Permanent mechanical circulatory support in patients of advanced age

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Abstract

Objective: This study details our initial results of long-term left ventricular assist device (LVAD) support in patients suffering from catecholamine-dependent end-stage heart failure or cardiogenic shock with age above 65 years or age above 60 and contraindications to cardiac transplantation.

Methods: Between September 2000 and July 2002, 27 patients received implantation of left ventricular assist devices (Micromed DeBakey (n = 15), Berlin Heart Excor (n = 6), Arrow Lion Heart (n = 4) and Novacor N100 (n = 2)). The mean age of this group was 66.2 ± 4.1 (60–77) years. The patients presented with the following features by the time of LVAD implantation: failure of weaning from inotropic support (78%), either profound cardiogenic shock (37%) or instable hemodynamic status (22%), high-dose inotropic (52%) or intraaortic balloon pump support (11%), dialysis (15%), artificial ventilation (15%), and at least one previous cardiac procedure (44%).

Results: The cumulative survival rate for the whole group was 63% at 30 days, 30% at 180 days, and 22% at 2 years. The presence of preoperative cardiogenic shock was associated with a higher perioperative mortality rate. Late complications (n = 7) included replacement of two thrombosed DeBakey LVADs and five late deaths secondary to thrombembolism/intracranial hemorrhage (DeBakey LVAD, n = 3) or septicemia (n = 2). As of May 15, 2003, six patients remain on LVAD support for an average of 653 (339–953) days, three patients now for more than 2 years. Ten patients were discharged home to spend 73% of their life span on out-of-hospital long-term LVAD support.

Conclusion: This study reports the first single-center experience of permanent LVAD support in patients of advanced age. For this initial experience, many patients with critical circulatory status and previous cardiac operations were included and a high postoperative mortality rate was encountered among them. Older age and associated multimorbidity are the key determinants rendering the conditions of LVAD therapy for this patient cohort to be different from the bridge-to-transplant experience. The LVADs employed in this study showed different capabilities with regard to long-term support. Our experience shows that permanent mechanical circulatory support does have the potential to evolve as a treatment option in selected elderly patients with end-stage heart failure.

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Keywords: Heart failure; Cardiogenic shock; Cardiac transplantation; Left ventricular assist device; Ventricular assist device; Circulatory support

1. Introduction

End-stage heart failure may progress to require heart replacement by cardiac transplantation. If an acute deterioration of the patient’s hemodynamic status occurs before a donor heart is available, the intermediate use of ventricular assist devices or the total artificial heart as a bridge to heart transplantation remains a valuable option. Despite being very successful as a casuistic therapy for those patients benefiting from timely allocation of a donor heart [1], cardiac transplantation often will not be available for older patients (above 65 years of age) or in the presence of established contraindications. The situation is further complicated if such patients do not have the option of corrective heart surgery such as resection of left ventricular aneurysms [2] or mitral valve repair [3] to provide relief of symptomatic heart failure. It was for such patients that we considered the option of long-term mechanical circulatory support.

2. Materials and methods

2.1. Patient selection

Patients were considered to be candidates for long-term LVAD support if they presented with the diagnosis of...
end-stage heart failure and met the following inclusion criteria: (1) no option of organ preserving cardiac operative procedures, (2) age beyond 65 years or age above 60 years in presence of established contraindications for heart transplantation, such as diabetes mellitus with secondary organ damage, or severe peripheral vascular disease, (3) end-stage heart failure of NYHA class IV or catecholamine-dependent heart failure or acute hemodynamic deterioration/profound cardiogenic shock (including high-dose catecholamine support, intraaortic balloon pump support (IABP), mechanical ventilation, or hemofiltration/dialysis). Previous cardiac operative procedures were not considered a contraindication for LVAD support.

Between September 2000 and July 2002, a total of 27 male patients (mean age 66 ± 4 years, range 60–77) were selected for long-term LVAD support. Four patients (15%) were above 70 years of age by the time of LVAD implantation. The underlying cardiac pathology was dilative cardiomyopathy (n = 8) or end-stage heart failure from ischemic heart disease (n = 19). Twelve patients (44%) had previously undergone cardiac operative procedures; four of these (15%) had already had two previous cardiac operations. In one patient, three operative procedures had been performed before, namely coronary artery bypass grafting, followed by resection of LV aneurysm and finally, cardiomypoplasty. Eleven patients (41%) had received implantable cardioverter-defibrillators (ICDs) earlier (Table 1).

The majority of patients were referred from remote hospitals where recompensation from heart failure had been attempted previously. After admission to our unit, intravenous inotropic support became necessary or had to be re-instituted (initial cardiac index 1.58 ± 0.41 l/min per m², range 0.8–2.4 l/min per m²) in 21 out of 27 patients (78%) despite optimal oral medication, including angiotensin-converting enzyme (ACE) inhibitors, β-blockers and loop diuretics (Table 1). One patient was transferred with the IABP in place; two further patients required insertion of an IABP because of acute deterioration of their hemodynamic status after admission (Table 1). Management of heart failure included inotropic support (dopamine and dobutamine) according to the actual hemodynamic status as determined by continuous assessment of cardiac output (Vigilance®, Edwards Lifesciences, Unterschleißheim, Germany). If the patients’ hemodynamic status did not improve under these measures, epinephrine and/or enoximone were administered in addition (Table 1).

Only six patients did not require intravenous inotropic support immediately prior to LVAD implantation (Table 1). Weaning from intravenous inotropic support was not possible in any of the other 21 patients. Only five out of these 21 patients could be stabilized on a minor dosage of

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit of measurement</th>
<th>No inotropic support</th>
<th>Inotropic support</th>
<th>Cardiogenic shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>n</td>
<td>6</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>years</td>
<td>65.5 ± 3.9</td>
<td>67.3 ± 4.3</td>
<td>65.5 ± 4.6</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td></td>
<td>1.92 ± 0.15</td>
<td>1.87 ± 0.16</td>
<td>1.88 ± 0.18</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>%</td>
<td>14 ± 4</td>
<td>17 ± 5</td>
<td>15 ± 3</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td></td>
<td>76 ± 3</td>
<td>74 ± 4</td>
<td>74 ± 7</td>
</tr>
<tr>
<td>Previous operations</td>
<td>n</td>
<td>2</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>ICD</td>
<td>n</td>
<td>2</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Dopa + dobu</td>
<td>µg/kg per min</td>
<td>0</td>
<td>7.65 ± 3.52</td>
<td>9.85 ± 3.79</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>µg/kg per min</td>
<td>0</td>
<td>0</td>
<td>0.23 ± 0.09</td>
</tr>
<tr>
<td>Enoximone</td>
<td>µg/kg per min</td>
<td>0</td>
<td>3</td>
<td>3.43 ± 1.99</td>
</tr>
<tr>
<td>Mechan. ventilation</td>
<td>n</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Hemofiltration</td>
<td>n</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>IABP</td>
<td>n</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Micromed DeBakey</td>
<td>n</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Berlin Heart</td>
<td>n</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Lion Heart</td>
<td>n</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Novacor</td>
<td>n</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Left thoracotomy implant technique</td>
<td>n</td>
<td>3</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>

The demographic data, parameters indicating cardiac function and circulatory status, and choice of LVADs are shown for 27 patients of advanced age immediately before LVAD implantation. The patients are grouped according to their pre-LVAD circulatory status (no inotropic support, necessity of inotropic support, persistent cardiogenic shock). LVAD, left ventricular assist device; Dopa + dobu, combined dosage of dopamine and dobutamine; LVEF, left ventricular ejection fraction; LVEDD, left ventricular enddiastolic diameter; ICD, implantable cardioverter-defibrillator; IABP, intraaortic balloon pump, some data are presented as the mean ± SD. For further details refer text.
dopamine and dobutamine (4.37 $\pm$ 1.37 $\mu$g/kg per min). The six patients without and the five patients with only minor inotropic support were judged from their clinical presentation as to have stable circulatory patterns before LVAD insertion. In contrast, in the remaining 16 patients judged as unstable, catecholamine-dependent heart failure progressed to require high-dose administration of dopamine and dobutamine (10.05 $\pm$ 3.14 $\mu$g/kg per min); in the majority of the latter patients, epinephrine ($n = 7$, 0.23 $\pm$ 0.09 $\mu$g/kg per min) and/or enoximone ($n = 9$, 3.92 $\pm$ 2.43 $\mu$g/kg per min) were administered in addition. Advanced cardiogenic shock persisted or developed in 10 out of the 16 unstable patients despite all conventional measures; mechanical ventilation and hemofiltration/dialysis became necessary in four patients each (Table 1).

2.2. Selection of LVADs

With the patients being scheduled for permanent circulatory support, implantable LVADs have been our first choice. The Micromed DeBakey LVAD (Micromed Technology Inc., Houston, TX, USA) [4,5] was implanted in 15 patients and, in this series of patients, succeeded the Novacor N100 LVAS (World Heart Inc., Oakland, CA, USA) [6], which was only used in two early cases, as an implantable blood pump. Four hemodynamically stable patients received implantation of the first totally implantable LVAD, the Arrow Lion Heart LVD 2000 (Arrow Intl. Inc., Reading, PA, USA) [7] between September 2000 and July 2001. The Berlin Heart Excor pneumatic LVAD (Berlin Heart AG, Berlin, Germany) [8,9] was implanted in six cases between September 2000 and September 2001.

With its proven hemodynamic efficiency and utilizing a left lateral implantation technique, the Berlin Heart Excor LVAD found its major application in patients with instable hemodynamic patterns and previous cardiac procedures (Table 1).

The Micromed DeBakey LVAD (Fig. 1) [4,5] is a small, light-weight (<100 g) axial flow blood pump. While the blood pump itself resides within the chest, a percutaneous driveline has to be brought out through the skin in the right lower abdomen and connects the blood pump to the external controller and battery pack, which are worn by the patient in a shoulder bag. During the year 2001, the DeBakey LVAD was modified to bear a Cameda® heparin coating of the interior blood-contacting surfaces. The Berlin Heart Excor LVAD [8,9] is a paracorporeal, pneumatically accentuated blood pump. Both in- and outflow cannulas are brought out through the skin in the upper abdomen and are connected to the paracorporeally situated blood pump. The blood pumps of the Berlin Heart Excor LVAD have had a Cameda® heparin coating since 1994. A portable external pneumatic driver (Excor®) provides enhanced patient mobility (Fig. 2) and allows the patients to ambulate freely and to be discharged home. Like all implantable electromechanically driven pulsatile flow blood pumps, both the Novacor N100 LVAS [6] and the Lion Heart LVD 2000 require the creation of a pump pocket underneath the left rectus abdominal muscle. In the case of the Novacor, a percutaneous
The LVADs were implanted using the standard median sternotomy approach and partial cardiopulmonary bypass in eleven cases. In 16 out of the 27 patients (59%) an alternative LVAD implantation technique was used (in 5/6 patients with the Berlin Heart LVAD and in 11/15 patients with the Micromed DeBakey LVAD): after a full left lateral thoracotomy and aided by partial cardiopulmonary bypass instituted via cannulation of the femoral vessels, the LVAD was connected to the left ventricular apex and the outflow was directed towards the descending thoracic aorta (Fig. 1) [10]. This technique has now been used in our institution in more than 27 patients for implantation of the Berlin Heart Excor pneumatic LVAD alone since 1997 [11]. Originally inaugurated as an alternative surgical technique to provide LVAD support and to avoid a re-sternotomy in patients with previous cardiac operative procedures, it’s utilization has been extended to four further patients without previous operations in this series. Our institutional ethics committee on human research granted approval for use of the Arrow Lion Heart LVD 2000 (application no. 191/2000, final approval of latest submissions November 6, 2000) and for use of the Micromed DeBakey LVAD (application no. 18/2002, final approval of latest submissions January 27, 2002).

Long-term anticoagulation management was similar for all LVADs and included the administration of phenprocoumon (INR 3.0–3.5), aspirin and dipyramidole [9]. During the phase of in-hospital rehabilitation after LVAD implantation, the patients were trained in the self-assessment of INR and corresponding daily adjustment of the phenprocoumon dosage. Ambulatory care was provided by our institution through a designated outpatient clinic, where the patients were monitored in intervals of 2–6 weeks. In the patient with the Lion Heart LVAD, the pressure within the volume compensation compartment was checked every 2–3 weeks through the access port and an appropriate amount of gas was refilled.

Kaplan–Meier estimates of cumulative survival were calculated using commercially available software (SPSS Inc., Chicago, IL, USA). In case the analysis was stratified according to a factor, the log rank statistics, the Tarone-Ware and Breslow statistics were applied to each analysis to test the equality of the survival distributions for different levels of the factor.

3. Results

3.1. Survival

The cumulative survival rate for the whole group of patients was 63% at 30 days, 32% at 180 days, and 22% at 1 and 2 years following LVAD implantation (Fig. 3). No deaths have occurred so far in patients beyond 235 days of LVAD support. Fourteen patients died early after LVAD implantation (25 ± 19 days), seven patients died later (158 ± 58 days) during LVAD support. The major causes of early mortality were septicemia/multiorgan failure (n = 11) and visceral ischemia (n = 1). Two further patients died early after implantation of the DeBakey LVAD via a left lateral thoracotomy as a consequence of multiple arterial embolization including the cerebral and visceral regions; in these cases, the most likely source of emboli was a heavily calcified descending thoracic aorta encountered during implantation of the LVAD.

Whether patients were judged as presenting with stable (n = 11) or instable hemodynamic status (n = 16) prior to LVAD implantation (see above), did not translate into statistically significant differences in early outcome: if a Kaplan–Meier estimate of cumulative survival is applied, a 32% advantage with regard to survival rate at 30 days (P = 0.1281, log rank statistic) in favour of patients with stable circulation prior to LVAD implantation is found. Contrasting the patients with cardiogenic shock prior to LVAD implantation against all others (Fig. 4), however, resulted in a significantly inferior early survival rate (30 versus 82%, P = 0.0090) at 30 days, but this difference already diminished at 90 days (30 versus 53%, P = 0.1028). If the patient cohort is grouped as those presenting with no requirements for inotropic support (n = 6), necessity of
inotropic support (n = 11) or advanced circulatory instability/cardiogenic shock (n = 10) prior to LVAD implantation (Table 1), large differences in the mortality rates become apparent (Fig. 5): at 30 days, no deaths were observed in patients without prior inotropic support versus 73% survival in the inotropic support group and 30% survival in patients with preoperative shock (P = 0.0113, log rank statistics, ‘No inotropes’ versus ‘Shock’ group). These differences in survival rates remained true at 90 days, and the overall survival approaches—but does not reach—a statistically significant difference between the subgroups (P = 0.0636, subgroups ‘Shock’ versus ‘No inotropes’).

There was a trend towards a reduction in overall survival after LVAD implantation for patients with the diagnosis of dilative cardiomyopathy (n = 8) when compared to patients with end-stage heart failure secondary to ischemic heart disease as demonstrated by the Kaplan–Meier survival analysis (P = 0.0664). Older age, by itself, was not a determinator of early or late survival in this series. If the patients were grouped according to the clinically important age barrier of 65 years, for example, there was no difference in early or late outcome as demonstrated by the Kaplan–Meier survival estimate (P = 0.7615, log rank statistic).

3.2. Long-term support

Eleven out of 13 long-term supported patients were either discharged home after physical rehabilitation and appropriate training in device management and self-assessment of the INR (n = 10) or transferred to a remote hospital for further rehabilitation (n = 1). Seven late deaths occurred during long-term follow-up: two patients died secondary to recurrent pneumonia/septicemia at 118 ± 43 days following Berlin Heart LVAD implantation and after initial recovery and mobilization. The remaining five late deaths were observed at 205 ± 46 days in patients with the DeBakey LVAD who had been discharged home long before (n = 4) or transferred to a remote hospital after uneventful recovery (n = 1, 91 days) (Table 2). In the first case, the patient was readmitted with a largely asymptomatic intracranial bleeding, low LVAD flow and laboratory evidence of device-related hemolysis. The patient recovered from the intracranial bleeding without sequelae, but the LVAD flow remained low. Later the LVAD arrested and the DeBakey LVAD was replaced. The patient recovered quickly after LVAD replacement and was fully mobilized a few days after the operation. He died from a sudden massive secondary intracranial bleeding 16 days after LVAD exchange. The second patient was readmitted with a minor intracranial hemorrhage after more than 7 months following LVAD implantation. Two weeks later, the DeBakey LVAD arrested and a major stroke occurred. The third patient was readmitted with low LVAD flow and clinical evidence of a minor stroke. A lysis therapy was initiated to save the thrombosed LVAD, but an intracranial hemorrhage developed. The fourth patient was readmitted with intermittent low LVAD flow, hematuria and poor physical condition in general. Presence of a colon carcinoma was suspected on the grounds of his clinical presentation and endoscopic findings; however, histology remained negative. Two weeks later the LVAD arrested and was replaced by a Berlin Heart Excor LVAD. The patient died later from right ventricular and multiorgan failure. The fifth patient, at the age of 77 years, died from sudden spontaneous intracranial hemorrhage after previous...
recovery and full mobilization following LVAD implantation.

Other technical defects of the implanted LVADs were infrequently observed (Table 2). Controller failures necessitated the elective replacement of external VAD components in some DeBakey LVADs. In the one patient with the Lion Heart an electronic defect of the implanted internal controller without effects on blood pump performance was suggested by transcutaneous data transmission. Replacement of the internal controller was advised and was scheduled after 18 months after LVAD implantation. Subsequent infection of the operative site necessitated two further surgical revisions, implantation of a replacement internal controller and prolonged hospitalization (Table 2). In him, also the external coil of the TETS system had to be replaced once because it tended to overheat. Technical failures of the LVAD system, LVAD-associated infections and other non-cardiac events were the three most frequent causes for hospital readmission in these patients (Table 3). In the patient with the Lion Heart, the pre-existing severe peripheral arterial occlusive disease necessitated the amputation of the left upper limb and right forefoot amputation resulting in substantially extended hospitalization (Table 3).

The total LVAD support time was $470 \pm 316$ days ($152–953$ days) in the 10 patients discharged home. The LVAD support time after their initial hospital discharge accounted for $411 \pm 304$ days (Table 3). With the use of LVADs, the patients were able to spend an average of 73% of their respective life time out of hospital after initial hospital discharge (Table 3). Older age and associated multimorbidity of these patients might necessitate secondary hospitalization for a variety of reasons. To assess the restrictions on out-of-hospital LVAD support imposed only by complications associated with the LVAD use, the ‘LVAD adjusted’ duration of out-of-hospital LVAD support has been calculated (Table 3): the patients spent an average of 79% of their respective LVAD support time after initial hospital discharge at home.

### 4. Discussion

Cardiac transplantation remains the most successful single therapy for patients with end-stage heart failure.

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### Table 2
LVAD-associated complications during long-term support

<table>
<thead>
<tr>
<th>Type LVAD</th>
<th>No. (n)</th>
<th>Time LVAD support (days)</th>
<th>Sum of patient days (days)</th>
<th>Technical defects (n)</th>
<th>VAD arrest (n)</th>
<th>VAD pump replacement (n)</th>
<th>VAD component replacement (n)</th>
<th>Stroke/ICB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berlin Heart</td>
<td>2/6</td>
<td>883 ± 100</td>
<td>1765</td>
<td>0</td>
<td>0</td>
<td>4(^a)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DeBakey</td>
<td>7/15</td>
<td>286 ± 126</td>
<td>2002</td>
<td>1</td>
<td>4(^a)</td>
<td>2</td>
<td>2</td>
<td>7(^c)</td>
</tr>
<tr>
<td>Lion Heart</td>
<td>1/4</td>
<td>933</td>
<td>933</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1(^d)</td>
</tr>
<tr>
<td>Total</td>
<td>10/27</td>
<td>470 ± 316</td>
<td>4700</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

\(^a\) Pump replacement is routinely performed with evidence of fibrin deposits or thrombus formation within the blood pump or cannulas during inspection.

\(^b\) In three patients.

\(^c\) In four patients.

\(^d\) No residual neurology.

### Table 3
Duration of out-of-hospital LVAD support and readmissions

<table>
<thead>
<tr>
<th>Type LVAD</th>
<th>No.</th>
<th>DAD (days)</th>
<th>DOH (days)</th>
<th>LOH gain (%)</th>
<th>LVAD adjusted DOH (days)</th>
<th>LOH LVAD adj. gain (%)</th>
<th>VAD tech. (days)</th>
<th>VAD infect. (days)</th>
<th>Other reasons (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berlin Heart</td>
<td>2/6</td>
<td>805 ± 129</td>
<td>770 ± 135</td>
<td>95 ± 1</td>
<td>778 ± 129</td>
<td>97 ± 1</td>
<td>0</td>
<td>23 ± 4</td>
<td>2 ± 3</td>
</tr>
<tr>
<td>DeBakey</td>
<td>7/15</td>
<td>234 ± 123</td>
<td>164 ± 96</td>
<td>69 ± 16</td>
<td>177 ± 116</td>
<td>73 ± 17</td>
<td>19 ± 30</td>
<td>23 ± 42</td>
<td>18 ± 30</td>
</tr>
<tr>
<td>Lion Heart</td>
<td>1/4</td>
<td>857</td>
<td>475</td>
<td>55</td>
<td>706</td>
<td>82</td>
<td>51</td>
<td>48</td>
<td>231</td>
</tr>
<tr>
<td>Total</td>
<td>10/27</td>
<td>411 ± 304</td>
<td>317 ± 273</td>
<td>73 ± 18</td>
<td>355 ± 294</td>
<td>79 ± 17</td>
<td>18 ± 28</td>
<td>25 ± 35</td>
<td>36 ± 73</td>
</tr>
</tbody>
</table>

Shown are the duration of LVAD support and the time spent out of hospital together with three most frequent causes for hospital readmission in 10 out of 27 elderly patients on long-term LVAD support. The total survival time was $470 \pm 316$ days on LVAD support. The patients were able to spend an average of 73%, resp. 79%, of their life span out of hospital after their initial discharge. For further discussion refer text. DAD, duration of LVAD support after initial discharge; DOH, duration of LVAD support out of hospital; LOH gain, percentage of life span out of hospital gained by using LVADs; LVAD adjusted DOH, duration of out of hospital LVAD support calculated by accounting only for all-cause LVAD-associated hospital readmissions; LOH LVAD adjusted gain, percentage of life span out of hospital gained by using LVADs when only LVAD-associated hospital readmissions are regarded; VAD tech./infect., LVAD-associated readmissions for technical failures or low LVAD flow/infections; Other reasons, all other diagnoses leading to hospital readmission.
with long-term survival rates of 60% at 5 and 50% at 10 years [1]. It has established a standard to which alternative therapeutic strategies will have to be compared on the basis of equivalent patient selection. While selected patients obviously continue to benefit from resection of left ventricular aneurysms [2] or mitral valve reconstruction [3], both partial left ventriculectomy [12] or dynamic cardiomypolasty [13] fell short in achieving comparable long-term survival rates. Dynamic cardiomypolasty and, more recently, the application of passive containment devices [14] or the myosplint procedure [15] do not achieve a comparable gain in relief from heart failure or their applicability is limited to patients with a less severe degree of heart failure.

To address this problem we used permanent mechanical circulatory support in elderly patients above 65 years of age or for those not qualifying for cardiac transplantation or bridge-to-transplant procedures because of established contraindications and age above 60 years. For this initial experience with permanent circulatory support, elderly patients with highly critical hemodynamic status, previous IABP support, intubation or renal failure were accepted (Table 1). Although our experience is still limited with the regard to the total number of cases, we can now prove a strong association between the preoperative circulatory status and early outcome (Figs. 4 and 5). In other terms, more selective inclusion of patients will clearly improve on the high early mortality rates observed in patients with preoperative shock.

The majority of patients in this series received the Micromed DeBakey LVAD. The DeBakey LVAD with its compact design and comparatively simple implantation technique—and the possibility of implantation via the left thoracotomy approach in cases with previous cardiac procedures—was anticipated to be advantageous when employed in patients as selected for this clinical series. However, the incidence of VAD thrombosis and stroke/intracranial hemorrhage encountered with the DeBakey LVAD between 143 and 230 days of LVAD support was largely responsible for the late mortality in this series.

Younger patients who are considered for LVAD implantation within bridge-to-transplant procedures and who present with a range of hemodynamic patterns similar to those observed in this series in general are expected to have a better early and late outcome than the patients in this series. It is therefore our impression that older age and the associated multimorbiditiy set the conditions for LVAD therapy in these patients apart from those of other patient groups, as for example, the bridge-to-transplant experience. Furthermore, this series stands out because of the high number of patients who were included despite previous cardiac operative procedures (44%).

More importantly, we were able to demonstrate that permanent LVAD use enables even such elderly patients to spend 73%, resp. 79% (Table 3), of their remaining life span on out-of-hospital LVAD support after their initial discharge from hospital. In addition, no patient has died so far beyond 235 days of LVAD support. Remarkably, the two long-term surviving patients with the Berlin Heart Excort LVAD required exceptionally few hospital readmissions resulting in a 95% out-of-hospital LVAD support time (Table 3). While this is also important to note in economical terms, it means that permanent LVAD support clearly is an option for this patient cohort. When evaluating the length of hospitalization in these patients, one has to bear in mind that such hospitalizations are very often longer than if treatment of the diagnosed illness alone led to readmission. The reason is that, at present, there is a lack of secondary caregivers and professional out-of-hospital ambulatory care for such patients in our health system.

This series of patients can be compared to two other clinical trials being conducted on similar patient cohorts and within the same time frame—the REMATCH trial (May 1998 to July 2001) [16] which was a double-armed US multicenter trial enrolling 68 patients for the treatment arm with permanent LVAD support using the partially implantable vented-electric Heartmate LVAS (Thoratec Corp., Pleasanton, CA, USA), and the single arm Lion Heart [7] European CUBS trial (Clinical Utility Baseline Study) [17], which enrolled 22 patients between October 1999 to December 2002. The 1 and 2 years survival rates in the REMATCH trial were 52% and 23%, and in the CUBS trial the survival rates were at 41% and 36%, respectively, which suggests these results to be on par or to provide some improvement over the 22% survival rates at 1 and 2 years in our series. In contrast to both the REMATCH and the CUBS trials, our series, however, included a high percentage of patients with advanced circulatory failure before LVAD implantation or previous operative cardic procedures, which were not present there. Regarding demographic data and the results, strong similarities between the REMATCH trial and our series become evident: the patients’ mean age, average survival time, long-term survival rates and average number of days spent out of the hospital are well within comparison.

In summary, the overall survival rates during permanent circulatory support in patients of advanced age in this study—as well as in similar series at that time—were lower than anticipated. Because of the high early mortality encountered, the inclusion of patients presenting with the combination of advanced age and profound cardiogenic shock cannot be recommended in general and the indication for LVAD support in such cases should be assessed on an individual basis. Long-term VAD support using the Micromed DeBakey LVAD, in our experience, provided less favourable results. The survival rates remained rather stable in patients beyond 250 days of LVAD support, and these patients could be maintained on out-of-hospital LVAD support for most of the time, clearly indicating that permanent circulatory support already has evolved as a treatment option for such patients. We would anticipate that, with the appropriate selection of patients and the LVAD technology available to us today, survival rates of 40–50%
at 2 and 3 years might well be achieved in elderly patients with end-stage heart failure in the near future.

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References


Appendix A. Conference discussion

Dr T. Aberg (Umea, Sweden): This is indeed a very important contribution. If you look at society’s possibilities to fund this kind of treatment, have you done any economic calculation about how successful the treatment must be in order to be economically viable for society?

Dr Jurmann: Not yet.

Dr Aberg: Are you planning to do so?

Dr Jurmann: Yes.

Dr Aberg: From my point of view, I think the treatment of chronic heart failure will be one of the issues that heart surgeons are going to be involved in. So I think these early attempts at mechanical support are indeed extremely important and worthy of a good discussion.

Dr V. DiSesa (West Chester, Pennsylvania): You used a relatively small number of a relatively large number of different devices. Based on at least this experience, have you got a favorite now or is there one that you use or are you still evaluating all of them?

Dr Jurmann: Performing a VAD implantation in an older patient with terminal heart failure or cardiogenic shock obviously means to perform a large operation in old and critically ill patient. We had to experience early throughout this series that such patients just did not recover as well as younger patients receiving VAD implantation in a similar preoperative condition.

The DeBakey VAD is a pretty small, light-weighted design, and during implantation, it gives you the impression that this is much less of an operation than implanting some other pulsatile pumps, for example. It has therefore been the hope that we had associated with the introduction of the DeBakey VAD, that the DeBakey VAD would enable us to downsize the invasiveness of the VAD implantation procedure itself. It didn't work out for us and during this series actually, and we are very unfortunate to tell this. So the DeBakey would have been an ideal solution; it is a small device per se. So, for the moment, I think pulsatile pumps like the Lion Heart, Novacor or the Berlin Heart Excor seem to be in favor in terms of long-term support. This is what I can say at the moment.

Dr F. Mohr (Leipzig, Germany): Your results match the results of the REMATCH trial more or less, and I am not sure whether we should be encouraged or discouraged by these results, because if you look at it from the perspective of an insurance company, I think there is a big question mark whether we can go ahead to do that.

My question for you is in terms of those patients you operated upon in cardiogenic shock, your survival rate is only 10%. If you would like to stimulate us to continue with such support or assist treatments, shouldn’t we exclude those patients in cardiogenic shock as a candidate, because otherwise it is my opinion we will have a problem to justify it.

Dr Jurmann: Regarding these results, the numbers are still a little too small to do some meaningful detailed statistical analysis, like a multivariate analysis of associated risk factors. Related to your comment about the patients in severe cardiogenic shock, one clear message from these data is, however, that VAD implantation in older patients in severe cardiogenic shock might not be recommended in general. Such cases will have to be evaluated on an individual basis. On the other hand, I will have to remind you, that, by comparison, the expected survival of such patients is zero.
So, the results from this series might be ambivalent: there is a higher than anticipated early mortality which was the consequence of our patient selection, advanced age and multimorbidity, as demonstrated, and there were late complications with one of the VAD types chosen. But there are also rather stable survival rates in patients beyond 260 days of VAD support, clearly indicating that permanent VAD support is an option for such patients.

Dr A. Franco-Cereceda (Stockholm, Sweden): Have you seen any recovery of cardiac function in those patients leading to a possibility of explanting the devices, and if so, do you have any opinion on pulsatile or continuous flow pumps and how long they should be used, and particularly on what kind of dilated cardiomyopathies we should use them?

Dr Jurmann: I think in this age group, above 60 years, it is very unlikely to expect myocardial recovery from chronic heart failure, as most of those are so-called ischemic cardiomyopathies, which means end-stage coronary artery disease patients. Whenever we saw recovery happen, it was mostly in dilated cardiomyopathy, and it was in younger patients certainly. None of these patients really improved his cardiac function on the device. So if his ejection fraction was 10, it just remained 10. It is also not what we expect to happen in these patients basically.

Most of the recovery experience we had so far, though, was accumulated with pulsatile pumps, although it does not mean that it cannot occur with axial flow pumps, since we have one patient right now who seems to recover his heart on an axial flow pump and might be explanted next week.

Dr T. Wahlers (Jena, Germany): With regard to your indications applied one has to know, that in the Clinical Utility Baseline trial for the Lion Heart it is not allowed to include patients under emergency conditions. Don’t we have to define a patient group as a surgical society in which we should not proceed with these types of implantations, in patients for example, being in the emergency state?

And as a second comment, I was a little bit surprised with regard to the REMATCH data that you haven’t implanted the TCI HeartMate device, because, in my opinion, also in the long term, perhaps the results might be a little better as compared to the results presented by your group.

Dr Jurmann: About cardiogenic shock, we had this as a comment from Dr Mohr, it is something which might be excluded from such trials if the patients are above 60 or 65 years. However, we didn’t know this two years ago. We know this by now.

With regard to the choice of devices, all the devices, no matter if it is Novacor, if it is TCI, if it is a DeBakey VAD or something else, there has been some experience already, they have been implanted in a large number of cases, and many of those were for medium term to so-called long term support. The overall results of this series have been influenced, in part, by late device-related complications, as detailed previously. We would have had hoped that the DeBakey VAD would have improved our results, and we are unfortunate to tell that this has not happened.