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Thrombus Formation Following Transcatheter Aortic Valve Replacement

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ABSTRACT

OBJECTIVES This paper reviews the published data and reports 3 cases of thrombosis involving CoreValve (Medtronic, Minneapolis, Minnesota) and 1 involving Edward Sapien (Edwards Lifesciences, Irvine, California) devices. Three of these cases had pathological findings at autopsy.

BACKGROUND Only a limited number of cases of valve dysfunction with rapid increase of transvalvular aortic gradients or aortic insufficiency post-transcatheter aortic valve replacement (TAVR) have been described. This nonstructural valvular dysfunction has been presumed to be because of early pannus formation or thrombosis.

METHODS Through reviews of the published reports and 4 clinical cases, pathological and clinical findings of early valve thrombosis are examined to elucidate methods for recognition and identifying potential causes and treatments.

RESULTS This paper presents 4 cases, 2 of which had increasing gradients post-TAVR. All 3 pathology cases showed presence of a valve thrombosis in at least 2 TAV leaflets on autopsy, but were not visualized by transthoracic echocardiogram or transesophageal echocardiogram. One case was medically treated with oral anti coagulation with normalization of gradients. The consequence of valve thrombosis in all 3 pathology patients either directly or indirectly played a role in their early demise. At least 18 case reports of early valve thrombosis have been published. In 12 of these cases, the early treatment with anticoagulation therapy resolved the thrombus formation and normalized aortic pressures gradients successfully.

CONCLUSIONS These 4 cases elucidate the occurrence of valve thrombosis post-TAVR. Consideration should be given to treatment with dual antiplatelet therapy and oral anticoagulation in patients post-TAVR with increasing mean pressure gradients and maximum aortic valve velocity. Further research should be conducted to create guidelines for antithrombotic therapy following TAVR procedure. (J Am Coll Cardiol Intv 2015;8:728–39) © 2015 by the American College of Cardiology Foundation.

Calcific aortic stenosis (AS) remains the most prevalent valvular disease in the elderly population, and the prevalence of AS continues to grow as our population ages (1–3). Transcatheter aortic valve replacement (TAVR) has become the therapy of choice for patients with severe AS clinically deemed to be at high risk or considered nonsurgical for conventional surgical aortic

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valve replacement (SAVR) (1,4–10). Although limited TAVR procedures to date have shown a similar rate of failure to those individuals treated with surgical aortic valve (11–14). However, there has been insufficient time to track full outcomes of TAVR procedures (≥5 years) due to the introduction and approval of this procedure spanning just over a decade.

Only a limited number of cases of early valvular dysfunction with rapid increase of transvalvular aortic gradients or aortic insufficiency (AI) have been described (15–17). These valve failures have been presumed to be because of either early pannus formation or thrombosis. This paper reviews the published data and reports 4 additional cases, of which 3 had further autopsy pathology reports. The first patient treated with a CoreValve bioprosthesis (Medtronic, Inc., Minneapolis, Minnesota) manifested with early post-procedure elevation in transvalvular gradient and insufficiency, requiring treatment with a second valve-in-valve TAVR (**Figure 1**). In 2 other patients, valve failure was noted at autopsy. The patient that underwent the valve-in-valve procedure died 1 month after the procedure, and an autopsy was performed that elucidates the mechanisms of early valvular failure, whereas the other 2 died 48 days (Sapien, Edwards Lifesciences, Irvine, California) and 15 days (CoreValve) after the procedure. The last case had post-TAVR severe AS 10 months following implantation (CoreValve) that was treated medically with oral anticoagulation.

CASE SERIES

CASE 1. Initial TAVR procedure. A 68-year-old woman presented with symptomatic severe AS, with a previous medical history of congestive heart failure, moderate chronic obstructive pulmonary disease (COPD), stage IV chronic kidney disease, chronic iron deficiency anemia, and a New York Heart Association (NYHA) functional class III. The patient had been deemed inoperable by 4 cardiac surgeons because of a calcified ascending aortic root. The patient's screening transthoracic echocardiogram (TTE) revealed severe AS with a calculated mean pressure gradient (P_{mean}) of 43.5 mm Hg, a maximum aortic valve velocity (V_{max}) of 4.3 m/s, and an aortic valve area (AVA) of 0.4 cm^2. Her calculated Society of Thoracic Surgeons (STS) mortality score was 4%, and her EuroSCORE (European System for Cardiac Operative Risk Evaluation) was 3.5%. There were no unusual findings regarding the aortic root's characteristics, with normal size sinus of Valsalva (SOV), that would predispose to a thrombotic setting. Under general anesthesia, she underwent a successful TAVR, with a 26-mm CoreValve bioprosthesis implanted through a left subclavian approach due to severe peripheral vascular disease. The valve was mounted by usual characteristics and deployed by fluoroscopy guidance on the first attempt with an implantation depth of 8 mm. There was no evidence of AI and post-dilation was not considered necessary. On follow-up TTE, there was evidence of mild AI.

Post-TAVR TTE measurements revealed a P_{mean} of 16 mm Hg, a V_{max} of 2.8 m/s, and an AVA of 1.3 cm^2. The patient had a 5-day hospital stay in which she had worsening anemia, with a hemoglobin decrease from 11.9 mg/dl to 8.6 mg/dl, requiring a transfusion of 2 units of packed red blood cells. She also developed transient thrombocytopenia, with a platelet count of 6×10^3 platelets/μl. A possible heparin-induced thrombocytopenia was suspected, so heparin and clopidogrel were discontinued. Platelet factor 4 was ordered, and the results were negative. On discharge, the TTE values were in normal ranges with a P_{mean} of 15.1 mm Hg, a V_{max} of 2.7 m/s, and an AVA of 1.3 cm^2. The patient was discharged home on antiplatelet monotherapy of aspirin 81 mg/day due to her bleeding risk.

1-month follow-up. At 1-month follow-up post-TAVR, the patient referred to be "feeling better," but still required oxygen support because of her COPD. Her NYHA functional class improved from III to II. Her cardiovascular physical examination revealed an aortic outflow murmur, with preserved second heart sounds and no indication of AI. TTE revealed an increase in P_{mean} to 43 mm Hg, as well as an increase in V_{max} to 4.3 m/s, and a decrease of the AVA to 0.5 cm^2. Mild perivalvular AI was seen on TTE. Although a high transvalvular velocity was documented, the clinical presentations showed improvement and the physical examination did not support the echocardiographic findings. Because the patient's symptoms were improved, she was followed up clinically and continued on the same antiplatelet monotherapy.

6-month follow-up. At 6-month follow-up, there was worsening of the NYHA functional class to III. The patient's TTE revealed a P_{mean} of 50 mm Hg, a V_{max} of 4.6 m/s, and an AVA of 0.6 cm^2, with moderate AI. The patient was evaluated with a cardiac catheterization that confirmed moderate to severe AS of the bioprosthesis as well as a 2+ AI with a central jet. The CoreValve dysfunction was presumed to be from early pannus formation. On the basis of hemodynamic evidence of early valve failure, it was decided to perform a valve in valve TAVR.

ABBREVIATIONS AND ACRONYMS

AI = aortic insufficiency

AS = aortic stenosis

AVA = aortic valve area

COPD = chronic obstructive pulmonary disease

NYHA = New York Heart Association

P_{mean} = mean pressure gradient

SAVR = surgical aortic valve replacement

SOV = sinus of Valsalva

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

TTE = transthoracic echocardiogram

V_{max} = maximum aortic valve velocity