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Transcatheter Aortic and Mitral Valve-in-Valve Implantation for Failed Surgical Bioprosthetic Valves

An 8-Year Single-Center Experience

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ABSTRACT

OBJECTIVES We report our 8-year experience in transcatheter aortic and mitral valve-in-valve (VinV) implantation.

BACKGROUND Feasibility and good early outcomes associated with transcatheter aortic and mitral VinV implantation into failed surgical bioprostheses have been confirmed, but the mid-term and long-term outcomes of transcatheter aortic and mitral VinV is unknown.

METHODS A total of 73 patients with aortic (n = 42) and mitral (n = 31) bioprosthetic valve dysfunction underwent transcatheter VinV implantation between April 2007 and December 2013. Edwards balloon-expandable transcatheter valves (Edwards Lifesciences Inc., Irvine, California) were used. Median follow-up was 2.52 years with a maximum of 8 years.

RESULTS Seventy-two patients (mean age 79.7 ± 9.4 years, 32 women) underwent successful VinV implantation (success rate 98.6%). At 30 days, all-cause mortality was 1.4%, disabling stroke 1.4%, life-threatening bleeding 4.1%, acute kidney injury requiring hemodialysis 2.7%, and coronary artery obstruction requiring intervention 1.4%. No patient had greater than mild paravalvular leak. Estimated survival rates were 88.9%, 79.5%, 69.8%, 61.9%, and 40.5% at 1, 2, 3, 4, and 5 years, respectively. The small surgical valve size (19 and 21 mm) was an independent risk factor for reduced survival in aortic VinV patients. At 2-year follow-up, 82.8% of aortic and 100% of mitral VinV patients were in New York Heart Association functional class I or II.

CONCLUSIONS Transcatheter VinV for failed surgical bioprostheses can be performed safely with a high success rate and minimal early mortality and morbidity. Transcatheter VinV provides encouraging mid-term clinical outcomes in this high-risk elderly cohort of patients. Transcatheter VinV is an acceptable alternative therapy for failed aortic or mitral bioprostheses in selected high-risk patients. (J Am Coll Cardiol Intv 2015;8:1735–44) © 2015 by the American College of Cardiology Foundation

Although open-heart aortic or mitral valve replacement remains the standard therapy for failed prosthetic valves and can be performed with clinically acceptable operative mortality and morbidity in many patients, there are some patients with prosthetic dysfunction/degeneration who are either elderly or at high risk for reoperation in terms of mortality and/or morbidity (1,2). Such

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ABBREVIATIONS AND ACRONYMS

AVR = aortic valve replacement

LVEF = left ventricular ejection fraction

MVR = mitral valve replacement

NYHA = New York Heart Association

TAVI = transcatheter aortic valve implantation

VinV = valve-in-valve

patients are often declined, or not referred, for redo aortic valve replacement (AVR) or mitral valve replacement (MVR).

The feasibility and good early outcomes of transcatheter aortic and mitral valve-in-valve (VinV) implantation into failed surgical bioprostheses have been demonstrated (3–12). A lesser invasive approach for failed surgical bioprostheses is desirable for this ever-expanding high-risk elderly population.

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We report our 8-year experience in transcatheter aortic and mitral VinV implantation in 73 consecutive patients with surgical biological valve dysfunction.

METHODS

PATIENT SELECTION. From April 2007 to December 2013, 73 consecutive patients with symptomatic severe aortic (n = 42) and mitral (n = 31) bioprosthetic valve dysfunction underwent transcatheter aortic and mitral VinV implantation, respectively, at a single center (St. Paul's Hospital, Vancouver, British Columbia, Canada). All patients had previous AVR or MVR with bioprostheses and were reviewed at our multidisciplinary transcatheter valve rounds. The indications for reoperative AVR or MVR generally followed the American College of Cardiology/American Heart Association guidelines for valve surgery (13). Patients who were deemed to be too high risk for conventional redo valve replacement by cardiac surgeons were considered as potential candidates for transcatheter VinV implantation. Written and informed consents were obtained. Echocardiography and clinical follow-up was performed pre- and post-operatively.

VinV IMPLANTATION. Balloon-expandable transcatheter valves (Edwards Lifesciences, Inc., Irvine, California) were used in all cases. Various generations of valves and delivery systems were used from April 2007 to December 2013. The first-in-human aortic and mitral VinV implantations were performed by the implantation of 23- and 26-mm Cribier-Edwards equine valves, respectively, using a transapical approach (4,14). In all subsequent cases, bovine Edwards SAPIEN and SAPIEN XT valves were implanted through either a transfemoral or transapical approach. Transapical access was the only approach that was used for mitral VinV implantation. All operations were performed in our hybrid operating room equipped with standby cardiopulmonary bypass support. The techniques of transcatheter aortic and mitral VinV implantation were described previously (4,14,15). Balloon valvuloplasty of the bioprosthesis was utilized in our initial experience, but was subsequently not utilized during transapical VinV implantation. During transfemoral aortic VinV implantation, balloon valvuloplasty was used in some cases with critical bioprosthetic stenosis. Selection of an appropriately sized SAPIEN or SAPIEN XT valve depended on the internal diameter of the pre-existing surgical bioprosthesis as reported by the manufacturer. Fluoroscopic and/or transesophageal echocardiography imaging were sufficient for valve positioning. Intraoperative conventional aortography was not performed during transapical VinV implantation, but occasionally performed prior to transfemoral aortic VinV implantation and/or following aortic VinV implantation to assess coronary ostia. Contrast was not utilized during mitral VinV procedures. Optimal positioning of the transcatheter valve was achieved with rapid ventricular pacing immediately prior to valve deployment. Post-operatively, patients were instructed to take aspirin indefinitely and clopidogrel for at least 3 months. Warfarin and aspirin were used for mitral VinV implantation or if other indications were present, such as atrial fibrillation.

FOLLOW-UP AND DATA COLLECTION. All patients were followed-up by transcatheter valve therapy team staff or clinical fellows. Follow-up included telephone interviews and office visits. Data were prospectively collected and entered into our transcatheter aortic valve implantation (TAVI) database. The median follow-up period was 2.52 years, with longest follow-up of 8 years. Procedural success and complications were reported according to Valve Academic Research Consortium-2 definitions (16).

STATISTICAL ANALYSIS. Continuous variables were summarized using mean ± SD or median with interquartile range (IQR) and compared between aortic surgical valve sizes (≤21, 23, or >23 mm) or surgical types (aortic valve vs. mitral valve) with the use of the Student *t* test or Wilcoxon rank sum test. Categorical variables were summarized using frequencies and percentages and compared between surgical valve sizes or surgical types with the use of the Fisher exact test or chi-square test. The Kaplan-Meier method was used to obtain the survival curves on the basis of time-to-event data. Cox proportional hazards regression analyses were conducted to evaluate risk factors influencing mid-term survival rates. The proportional hazards assumption of the Cox regressions was satisfied for the models. Follow-up echocardiographic

data were evaluated by the paired *t* test or Wilcoxon signed rank test, and the longitudinal model with covariance structure for continuous variables. The covariance structure, heterogeneous compound symmetry was chosen for modeling for pulmonary artery systolic pressure (PASP), and the covariance structure, autoregressive with heterogeneous variance was selected for modeling for mean gradient. Dichotomized New York Heart Association (NYHA) data obtained at baseline and follow-ups were compared using McNemar's test. All tests were 2-sided, and a p value <0.05 was considered statistically significant. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, North Carolina) and R software version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

PATIENTS. The mean ages were 80.5 ± 9.8 years and 78.7 ± 8.8 years in patients undergoing aortic and mitral VinV implantation, respectively. Patients undergoing mitral VinV were more likely to be female relative to those undergoing aortic VinV (58.0% vs. 32.3%). Surgical bioprosthetic valves included Carpentier-Edwards porcine and pericardial (Edwards Lifesciences, Inc., Irvine, California), Mosaic (Medtronic, Minneapolis, Minnesota), Mitroflow (Sorin Group, Milan, Italy), Trifecta (St. Jude Medical, Minneapolis, Minnesota), and Ionescu-Shiley (Shiley Inc., Irvine, California) valves. Surgical aortic and mitral valves were implanted 13.4 ± 5.5 years and 9.3 ± 3.1 years before the VinV procedure, respectively. Baseline demographics are listed in Table 1.

The median of the calculated Society of Thoracic Surgeons risk score was 9.6 (IQR: 6.2 to 11.4) and 9.7 (IQR: 5.0 to 16.6) in patients with aortic and mitral VinV implantation, respectively. Mechanisms of bioprosthetic failure included stenosis, regurgitation, and mixed stenosis and regurgitation (Table 1). No patient had significant perivalvular bioprosthetic regurgitation. The manufacturers' labeled size ranged from 19 to 29 mm and 25 to 33 mm for aortic and mitral bioprostheses, respectively.

INTRAOPERATIVE OUTCOMES. The transcatheter valve was successfully implanted within the failed surgical valve in 72 of 73 patients (98.6%). Major intraoperative complications were observed in 3 patients (4.1%). Embolization of a SAPIEN valve into the left ventricle occurred in 1 patient due to an extremely poor implantation angle during a transapical aortic VinV procedure. Emergency conversion to open-heart surgery was required, and the patient survived. Left main coronary obstruction occurred in 1 patient following implantation of a SAPIEN valve into a Sorin Mitroflow aortic valve. Despite emergency conversion to open-heart AVR, the patient died the following day (17). A third patient with a failed mitral bioprosthesis required implantation of a second valve because of an initial implant placed distal (more apical) to the mitral annulus.

TABLE 1 Baseline Characteristics

	All (n = 73)	Aortic (n = 42)	Mitral (n = 31)
Age, yrs	79.7 ± 9.4	80.5 ± 9.8	78.7 ± 8.8
Male	41 (56.2)	28 (67.7)	13 (42.0)
Diabetes mellitus	17 (23.3)	10 (23.8)	7 (22.6)
Coronary artery disease	45 (61.6)	29 (69.0)	16 (51.6)
PASP ≥60 mm Hg	20 (27.4)	7 (16.7)	13 (41.9)
Coronary artery bypass grafting	32 (43.8)	19 (45.2)	13 (41.9)
NYHA functional class III or IV	69 (94.5)	39 (92.9)	30 (96.8)
COPD (moderate + severe)	11 (15.1)	4 (9.5)	7 (22.6)
Cerebrovascular accident	17 (23.3)	7 (16.7)	10 (32.3)
Surgical valve size <23 mm	8 (11.0)	8 (19.0)	0 (0.0)
Peripheral vascular disease	17 (23.3)	13 (31.0)	4 (12.9)
Left ventricular ejection fraction, %	60 (45, 65)	57.5 (47, 65)	60 (40, 65)
Creatinine 100–149 mmol/l	32 (43.8)	20 (47.6)	12 (38.7)
Creatinine ≥150 mmol/l	11 (15.1)	9 (21.4)	2 (6.5)
STS score, %	9.6 (5.9, 13.4)	9.6 (6.2, 11.4)	9.7 (5, 16.6)
Failed surgical valves			
Stenosis	34 (46.6)	22 (52.4)	12 (38.7)
Regurgitation	27 (37.0)	13 (31.0)	14 (54.2)
Mixed	12 (16.4)	7 (16.7)	5 (16.1)

Values are mean ± SD, n (%), or median (quartile 1, quartile 3).
COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; STS = Society of Thoracic Surgeons.

EARLY CLINICAL OUTCOMES. Life threatening bleeding (packed red blood cells ≥4 U) and major bleeding (2 to 3 U) occurred in 3 (4.1%) aortic and 6 (8.2%) mitral VinV patients. No patient required reoperation for bleeding or tamponade. One patient (1.4%) had an in-hospital disabling stroke following mitral VinV implantation. Two patients (2.7%) had stage III acute kidney injury by Valve Academic Research Consortium-2, requiring temporary renal replacement therapy. One patient with chronic atrial fibrillation required a pacemaker following mitral VinV implantation due to pre-existing sick sinus syndrome. One patient, who had left main obstruction and was converted to open-heart surgery, died on the first day following the procedure, resulting in an overall 30-day mortality of 1.4% (Table 2). The median of the hospital length of stay was 5 days (IQR: 3 to 7 days).

MID-TERM CLINICAL OUTCOMES. Overall survival in 73 patients who underwent either aortic or mitral

TABLE 2 Early and Late Complications

	Aortic VinV (n = 42)		Mitral VinV (n = 31)	
	30 Days	>30 Days	30 Days	>30 Days
Major bleeding (2-3 U PRBC)	0	0	6	0
Life-threatening bleeding (≥4 U PRBC)	2	1	1	0
Conversion to open surgery	1	0	0	0
Valve migration	0	0	0	1
ARF requiring hemodialysis	1	0	1	0
Myocardial infarction	0	0	0	0
Major vascular complication	0	0	0	0
Disabling stroke	0	0	1	1
Left main obstruction	1	0	0	0
Endocarditis	0	0	0	0
Valve thrombosis	0	2	0	2
Failed valve (structural)	0	1	0	0
THV-in-THV deployment	0	0	1	0
Permanent PM implantation	0	0	1	0

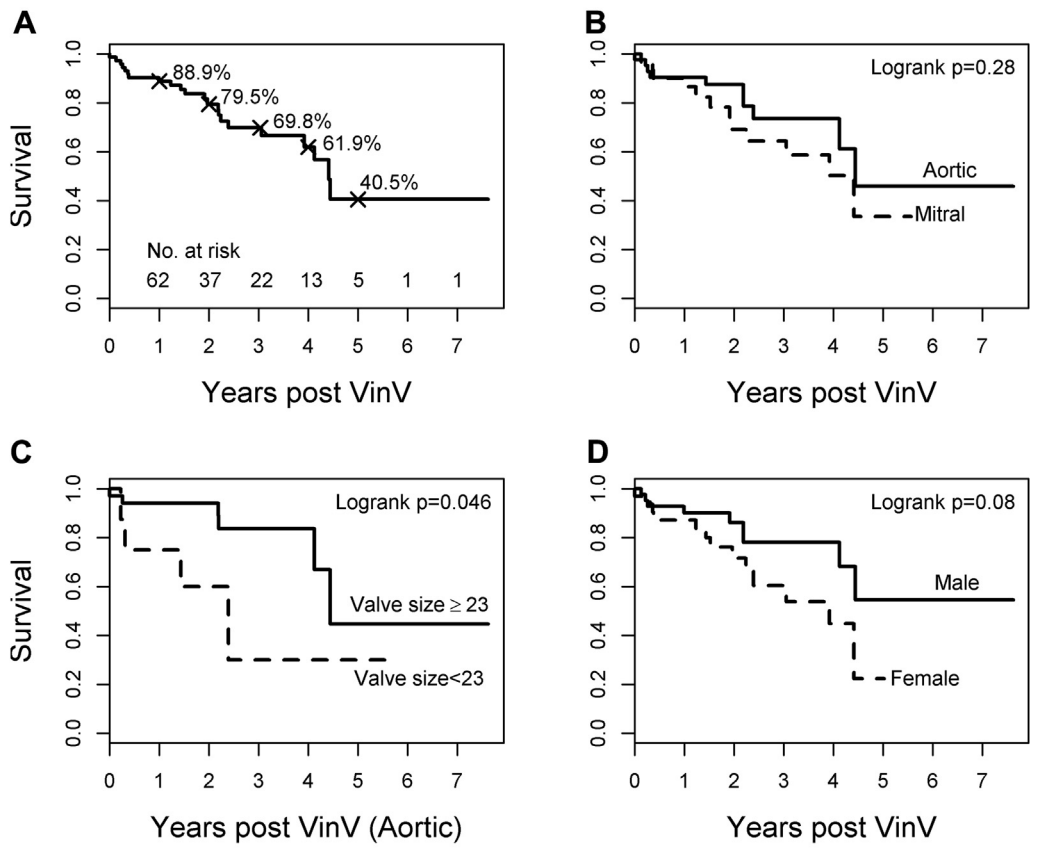
Values are n.

ARF = acute renal failure; PM = pacemaker; PRBC = packed red blood cells; THV = transcatheter heart valve; VinV = valve-in-valve.

VinV implantation was 88.9%, 79.5%, 69.8%, 61.9%, and 40.5% at 1, 2, 3, 4, and 5 years, respectively (Figure 1A). Peripheral vascular disease and previous stroke were independent risk factors for reduced mid-term survival, with hazard ratios of 3.2 and 3.0, respectively (Table 3). Female patients appeared to have relatively poor survival (Figure 1D). There was no significant difference in late survival between patients undergoing aortic and mitral VinV implantation (Figure 1B). The median survival rates were 4.5 and 4.4 years following aortic and mitral VinV implantation, respectively.

Multivariate model showed that the small size (19 and 21 mm) of failed aortic surgical valves was an independent risk factor for reduced mid-term survival, with a hazard ratio of 6.2 in patients with aortic VinV implantation (Table 4). Poorer estimated survival was observed in patients who had small aortic surgical valves (19 and 21 mm) relative to those with surgical valves of ≥23 mm (p = 0.046)

FIGURE 1 Kaplan-Meier Survival Rates Following Transcatheter VinV Implantation



(A) All 73 patients, **(B)** aortic versus mitral patients, **(C)** patients with different surgical valve sizes, and **(D)** male versus female patients. VinV = valve-in-valve.

(Figure 1C). There were significant smaller aortic valve area and higher mean transaortic pressure gradient following aortic VinV implantation in patients with surgical valve sizes of 19 and 21 mm relative to those with surgical valve sizes of >23 mm (Table 5). There was no difference in survival following aortic VinV implantation between the patients with bioprosthetic stenosis and those with bioprosthetic regurgitation.

Cumulative valve-related complications were listed in Table 2. Delayed valve migration occurred in 1 patient following uneventful mitral VinV implantation with a 26-mm SAPIEN prosthesis into a failed 27-mm Edwards Perimount pericardial valve (Edwards Lifesciences, Inc.). In this patient, acute heart failure 2 months after the procedure resulted from atrial migration of the SAPIEN valve and severe peri-paravalvular regurgitation. A second transapical mitral VinV implantation with a 29-mm SAPIEN valve was performed without complications, and the patient survived for 21 months. Four patients (5.5%) who underwent aortic or mitral VinV implantation and received ASA and clopidogrel antiplatelet therapy post-operatively developed valve thrombosis, which was resolved with anticoagulation using warfarin. One patient developed congestive heart failure symptoms 1 year after transfemoral aortic VinV implantation of a 23-mm SAPIEN valve into a 23-mm Mitroflow surgical aortic tissue valve and subsequently underwent successful conventional redo AVR. Pathology of the explanted SAPIEN valve showed mild calcification. In this patient, residual aortic stenosis was observed immediately following VinV implantation (mean transaortic pressure gradient 39 mm Hg and aortic valve area 0.8 cm^2 at 1-month follow-up). One patient with aortic VinV experienced cerebral hemorrhage due to a fall and warfarin, which was resolved.

Significant clinical improvement in heart failure symptoms was observed following VinV implantation in the majority of patients. In all patients who had 2-year follow-up data, NYHA functional class I and II was observed in 82.8% and 100% patients with aortic and mitral VinV implantation, respectively (Figure 2). The majority of patients who had longer follow-up after VinV implantation had NYHA functional class I and II heart failure symptoms: 27 of 27 patients at the third year, 14 of 15 patients at the fourth year, 6 of 6 patients at the fifth year, and 4 of 4 patients at the sixth year. One patient remained at NYHA functional class I at 8 years.

PERFORMANCE OF TRANSCATHETER VALVES. Transcatheter valve performance was determined by echocardiography. A significant reduction in prosthetic valvular pressure gradients and an increase in aortic prosthetic valve areas were seen at 12-month follow-up in the survivors with aortic VinV implantation (Figures 3E and 3G). A significant reduction in mean transmitral pressure gradient was also observed in patients following transcatheter mitral VinV implantation (Figure 3F). Aortic VinV implantation resulted in significant improvement in left ventricular ejection fraction (LVEF) within 1-year follow-up in patients who had baseline LVEF of ≤50% (Figure 3A). By contrast, there was no improvement in LVEF in patients following mitral VinV implantation (Figure 3B). PASP was significantly decreased within 1 year following aortic VinV implantation in the patients who had baseline PASP of >50 mm Hg ($p < 0.001$) (Figure 3C), but there was only a trend toward a decrease in PASP in the patients who had mitral VinV implantation ($p = 0.08$) (Figure 3D). Further analysis (F test on the basis of longitudinal models with covariance structure) showed that PASP and mean

TABLE 3 Factors Influencing Survival (n = 73)

	Univariate Model		Multivariate Model	
	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value
Female	2.136 (0.904–5.049)	0.084	2.570 (0.983–6.719)	0.054
PVD	1.466 (0.590–3.644)	0.411	3.153 (1.070–9.288)	0.037
PASP ≥60 mm Hg	1.880 (0.775–4.556)	0.162	2.941 (0.963–8.982)	0.058
LVEF <50%	1.459 (0.611–3.482)	0.395	2.658 (0.891–7.931)	0.080
COPD (moderate + severe)	0.645 (0.151–2.763)	0.555		
CABG ± CAD	1.231 (0.479–3.160)	0.666		
Creatinine 100–149 mmol/l	1.116 (0.325–3.835)	0.862		
Creatinine ≥150 mmol/l	1.532 (0.593–3.958)	0.379		
DM	1.447 (0.530–3.948)	0.471		
CVA	2.001 (0.794–5.046)	0.142	2.956 (1.033–8.461)	0.043

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CI = confidence interval; CVA = cerebrovascular accident; DM = diabetes mellitus; LVEF = left ventricular ejection fraction; PVD = peripheral vascular disease; other abbreviations as in Table 1.

TABLE 4 Factors Influencing the Survival of Aortic VinV Patients (n = 42)

	Univariate Model		Multivariate Model	
	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value
Female	2.485 (0.614–10.07)	0.202		
PVD	2.752 (0.747–10.14)	0.128		
PASP ≥60 mm Hg	2.906 (0.692–12.21)	0.145		
LVEF <50%	1.742 (0.489–6.207)	0.392	2.945 (1.472–25.99)	0.049
CABG ± CAD	0.784 (0.177–3.475)	0.749		
Creatinine 100–149 mmol/l	0.925 (0.127–6.749)	0.938		
Creatinine ≥150 mmol/l	2.126 (0.428–10.57)	0.357		
DM	2.601 (0.639–10.59)	0.182	4.779 (0.741–11.71)	0.125
CVA	0.773 (0.995–6.304)	0.810		
Surgical valve size <23 mm	3.420 (0.951–12.30)	0.060	6.186 (1.001–22.82)	0.013

Abbreviations as in Tables 1 and 3.

TABLE 5 Influence of Surgical Valve Sizes on Transcatheter Valve Hemodynamics in Aortic VinV Patients

Group	Surgical Valve Size (mm)	THV Size (mm)	Post-Op AVA (cm^2)	Post-Op MG (mm Hg)
I (n = 8)	19 or 21	20 or 23	0.88 ± 0.15	25.7 ± 9.5
II (n = 14)	23	23 or 26	1.02 ± 0.17*	22.5 ± 7.9
III (n = 19)	25, 27, or 29	23, 26, or 29	1.35 ± 0.27*†	15.8 ± 6.2*†

Values are mean ± SD unless otherwise indicated. *p < 0.05 vs. Group I. †p < 0.05 vs. Group II.
AVA = aortic valve area; MG = mean gradient; Post-Op = post-operative; THV = transcatheter heart valve; VinV = valve in valve.

gradient significantly decreased with time following either aortic or mitral VinV implantation (p < 0.001). There was a continuing decrease in PASP from 12 to 36 months following mitral VinV implantation (Figure 4).

Of the patients who underwent aortic VinV implantation, 4 (9.5%) had mild regurgitation and 38 (90.5%) had no or trivial regurgitation at up to 8-year follow-up. In patients who underwent mitral VinV implantation, 4 (12.9%) and 27 (87.1%) had mild and no or trivial regurgitation at up to 5-year follow-up, respectively. Following VinV implantation, no patient had greater than mild regurgitation during follow-up.

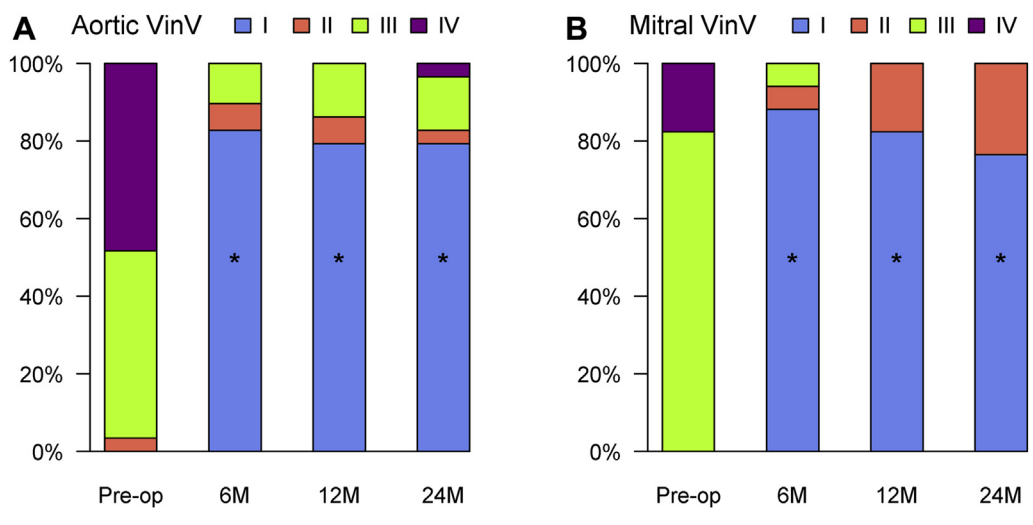
DISCUSSION

Feasibility and good early outcomes associated with transcatheter aortic and mitral VinV implantation into failed surgical bioprostheses have been confirmed, but the mid-term and long-term outcomes of transcatheter aortic and mitral VinV is unknown. This study has demonstrated that transcatheter VinV implantation provides encouraging mid-term clinical and hemodynamic outcomes in this high-risk elderly cohort of patients. The small surgical valve size (19 and 21 mm) was an independent risk factor for reduced survival in aortic VinV patients. Long-term follow-up in a larger sample size is needed to understand independent risk factors for reduced survival, which will optimize patient selection for the VinV procedure.

SURGICAL TECHNIQUES. In our center, transcatheter aortic VinV implantation was initially performed using transapical access, which provided the most direct, shortest, and coaxial access to the aortic valve. However, more recently, the transfemoral approach has gained favor, as it is similarly effective but relatively less invasive. Transcatheter mitral valve implantation has remained exclusively a transapical procedure. Although the procedure can be replicated with direct transseptal access, this remains a complex procedure (18).

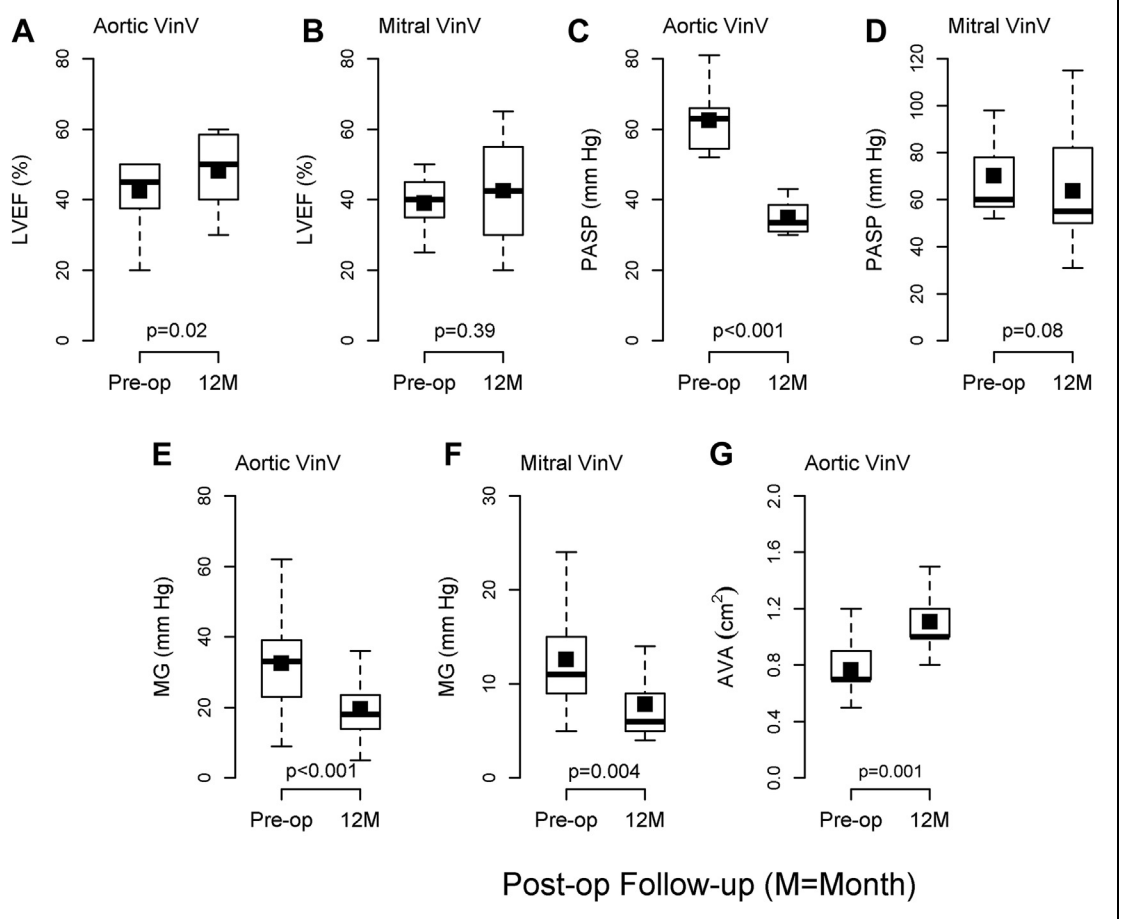
Initially, we routinely utilized valvuloplasty prior to valve implantation. However, this has been found largely unnecessary. Currently, we do not utilize balloon valvuloplasty during transapical procedures, although valvuloplasty still remains necessary in

FIGURE 2 Pre-Op and Post-Op NYHA Functional Class



Pre-operative (pre-op) and post-operative (post-op) New York Heart Association (NYHA) functional class following **(A)** aortic or **(B)** mitral valve-in-valve (VinV) implantation in patients who had 24-month follow-up data. *p < 0.001 versus pre-op percentage of NYHA functional class III and IV. M = month follow-up.

FIGURE 3 Echocardiographic Outcomes Following Either Aortic or Mitral VinV Implantation In Patients Who Had 12-Month Follow-Up Data



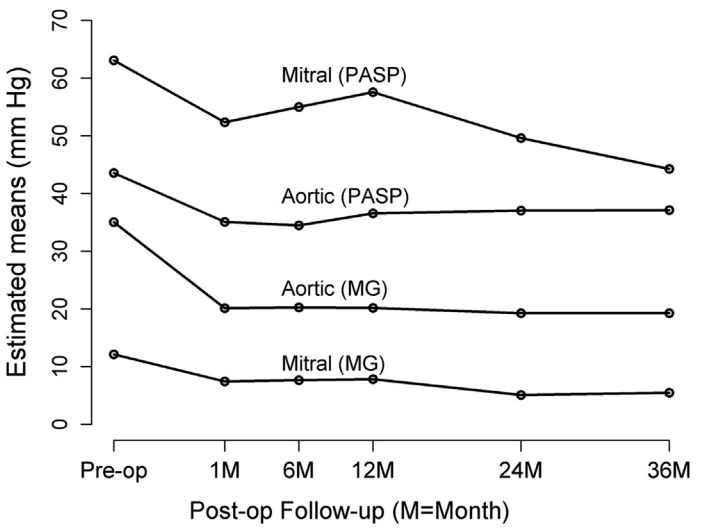
(A and B) Left ventricular ejection fraction (LVEF) changes in patients with left ventricular dysfunction (pre-operative LVEF of ≤50%), **(C and D)** changes in pulmonary artery systolic pressure (PASP) in patients with pulmonary hypertension (PASP >50 mm Hg), **(E and F)** changes in mean transvalvular pressure gradient (MG), and **(G)** aortic valve area (AVA). Abbreviations as in Figure 2.

some patients with severe bioprosthetic aortic stenosis undergoing a transarterial access procedure. Final fine adjustment of transcatheter valve positioning is usually required during rapid ventricular pacing to achieve an optimal positioning, as surgical valve motion particularly at the mitral position is significant during cardiac cycles. Therefore, slow inflation of a balloon during valve deployment is strongly recommended for VinV implantation.

EARLY CLINICAL OUTCOMES. A recent report from the Global registry documented a 9.4% 30-day all-cause mortality rate after aortic VinV implantation in patients with an average Society of Thoracic Surgeons predicted risk of 11.8 ± 9.9%. (19). Our 1.4% 30-day all-cause mortality compares very favorably, possibly due to our relatively large TAVI experience prior to initiating VinV procedures. The size of surgical mitral valves is generally much larger than that of aortic surgical valves, which leads to better hemodynamic outcomes following mitral VinV implantation. Our 30-day mortality following mitral VinV implantation was 0%.

Stroke following aortic TAVI is one of the major concerns in patients with native aortic stenosis. Degenerated bioprosthetic valve leaflets are generally more friable than stenotic native valve leaflets and prone to tearing, which theoretically leads to a higher risk of acute neurological events. However, the incidence of stroke in patients with VinV implantation is equivalent to those in patients with TAVI for native aortic stenosis. Our stroke rate was 1.4% following

FIGURE 4 Changes in Estimated Means of PASP and MG With Time Following VinV Implantation



F test on the basis of longitudinal models with covariance structure showed that PASP and MG significantly decreased with time following either aortic or mitral VinV implantation ($p < 0.001$). Abbreviations as in Figures 2 and 3.

VinV, which is similar to the global registry data (2%). Heart block or aortic rupture was an extremely rare complication because the transcatheter valve is implanted into failed surgical valves without contacting the aortic root or annulus.

Left main occlusion is a potentially fatal complication of TAVI, and may be even more common in association with aortic VinV implantation. In this VinV series, 1 patient experienced left main coronary obstruction following aortic VinV implantation into a failed Mitroflow aortic tissue valve. Following this case, we initiated more extensive pre-operative assessment for the risk of left main occlusion, including routine screening with computed tomographic angiography. The size of sinus of Valsalva, the height of a coronary ostium related to the height of a surgical bioprosthetic leaflet, and the bulk of a surgical bioprosthetic leaflet are the major determinants of the risk for coronary ostial obstruction. Generally speaking, stentless bioprosthetic valves or those that are internally stented (e.g., Mitroflow and Trifecta) may be at a slightly higher risk, as the leaflets of these surgical valves may extend outward in a tubular fashion following VinV implantation (17). To avoid this significant complication, careful pre-operative assessment of the aortic root is still important in patients undergoing the aortic VinV procedure.

MID-TERM CLINICAL OUTCOMES. Mid-term clinical outcomes following VinV implantation were encouraging, with a 1-year survival of 88.9% and 5-year survival of 40.5% in a very high-risk cohort. There was no significant difference in the survival following aortic versus mitral VinV implantation. However, later 5-year survival was relatively poor (40.5%), likely a consequence of the multiple comorbidities and advanced age of our patients, with the majority of patients over age 80 years at the time of VinV implantation. Peripheral vascular disease and history of cerebrovascular accident are independent risk factors for reduced survival following VinV implantation. Female patients and patients with severe pulmonary hypertension (pulmonary artery systolic pressure of ≥60 mm Hg) appear to have poor survival following VinV implantation. This study has also demonstrated the significant effect of failed surgical valve size on clinical outcomes in patients undergoing aortic VinV implantation. The patients with small aortic surgical valve sizes (<23 mm) are associated with significantly poorer survival compared with those with aortic valve sizes of ≥23 mm. Multivariate analysis has demonstrated that the small size of the aortic surgical valve is the only independent risk factor of reduced survival.

Transcatheter VinV implantation provides significantly symptomatic relief and improved quality of life in the majority of patients with either aortic or mitral prosthetic disease. Symptomatic improvement following VinV implantation is also seen in patients with small surgical bioprostheses sizes despite relatively suboptimal hemodynamic performance (small effective orifice valve area and high residual mean transaortic pressure gradient). The improvement in symptoms and quality of life are persistent in all survival patients during up to 8-year follow-up.

TRANSCATHETER VALVE PERFORMANCE. The hemodynamic performance of transcatheter valves following VinV implantation is largely dependent on the surgical valve size. The larger the surgical valve size, the better the hemodynamics. The hemodynamic performance of all mitral implants and in aortic patients with surgical valve sizes of >23 mm is excellent, with a low residual pressure gradient and a relatively large effective orifice. Residual stenosis of an implanted transcatheter valve is rare in mitral patients, as mitral surgical valves are generally ≥25 mm. In contrast, this is frequently seen in patients with smaller aortic tissue valves (19 and 21 mm).

Left ventricular systolic function improves significantly following aortic VinV implantation, but not

following mitral VinV implantation. This is consistent with the report following conventional aortic or mitral valve replacement (20–22).

A significant reduction in pulmonary artery pressure following VinV implantation was observed in both aortic and mitral patients. Unexpectedly, the maximal reduction was immediately observed following aortic VinV implantation, whereas in patients with mitral VinV implantation, a continuing decline in pulmonary artery pressure was observed from 12 to 36 months. Although speculative, the pulmonary hypertension is probably more chronic in patients with mitral regurgitation than in patients with aortic stenosis, which therefore requires more time for the recovery following mitral VinV implantation. In addition, this may be due to the higher incidence of chronic lung disease in the mitral group.

Importantly, significant paravalvular regurgitation was not observed following VinV implantation into either aortic or a mitral surgical bioprostheses.

The durability of aortic or mitral VinV implants is encouraging at a median follow-up of 2.52 years with maximum of 8 years follow-up. Structural failure of transcatheter valves or valve reoperation was observed only in 1 patient in our series. In this patient who developed congestive heart failure and underwent conventional redo AVR at 1 year following aortic VinV implantation, the newly developed symptoms are likely due to mismatch (small surgical valve), rather than true structural valve dysfunction. This is also supported by pathological study of the explanted valve. Furthermore, the patient was only 53 years of age when she had the VinV implantation and was also on hemodialysis; both are known to be major risk factors for reduced longevity of surgical bioprostheses.

CONSIDERATIONS OF SURGICAL VALVE SIZE. VinV implants in smaller (19 and 21 mm) surgical aortic valves were associated with significant symptomatic improvement. However, late survival was disappointing. Whether this is the result of patient-prosthesis mismatch and inadequate relief of aortic stenosis or the consequence of the multiple factors that lead to implantation of small surgical bioprostheses is unknown. It is also unknown if the outcomes of redo surgical valve replacement in conjunction with aortic root enlargement would be better. However, it seems reasonable to recommend caution when implanting intra-annular balloon-expandable Sapien-type valves in small bioprostheses. There is some evidence to suggest that better hemodynamic outcomes may be achieved with transcatheter valves that incorporate supra-annular leaflets (19,23,24), or smaller balloon-expandable transcatheter valves (20 mm) (25).

In contrast, hemodynamic function was excellent with encouraging clinical outcomes when VinV implantation into larger (>23 mm) surgical bioprostheses. It seems reasonable to conclude that surgeons should make every effort to implant surgical aortic bioprostheses of at least 23 to 25 mm, particularly in young patients. At the same time, it is suggested to keep the valve away from the coronary ostia to avoid coronary occlusion with VinV implantation. If necessary to achieve these goals, enlargement of the aortic annulus and/or aortic root (sinus Valsalva) may be considered to allow future VinV therapy with satisfactory outcomes. As an alternative, a more durable mechanical valve might be considered.

POST-OPERATIVE ANTICOAGULATION. It has been our practice to recommend aspirin indefinitely and clopidogrel for at least 3 months to patients following native aortic valve TAVI. In aortic VinV patients, we continue using the same protocol that is used in patients with TAVI. However, the observation of mitral valve thrombus in 2 patients has led to our current practice of aspirin indefinitely with the addition of warfarin for at least 3 months following mitral VinV implantation in patients without atrial fibrillation. An embolic complication from either aortic or mitral valve thrombosis appears rare, as we did not observe this in our patients who were diagnosed with valve thrombosis. Clearly, optimal anticoagulation following VinV therapy requires further study.

CONCLUSIONS

Transcatheter VinV implantation with balloon-expandable valves for failed aortic or mitral surgical bioprostheses can be performed safely with a high success rate and minimal early mortality and morbidity. Transcatheter VinV implantation provides encouraging mid-term clinical and hemodynamic outcomes in this high-risk elderly cohort of patients. The appeal of this less-invasive approach to bioprosthetic valve failure may be compelling in patients for whom repeat surgery would be high risk. In patients undergoing conventional surgery with a bioprosthesis, efforts should be made to implant a bioprostheses large enough to allow for a future VinV implant with optimal hemodynamics and clinical outcomes.

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PERSPECTIVES

WHAT IS KNOWN? Feasibility and good early outcomes associated with transcatheter aortic and mitral VinV implantation into failed surgical bioprostheses have been confirmed, but the mid-term and long-term outcomes of transcatheter aortic and mitral VinV is unknown.

WHAT IS NEW? Transcatheter VinV implantation provides encouraging mid-term clinical and hemodynamic outcomes in this high-risk elderly cohort of patients. The small surgical valve size (19 and 21 mm) was an independent risk factor for reduced survival in aortic VinV patients.

WHAT IS NEXT? Long-term follow-up in a larger sample size is needed to understand independent risk factors for reduced survival, which will optimize patient selection for the VinV procedure.

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