure development after LVAD support among the preoperative hemodynamics and characteristics of patients who received Novacor (World Heart Inc., Ottawa, Ontario, Canada) and then establishing criteria for the patient selection.
Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>RV failure group</th>
<th>No RV failure group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>12.3</td>
<td>10.25</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.83±8.17</td>
<td>50.21±7.77</td>
<td>NS</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.81±0.17</td>
<td>1.80±0.26</td>
<td>NS</td>
</tr>
<tr>
<td>Myocarditis (%)</td>
<td>7.8</td>
<td>10.25</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-operative IABP (%)</td>
<td>33.3</td>
<td>33.3</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-operative mechanical ventilation (%)</td>
<td>25</td>
<td>5.12</td>
<td>0.001</td>
</tr>
<tr>
<td>Pre-operative ECMO (%)</td>
<td>8.3</td>
<td>5.12</td>
<td>NS</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>2.1±1.67</td>
<td>2.41±3.68</td>
<td>NS</td>
</tr>
<tr>
<td>AST (U/l)</td>
<td>800.22±346.5</td>
<td>123.34±4.95</td>
<td>0.013</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>467.22±195.30</td>
<td>237.40±44.56</td>
<td>0.02</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>84.1±27.57</td>
<td>70.73±6.02</td>
<td>0.025</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.69±0.67</td>
<td>1.32±0.02</td>
<td>0.015</td>
</tr>
<tr>
<td>White blood count./mm³</td>
<td>15332±5102</td>
<td>9928±1931</td>
<td>NS</td>
</tr>
<tr>
<td>Platelet count./mm³</td>
<td>167100±9754</td>
<td>206539±11020</td>
<td>NS</td>
</tr>
</tbody>
</table>

AST = aspartate aminotransferase; ALT = alanine aminotransferase; BSA= body surface area; BUN = blood urea nitrogen; ECMO = extracorporeal membrane oxygenation; IABP = intraaortic balloon pump; NS = not significant; RV = right ventricular.

2. Materials and methods

From November 1992 to January 2005, Novacor LVADs (World Heart Inc., Ottawa, Ontario, Canada) were implanted in 54 patients at San Matteo Hospital (Pavia, Italy). The pump uses a dual pusher plates mechanism with a maximum stroke of 65 ml. The LVAD was implanted as bridge to transplant in 51 patients, destination therapy in 2 patients and bridge to recovery in 1 patient. The 2 patients selected for destination therapy presented formal contraindication to transplantation: age 65 years and colon cancer. The bridge to recovery was attempted in a female patient who was myocarditis affected. There were 48 males and 6 females with a mean age of population of 51.4 years (range 29–68 years). The underlying diseases were dilated cardiomyopathy in 34 patients, ischemic cardiomyopathy in 13 patients, myocarditis in 1 patient. The four cases of post-cardiothomy heart failure and the two rejections of heart transplantation have been excluded because, for these pathologies, biventricular assist device is more often needed. All the patients presented with advanced heart failure: dependence on intravenous inotropic and vasodilatory therapy (43 patients), intra-aortic balloon pump support (13 patients) and centrifugal pump support (3 patients). In every patient we performed ECG, chest radiography, cardiac biomarkers, coronarography, echocardiography and right heart catheterization for the right heart failure diagnosis; the evidence of right heart failure is an exclusion criteria for left ventricular assist device insertion.

To identify the pre-operative risk factors for RV failure during LVAD support, we divided the remaining 48 patients into two groups: the ‘RV failure’ group presented, after LVAD assistance, systolic artery pressure < 80 mmHg, cardiac output < 2 l/min, acute massive tricuspid regurgitation at transesophageal echocardiography, evidence of RV dysfunction at the direct observation on the operative field, requirement of intravenous inotropes, nitric oxide inhalation, and right side centrifugal pump for cadiopulmonary bypass weaning; the same criteria were used by the Cleveland Clinic Foundation group [6,7] and in the Columbia Presbyterian interim experience [10]. The management of RV failure was performed through accurate fluid loading on the basis of the pulmonary artery catheterization data and the transesophageal echocardiography monitoring, inotropic and vasopressor support with epinephrine, dopamine, dobutamine, enoximone, norepinephrine in various associations according to the circumstances. We also commonly used inhaled nitric oxide as selective pulmonary vasodilator to decrease RV afterload. In spite of this kind of support, the patients in RV failure group needed right side centrifugal pump for cadiopulmonary by-pass weaning.

Pre-operative hemodynamic parameters were measured in the week preceding the intervention after the introduction of the therapy to optimize RV function. We used rapid-response thermistor pulmonary artery catheter (Swan-Ganz catheter, Edwards Lifesciences LLC, Irvine, CA) to obtain the mean pulmonary arterial pressure (PAP), the right atrial pressure (RAP), the cardiac output, RV ejection fraction (EF), the pulmonary wedge capillary pressure. Then we derived transpulmonary gradient; cardiac index, pulmonary vascular resistance, pulmonary vascular resistance index and right ventricular stroke index. Also many clinical factors, reported in literature as predictors of RV failure, were evaluated: preoperative fever, preoperative laboratory tests for liver and renal function, quantitative bleeding amount. We express the data as the mean ± standard deviation; we performed statistical analysis by χ² test or unpaired Student t-test. Difference was considered significant at the level of P<0.05.

Multivariate analysis has not been performed for the relative number of the patients, and because, on the basis of the univariate analysis, only two variables would enter into the multivariable logistic regression model.

3. Results

Table 1 summarizes patients’ pre-operative characteristics and laboratory data for each group. The two groups did not show any significant difference about the diagnosis of the underlying disease. The need of a pre-operative intraaortic balloon pump or extracorporeal membrane oxygenation support is not a risk factor for RV failure development, but pre-operative mechanical ventilation shows a significant correlation with RV failure, but the patients are...
Heart failure represents a major public health issue in the Western World. Heart transplantation is the therapy for end stage heart failure, but the main impediment is the discrepancy between the number of donors and recipients. In our experience LVAD was used, for the main part, as bridge to transplantation in patients who could not wait for a donor only on medical therapy. The quality of life on assistance was reasonable and many patients were discharged from the hospital. The aim of this retrospective study is the identification of the pre-operative risk factors for severe RV failure after LVAD insertion to improve patient selection for isolated LVAD insertion. We analyzed pre-operative demographic, hemodynamic and laboratory data and the intraoperative variables reported as risk factors in the previous studies. The literature does not report a firm conclusion, so it is still difficult to define universal criteria for patient selection for univentricular or biventricular assist device implantation.

### 4. Discussion

Heart failure represents a major public health issue in the Western World. Heart transplantation is the therapy for end stage heart failure, but the main impediment is the discrepancy between the number of donors and recipients. In our experience LVAD was used, for the main part, as bridge to transplantation in patients who could not wait for a donor only on medical therapy. The quality of life on assistance was reasonable and many patients were discharged from the hospital. The aim of this retrospective study is the identification of the pre-operative risk factors for severe RV failure after LVAD insertion to improve patient selection for isolated LVAD insertion. We analyzed pre-operative demographic, hemodynamic and laboratory data and the intraoperative variables reported as risk factors in the previous studies. The literature does not report a firm conclusion, so it is still difficult to define universal criteria for patient selection for univentricular or biventricular assist device implantation.

Considering the demographic variables and the diagnosis of the underlying disease, our patients did not present any significant differences; Ochiai and associates [7] found significant difference in female gender, result not confirmed after adjusting for body surface area, and in the non-ischemic etiology as a predictor of RV failure after LVAD support, in accordance with Thoratec experience [11], which reported that the need of biventricular support was more frequent in dilated cardiomyopathy rather than coronary artery disease.

Pulmonary hypertension with elevated PVR has been retained as a contraindication for LVAD use of high risk RV failure development [3], but recent studies indicated that when RV contractility is severely impaired in presence of a high PVR, RV is not able to elevate PAP [4–7]. Our data confirm the latest hypothesis: mean PAP was >42 mmHg in the 92% of the patients in the ‘no RV failure’ group and in none of the patients in the ‘RV failure’ group. The two groups, however, did not significantly differ for RV EF, but this finding also suggests that the RV contractility was lower in the RV failure group. If the RV contractility was the same in the two groups RV EF should have been higher in the patients with lower PAP (‘RV failure’ group), due to afterload dependence of the EF. Among the hemodynamic variables, Levin and associates [12] identified also a high value of RAP as a risk factor for RV failure after LVAD insertion. In our analysis, RAP was not significantly different between the two groups.
The RV afterload seemed to be less important than the RV contractility for the RV function during LVAD support (no significant difference in the TPG, PVR or PVRI).

Among the laboratory tests for liver and renal function creatinine, aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen showed a significant difference between the two groups. These data may testify a chronic preoperative RV failure state at a higher degree with venous congestion in the patients at high risk for RV failure after LVAD support, as reported in a previous study [6]. In the light of this observation, our pre-operative diagnostics patients affected with heart failure may under-estimate the presence of RV failure.

Other studies [13] reported fever without infection, peri-operative blood transfusions, and increased need for pre-implant isotropic support as a risk factor for RV failure, that did not reach significant difference in our current study. Pagani et al. [14] reported that the incidence of RV failure after LVAD insertion was higher in patients supported with ECMO before LVAD. The authors attributed this finding to a lung injury exacerbated by ECMO or may reflect the overall increased severity of illness. The Pittsburgh group [15] and Thoratec [11] experience confirmed this finding. In our series ECMO was applied only in three cases; we found significant difference in the need of mechanical ventilation in the pre-operative period, but there were only 5 cases. Unfortunately, our experience with levothrombom is limited only to the latest two cases, and so we cannot draw our conclusion about its use in supporting failing right ventricle.

In our series, RV failure complicated the 16% of LVAD insertions confirming the observation of the previous studies. RV failure is one of the most serious complications of the LVAD support, because the survival to heart transplant was significantly lower than the RV failure group (25%) when compared with the other group (85%). Both the study of Frazier and associates [3] and the one of Goldstein et al. [5] reported significantly negative correlation with the outcome. For this reason, the prediction of RV failure is very important for the selection of patients [19]. Although several studies have attempted to identify risk factors for RV failure after LVAD support, few data are available to predict RV failure before the operation, and more data are needed.

5. Conclusions

The RV failure incidence after LVAD support was 16%, and it had negative correlation with the outcome. Preoperative low PAP was a significant risk factor for RV failure development. Additional risk factors included laboratory tests deposing for chronic congestive RV failure in the preoperative screening (creatinine, aspartate aminotransferase, alanine aminotransferase and blood urea nitrogen). This information may be useful for the patient selection for isolated LVAD implantation, but other studies are necessary before establishing criteria for patient selection for univentricular support are universally accepted.

References


