Case Report

Anticoagulation dilemma in a high-risk patient with On-X valves

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ABSTRACT

Thromboembolism continues to be a major concern in patients with mechanical heart valves, especially in those with unsatisfactory anticoagulation levels. The new On-X valve (On-X Life Technologies, Austin, TX, USA) has been reported as having unique structural characteristics that offer lower thrombogenicity to the valve. We report a case where the patient received no or minimal systemic anticoagulation after placement of On-X mitral and aortic valves due to development of severe mucosal arterio-venous malformations yet did not show any evidence of thromboembolism. This case report reinforces the findings of recent studies that lower anticoagulation levels may be acceptable in patients with On-X valves and suggests this valve may be particularly useful in those in whom therapeutic levels of anticoagulation cannot be achieved due to increased risk of bleeding.

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INTRODUCTION

Currently available mechanical heart valves (MHVs) have acceptable durability and hemodynamics, however, thromboembolism continues to be a concern, especially in patients with unsatisfactory anticoagulation levels.[1] A relatively new MHV, the bileaflet On-X valve (On-X Life Technologies, Austin, TX, USA) is believed to have greater thromboresistance because of its all-carbon manufacturing and improved flow dynamics. Preliminary short- and intermediate-term studies have shown that this valve could possibly reduce anticoagulation requirements.[2-7] In this case report, we discuss the critical need to balance anticoagulation therapy with the potential for life-threatening protracted bleeding in a patient with two freshly implanted On-X valves.

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CASE REPORT

A 57-year-old woman with severe rheumatic mitral stenosis, severe aortic stenosis, and severe tricuspid regurgitation underwent implantation of a 25 mm mitral and a 19 mm aortic On-X valve, a de Vega tricuspid annuloplasty, and Maze procedure. The cardiopulmonary bypass and aortic cross-clamp times were 174 and 134 min, respectively. She had chronic atrial fibrillation, hypertension, and pacemaker placement for sick sinus syndrome, and was on warfarin, but denied any history of bleeding in the past. Her preoperative echocardiogram and right heart catheterization revealed severe pulmonary hypertension with pulmonary arterial systolic pressures of 75 mmHg and severe right ventricular dilatation.

She came to the intensive care unit (ICU) intubated and on high infusion rates of inotropic and vasopressor agents including epinephrine, norepinephrine, vasopressin, and milrinone. Despite multiple blood component therapy intraoperatively, she continued to be severely hypocoagulable, with thrombocytopenia, hypofibrinogenemia, and elevated international normalized ratio (INR) levels [Figures 1 and 2]. As her coagulation parameters began to normalize, she was started on subcutaneous heparin 5000 IU every 12 h for prophylaxis against deep vein thrombosis on

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postoperative day (POD) 8. However, neither antiplatelet therapy nor therapeutic heparinization was initiated due to the patient's precarious medical condition. Despite this, immediately after removal of the epicardial pacing wires on POD 9, she developed pericardial tamponade requiring emergent opening of the sternum. This led to progressive worsening of pulmonary hypertension, causing severe right heart failure and eventually biventricular failure, necessitating placement of an intra-aortic balloon pump and inhalational epoprostenol therapy. The patient developed renal failure which required continuous renal replacement therapy and compounded coagulopathy by causing consumptive thrombocytopenia and thrombocytopathia.

Three weeks after surgery, she progressed to disseminated intravascular coagulopathy (DIC) and was given multiple blood component transfusions including desmopressin, cryoprecipitate, and factor VII. After the DIC was resolved, she exhibited waxing and waning coagulopathy and thrombocytopenia [Figures 1 and 2]. Interestingly, around 6 weeks into her ICU stay, she developed profuse, life-threatening bleeding from the respiratory and upper gastrointestinal tracts and natural orifices in response to any attempts to initiate anticoagulation, even with prophylactic doses of heparin. Diagnostic bronchoscopy and upper and lower gastrointestinal endoscopies revealed extensive arteriovenous malformations (AVMs) throughout her respiratory and gastrointestinal tracts. Due to the lack of preoperative endoscopy and the fact that AVMs were not restricted to the colon, making a definitive diagnosis of Heyde's syndrome with acquired von Willebrand factor deficiency was difficult. However, there is also a possibility that some degree of aortic valve patient-prosthetic mismatch could have caused a variant of Heyde's syndrome. The patient therefore received little or no anticoagulation for almost her entire hospital stay. During her 5 months in the ICU, frequent transthoracic and transesophageal echocardiographic examinations revealed no valve thrombi. She was discharged to a long-term acute care facility on aspirin and warfarin with a subtherapeutic INR of 1.6, in view of her higher risk for bleeding. There was no history of thromboembolism and no further bleeding episodes. She died about 3 months later at an outside hospital due to pulmonary aspiration and sepsis.

DISCUSSION

In the USA, there is a growing number of valve replacements in patients of all age groups.[1] While MHVs are more durable than tissue valves, they are also thrombogenic and, therefore, require life-long anticoagulation based on American Heart Association (AHA) guidelines to prevent valve thrombosis. These guidelines may not be achievable in those at high-risk of bleeding, creating a therapeutic dilemma as thromboembolism due to inadequate anticoagulation can have dire consequences at any age. The new On-X valve is said to have several structural characteristics that may confer a certain degree of thromboresistance as compared to the other MHVs and may prove to be especially beneficial in such circumstances.

The On-X valve – Structural and hemodynamic characteristics

The US Food and Drug Administration approved the On-X aortic valve in 2001 and the On-X mitral valve in 2002. The pure pyrolytic carbon used in the construction of these valves makes them more wear-resistant without the need for silicon carbide.[8,9] The absence of silicone alloy allows for a smoother finish and greater biocompatibility, which may decrease thrombogenicity. According to the manufacturer, several properties of the valve including flared inlet design, elongated orifice, smooth contours of the pivots, and opening of the valve leaflets to a full 90 degrees, may improve flow dynamics across the valve and provide more thromboresistance than other MHVs (On-X Life Technology information. Available at: http://www.onxlti.com/. Accessed April 01, 2015) [Figure 3].

Intraoperative and early postoperative echocardiographic data have shown increased effective orifice area and reduced transvalvular gradients as compared to St. Jude MHVs (St. Jude Medical Inc., St. Paul, MN, USA).[10,11] In a randomized comparison with the Carbomedics Top Hat valve (Carbomedics Inc., Austin, TX, USA), the On-X valve had a significantly better hemodynamic profile, including effective orifice area, peak velocity, and peak and mean pressure drop across the valve in the immediate postoperative period.[12] MHVs in general cause significant hemolysis with reports of lactate dehydrogenase (LDH) levels increasing up to 200% of upper normal. However, both aortic and mitral On-X valves have shown much lower LDH levels at up to 1 year after implantation.[13]

The On-X valve – Anticoagulation profile

Coagulation-related complications of MHVs range from a fatal thromboembolism due to inadequate anticoagulation at one end of the spectrum to equally devastating anticoagulation-induced bleeding at the other end. In several short- and intermediate-term multi-center

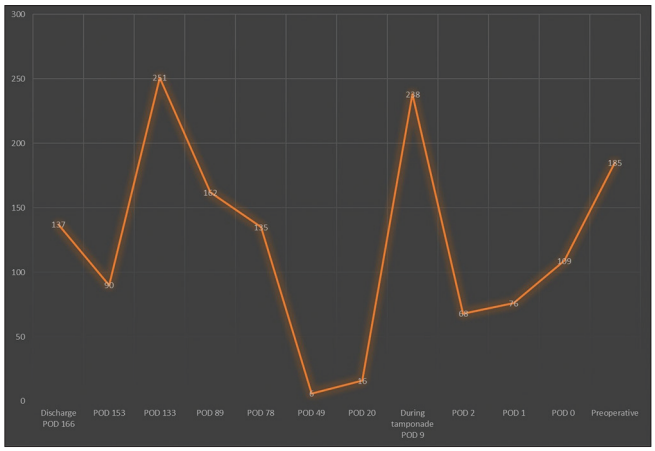

Figure 1: Wild fluctuations in platelet count from preoperative visit until discharge on postoperative day 166. Intervals between time points on the x-axis are variable

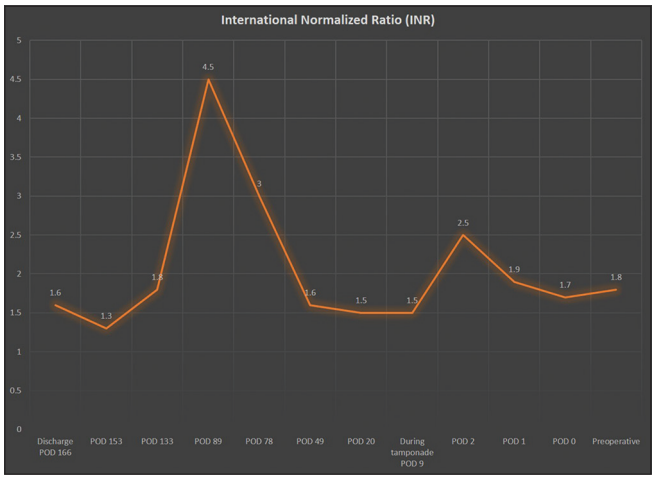

Figure 2: Patient's international normalized ratio (INR) from preoperative visit until discharge on postoperative day 166, showing subtherapeutic INR at multiple time points throughout the Intensive care unit stay

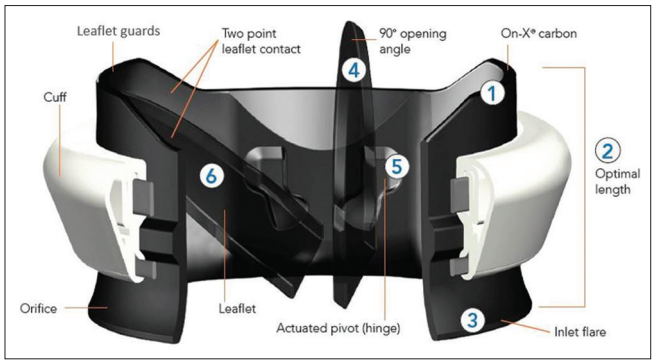

Figure 3: On-X prosthetic heart valve design and features. (1) Pure carbon, (2) Optimal longer length (3) Inlet flared orifice, (4) Full 90° leaflet opening, (5) Stasis-free pivots, (6) Two-point leaflet closure (with permission from On-X Life Technologies, Inc., Austin, Texas, USA)

American and European studies, On-X valves have performed favorably compared to other MHVs.[2-6]

Most recently, in a 5-year prospective observational study, 737 patients who underwent On-X valve replacement in aortic and/or mitral positions were maintained at an INR of 2.0–2.5 for aortic valve replacements (AVR) and 2.0–3.0 for mitral valve replacements (MVR). The results showed a 5-year freedom from major thromboembolism of 96.5% for AVR and 97.7% for MVR and from hemorrhage of 93.6% for AVR and 95.7% for MVR. Thromboembolism and hemorrhage were seen only when there was a deviation in the desired INR ranges.[7]

In another study, clinical performance of the On-X valves was compared with the Carbomedics and Medtronic Hall valves (Medtronic, Inc., Minneapolis, MN, USA) in the challenging setting of a Third World population. Target INR was 1.5–2.5 to minimize bleeding, with several patients receiving either no or incomplete anticoagulation coverage. This study showed that in the aortic position, there were no significant differences in thromboembolic complications among the three valves; however in the mitral position, both Medtronic Hall and On-X valves performed favorably as compared to the Carbomedics valve (Carbomedics Inc., Austin, TX, USA).[14]

Anticoagulation for mechanical and tissue valves versus On-X valves

According to current AHA guidelines, patients with mechanical and tissue valves should be anticoagulated for 3 months postoperatively for an INR between 2.5 and 3.5. While biological valve patients may be switched over to aspirin after that, those with MHVs should be continued on warfarin to maintain INR levels of 2.0–3.0 for low-risk AVR patients without risk of thromboembolism and 2.5–3.5 for all MVR patients and high-risk AVR patients.[15]

At this time, no standard INR ranges to prevent thromboembolism are recommended for On-X valves. The Prospective Randomized On-X Valve Reduced Anticoagulation Clinical Trial is presently underway to examine whether a lower level of anticoagulation may be acceptable.[16] In the protocol, all patients will receive standard anticoagulation therapy for the first 3 months followed by aspirin 325 mg/day and clopidogrel 75 mg/day for low-risk AVR; warfarin to maintain INR of 1.5–2.0 paired with aspirin 81 mg/day for high-risk AVR; and warfarin to maintain INR of 2.0–2.5 along with aspirin 81 mg/day for all MVRs. Results of the phase I study involving high-risk AVRs showed reduced frequency of minor and major bleeding events without increased risk of

thromboembolism in the test group receiving warfarin to maintain INR of 1.5–2.0 and low-dose aspirin therapy.[16]

Retrospective studies have shown that anticoagulation has been safely held for 1–2 weeks in MHV patients with intracranial hemorrhages or ischemic strokes who are at a very high-risk for worsening of hemorrhage or conversion to a hemorrhagic stroke.[17,18] However, our patient remained off any type of anticoagulation for several months without any clinical evidence of valve thrombosis or embolism. While we do not endorse defying those recommendations, based on recent data that have suggested lower thrombogenicity of On-X valves and the absence of thromboembolism in our patient, it may be possible to accept lower anticogulation levels in those at a very high-risk of bleeding. In the future, the On-X valve could well become the valve of choice for such patients; however, further randomized trials are needed to determine the safety and efficacy of maintaining lower anticoagulation levels.

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