Annals of Surgical Case Reports

Case Report
Published: 18 Jun, 2019

Use of Apixaban for Anticoagulation in a Patient with Recurrent Pericardial Effusion in the Setting of Left Ventricular Assist Device: A Heartmate 3 Experience

Demetrios N Mallios*, Amy E Hackmann and Armin Kiankhooy

Department of Surgery, University of Southern California, USA

Abstract

Bleeding complications associated with long-term anticoagulation and antiplatelet therapy in the setting of Left Ventricular Assist Device (LVAD) are well-documented. We report the use of apixaban for anticoagulation in a patient who suffered recurrent pericardial effusion and tamponade while on aspirin and unfractionated heparin, necessitating multiple mediastinal re-explorations. Upon initiation of apixaban therapy in exchange for aspirin and unfractionated heparin, the patient had no subsequent bleeding episodes and was ultimately discharged to home on apixaban without further complication. In carefully chosen patients with otherwise limited options, use of apixaban may be an appropriate anticoagulation strategy in the setting of the HeartMate 3 LVAD.

Introduction

As the prevalence of heart failure continues to rise in both the United States and around the world, new treatment strategies for this difficult patient population are always being explored [1]. Recently, the use of Left Ventricular Assist Devices (LVAD) has become more common, particularly in patients with end stage disease. But as with any developing treatment paradigm, increasing implantation of LVADs is not without complication. Of particular importance is the bleeding risk associated with LVADs, principally due to use of long-term anticoagulation and antiplatelet therapy so as to prevent pump thrombosis. These bleeding complications range from the seemingly innocuous, such as increased bruising, all the way to the life threatening. In a deviation from the "usual" anticoagulation strategy, we report use of apixaban as an alternative in an LVAD patient who suffered recurrent pericardial effusion and tamponade while on aspirin and unfractionated heparin, despite laboratory measures of coagulation remaining within the intended therapeutic range.

Case Report

A 67-year-old male with a history of dilated, ischemic cardiomyopathy was admitted to our institution with decompensated heart failure. Despite medical optimization, the patient remained dependent on continuous vasopressor and inotropic support. As his condition further deteriorated, intra-aortic balloon pump was placed. Although the patient stabilized, he remained dependent on the aforementioned support and was unable to tolerate weaning. As such, the decision was made in concert with patient and family to move forward with placement of HeartMate 3 LVAD for durable circulatory support.

Device implantation was uncomplicated and the patient tolerated the procedure well. However, on postoperative day two, there was acute cardiovascular compromise with concern for tamponade physiology. The patient was taken to the operating room emergently. Diffuse oozing was noted and copious clot was evacuated with immediate improvement in hemodynamics and LVAD flows. Notably, all suture lines were found to be hemostatic without discrete focus of significant bleeding.

In light of this bleeding event, antiplatelet therapy and anticoagulation were initially held. However, by postoperative day four, the decision was made to start daily aspirin at a dose of 81 mg, along with unfractionated heparin drip for a goal Partial Thromboplastin Time (PTT) of 50 secs to 60 secs. On postoperative day seven, the PTT goal was increased to 60 secs to 70 secs without incident. Five days later, the patient developed progressive shortness of breath with opacification of right hemithorax on chest X-ray. Urgent bronchscopy was done to rule out mucus plugging or other tracheobronchial abnormality followed by bedside ultrasound which demonstrated a sizable

OPEN ACCESS

****Correspondence:***
Demetrios N Mallios, Divison of Cardiothoracic Surgery, Department of Surgery, Keck School of Medicine of USC, University of Southern California, California, USA,
E-mail: mallios.demetrios@gmail.com

Received Date: *29 May 2019*
Accepted Date: *16 Jun 2019*
Published Date: *18 Jun 2019*

Citation:
Mallios DN, Hackmann AE, Kiankhooy A. Use of Apixaban for Anticoagulation in a Patient with Recurrent Pericardial Effusion in the Setting of Left Ventricular Assist Device: A Heartmate 3 Experience. Ann Surg Case Rep. 2019; 2(2): 1015.

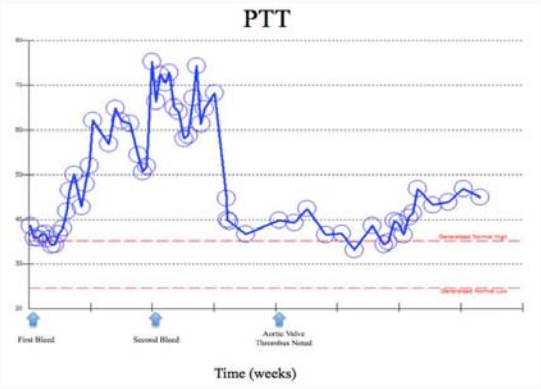

Figure 1: Postoperative PTT trend with significant events. The patient's PTT values remained within the target therapeutic range for the duration of his hospitalization.

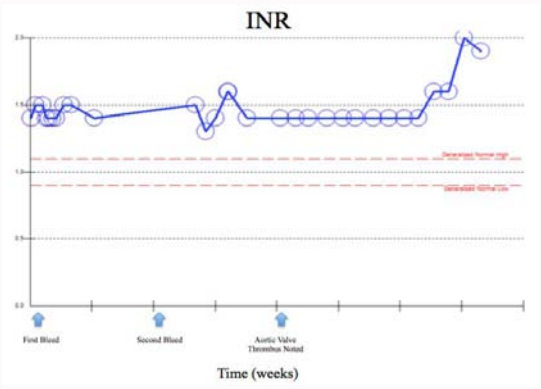

Figure 2: Postoperative INR trend with significant events.

pericardial effusion. Upon mediastinal re-exploration, significant clot burden was found and evacuated, but no discrete bleeding was seen. Once again, diffuse oozing seemed to be the culprit.

Of note, lab studies for coagulation had remained within the intended therapeutic range for the duration of the postoperative period. Peak PTT was 75.6 secs, while peak International Normalized Ratio (INR) was 1.6 (Figure 1 and 2). But given two prior episodes of significant bleeding and need for re-operation, the decision was made to again hold antiplatelet therapy and anticoagulation. However, over a period of eight days during which anticoagulation was being held, the patient unfortunately developed aortic valve thrombus as noted on bedside transthoracic echocardiogram that was being done serially to monitor for accumulation of recurrent pericardial effusion (Figure 3). It was clear that anticoagulation therapy needed to be restarted at this time, but the prior bleeding episodes made the decision difficult.

In considering alternative strategies, it was noted that the patient had previously tolerated apixaban as an outpatient for atrial fibrillation. Importantly, he had no history of prior bleeding episodes or thrombotic events, despite extended use of apixaban. And given that prior use of unfractionated heparin and antiplatelet therapy had been unsuccessful, it seemed reasonable to trial the patient on apixaban therapy knowing he had used it and tolerated it well in the past. After expressing our concerns and discussing different strategies with the family, we decided to start apixaban at a dose of 5 mg twice daily in hopes of minimizing the risk of further bleeding complications while at the same time addressing the newly-formed

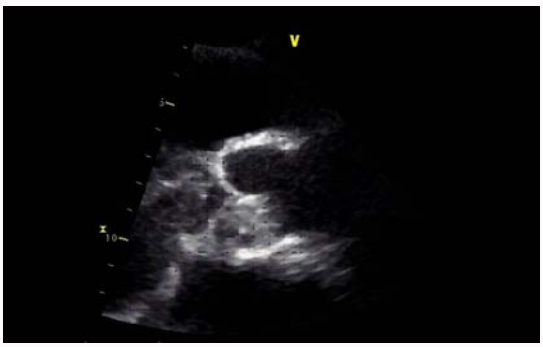

Figure 3: Note the large, round thrombus adherent to the aortic valve leaflet.

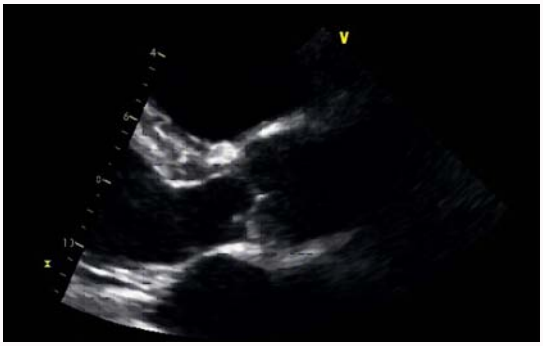

Figure 4: Resolution of the aortic valve thrombus.

aortic valve thrombus and preventing pump thrombosis. Ultimately, this strategy proved effective. The patient suffered no further bleeding complications through day of discharge. Likewise, no new thrombotic complications occurred, and follow-up transthoracic echocardiogram demonstrated resolution of the aortic valve thrombus, as well (Figure 4). Furthermore, lactate dehydrogenase levels remained stable after the initiation of apixiban without any significant increase, which suggests that the LVAD continued to operate smoothly without excessive hemolysis. At this time, the patient is still doing well with apixaban monotherapy in the absence of antiplatelet therapy or other anticoagulation.

Discussion

While we report the first use of apixaban as anticoagulation in HeartMate 3 LVAD, it is important to acknowledge that apixaban use has been previously described in a patient with HeartMate 2 LVAD who suffered from recurrent gastrointestinal bleeding while on conventional antiplatelet therapy and anticoagulation [2]. In their report, Pollari and colleagues likewise demonstrate feasibility and safety of use of apixaban in a complex LVAD patient with limited anticoagulation options in the face of recurrent bleeding.

Along with the bleeding risk that comes with anticoagulation, it is important to consider the effects of the LVAD itself. Similar to cardiopulmonary bypass and extracorporeal membrane oxygenation systems, LVAD use predisposes to consumptive coagulopathy and platelet dysfunction. The consequences and implications of these effects have not been well studied and are difficult to quantify, particularly in a patient who is already therapeutically anticoagulated. However, it is necessary to consider the likelihood that such changes could serve as an additive risk for bleeding in patients with LVAD, further complicating the situation.

On the flip side, it is also important to consider the risk of pump thrombosis and other thrombotic complications associated with LVAD use. While pump thrombosis was a serious concern in the past, it seems to be less of an issue with the fully magnetically levitated, centrifugal flow HeartMate 3 as compared to the axial flow HeartMate 2. In fact, over two years of follow up in the MOMENTUM 3 trial, only two episodes of thrombosis were seen in a cohort of 190 HeartMate 3 patients [3]. Further, these were not confirmed to be de novo thromboses within the pump; more likely, these episodes represent inflow thromboses that formed elsewhere within the heart (for example, the left atrial appendage) and migrated to the pump. Another recent study by Schmitto and colleagues confirmed the excellent hemocompatibility of the HeartMate 3 LVAD without a single pump thrombosis in 50 patients over two years of follow up [4]. Despite these findings, anticoagulation in these patients will continue to play an important role in the immediate future.

Although prospective studies investigating optimal anticoagulation strategy in the setting of LVAD are lacking, an extensive review and summary of the literature by Rossi and colleagues does suggest that long-term use of warfarin and antiplatelet therapy offers the lowest risk of thromboembolic events in LVAD patients when compared to unfractionated heparin and low molecular weight heparin [5]. At our institution, the typical postoperative regimen for LVAD patients includes initiation of unfractionated heparin drip as a bridge to long-term anticoagulation with warfarin and daily aspirin at a dose of 81 mg. The target therapeutic range varies depending on the patient and circumstances, but generally we aim for PTT 60 secs to 70 secs with INR 2.5 to 3.To minimize the risk of thrombosis while at the same time mitigating bleeding risk, we advocate for careful monitoring of coagulation parameters in all patients and serial lab studies while the patient is hospitalized. Our dosing strategy is reassessed daily in concert with an anticoagulation pharmacist so as to stay within the intended therapeutic range as much as possible. Transitioning to the outpatient setting, we feel it is of paramount importance that patients are thoroughly educated on the use, dosing, and side effects associated with warfarin in particular. Regular clinic appointments and labs studies are necessary, and the help of a dietitian can also be worthwhile.

But for the patient who is unable to tolerate these conventional strategies for any reason, what is the best alternative? We contend that apixaban monotherapy may be a reasonable option, though we realize this is based solely on anectodal experience. Whereas use of apixaban has been studied extensively in patients with atrial fibrillation, apixaban in LVAD patients has not been rigorously investigated [6]. Moving forward, we do hope to see further studies on apixaban and other novel oral anticoagulants in both LVAD patients and other patients in need of anticoagulation. If demonstrably safe and effective, such agents offer ease of use and dosing compared to warfarin, no requirement for regular blood draws to track INR, and fewer clinic appointments. Furthermore, in patients who have used such agents in the past without complication, continuing with said agent may be preferable to initiating a new agent like warfarin. Recent FDA approval for Andexxa, an apixaban reversal agent, makes apixaban an even more attractive alternative [7]. Additionally, the significant decrease in rate of pump thrombosis seen in the HeartMate 3 as compared to HeartMate 2 (likely owing to improved engineering, centrifugal flow, and intrinsic pulsatility) may be an early sign that a lower therapeutic dose of anticoagulation could be reasonable for LVAD patients in the future. In the meantime, though, conventional anticoagulation strategies as described above will remain the gold standard with deviation from established protocol reserved for unique cases.

References

1. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Card Fail Rev. 2017;3(1):7-11.
2. Pollari F, Fischlein T, Fittkau M, Santarpino G. Anticoagulation with apixaban in left ventricular assist device patient with gastrointestinal bleeding: a viable alternative to warfarin? J Thorac Cardiovasc Surg. 2016;151:79-81.
3. Mehra MR, Goldstein DJ, Uriel N, Cleveland JC Jr, Yuzefpolskaya M, Salerno C, et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. N Engl J Med. 2018;378(15):1386-95.
4. Schmitto JD, Pya Y, Zimpfer D, Krabatsch T, Garbade J, Rao V, et al. Long-term evaluation of a fully magnetically levitated circulatory support device for advanced heart failure-two-year results from the HeartMate 3 CE Mark study. Eur J Heart Fail. 2018;27.
5. Rossi M, Serraino GF, Jiritano F, Renzulli A. What is the optimal anticoagulation in patients with a left ventricular assist device? Interact Cardiovasc Thorac Surg. 2012;15(4):733-40.
6. Hylek EM, Held C, Alexander JH, Lpes RD, De Caterina R, Wojdyla DM, et al. Major bleeding in patients with atrial fibrillation receiving apixaban or warfarin: The ARISTOTLE Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation): predictors, characteristics, and clinical outcomes. J Am Coll Cardiol. 2014;63(20):2141-7.
7. Andexxa-An Antidote for Apixaban and Rivaroxaban. JAMA. 2018;320(4):399-400.