

Impact of aortic annular size and valve type on haemodynamics and clinical outcomes after transcatheter aortic valve implantation

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ABSTRACT

Introduction: Data on patients with small aortic annuli (SAA) undergoing transcatheter aortic valve implantation (TAVI) are limited. We aim to describe the impact of aortic annular size, particularly SAA and TAVI valve type on valve haemodynamics, durability and clinical outcomes.

Method: All patients in National Heart Centre Singapore who underwent transfemoral TAVI for severe symptomatic native aortic stenosis from July 2012 to December 2019 were included. Outcome measures include valve haemodynamics, prosthesis-patient mismatch (PPM), structural valve degeneration (SVD) and mortality.

Results: A total of 244 patients were included. The mean Society of Thoracic Surgeons score was 6.22 ± 6.08 , with 52.5% patients with small aortic annulus ($<23\text{mm}$), 33.2% patients with medium aortic annulus ($23\text{--}26\text{mm}$) and 14.3% patients with large aortic annulus ($>26\text{mm}$). There were more patients with self-expanding valve (SEV) (65.2%) versus balloon-expandable valve (BEV) (34.8%). There were no significant differences in indexed aortic valve area (iAVA), mean pressure gradient (MPG), PPM, SVD or mortality across all aortic annular sizes. However, specific to the SAA group, patients with SEV had larger iAVA (SEV $1.19 \pm 0.35\text{cm}^2/\text{m}^2$ vs BEV $0.88 \pm 0.15\text{cm}^2/\text{m}^2$, $P < 0.01$) and lower MPG (SEV $9.25 \pm 4.88\text{ mmHg}$ vs BEV $14.17 \pm 4.75\text{ mmHg}$, $P < 0.01$) at 1 year, without differences in PPM or mortality. Aortic annular size, TAVI valve type and PPM did not predict overall mortality up to 7 years. There was no significant difference in SVD between aortic annular sizes up to 5 years.

Conclusion: Valve haemodynamics and durability were similar across the different aortic annular sizes. In the SAA group, SEV had better haemodynamics than BEV at 1 year, but no differences in PPM or mortality. There were no significant differences in mortality between aortic annular sizes, TAVI valve types or PPM.

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INTRODUCTION

The management of severe aortic stenosis (AS) in patients with small aortic annulus (SAA) represents a therapeutic challenge due to the increased mortality and major adverse cardiac events (MACE) seen in this group of patients even after surgical aortic valve replacement (SAVR).^{1,2}

In recent times, the role of transcatheter aortic valve implantation (TAVI) has expanded significantly to include even those with low surgical risk.³ With the

increased life expectancy in this low-risk group, it has become imperative to understand the impact of aortic annular size and TAVI valve type on prosthesis-patient mismatch (PPM), structural valve degeneration (SVD) and other clinical outcomes. While the negative impact of PPM has been well elucidated in SAVR, the data within TAVI cohorts have been controversial.⁴⁻⁶ Several studies have evaluated the medium-to-long-term valve durability of TAVI,⁷⁻¹¹ but there is limited data on patients with SAA especially in Western cohorts where

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CLINICAL IMPACT

What is New

- To the best of our knowledge, this is the first study in Southeast Asia evaluating the impact of aortic valve annular size, with a focus on small aortic annulus (SAA), for patients with aortic stenosis undergoing transcatheter aortic valve implantation (TAVI).

Clinical Implications

- There were no significant differences in mortality between aortic annular sizes, TAVI valve types or prosthesis-patient mismatch (PPM) at 1 year.
- In the SAA group, while self-expanding valves may be considered given better haemodynamics and lower PPM than balloon expandable valves at 1 year, there was no significant differences in mortality.

patients with larger annular areas predominate; this information gap would be particularly useful in an Asian population, where a significant proportion have SAA.

This study aims to describe the impact of aortic annular sizing and TAVI valve type on valve haemodynamics and durability, as well as clinical outcomes in patients undergoing TAVI, with a particular focus on patients with SAA.

METHOD

All consecutive patients with severe symptomatic AS treated with TAVI at National Heart Centre Singapore from July 2012 to December 2019 were prospectively recruited into the registry (Centralised Institutional Review Board Reference 2014/2165). Details of the registry have been previously published.^{12,13} In summary, a heart team was involved in the selection of patients, type of transcatheter aortic valve used, and approach. Registry participation did not impact clinical management. Written informed consent was obtained from all patients and ethical approval for the study was procured from the institutional review board. The TAVI procedure was carried out as per previously published standard protocols.^{14,15} All patients underwent echocardiographic evaluation at baseline prior to intervention, before discharge, at 3 months follow-up and yearly thereafter.

All patients who had transfemoral TAVI performed for severe native aortic valve stenosis, and those with a

computed tomography (CT) performed for valve sizing were included. Patients with severe aortic regurgitation, non-transfemoral TAVI, valve-in-valve TAVI, and use of other modalities for valve sizing (e.g. transoesophageal echocardiogram) were excluded.

All patients underwent pre-operative evaluation of the aortic valve and aortic root, as well as the aorto-ilio-femoral vasculature anatomy, with either a 64-detector or 320-detector row CT scanner (Canon Medical Systems Corp, Otawara, Japan). Acquisition protocols of multidetector computed tomography (MDCT) data were acquired as per recommended.¹⁶⁻¹⁸ In brief, contrast-enhanced ECG-gated acquisition of the aortic root was performed after the injection of iodinated contrast, with the region of interest placed in the ascending aorta and axial slice of <1mm. All the MDCT data sets were recorded and stored for post-processing using 3mensio (3mensio Medical Imaging BV, Bilthoven, The Netherlands).¹⁹ From the 3 multiplanar reformation planes and the 3-dimensional reconstruction, automatic segmentation of the aortic root and a centre line crossing the aortic lumen is provided. After validation of the lowest insertion points of all the aortic cusp and the perpendicular plane, the maximum, minimum and mean diameters, area and perimeter of the aortic valve annulus are measured using the systolic images, at 30–40% of the RR interval of the contrast-enhanced MDCT scans, for sizing of the device. This is based on either the annular area (for balloon-expandable valve [BEV]) or the perimeter (for self-expanding valve [SEV]) of the annular dimension. In addition, the coronary heights and the respective sinus of Valsalva, sinotubular junction and ascending aorta dimensions were obtained, as recommended.¹⁶⁻¹⁸ Patients were stratified based on the aortic annular diameter derived on MDCT, either by area-derived (for BEVs) or perimeter-derived (for SEVs) method, with small annulus defined as <23mm, medium as 23–26mm, and large as ≥26mm, respectively.

Patients included in the registry were followed up based on a fixed schedule, with all patients completing in-hospital follow-ups, although not all patients completed 1-year follow-up. Outcome measures were based on Valve Academic Research Consortium 3-defined endpoints.²⁰ The primary outcome of this study was 1-year all-cause mortality. Secondary outcomes included in-hospital mortality, post-procedure complications, PPM and SVD. PPM was defined as an indexed aortic valve area (iAVA) of <0.85cm²/m² based on the post-TAVI echocardiogram performed prior to the patient discharged on index admission for TAVI, with those between 0.65 and 0.85cm²/m² classified as moderate, and <0.65cm²/m² classified as severe. SVD

was defined by changes in mean pressure gradient (MPG) and aortic valve area (AVA) and/or new occurrence of aortic regurgitation (AR) compared with serial echocardiographic assessments performed post-procedure. Moderate SVD was defined as an increase in $\text{MPG} \geq 10 \text{ mmHg}$ resulting in the mean gradient $\geq 20 \text{ mmHg}$ with a concomitant decrease in $\text{AVA} \geq 0.3 \text{ cm}^2$ or $\geq 25\%$, and/or a new occurrence or increase of ≥ 1 grade of intraprosthetic AR resulting in $\geq$ moderate AR. Severe SVD was defined as an increase in $\text{MPG} \geq 20 \text{ mmHg}$ resulting in mean gradient $\geq 30 \text{ mmHg}$ with concomitant decrease in $\text{AVA} \geq 0.6 \text{ cm}^2$, and/or new occurrence, or increase of ≥ 2 grades of intraprosthetic AR, resulting in severe AR.

Continuous variables were expressed as mean $\pm$ standard deviation (SD) and categorical data was expressed as proportions and percentages. Echocardiographic outcomes were limited in some patients and the percentages calculated for echocardiographic outcomes were based on the denominator of those with such parameters measured. Comparison between continuous data was performed using the independent t-test or one-way analysis of variance, while categorical data were compared using chi-square test or Fisher's exact test. Short-term outcomes between the different aortic annular sizes were compared using logistic regression, and longer-term outcomes were compared using cox regression with the corresponding hazard ratios (HRs) and 95% confidence intervals calculated. Subgroup analyses based on TAVI valve type and PPM were also performed. Univariate analysis was performed for clinically significant variables with $P < 0.10$, and multivariate analyses was subsequently done to adjust for confounders. Statistical analyses were conducted using Stata version 16 (StataCorp, College Station, Texas).

RESULTS

A total of 244 patients with mean Society of Thoracic Surgeons (STS) score of 6.22 ± 6.08 were included. The mean duration of follow-up was $1,147 \pm 798$ days.

The majority of patients had a SAA, with 128 (52.5%) small ($< 23 \text{ mm}$), 81 (33.2%) medium ($23\text{--}26 \text{ mm}$) and 35 (14.3%) large ($\geq 26 \text{ mm}$). There were more patients with SEV (65.2%) versus BEV (34.8%). Compared with other groups, patients with SAA weighed less (small $58.82 \pm 12.15 \text{ kg}$ vs medium $62.83 \pm 14.13 \text{ kg}$ vs large $64.73 \pm 12.45 \text{ kg}$, $P < 0.001$), were shorter (small $154.02 \pm 8.24 \text{ cm}$ vs medium $159.77 \pm 8.39 \text{ cm}$ vs large $165.26 \pm 8.66 \text{ cm}$, $P < 0.001$), had lower body surface area (BSA) (small $1.55 \pm 0.18 \text{ m}^2$ vs medium $1.66 \pm 0.2 \text{ m}^2$ vs large $1.71 \pm 0.19 \text{ m}^2$, $P < 0.001$) and were predominantly female (small 64.84% vs medium

37.16% vs large 14.39%, $P < 0.001$). There was also a lower proportion of patients with bicuspid valves (small 5.08% vs medium 18.75% vs large 29.41%, $P < 0.001$). Mean left ventricular ejection fraction was higher for patients with SAA (small $57.16 \pm 11.24\%$ vs medium $49.80 \pm 14.49\%$ vs large $48.31 \pm 17.26\%$, $P < 0.001$), as seen in Table 1.

The CT parameters for the different aortic valve annuli are also reflected in Table 1. Of note, aortic calcium score was significantly lower for patients with smaller aortic valve annulus (small $2,179.78 \pm 1,281.58$ vs medium $27,86.05 \pm 22,076.32$ vs large $3,221.67 \pm 1,740.49$, $P < 0.007$). There was, however, no significant difference for the presence of porcelain aorta.

In terms of pertinent periprocedural complications, there was no significant difference with regards to permanent pacemaker implantation (small 8.59% vs medium 7.41% vs large 8.57%, $P > 0.05$) across the 3 groups.

Comparing haemodynamic outcomes, there was no significant difference in terms of PPM across different aortic annular sizes. While patients with SAA have a smaller AVA post-procedure (small $1.66 \pm 0.43 \text{ cm}^2$ vs medium $1.75 \pm 0.45 \text{ cm}^2$ vs large $1.93 \pm 0.52 \text{ cm}^2$, $P = 0.0016$) after correcting for BSA, iAVA did not show any significant difference (small 1.08 ± 0.29 vs medium 1.09 ± 0.32 vs large 1.12 ± 0.25 , $P = 0.821$). This is also corroborated by no significant differences for MPG between the different aortic annuli. At 1 year, however, there were significantly more patients with larger annulus with at least moderate paravalvular AR (small 10% vs medium 15.38% vs large 33.33%, small vs medium $P = 0.358$, small vs large $P = 0.036$).

In terms of mortality, there were no significant differences with regards to in-hospital or 1-year mortality (Table 2), or throughout the entire follow-up period as demonstrated in the Kaplan-Meier survival curve (Fig. 1) ($P > 0.05$).

From a valve durability standpoint, there were no patients who developed severe SVD up to 5 years of follow-up. Comparing the 3 groups, there was no significant difference in terms of SVD (Table 3). There were also no marked changes in AVA and MPG up to 5 years (Fig. 2).

Among those with SAA, patients who underwent SEV had a larger AVA (SEV $1.76 \pm 0.49 \text{ cm}^2$ vs BEV $1.39 \pm 0.25 \text{ cm}^2$, $P = 0.001$), larger iAVA (SEV $1.19 \pm 0.35 \text{ cm}^2/\text{m}^2$ vs BEV $0.88 \pm 0.15 \text{ cm}^2/\text{m}^2$, $P < 0.001$) and lower MPG (SEV $9.25 \pm 4.88 \text{ mmHg}$ vs BEV $14.17 \pm 4.75 \text{ mmHg}$, $P < 0.001$), at 1 year as illustrated in Fig. 3. However, there was no significant difference in

Table 1. Baseline and procedural characteristics of patients stratified by aortic annular size

Aortic annular size	Overall	<23mm	23–26mm	≥26mm	P value
	n=244	n=128	n=81	n=35	
Baseline characteristics					
Age, mean±SD, years	77.56±8.80	78.82±7.04	76.51±10.08	75.37±10.75	0.050
Male, no. (%)	134 (54.92)	45 (35.16)	59 (72.84)	30 (85.71)	<0.001
Body mass index, kg/cm ²	24.18±4.90	23.99±4.83	24.71±5.21	23.60±4.40	0.445
Weight, mean±SD, kg	59.95±13.26	56.82±12.15	62.83±14.13	64.73±12.45	<0.001
Height, mean±SD, cm	157.52±9.26	154.02±8.24	159.77±8.39	165.26±8.66	<0.001
Body surface area, mean±SD, m ²	1.61±0.20	1.55±0.18	1.66±0.20	1.71±0.19	<0.001
Smoker, no. (%)	38 (15.57)	14 (10.94)	17 (20.99)	7 (20.00)	0.110
Diabetes mellitus, no. (%)	92 (37.70)	45 (35.16)	32 (39.51)	15 (42.86)	0.650
Hypertension, no. (%)	203 (83.20)	111 (86.72)	64 (79.01)	28 (80.00)	0.300
Dyslipidaemia, no. (%)	179 (73.36)	96 (75.00)	62 (76.54)	21 (60.00)	0.150
Cerebrovascular disease, no. (%)	34 (13.93)	24 (18.75)	6 (7.41)	4 (11.43)	0.063
Chronic liver disease, no. (%)	14 (5.74)	8 (6.25)	3 (3.70)	3 (8.57)	0.548
Peripheral vascular disease, no. (%)	20 (8.23)	12 (9.45)	5 (6.17)	3 (8.57)	0.702
Obstructive lung disease, no. (%)	27 (11.07)	15 (11.72)	8 (9.88)	4 (11.43)	0.916
Coronary artery disease, no. (%)	174 (71.31)	93 (72.66)	59 (72.84)	22 (62.86)	0.490
Previous percutaneous coronary intervention, no. (%)	113 (46.31)	65 (50.78)	38 (46.91)	10 (28.57)	0.065
Previous coronary artery bypass graft, no. (%)	37 (15.23)	15 (11.81)	15 (18.52)	7 (20.00)	0.294
Atrial fibrillation, no. (%)	47 (19.26)	24 (18.75)	15 (18.52)	8 (22.86)	0.843
Estimated glomerular filtration rate, mean±SD	47.63±26.70	49.69±26.30	42.93±25.81	51.04±29.45	0.151
NYHA class III–IV, no. (%)	99 (40.57)	47 (36.72)	40 (49.38)	12 (34.29)	0.137
STS score	6.22±6.08	5.96±4.35	6.16±4.90	7.33±11.63	0.493
EuroScore II	5.57±6.94	5.09±5.35	5.75±6.55	6.97±11.69	0.369
Computed tomography measurements					
Aortic calcium score, mean±SD	2542.87±1698.76	2179.78±1281.59	2786.05±2076.32	3221.67±1740.49	0.007
Maximum diameter, mean±SD, mm	25.58±2.80	23.58±1.47	26.77±1.54	30.12±1.62	<0.001
Minimum diameter, mean±SD, mm	20.52±2.23	19.07±1.31	21.41±1.55	23.76±1.69	<0.001
Mean diameter, mean±SD, mm	23.03±2.31	21.29±1.18	24.08±0.89	26.94±1.13	<0.001
Area, mean±SD, mm ²	411.31±86.80	347.60±46.23	447.64±30.92	560.25±48.52	<0.001
Perimeter, mean±SD, mm	72.78±8.47	67.45±3.64	75.66±8.11	85.62±3.54	<0.001
Sinus of Valsalva average, mean±SD, mm	30.29±3.58	28.33±2.88	31.32±2.42	35.09±2.43	<0.001
Sintotubular junction, mean±SD, mm	26.04±3.52	24.50±3.10	26.93±2.78	29.57±3.28	<0.001
Sintotubular junction height, mean±SD, mm	19.69±2.76	18.40±2.04	20.41±2.36	22.74±3.00	<0.001
Ascending aorta diameter, mean±SD, mm	32.74±4.75	31.70±4.28	33.37±4.15	35.05±6.46	<0.001
Left main height, mean±SD, mm	13.83±7.70	13.21±10.24	14.04±2.97	15.63±2.74	0.249

Table 1. Baseline and procedural characteristics of patients stratified by aortic annular size (Cont'd)

Aortic annular size	Overall n=244	<23mm n=128	23–26mm n=81	≥26mm n=35	P value
Right coronary height, mean±SD, mm	16.39±2.53	15.26±2.17	17.03±2.04	19.03±2.31	<0.001
Porcelain aorta, no. (%)	36 (14.81)	18 (14.17)	16 (19.75)	2 (5.71)	0.142
Baseline echocardiographic parameters					
AvMPG, mean±SD, mmHg	48.31±16.30	47.64±16.14	49.71±17.32	47.52±14.58	0.648
AVA, mean±SD, cm ²	0.72±0.21	0.70±0.21	0.72±0.18	0.78±0.24	0.102
iAVA, mean±SD, cm ² /m ²	0.45±0.13	0.45±0.14	0.43±0.11	0.47±0.14	0.367
LVEF, mean±SD, %	53.43±13.87	57.16±11.24	49.80±14.49	48.31±17.26	<0.001
Aortic valve type					<0.001
Bicuspid, no. (%)	31 (13.36)	6 (5.08)	15 (18.75)	10 (29.41)	
Tricuspid, no. (%)	201 (86.64)	112 (94.92)	65 (81.25)	24 (70.59)	
Pre-procedure AR (≥moderate), no. (%)	73 (30.67)	42 (33.60)	22 (27.85)	9 (26.47)	0.582
Procedural details					
Contrast volume, mean±SD, mL	141.98±66.54	139.17±71.47	138.05±56.79	160.26±67.35	0.220
Procedural time, mean±SD, minutes	113.15±57.23	116.16±59.28	111.14±59.38	105.92±43.13	0.701
Valve type					0.017
BEV, no. (%)	81 (34.76)	33 (26.83)	31 (40.79)	17 (50.00)	
SEV, no. (%)	152 (65.24)	90 (73.17)	45 (59.21)	17 (50.00)	

AR: aortic regurgitation; AvMPG: aortic valve mean pressure gradient; AVA: aortic valve area; BEV: balloon-expandable valve; iAVA: indexed aortic valve area; LVEF: left ventricle ejection fraction; NYHA: New York Heart Association; STS: Society of Thoracic Surgeons; SD: standard deviation; SEV: self-expanding valve

terms of PPM. There were also no significant differences with regard to the presence of AR or pacemaker implantation. Both inpatient and 1-year mortality was not significantly different between the groups ($P>0.05$) (Table 4).

Among patients with large aortic annuli, while there was a significant difference in iAVA during the index hospitalisation in those who underwent SEV compared to BEV (1.22 ± 0.24 vs 1.02 ± 0.24 , $P=0.042$), there were no differences in aortic valve MPG. In addition, these differences were not seen at 1-year follow-up.

As seen in Table 5, for both medium and large aortic annuli, there were no significant differences in inpatient or 1-year mortality ($P>0.05$). Additionally, regardless of annular size, having at least moderate PPM did not have any significant differences in inpatient and 1-year clinical outcomes ($P>0.05$).

In the overall cohort, multivariate analyses (Table 6) demonstrated that aortic annular size (reference group small, medium HR 1.03, 95% confidence interval [CI]

0.54–1.98, $P=0.929$, large HR 1.85, 95% CI 0.83–4.09, $P=0.133$), TAVI valve type (reference group BEV, SEV HR 1.45, 95% CI 0.78–2.68, $P=0.240$) and moderate to severe PPM (HR 1.72, 95% CI 0.86–3.44, $P=0.113$) were not significant predictors of mortality. Independent predictors of mortality include obstructive lung disease (HR 2.21, 95% CI 1.05–4.64, $P=0.036$) and a lower estimated glomerular filtration rate (eGFR) (HR 1.02 95% CI 1.01–1.03, $P=0.001$).

DISCUSSION

In this study, we evaluated the impact of aortic annular sizing and TAVI valve type on valve haemodynamics and durability, as well as clinical outcomes in patients undergoing TAVI. In particular, there were substantial data on patients with SAA. We observed several significant findings: (1) annular size had no impact on valve haemodynamics, PPM or mortality; (2) in patients with small annular size, SEV had better valve haemodynamics than BEV but no differences in mortality; (3) moderate or severe PPM did not impact

Table 2. Inpatient and 1-year outcomes stratified by aortic annular size

	Overall	<23mm	23–26mm	≥26mm	P value (overall)	
	n=244	n=128	n=81	n=35	<23 vs 23–26	<23 vs ≥26
Inpatient outcomes						
AVA, mean±SD, cm ²	1.73±0.46	1.66±0.43	1.75±0.45	1.93±0.52	0.016	
iAVA, mean±SD, cm ² /m ²	1.09±0.30	1.08±0.29	1.09±0.32	1.12±0.25	0.821	
AvMPG, mean±SD, mmHg	10.63±4.85	10.37±5.02	11.27±5.02	10.03±3.62	0.331	
≥Moderate AR, no. (%)	28 (11.91)	16 (13.22)	7 (8.75)	5 (14.71)	0.333	0.823
≥Moderate PPM, no. (%)	43 (21.18)	24 (22.86)	15 (21.74)	4 (13.79)	0.863	0.293
Moderate PPM, no. (%)	30 (14.78)	18 (17.14)	9 (13.04)	3 (10.34)	0.466	0.378
Severe PPM, no. (%)	13 (6.40)	6 (5.71)	6 (8.70)	1 (3.45)	0.451	0.631
Cardiovascular death, no. (%)	4 (1.64)	2 (1.56)	1 (1.23)	1 (2.86)	0.846	0.619
MACE, no. (%)	16 (6.64)	7 (5.56)	6 (7.41)	3 (8.82)	0.593	0.489
Death, no. (%)	7 (2.87)	5 (3.91)	1 (1.23)	1 (2.86)	0.286	0.771
Myocardial infarction, no. (%)	3 (1.24)	1 (0.79)	1 (1.23)	1 (2.94)	0.754	0.351
Stroke, no. (%)	7 (2.87)	2 (1.56)	4 (4.94)	1 (2.86)	0.177	0.619
Major bleeding, no. (%)	1 (0.41)	1 (0.79)	0	0	-	-
New pacemaker implantation, no. (%)	20 (8.20)	11 (8.59)	6 (7.41)	3 (8.57)	0.76	1.00
1-year outcomes						
AVA, mean±SD, cm ²	1.70±0.42	1.64±0.45	1.73±0.38	1.94±0.31	0.043	
iAVA, mean±SD, cm ² /m ²	1.08±0.31	1.08±0.33	1.05±0.28	1.18±0.25	0.416	
AvMPG, mean±SD, mmHg	11.22±5.19	11.05±5.53	11.74±4.90	10.15±4.18	0.566	
≥Moderate AR, no. (%)	20 (13.89)	8 (10.00)	8 (15.38)	4 (33.33)	0.358	0.036
Death, no. (%)	19 (8.88)	8 (7.14)	6 (8.33)	5 (16.67)	0.779	0.119
Cardiovascular death, no. (%)	10 (4.67)	4 (3.57)	3 (4.17)	3 (10.00)	0.840	0.158

AR: aortic regurgitation; AvMPG: aortic valve mean pressure gradient; AVA: aortic valve area; iAVA: indexed aortic valve area; MACE: major adverse cardiac events comprising death, myocardial infarction and stroke; PPM: prosthesis-patient mismatch; SD: standard deviation

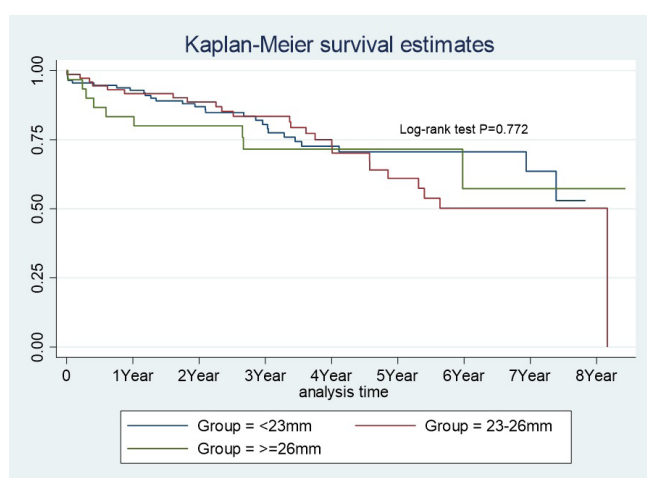


Fig. 1. Kaplan-Meier survival curve based on aortic annular size.

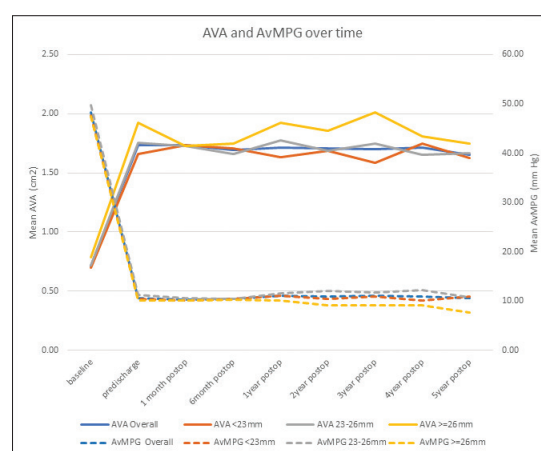


Fig. 2. Comparison of aortic valve area and mean pressure gradient over time based on aortic annular size.

AvMPG: aortic valve mean pressure gradient; AVA: aortic valve area

Table 3. Comparison of structural valve degeneration over time based on aortic annular size

	Overall		<23mm		23–26mm		≥26mm		P value
	n=244		n=128		n=81		n=35		
Moderate SVD	n/total	%	n/total	%	n/total	%	n/total	%	
1 year	13/122	10.66	6/65	9.23	6/46	13.04	1/11	9.09	0.802
2 year	10/105	9.52	3/56	5.36	6/38	15.79	1/11	9.09	0.239
3 year	8/75	10.67	3/36	8.33	4/30	13.33	1/9	11.11	0.806
4 year	5/57	8.77	3/26	11.54	2/25	8.00	0/6	0	0.656
5 year	3/34	8.82	1/14	7.14	2/17	11.76	0/3	0	0.770

SVD: structural valve degeneration

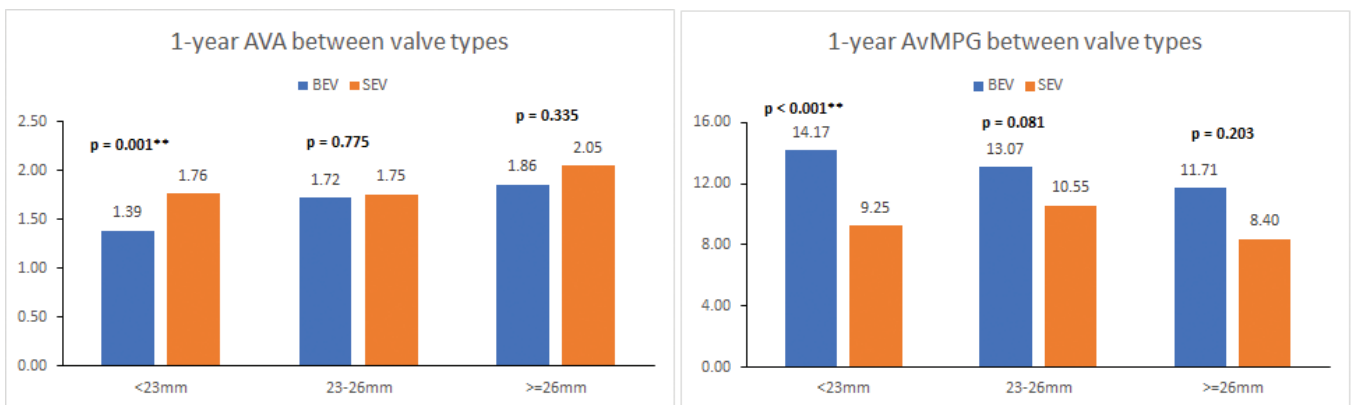


Fig. 3. Comparison of aortic valve area and mean pressure gradient over time based on aortic annular size and stratified by TAVI valve type. AvMPG: aortic valve mean pressure gradient; AVA: aortic valve area; BEV: balloon-expandable valve; SEV: self-expanding valve

on mortality, at least at 1 year; and (4) annular size did not impact on longer-term SVD.

In terms of anatomic features, aortic annular size appears to be one of the most relevant factors that could theoretically play a major role in influencing valve haemodynamic performance and clinical outcomes.²¹⁻²³ In our cohort, however, we found that this theoretical risk with the SAA group was not apparent; the SAA group had similar valve haemodynamics, especially after correcting for BSA, and clinical outcomes as the other groups. These findings are corroborated by other similar studies, especially in other Asian populations where there are significant groups of patients with SAA.^{22,24,25} Additionally, the SAA group in our cohort also had lower rates of paravalvular regurgitation post-intervention when compared to patients with larger aortic annulus. This is consistent with other studies with the postulation that the presence of an SAA minimises prosthesis-annulus incongruity, and allows for better apposition of the prosthesis to the native valve.²⁶ This might be clinically relevant in the long term as AR is known to be a determining factor of long-term mortality after TAVI.^{27,28} On balance, longer observation and larger patient

numbers may be required to validate a potential impact on long-term survival.

Studies have shown that SEV have better valve haemodynamics and lower PPM rates than BEV.^{29,30} Anatomically, the result of better haemodynamics may be driven by the supra-annular location in SEV compared with intra-annular location in BEV.²¹ These findings were also seen in our study but primarily in the SAA group. Importantly, there was no impact on mortality at 1 year regardless of valve type.

In terms of PPM, subgroup analyses of our cohort showed that moderate or severe PPM had no significant impact on mortality, at least at 1 year. The presence of severe PPM had been associated with negative outcomes, especially for patients post-SAVR.³¹ However, the impact of PPM appears mixed for patients post-TAVI, with some reporting an increased risk of mortality,⁴ while more recent studies showing no difference in clinical outcomes.^{5,6,32} The theoretical negative impact of PPM can be explained by poorer haemodynamics resulting in a delay of regression of post-operative left ventricular hypertrophy, which may result in increased morbidity (through limitations in

Table 4. Inpatient and 1-year outcomes stratified by TAVI valve type for small, medium and large aortic annular size

	BEV	SEV	P value
Small	n=33	n=90	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.55±0.41	1.72±0.43	0.076
iAVA, mean±SD, cm ² /m ²	0.97±0.27	1.15±0.28	0.006
AvMPG, mean±SD, mmHg	±4.72	9.25±4.52	0.004
≥Moderate AR, no. (%)	2 (6.45)	13 (15.29)	0.348
≥Moderate PPM, no. (%)	8 (29.63)	12 (16.22)	0.162
Moderate PPM, no. (%)	5 (18.52)	10 (13.51)	0.538
Severe PPM, no. (%)	3 (11.11)	2 (2.70)	0.117
Cardiovascular death, no. (%)	0	2 (2.22)	1.000
MACE, no. (%)	3 (9.09)	4 (4.55)	0.389
Death, no. (%)	3 (9.09)	2 (2.22)	0.119
Myocardial infarction, no. (%)	0	1 (1.14)	1.000
Stroke, no. (%)	0	2 (2.22)	1.000
Major bleeding, no. (%)	1 (3.03)	0	0.273
New pacemaker implantation, no. (%)	2 (6.06)	6 (6.67)	1.000
1-year outcomes			
AVA, mean±SD, cm ²	1.39±0.25	1.76±0.49	0.001
iAVA, mean±SD, cm ² /m ²	0.88±0.15	1.19±0.35	<0.001
AvMPG, mean±SD, mmHg	14.17±4.75	9.25±4.88	<0.001
≥Moderate AR, no. (%)	2 (8.70)	5 (9.62)	1.000
Death, no. (%)	3 (9.68)	5 (6.58)	0.688
Cardiovascular death, no. (%)	0	4 (5.26)	0.321
Medium	n=31	n=45	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.78±0.36	1.79±0.48	0.920
iAVA, mean±SD, cm ² /m ²	1.09±0.27	1.12±0.34	0.703
AvMPG, mean±SD, mmHg	11.07±4.21	11.27±5.61	0.868
≥Moderate AR, no. (%)	1 (3.23)	6 (13.64)	0.228
≥Moderate PPM, no. (%)	5 (19.23)	7 (18.42)	1.000
Moderate PPM, no. (%)	3 (11.54)	5 (13.16)	1.000
Severe PPM, no. (%)	2 (7.69)	2 (5.26)	1.000
Cardiovascular death, no. (%)	0	1 (2.22)	1.000
MACE, no. (%)	2 (6.45)	4 (8.89)	1.000
Death, no. (%)	0	1 (2.22)	1.000
Myocardial infarction, no. (%)	1 (3.23)	0	0.408
Stroke, no. (%)	1 (3.23)	3 (6.67)	0.641

Table 4. Inpatient and 1-year outcomes stratified by TAVI valve type for small, medium and large aortic annular size (Cont'd)

	BEV	SEV	P value
Major bleeding, no. (%)	0	0	-
New pacemaker implantation, no. (%)	1 (3.23)	4 (8.89)	0.643
1-year outcomes			
AVA, mean±SD, cm ²	1.72±0.39	1.75±0.39	0.775
iAVA, mean±SD, cm ² /m ²	1.04±0.30	1.07±0.28	0.680
AvMPG, mean±SD, mmHg	13.07±5.58	10.55±4.19	0.081
≥Moderate AR, no. (%)	2 (10.53)	5 (17.24)	0.687
Death within 1 year, no. (%)	0	5 (11.63)	0.151
Cardiovascular death within 1 year, no. (%)	0	3 (6.98)	0.548
Large	n=17	n=17	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.77±0.44	2.09±0.57	0.109
iAVA, mean±SD, cm ² /m ²	1.02±0.24	1.22±0.24	0.042
AvMPG, mean±SD, mmHg	10.71±3.33	9.67±3.75	0.416
≥Moderate AR, no. (%)	2 (11.76)	3 (18.75)	0.656
≥Moderate PPM, no. (%)	2 (15.38)	2 (13.33)	1.000
Moderate PPM, no. (%)	1 (7.69)	2 (13.33)	1.000
Severe PPM, no. (%)	1 (7.69)	0	0.464
Cardiovascular death, no. (%)	1 (5.88)	0	1.000
MACE, no. (%)	2 (11.76)	1 (6.25)	1.000
Death, no. (%)	1 (5.88)	0	1.000
Myocardial infarction, no. (%)	1 (5.88)	0	1.000
Stroke, no. (%)	0	1 (5.88)	1.000
Major bleeding, no. (%)	0	0	-
New pacemaker implantation, no. (%)	1 (5.88)	2 (11.76)	1.000
1-year outcomes			
AVA, mean±SD, cm ²	1.86±0.30	2.05±0.37	0.335
iAVA, mean±SD, cm ² /m ²	1.13±0.28	1.25±0.23	0.435
AvMPG, mean±SD, mmHg	11.71±3.64	8.40±4.83	0.203
≥Moderate AR, no. (%)	2 (28.57)	2 (50.00)	0.576
Death within 1 year, no. (%)	2 (13.33)	3 (21.43)	0.651
Cardiovascular death within 1 year, no. (%)	1 (6.67)	2 (14.29)	0.598
Overall	n=81	n=152	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.69±0.41	1.79±0.47	0.144
iAVA, mean±SD, cm ² /m ²	1.03±0.27	1.15±0.30	0.007
AvMPG, mean±SD, mmHg	11.40±4.24	9.92±4.87	0.024

Table 4. Inpatient and 1-year outcomes stratified by TAVI valve type for small, medium and large aortic annular size (Cont'd)

	BEV	SEV	<i>P</i> value
≥Moderate AR, no. (%)	5 (6.33)	22 (15.17)	0.052
≥Moderate PPM, no. (%)	15 (22.73)	21 (16.54)	0.295
Moderate PPM, no. (%)	9 (13.64)	17 (13.39)	0.961
Severe PPM, no. (%)	6 (9.09)	4 (3.15)	0.094
Cardiovascular death, no. (%)	1 (1.23)	3 (1.97)	1.000
MACE, no. (%)	7 (8.64)	9 (6.04)	0.459
Death, no. (%)	4 (4.94)	3 (1.97)	0.241
Myocardial infarction, no. (%)	2 (2.47)	1 (0.67)	0.251
Stroke, no. (%)	1 (1.23)	6 (3.95)	0.426
Major bleeding, no. (%)	1 (1.25)	0	0.348
New pacemaker implantation, no. (%)	4 (4.94)	12 (7.89)	0.587
1-year outcomes			
AVA, mean±SD, cm ²	1.59±0.37	1.78±0.45	0.014
iAVA, mean±SD, cm ² /m ²	0.98±0.25	1.15±0.32	0.002
AvMPG, mean±SD, mmHg	13.39±4.94	9.63±4.65	<0.001
≥Moderate AR, no. (%)	6 (12.24)	12 (13.95)	0.779
Death within 1 year, no. (%)	5 (7.14)	13 (9.77)	0.531
Cardiovascular death within 1 year, no. (%)	1 (1.43)	9 (6.77)	0.169

AR: aortic regurgitation; AvMPG: aortic valve mean pressure gradient; AVA: aortic valve area; BEV: balloon-expandable valve; MACE: major adverse cardiac events comprising death, myocardial infarction and stroke; PPM: prosthesis-patient mismatch; SEV: self-expanding valve; TAVI: transcatheter aortic valve implantation

Table 5. Inpatient and 1-year outcomes stratified by presence of PPM for small, medium and large aortic annular size

	Without PPM	≥Moderate PPM	<i>P</i> value
Small	n=81	n=24	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.82±0.34	1.13	<0.001
iAVA, mean±SD, cm ² /m ²	1.20±0.22	0.69	<0.001
AvMPG, mean±SD, mmHg	8.98±3.68	14.86	<0.001
≥Moderate AR, no. (%)	10 (12.35)	3 (12.50)	1.000
Cardiovascular death, no. (%)	0	1 (4.17)	0.229
MACE, no. (%)	1 (1.25)	2 (8.70)	0.124
Death, no. (%)	0	2 (8.33)	0.051
Myocardial infarction, no. (%)	0	1 (4.35)	0.223
Stroke, no. (%)	1 (1.23)	0	1.000
Major bleeding, no. (%)	0	0	-
New pacemaker implantation, no. (%)	6 (7.41)	4 (16.67)	0.231
1-year outcomes			

Table 5. Inpatient and 1-year outcomes stratified by presence of PPM for small, medium and large aortic annular size (Cont'd)

	Without PPM	≥Moderate PPM	P value
AVA, mean±SD, cm ²	1.65±0.47	1.48±0.29	0.184
iAVA, mean±SD, cm ² /m ²	1.10±0.34	0.96±0.21	0.122
AvMPG, mean±SD, mmHg	10.74±5.82	13.44±4.69	0.095
≥Moderate AR, no. (%)	4 (7.69)	2 (12.50)	0.620
Death, no. (%)	2 (2.94)	3 (13.64)	0.092
Cardiovascular death, no. (%)	1 (1.47)	2 (9.09)	0.147
Medium	n=54	n=15	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.90±0.37	1.22±0.23	<0.001
iAVA, mean±SD, cm ² /m ²	1.19±0.27	0.71±0.11	<0.001
AvMPG, mean±SD, mmHg	9.65±4.12	16.20±5.13	<0.001
≥Moderate AR, no. (%)	6 (11.11)	0	0.327
Cardiovascular death, no. (%)	0	0	-
MACE, no. (%)	2 (3.70)	1 (6.67)	0.527
Death, no. (%)	0	0	-
Myocardial infarction, no. (%)	1 (1.85)	0	1.000
Stroke, no. (%)	1 (1.85)	1 (6.67)	0.390
Major bleeding, no. (%)	0	0	-
New pacemaker implantation, no. (%)	4 (7.41)	2 (13.33)	0.604
1-year outcomes			
AVA, mean±SD, cm ²	1.78±0.37	1.55±0.36	0.075
iAVA, mean±SD, cm ² /m ²	1.10±0.28	0.92±0.21	0.057
AvMPG, mean±SD, mmHg	10.39±3.85	15.50±5.64	0.001
≥Moderate AR, no. (%)	7 (20.00)	0	0.171
Death within 1 year, no. (%)	4 (8.33)	1 (7.69)	1.000
Cardiovascular death within 1 year, no. (%)	2 (4.17)	0	1.000
Large	n=25	n=4	
Inpatient outcomes			
AVA, mean±SD, cm ²	2.02±0.50	1.30±0.12	0.009
iAVA, mean±SD, cm ² /m ²	1.18±0.21	0.73±0.10	<0.001
AvMPG, mean±SD, mmHg	9.84±3.58	12.00±3.56	0.274
≥Moderate AR, no. (%)	5 (20.00)	0	1.000
Cardiovascular death, no. (%)	1 (4.00)	0	1.000
MACE, no. (%)	3 (12.50)	0	1.000
Death, no. (%)	1 (4.00)	0	1.000
Myocardial infarction, no. (%)	1 (4.17)	0	1.000
Stroke, no. (%)	1 (4.00)	0	1.000

Table 5. Inpatient and 1-year outcomes stratified by presence of PPM for small, medium and large aortic annular size (Cont'd)

	Without PPM	≥Moderate PPM	<i>P</i> value
Major bleeding, no. (%)	0	0	-
New pacemaker implantation, no. (%)	3 (12.00)	0	1.000
1-year outcomes			
AVA, mean±SD, cm ²	1.93±0.29	2.13±0.47	0.432
iAVA, mean±SD, cm ² /m ²	1.17±0.24	1.23±0.27	0.755
AvMPG, mean±SD, mmHg	10.67±3.94	5.50±2.12	0.114
≥Moderate AR, no. (%)	4 (44.44)	0	1.000
Death within 1 year, no. (%)	5 (23.81)	0	0.549
Cardiovascular death within 1 year, no. (%)	3 (14.29)	0	1.000
Overall	n=160	n=43	
Inpatient outcomes			
AVA, mean±SD, cm ²	1.88±0.38	1.18±0.23	<0.001
iAVA, mean±SD, cm ² /m ²	1.19±0.24	0.70±0.12	<0.001
AvMPG, mean±SD, mmHg	9.34±3.82	15.07±6.18	<0.001
≥Moderate AR, no. (%)	21 (13.13)	3 (6.98)	0.424
Cardiovascular death, no. (%)	1 (0.63)	1 (2.33)	0.316
MACE, no. (%)	6 (3.80)	3 (7.14)	0.400
Death, no. (%)	1 (0.63)	2 (4.65)	0.114
Myocardial infarction, no. (%)	2 (1.27)	1 (2.38)	0.509
Stroke, no. (%)	3 (1.88)	1 (2.33)	1.000
Major bleeding, no. (%)	0	0	-
New pacemaker implantation, no. (%)	13 (8.13)	6 (13.95)	0.244
1-year outcomes			
AVA, mean±SD, cm ²	1.72±0.43	1.55±0.36	0.050
iAVA, mean±SD, cm ² /m ²	1.11±0.31	0.96±0.22	0.020
AvMPG, mean±SD, mmHg	10.61±4.99	13.67±5.43	0.005
≥Moderate AR, no. (%)	15 (15.46)	2 (7.14)	0.357
Death within 1 year, no. (%)	11 (8.03)	4 (10.26)	0.745
Cardiovascular death within 1 year, no. (%)	6 (4.38)	2 (5.13)	1.000

AR: aortic regurgitation, AvMPG: aortic valve mean pressure gradient, AVA: aortic valve area, MACE: major adverse cardiac events comprising death, myocardial infarction and stroke, PPM: prosthesis-patient mismatch, SEV: self-expanding valve

physical activity) and mortality in the long run. With improvements and advances in the bioprosthetic valve hemodynamic performance in the past decades, the negative effects of PPM may be attenuated.³² Our study adds to the growing evidence that PPM may not necessarily be related to increased mortality at least at 1 year, although this warrants longer follow-up to evaluate its effects on medium-to-long-term mortality.

In terms of valve durability, our study showed that annular size did not have an impact on SVD. While the medium-to-long-term valve durability of TAVI has been evaluated,⁷⁻¹¹ these have been mainly in Western cohorts of patients with predominantly larger annular areas. In summary, these studies have shown that valve haemodynamics remained consistent for up to 7 years, with similar freedom from severe SVD for TAVI when

Table 6. Multivariate analysis for independent predictors of overall mortality

	Hazard ratio	95% Confidence interval	P value
Aortic annular size			
<23mm	(reference)	(reference)	(reference)
23–26mm	1.03	0.54–1.97	1.97)
≥26mm	1.84	0.83–4.07	0.133
Decreased eGFR	0.98	0.97–0.99	0.001
NYHA III/IV	1.35	0.75–2.45	0.317
Obstructive lung disease	2.21	1.05–4.64	0.036
Moderate or severe prosthesis patient mismatch	1.75	0.88–3.50	0.113
Valve type			
BEV	(reference)	(reference)	(reference)
SEV	1.45	0.78–2.68	0.240

BEV: balloon-expandable valve; eGFR: estimated glomerular filtration rate; NYHA: New York Heart Association; SEV: self-expanding valve

compared to SAVR. Given that severe PPM and small prosthesis size have been postulated to be potential factors leading to accelerated bioprosthetic degeneration,³³ data from patients with SAA is valuable. This study adds further knowledge in this burgeoning field, demonstrating the stability of valve haemodynamics especially in the SAA cohort up to 5 years. We acknowledge that longer-term studies are warranted—especially among younger patients with smaller bioprostheses who are at risk of requiring future interventions through valve-in-valve TAVI or redoing SAVR in the longer term.

Intrinsic limitations in our non-randomised prospective observational single-centre study are the possibility of bias that may not be fully accounted for even with the adjustment of confounders. Furthermore, the smaller patient numbers may not have been enough to detect smaller differences. However, the data do provide valuable insights, especially in a cohort with a significant proportion of patients with SAA. Lastly, there were fewer patients with long-term follow-up data; such information may be needed, especially for studying the outcome of SVD and the impact of PPM. Nevertheless, interesting hypotheses have been raised, which will be the work for future research.

CONCLUSION

Valve haemodynamics and durability were similar across the different aortic annular sizes. In the SAA group, SEV had better haemodynamics than BEV at 1 year, but no differences in PPM or mortality. There were no significant differences in mortality between aortic annular sizes, TAVI valve types or PPM.

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