Treatment of Thrombus Formation Associated With the MicroMed DeBakey VAD Using Recombinant Tissue Plasminogen Activator

Markus Rothenburger, MD; Markus J. Wilhelm, MD; Dieter Hammel, MD; Christoph Schmidt, MD; Tonny D.T. Tjan, MD; Dirk Böcker, MD; Hans H. Scheld, MD; Christof Schmid, MD

Background—The latest generation of left ventricular assist devices consists of nonpulsatile impeller pumps. In these small pumps, thrombus formation inside the device does not lead to thromboembolic end-organ dysfunction but may dramatically impair pump flow. We report on our experience with thrombus-related pump dysfunctions of the MicroMed DeBakey left ventricular assist device and its treatment.

Methods—Eight of 22 patients with a MicroMed DeBakey VAD presented with a critically reduced pump flow. In 7 cases, an increased power demand indicative of progressive thrombus formation associated with the device was evident, whereas 1 case presented with thrombus formation within the inflow conduit associated with a very low power demand. Brief spontaneously resolving pump stops had been noted in 6 patients. All 8 patients were treated with 100 mg of recombinant tissue plasminogen activator (rt-PA), administered via an IV line.

Results—Rt-PA lysis led to an increase of pump flow along with a reduction of power demand within a short time in all patients. No severe bleeding complications occurred. However, 4 patients experienced transient epistaxis. All patients could be discharged from intensive care immediately after discontinuation of thrombolytic therapy.

Conclusion—Rt-PA lysis is a very effective tool for thrombus-related pump dysfunction in patients with impeller pumps, which renders emergency surgical exchange unnecessary in most cases. (Circulation. 2002;106[suppl I]:I-189-I-192.)

Key Words: MicroMed DeBakey LVAD ■ thrombus formation ■ thrombolytic therapy ■ recombinant tissue plasminogen activator (rt-PA)

Left ventricular assist devices (LVAD) are commonly used as a bridge to heart transplantation in end-stage heart failure patients. Most of the LVADs are based on a pulsatile blood flow, such as the Novacor N100 (Baxter, Oakland, Calif) or the HeartMate system (Thoratec, Pleasanton, Calif). It has been reported that up to 47% of all patients with a pulsatile LVAD develop thromboembolic complications during support. The MicroMed DeBakey VAD (MicroMed Technology, Houston, Tex) has been introduced recently and generates continuous blood flow by using an impeller pump. In these patients, the thromboembolic hazard seems to be much lower, but thrombus formation inside the left ventricle may lead to malfunction of the device, causing a high risk of fatal outcome. In such a situation, restoring adequate flow within a very short period is necessary. One possibility is surgical device exchange, but this is associated with all the problems of an urgent redo procedure. The aim of our study was to investigate thrombolysis as an alternative treatment strategy.

Methods

Patients

Twenty-two patients, 20 men and 2 women, were enrolled in the study. The age ranged from 17 to 63 years, with a mean of 43.7±14.3 years. In 8 patients, thrombus formation developed during long-term mechanical support with the DeBakey VAD.

Device

The MicroMed DeBakey LVAD achieves axial blood flow by a valveless rotary blood pump (7.500 to 12.500 rpm) with inflow from the left ventricular apex and an outflow graft into the ascending aorta.

Anticoagulation Management

In all patients, the same anticoagulation protocol was applied, mainly based on heparin. Before implantation, a partial thromboplastin time of 40 to 60 seconds was maintained. During cardiopulmonary bypass, full heparinization was achieved routinely. Postoperatively, intravenous heparin administration was continued, the goal being a partial thromboplastin time of 60 to 100 seconds. After cessation of drainage losses and hemodynamic stabilization, all patients were switched to oral anticoagulation with an international normalized ratio of 2.0 to 3.0.
ratio (INR) between 2.5 and 3.5, and aspirin (300 mg) and dipyramidole (75 mg) were added.

Device Control
Device function was supervised by an external controller module with audible and visible alarm signals and a laptop-based Clinical Data Acquisition System. As recently described, this system stores pump-operating data and displays pump and physiologic information like flow rate (L/min), power demand (watts), pump speed (rpm), and current (amps).5

Diagnosis of Device-Related Thrombus Formation
Diagnosis of thrombus formation was mainly established by indirect evidence. In our early experience with the MicroMed DeBakey VAD, 2 patients underwent emergency device exchange, not thrombolytic therapy, because of markedly reduced pump flow and increased power demand. Recurrent pump stops had occurred before surgical treatment. The examination of the explanted devices demonstrated thrombotic material inside the MicroMed DeBakey VAD (Figures 1, 2). Because of this experience, diagnosis of thrombus formation inside or dislodgement into the device was made from characteristic changes of flow rate and power demand of the device; ie, decrease of flow rate and increase of power demand markedly differing from the patient’s baseline were considered indicative of thrombus formation. Transesophageal echocardiography always failed to visualize a thrombus adhering to the inflow conduit. An angiography was considered too dangerous in an acute low output situation. In 1 patient with an unusual low power demand and low flow, we suspected that a major thrombus formation within the inflow conduit was tremendously hindering pump inflow.

Treatment With rt-PA
Thrombolytic treatment was standardized with an IV infusion of 100 mg recombinant tissue plasminogen activator (rt-PA). Initially, 50 mg of rt-PA was given as a bolus, followed by another 50 mg administered over an interval of 1 to 2 hours. Since partial thromboplastin time (PTT) frequently increases during rt-PA lysis, the IV heparin dose was lowered and coagulation parameters monitored hourly. Following rt-PA lysis, PTT was augmented from 60 seconds to 100 seconds, and antiplatelet therapy was intensified.

Results
Device-Related Complications
Eight of the 22 patients with a MicroMed DeBakey VAD developed 10 episodes suspicious of thrombus formation

### Table 1. Patient Characteristics and Clinical Data of the Patients With Thrombus Formation Associated With the MicroMed DeBakey VAD

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex (m/f)</th>
<th>Age (y)</th>
<th>NYHA Class</th>
<th>LV-EF (%)</th>
<th>Underlying Disease</th>
<th>Device Exchange (d)</th>
<th>Device Support at Lysis (d)</th>
<th>Transplantation Performed on Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>m</td>
<td>43</td>
<td>IV</td>
<td>21</td>
<td>ICM</td>
<td>78</td>
<td>156 (78 d)*</td>
<td>167</td>
</tr>
<tr>
<td>2</td>
<td>m</td>
<td>18</td>
<td>IV</td>
<td>20</td>
<td>CHF</td>
<td>78</td>
<td>194/215 (116/137 d)*†</td>
<td>280</td>
</tr>
<tr>
<td>3</td>
<td>m</td>
<td>28</td>
<td>IV</td>
<td>22</td>
<td>CHF/ASD I</td>
<td>290</td>
<td>430 (140 d)*</td>
<td>437</td>
</tr>
<tr>
<td>4</td>
<td>m</td>
<td>42</td>
<td>IV</td>
<td>25</td>
<td>ICM</td>
<td>...</td>
<td>116</td>
<td>Dead on VAD support (day 258)</td>
</tr>
<tr>
<td>5</td>
<td>m</td>
<td>47</td>
<td>IV</td>
<td>24</td>
<td>ICM</td>
<td>...</td>
<td>58</td>
<td>107</td>
</tr>
<tr>
<td>6</td>
<td>m</td>
<td>55</td>
<td>IV</td>
<td>23</td>
<td>ICM</td>
<td>...</td>
<td>37/43/65†</td>
<td>73</td>
</tr>
<tr>
<td>7</td>
<td>f</td>
<td>24</td>
<td>IV</td>
<td>21</td>
<td>CHF</td>
<td>...</td>
<td>53</td>
<td>Dead on VAD support (day 128)</td>
</tr>
<tr>
<td>8</td>
<td>m</td>
<td>48</td>
<td>IV</td>
<td>23</td>
<td>ICM</td>
<td>...</td>
<td>296</td>
<td>299</td>
</tr>
</tbody>
</table>

NYHA class indicates New York Heart Association heart failure classification; LV-EF, left ventricular ejection fraction; ICM, ischemic cardiomyopathy; CHF, congestive heart failure; and ASD I, atrial septal defect type I.

*All thrombolytic therapies of these patients were performed with the second pump after emergency device exchange. †Repeat thrombolytic therapy. (a: 78 days; b: 116/137 days; c: 140 days).

Figure 1. Thrombus formation in the inflow conduit of a MicroMed DeBakey VAD.

Figure 2. Thrombus formation around the impeller of an exchanged MicroMed DeBakey VAD.
inside the device and 1 episode of suspected involvement of the inflow conduit (Table 2). Six patients had a history of recurrent pump stops.

Effect of Thrombolytic Therapy With rt-PA
Table 2 depicts the effects of thrombolytic therapy on device function as well as the associated adverse effects. Immediately after termination of thrombolytic therapy, usually within 3 hours, the aspired increase of flow rate and decrease of power demand could be noted (Table 2). All patients survived thrombolytic therapy. No severe bleeding complications were observed, and there was no evidence of intracranial hemorrhage. No device exchange was necessary after thrombolytic therapy with rt-PA. However, 4 patients experienced epistaxis for 3 days, and 1 patient needed a nasal tamponade for 2 days.

Repeat Thrombolysis and Outcome
One patient underwent 2 and another patient 3 thrombolytic therapies with rt-PA during long-term mechanical support. In all instances, device malfunction resolved completely and without severe complications, similar to previous treatments. Six patients could be forwarded to successful heart transplantation. Two patients died during LVAD support because of multiorgan failure after 258 and 128 days on support (142 and 75 days after thrombolytic therapy, respectively).

Discussion
The underlying cause of thrombus formation despite effective anticoagulation is still unclear. At explantation, we always observed some thrombus formation inside the inflow conduit and sometimes also within the pump. There seems to be no relationship with heating or an association with the bearings. Because the company presumed a problem with the inner surface of the inflow conduit, the latter has been coated with heparin. With these heparin-coated devices we have not experienced that problem. It remains to be seen whether this modification really prevents thrombus formation. Nonetheless, a thrombus inside the left ventricle may dislodge into the pump and lead to a pump dysfunction. A suboptimal implantation technique as a potential cause for increased thrombus formation reflecting a learning-curve effect can be excluded, since the surgical technique is more or less identical to the one for the first-generation devices such as the Novacor. After more than 6 months of LVAD support, cerebral embolization was evident in 2 patients and was unrelated to thrombolysis. Liver or spleen infarction never occurred. Even if it were proven, we think that a thrombus drawn into the pump is split into minuscule pieces, unless a pump stop occurs, which may explain the low rate of thromboembolism. It may well be that silent thromboembolism occurs, but there is no clinical evidence.

Thrombolytic therapy using rt-PA is well known for several indications like stroke, pulmonary embolism, left or right ventricular thrombi, or acute myocardial infarction. The only case in the literature about lysis in a patient with a left ventricular assist device has been reported from Kasirajan et al. They performed an intraarterial urokinase lysis after a cerebral thromboembolic complication in a patient with a Novacor LVAD. This case demonstrated for the first time the possibility of local lysis in patients with ongoing LVAD support.

Table 2. Effect of rt-PA Lysis on Device Function and Complications

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21.1</td>
<td>1.2</td>
<td>9.0</td>
<td>4.2</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>20.4</td>
<td>2.3</td>
<td>6.6</td>
<td>4.1</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>17.8</td>
<td>1.5</td>
<td>8</td>
<td>3.2</td>
<td>Yes</td>
<td>Epistaxis, minor bleeding</td>
</tr>
<tr>
<td>3</td>
<td>16.6</td>
<td>2.1</td>
<td>8.7</td>
<td>3.5</td>
<td>No</td>
<td>Epistaxis, skin bleeding</td>
</tr>
<tr>
<td>4</td>
<td>13.5</td>
<td>2.3</td>
<td>8.4</td>
<td>5.7</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>6.9</td>
<td>1.9</td>
<td>10.2</td>
<td>5.4</td>
<td>No</td>
<td>Epistaxis</td>
</tr>
<tr>
<td>6</td>
<td>11.3</td>
<td>0.6</td>
<td>9.9</td>
<td>5.4</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>12.5</td>
<td>1.5</td>
<td>8.9</td>
<td>5.1</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>12.7</td>
<td>1.6</td>
<td>8.6</td>
<td>5.2</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>17.9</td>
<td>0.4</td>
<td>10.8</td>
<td>3.4</td>
<td>No</td>
<td>Epistaxis, skin bleeding</td>
</tr>
<tr>
<td>8</td>
<td>23.1</td>
<td>1.0</td>
<td>9.2</td>
<td>3.1</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
treated a patient who had a pump stop by using ligation of the outflow graft to prevent deleterious regurgitant flow. Because of mild recovery of ventricular pump function, the patient survived the waiting period to heart transplantation, which was performed 2 days later. Because most patients on mechanical support are unable to survive ligation of the outflow graft, this procedure cannot be considered an appropriate alternative to thrombolytic therapy.

In conclusion, thrombolytic therapy with rt-PA is an effective and easily applicable treatment for thrombus formation inside the MicroMed DeBakey VAD and has an acceptable risk for the patients.

References
Treatment of Thrombus Formation Associated With the MicroMed DeBakey VAD Using Recombinant Tissue Plasminogen Activator
Markus Rothenburger, Markus J. Wilhelm, Dieter Hammel, Christoph Schmidt, Tonny D. T. Tjan, Dirk Böcker, Hans H. Scheld and Christof Schmid

Circulation. 2002;106:I-189-I-192
doi: 10.1161/01.cir.0000032913.33237.f5
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/106/12_suppl_1/I-189

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/