Pulsatile Flow in Patients With a Novel Nonpulsatile Implantable Ventricular Assist Device

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Background—Ventricular assist devices (VADs) are an accepted therapy for patients with end-stage heart failure. The implantable devices that are available produce a pulsatile flow and are very large. In 6 patients, beginning in November 1998, we started to use the continuous-flow implantable DeBakey VAD device, which weighs 93 g. To detect the flow in peripheral vessels, we measured transcranial Doppler signals in patients after implantation.

Methods and Results—Transcranial Doppler studies were performed with the MULTI-DOP X4 device with two 2-MHz probes (for the middle cranial arteries) in 4 patients for up to 12 weeks twice weekly after implantation. The blood velocity was measured, and the pulsation index (PI) calculated. The measured pump flow and rotations per minute were registered. The preoperative echocardiographic assessment values were compared with those acquired 6 weeks after implantation. The PI increased continually in all patients after VAD implantation, left ventricular (LV) ejection fraction did not improve, but right ventricular (RV) ejection fraction after implantation improved compared with preoperative values. The LV end-diastolic diameter after implantation decreased between 11% and 46% intraindividually. There was no correlation between PI and blood pressure or, except in 1 patient, between PI and blood flow through the VAD.

Conclusions—The DeBakey VAD unloads the LV, which leads to a decrease in LV end-diastolic LV diameter and to the restoration of RV function. The unloaded LV and partially recovered RV provide a nearly physiological pulsatile flow despite the continuous flow of the VAD. Pulsatility is independent of peripheral vascular resistance. The first clinical experience with the DeBakey VAD was positive and has resulted in its continued use. (Circulation. 2000;102[suppl III]:III-183-III-187.)

Key Words: ventricular assist device • echocardiography • blood flow • heart failure

Pulsatile mechanical ventricular assist devices (VADs) have become an accepted therapy for the support of patients with severe heart failure as a ‘bridge to transplantation’ or in a small part as an aid to recovery.1–3 Patients are usually treated with pulsatile VADs. These devices are very large and cannot be implanted into small adults, women, and children. The continuous-flow VADs are much smaller, they do not have any artificial valves, and the theoretically thrombogenic foreign surface is smaller. However, the nonpulsatile flow is not physiological. The debate regarding the effect of nonpulsatile flow on organ function and the hormonal situation is extensive and remains controversial.4–7

In November 1998, for the first time, we used the novel implantable continuous-flow DeBakey VAD (Micromed Inc) with blood flow that is generated by a turbine, which produces 7500 to 12 500 rpm. The pump is small and weighs 93 g.8

In view of the effect of the long-term continuous flow created by the turbine of the VAD on the flow in the peripheral vessels, especially in cerebral vessels, we performed transcranial Doppler (TCD) measurements of flow parameters in the middle cerebral arteries (MCAs) in 4 patients after the implantation of the DeBakey VAD.

Methods

Since November 1998, the new DeBakey VAD was implanted in 6 patients with end-stage cardiac failure class IV, which could not be stabilized with medical means. The patients’ diagnosis, clinical status before VAD implantation, demographic data, and clinical outcomes are given in Table 1. All patients were extubated after surgery. In 4 patients, the study of TCD measurements was performed. The first 2 patients did not undergo assessment due to the initial unavailability of the TCD equipment.

TCD Imaging

TCD studies were performed with the MULTI-DOP X4 device (DWL Elektronische Systeme GmbH) with two 2-MHz probes (left and right) with a diameter of 1.7 cm. They were fixed around the patient’s head with a special elastic tape to minimize movement artifacts. The device permitted bilateral MCA monitoring. The
TABLE 2. Results of TCD Measurements, Echocardiographic Data Before Surgery and 6 Weeks After Implantation, and Performance of the DeBakey VAD

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Age, y</th>
<th>Weight, kg</th>
<th>Diagnosis</th>
<th>Clinical Status Before VAD Implantation</th>
<th>CI Before VAD Implantation, L·min⁻¹·m⁻²</th>
<th>Duration of Support, d</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>55</td>
<td>90</td>
<td>CHD</td>
<td>Inotropic medication, IABP, on ventilator</td>
<td>1.8</td>
<td>47</td>
<td>Died of sepsis</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>37</td>
<td>77</td>
<td>CMP</td>
<td>Inotropic medication</td>
<td>1.7</td>
<td>9</td>
<td>Pump stoppage; switch to pulsatile LVAD</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>37</td>
<td>92</td>
<td>CMP</td>
<td>Inotropic medication</td>
<td>1.9</td>
<td>87</td>
<td>HTx</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>62</td>
<td>73</td>
<td>CHD</td>
<td>Inotropic medication</td>
<td>1.9</td>
<td>53</td>
<td>Pump stoppage (connector problem); switch to pulsatile LVAD</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>46</td>
<td>60</td>
<td>CHD</td>
<td>Inotropic medication, IABP, on ventilator</td>
<td>1.8</td>
<td>109</td>
<td>Died of sepsis</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>33</td>
<td>71</td>
<td>CMP</td>
<td>Inotropic medication</td>
<td>1.8</td>
<td>91</td>
<td>HTx</td>
</tr>
</tbody>
</table>

CHD indicates coronary heart disease; CI, cardiac index; CMP, cardiomyopathy; HTx, heart transplantation; and IABP, intra-aortic balloon pump.

Measurements were performed with the patients in the half-sitting position and at regular intervals (ie, twice a week).

Echocardiographically measured (transthoracic approach) left and right ventricular ejection fraction (LVEF and RVEF, respectively) and LV end-diastolic diameter (LVIDd) were compared before surgery and 6 weeks after implantation.

Both MCAs were isolated transtemporally. We used a low gain for spectra display and a low acoustic intensity (33 mW/cm²). The 5-mm pulsed-wave sample volume was placed on the first segment of the vessel and ranged in depth from 47 to 63 mm (deeper volume). A 64-point fast Fourier transform with length of 2 ms and an overlap of 60% was set. These parameters were kept constant throughout the study. A total of 60 measurements were performed in 4 mobilized patients for up to 12 weeks after device implantation. In each session, blood velocity (V) was measured and the Gosling pulsation index (PI) \((V_{\text{max}}-V_{\text{min}})/V_{\text{max}}\) was calculated for both MCAs.

Anticoagulation

Anticoagulation was performed early after surgery with a continuous intravenous infusion of heparin to maintain an activated clotting time of 140 to 160 seconds. After stabilization of the patient’s condition and the removal of all of the drains and central catheters, phenprocoumon was administered with the target of the international normalized ratio, which ranged between 2.5 and 3.5. No platelet antiaggregation drugs were administered.

Performance of the DeBakey VAD

During this present study, the revolutions of the impeller were documented. The VAD data are given in Table 2.

Statistical Analysis

Statistical analyses of the data were performed with SPSS 9.0 for Windows. The normally distributed data are reported as mean±SD values, and the abnormally distributed data are reported as median and range values. Significant differences were confirmed with a Mann-Whitney U test (independent data) and Wilcoxon’s test (related data). Pearson’s test was applied to evaluate correlation. A value of \(P<0.05\) was considered statistically significant.

**Results**

The PI in both MCAs continually increased in all patients after VAD implantation (median 0.21 versus 0.37; \(P=0.022\)). The course of mean PI after implantation is shown in Figure 1. No correlation occurred between PI and mean arterial blood pressure (BP) in any patient. Apart from patient 4, no correlation occurred between PI and blood flow through the VAD. These parameters are shown in Table 2. The median LVEF did not improve 6 weeks after VAD implantation (0.17 [range 0.15 to 0.2] versus 0.2 [range 0.35 to 0.45]; \(P=0.25\)). The median RVEF measured 6 weeks after implantation improved compared with the median preoperative RVEF (0.25 [range 0.24 to 0.4] versus 0.4 [range 0.35 to 0.45]; \(P=0.25\)), but the difference did not reach a significant level due to the small number of patients and the heterogeneity of sensor on the outflow graft, and the power consumption were documented. The VAD data are given in Table 2.

**TABLE 2. Results of TCD Measurements, Echocardiographic Data Before Surgery and 6 Weeks After Implantation, and Performance of the DeBakey VAD During the Study Period**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>LVEF Before VAD, mm</th>
<th>RVEF Before VAD, mm</th>
<th>LVIDd Before VAD, mm</th>
<th>LVIDd With VAD, mm</th>
<th>Mean PI Early/Late After Surgery, Vmean/BP, r</th>
<th>Correlation Vmean/Flow, r</th>
<th>Correlation PI/Flow, r</th>
<th>Correlation PI/BP, r</th>
<th>Mean Revolutions, RPM</th>
<th>Mean Pump Flow, W</th>
<th>Mean Power Consumption, W</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.15</td>
<td>0.35</td>
<td>82</td>
<td>0.17</td>
<td>0.17</td>
<td>65</td>
<td>...</td>
<td>...</td>
<td>9.8±0.2</td>
<td>4.9±0.5</td>
<td>10.5±1.2</td>
</tr>
<tr>
<td>2</td>
<td>0.15</td>
<td>0.2</td>
<td>69</td>
<td>0.35</td>
<td>0.35</td>
<td>65</td>
<td>...</td>
<td>...</td>
<td>9.5±0.3</td>
<td>4.5±0.5</td>
<td>10.6±1.3</td>
</tr>
<tr>
<td>3</td>
<td>0.18</td>
<td>0.4</td>
<td>78</td>
<td>0.2</td>
<td>0.2</td>
<td>64</td>
<td>0.23/0.37</td>
<td>0.54/0.53</td>
<td>0.51/0.06</td>
<td>-0.26</td>
<td>-0.15</td>
</tr>
<tr>
<td>4</td>
<td>0.18</td>
<td>0.25</td>
<td>66</td>
<td>0.2</td>
<td>0.2</td>
<td>36</td>
<td>0.19/0.37</td>
<td>0.66/0.33*</td>
<td>0.55/0.12</td>
<td>0.93†</td>
<td>-0.05</td>
</tr>
<tr>
<td>5</td>
<td>0.15</td>
<td>0.2</td>
<td>61</td>
<td>0.15</td>
<td>0.15</td>
<td>36</td>
<td>0.13/0.46</td>
<td>0.66/0.62</td>
<td>0.49/0.44*</td>
<td>-0.51</td>
<td>0.34</td>
</tr>
<tr>
<td>6</td>
<td>0.2</td>
<td>0.25</td>
<td>65</td>
<td>0.2</td>
<td>0.45</td>
<td>58</td>
<td>0.24/0.37</td>
<td>0.51/0.46</td>
<td>0.03/0.05</td>
<td>0.13</td>
<td>0.15</td>
</tr>
</tbody>
</table>

No TCD measurements were performed on patients 1 and 2. No postoperative echocardiographic data were available for patient 2 due to short support time (9 days).

\(^{*} P<0.05, \text{†} P<0.01\)
preoperative values. The median preoperative LVIDd was 67.5 mm (range 61 to 82 mm), and it decreased significantly at 6 weeks after implantation ($P = 0.04$) to a median of 58 mm (range 36 to 65 mm). The intraindividual decrease in LVIDd was between 11% and 45%. Echocardiography confirmed the correct position of the inflow cannula in all patients.

The average $V_{\text{mean}}$ value was 0.53±0.11 m/s in patient 3 (range 0.40 to 0.82 m/s), 0.66±0.16 m/s in patient 4 for the left MCA (range 0.46 to 0.09 m/s), and 0.33±0.11 m/s in patient 4 for the right MCA (range 0.22 to 0.6 m/s; $P=0.00002$). In patient 5, the average $V_{\text{mean}}$ value was similar for both sides (0.65±0.15 m/s, range 0.34 to 0.85 m/s). This was also true for patient 6 (0.49±0.09 m/s, range 0.38 to 0.69 m/s). In 3 patients, the intrapatient variability of $V_{\text{mean}}$, which occurred more frequently in the left MCA, correlated moderately with BP and was more marked on the left side. In patient 6, there was no correlation between $V_{\text{mean}}$ and mean BP (Table 2). The $V_{\text{mean}}$ value decreased slightly in all patients after 6 weeks of support (median 0.71 versus 0.48 m/s, $P=0.07$).

**Discussion**

Patients with severe heart failure can be kept alive with a continuous-flow VAD. During long-term support, the continuous-flow DeBakey VAD generates, after a short period of nonpulsatility, a nearly physiological pulsatility with regard to pulsatile preload of the pump, produced through contraction of the unloaded LV and partially recovered RV.

The use of a pulsatile VAD for end-stage cardiac failure has become an established therapy as a bridge to transplantation or occasionally as temporary support. Several different types of implantable VAD are now in use. A frequent problem with these large implantable devices is the difficulty of implantation into small adults, women, and children. Moreover, these devices, except for totally artificial hearts, cannot be used in a biventricular mode. Extracorporeal devices can be used as an alternative, even in newborns, but discharge from hospital with biventricular VADs is difficult. The continuous-flow DeBakey VAD is smaller and does not have any artificial valves, and the theoretically thrombogenic foreign surface area is smaller (Figure 2), but the continuous, nonpulsatile flow remains nonphysiological.

The debate with regard to the effect of short-term nonpulsatile flow on organ function is extensive and has existed since cardiopulmonary bypass became routinely used. However, the pathophysiology of long-term nonpulsatile flow is poorly understood. The benefit of pulsatile perfusion on peripheral organs is probably mediated by its effect on systemic vascular resistance and on the microcirculation as a result of less endothelial damage and normalized NO release. The pulsatility improves splanchnic perfusion and plays a fundamental role in the movement of lymph into and out of the intestine, the prevention of edema, and the maintenance of capillary patency through the prevention of sludging. The brain microcirculation and cerebrospinal fluid movement are reported to be improved with pulsatility. Pulsation improves aerobic tissue metabolism. The influence of nonpulsatile flow on the renin-angiotensin system and catecholamine release remains controversial.

The first positive clinical experience with the DeBakey VAD led us to investigate the influence of long-term nonpulsatile flow on peripheral perfusion. The typical TCD signal immediately after implantation is shown in Figure 3. We have seen that the flow pulsatility in the peripheral vessels increased continually after VAD implantation in all patients (Figure 4), whereas simultaneous echocardiography during some TCD measurements demonstrated that the aortic valve did not open. The question then arose as to what could be the origin of this pulsation. We believe that the contractions of an
unloaded LV and the recovery of RV function account for this phenomenon. The calculated LVEF did not improve, but the aortic valve did not open during measurements. However, the LV was satisfactorily unloaded, and therefore, the LVEF could not be correctly calculated. The unloading of LV could be detected through a significant decrease in LVIDd after implantation (Table 2). This may have led to a change in the geometry of the RV, which plays an important role in the improvement of RV function.16–18 Afterload reduction is the most likely mechanism by which the RV ejection fraction improves after LV assist device (LVAD) implantation.19 The importance of good RV function in patients with an LVAD has been previously emphasized.18,20,21 We prevented RV dysfunction in the patients after implantation of the DeBakey VAD through the routine use of nitric oxide inhalation immediately after implantation and the maintenance of a moderate cardiac index to reduce preload of the RV.20 The mean RVEF rose after VAD implantation from 0.25 to 0.4. However, in 2 patients with good RVEF before surgery, this did not significantly change after implantation. Similar improvements in RV function during support with the pulsatile Novacor LVAD have been reported.19,21–23 This constellation may explain the pulsatile flow in the peripheral vessels despite the nearly constant revolutions of the turbine of the VAD. The well-recovered RV provides some pulsatile flow through the lung. After unloading of the LV, contractions of the unloaded LV provide pressure changes at the pump inlet and accelerate and modulate the flow through the pump, which augments these pressure changes at a higher level, and thus the flow in the outflow graft, aorta, and its branches becomes pulsatile. The flow sensor on the outflow graft and invasive BP monitoring with a bedside control unit showed pulsatile flow through the outflow graft and in the peripheral vessels (Figure 5).

The pulsatility of blood flow increased continually in all patients due to the improvement in LV and RV function and was seen in the PI as between 0.3 and 0.5 after weeks of support, and in patients 5 and 6 values of up to 0.6 to 0.7 sometimes occurred (Figure 1). A nearly normal relationship was seen between systolic and diastolic blood flow acceleration in patient 5 as early as 4 weeks after the commencement of support (Figure 4). The pulsatility was not dependent on the pump flow or the BP. However, in the patient with low pump flow, due to deformation of the outflow graft (patient 4), a high correlation occurred between PI and pump flow.

The continuous increase in pulsatility during support reduced sympathetic nerve activity24; this effect was seen in all patients on the basis of the decrease in $V_{\text{mean}}$ and only moderate correlation between $V_{\text{mean}}$ and BP with constant pump flow in 3 patients during support. The correlation was more marked on the left MCA. In 1 patient, no correlation occurred. The moderate correlation between $V_{\text{mean}}$ and BP (Table 2) showed a preserved autoregulation of cerebral blood flow. Only patient 5, in whom this correlation was significant, experienced instances of orthostatic collapse.

The goal of the use of the DeBakey VAD is to maintain the pump flow at a level equivalent to a cardiac index of $\geq 2 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. Lower pump flow during routine support would not provide adequate hemodynamic support if the cardiac function is deteriorated but would be used in a weaning protocol.

**Conclusions**

Patients with severe heart failure can be kept alive with a continuous-flow VAD. The use of the DeBakey VAD results
in normal organ function and provides unloading of the LV, which can lead to partially restored myocardial function. Despite of nonpulsatile flow produced with the turbine of the DeBakey VAD, the pressure changes due to contractions of the unloaded LV and the partially recovered RV provide a nearly physiological pulsatile flow. The pulsatility was not dependent on pump flow or peripheral resistance. The first clinical experience with the DeBakey VAD was positive and has lead to its continued use.

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References
5. Shevde K, DeBois W. Pro: pulsatile flow is preferable to nonpulsatile flow and provides unloading of the LV, and the partially recovered RV provide a nearly physiological pulsatile flow. The pulsatility was not dependent on pump flow or peripheral resistance.

4. Finlayson D. Con: nonpulsatile flow is preferable to pulsatile flow during cardiopulmonary bypass.
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