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

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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).1,2 It has been reported that up to 47% of all patients with a pulsatile LVAD develop thromboembolic complications during support.1,3,4 The MicroMed DeBakey VAD (MicroMed Technology, Houston, Tex) has been introduced recently and generates continuous blood flow by using an impeller pump.5,6 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. Demographic data and patient characteristics are described in table 1.

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.5

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 2.5.
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

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<th>LV-EF (%)</th>
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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).
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. Immedi-
ately 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 hemor-
rhage. No device exchange was necessary after thrombolytic
therapy with rt-PA. However, 4 patients experienced epi-
staxis 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 transplan-
tation. 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. Nonethe-
less, a thrombus inside the left ventricle may dislodge into the
pump and lead to a pump dysfunction. A suboptimal implan-
tation 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.7
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.8–11
The only case in the literature about lysis in a patient with a
left ventricular assist device has been reported from Kasirajan
et al.12 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.

Noon et al reported increased power rates and reduced
pump flows following cardiac catheterization after placement
of a DeBakey VAD using highly viscous radiopaque contrast
agents.5 They proposed that thrombolytic therapy be per-
formed if a thrombus inside the pump is present but never
actually performed thrombolysis.5

We performed thrombolytic therapy with 100 mg of rt-PA
in our patients with suspected thrombus formation or throm-
bus dislodgement into the MicroMed DeBakey VAD. All
patients recovered from device malfunction within 3 hours
after lysis and without severe bleeding complications. We
were well aware of the risk of intracranial bleeding; however,
especially surgical device exchange was considered a greater
hazard.

Wieselthaler et al reported their single center experience on
thrombus formation in 1 of 6 patients.6 They surgically

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