Prevalence, Predictors and Survival Outcome of Prosthesis-Patient Mismatch After Transcatheter Aortic Valve Replacement: A Single-Center Experience

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Abstract

INTRODUCTION: Prosthesis-patient mismatch (PPM) after surgical or transcatheter aortic valve replacement (SAVR or TAVR, respectively), remains a significant concern in large registries and has potentially affected clinical outcomes including mortality. This study aimed to determine the prevalence, predictors and survival outcome of patients with and without PPM post-TAVR at St. Luke's Medical Center–Global City (SLMC-GC), Philippines.

METHODS: This was a retrospective cohort analysis among patients who underwent TAVR at SLMC-GC between 2012 and 2018. We reviewed the procedural and follow-up records of patients from the TAVR clinic at SLMC-GC and identified those with PPM. The prevalence of PPM was computed and the characteristics and survival of those with and without PPM were compared.

RESULTS: There were 133 patients included in the study. Severe and moderate PPM were observed in 4.5% and 11.3% of patients, respectively. No clinical, procedural or echocardiographic characteristic was identified as a significant independent predictor of PPM post-TAVR. The estimated mean survival of patients using the Kaplan–Meier method was 64.9 months (95% CI 52.7, 77.2 months) in the PPM group vs 62.1 months (95% CI 55.9, 68.4 months; log-rank p=0.72), which were not significantly different between groups.

CONCLUSION: The incidence of moderate to severe PPM post-TAVR in our institution was 15.8%. The clinical, procedural and echocardiographic characteristics of patients with and without PPM post-TAVR did not significantly differ between groups. PPM has no significant impact on mortality among post-TAVR patients in Filipinos.

KEYWORDS: Prosthesis-patient mismatch, Transcatheter aortic valve replacement, effective orifice area, Philippines

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has been established as a less invasive treatment option for patients with severe, symptomatic aortic valve stenosis who have intermediate, high, or extreme surgical risk.[1-3] In the Philippines, there is a growing number of patients availing of TAVR especially among those with high surgical risk. A continuing concern after aortic valve replacement is valve prosthesis–patient mismatch (PPM), which has a significant negative impact on clinical outcomes, such as an increased all-cause and cardiac-related mortality.[4-7] PPM occurs when a normally functioning implanted valve prosthesis has a small effective orifice in relation to the patient's body size, causing abnormally high transvalvular gradients.[5-7]

The indexed effective orifice area (iEOA) is used to characterize PPM and is defined as the effective orifice area (EOA) of the prosthetic valve divided by the patient's body surface area (BSA).[5-7]

In surgical aortic valve replacement (SAVR), the reported incidence of PPM ranges from 20% to 70%.[4,5] However, the PARTNER trial (Placement of AoRTic TraNscathetER Valve Trial) showed that PPM is less common and less severe after TAVR compared with SAVR.[4] Various studies have also reported PPM in 35% to 46.4% of patients after TAVR, which was associated with adverse impact on post-procedural myocardial mechanics (e.g., lesser left ventricular mass regression and reverse left ventricular remodeling), morbidity (e.g., heart failure hospitalization) and mortality.[4-8]

One report from the OCEAN-TAVI (Optimized transCathEter vAlvular iNtervention) Japanese multicenter registry showed that the incidence of PPM was 9.6%, with no significant impact on overall mortality.[9] However, the incidence of post-TAVR PPM has not been established in other Asian countries, including the Philippines, although some studies suggest that the outcomes of TAVR among Asians were similar to those observed in western cohorts.[10] Given the paucity of local data, we sought to investigate the prevalence, predictors and survival outcome of PPM among patients who underwent TAVR at St. Luke's Medical Center–Global City (SLMC-GC) between 2012 and 2018.

METHODS

This was a retrospective cohort analysis among patients who underwent TAVR at SLMC-GC between 2012 and 2018. The study protocol was duly reviewed and approved by the institutional ethics review committee of the center.

The study population included all consecutive patients who underwent successful TAVR at our center during the study period. We excluded patients whose pre-procedural or post-TAVR echocardiographic reports were not available. The relevant clinical, surgical, computed tomography and echocardiography data of included patients were recorded and tabulated for analysis. The primary outcome in this study was the prevalence of PPM after successful TAVR among patients undergoing TAVR at SLMC-GC. Successful TAVR procedure was defined as the delivery of the transcatheter heart valve in the aortic position. The type of prosthesis used (e.g., Lotus, CoreValve, Evolute R), the prosthesis size (mm), and the delivery approach (e.g., transfemoral/transiliac, transaxillary/subclavian or transaortic) were recorded. Transcatheter valve size referred to the external dimension from the manufacturer.

Patients were then assigned to the PPM and non-PPM groups based on the observed iEOA post-TAVR using available echocardiographic reports on discharge. The PPM group included patients with moderate and severe PPM whereas the non-PPM group had none or mild PPM. Mild or no PPM was defined as iEOA>0.85 cm^2/m^2; moderate PPM as iEOA of 0.65 to 0.85 cm^2/m^2; and severe PPM as iEOA<0.65 cm^2/m^2.[13,14] For obese patients (body mass index [BMI] >30 kg/m^2), the corresponding iEOA cutoffs were >0.70 cm^2/m^2, 0.70 to 0.56 cm^2/m^2, and <0.55 cm^2/m^2, respectively.[14] BSA was computed using the Du Bois Formula.[15] Pre-procedural aortic valve area (AVA) was determined using the continuity equation and was then indexed to the BSA (iAVA).[14,16] The aortic annular diameter and the number of aortic valve cusps, whether tricuspid or bicuspid, were also noted.

Mortality was recorded as death from any cause after the TAVR. Immediate, short-term, mid-term and long-term mortality were reported as death from any cause prior to discharge up to <3 months, until six months, until one year and >1 year post-TAVR, respectively.

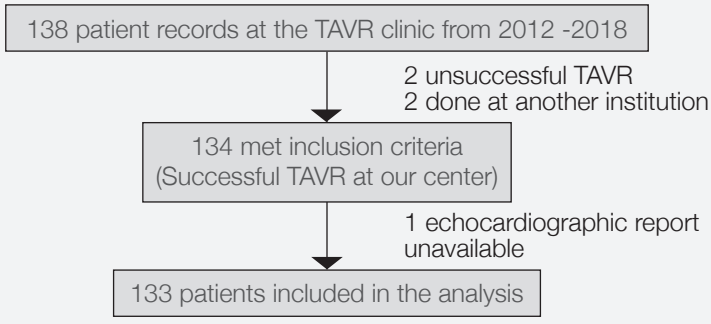
Statistical Analysis

Frequency, percentage, mean, standard deviation, median, and range were used to describe the clinical characteristics, procedural characteristics, and echocardiographic characteristics of the patients who underwent TAVR from 2012 to 2018. Quantitative variables were compared using the unpaired Student's t-test or the Mann-Whitney test. The chi-square test or Fisher exact test was used to compare qualitative variables. Univariate or multivariate logistic regression analyses were performed to identify which of the characteristics predict risk for PPM. Cumulative survival rates were analyzed using the Kaplan-Meier method, and differences will be assessed the log rank test. A p-value <0.05 was considered significant. Stata version 15.0 was used for the statistical analyses.

RESULTS

We reviewed the records of 138 TAVR patients at SLMC-GC and 133 were included in our analysis (Figure 1).

Figure 1. Patient flow chart



There were 133 patients included in the study, with a mean age of 76.5 years and with more males (57.9%) than females. The prevalence of bicuspid aortic valve was 11.3%. More than half of the patients received CoreValve (54.9%). The average size of the prosthetic valve used was 28 mm.

Pre-procedural aortic annular diameter values were reported in only 32 patients (24.1%) and were not included in further analysis.

Twenty-one patients (15.8%) had significant PPM. Severe and moderate PPM were observed in six (4.5%) and 15 (11.3%) patients, respectively. Table 1 shows the clinical, procedural and echocardiographic characteristics of the patients in the PPM and non-PPM groups. The mean age among patients who developed PPM post-TAVR was 74.0 ± 8.9 years; the mean BSA was 1.85 ± 0.25 m2 and the mean BMI was 27.6 ± 6.2 kg/m2. These observations were not significantly different from those without PPM. There were also no significant differences between the PPM and non-PPM groups in terms of procedural and echocardiographic characteristics. Logistic regression analysis also did not identify any characteristic as a significant independent predictor of PPM post-TAVR.

Table 1. Clinical, procedural and echocardiographic characteristics of the patients with and without PPM

Characteristics	PPM (N=21)	Non-PPM (N=112)	Risk Ratio (95% CI)	P-value
Sex (n,%)				
Male	12 (57.1%)	65 (58.0%)	0.96 (0.38-2.47)	0.94
Female	9 (42.9%)	47 (42.0%)		
Age on date of procedure	74.0 ± 8.9	77.0 ± 8.2	0.96 (0.91-1.01)	0.13
Pre-op weight (kg)	75.45 ± 18.5	69.2 ± 13.9	1.03 (0.1-1.06)	0.08
Pre-op height (cm)	165.0 ± 9.6	161.8 ± 9.8	1.03 (0.1-1.09)	0.18
Pre-op BMI (kg/m^2)	27.6 ± 6.2	26.4 ± 4.6	1.05 (0.96-1.15)	0.27
Pre-op BSA (m^2)	1.85 ± 0.25	1.76 ± 0.21	6.96 (0.8-60.39)	0.08
Aortic Valve Anatomy				
Bicuspid	4 (19.1%)	11 (9.8%)	2.16 (0.62-7.57)	0.23
Tricuspid	17 (81.0%)	101 (90.2%)		
Procedural Characteristics				
Access				
Transfemoral/Transiliac	18 (85.7%)	99 (88.4%)	0.37 (0.08-2.53)	0.46
Subclavian/Axillary	1 (4.8%)	8 (7.1%)	0.39 (0.02-4.41)	0.31
Transaortic	2 (9.5%)	5 (4.5%)		
Valve Type				
Core Valve	13 (61.9%)	60 (53.6%)	0.7 (0.2-2.51)	0.59
Evolute R	4 (19.1%)	39 (34.8%)	0.33 (0.07-1.53)	0.16
Lotus	4 (19.1%)	13 (11.6%)		
TAVI Size (mm)	27.52 ± 2.69	28.29 ± 3.28	0.926 (0.8-1.08)	0.32
Echocardiographic characteristics				
AVA	0.77 ± 0.51	0.71 ± 0.3	1.53 (0.46-5.13)	0.49
iAVA	0.41 ± 0.24	0.41 ± 0.17	1.16 (0.09-14.74)	0.91
Mean Gradient	46.06 ± 20.21	44.63 ± 19.97	1.0 (0.98-1.02)	0.762

AVA, aortic valve area; BMI, body mass index; BSA, body surface area; iAVA, indexed AVA; PPM, prosthesis-patient mismatch; TAVI, transaortic valve implant.

There was no significant difference in the immediate, short-term and mid-term mortality rates between groups (Table 2). Of note, all-cause mortality at one year post-TAVR was numerically higher in patients without PPM (16/112, 14.3%) compared with those who had PPM (1/21, 4.8%); however, this difference was not statistically significant (p=0.998).

Table 2. Immediate, short-term and mid-term mortality of patients with and without PPM post-TAVR

Timeframe	Mortality		P-value
	No PPM (n=112)	With PPM (n=21)	
0 - 3 months	12 (10.7%)	1 (4.8%)	0.23
3 - <6 months	3 (2.7%)	0	0.998
6 - 12 months	1 (0.9%)	0	0.998

The median follow-up duration for long-term mortality was 27 months. Figure 2 shows the Kaplan-Meier survival estimates beyond one year post-TAVR. The estimated mean survival of patients using the Kaplan–Meier method was 64.9 months (95% CI 52.7, 77.2 months) in the PPM group vs 62.1 months (95% CI 55.9, 68.4 months; log-rank p=0.72), which were not significantly different.

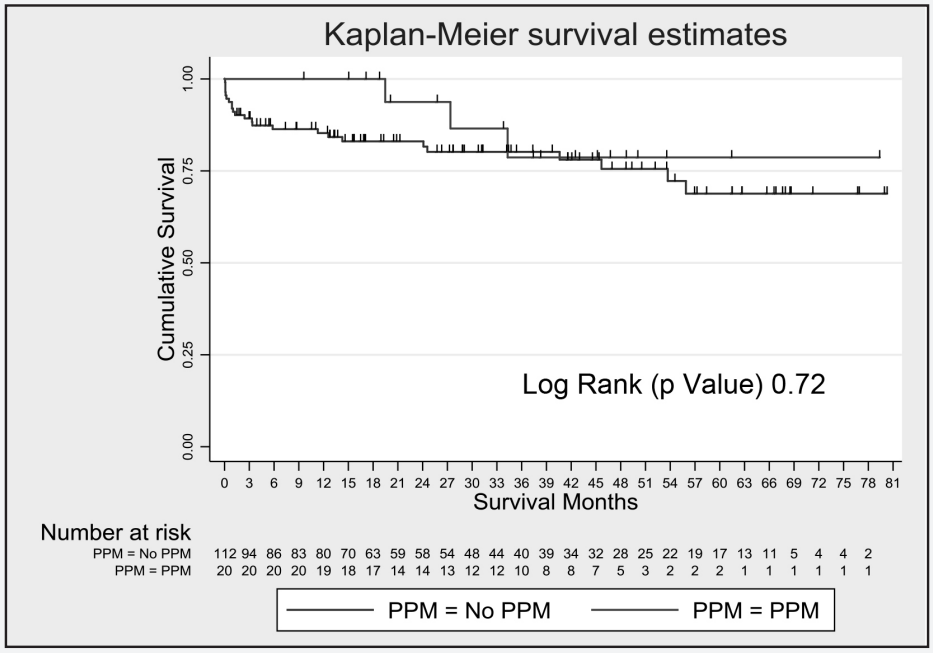


Figure 2. Kaplan-Meier Survival Curves of patients with and without PPM post-TAVR

DISCUSSION

This study showed that TAVR at our institution was associated with a 15.8% rate of moderate and severe PPM and there were no significant differences in the clinical, procedural and echocardiographic characteristics of patients with and without PPM post-TAVR. The cumulative survival rates for the PPM and the non-PPM groups were similar.

The incidence of PPM in this study (15.8%) was higher than that observed among the Japanese in the OCEAN-TAVI registry (9.6%).[9] On the other hand, our study demonstrated a lower prevalence of PPM compared to the Western registries (35% to 46%).[4-8] Previous studies hypothesized that differences in BSA may explain the lower incidence of PPM among Asian patients who have relatively smaller body sizes.[8,9] The mean BSA of patients in the OCEAN-TAVI registry[9] was 1.38 m^2 compared to 1.81 to 1.87 m^2 in Caucasian cohorts.[6,8] In this Philippine study, the mean BSA was 1.8 m^2, which was closer to the mean BSA of Western studies. With a larger BSA, the ratio of the native aortic annulus size and the eventual TAVR prosthetic size to the BSA would expectedly be smaller.

In both Asian and Caucasian studies, the mean BSA of patients with PPM was significantly larger than those with no PPM.[6,8,9] However, our study showed that the characteristics of patients who had PPM did not significantly differ from those without PPM post-TAVR in terms of BSA, procedural and echocardiographic characteristics. The low PPM rate and the accompanying low statistical power of the analysis may have contributed to this lack of difference.

Other than larger BSA, reported predictors of severe PPM post-TAVR in earlier studies included small (≤23-mm) valve prosthesis size, valve-in-valve procedure, female sex, younger age, non-white/Hispanic race, lower ejection fraction, atrial fibrillation, severe mitral or tricuspid regurgitation, smaller aortic valve area, smaller annulus area, no balloon post-dilatation, and use of Edwards Sapien 3 (Edwards Lifesciences, Irvine, California).[6,8,10,11,17-19] These studies were prospective investigations with standardized measurements and recording of patient variables in a larger cohort of patients. Nonetheless, similar to these reports, we observed a non-significant trend towards a younger age, larger BSA and smaller prosthesis size in patients with PPM post-TAVR.

This Philippine cohort has a higher percentage of patients with bicuspid aortic valve (11.3%) compared to the OCEAN-TAVI registry (1.2%).[9] The reported higher prevalence of bicuspid valve among Asian patients has been raised as a concern during TAVR.[10,20,21] While our results did not show that bicuspid aortic valve morphology was significantly associated with the development of PPM post-TAVR, further studies are recommended to continue investigating the impact of this variable and other factors on the risk of PPM.

Our study found that PPM post-TAVR was not associated with significantly increased mortality. This observation is consistent with the conclusion of the OCEAN-TAVI registry[9] that among Asian patients, PPM post-TAVR does not impair survival. An earlier observation among patients receiving a bioprosthetic valve through SAVR[22] showed that PPM was significantly associated with impaired survival for patients with BSA >1.7m^2 whereas the impact of PPM was not significant among smaller patients (BSA <1.7m^2). This does not negate the conclusions of OCEAN-TAVI, which enrolled patients with an average BSA <1.7m^2. However, our study had larger patients with a mean BSA of 1.8 m^2 and yet had the same observation regarding mortality. This may be attributed to the larger size of prosthetic valves used for our larger patients. The average size of the prostheses used in our study was 28 mm versus 24.47 mm in the OCEAN-TAVI registry.[9] Among SAVR patients, higher mortality rates were also observed among those receiving smaller-sized bioprosthetic valves.[22] Thus, even with a larger BSA, implanting a larger prosthetic valve may help prevent a small ratio for iEOA and minimize the impact on mortality post-TAVR.

Our findings on mortality differ from the recent findings of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) registry and the PARTNER trial.[4,8] These studies found higher mortality in patients with PPM post-TAVR. However, these two larger registries, unlike the OCEAN-TAVI group, reported the association of mortality specifically with severe PPM (iEOA <0.65 cm^2/m^2). Future investigation on a larger Philippine cohort may be conducted to be able to perform subgroup analysis of patients according to PPM severity.

This was a pilot investigation among our local patients and some limitations of this study must be mentioned. First, this was a retrospective study done in a single center. The data was largely based on clinical reports gathered post-procedure. This study also lacked evaluation of other clinical outcomes post-TAVR and their association with PPM. Second, since the experience with TAVR in the country is still growing, a larger population size will help provide more definitive conclusions. Our study group intends to continue further investigation as the experience with TAVR grows.

CONCLUSION

The prevalence of PPM post-TAVR among patients in the Philippines was 15.8%; 4.5% had severe and 11.3% had moderate PPM. This was higher than that observed among the Japanese population but lower than those reported among larger Western registries. There was no difference in the clinical, procedural, and echocardiographic characteristics of patients with and without PPM post TAVR. Survival outcome of patients with PPM post-TAVR was similar to those without PPM. These findings indicate that PPM post TAVR has no significant impact on mortality among patients in the Philippines.

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