Outcome of Patients Having Transcatheter Mitral Valve Implantation for the Treatment of Degenerated Mitral Bioprostheses

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Transcatheter mitral valve implantation (TMVI) is at various levels of preclinical investigation and has proven to be more challenging than transcatheter aortic valve implantation due to more complex anatomy. The purpose of this study is to evaluate the short-term and long-term outcomes of high-risk patients who underwent TMVI for degenerated mitral bioprostheses. In this retrospective, observational study, we reviewed data on the first 26 patients with previous surgical mitral valve replacement or repair with annular ring that underwent TMVI using the balloon-expandable heart-valve system at our institution from 2014 to 2019. We reviewed pre/postprocedure echocardiographic data, in-hospital, 30-day data and 1-year outcomes. The indication for TMVI was mitral regurgitation (MR) in 9 patients, mitral stenosis in 9 patients and mixed mitral disease in 8 patients. There was a 100% device implantation success rate and a 96% in-hospital survival rate. Survival was 96% at 30 days and 85% at 1 year. Mean mitral gradient (MMG) improved postprocedure (13.3 mm Hg to 6.8 mm Hg, p <0.0001) and was sustained at 1 year (13.3 mm Hg to 7.2 mm Hg, p <0.0001). MR grade improved postprocedure (3+ to 1+, p <0.0001) and was sustained at 1 year (3+ to 0, p <0.0001). Additionally there was significant 30-day and 1-year improvements in patients' Kansas City Cardiomyopathy Questionnaire score after TMVI (47.8 to 75.7 to 84.0, p = <0.0001). In conclusion, our early experience with treatment of degenerated mitral bioprostheses using TMVI in high-risk patients resulted in significant short-term and sustained long-term improvements in mean mitral gradient, MR and heart failure symptoms. **(Am J Cardiol 2020;131:99−103)**

The last 2 decades have seen the unprecedented emergence of transcatheter therapies for the treatment of valvular heart disease. In 2002 the first transcatheter aortic valve implantation (TAVI) was performed.[1] It represented a breakthrough in the treatment of aortic stenosis. In the years that followed, technologic advancements and refinements have led to an exponential use of TAVI for multiple patient populations.[2-5] As the landscape of interventional cardiology evolves, there is a renewed focus on the treatment of mitral valve disease using transcatheter therapies. Clinical trials are ongoing, designed to evaluate several transcatheter heart valve devices for the treatment of mitral regurgitation (MR) with transcatheter mitral valve implantation (TMVI).[6,7] Registry data suggest that the use of TAVI valves in the mitral position for treatment of failed bioprostheses can be successful as anticipation builds for completion of ongoing TMVI trials.[8,9] Our heart team has performed >1,800 TAVIs since 2012. Since 2014, we have performed 26 TMVIs using the balloon-expandable heart-valve system for the treatment of degenerated bioprostheses. The purpose of our study was to contribute a real world, experienced single center perspective of TMVI with long-term follow-up, to the literature.

Methods

This was a retrospective, observational study of the first 26 patients with prior surgical mitral valve replacement or mitral valve repair with annular ring that underwent TMVI using the second-generation balloon-expandable SAPIEN XT (Edwards Lifesciences, Irvine, CA) or third-generation balloon-expandable SAPIEN 3 heart-valve system (Edwards Lifesciences, Irvine, CA) at our institution from 2014 to 2019. Data were collected regarding demographic information, co-morbidities, mitral valve baseline criteria, procedural details, outcomes such as mortality and morbidity including in-hospital and at 1 year, and quality of life. Patients had either severe bioprosthetic MR, severe bioprosthetic mitral stenosis or mixed mitral disease. All patients had New York Heart Association functional class IV symptoms at time of TMVI. This study was HIPAA compliant and reviewed by our institutional review board and deemed exempt. Written informed consent was obtained from all patients for the TMVI prior to the procedure. Study data were collected and managed using Research Electronic Data Capture, a secure electronic data capture tool hosted at our institution.[10] The TMVI procedure was performed in a sterile hybrid cardiac catheterization laboratory and patients were placed under general anesthesia. Access was

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obtained through either the transfemoral vein with transesophageal echocardiographic-guided transseptal puncture or percutaneous transapical approach. Initial literature described TMVI through the transapical approach, which we utilized early.[11] Eventually this was replaced by the transseptal approach in our institution. For patients who underwent transfemoral vein TMVI with transseptal puncture, venous access was obtained using a Swartz sheath. This was then switched out for an Agilis sheath after transseptal puncture. A confida wire was then placed anterograde into the left ventricle. A wide septostomy was then performed using an Atlas balloon. The valve was then crimped onto the delivery system and deployed using rapid pacing. Transesophageal echocardiogram was used to confirm a well-sealed bioprosthetic valve. The guidewire and delivery system were removed and venous hemostasis was achieved using a figure-of-eight stitch. For patients who underwent transapical TMVI, a left anterior thoracotomy was performed. The cardiothoracic surgeon then placed 2 full-thickness concentric 2-0 Prolene pursestring sutures with intervening pledgets. The apex was then punctured with a 16-gauge Angiocath. An extra stiff Amplatzer guidewire with a soft tip as placed through the apex. The valve was then crimped onto the delivery system and deployed using rapid pacing. Transesophageal echocardiogram was used to confirm a well-sealed bioprosthetic valve. The guidewire and delivery system were removed and using ventricular pacing the 2 pursestring sutures were tied down. This resulted in excellent hemostasis of the apex. The subcutaneous tissues were irrigated with warm saline and closed in a multilayer fashion. Dermabond followed by dry dressing was then applied. All patients had deployment of either the balloon-expandable Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA) valve or the balloon-expandable Edwards SAPIEN 3 (Edwards Lifesciences, Irvine, CA) valve. Access and valve sizing was dependent on operator discretion after thorough review of preprocedure multidetector computed tomography and patient charts. All patients underwent a preprocedure retrospective electrocardiogram (ECG)-gated chest and nongated abdomen pelvis scan using a Siemens Somatom Definition AS 128-slice multidetector computed tomography Scanner prior to TMVI. Image reconstruction and analysis was done offline on a Syngo.via Workstation (Siemens Healthcare, GmbH, Germany). Multidetector computed tomography was performed to aid in prosthesis sizing. Additionally, all patients underwent careful assessment of the mitral valve using preprocedure transthoracic echocardiogram and transesophageal echocardiogram. All patients underwent postprocedure transthoracic echocardiogram 1 to 3 days after TMVI. Follow-up transthoracic echocardiogram was carried out during prescheduled outpatient clinic visits at 30 days and 1 year. Results were interpreted by experienced level 3 echocardiographers, who were not involved in the preprocedure evaluations. The primary outcomes of interest were in-hospital, 30-day and 1-year all-cause mortality. Additional outcomes of interest were procedural complications rates of postprocedure atrial fibrillation (AF), stroke, new requirements for dialysis, major and minor bleeding, left ventricular outflow tract obstruction. We further evaluated length of stay, in-hospital echocardiographic changes, readmissions at 30 days and 1 year, and at 1 year, changes in Kansas City Cardiomyopathy Questionnaire scores at 30 days and 1 year. Follow-up was carried out during prescheduled outpatient clinic visits or by telephone contact at 30 days and 1 year. In addition, records from referring cardiologists' offices and outside hospitals were obtained when necessary to complete follow-up. Patients' demographic and clinical characteristics were summarized using mean ± standard deviation, and frequency (percent). Comparisons between categorical variables were performed using Wilcoxon signed rank test. Comparisons between continuous variables were performed using 2-sided *t* test. A p value of less than 0.05 was considered statistically significant. All analyses were done using SAS 9.4 (Figure 1).

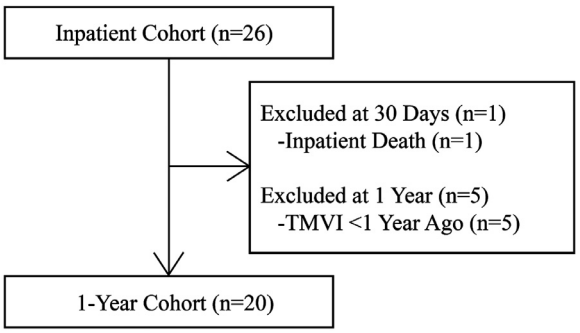

Figure 1. Patients included and excluded in our study.

Results

Our analysis of in-hospital outcomes included all 26 patients. The 26 patients had a mean age of 71.0 ± 11.1 years and were 35% male. The average Society of Thoracic Surgeons risk score for surgical mitral valve replacement was 13% in our population. The Society of Thoracic Surgeons risk score uses an algorithm that is based on the presence of co-morbidities to estimate the 30-day postoperative mortality.[12] The remainder of the patients' baseline clinical characteristics is shown in Table 1. The mean time from prior surgical mitral valve replacement or repair with annular ring to TMVI was 103.1 ± 66.6 months. Of the 26 patients, 20 had prior surgical mitral valve replacement and 6 had prior repair with annular ring. The primary indication for TMVI was bioprosthetic MR in 9 patients, bioprosthetic mitral stenosis in 9 patients and mixed mitral disease in 8 patients (Table 2). TMVI was performed using the balloon-expandable Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA) valve in 7 patients and using the balloon-expandable Edwards SAPIEN 3 (Edwards Lifesciences, Irvine, CA) valve in the remaining 19 patients. TMVI was performed through the transseptal approach in 73% (n = 19) of patients and through the transapical approach in 27% (n = 7) of patients. Preprocedure valvuloplasty was performed in 15% (n = 4) of patients. Procedural data are summarized in Table 3. Our primary outcome of in-hospital mortality occurred in 4% (n = 1) of patients after TMVI. The remaining 25 patients who survived the index hospitalization were included in our 30-day analysis and their mortality was 4% (n = 1). The 1 30-day

Table 1
Baseline characteristics of patients (n = 26)

Variable	
Age (years)	71.0 ± 11.1
Men	9 (35%)
Hypertension	26 (100%)
Body mass index (kg/m^2)	28.1 ± 5.9
Diabetes mellitus	8 (31%)
Insulin dependent	3 (12%)
Atrial fibrillation	18 (69)
Coronary artery disease	10 (39%)
Prior myocardial infarction	4 (15%)
Prior percutaneous coronary intervention	4 (15%)
Prior coronary artery bypass grafting	7 (27%)
Prior cerebrovascular accident	2 (8%)
Peripheral artery disease	5 (19%)
Hostile chest	3 (12%)
Chronic obstructive pulmonary disease	8 (31%)
Home oxygen requirement	1 (4%)
Smoker	1 (4%)
Hemoglobin (g/dl)	11.7 ± 1.8
Baseline creatinine (mg/dl)	1.2 ± 0.7
End stage renal disease on hemodialysis	2 (8%)
B-type natriuretic peptide (pg/ml)	454.2 ± 429.9
Immunosuppressed	7 (27%)

Table 2
Baseline characteristics of mitral valve (n = 26)

Variable	
Time since prior mitral valve surgery (months)	103.1 ± 66.6
Type of prior mitral valve surgery	
Surgical mitral valve replacement	30 (77%)
Surgical mitral valve repair with annular ring	6 (23%)
Indication for TMVI	
Bioprosthetic MR	9 (35%)
Bioprosthetic MS	9 (35%)
Mixed bioprosthetic disease	8 (31%)

Table 3
Procedural metrics (n = 26)

Variable	
TMVI approach	
Transseptal	19 (73%)
Transapical	7 (27%)
Pre-TMVI valvuloplasty	4 (15%)
Procedure time (minutes)	125.7 ± 58.2
Fluoroscopy time (minutes)	34.8 ± 26.5
Contrast volume (ml)	31.0 ± 48.7
Procedural success	26 (100%)

mortality was of a patient who was readmitted for acute on chronic decompensated heart failure with cardiogenic shock refractory to inotropes. Of the 25 patients who survived the index hospitalization, 20 were included in our mortality analysis at 1 year, with 5 not having yet reached 1 year since their TMVI. Their 1-year mortality was 15% (n = 3). The mean intensive care unit length of stay was 56.0 ± 71.8 hours. The mean length of stay was 5.3 ± 5.0 days. In-hospital AF occurred in 0% of patients. In-hospital stroke occurred in 8% (n = 2) of patients. New requirement for dialysis did not occur. Valve Academic Research Consortium-2 minor bleeding occurred in 35% (n = 9) of patients. Left ventricular outflow tract obstruction after valve deployment occurred in 4% (n = 1) of patients. That patient underwent successful emergency alcohol septal ablation with resolution of the left ventricular outflow tract obstruction. In-hospital Valve Academic Research Consortium-2 major bleeding occurred in 12% (n = 3) of patients. The first patient had postprocedural hemothorax, which resolved after thoracentesis and multiple transfusions, ultimately discharged home in stable condition. The second patient was a transfer to our hospital in cardiogenic shock requiring Impella. This patient suffered from significant access site bleeding requiring transfusions ultimately dying on post-procedure day 16. The final patient presented with acute flail leaflet with wide-open MR requiring extracorporeal membranous oxygenation. This patient suffered from significant access site bleeding as well, requiring transfusions but was subsequently discharged home. There was significant 30-day and 1-year improvements in patients' Kansas City Cardiomyopathy Questionnaire score after TMVI (47.8 to 75.7 to 84.0, p = <0.0001), with 24% (n = 6) of patients being readmitted in the 30 days after TMVI and 65% (n = 13) of patients being readmitted in the 1 year after TMVI. There was significant improvement in systolic pulmonary artery pressure post-TMVI (59.8 mm Hg to 49.1 mm Hg, p = 0.0225). There was no 1-year change in EF after TMVI (49% to 44%, p = 0.5197). MR grade improved immediately after TMVI (3+ to 1+, p <0.0001) and these improvements were sustained at 1 year (3+ to 0, p <0.0001). Mean mitral gradient (MMG) improved immediately after TMVI (13.3 mm Hg to 6.8 mm Hg, p <0.0001) and these improvements were sustained at 1 year (13.3 mm Hg to 7.2 mm Hg, p <0.0001; Table 4).

Discussion

The field of interventional cardiology continues to advance toward more complex structural interventions. TAVI has become a revolutionary therapy for a growing

Table 4
Summary of echocardiographic changes (n = 26)

Variable	Pre-TMVI	Post-TMVI	1-year post-TMVI	p value
Baseline left ventricular ejection fraction (percent)	48.6% ± 13.6%	46.1% ± 14.2%	43.7% ± 15.9%	0.5197
Median mitral regurgitation grade (1+, 2+, 3+, or 4+)	3+ (2+, 4+)	1+ (1+, 2+)	0+ (0+, 1+)	<0.0001
Mean mitral gradient (mm Hg)	13.3 ± 6.5	6.8 ± 2.8	7.2 ± 6.3	<0.0001

patient population with worldwide application. The emergence of TAVI has ignited the search for a mitral valve equivalent. There is an enormous unmet need for patients with debilitating chronic MR. Despite the complexities of the mitral valve, development of a safe and effective TMVI device is inevitable and will be a breakthrough in the treatment for patients with inoperable MR. In the interim, many centers have begun using TAVI devices in the mitral position for degenerated mitral bioprostheses (valve or ring).[9,8] The largest publication to date, regarding the use of a TAVI valve for TMVI, was from the 2016 report of the transcatheter valve therapy registry.[9] The reviewed the off label use of the second-generation balloon-expandable SAPIEN XT heart-valve system (Edwards Lifesciences, Irvine, CA) for either TMVI in valve (76%) or TMVI in ring (24%) in 349 patients at high-risk for re-do surgical mitral valve replacement across 98 centers.[9] This patient population had a mean age of 76 years and was predominantly female (61%) with an STS PROM of 11%. In hospital mortality was 7% and at 30 days was 9%, less than the STS PROM of 11%. Postprocedure, only 84% of patients had an echocardiogram, which showed that MR had been reduced to at most mild (1+) in 81% of patients and the MMG was 6 mm Hg. Another subset of 311 patients was reviewed from the transcatheter valve therapy registry. These data demonstrated a reduction in heart failure symptoms in more than 85% of patients and lower mortality rates that the STS PROM. These data led the Food and Drug Administration to approve the third-generation balloon-expandable SAPIEN 3 heart-valve system (Edwards Lifesciences, Irvine, CA) for use in severely degenerated mitral bioprostheses in 2017.[8] Our study contributes the first single center perspective of TMVI using balloon-expandable heart valves for the treatment of degenerated mitral bioprostheses with long-term 1-year follow-up to the literature. Our results indicated that TMVI for the treatment of degenerated bioprostheses can be safely performed in the hands of an experienced heart team using balloon-expandable heart valves with meaningful hemodynamic and clinical improvements. TMVI of degenerated mitral bioprostheses using balloon-expandable heart valves yielded a 100% procedural success rate for our heart team. One patient (4%) developed left ventricular outflow tract obstruction immediately post-TMVI, which was successfully treated with alcohol septal ablation. Left ventricular outflow tract obstruction is a potentially life-threatening complication of TMVI reported to be 7% to 9% in the literature.[13] Use of multidetector computed tomography can help determine the risk of neo-left ventricular outflow tract obstruction pre-TMVI and aide in planning. This is something that we now routinely perform pre-TMVI. Additionally, there was 96% in-hospital survival, 96% 30-day survival and 85% 1-year survival. Despite treating a higher risk group (mean Society of Thoracic Surgeons score of 13% compared with 11%), our 30-day mortality (4%) was lower than the 30-day mortality of the multicentered 2016 transcatheter valve therapy registry data (9%). There is a dearth of data regarding the long-term follow-up of patients who underwent TMVI. Out study demonstrated a 1-year mortality of 15% in this high-risk group of patients. Initial improvements immediately after TMVI in MR grade and MMG were sustained at 1 year in our cohort. Additionally, early improvements of functional ability persisted in those that survived to 1 year. This study was an observational, retrospective study limited to 1 TMVI center. The results of our study require prospective randomized validation in a larger multicentered cohort of patients. Experience using balloon-expandable transcatheter heart valve for the treatment of severely degenerated mitral bioprostheses is growing. Early transcatheter valve therapy registry data from multiple centers support the use for patients with prohibitive surgical risk for re-do surgical mitral valve replacement. Our study contributes to that body of evidence, with robust short-term and long-term results. TMVI using predominantly the third-generation balloon-expandable SAPIEN 3 heart-valve system (Edwards Lifesciences, Irvine, CA) resulted in a 100% procedural success rate with 96% in-hospital survival and 96% survival at 30 days. There were clear and sustained improvements in MMG and MR grade which translated to meaningful improvements in patients' functional ability at 1 year.

Authors' Contribution

Giorgio A. Medranda: conceptualization of ideas, methodology, formal analysis, investigation and data collection, data curation, writing the original draft, visualization of data, project administration.

Kunal Brahmbhatt: conceptualization of ideas, methodology, investigation and data collection, project administration.

Kevin Marzo: conceptualization of ideas, methodology, project administration.

Khaled Salhab: conceptualization of ideas, methodology, project administration.

Richard Schwartz: conceptualization of ideas, methodology, project administration.

Stephen J. Green: conceptualization of ideas, methodology, project administration.

Disclosures

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

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