Title: Aortic Root Thrombosis leading to STEMI in a Heartmate 3 Patient

Author:

Onyedika J. Ilonze MD, MPH[1], Asad Torabi MD[1], Maya Guglin MD, PhD[1], Kashif Saleem MD[2], Roopa Rao MD[1]

Affiliation

Division of Cardiovascular Medicine, Indiana University School of Medicine, Indianapolis, IN

Division of Cardiovascular Surgery, Indiana University School of Medicine, Indianapolis, IN

Corresponding author:
Onyedika J. Ilonze MD, MPH
Division of Cardiovascular Medicine, Indiana University School of Medicine
1801 N. Senate Boulevard Suite 2000, Indianapolis, IN 46202
Email address: oilonze@iu.edu
Phone number: 317-962-9700 **Fax number:** 317-962-9657

Key Words: Left ventricular assist device, Myocardial infarction; STEMI, Aortic root thrombosis

Source of Funding Statement: None

Abstract Word Count: 233

Manuscript Word Count: 1378

Ilonze, O. J., Torabi, A., Guglin, M., Saleem, K., & Rao, R. (2023). Aortic root thrombosis leading to STEMI in a Heartmate 3 patient. Journal of Artificial Organs: The Official Journal of the Japanese Society for Artificial Organs, 26(1), 73–78. https://doi.org/10.1007/s10047-022-01339-y

Abstract

Despite left ventricular assist device (LVAD) therapy becoming established for end stage heart failure (HF), complications remain. Thromboembolic complications are rare with the newest iteration of LVADs. We managed a case of a continuous flow LVAD-related thromboembolic event that presented as an acute myocardial infarction. A 64-year-old male who underwent Heartmate III® LVAD implantation had crushing substernal chest pain and ventricular tachycardia with acute anterolateral myocardial infarction on electrocardiogram on post-operative day 9. Echocardiography showed closed aortic valve and mild aortic regurgitation, but CT angiography showed thrombus within the left coronary cusp despite full anticoagulation. Continuous suction of blood from the left ventricle despite pulsatile flow into the ascending aorta resulted in a minimally opening aortic valve and stagnation of blood leading to thrombosis on the coronary cusp. Apart from post-operative ventricular tachycardia and right ventricular failure; he had adequate body size (body surface area 2.13 m^2) and no post-operative or coagulopathy which could predispose him to thrombosis. Coronary angiography revealed stable severe three vessel disease and thrombus in left main and proximal circumflex artery, and he had aspiration thrombectomy, and international normalized ratio target was increased to 3-3.5 with aspirin 325 mg daily. He survived to discharge but died 60 days after LVAD implant with multiple low flow alarms, and cardiac arrest. We review the literature and propose a management algorithm for patients with impaired AV opening and aortic root thrombosis.

Case Presentation:

A 64-year-old male with end stage ACC/AHA stage D HF secondary to ischemic dilated cardiomyopathy (left ventricular ejection fraction of 15%) secondary to severe native 3-vessel coronary artery disease (EF 15%). He had adequate body size with body surface area of 2.13 m^2 and was INTERMACS class 3 with New York Heart Association (NYHA) class IV symptoms. Pre-operative transthoracic echo showed severe LV dysfunction with LVEF 15%, severe LV dilatation (LV diastolic and systolic dimensions, 68 and 55 mm, respectively) and normally opening aortic valve without thrombosis. Right ventricular function was normal. He underwent Heartmate III® left ventricular assist device (LVAD) implantation as a bridge to transplant. After LVAD implantation, echocardiography revealed a decrease in LV dimensions (LV diastolic and systolic dimensions, 56 and 52 mm, respectively) and RV could not be adequately visualized.

The aortic valve did not open, even at pump speeds of 5000 rpm or lower, so the pump speed was kept at 5200 rpm for this patient. Hemodynamics were acceptable and had post-operative right heart failure with central venous pressure (CVP) of 15 mmHg with abnormal RV function which was treated with inotrope infusion and diuretics postoperatively. LVAD parameters were as follows: pump speed: 5,200 rpm; pulse index: 3–3.5; and pump power, 3.6–4 W. On postoperative day 1, we began single antiplatelet therapy with 325 mg of aspirin daily and warfarin then started heparin bridge therapy on postoperative day 3 and he attained target international normalized ratio (INR) in the range of 2.0–3.0 within 48 hours of anticoagulation. On post-operative day 4, he developed sudden onset of post-operative atrial fibrillation with rapid ventricular response and underwent conscious sedation and direct current cardioversion with restoration of sinus rhythm.

On postoperative day 9, he suddenly complained of severe chest pain and hypotension. 12-lead electrocardiogram (ECG) showed ventricular tachycardia (VT) and ST-segment elevation in leads I, aVL, and V2–V6 were documented implying widespread anterolateral ischemia. He received intravenous amiodarone with no response then had conscious sedation and underwent cardioversion with restoration of sinus rhythm and then taken emergently to the catheterization lab. He had known stable severe three vessel disease. However, a coronary catheter with contrast angiography confirmed the presence of thrombus in the left main and left circumflex arteries **(Figure 1)** and he underwent successful aspiration thrombectomy which prevented ongoing myocardial injury and ventricular arrhythmias. Computed tomography angiography (CTA) showed a large thrombus within the left coronary cusp despite full anticoagulation **(Figure 2)**. High sensitivity troponin was 503 ng/L but peaked at 51,222 ng/L 24 hours after the onset of symptoms. Echocardiography revealed normal LV size, minimally opening aortic valve (once every 4-5 beats) and new RV and right atrial (RA) dilatation and hypokinesis representing RV failure. He had intravenous diuretics and inotropes and RV function improved.

Hypercoagulability workup was negative for inherited coagulopathies, collagen diseases, and cancer. We continued warfarin and used a higher INR target of 3-3.5 and aspirin 325 mg daily. The patient survived to discharge but 60 days later died on arrival to the emergency room later with multiple low flow alarms, and cardiac arrest.

Discussion

The seventh INTERMACS report showed that MI remains a rare complication of LVAD therapy and occurred at a rate of 0.06 events per 100 patient-months in the first 12 months post

LVAD-implant.[1] Aortic root thrombosis as a cause of myocardial infarction (MI) is uncommon in LVAD patients. The etiology of STEMI in this case was likely aortic valve thrombosis but may have also been in stent restenosis given known severe three vessel CAD prior to LVAD implant.

The Heartmate II® LVAD is an axial, mechanical (blood washed) pump that is typically run at speeds of 8,000-10,000 rpm and has been known to have high rates of LVAD thrombosis.[2] In contrast, the Heartmate III® is a fully magnetically levitated centrifugal-flow LVAD run at lower speeds (5,000-6,000 rpm) which is associated with less frequent need for pump replacement than axial-flow devices and was superior with respect to survival free of disabling stroke or reoperation to replace or remove a malfunctioning device.[3] The magnetically levitated design of the Heartmate III should make it less predisposed to aortic valve thrombus formation.

The angle and the position of the outflow graft was acceptable. The closed aortic valve and blood stasis led to a large thrombus on the LCC and the development of acute anterolateral myocardial infarction. Postoperative RV failure likely secondary to stunning from VT can lead to limited AV opening, worsen blood stagnation near the coronary cusp through insufficient LV preload, and reduced pump flow to the ascending aorta. This can also be worsened in cases of small patients with small body surface area[4] although our patient had a normal body surface area. Due to the risk of post-operative bleeding and the low rates of thrombosis of the HeartMate III LVAD, we started anticoagulation slowly and INR on the day of STEMI presentation was 2.1. Our therapeutic strategy was to prevent the formation of pathological thrombi without excessively increasing the risk of major hemorrhage. However, in retrospect we speculate that the patient's anticoagulation was sub-optimal given the relatively low LVAD speed (5200 rpm)

and the high propensity to form thrombus so early after surgery. We also postulated that a higher intensity of heparin anticoagulation [(higher target partial thromboplastin time (PTT)] in addition to warfarin until therapeutic INR was achieved may have prevented the acute myocardial infarction. We transiently increased his INR target to 3-3.5 and increased antiplatelet therapy to aspirin 325 mg daily. Patient was discharged but died 60 days after LVAD implantation with multiple low flow alarms, cardiac arrest, and death on arrival at the emergency room.

Aortic root thrombosis appears to be commoner within the first 30 days post-LVAD implant.[4-6] The left coronary cusp and the non-coronary cusps are most commonly affected.[5-7] Leaflet fusion, aortic insufficiency, and stasis in the noncoronary sinus may predispose patients to thrombus formation. Aortic root thrombosis is not a benign condition. Outcomes after diagnosis have ranged from survival to discharge,[4, 5, 7] death [5, 8, 9] (index case), and orthotopic heart transplantation [5, 10] despite all patients receiving intensified anticoagulation. **Table 1** lists the published cases of STEMI in HeartMate II LVAD patients. Thrombus formation in implanted continuous flow LVADs may be the result of continuous suction of blood from the LV and non-pulsatile flow into the ascending aorta which leads to closure of the aortic valve and stasis of blood on the left coronary cusp (LCC) in patients with severely reduced LV contractility.[11] Thrombus formation on the coronary cusp seems to be a complication mainly observed in patients with continuous flow pumps and not in pulsatile- flow pumps.[10]
Our patient represents the first Heartmate III® LVAD patient in the literature to have a STEMI with sub-optimal anticoagulation (INR 2.1 otherwise bridged with heparin). A thrombus within the left coronary cusp which was seen in the CTA in our case was also present in other cases.[4-6]

It is well-known that some LVAD patients have closed aortic valves and while some develop thrombus, others do not. Extra-valvular factors seen in our patient including suboptimal anti-coagulation, post-operative right heart failure, post-operative arrhythmias (atrial fibrillation and ventricular fibrillation), and cardioversion could all be contributory to thrombosis formation. No consensus exists for treating thrombi on the coronary cusp in patients with LVADs.

Based on our experience and review of the literature, we propose an algorithm for the management of persistently closed aortic valves in LVAD patients **(Figure 3).** We recommend a strategy of routine imaging screening for aortic valve thrombosis in patients with closed aortic valve throughout the cardiac cycle to facilitate early detection of aortic valve thrombosis. CTA can be complementary to further assess thrombosis burden. Reduction of LVAD speed, if possible, to enable aortic valve opening and intensification of anticoagulation regimen could be attempted. Aspiration thrombectomy in STEMI could be an initial step but for persistent thrombosis, surgical removal of the thrombus with the aid of cardiopulmonary bypass can be considered. We hope that this report adds awareness to this potential complication which may become more common as patients are living longer with continuous-flow LVADs. Further research is needed to determine the mechanisms contributing to aortic valve thrombosis and acute myocardial infarction to establish proven preventive and therapeutic strategies.

Conflict of interest: None

Legend

Figure 1 RAO Caudal view showing the thrombotic circumflex artery before aspiration thrombectomy

Figure 2 CT angiogram showing thrombus on left coronary cusp (LCC)

Figure 3 Suggested algorithm for managing patients with aortic valve thrombosis

Table 1 Cases of aortic valve thrombosis in HeartMate II LVAD patients reported in the literature

References

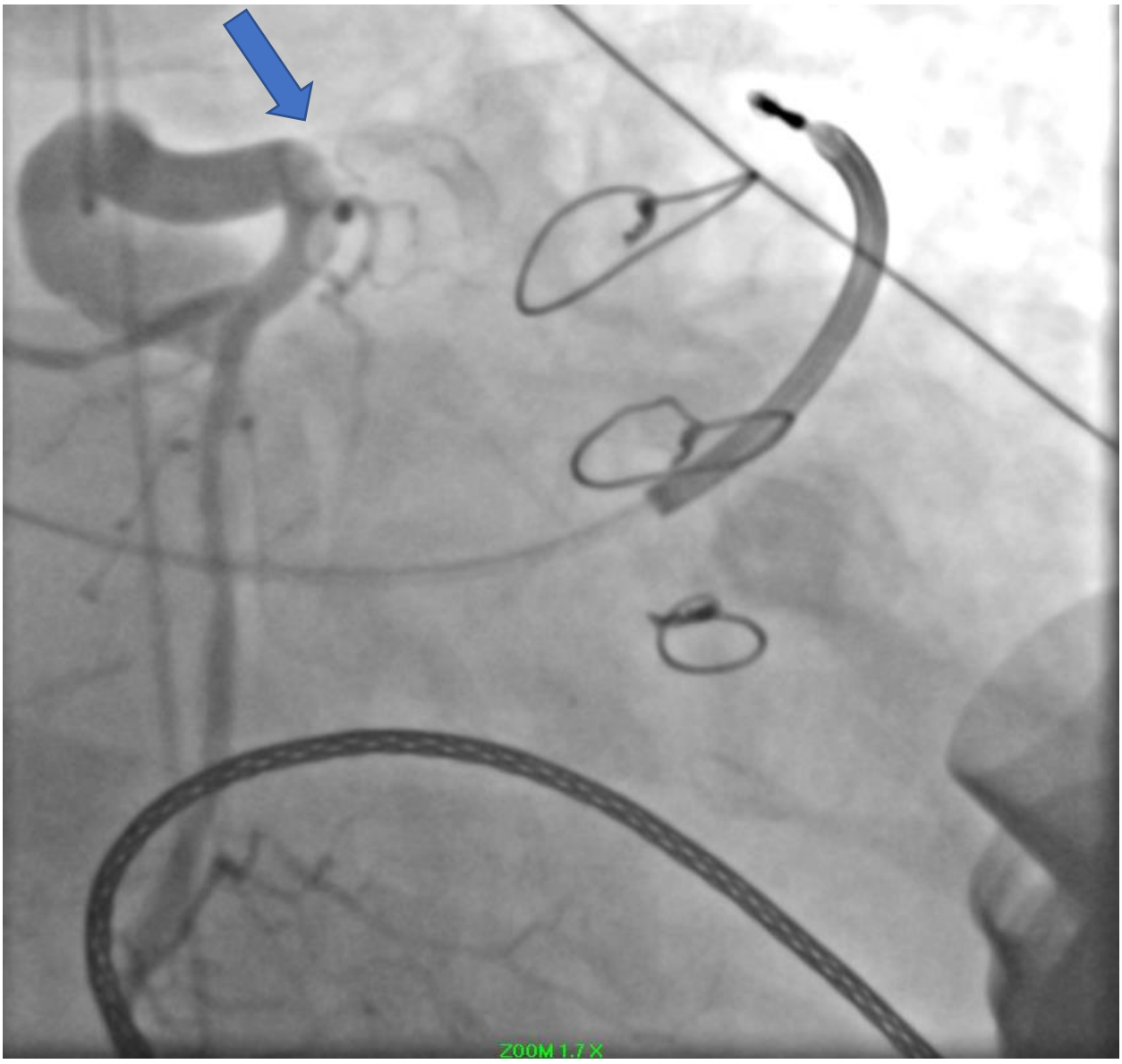
1. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, et al. Seventh INTERMACS annual report: 15,000 patients and counting. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation. 2015;34(12):1495-504.
2. Starling RC, Moazami N, Silvestry SC, Ewald G, Rogers JG, Milano CA, et al. Unexpected abrupt increase in left ventricular assist device thrombosis. The New England journal of medicine. 2014;370(1):33-40.
3. Mehra MR, Uriel N, Naka Y, Cleveland JC, Jr., Yuzefpolskaya M, Salerno CT, et al. A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. The New England journal of medicine. 2019;380(17):1618-27.
4. Nakajima S, Seguchi O, Murata Y, Fujita T, Hata H, Yamane T, et al. Left coronary artery occlusion caused by a large thrombus on the left coronary cusp in a patient with a continuous-flow ventricular assist device. J Artif Organs. 2014;17(2):197-201.
5. Fried J, Han J, Naka Y, Jorde UP, Uriel N. Myocardial infarction after left ventricular assist device implantation: clinical course, role of aortic root thrombus, and outcomes. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation. 2014;33(1):112-5.
6. Shah S, Mehra MR, Couper GS, Desai AS. Continuous flow left ventricular assist device related aortic root thrombosis complicated by left main coronary artery occlusion. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation. 2014;33(1):119-20.
7. Tanna MS, Reyentovich A, Balsam LB, Dodson JA, Vainrib AF, Benenstein RJ, et al. Aortic root thrombus complicated by left main coronary artery occlusion visualized by 3D echocardiography in a patient with continuous-flow left ventricular assist device. Echocardiography. 2017;34(2):306-10.
8. Dickerman RD, Schaller F, McConathy WJ. Left ventricular wall thickening does occur in elite power athletes with or without anabolic steroid Use. Cardiology. 1998;90(2):145-8.
9. Rajagopalan NW, RE. ST-Segment Elevation Myocardial Infarction in Patient with Left Ventricular Assist Device. The VAD Journal. 2015.
10. Demirozu ZT, Frazier OH. Aortic valve noncoronary cusp thrombosis after implantation of a nonpulsatile, continuous-flow pump. Tex Heart Inst J. 2012;39(5):618-20.
11. Freed BH, Jeevanandam V, Jolly N. Aortic root and valve thrombosis after implantation of a left ventricular assist device. J Invasive Cardiol. 2011;23(4):E63-5.

Table 1

Cases of Aortic Valve Thrombosis in HeartMate II Left Ventricular Assist Device patients Reported in the Literature

	Patient	Device	Duration from device implant to presentation	Location of thrombus in AV	AV opening	Outcome
Demirozu et al. 2012	61-year-old female	HeartMate II	30 days	Non coronary cusp thrombosis	Closed	Died 30 days post-implant
Demirozu et al. 2012	62-year-old male	HeartMate II	5 days	Non coronary cusp thrombosis	Closed	Died 150 days after implant
Demirozu et al. 2012	65-year-old male	HeartMate II	11 months	Non coronary cusp thrombosis	Closed	Orthotopic heart transplant
Demirozu et al. 2012	50-year-old male	HeartMate II	2 days	Non coronary cusp thrombosis	Closed	Orthotopic heart transplant
Nakajima et al. 2014	26-year-old female	HeartMate II	5 months	Left coronary cusp thrombosis	Closed	Survived to discharge
Shah et al. 2014	48-year-old female	HeartMate II	4 days	Left coronary cusp thrombosis	Opens intermittently	Alive at time of report
Fried et al. 2014	46-year-old	HeartMate II	2 days	Left coronary cusp thrombosis	Closed	Died after 35 days
Fried et al. 2014	67-year-old male	HeartMate II	3 days	Non coronary cusp thrombosis	Closed	Survived to discharge
Fried et al. 2014	45-year-old female	HeartMate II	2 days	Non coronary and left coronary cusp thrombosis	Closed	Heart transplantation
Tanna et al. 2017	71-year-old male	HeartMate II	18 months	Non coronary cusp thrombosis	Closed	Survived to discharge

Figure 1 – RAO Caudal view showing the thrombotic circumflex artery before aspiration thrombectomy



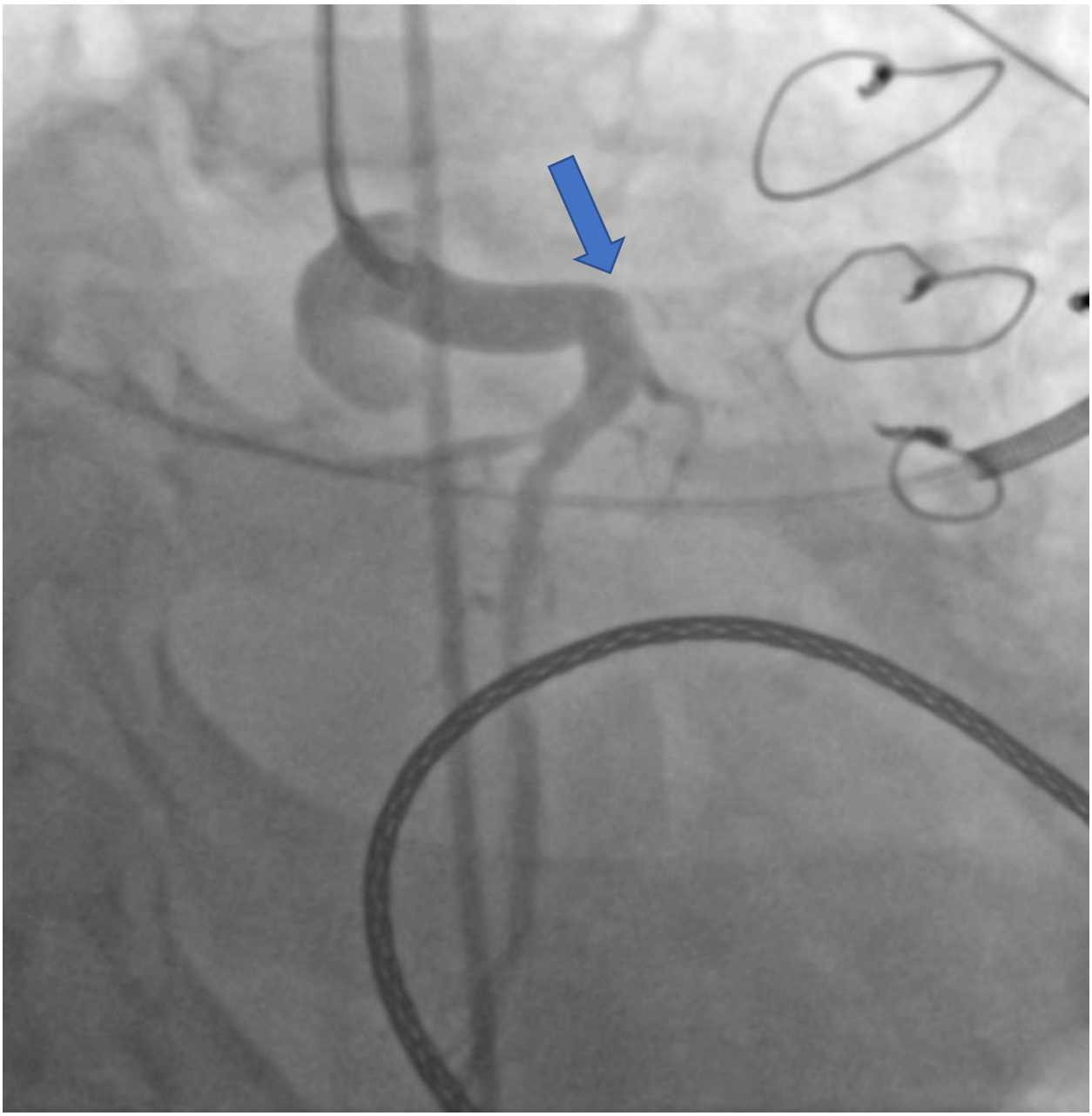
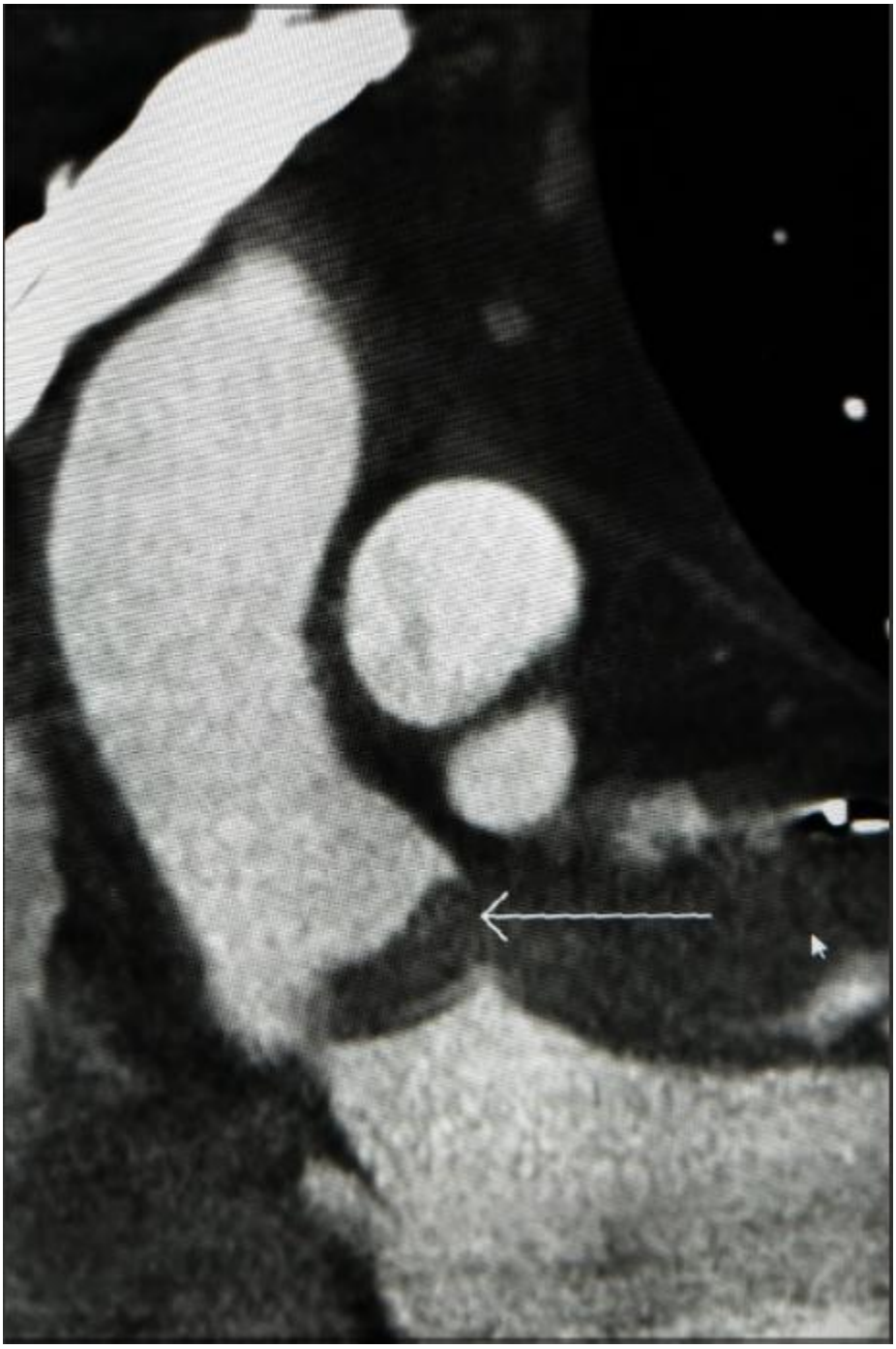


Figure 1 – RAO Caudal view showing the thrombotic circumflex artery after aspiration thrombectomy

Figure 2 – CTA showing thrombus on left coronary cusp (LCC)



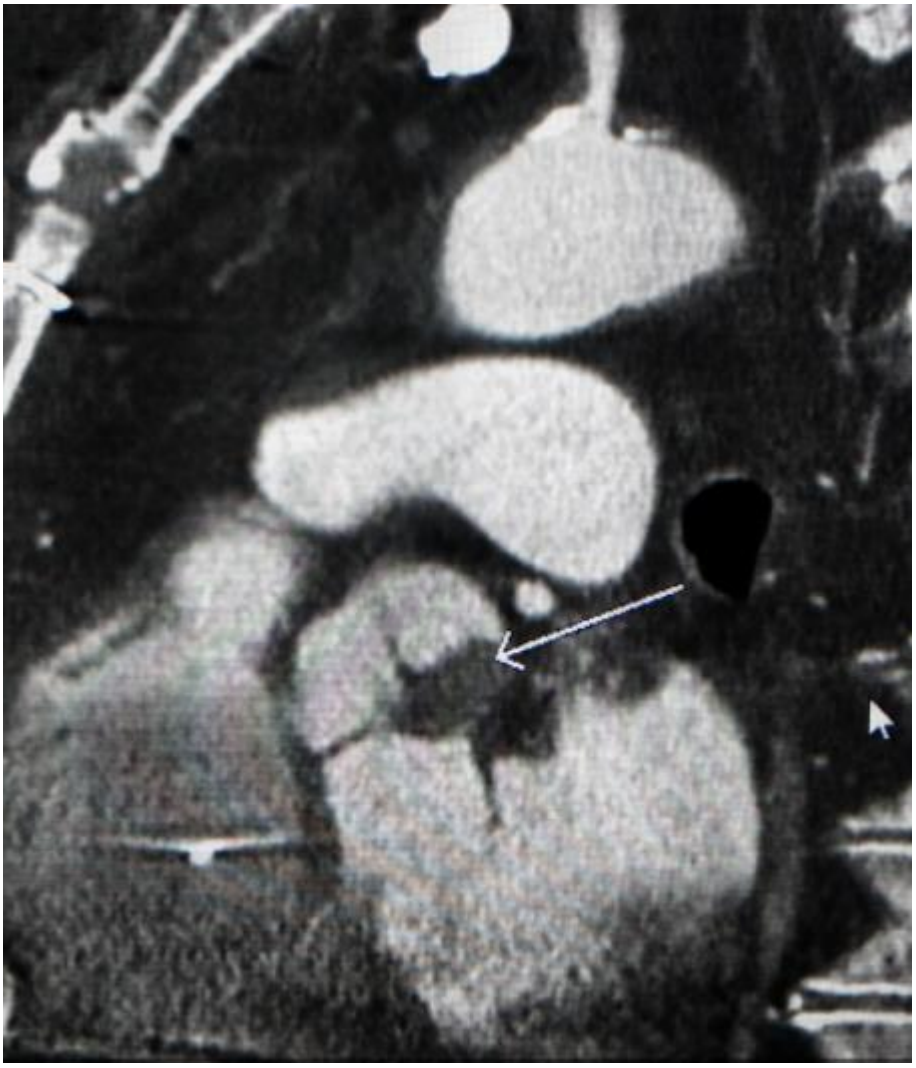


Figure 3

Figure 3 – Suggested Algorithm for Managing Patients with Aortic Valve Thrombosis Post-Heartmate 3 Left Ventricular Assist Device

VT – Ventricular tachycardia; A fib – Atrial fibrillation; AFL – Atrial flutter; RHF – Right heart failure; AC – Anticoagulation; INR – International normalized ratio, AMI – Acute myocardial infarction