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# Advantages and disadvantages of using intravenous tissue Plasminogen activator as salvage therapy for inoperable HeartWare thrombosis

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## Abstract

Device thrombosis is a devastating complication of left ventricular assist devices. The definitive treatment has been device exchange or explant. Evidence of increasing morbidity and mortality with device exchange has shifted strategies toward conservative management. In this report, we detail the use of thrombolytics as salvage therapy in a patient with an occlusive HeartWare ventricular assist device (HeartWare Inc., Framingham, MA) thrombus, resulting in long-term survival without further intervention.

## 1 | INTRODUCTION

The use of left ventricular assist device (LVAD) in patients with advanced heart failure has increased secondary to device-related improvements in survival and limited donor availability for transplantation.[1,2] Although the risk of device-related thrombosis is small, recent evidence suggests it is increasing.[1,3] The definitive treatment of LVAD thrombosis has been device exchange or explantation; however, this results in increased morbidity and mortality. As a result, alternative management strategies have been suggested. Successful pharmacologic management of device thrombosis has been published; however, the definition of success has differed significantly, including patients with brief resolution of hemolysis who later receive surgical treatment with pump exchange, removal, or transplantation.[4–7] One publication reports two patients administered intravenous (IV) tissue plasminogen activator (tPA) with unfractionated heparin (UFH) who remained asymptomatic for an undefined time period.[6] However, the dose was not described and patients with end-organ dysfunction or hemodynamic instability received surgical, not medical, management. Another publication described one patient who survived a year after tPA, but all patients with hemolysis (even in the absence of increased pump parameters) were considered a pump thrombosis, potentially resulting in treatment of patients without true thrombosis.[4] Lastly, in a report of 15 events treated successfully with medical therapy, the pharmacologic agents were not described and outcomes were only evaluated up to 1 month after therapy. One patient who survived for over 1 year is described, but re-thrombosis occurred requiring re-treatment. No other information is given regarding severity of pump malfunction.[7] We report the use of tPA as a salvage therapy in an inoperable patient with an LVAD thrombosis and demonstrate the advantages and disadvantages of this treatment strategy.

  

## 2 | PATIENT PROFILE

A 66-year-old male with ischemic cardiomyopathy received an HeartWare (HVAD®) ventricular assist device (HeartWare Inc, Framingham, MA). Postoperative course was complicated by driveline infection, *Staphylococcus* bacteremia, and *Clostridium difficile* infection. The patient was discharged to a rehabilitation center and readmitted a year after implantation after a mechanical fall. Device flows decreased from 5.1 to 1.7 L/min and mean arterial pressure (MAP) was 110 mmHg (Fig. 1). The patient did not exhibit overt signs of heart failure or hemolysis. UFH infusion was initiated for a subtherapeutic international normalized ratio (INR) of 1.9. A transthoracic echocardiogram showed reduced left ventricular ejection fraction (10%) and a possible echo density within the left ventricle. A head computed tomography (CT) showed no abnormalities. Transesophageal echocardiogram showed a large, occlusive thrombus around the inflow cannula (Fig. 2). The patient's clinical status deteriorated (serum creatinine increased from 2.1 to 3.1 mg/dL, MAP decreased requiring vasopressors, and hemolysis developed [changes in haptoglobin and lactate dehydrogenase] (Fig. 3). Blood and urine cultures showed *Staphylococcus* and *Enterobacter*, respectively. The patient was not a surgical candidate secondary to frailty (bed ridden with 17% weight loss over 7 months) and acute on chronic infection. The decision was made to administer IV tPA. The INR was now 2.8 despite holding warfarin. Partial thromboplastin time was therapeutic on UFH infusion. Residual warfarin effect was reversed with IV phytonadine 2 h prior to tPA, and UFH was continued throughout the thrombolytic period. The patient received 50 mg of IV tPA (10 mg bolus, 40 mg infusion over 2 h). Thirty minutes after tPA initiation, device flows increased (1.7–2.6 L/min) and reached 3.7 L/min by the end of the infusion (Table 1). Forty-five minutes after tPA initiation, the patient developed altered mental status. CT angiography of the head showed small, acute ischemic infarcts in the left occipital and right parietal lobes without hemorrhage. The UFH infusion was continued. Less than 24 h later, the patient followed all commands, spoke in full sentences, with no focal deficits. After completion of tPA and with continued UFH, markers of hemolysis, HVAD flows, and clinical status improved (Fig. 1 and Table 1). The patient was discharged 24 days after thrombolytic

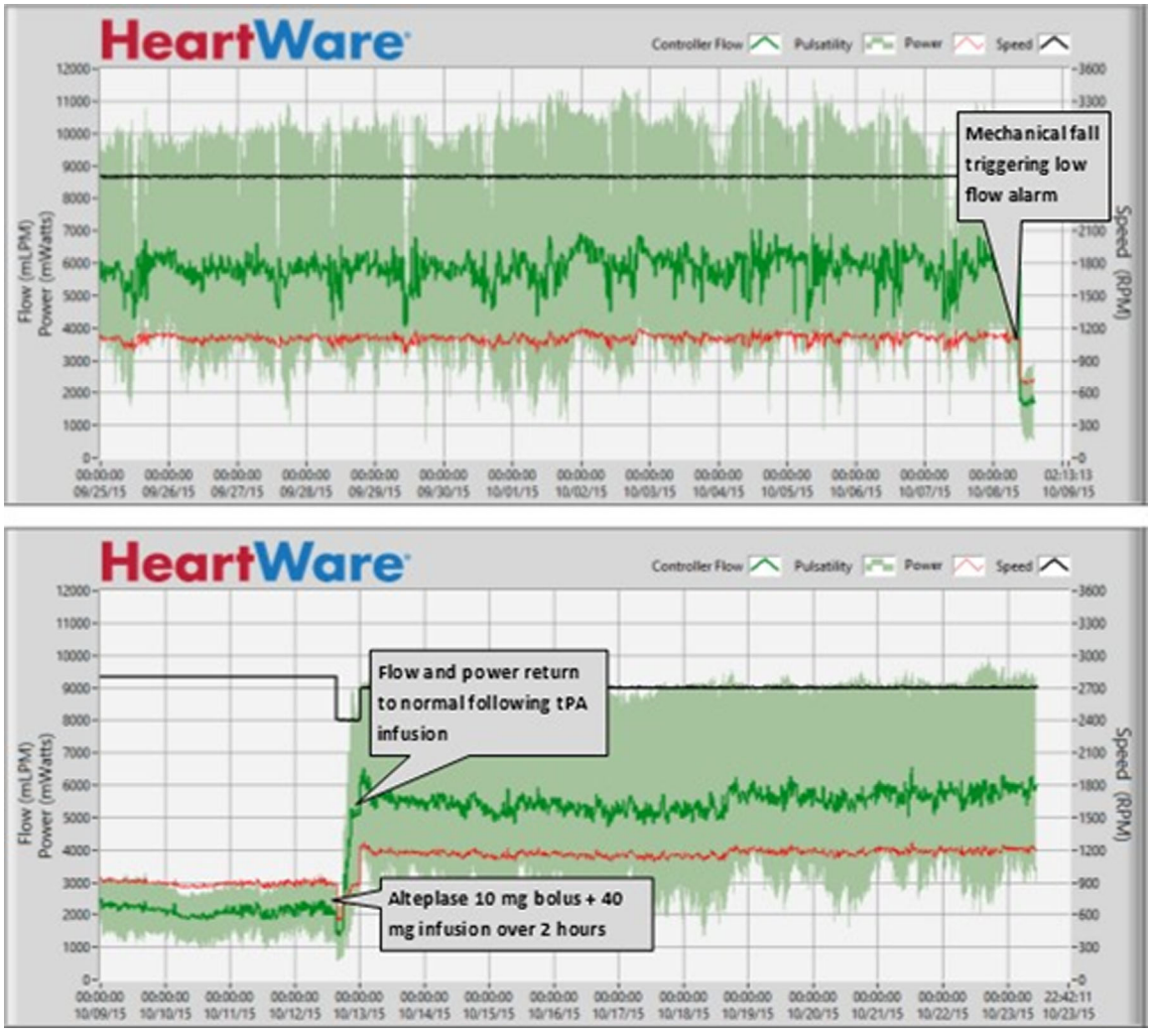


**FIGURE 1** Flow and power readings dropped abruptly and remained low until completion of tissue plasminogen activator

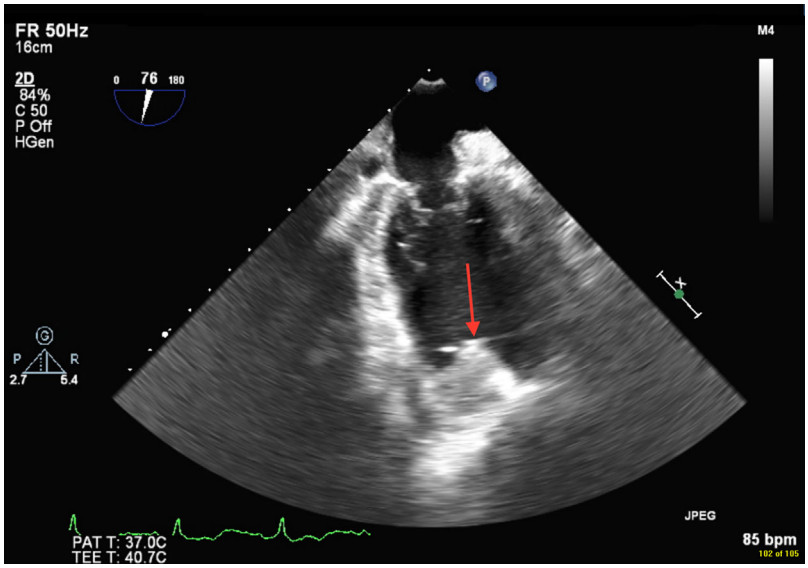


**FIGURE 2** Transesophageal echocardiogram with arrow pointing to large thrombus obstructing the inflow cannula

therapy receiving warfarin alone, and remains without rehospitalization or intervention for 18 months. Device parameters 1 year after discharge showed Flow 4.6 L/min, RPM 2700, and Power 4.0.

## 3 | DISCUSSION

The definitive treatment for device thrombus has been surgical intervention; however, increased morbidity has been documented.[8] Emerging evidence supports preventative monitoring of device flows and power as markers of device thrombosis.[9] One paper shows an algorithm predicting the likelihood of successful medical treatment based on characteristic rises in log parameters.[9] Our patient did not meet criteria for these identified categories as log parameters changed abruptly, indicating a device occlusion. Given the lack of consensus on thrombolytic dosing, we extrapolated a regimen from the existing literature for this high-risk patient.[5] We reversed the INR with phytonadione prior to tPA administration while a therapeutic UFH infusion was continued to mitigate any continued warfarin effects should a hemorrhagic complication occur. It is doubtful that phytonadione had any bearing on the embolic events that ensued, given the timing of administration, and concurrent therapeutic UFH infusion. Although the patient achieved successful lysis of the device thrombus, he suffered small embolic strokes, in contrast to the hemorrhagic complications most frequently published. Fortunately, there were no long-term deficits, the patient was successfully

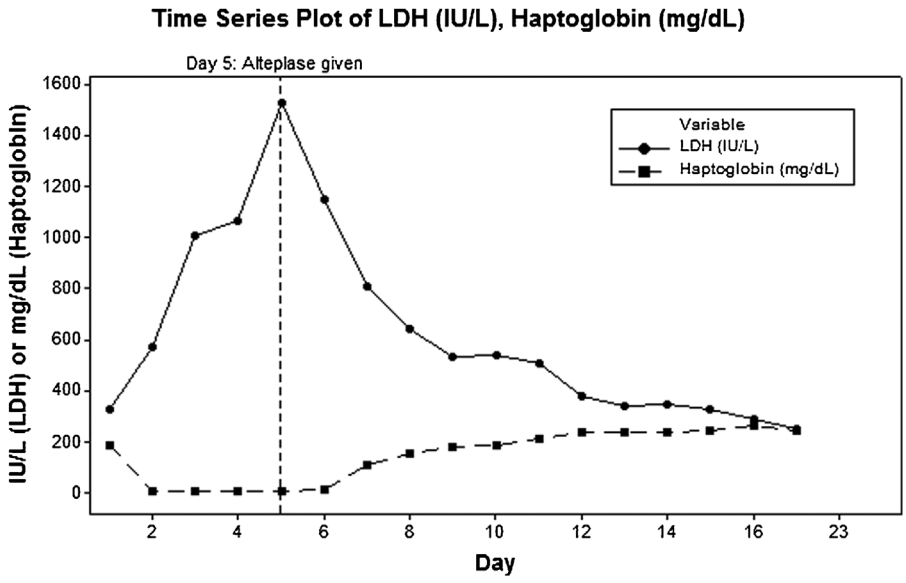


**FIGURE 3** Graphical representation of lactate dehydrogenase and haptoglobin values prior to and after administration of intravenous tissue plasminogen activator

**TABLE 1** HVAD parameters during and after IV tPA

| Time (min) | Motor speed (RPM) | Motor power (W) | Flow (L/Min) |
|---|---|---|---|
| 0 | 2401 | 1.91 | 1.5 |
| 15 | 2403 | 1.92 | 1.5 |
| 30 | 2401 | 2 | 1.7 |
| 45 | 2395 | 2.26 | 2.6 |
| 50 | 2397 | 2.39 | 3 |
| 65 | 2401 | 2.44 | 3.3 |
| 80 | 2401 | 2.32 | 2.8 |
| 95 | 2400 | 2.55 | 3.6 |
| 110 | 2400 | 2.47 | 3.4 |
| 125 | 2397 | 2.58 | 3.7 |
| 140 | 2398 | 2.56 | 3.7 |
| 155 | 2396 | 2.76 | 4.3 |
| 170 | 2399 | 2.67 | 4.1 |
| 185 | 2405 | 2.75 | 4.4 |
| 200 | 2400 | 2.88 | 5.1 |

HVAD, HeartWare ventricular assist device; IV, intravenous; RPM, revolutions per minute; tPA, tissue plasminogen activator.

discharged and remains free of readmissions or device malfunction. Our report details the use of IV tPA as a potential salvage modality, with long-term success, in a patient with occlusive HVAD thrombosis, and limited treatment options. However, in view of the potential for thromboembolism which may result in end organ dysfunction, tPA administration for LVAD thrombosis should only be used in those patients who are truly "inoperable."

## CONFLICTS OF INTEREST

None.

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