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Valve-in-Valve Transcatheter Valve Implantation in the Non-Aortic Position

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Abstract

Background—Transcatheter valve-in-valve (VIV) procedures are an alternative to standard surgical valve replacement in high risk patients.

Methods—Cases in which a commercially approved transcatheter aortic valve replacement (TAVR) device was used for a non-aortic VIV procedure between November 2013 and September 2015 are reviewed. Clinical, echocardiographic, and procedural details, patient survival, and symptom severity by NYHA class at follow-up were assessed.

Results—All patients were heart-team determined high-risk for conventional redo surgery (mean STS PROM = $6.8 \pm 2.2\%$). Five patients underwent VIV replacement in the non-aortic position, 4 for bioprosthetic mitral valve dysfunction and one for bioprosthetic tricuspid valve dysfunction. Bioprosthetic failure was due to stenosis in 3 patients and regurgitation in 2 others. A balloon-expandable device was used for all patients (Edwards Lifesciences, Irvine, CA). Transcatheter VIV replacement was accomplished by the transapical (mitral) and transfemoral venous (tricuspid) approaches. Median post-operative length of stay was 5 days (range 3-12). No deaths occurred at a mean follow-up of 21 months. NYHA class at follow-up decreased from class IV at baseline to class I or II for all patients. No paravalvular leaks greater than trivial were encountered. Median mean gradient following mitral replacement was 6.5 mmHg (range 6-13 mmHg), and following tricuspid replacement was 4 mmHg. Post-operative complications included hematuria, epistaxis, acute kidney injury, and atrial fibrillation.

Conclusions—Transcatheter VIV implantation in the non-aortic position for dysfunctional bioprostheses can be performed safely with favorable clinical outcomes using a balloon expandable TAVR device.

INTRODUCTION

As patient longevity improves, bioprosthetic degeneration frequently requires repeat surgical valve replacement. An estimated 20-30% of bioprosthetic valves fail at 10 years and 50%

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fail at 15 years (1). Since many of these patients have progressed to high surgical risk by the time of valve failure, transcatheter heart valve (THV) replacement has provided a less invasive alternative in this setting (2, 3). This valve-in-valve (VIV) technique for degenerative bioprostheses has shown promising results particularly in patients with failed aortic valves. The broader application to the replacement of bioprosthetic valves in the non-aortic position has been suggested, however; this off-label approach warrants careful study in order to optimize patient selection and demonstrate feasibility with the current technology. We report our experience using transcatheter valve-in-valve (VIV) procedures in the mitral and tricuspid positions.

MATERIALS AND METHODS

Patients

Institutional Review Board approval was obtained for this retrospective single-cohort review. Patients who underwent transcatheter VIV implantation in the non-aortic position between November 2013 and September 2015 were included in the study. Patients were previously identified as high operative risk by a multidisciplinary team including a cardiothoracic surgeon and interventional cardiologist. High risk characteristics included but were not limited to advanced age, multiple or major prior cardiothoracic surgery, chronic obstructive pulmonary disease, pulmonary hypertension, Jehovah's Witness status with refusal of allogeneic blood products, and frailty. Patient demographics and comorbidities were obtained from the medical record. Operative reports and radiological images were reviewed for procedural and implant details. Hospital course and outcomes during a variable follow-up period were included in the review. As a descriptive study, standard non-comparative statistics were used to illustrate our results.

Techniques

The nature of VIV implantation in the non-aortic position was discussed with each patient as part of the informed consent process. All procedures were performed in a hybrid operating room under general anesthesia.

A representative outline of our transcatheter mitral valve replacements began with femoral arterial access with a 5 French catheter. Bilateral femoral venous access was achieved for placement of a temporary pacing wire and for potential femoral vessel cannula placement in the event of a need for expeditious cardiopulmonary bypass. A small left anterior thoracotomy was used to facilitate the transapical approach. The left ventricular (LV) apex was palpated, pledgeted mattress stay sutures placed, and under transesophageal echocardiographic (TEE) guidance, a 7 Fr sheath was placed in the LV apex and the mitral prosthesis was crossed using a Berenstein catheter (AngioDynamics, Queensbury, NY) and J-tipped 0.035" Glidewire (Terumo Interventional Systems, Somerset, NJ). The Berenstein catheter was advanced into the left atrium and the Glidewire was exchanged for a 0.035" × 145" extra-stiff J-tipped guidewire. This guidewire was used to insert the Edwards delivery sheath. Balloon valvuloplasty was performed first during rapid ventricular pacing at a rate of 180 beats per minute. The Edwards SAPIEN or SAPIEN XT (Edwards Lifesciences, Irvine,

CA) valves were used for mitral replacement. Both valve deployment and removal of the intramyocardial sheath were performed under rapid pacing.

Transcatheter tricuspid valve implantation began with bilateral femoral venous access. A balloon tipped catheter was used to cross the tricuspid valve prosthesis and was advanced into the pulmonary artery. A 0.035" × 260" extra stiff J-tipped guidewire was placed into the pulmonary artery. The Edwards 20 Fr sheath was inserted into the right femoral vein to the level of the hepatic veins. Balloon tricuspid valvuloplasty was performed prior to deployment of the valve. The Edwards SAPIEN XT was deployed during rapid ventricular pacing at a rate of 180 beats per minute.

All procedures concluded with assessment of valvular flow characteristics and hemodynamics immediately following implantation. Valve position was assessed using real-time fluoroscopy and TEE. It is our practice to then prescribe 3 months of oral dual antiplatelet therapy for these transcatheter valves (aspirin 81 mg, clopidogrel 75 mg). If a patient is chronically anticoagulated with a vitamin K antagonist or novel agent, we generally prescribe dual antiplatelet therapy for one week, followed by resumption of their home anticoagulation regimen.

RESULTS

Five patients were identified in this cohort. Four underwent mitral valve replacement and one underwent tricuspid valve replacement. Bioprosthesis failure was due to stenosis in three patients and regurgitation in two patients. Median age was 79 years (range 65-85 years) with estimated operative risk range of 5-10% according to the Society of Thoracic Surgeons Risk Score. All patients were New York Heart Association (NYHA) class IV prior to THV replacement. The median time interval between the most recent surgical valve replacement and THV replacement was 12 years (range 10-16 years). THV implantation was successfully performed in all five patients. A brief synopsis of each patient is described below and summarized in Table 1.

Patient #1 is a 71 year old female who had undergone mitral valve replacement (MVR) (27 mm CE bioprosthetic) (Edwards Lifesciences, Irvine, CA) for rheumatic mitral valve disease and left atrial appendage ligation 12 years prior to transcatheter mitral valve implantation. She was deemed to be high risk by the heart team for redo operation given prior cardiac surgery, pulmonary hypertension, and Jehovah's Witness status (STS risk 5%). Additional comorbidities included COPD and moderate aortic insufficiency. She originally presented with dyspnea on exertion, orthopnea, and fatigue, and had been hospitalized twice in the year prior to THV for heart failure symptoms and was thus evaluated for THV implantation. Pre-operative echocardiography demonstrated severe pulmonary insufficiency (PI), moderate aortic insufficiency (AI), severe mitral stenosis (MS) (peak gradient 21 mmHg, mean gradient 14 mmHg) with mild mitral regurgitation (MR), and an EF > 55% with a dilated, hypokinetic right ventricular (RV). Following thoracotomy and palpation of the LV apex, persistent ventricular tachycardia prompted the need for cardiopulmonary bypass. The procedure continued with transapical deployment of a 26 mm Edwards SAPIEN valve in the mitral position and weaning from bypass. Post-operatively, the patient sustained an acute

kidney injury (AKI) not requiring renal replacement therapy as well as atrial fibrillation treated with amiodarone resulting in chemical cardioversion to sinus rhythm. Her post-operative length of stay was 12 days. At most recent follow-up of 30 months the patient remains as NYHA class I. Post-operative echo the following day revealed a peak gradient of 11 mmHg and a mean gradient of 6 mmHg, and EF 50%.

Patient #2 is a 65 year old female with a history of Holt-Oram syndrome. Twenty years prior to THV she had undergone atrial septal defect repair complicated by bradycardia requiring a permanent pacemaker with epicardial ventricular leads. Soon after she underwent tricuspid annuloplasty followed by eventual tricuspid valve replacement with a 29 mm CE bioprosthetic 13 years prior to THV. This operation also included a repair of the sinus venosus defect, repair of partially anomalous pulmonary venous return, reopening of a coronary sinus occlusion, and MAZE procedure. Years later she underwent tricuspid balloon valvuloplasty but continued to experience dyspnea on exertion and orthopnea resulting in one hospital admission within the year prior to THV. Pre-operative echocardiography was notable for mild MR, severe TR and TS (peak gradient 7 mmHg, mean gradient 4 mmHg), EF > 55% and normal RV function. Right heart catheterization demonstrated pulmonary arterial pressure (PAP) of 55/27 mmHg (mean 36 mmHg). Additional medical history included chronic atrial fibrillation and persistent left SVC. Her STS risk was 5% although she was determined to be high risk for redo surgery by the heart team given her history of complex congenital heart disease, multiple prior cardiac surgeries, and hostile mediastinum. Pre-operative cross sectional imaging facilitated adequate sizing of the implant and operative planning (Figure 1). The femoral vein was used for access to the tricuspid valve. Following initial balloon valvuloplasty, the tricuspid valve was traversed and a 29 mm Edwards SAPIEN XT was deployed in the tricuspid position (Figure 2). The procedure was well-tolerated without any post-operative complications. The patient was discharged on post-operative day 3 and was NYHA class I at a follow-up of 9 months. Follow-up echocardiography five months after surgery was notable for mild MR, resolution of TR with peak 15 mmHg and mean 8 mmHg, EF > 55% and moderate RV dysfunction.

Patient #3 is a 79 year old female who underwent MVR with a 25 mm Baxter Porcine valve (Baxter Healthcare Corp, Irvine, CA) for rheumatic mitral valve disease 16 years prior to THV. Additional medical history included partial left pneumonectomy for bronchiectasis, chronic atrial fibrillation, chronic obstructive pulmonary disease, and transient ischemic attack. The patient was deemed high surgical risk due to advanced age of 79, significant prior thoracic surgery, and frailty (STS risk 10%). The patient originally presented with dyspnea and fatigue had been hospitalized twice in the year prior to THV for worsening symptoms. Pre-operative cross sectional imaging facilitated valve sizing and operative planning for the transapical approach (Figure 3). Pre-operative echocardiography demonstrated trace AI, mild PI, severe MR and mild MS (peak 21 mmHg and mean 7 mmHg), moderate TR, EF > 55% and mild RV dysfunction. Right heart catheterization showed PAP of 75/18 mmHg (mean 40 mmHg). Femoral arterial and venous access was used for the procedure. After traversing the mitral valve a 23 mm Edwards SAPIEN XT valve was deployed (Figure 4). The patient tolerated the procedure well. There were no significant complications although the patient did have post-operative nausea and anxiety attributed to analgesic medications. The patient was discharged on post-operative day 5 and

was NYHA class I at a follow-up of 9 months. Post-operative echocardiography in the month following surgery was notable for mild TR, mild PI, trivial MR (peak gradient 24 mmHg, mean gradient 13 mmHg), EF > 55% and mild RV dysfunction (Figure 5).

Patient #4 is an 85 year old male who underwent MVR (25 mm CE Perimount) (Edwards Lifesciences, Irvine, CA) 10 years prior to THV as well as a bioprosthetic aortic valve replacement with redo sternotomy in the interim. Additional history included atrial fibrillation, abdominal aortic aneurysm treated with an endovascular stent graft, coronary stenting, hypertension, hyperlipidemia, permanent pacemaker implantation for complete heart block, and moderate to severe pulmonary hypertension. The patient originally presented with worsening dyspnea. Pre-operative echocardiography was notable for mild MR and severe MS (peak gradient 18 mmHg, mean gradient 13 mmHg), EF 45-55% and mild RV dysfunction. Right heart catheterization showed PAP 68/30 mmHg (mean 45 mmHg). The patient was deemed high risk due to advanced age of 85 and two prior cardiac surgeries (STS risk 8%). Femoral arterial and venous access was used for the procedure. A 26 mm Edwards SAPIEN valve was deployed in the mitral position using the transapical approach. Post-operative complications were limited to hematuria which required urologic consultation and continuous bladder irrigation. Post-operative length of stay was 5 days and the patient was found to be NYHA class II at a follow-up of 25 months. Post-operative echocardiography 15 months after surgery was notable for mild AI, a peak mitral gradient of 15 and mean gradient 7 mmHg, moderate TR, mild PI, EF > 55% and mild RV dysfunction.

Patient #5 is a 79 year old male who underwent MVR (33 mm Mosaic) (Medtronic, Minneapolis, MN) and single-vessel coronary artery bypass grafting 10 years prior to THV. Additional comorbidities included hypertension, hyperlipidemia, chronic atrial fibrillation, deep vein thrombosis, and pulmonary embolism. The patient was determined to be high risk by the heart team given his prior cardiac surgery, pulmonary hypertension, and pulmonary thromboembolic disease (STS risk 6%). He originally presented with worsening dyspnea, orthopnea, and mild weight gain and was admitted to the hospital one week prior to THV for optimization given recent worsening of heart failure symptoms. Pre-operative echocardiography was notable for trace PI, thickened, flail, calcified mitral leaflets with severe MR with moderate MS (peak 18 mmHg, mean 8 mmHg), EF 45-55% and severe RV dysfunction. Right heart catheterization showed PAP 82/42 mmHg (mean 60 mmHg). Femoral arterial and venous access was used for the procedure. The mitral valve was accessed using the transapical approach and a 29 mm Edwards SAPIEN XT valve was deployed in the mitral position. The patient tolerated the procedure well. Post-operative epistaxis was encountered which was treated conservatively. The patient was discharged on post-operative day 5 and was in NYHA class II at a follow-up of 21 months. Post-operative echocardiography the month of surgery showed a peak gradient 11 and mean gradient 6 mmHg, trivial TR, mild PI, EF 50% and moderate RV dysfunction.

DISCUSSION

This series of five patients represents the successful adaptation of THV replacement for bioprosthetic valves in the non-aortic position. The balloon-expandable Edwards SAPIEN platform was chosen due to a lower profile more suitable for the non-aortic position. Despite

a variety of complications, these patients all left the hospital with significantly improved NYHA status maintained through a median follow-up of 21 months and without lasting or permanent morbidity at follow-up. As such, this report demonstrates the feasibility of the off-label use of current transcatheter implantable valves in the non-aortic position.

The current literature emphasizes the use of aortic VIV procedures and few studies report their experience with non-aortic techniques. The largest series by Cheung et al includes 23 patients undergoing transcatheter mitral VIV replacement. Valve deployment was successful in all cases with 0% 30-day mortality and only 9.6% long-term mortality at a mean follow-up of 25.1 months (4). The transapical approach was used in this cohort with 10% valve upsizing from the manufacturer ID. This series was a follow-up from earlier experiences whose outcomes now reported an early stroke attributed to thrombus at the LV apex (5, 6). This patient recovered from the insult but succumbed to death by pneumonia-related sepsis. LV apex complications have been seen in other series as well, some requiring re-thoracotomy and resuscitation (7). Further success was reported in a case series of seven patients undergoing mitral VIV replacement with the Edwards SAPIEN valve. Only one death due to pneumonia on post-operative day 34 was reported, with no other deaths at follow-up. NYHA class was improved from III to I/II (8). The most comprehensive review to date is that of Paradis et al which compiles results from several mitral VIV procedures. Additional reports on the use of valve-in-ring procedures were also included in this study, demonstrating similar procedural success although with higher long-term mortality (1).

The use of THV replacement in additional positions has also been described. In a series of 26 high risk patients, adequate valve performance and a low 30-day mortality of 4.2% was reported (9). Of these patients, there were 10 aortic, 7 mitral, 6 pulmonary, and 1 tricuspid VIV procedures were performed. The volume of reports pertaining to tricuspid and pulmonary valves is exceedingly low. Alternative approaches have also been described with less enthusiasm, such as the trans-septal mitral valve approach, which proved to be technically challenging despite favorable outcomes (10).

Non-aortic transcatheter VIV implantation is a relatively uncommon experience among individual centers. These TAVR devices were used “off-label” for VIV procedures before FDA approval for VIV AVR procedures. Use of TAVR devices for dysfunctional bioprosthetic AVRs with either the SAPIEN XT or CoreValve Evolut device are now approved by the FDA, but use in the non-aortic position remains off-label. Direct comparison is lacking throughout the literature but we expect this to change as the population of aging patients with failed bioprosthetic valves increases. In addition to the outcomes of non-aortic THV replacement, the technical aspects are also worth investigation. To date we have utilized the Edwards SAPIEN or SAPIEN XT valve which is intended for use in the aortic position only. Tailoring these valves to each non-aortic position will be critical for minimizing the sizing discrepancies inherent to VIV replacement. Bapat elaborates on this challenge by accounting for leaflet deformation using various methods in relation to the stent ID. Although modest oversizing has allowed for better fitting valves, incomplete deployment was a considerable hazard (11). Among factors that would lead us to consider a patient not to be a VIV candidate in the non-aortic position, at present we include a prosthetic valve ID for which a suitable THV device is not available, echocardiographic

evidence of an intra-cardiac mass, thrombus, or vegetation, and standard exclusion criteria for TAVR such as presence of non-cardiac comorbidities that would preclude any benefit with THV replacement.

In conclusion, THV implantation for patients with failed prior non-aortic bioprostheses is a viable alternative therapy for patients at high risk for reoperation. Increased use of this treatment strategy will facilitate future clinical comparisons and assist in the development and differentiation of further transcatheter heart valve technologies.

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Figure 1.
Preoperative planar (left) and sagittal (right) views of the tricuspid bioprosthesis.

Figure 2. Transcatheter tricuspid valve implantation over pre-existing bioprosthetic valve. (a) alignment of new prosthetic inside the tricuspid orifice, (b) initial balloon expansion of the implant, (c) full balloon expansion of the implant, and (d) final positioning of the valve-in-valve implant.

Figure 3.
Preoperative planar (left) and coronal (right) views of the mitral bioprosthetic valve.

Figure 4.

Transcatheter mitral valve implantation over pre-existing bioprosthesis. (a) alignment of new prosthetic inside the mitral orifice, (b) initial balloon expansion of the implant, (c) full balloon expansion of the implant, and (d) final positioning of the valve-in-valve implant.

Figure 5.

(a) Intra-operative TEE images prior to implantation demonstrating severe mitral regurgitation and (b) post-implantation of SAPIEN valve demonstrating trivial residual mitral regurgitation.

Table 1**Patient and Valve Characteristics**

Patient ID	1	2	3	4	5
Age (years)	71	65	79	85	79
Degenerative Valve	Mitral	Tricuspid	Mitral	Mitral	Mitral
Initial Bioprosthetic Valve	CE Perimount	CE Perimount	Baxter Porcine	CE Perimount Plus	Medtronic Mosaic
Labeled ED (mm)	27	29	25	25	33
Labeled ID (mm)	25	27	23	23	28
Mechanism of Failure	Stenosis	Stenosis	Regurgitation	Stenosis	Regurgitation
Pre-Op Echo					
Valvular	Mild MR, Severe MS	Severe TR, Severe TS	Severe MR, Mild MS	Mild MR, Severe MS	Severe MR, Moderate MS
Peak Gradient (mmHg)	21	13	24	32	31
Mean Gradient (mmHg)	14	8	11	23	11
EF (%)	>55	>55	>55	>55	50
Mean Annulus Diameter (mm)	24.2	23.8	20.4	21.2	27.4
Valve Area (cm ²)		4.44	3.26	3.53	5.90
STS Risk Score	5%	5%	10%	8%	6%
NYHA Class at Admission	IV	IV	IV	IV	IV
Interval to THV (years)	12	13	16	10	10
Type of THV	SAPIEN	SAPIEN XT	SAPIEN XT	SAPIEN	SAPIEN XT
THV Size (mm)	26	29	23	26	29
Post-Op Echo					
Valvular	Mild MR, No MS	No TR, No TS	No MR	Indeterminate	Indeterminate
Peak Gradient (mmHg)	11	7	24	15	11
Mean Gradient (mmHg)	6	4	13	7	6
EF (%)	50	45	>55	>55	50
Paravalvular Leak	Trace	None	Trace	Trivial	Trivial
Complications	AFIB, AKI	None	Nausea	Hematuria	Epistaxis
Length of Stay (days)	12	3	5	5	5
Follow-Up (months)	30	9	9	25	21
NYHA Class at Discharge	I	I	I	II	II

ED = external diameter, ID = internal diameter, EF = ejection fraction, STS = Society of Thoracic Surgeons, NYHA = New York Heart Association, THV = transcatheter heart valve, MR = mitral regurgitation, MS = mitral stenosis, TR = tricuspid regurgitation, TS = tricuspid stenosis, AFIB = atrial fibrillation, AKI = acute kidney injury