# Eptifibatide for the Treatment of HeartMate II Left Ventricular Assist Device Thrombosis

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Left ventricular assist device (LVAD) thrombosis is a life-threatening complication occurring in ≈6% of patients receiving a HeartMate II (HMII) LVAD (Thoratec Corp, Pleasanton, CA) within 24 months after implantation.[1] Prophylactic therapy with aspirin and warfarin to an international normalized ratio (INR) of 1.5 to 2.5 is recommended to prevent LVAD thrombosis in most HMII recipients.[2] For device malfunction because of pump thrombosis, surgical device exchange may be necessary but carries a high risk of morbidity and mortality. Alternate treatment approaches include the addition of clopidogrel, tirofiban, and thrombolysis.[3] We report our experience with eptifibatide (Merck & Co, Inc, Whitehouse Station, NJ), a platelet glycoprotein IIb/IIIa receptor inhibitor, for the treatment of LVAD thrombosis in 2 patients.

## Case I

A 66-year-old male with ischemic cardiomyopathy who underwent HMII implantation as a bridge to cardiac transplantation developed LVAD thrombosis 42 days after his surgery while taking 325 mg of aspirin and warfarin. His INR was subtherapeutic at 1.3. Hematuria, a lactate dehydrogenase level of 2326 IU/L, direct bilirubin of 0.8 mg/dL, a lower pulsatility index, and pump flow compared with previous levels, which suggested hemolysis and possible device thrombosis (Table 1). The patient was initially treated with weight-based intravenous unfractionated heparin to target an activated partial thromboplastin time between 60 and 80 seconds (1.5–2.5×normal) for 5 days without significant improvement in serological markers of hemolysis or device parameters. Given the lack of clinical response, eptifibatide, 180 μg/kg bolus followed by a 1 μg/kg per minute infusion, was initiated in addition to intravenous unfractionated heparin with marked improvement of hemolysis indexes and LVAD pulsatility index at 72 hours. A transthoracic echocardiogram at the time of presentation revealed opening of the aortic valve with every cardiac cycle and intermittent opening after resolution of the thrombus. His hospital course was complicated by upper gastrointestinal bleeding secondary to peptic ulcer disease on day 3 of eptifibatide therapy after the improvement of LVAD parameters. This was treated successfully with local epinephrine injection therapy, clip placement, and blood transfusion. There was no clinical evidence of systemic embolization. The patient has had no further LVAD thrombosis (day 386 since HMII LVAD implantation).

## Case II

A 25-year-old woman with doxorubicin-induced cardiomyopathy who underwent HMII LVAD placement as a bridge to transplantation developed LVAD thrombosis 33 days after surgery while taking 325 mg of aspirin and warfarin. Her INR was subtherapeutic at 1.4. Her HMII LVAD parameters revealed an increased power spike, and laboratory workup revealed hemolysis with a lactate dehydrogenase of 1292 IU/L and a direct bilirubin of 1.0 mg/dL. Computed tomographic angiography of the chest identified a laminar thrombus in both the inflow and outflow cannulas (Figure). Weight-based intravenous unfractionated heparin to target an activated partial thromboplastin time between 60 and 80 seconds was initiated and overlapped with warfarin therapy. Given the lack of clinical response 24 hours after admission, eptifibatide, 180 μg/kg bolus followed by a 2-μg/kg per minute infusion, was subsequently initiated with dramatic improvement of her hemolysis indexes within 48 hours. Once her INR was therapeutic (1.5–2.5), intravenous unfractionated heparin was discontinued, and eptifibatide monotherapy was continued for 4 additional days. Her LVAD power returned to baseline levels at the time of discharge (Table 2). She developed upper gastrointestinal bleeding on the first day of eptifibatide infusion secondary to a Dieulafoy lesion that was treated successfully with clip placement and 4 units of packed red blood cells. There was no clinical evidence of systemic embolization. She subsequently underwent successful cardiac transplantation at day 98 after her original LVAD surgery. At the time of transplantation, visual inspection of the VAD inflow and outflow cannulae did not reveal any evidence of thrombosis.

## Discussion

Mechanisms promoting LVAD thrombosis may include platelet activation, heat-induced coagulation, excessive shear forces within the device, systemic inflammation, or ingestion of a preexisting thrombus within the left ventricle or

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**Table 1. Clinical Variables: Patient 1**

| Day* | PI | RPM | Flow | Power | Heparin | Eptifibatide | Hg | LDH |
|---|---|---|---|---|---|---|---|---|
| Baseline | 4.4–5.0 | 8800 | 4.7–5.1 | 5.4–6.0 | – | – | 12.5 | 214 |
| 0 | 2.4–2.9 | 8600 | 3.4–4.9 | 4.8–5.6 | X | – | 10.3 | 2120 |
| 1 | 2.5–2.8 | 8600 | 3.7–4.6 | 4.8–5.6 | X | – | 9.5 | 2326 |
| 2 | 2.7–3.0 | 8600 | 3.5–3.9 | 4.8–5.4 | X | – | 8.9 | 1711 |
| 3 | 2.6–3.1 | 8600 | 3.2–4.6 | 4.8–5.4 | X | – | 9.5 | 1663 |
| 4 | 2.7–3.2 | 8600 | 3.2–4.2 | 4.8–5.1 | X | – | 9.3 | 1573 |
| 5 | 2.5–2.9 | 8600 | 3.4–4.0 | 4.8–5.6 | X | X | 9.0 | 1521 |
| 6 | 2.5–3.0 | 8600 | 3.5–4.0 | 4.8–5.1 | X | X | 9.1 | 1278 |
| 7 | 2.8–3.1 | 8600 | 3.3–4.0 | 4.8–5.1 | X | X | 8.5 | 1254 |
| 8 | 3.0–5.1 | 8600 | 4.0–5.4 | 5.2–6.0 | X | X | 8.2 | 1166 |
| 9 | 4.1–5.0 | 8600 | 4.2–6.0 | 5.2–6.4 | X | – | 6.9 | 936 |
| 10 | 4.6–4.8 | 8600 | 4.1–5.7 | 5.1–5.8 | X | – | 6.6 | 922 |
| 11 | 4.1–5.3 | 9800 | 4.3–6.1 | 5.1–7.8 | X | – | 8.1 | 1062 |
| 71 | 4.4 | 8800 | 5.1 | 6.0 | – | – | 13.2 | 378 |

PI indicates pulsatility index; RPM, rotations per minute; LDH, lactate dehydrogenase; X, receiving therapy; –, not receiving therapy.
*Baseline denotes left ventricular assist device (VAD) flows and laboratory parameters at the time of first hospital discharge post-VAD placement.

aortic root.[1–3] Recently, 2 types of HMII LVAD thrombi were reported: (1) firm, brittle, and platelet-rich (white thrombi), or (2) red, soft, and fibrin-rich (red thrombi). In the present study, formation of a white thrombus was thought to develop from heat-induced coagulation generated by the LVAD.[4] In our series, marginally subtherapeutic INR levels may have contributed to the LVAD thrombosis as both patients presented with INR levels below the therapeutic window. We hypothesized that eptifibatide, a potent platelet glycoprotein IIb/IIIa receptor inhibitor historically studied in acute coronary syndromes, would be effective in treating LVAD associated white thrombi. Our findings have several important clinical implications. First, we identify thrombosis as an important cause of heart failure and hemolysis in LVAD recipients. Second, we report that eptifibatide can be used clinically to improve LVAD function in the setting of thrombosis possibly through the inhibition of platelet adhesion. Third, we identify that bleeding is an important complication of eptifibatide for this complex population, suggesting that alternative approaches to antiplatelet therapy should be investigated. Despite our successful outcomes, the role of eptifibatide in the treatment of LVAD thrombosis remains unclear particularly in light of the associated bleeding risks. In conclusion, our report highlights the critical need for better algorithms to diagnose and manage LVAD thrombosis in this ever-growing population of patients.

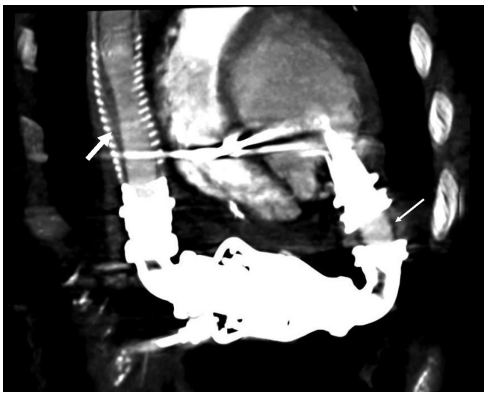

**Figure.** Chest computed tomographic image of left ventricular assist device thrombus in patient 2. Coronal view demonstrating thrombus in the inflow cannula (**thin arrow**) and outflow cannula (**thick arrow**).

## Disclosures

Drs Pham and Kapur received consulting fees of <$10 000 from Thoratec Corp (Pleasanton, CA) in the past 2 years. The other authors have no conflicts to report.

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**Key Words:** anticoagulation ■ eptifibatide ■ glycoprotein IIb/IIIa inhibitor ■ HeartMate II ■ heparin ■ left ventricular assist device ■ thrombosis

**Table 2. Clinical Variables: Patient 2**

| Day* | PI | RPM | Flow† | Power | Heparin | Eptifibatide | Hg | LDH |
|---|---|---|---|---|---|---|---|---|
| Baseline | 5.2 | 9200 | 5.4 | 7.7 | – | – | 8.2 | 289 |
| 0 | 4.0–5.1 | 9200 | +++ | 7.8–9.7 | X | – | 8.0 | 986 |
| 1 | 4.0–5.0 | 9200 | +++ | 7.7–8.6 | X | X | 7.9 | 1292 |
| 2 | 4.5–5.3 | 9200 | +++ | 6.6–9.6 | – | X | 6.9 | 1004 |
| 3 | 4.6–4.9 | 9200 | +++ | 8.0–9.2 | – | X | 8.4 | 698 |
| 4 | 3.9–5.4 | 9200 | +++ | 6.7–9.0 | – | X | 7.7 | 623 |
| 5 | 4.3–5.3 | 9200 | +++ | 6.6–9.0 | – | X | 7.0 | 570 |
| 6 | 3.9–4.6 | 9200 | +++ | 8.2–8.9 | – | X | 8.2 | 422 |
| 7 | 4.1–5.0 | 9200 | +++ | 8.5–9.3 | – | – | 7.6 | 378 |
| 8 | 4.2–4.9 | 9200 | +++ | 6.7–9.0 | – | – | 7.0 | 353 |
| 9 | 5.0–5.5 | 9200 | 5.6–6.0 | 6.6–6.7 | – | – | 7.5 | 355 |
| 54 | 5.8 | 9300 | 5.3 | 6.7 | – | – | 10.4 | 495 |

PI indicates pulsatility index; RPM, rotations per minute; LDH, lactate dehydrogenase; X, receiving therapy; –, not receiving therapy.

*Baseline denotes left ventricular assist device (VAD) flows and laboratory parameters at the time of first hospital discharge post-VAD placement.

†+++, VAD estimated flow is above the expected physiologic flow range.

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