Thoratec paracorporeal biventricular assist device therapy: the Freiburg experience†

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Abstract

OBJECTIVE: The treatment of severe biventricular (BV) contractile failure using mechanical circulatory support is challenging. We analyzed our center's results following implantation of a biventricular assist device (BV AD).

METHODS: We implanted 39 BV ADs between September 2001 and January 2009. All patients were qualified candidates for heart transplantation, without an organ available at time of BV AD implantation. Fifteen patients without a history of chronic cardiomyopathy suffered from acute BV failure (group 1), whereas the other 24 suffered from severe chronic cardiomyopathy (group 2). The indication for BV AD implantation was determined in reference to echocardiography, the degree of end-organ damage, and whether the patient qualified for a heart transplant or was a candidate for bridge to recovery.

RESULTS: Both groups were similar regarding their preoperative hemodynamics, intraoperative and early postoperative findings, and adverse events. Patients in group 1 were younger (mean age 37 ± 17 years) than those in group 2 (51 ± 12 years). Mean duration of support in group 1 was 137 ± 109 days, and 65 ± 61 days in group 2. In group 1, 33% (5/15) were weaned off the device and 53% (8/15) underwent heart transplantation, whereas 8/24 patients (42%) in the chronic group were transplanted. Group 1's mortality on the device was lower than that of group 2 (13% vs 67%). Furthermore, 11 patients of group 1 survived for 1 year compared with four in group 2 (73% vs 17%).

CONCLUSION: Implantation of a BV AD in patients with chronic heart failure and acute decompensation is associated with a high mortality and morbidity rate. By contrast, BV AD implantation can achieve excellent results in patients with acute BV failure without a history of chronic cardiomyopathy, even if they are in cardiogenic shock upon admission.

Keywords: Congestive heart failure • Biventricular assist device • Outcome • Acute heart failure

INTRODUCTION

Surgical treatment of patients with biventricular (BV) heart failure (HF) unresponsive to medical therapy represents an enormous challenge. The causes of BV failure include acute myocarditis, acute myocardial infarction (MI), chronic cardiomyopathy with acute cardiac decompensation, and post-cardiotomy cardiac failure.

Potential surgical options in these situations are:

(1) Implantation of an extracorporeal life support system (ECLS).
(2) Placement on the highly urgent (HU) waiting list for cardiac transplantation.
(3) Implantation of a left-ventricular assist device (LVAD, e.g., Heartmate II®, INCOR (Berlin Heart)®, and HeartWare®).

However, if right-heart failure occurs postoperatively after LVAD implantation, the prognosis is dismal and mortality rates of up to 100% have been reported [1]. Strict patient and device selection might improve such poor outcomes [2, 3].

(4) Paracorporeal biventricular assist device (BVAD) implantation (e.g., EXCOR (Berlin Heart)® and ABIOCOR®), which offers the patient effective support for up to 2 years. Most patients undergo a heart transplant following BVAD implantation, although some have been successfully weaned off the system following organ recovery [4]. The Thoratec Paracorporeal Ventricular Assist Device® (Thoratec Corporation, Pleasanton, CA, USA) is a system that has been implanted over 4000 times.

However, mortality after BVAD implantation remains high despite complete unloading of the heart and high-flow organ perfusion [5, 6]. This stands in contrast to excellent results in patients after LVAD implantation [7, 8]. One could speculate that patients requiring BV cardiac support are sicker and suffer from more severe end-organ dysfunction, which leads to poor outcomes [9].

In general, there are two groups of patients requiring BV cardiac support: those suffering from an acute onset of HF,
usually in severe cardiogenic shock, and those with a history of chronic congestive HF accompanied by a sudden impairment of cardiac function. The purpose of this study is to analyze pre-, intra-, and postoperative results after BVAD implantation in patients with acute and chronic onset of severe cardiac failure.

**MATERIAL AND METHODS**

We implanted a Thoratec® BV AD in 44 patients out of a total of 173 patients receiving mechanical circulatory support between September 2001 and January 2009 at our institution (25% of VAD implantations). As many as 39 patients with a primarily implanted BVAD were included and five patients excluded from this study. Two after a device change from an LVAD to a BVAD: one due to acute right heart failure, and the other due to device-related problems with thrombus formation and additional severe rhythmic disorders making the BVAD the better option. Two patients with implantation of a BVAD because of graft failure after heart transplantation and one patient with pheochromocytoma as underlying cause of HF were excluded as well. Indication for BV support relied on echocardiographic parameters (severe contractile impairment of the left and right ventricles, tricuspid annular plane systolic excursion, and tricuspid regurgitation), end-organ damage (liver, kidney, and lung), and if the patient qualified for heart transplantation or weaning. Due to our study’s retrospective format, we could not quantify all echocardiographic and hemodynamic data for all patients. We are aware of different scoring systems for right-ventricle failure after LVAD implantation. Therefore, our decisions were based on the most common scoring systems published [2, 10–13]. All patients were classified as INTERMACS level 1 (critical cardiogenic shock) [14] at the time of implantation.

**Surgical technique**

The BVADs were implanted according to standard surgical technique. The inflow cannula of the left ventricle was inserted into the left-ventricular apex, and the inflow cannula of the right-ventricular assist device was implanted in the right atrium or in the right-ventricular apex. The outflow grafts were anastomosed to the ascending aorta and to the main pulmonary artery, respectively. The BVAD’s pumping rate was adjusted to the patient’s physiological range, and we aimed for a systolic ejection time of 300 ms. Anticoagulation for both systems was started with heparin with a target partial thromboplastin time (PTT) of 60–80 s and changed to phenprocoumon with a target international normalized ratio (INR) of 3.0–3.5 after removal of the chest drains and sufficient oral ingestion. Platelet aggregation was inhibited by acetylsalicylic acid (ASA) at a dose of 100 mg/day.

**Study groups**

We divided the patients into two groups: patients in group 1 (n = 15) suffered from acute onset of HF with no prior history of cardiomyopathy, whereas patients in group 2 (n = 24) presented with a long history of chronic HF and subsequently severe cardiac decompensation. Long history of HF was defined as known worsening of heart function over years; unfortunately, mean duration of history of HF cannot be given as the exact onset is unknown in most cases.

**Etiology of BV failure**

Myocarditis was the most common cause of acute onset of HF in the first patient group (7/15 patients: 47%), followed by ischemic cardiomyopathy (5/15 patients: 33%). Two patients had acute HF of unknown origin and one patient developed acute HF after resuscitation following catheter ablation for Lown–Ganong–Levine syndrome. Due to the nature of this cohort, no patient was listed for transplant prior to implantation.

Group 2’s etiology of cardiac failure was dilative (17/24 patients, 71%) and ischemic cardiomyopathy (3/24 patients, 13%). Two patients presented with muscular dystrophy. One patient suffered from restrictive cardiomyopathy and the cause of BV failure in another was severe aortic regurgitation. About half of the patients (11/24, 46%) had been listed for heart transplantation and spent a mean of 168 ± 281 days on the waiting list prior to BVAD implantation. The mean time between first presentation at our center for evaluation of listing for heart transplantation and BVAD implantation was 8 ± 5 years.

**Laboratory values**

All analyses were done according to standard protocols.

**Statistics**

Data are presented as mean values ± standard deviation for quantitative variables and as absolute and relative frequencies for qualitative variables. Group comparisons were made with unpaired Student’s tests and Wilcoxon signed rank tests for quantitative data, as appropriate, and with Fisher’s exact test for qualitative data. All significance tests were two-sided, and a p value of <0.05 was considered statistically significant. Data analysis was made using SAS software (SAS Institute, Cary, NC, USA).

Laboratory data were analyzed preoperatively and 1, 10, and 30 days after implantation. PASW Statistics 18 (SPSS Inc., Chicago, IL, USA) was used for all calculations. The Mann–Whitney test with subsequent Bonferroni correction was employed for comparisons between groups. Thus, an asymptotic p ≤ 0.008 for basic laboratory data and p ≤ 0.01 for kidney and liver data were considered significant. Changes within each group were examined using the Friedman univariate analysis of variance (ANOVA) and Wilcoxon tests.

**RESULTS**

**Demographics and preoperative data (Table 1)**

Group 1 patients were significantly younger than those of group 2 (37 ± 18 vs 51 ± 12 years, p = 0.003).

Two-thirds (67%) of the group 1 patients were ventilated prior to BVAD implantation, and all received inotropic support. Resuscitation was necessary in 33% (5/15), and 40% (6/15) needed ECLS. An intra-aortic balloon pump (IABP) had to be
implanted in 47% (7/15) to bridge the patients to BVAD implantation.

Except for inotropic support and the need for ECLS, there were no statistically significant preoperative differences between the groups. Inotropic support was necessary in only 63% (15/24) in group 2, whereas 100% (15/15) needed inotropes preoperatively in group 1 (p = 0.0069).

The preoperative laboratory values (using the Bonferroni correction) revealed that patients with chronic HF had higher total bilirubin, aspartate transaminase (AST), and alanine aminotransferase (ALT) values (p = 0.001, p = 0.012, and p = 0.036, respectively).

Intraoperative data

Intraoperative data were similar in both groups, whether referring to the duration of the operation (group 1: 397 ± 103 min vs group 2: 390 ± 93 min) or bypass time (group 1: 169 ± 57 min vs group 2: 152 ± 40 min). Aorta cross-clamping was necessary in four patients in group 2 (17%) and in no patient in group 1. Pump flow on the BVAD was similar in both groups: initial RV AD flow was 2.2 ± 0.5 l/min/m² in group 1 and 2.16 ± 0.26 l/min/m² in group 2. Flow on the LVAD was 2.45 ± 0.5 l/min/m² in group 1 and 2.45 ± 0.25 l/min/m² in group 2. Delayed sternal closure was necessary in 13% (2/15) of those in group 1 and 17% (4/24) in group 2. There was no difference in the amount of blood products given in both groups either. The implantation procedure (right-atrial vs right-ventricular cannulation) was similar in both groups. A full dosage of protamine was given at the end of bypass.

Postoperative course (Table 2)

No significant differences appeared between the two groups' postoperative data.

The amount of postoperative bleeding in the first 24 h was 1217 ± 554 ml in group 1 and 1490 ± 1281 ml in group 2, with six patients in group 1 (40%) and 12 patients in group 2 (50%) requiring re-exploration because of bleeding or tamponade. The amount and nature of blood products administered intra- and postoperatively were similar in both groups. Five patients in group 1 (33%) and seven patients in group 2 (29%) required NovoSeven® RT (Coagulation Factor VIIa (Recombinant) due to diffuse bleeding.

Laboratory values

On the first day and 1 month after BVAD implantation, chronic patients had higher total bilirubin than acute patients (p = 0.001 and p = 0.009) (Fig. 1), whereas blood urea nitrogen (BUN) was higher on day 10 (p = 0.002). Chronic patients tended

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### Table 1: Demographics and preoperative data

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute HF</td>
<td>Chronic HF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td>n = 24</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>37 ± 18</td>
<td>51 ± 12</td>
<td>0.0059</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>10/15</td>
<td>21/24</td>
<td>0.22</td>
</tr>
<tr>
<td>Preoperative data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation</td>
<td>10/15 (67%)</td>
<td>10/24 (42%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Inotropic support</td>
<td>15/15 (100%)</td>
<td>15/24 (63%)</td>
<td>0.0069</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>5/15 (33%)</td>
<td>4/24 (17%)</td>
<td>0.27</td>
</tr>
<tr>
<td>IABP</td>
<td>7/15 (47%)</td>
<td>13/24 (54%)</td>
<td>0.75</td>
</tr>
<tr>
<td>ECLS</td>
<td>6/15 (40%)</td>
<td>2/24 (8%)</td>
<td>0.037</td>
</tr>
<tr>
<td>Preoperative laboratory values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>60 ± 27</td>
<td>93 ± 50</td>
<td>0.077</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.2 ± 0.4</td>
<td>2.0 ± 1.0</td>
<td>0.052</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>1.8 ± 1.7</td>
<td>2.8 ± 1.1</td>
<td>0.001</td>
</tr>
<tr>
<td>AST (IU/1)</td>
<td>306 ± 300</td>
<td>1620 ± 4000</td>
<td>0.012</td>
</tr>
<tr>
<td>ALT (IU/1)</td>
<td>735 ± 1075</td>
<td>784 ± 1688</td>
<td>0.036</td>
</tr>
</tbody>
</table>

HF indicates heart failure; IABP, intra-aortic balloon pump; ECLS, extracorporeal life support; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine transaminase.

### Table 2: Postoperative data

<table>
<thead>
<tr>
<th>Postoperative data</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute HF</td>
<td>Chronic HF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 15</td>
<td>n = 24</td>
<td></td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>46 ± 35</td>
<td>37 ± 28</td>
<td>0.38</td>
</tr>
<tr>
<td>In hospital stay (days)</td>
<td>97 ± 78</td>
<td>56 ± 49</td>
<td>0.05</td>
</tr>
<tr>
<td>Time of intubation (hours)</td>
<td>256 ± 266</td>
<td>378 ± 504</td>
<td>0.39</td>
</tr>
<tr>
<td>Tracheotomy</td>
<td>3/15 (20%)</td>
<td>4/24 (17%)</td>
<td>1</td>
</tr>
<tr>
<td>Dialysis</td>
<td>5/15 (33%)</td>
<td>9/24 (38%)</td>
<td>1</td>
</tr>
<tr>
<td>MARS</td>
<td>1/15 (7%)</td>
<td>3/24 (13%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Neurologic comp...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>2/15 (13%)</td>
<td>0/24</td>
<td>0.14</td>
</tr>
<tr>
<td>PRIND</td>
<td>0/15</td>
<td>0/24</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>2/15 (13%)</td>
<td>5/24 (21%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3/15 (20%)</td>
<td>11/24 (46%)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

HF indicates heart failure; ICU, intensive care unit; MARS, molecular adsorbents recirculation system; TIA, transient ischemic attack; PRIND, prolonged reversible ischemic neurologic deficit.

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**Figure 1: Total bilirubin.** The rectangles in the box plots contain the middle 50% of the values (25th and 75th percentile), the median is marked. The whiskers indicate the upper and lower non-extreme values. Circles and asterisks mark outliers and extreme values, respectively.
to present higher ALT and AST values on day 1 ($p = 0.036$ and $p = 0.012$, respectively), and higher serum creatinine on day 10 and 30 ($p = 0.036$ and $p = 0.032$).

ALT and AST decreased rapidly in patients with acute HF while on BVAD support, also when compared with preoperative values. We noted a slight drop in AST and ALT in patients with chronic HF (Figs. 2 and 3).

**Support and outcome**

Total support time in group 1 was $137 \pm 109$ days (range: 8–362 days). Two patients died on the device (13%): one of multi-organ failure, and one was considered brain dead (due to unsuccessful resuscitation resulting in hypoxic brain damage prior to device implantation). One expired during heart transplantation and one were weaned off the device due to organ recovery.

Total support time in group 2 was $65 \pm 61$ days (range: 8–235 days). Sixteen patients died on the device (67%): eight of septic multi-organ failure, four of multi-organ failure, and four were considered brain dead (all because of massive cerebral hemorrhage). Four patients died after cardiac transplant within $50 \pm 67$ days (range: 1–143 days): two of graft failure and two of septic multi-organ failure. Four patients were successfully transplanted (4/24 patients: 17%).

Group 1’s mortality on the device was lower than in group 2 (13% vs 67%) (Fig. 4). The 30-day mortality was 13% in group 1 vs 42% in group 2. The 180-day mortality revealed a similar trend, with a mortality of 20% in group 1 and 79% in group 2. Overall, we observed a 1-year survival rate of 73% for the acute patients and 17% for the chronic patients, respectively.

**DISCUSSION**

There are various surgical options for patients suffering from acute or chronic severe BV HF, when medical therapy has proven ineffective. These include stabilizing the patient with ECLS (implanted via the groin or thorax), listing for a HU heart transplantation, and LVAD or BVAD implantation [15]. However, placement on the HU waiting list is not a reasonable alternative for most of these critically ill patients, as the mean waiting time here in Germany is longer than 45 days [16]. Therefore, BVAD implantation seems to be the treatment of choice, even though this patient population’s mortality rate is reported to be as high...
as 40% [7, 8]. The ratio at our institution of BVAD to LVAD implantation stands at 1:4.

In our study, mortality on the device for group 1 at 13% and for group 2 at 67% – reflecting a 1-year survival rate of 73% (group 1) and 17% (group 2) – reveals the biggest single difference between the two groups. Despite the disease's different etiologies, factors such as older age are known risk factors of dying on BVAD support [17]. This fact could be affirmed by our study as group 1 patients were younger than group 2 patients. This is probably because 47% of them had myocarditis, which is more likely to occur in children and young adults, taking a more severe course in those under 40 years of age [18]. However, both groups revealed a wide range of ages: 11–60 years in the acute group, and 26–65 years in the chronic group. Obviously, the chronic group also contained young patients with long-term cardiac disease.

The preoperative data (Table 1) reveal that group 1 patients were in worse hemodynamic condition prior to BVAD implantation. All required inotropic support and use of ECLS was also significantly higher than in group 2. Patients without previous cardiomyopathy, who develop severe BV contractile failure, often need early hemodynamic support, including ECLS [19].

There were no differences between the groups intra-operatively. Both underwent the same surgical technique and spent similar times in surgery; there was no significant difference in the numbers of blood products used or in secondary bleeding. We had expected a higher rate of coagulopathy in group 1 [20] due to their chronically malperfused livers. Their higher preoperative bilirubin values might support this assumption. However, conscientious and effective intraoperative management seems to compensate for this malfunction.

We observed no significant differences in postoperative ventilation times, intensive care unit (ICU) or hospital stays, or complication rates. Yet, group 1’s mortality on the device (13%) is much lower than group 2’s (67%). This is probably due to group 1’s rapid onset of HF out of good general health, that is, they had not suffered for months or years from chronic end-organ malperfusion, as was the case with group 2’s chronic patients. Cardiac cachexia is also a serious problem in patients with chronic HF.

In our study, those patients with a longer history of cardiomyopathy and irreversible end-organ damage (as indicated by creatinine, bilirubin, AST, and ALT values) have a worse outcome than acutely ill patients in whom organ recovery is possible. This observation has also been made in other studies [17, 21, 22].

The chronic patients had higher pre- and post-BVAD implantation bilirubin values than the acute patients, who also demonstrated a faster postoperative reduction in AST and ALT, indicating group 1’s faster end-organ recovery. That was true although both groups’ BVADs showed similarly efficient perfusion and flows. Due to their chronic HF, group 2’s organs have had a long time to adapt to being malperfused. Perhaps BV support causes a paradoxical reaction in the liver, kidneys, and lungs after long-standing malperfusion. This issue deserves more intensive investigation.

Total support time in group 1 was 137 ± 109 days (range: 8–362 days) vs group 2’s 65 ± 61 days (range: 8–235 days). The longer support in group 1 is related to the high incidence of myocarditis in this group. Longer ventricular unloading took place to allow myocardial recovery to occur [23]. As no cardiac recovery is anticipated in group-2 patients, they are often listed sooner for heart transplantation, making their support times shorter.

**Study limitations**

Several limitations are associated with this study. First, it is a retrospective study with a potential bias concerning the treatment strategies. Second, the extent of cardiac cachexia cannot be determined completely from the charts. Third, the extent of end-organ damage requires more detailed evaluation in a subsequent study.

**CONCLUSIONS**

BV myocardial failure associated with cardiogenic shock is not controllable by conventional medical treatment. In this scenario, the implantation of a paracorporeal BVAD remains the treatment of choice. However, the outcome is poor with a mortality rate of 50%, despite sufficient unloading of the right and left heart and effective circulatory support.

In this study, we could demonstrate that the outcome after BVAD implantation in patients with an acute onset of HF is significantly better compared with patients with a chronic course of the disease. For those chronic patients, we therefore suggest the implantation of a short-term ECLS system as a ‘bridge to decision making’. After hemodynamic stabilization, we assume that these patients will recover with subsequent implantation of a BVAD.

Future studies will have to demonstrate if the implantation of a paracorporeal BVAD is superior to the implantation of an intracorporeal LVAD and extracorporeal RVAD (i.e., Levitronics®).

**FUNDING**

This study is associated with the comprehensive project ‘Cardiac assist devices for long-term support in cardiac insufficiency’ supported by the German Research Society (DFG) (# PAK 350). Thoratec Corp. (Pleasanton, CA, USA) runs training workshops on assist devices in cooperation with our department and pays compensation for expenses incurred to the University Medical Center Freiburg.

Conflict of interest: none declared.

**REFERENCES**


[18] Dr M. Kirsch (Paris, France). I have quite some difficulties with your conclusion that BiVAD is a bad system for assisting chronic heart failure patients. I think you have such huge differences in the preoperative presentation of your patients, especially regarding liver failure, that you cannot compare those two groups. You should make a multivariate analysis and you will see very certainly that liver function is the main determinant of the bad outcome of your patients.

[19] Dr Brehm: Actually we have made a multivariate analysis and we couldn’t see that in these patients. What we saw is that patients on ECMO support and on inotropes prior to implantation had a better outcome. But that was because the acute patients were all on inotropes and 40% were on an ECMO prior to implantation of the BiVAD. But I think you can compare these two groups. When you have a chronic patient you have to decide what to do with that patient. You can implant a BiVAD and think, okay, that would be the best option. But obviously it’s not. We have to compare and need to have further studies to determine whether the alternative approaches are really a better option. We currently don’t know that, but we are investigating it.

[20] Biventricular assist device, and it was certainly not the same in every patient; the decision was made on the presentation. It was based on liver function, end-organ function, and on the echo data—the TAPSE, the tricuspid regurgitation, and the right ventricular function. So it was decided mainly on the presentation, the echo findings, and the end-organ damage.