Diagnosis and Treatment Algorithm for Blood Flow Obstructions in Patients With Left Ventricular Assist Device

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ABSTRACT

BACKGROUND Thrombosis is an uncommon, but severe complication of left ventricular assist devices (LVADs).

OBJECTIVES This study analyzed experience with obstruction of blood flow through the LVAD with the purpose of developing optimal diagnosis and treatment of LVAD-related thrombosis.

METHODS Between October 2009 and July 2015, a total of 652 LVAD were implanted in 557 patients. Blood flow abnormalities in patients with LVAD (n = 524) were identified and classified as “high-power” and “low-flow” events.

RESULTS Three types of late blood flow obstructions were identified: 1) pre-pump via thrombus obstructing the inflow cannula (26 events; 0.037 events per patient-year); 2) intra-pump (70 events; 0.1 events per patient-year); and 3) post-pump via thrombosis of the outflow graft or stenosis of the anastomosis to the aorta (4 events; 0.006 events per patient-year). Pre-pump obstruction was treated by washout maneuver in 9 cases (success rate, 100%), thrombolysis in 9 patients (success rate, 56%), and pump exchange in 9 cases (success rate, 100%); 1 patient died without treatment and 2 were weaned from LVAD. Intra-pump obstruction was treated by thrombolysis (n = 9; success rate, 33%), pump exchange (n = 53; success rate, 94%), and removal due to myocardial recovery (n = 3; success rate, 100%); 7 patients died without treatment and parameters spontaneously normalized in 2 cases. Post-pump obstruction was treated in 2 patients by stenting (success rate, 100%), and was left untreated in 2 cases.

CONCLUSIONS We identified 3 types of LVAD-related blood flow obstruction, and developed an algorithm for optimal diagnosis and treatment. (J Am Coll Cardiol 2016;67:2758-68) © 2016 by the American College of Cardiology Foundation.

The HeartWare HVAD (HeartWare International, Framingham, Massachusetts) is an implantable centrifugal pump that is designed as a left ventricular assist device (LVAD). Pump thrombosis is a major and severe complication, with a reported incidence of 0.04 to 0.09 events per patient-year (EPPY) (1-4). Most reports focus on pump thrombosis itself, in which the thrombus is trapped between the impeller and the housing. However, blood flow may be disturbed at different levels of the LVAD system via obstruction of the inflow cannula caused by large wedge thrombus, by thrombosis within the device, and by kinking or stenosis of the outflow graft. Different types of blood flow...
obstruction demonstrate different clinical and technical signs and require specific treatments. The aim of our study was to analyze our experience in the recognition and therapy of various patterns of blood flow abnormalities in patients supported with the HeartWare HVAD and to develop an algorithm for their diagnosis and treatment.

METHODS

We retrospectively analyzed data collected from all patients implanted with a HeartWare HVAD as an LVAD at the Deutsches Herzzentrum Berlin between October 2009 and July 2015. Under German law, retrospective data analysis of an institution’s own data does not require ethics committee approval.

Events involving blood flow abnormalities were identified using our institutional database and clinical and technical files and classified as high-power and low-flow events, according to the alarms generated from the pump.

“High power” was defined as a power increase that generated a high-power alarm (alarm threshold commonly set at 1 W above mean power consumption) or a power trend increase of more than 0.5 W above the 30-day peak values. “Low flow” was defined as a decrease of >2 l/min below patient-specific average value, with a distinction made between persistent immediate decrease and continuous slow decrease.

The alarms triggered by these derangements are “high-power alarm” and “low-flow alarm” and are easily detected by the patients themselves. Low-flow events caused by hypovolemia (bleeding or dehydration), hypertension, and arrhythmia were excluded from the analysis. All alarm events were managed by the VAD coordinator.

Anticoagulation was performed as described previously (2), and there were no changes in the anticoagulation protocol over time. Briefly, in the postoperative period anticoagulation based on the activated partial thromboplastin time is targeted to an activated partial thromboplastin time of 45 to 50 s on day 1, of 50 to 60 on day 2, and of 60 to 70 on day 3. In the case of heparin-induced thrombocytopenia type II, argatroban is administered intravenously with the same activated partial thromboplastin time target. Aspirin is added 7 to 10 days after surgery if platelet count and function have returned to nearly normal values as monitored by platelet aggregation tests. Clopidogrel can be used in the case of aspirin intolerance or according to specific indications. In all patients, oral anticoagulation is started on approximately post-operative day 10 after oral feeding has begun, chest tube and central venous catheters have been removed, and no relevant pericardial effusion is present. The target international normalized ratio is set at 2.5 to 3.0. In outpatients, the anticoagulation monitoring and adjustment are based on daily use of the CoaguChek (Roche Diagnostic, Mannheim, Germany) device and laboratory tests performed during visits to the outpatient department.

For the definition of hemolysis we used a threshold of 20 mg/dl plasma-free hemoglobin, which is lower than reported previously (5) and is used by the Interagency Registry for Mechanically Assisted Circulatory Support (6). We measure hemoglobin, total bilirubin, plasma-free hemoglobin, lactate dehydrogenase, and haptoglobin routinely during every outpatient visit and advise the general practitioners who care for these patients to do so too.

Analysis of actual flow curves, log-files of technical data downloaded from the controller, and the acoustic spectra was performed in all patients before discharge home, during outpatient visits, and in every case of blood flow abnormalities, as described elsewhere (7). Lavare cycle is routinely enabled on first day after implantation in all patients; it does not affect the log-file interpretation because of the presence of a blanking algorithm in the log-file viewer. Acoustic signal analysis has been part of our routine practice in the past 3 years (7).

The algorithm (Figure 1) was finalized and approved as an institutional standard operating procedure in October 2015.

DETECTION OF BLOOD FLOW OBSTRUCTIONS. The HeartWare HVAD log-file analysis permits in-depth analysis of power and flow trends in real time to distinguish between different kinds of blood flow obstructions (Central Illustration). The major discriminator is the power consumption. The next discriminator is the pattern of power decrease (e.g., immediate or slow). Acoustic analysis (7) and hemolysis parameters (5,8-14) increase precision of the diagnosis. In-pump blood flow obstructions can be relatively easily identified by the increase of power consumption and hemolysis and by acoustic analysis; differentiation between pre-pump and post-pump flow obstruction (both indicated by low-flow alarms and low power consumption) is related to the pattern of flow decrease. In cases of pre-pump flow obstruction caused by wedge thrombus occluding the inflow cannula, the onset of low flow is acute and within hours (Figure 2). By contrast, low flow caused by thrombus in the outflow graft, kinking of the graft, or
The figure explains our strategy in managing LVAD pump thrombosis. In the first part, in pink, the steps for the detection of blood flow obstruction through the system are outlined. In the second part, in blue, the steps for treatment are presented. Arrows indicate positive or negative answers to single fact or the result of an action. CT = computed tomography; fHb = plasma-free hemoglobin; GI = gastrointestinal; INR = international normalized ratio; LDH = lactate dehydrogenase; LVAD = left ventricular assist device.
Pump flow could be disturbed at different levels of the left ventricular assist device system. **Numbers** indicate the site of thrombus apposition and identify the types of pump thrombosis. **Number 1**, pre-pump thrombosis. **Number 2**, intra-pump thrombosis. **Number 3**, post-pump thrombosis at the level of outflow graft and aortic anastomosis.
anastomotic stenosis develops slowly over days or weeks (Figure 3). This pattern of decrease of power consumption is the main discriminator in our algorithm.

The theoretical possibility that inflow cannula migration with gradually increased obstruction could cause a slow decrease of power consumption and mimic post-pump blood flow obstruction was considered, but never happened in our experience. Two mixed alterations were recognized: occlusive thrombus causing low flow progresses into the pump between the rotor and housing in which the friction increase causes elevation of power consumption; and primary pump thrombosis with outflow graft thrombotic involvement in which high-power consumption would decrease to nearly normal values. In both situations “normalization” of power consumption could be misleading, despite minimal real blood flow. In mixed alterations, the hemodynamic status, an unloaded and ejecting left ventricle, and hemolysis guide the diagnosis, and the log-file analysis would indicate the primary event.

**STATISTICAL ANALYSES.** Overall survival was estimated by Kaplan-Meier analysis. Data were censored at end of follow-up. Duration of support is reported as median (interquartile range [IQR]). Time zero for death after pump thrombosis was the date of pump thrombosis. Cox proportional hazards analysis with device thrombosis as a time-dependent covariate was used to calculate survival for patients without thrombosis. For patients with multiple device placements Kaplan-Meier curves start at the first device placement only. Patients’ baseline characteristics were compared by analysis of variance or Kruskal-Wallis test in the case of continuous variables or chi-square test in the case of categorical variables. Data were analyzed using R software, version 3.03 (R Foundation for Statistical Computing, Vienna, Austria).

**TREATMENT OF BLOOD FLOW OBSTRUCTION.** Treatment depended on the diagnosis of the type of blood flow obstruction based on clinical status, hemodynamic values, echocardiographic evaluation including “ramp test” (15), level of hemolysis, and end organ function.

The treatment was defined as successful when it led to restoration of normal blood flow from left ventricle to aorta as measured by normalization of power consumption and/or parameters of hemolysis and acoustic signals.

Thrombolysis as “soft lysis” was performed with tirofiban (Aggrastat, Merck & Co., West Point, Pennsylvania) as an initial dose of 1.6 μg/kg/min in 30 min and continuous infusion of 0.4 μg/kg/min (both reduced by approximately 50% in the case of severe renal impairment) for at least 48 h and maximum of 72 h. Hemolysis parameters were monitored twice daily, including lactate dehydrogenase, plasma-free hemoglobin, hemoglobin, haptoglobin, total bilirubin, and hemoglobinuria, as well as the acoustics of the pump. In addition to continuous infusion, a starting dose of 25 μg/kg as a bolus is provided if international normalized ratio at presentation is <3.
For occlusive thrombus of the inflow cannula, we recently developed a noninvasive technique to “wash out” the thrombus (16), a procedure that is performed with direct carotid artery protection to minimize the risk of cerebral thromboembolism. The washout maneuver involves stopping and restarting the pump, while in both carotid arteries filters are introduced to capture thrombus released from the pump, and to prevent it traveling to the brain during the procedure. We used the filter-based cerebral protection system Sentinel Claret (Claret Medical, Santa Rosa, California), with endovascular positioning through the right radial or brachial artery (16) performed in a hybrid operating room.

Surgical treatment included surgical pump exchange as previously reported (17,18). All explanted pumps were disassembled and visually inspected for thrombus formation. In the case of outflow graft thrombosis or stenosis of the anastomosis with the aorta, the graft was stented. The graft was visualized by angiography and the stenosis confirmed by measurement of a pressure gradient across the graft. Stenting is performed under angiographic monitoring (19–22).

RESULTS

Since 2009, a total of 652 HeartWare HVAD pumps HVADs have been implanted in 557 patients. Of these, 524 patients had left ventricular, 5 right ventricular, and 28 biventricular support. The present analysis is based on the 586 pumps implanted as LVADs in 524 patients. The median duration of support for a patient was 293 days (IQR: 41 to 742 days) and for each pump 262 days (IQR: 32 to 597 days). Overall survival was 81.3% at 30 days, and 61.9%, 50.1%, and 44.3% at 1, 2, and 3 years, respectively (Figure 4). Forty-three patients received heart transplantation and 12 were weaned from the device following myocardial recovery.

Survival after event for patients who experienced thrombosis of the device was 69.7% at 30 days, and

Kaplan-Meier curve of survival of the whole population for 1, 2, and 3 years is shown. Patients at risk and confidence bounds are indicated below the curve. Patients who were weaned or transplanted are also included. Survival of patients with multiple device placements starts at the time of first placement only.
TABLE 1 Patient Data at Baseline

<table>
<thead>
<tr>
<th></th>
<th>Pre-Pump (n = 26)</th>
<th>Intra-pump (n = 70)</th>
<th>Post-Pump (n = 4)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>58 ± 13</td>
<td>52 ± 13</td>
<td>48 ± 12</td>
<td>0.01</td>
</tr>
<tr>
<td>Male</td>
<td>18 (69)</td>
<td>60 (86)</td>
<td>3 (75)</td>
<td>0.26</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27 ± 6</td>
<td>28 ± 7</td>
<td>31 ± 6</td>
<td>0.34</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.9 ± 0.4</td>
<td>2 ± 0.6</td>
<td>2 ± 0.1</td>
<td>0.34</td>
</tr>
<tr>
<td>Etiology of cardiomyopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>12 (46)</td>
<td>47 (67)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Dilative idiopathic</td>
<td>10 (38)</td>
<td>16 (23)</td>
<td>4 (100)</td>
<td></td>
</tr>
<tr>
<td>Post-infective</td>
<td>2 (8)</td>
<td>4 (5.8)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Corrected congenital heart disease</td>
<td>1 (4)</td>
<td>1 (1.4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Sarcoïdosis</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Post-partum</td>
<td>0</td>
<td>1 (1.4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Post-cardiomatic (nonischemic)</td>
<td>0</td>
<td>1 (1.4)</td>
<td>0</td>
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<tr>
<td>INTERMACS</td>
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<td>0.58</td>
</tr>
<tr>
<td>1</td>
<td>1 (4)</td>
<td>13 (19)</td>
<td>1 (25)</td>
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</tr>
<tr>
<td>2</td>
<td>8 (31)</td>
<td>25 (36)</td>
<td>1 (25)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15 (50)</td>
<td>27 (39)</td>
<td>2 (50)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3 (11)</td>
<td>5 (6)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Not available</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Duration of support, days</td>
<td>313 (85–463)</td>
<td>345 (50–621)</td>
<td>644 (278–934)</td>
<td>0.44</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>2 ± 0.9</td>
<td>2.5 ± 1</td>
<td>3.2 ± 1</td>
<td>0.02</td>
</tr>
<tr>
<td>Activated partial thromboplastin time, s</td>
<td>56 ± 19</td>
<td>54 ± 20</td>
<td>50 ± 10</td>
<td>0.7</td>
</tr>
<tr>
<td>Patients with anticoagulation below target range</td>
<td>6 (23)</td>
<td>16 (23)</td>
<td>1 (25)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Values are mean ± SD, n (%), or median (interquartile range).
INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support.

49.4%, 37.2%, and 31% at 1, 2, and 3 years, respectively. Survival for patients without thrombosis was 81.4% at 30 days and 62.3%, 53.7%, and 48.5% at 1, 2, and 3 years, respectively.

During the past 6 years, 100 events of blood flow abnormalities were recorded (0.143 EPPY): 70 high-power episodes (70%), and 30 low-flow events (30%). Over this period, with growing knowledge of the problem, 3 types of blood flow obstruction were identified (as shown in the Central Illustration). Most events were diagnosed as intra-pump thrombosis, 26 events were diagnosed as pre-pump, and 4 as post-pump thrombosis. In all investigated explanted pumps, thrombosis was confirmed by visual inspection; the exchanged pump could not be analyzed in only a single case. By the nature of the treatment, thrombosis could not be proven visually after backwash and lysis procedures. Indirectly, thrombosis was confirmed after backwash maneuver in 3 cases where post-procedural arterial angiography proved thrombus in peripheral arteries (femoral and popliteal artery).

Patients’ characteristics and data at the time of the thrombotic event are shown (Table 1). Hemolysis parameters at the time of presentation are shown for each type of blood flow obstruction (Table 2). Forty-eight hours after treatments, parameters diagnostic for intravascular hemolysis were significantly decreased.

Of the 145 nonsintered pumps (without sintered titanium microspheres covering one-half of the length of the inflow cannula) implanted from August 2009 to June 2011, a total of 31 developed thrombotic events (0.14 EPPY) with no difference in thrombosis rate compared with sintered pumps. In particular pre-pump thrombosis could be identified in 5 of the polished pumps (3.4%) compared with 21 events in sintered pumps (4%). However, intra-pump thrombosis was recognized in 26 (17.9%) of nonsintered and 44 (9.9%) of sintered pumps. Different therapeutic approaches were followed according to the supposed level of flow obstruction (Table 3).

PRE-PUMP THROMBOSIS. Low-flow events further identified as pre-pump obstruction because of wedged thrombus obstructing the inflow cannula occurred in 26 (26%) cases (0.037 EPPY). Median support duration until first event was 313 days (IQR: 85 to 463 days).

Pre-pump obstruction was treated by a washout maneuver in 9 patients (all successful), thrombolysis in 9 patients (5 successful; success rate, 56%), and pump exchange in 9 patients (all successful). One patient died and 2 were weaned from LVAD. Some patients received multiple treatment attempts. One patient was excluded from the analysis because of erroneous diagnosis and consequently inappropriate treatment.

INTRA-PUMP THROMBOSIS. High blood flow episodes identified as caused by a thrombus between the impeller and pump housing occurred in 70 cases (0.10 EPPY). Median support duration until first event of thrombosis was 345 days (IQR: 50 to 621 days). Acoustic analysis was positive in all cases (100%). Intra-pump obstruction was treated by thrombolysis in 9 patients (3 successful; success rate, 33%), pump exchange in 53 cases (49 successful; success rate, 94%), and removal for myocardial recovery (3 cases; success rate, 100%). Seven patients died (too sick for surgery or refused surgery) and in 2 cases the parameters spontaneously normalized.

POST-PUMP THROMBOSIS. Post-pump obstruction by thrombus inside the outflow graft or secondary to stenosis of the aortic anastomosis occurred in 4 patients (4%; 0.006 EPPY). Median support duration until first event was 644 days (IQR: 278 to 934 days). Post-pump obstruction was treated by stenting (2 cases; success rate, 100%) or left untreated (2 cases).

Based on this experience we developed an algorithm (Figure 1) for the diagnosis and treatment of blood flow abnormalities during support with the LVAD.
DISCUSSION

LVAD thrombosis is an important topic because of the increasing number of patients supported worldwide and the increasing duration of mechanical circulatory support. The clinical presentation may vary from slightly increased hemolysis or minimal changes in pump values and acoustic profile in an ambulatory patient to acute hemodynamic collapse, massive hemolysis with multigorgan failure, or critical thromboembolic complications (7).

Among 100 events of flow abnormalities in 586 HeartWare HVAD implanted as LVAD, most were caused by an intra-pump thrombosis (70%), just over a quarter by pre-pump obstruction (26%) attributed to wedge thrombus partially or totally occluding the inflow cannula, and only a few by outflow graft involvement (4%). The inferior survival rate of our patients compared with rates reported in the past may be explained by the elevated number of high-risk patients treated at our institution. In the last 2 years the number of patients who received LVAD implantation following acute extracorporeal life support doubled from 10% to 20%. Moreover, the institutional policy was to preferably use HeartWare HVAD in high-risk cases (e.g., on ECLS [extracorporeal life support], redo surgery, cachexia, biventricular assist device support, congenital heart disease) because of its small size, and simple, fast implantation compared with HeartMate II.

Earlier reports (1-3), including 1 from our team, showed pump thrombosis of between 0.04 EPPY (1) and 0.09 EPPY (3). However, in our previous report, we considered only cases with visually confirmed pump thrombus (3). In the present study, patients with successful thrombolysis and those not treated were also included in the calculation, leading to a slightly higher incidence of intra-pump thrombosis of up to 0.10 EPPY. Wedge thrombus formation as a cause for pre-pump flow obstruction may be partially attributed to the pump design, but we observed a more significant decrease in intra-pump thrombosis after the introduction of the sintered inflow cannula. Sintering probably reduces the development of fibrin layers along the inflow cannula (fibrin that could be mobilized, ingested, and then jammed in the hydrodynamic field) consequently reducing rates of intra-pump thrombosis. However, the process of sintering part of the device did not influence the therapy of pump thrombosis over time. Also, in our opinion post-pump flow obstruction is independent of pump design.

The main interest of the analysis is focused on the treatment of pump thrombosis. Because multiple strategies are available, we first localize where the flow is disturbed and then decide on the appropriate treatment on the basis of consequences of the abnormal flow in the patient.

PRE-PUMP THROMBOSIS. The leading symptom of pre-pump thrombosis is hemodynamic instability (if the myocardial function has not recovered); therefore emergency treatment is necessary. For fresh wedge thrombus occluding the inflow cannula, but not protruding into the pump between impeller and housing confirmed by absence of third harmonics, pump stop under protection of the carotid arteries (23,24) offers the possibility of less invasive treatment. In our experience this was completely successful. The time frame for successful washout is a matter of hours; later lysis is a viable option, but the success rate was lower (56%). The 4 patients in whom lysis failed then underwent washout maneuver (n = 2) and pump exchange (n = 2).

In the past, pump exchange was performed for pre-pump flow obstruction. For the past 3 years, however, we have regarded the washout maneuver as first choice. For 1 year it has been routinely performed with a cerebral protection system. Therefore, our overall treatment results are influenced by the introduction of the washout maneuver in our clinical practice.

INTRA-PUMP THROMBOSIS. Because early intervention is key for success, pump exchange is the definitive treatment for intra-pump thrombosis, and thrombolysis plays a secondary role in managing this complication. Technically, an increase of power consumption and detection of the third harmonic are the first signs of LVAD thrombosis. Clinically, hemolysis as a consequence of the unbalanced impeller with subsequent friction and destruction of all blood components is the leading symptom of intra-pump
Table 3: Treatment of Blood Flow Abnormalities and Success Rate According to the Obstruction Type

<table>
<thead>
<tr>
<th>Obstruction Site</th>
<th>Lysis, n (Success Rate)</th>
<th>Pump Exchange, n (Success Rate)</th>
<th>Washout Maneuver, n (Success Rate)</th>
<th>Spontaneous Normalization, n (Success Rate)</th>
<th>Stenting Outflow Graft, n (Success Rate)</th>
<th>Weaning, n (Success Rate)</th>
<th>No Treatment, n</th>
<th>Treatments Success Rate, n (%), No. of Successful Treatments/No. of Treatments</th>
<th>Hospital Discharge, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-pump (n = 26)</td>
<td>5/9 (56)</td>
<td>9/9 (100)</td>
<td>0</td>
<td>NA</td>
<td>2/2 (100)</td>
<td>1</td>
<td>23/27 (85)</td>
<td>23/26 (89)</td>
<td></td>
</tr>
<tr>
<td>Intra-pump (n = 70)</td>
<td>3/9 (33)</td>
<td>49/53 (94)</td>
<td>NA</td>
<td>2/2 (100)</td>
<td>3/3 (100)</td>
<td>7</td>
<td>54/64 (84)</td>
<td>42/70 (60)</td>
<td></td>
</tr>
<tr>
<td>Post-pump (n = 4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2/2 (100%)</td>
<td>0</td>
<td>2</td>
<td>2/2 (100)</td>
<td>2/4 (50)</td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%). Gastrointestinal bleeding after lysis was recorded in 1 patient with known angiodysplasia. Recurrence of thrombosis after successful lysis was observed in 4 patients. *Success is defined as restoration of normal blood flow. †With consequent death of the patient. ‡There were multiple treatment attempts.

NA = not applicable.

Thrombosis (5,8–14). However, hemolysis may take hours or days before laboratory or clinical signs appear, and the best threshold for defining hemolysis in LVADs remains to be defined. In the case of low hemolysis when the event started <3 days before, thrombolysis should be attempted. If hemolysis progresses despite thrombolysis, pump exchange should be performed immediately. Hemoglobinuria with dark urine, although not the defining symptom of hemolysis, nevertheless may indicate it is occurring even before the results of routine laboratory test are ready, and can therefore trigger the decision for pump exchange. Early pump exchange may prevent imminent renal failure. At our institution the sun should not go down or rise up over dark urine.

In our experience thrombolysis is successful if started immediately after the first signs of intra-pump thrombosis (power increase or acoustic signals or hemolysis) appear. However, the success rate is still inferior to that of pump exchange. Two of the 9 patients treated presented with another episode of high-power consumption and underwent surgical pump exchange in the long-term follow-up (after 2 and 6 months, respectively). From the literature, Stulak et al. (25) concluded that attempts to treat pump thrombosis medically have a low success rate and a high risk of hemorrhagic stroke and death. After differentiation into pre-pump, intra-pump, and post-pump blood flow obstructions, thrombolysis seems in our experience to be justified in intra-pump thrombosis only. We cannot exclude a lower success rate of “soft lysis” based on anti-platelet drugs compared with lysis with r-TPA (recombinant tissue plasminogen activator) (26), but soft lysis is safe and permits a staged approach not precluding surgical pump exchange. However, recently published data demonstrate high rate of intracranial bleeding complications (21%) in patients treated with thrombolytic agents. Additionally, this treatment is contraindicated in the case of early pump thrombosis (surgery <6 months) or after a recent bleeding episode during support (25–27).

Two weaned patients had been previously evaluated as having myocardial recovery and intra-pump thrombosis occurred coincidentally just days before scheduled pump explantation. It is not our strategy to perform “acute weaning” for pump thrombosis.

Post-Pump Thrombosis. We observed different patterns of the drop in power consumption and the calculated flow when blood flow obstruction occurred at the level of the aortic anastomosis inside the outflow graft. Computed tomography scan is a valuable tool for visualization of thrombosis of the outflow graft; however, neither case of anastomosis stenosis was recognized by computed tomography. Fluoroscopy, including ventriculography and injection of contrast into the proximal part of the outflow graft, is an excellent diagnostic tool and allows concomitant treatment (19–22).

In cases of low flow, we recommend that the patient be investigated in a hybrid operation room. The first step should be fluoroscopy and direct visualization of the LV with contrast medium. If pre-pump obstruction is detected, a washout maneuver under carotid protection should be attempted, with standby for surgical pump exchange. In successful cases, an angiogram should then be immediately performed to detect the location of the thrombus after the maneuver. If femoral occlusion is detected, embolectomy is performed. If there is no pre-pump obstruction, visualization of the outflow tract by catheterization of the tract with injection of contrast should be performed. Kinking of the outflow tract can be treated by stenting alone, and thrombosis of the outflow tract by stenting with a covered stent while using cerebral endovascular protection (23,24). A significant stenosis of the aortic anastomosis may not
be clearly visualized with contrast. In this case pressure should be measured along the outflow graft and in the aorta as the next step. A pressure drop between the outflow graft and aorta indicates stenosis. Pressure measurement may be also useful for measuring success after stenting.

Two of our patients were successfully treated with stenting; the others were too critical to undergo treatment, and died within a few days (1 was judged unsuitable for surgery and stenting was not considered; in 1 case the pressure drop was not documented).

Echocardiography may rule out other causes of hemolysis, such as aortic insufficiency. Echo measurement of blood velocity through the outflow graft is feasible and the detection of abnormalities should prompt fluoroscopic assessment of the graft.

We were able to restore normal blood flow in almost all of our patients, in some after 2 or more different attempts. The exceptions were a few patients for whom surgery was not suitable or who declined further treatment. Our overall success rate was 84.9% (79 of 93 attempts). In some patients, despite restoration of blood flow and release of hemolysis, multiorgan failure caused by severe hemolysis or hemodynamic collapse was not reversible and the patients died. Therefore early detection of blood flow obstruction, localization of the thrombus/stenosis site, and rapid restoration of blood flow and resolution of hemolysis are crucial.

STUDY LIMITATIONS. There are several limitations to this retrospective analysis. This is a single center study with a small team implanting and managing these devices, and a multicentered collaborative approach would lend greater weight to the results. Furthermore, the detection and management algorithm has evolved through the course of the study as the center learned “best practice.” Therefore during the past 6 years our diagnosis and treatment have changed with growing experience. In earlier days, some cases of pre-pump thrombosis were treated by pump exchange, whereas now we attempt the washout maneuver first. Similarly, it is probable that some post-pump thrombosis was not recognized and was treated by pump exchange.

CONCLUSIONS

Blood flow abnormalities are not rare in patients supported with the HeartWare HVAD. In most cases this complication can be successfully treated using an algorithmic approach. Our treatment strategy is based on grade of hemolysis and hemodynamic status. Severe hemolysis as indicated by dark urine or anuria, or hemodynamic instability, triggers emergency surgery. In our opinion, the best treatment for each condition was primary washout maneuver with carotid protection for pre-pump obstruction, pump exchange for intra-pump obstruction, and stenting of the outflow graft for post-pump obstruction.

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