The VAD Journal: *The journal of mechanical assisted circulation and heart failure*

Peer-Reviewed Case Report

Normal Lactate Dehydrogenase Does Not Exclude Pump Thrombosis in Left Ventricular Assist Devices

Julie Shelton*, Bennet George, Amanda Hart, and Maya Guglin

University of Kentucky, Lexington, KY

* Corresponding author: jsh253@uky.edu

Citation: Shelton, J et al.(2016). " Normal Lactate Dehydrogenase Does Not Exclude Pump Thrombosis in Left Ventricular Assist Devices"

The VAD Journal, 2. doi: http://dx.doi.org/10.13023/VAD.2016.15

Editor-in-Chief: Maya Guglin, University of Kentucky

Received: April 25, 2016

Accepted: June 30, 2016

Published: June 30, 2016

Funding: Not applicable

Competing interests: Not applicable

Abstract

Left ventricular assist device (LVAD) pump thrombosis is a well-known complication of LVAD placement. Elevated lactate dehydrogenase (LDH) has classically been the first objective marker of pump thrombosis. In this case, we present a patient found to have normal serum LDH values but was ultimately found to have significant pump thrombosis.

Keywords: LVAD, heart failure, ventricular assist device, pump thrombosis

Introduction

Pump thrombosis is a well-known complication of left ventricular assist device (LVAD). Elevated lactate dehydrogenase (LDH) has classically been the first and most consistent objective marker of this condition. In this case, we present a patient with completely normal serum LDH values who was ultimately found to have pump thrombosis.

Case Presentation

A 64-year-old gentleman with a Heartware® HVAD left ventricular assist device (LVAD) initially presented to an outside emergency department with progressive fatigue, melena for one week, along with an abrupt drop in the flow rate noted on his device's controller. His LVAD was placed two years prior to presentation in the setting of chronic systolic heart failure secondary to ischemic cardiomyopathy.

The patient's home anticoagulation regimen consisted of aspirin 81 mg daily and warfarin titrated to a target INR of 1.5-1.8. In the year and a half since implantation, he experienced multiple episodes of gastrointestinal bleeding and

underwent multiple endoscopic procedures, including eight colonoscopies. The procedures were unrevealing with no overt source of bleeding identified. While he had felt fatigued over one week, he acutely felt worse on the day of presentation. Furthermore, the patient noticed that the flow on his LVAD controller dropped from 4.5 L/min to less than 1 L/min. On review of systems, the patient mentioned he had recurrence of melena over the last week. Subsequent interrogation of his LVAD in the emergency room confirmed flows less than 1 L/min as well as absent pulsatility on the flow waveform. He was found to be anemic and two units of packed red blood cells along with 1 L of intravenous fluids was administered. A continuous dopamine infusion was started for hypotension. The patient was transferred to our institution for further care.

On arrival, the patient was in mixed cardiogenic and hypovolemic shock in the setting of gastrointestinal bleeding. He was afebrile with a heart rate of 70 beats/min and a blood pressure of 92/75 mmHg. Laboratory data revealed a hemoglobin of 6.7 g/dL with a hematocrit of 21.1%, platelet count of 254 k/µL, INR of 2.0, serum creatinine of 1.79 mg/dL (baseline of 0.7 mg/dL), serum lactate dehydrogenase (LDH) of 195 U/L (institutional reference range: 116-250 U/L), and plasma free hemoglobin (pfHb) less than 3 mg/dL. LDH was checked repeatedly, and remained within normal limits.

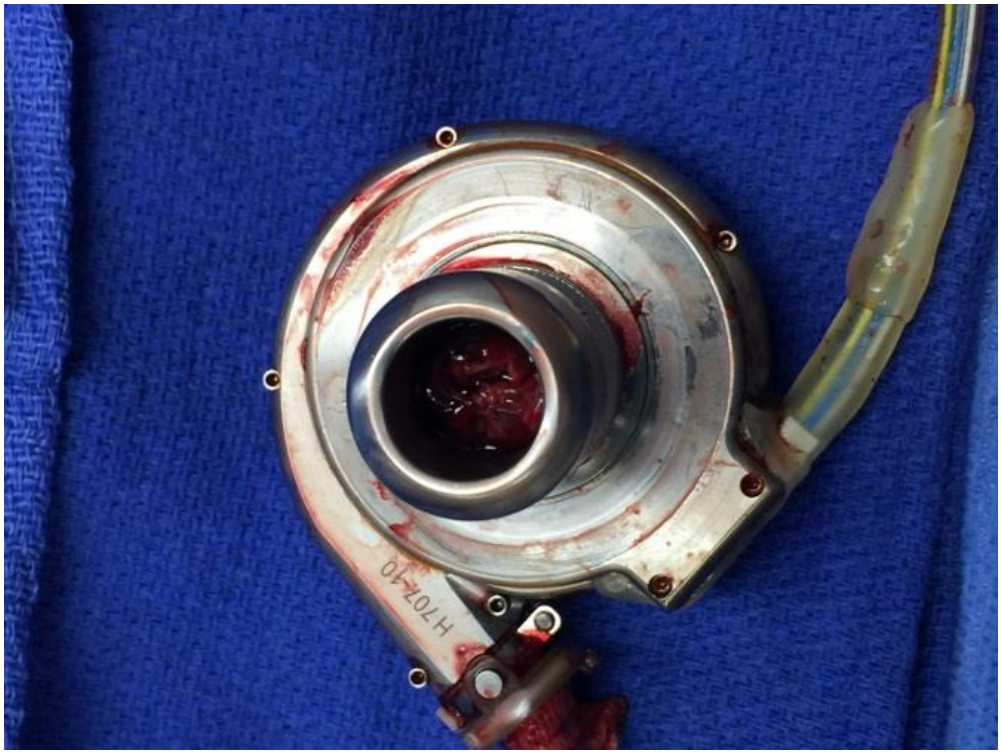
Over next several days, the patient became anuric with worsening serum creatinine. He was referred for right heart catheterization to assess intracardiac hemodynamics. Elevated right and left-sided filling pressures were seen with a right atrial pressure of 20 mmHg, a pulmonary artery pressure of 74/29 mmHg (mean 46 mmHg), and a pulmonary capillary wedge pressure of 27 mmHg. Mixed venous oxygen saturation was 43%. Transthoracic echocardiography demonstrated an ejection fraction of 20-30% with moderate to severe hypokinesis of the left ventricle. His aortic valve opened with each beat.

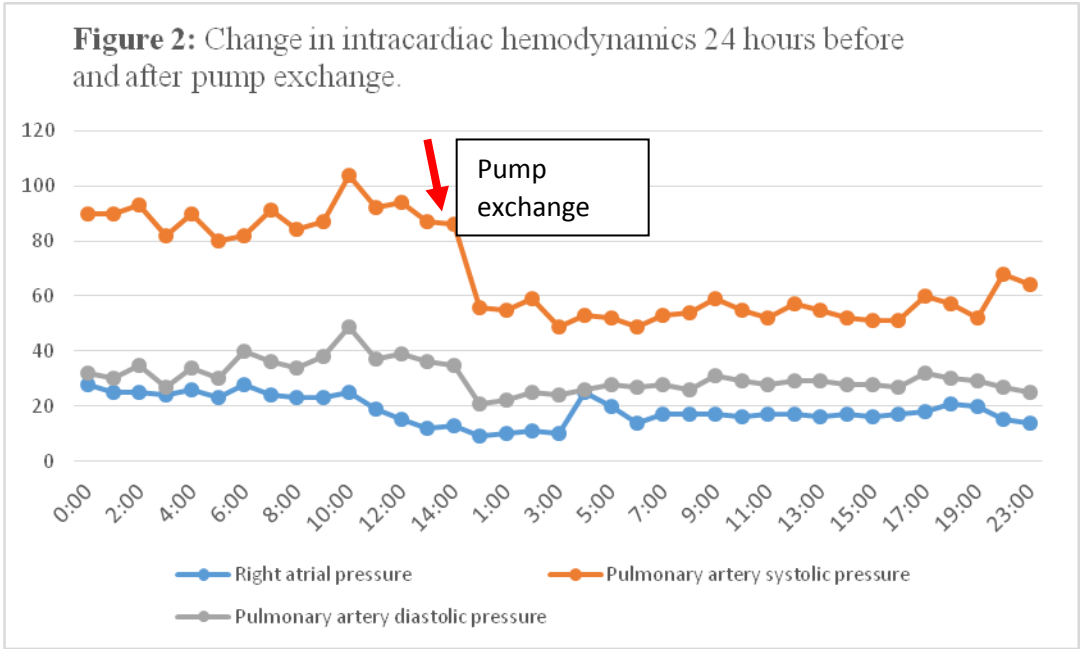
Despite adequate volume resuscitation, including blood products, and the escalation to three vasopressors, the patient's LVAD flows remained low at about 2 L/min. We attempted to increase the pump speed to 3000 revolutions per minute (rpms) but this did not result in a flow increase. Despite a normal hemolytic work-up, our suspicion for pump thrombosis remained high. Cardiothoracic surgery was consulted and the patient was taken to the operating room for LVAD exchange. The hardware was found to have complete inflow and outflow thrombus occlusion as well as thrombus within the left ventricle (Figure 1).

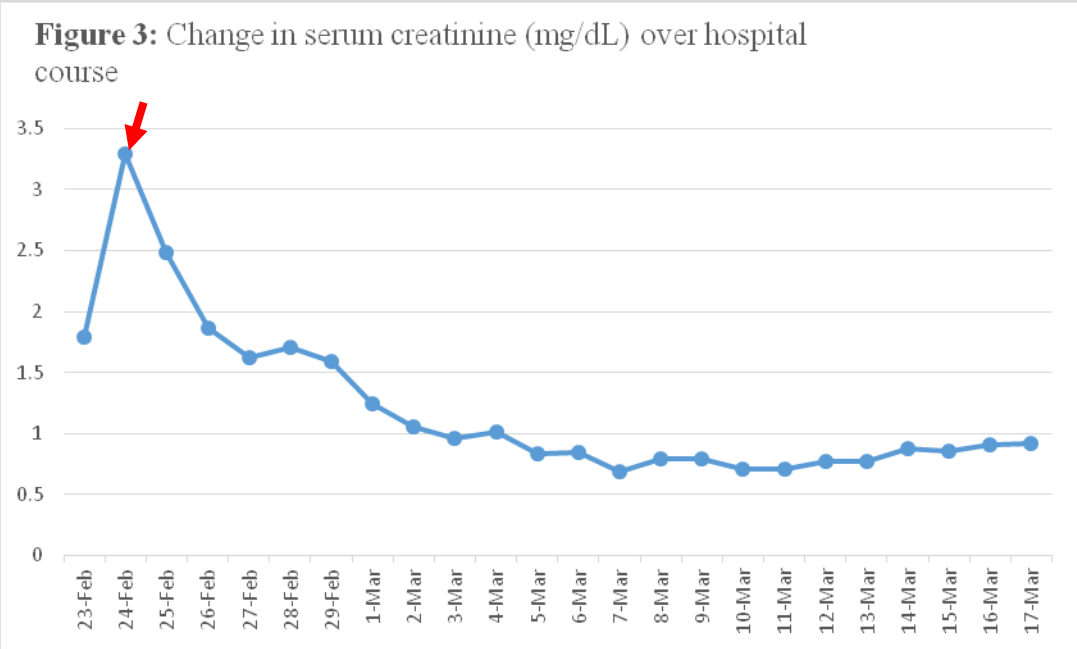
Figure 2 demonstrates the changes in intracardiac hemodynamics prior to and shortly after pump exchange. Right atrial pressures decreased from an average of 22 mmHg for the 14 hours prior to surgery to 16 mmHg in the 19 hours after surgery. Similarly, pulmonary artery systolic pressures ranged from 84-104 mmHg preoperatively and improved to a range of 49-68 mmHg after pump exchange.

LVAD flows improved and the patient was able to be weaned off of all vasopressors. Figure 3 demonstrates the normalization of his serum creatinine as his urine output increased and acute kidney injury resolved. The red arrow indicates the pump exchange.

Figure 1: Inflow cannula demonstrating complete thrombosis.







The patient's hospital course was complicated by sustained ventricular tachycardia requiring defibrillation as well as postoperative respiratory insufficiency with a left pleural effusion requiring decortication. His gastrointestinal bleeding resolved without intervention. He was later transplanted with no complications.

Discussion

The use of left ventricular assist devices (LVADs) is increasing in the management of refractory end-stage heart failure[1-2]. As LVAD technology improves, there has been a reduction in adverse events; however, pump thrombosis remains a life-threatening complication[3-4]. The advantages of continuous flow LVADs are the lower incidence of bleeding complications as well as the reduced rates of infection when compared to pulsatile flow LVADs. Unfortunately, the challenges of pump thrombosis, gastrointestinal bleeding, and aortic insufficiency persist[3-4]. In a multicenter study, Starling et al. documented an increase in the rate of device thrombosis in patients receiving the HeartMate II LVAD when compared to the pre-approval clinical trials. In the last two years of the study, their group found that the occurrence of pump thrombosis increased from 2.2% to 8.4% at three months post-implantation[10]. Multiple other studies cite rates of confirmed pump thrombosis between 0.9-14%[3-12]. Early detection and a high index of suspicion for these complications are critical, as thromboembolic events and pump thrombosis carry significant morbidity and mortality[3,9-10].

Pump thrombosis is defined as clot within the flow path in any portion of the LVAD device and should be suspected with clinical signs of heart failure, abnormal pump parameters (such as sustained power spikes), elevated LDH, or clinical signs or

symptoms of hemolysis [5, 11-12]. The rise in LDH usually precedes a pump thrombosis event, and routine monitoring is indicated to allow for early recognition of possible pump thrombosis[3]. Cowger et al. have shown that an elevated LDH was associated with increased adverse events in LVAD patients, and LDH monitoring parameters may allow for earlier detection of pump thrombosis. In the setting of hemolysis, elevations in LDH may occur as many as 4 months before changes in pfHb with clinical signs of hemolysis[11]. Guidelines from the International Society for Heart and Lung Transplantation recommend to follow biologic markers for hemolysis as a sign of thrombosis[13]. Akin et al. report a sensitivity and specificity of LDH greater than three times the upper limit of normal of 88% and 97%, respectively[12]. Similarly, Uriel et al. found that an LDH greater than four times the upper limit of normal was 100% sensitive and 92.5% specific for pump thrombosis at the time of diagnosis[9]. Of note, a study by Shah, et al found that LDH levels associated with centrifugal (e.g. Heartware) LVADs are, in general, lower than with axial flow (e.g. HeartMate II) LVADs. Not only did they show LDH was more sensitive for pump thrombosis than pfHb, but extrapolation of their data indicated that a lower threshold of LDH elevation may be required to evaluate for pump thrombosis in Heartware LVADs[14]. Thus, LDH has been shown to be an important adjunct in early diagnosis of LVAD-related thrombosis.

After an extensive literature review, this is the first case report we have come across where there was no clear evidence of hemolysis appreciated prior to confirmed pump thrombosis. Our patient, in fact, had an LDH and plasma free hemoglobin within the normal limits of our laboratory values. He did have evidence of pump failure given minimal flow upon LVAD interrogation, as well as clinical signs of heart failure evidenced by worsening pulmonary and peripheral edema, anuria, and worsening intracardiac hemodynamics. Given such a clear clinical picture of LVAD pump failure, our index of suspicion for pump thrombosis remained high. Ultimately, the fact that this patient had normal hemolysis biomarkers in the setting of significant pump thrombosis suggests that we must question the sensitivity of LDH as an early detector of this significant complication.

Hemolysis occurs due to mechanical damage to red blood cells (RBCs). Turbulent flow and high shear stress on RBCs, especially during periods of hemodynamic instability, contribute to hemolysis. Heat generation as well as the rough, textured surfaces of the device may also play a role[5,7-8]. All of these factors rely on blood flow through the pump in order for mechanical damage to RBCs to occur. In our patient, the complete occlusion of the pump meant he had no blood flow through his device and, therefore, no cellular damage or hemolysis. While he did have a pump thrombosis leading to pump failure, hemolysis biomarkers were not helpful in the diagnosis. The diagnosis of pump thrombosis can be challenging, but in a patient with pump failure and clinical evidence of worsened heart failure it must remain on the differential.

References

1. Haeck ML, Hoogslag GE, Rodrigo SF, et al. Treatment options in end-stage heart failure: where to go from here? *Neth Heart J*. 2012; 20: 167-75.

2. Manintveld OC. Left ventricular assist device for end-stage heart failure: results of the first LVAD destination program in the Netherlands : Towards LVAD destination therapy in the Netherlands. *Neth Heart J*. 2015; 23: 100-1.

3. Goldstein DJ, John R, Salerno C, Silvestry S, et al. Algorithm for the diagnosis and management of suspected pump thrombus. *J Heart Lung Transplant*. 2013; 32: 667-70.

4. Boyle AJ, Russell SD, Teuteberg JJ, et al. Low thromboembolism and pump thrombosis with the HeartMate II left ventricular assist device: analysis of outpatient anti-coagulation. *J Heart Lung Transplant*. 2009; 28: 881-7.

5. Whitson BA, Eckman P, Kamdar F, et al. Hemolysis, pump thrombus, and neurologic events in continuous-flow left ventricular assist device recipients. *Ann Thorac Surg*. 2014; 97: 2097-103.

6. Katz JN, Jensen BC, Chang PP, Myers SL, Pagani FD and Kirklin JK. A multicenter analysis of clinical hemolysis in patients supported with durable, long-term left ventricular assist device therapy. *J Heart Lung Transplant*. 2015; 34: 701-9.

7. Hasin T, Deo S, Maleszewski JJ, et al. The role of medical management for acute intravascular hemolysis in patients supported on axial flow LVAD. *ASAIO J*. 2014; 60 :9-14.

8. John R, Kamdar F, Liao K, et al. Low thromboembolic risk for patients with the Heartmate II left ventricular assist device. *J Thorac Cardiovasc Surg*. 2008; 136: 1318-23.

9. Uriel N, Han J, Morrison KA, et al. Device thrombosis in HeartMate II continuous-flow left ventricular assist devices: a multifactorial phenomenon. *J Heart Lung Transplant*. 2014; 33: 51-9.

10. Starling RC, Moazami N, Silvestry SC, et al. Unexpected abrupt increase in left ventricular assist device thrombosis. *The New England journal of medicine*. 2014; 370: 33-40.

11. Cowger JA, Romano MA, Shah P, et al. Hemolysis: a harbinger of adverse outcome after left ventricular assist device implant. *J Heart Lung Transplant*. 2014; 33: 35-43.

12. Akin S, Soliman OI, Constantinescu AA, et al. Haemolysis as a first sign of thromboembolic event and acute pump thrombosis in patients with the continuous-flow left ventricular assist device HeartMate II. *Neth Heart J*. 2016; 24: 134-42.

13. Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant*. 2013; 32: 157-87.

14. Shah P, Mehta V, Cowger J, et al. Diagnosis of hemolysis and pump thrombosis with lactate dehydrogenase during left ventricular assist device support. *J Heart Lung Transplant.* 2014; 33: 102-4.