Impact of Flow Status on Effective Orifice Area in Transcatheter Heart Valves: A COMPARE-TAVI 1 Substudy

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Objective: The aim of this study was to study the impact of flow status on effective orifice area (EOA) in patients treated with the balloon-expandable Myval and Sapien transcatheter heart valves (THVs).

Methods: We collected the core laboratory-measured EOA, mean and peak gradients, Doppler velocity index (DVI), and stroke volume index (SVi) from the 30-day echocardiograms in patients treated with the balloon-expandable Myval and Sapien THVs in the COMPARE-TAVI 1 trial. Patients were stratified according to flow into low flow (SVi <35 mL/m^2), normal flow (SVi 35-50 mL/m^2), and high flow (SVi >50 mL/m^2).

Results: A total of 1,031 patients were included in COMPARE-TAVI 1. Myval THVs (20.0-32.0 mm) exhibited overall higher mean EOA and lower mean gradients (1.99 ± 0.55 cm^2, 9.46 ± 3.84 mm Hg) compared to Sapien THVs (20-29 mm; 1.81 ± 0.56 cm^2, 11.47 ± 4.47 mm Hg). Compared to normal-flow patients, low-flow patients exhibited smaller EOA (P < .001) and lower DVI (P < .001) in all valve sizes irrespective of THV platform, while high-flow patients had larger EOA (P < .001) and higher DVI (P < .001). Female sex was associated with lower stroke volume, resulting in lower mean and peak gradients independent of valve size and platform (P < .001).

Conclusion: The study indicates that EOA may be underestimated after TAVI in patients with low-flow status, which can impact the assessment of prosthesis-patient mismatch. (J Am Soc Echocardiogr 2025;■:■-■.)

Keywords: TAVI, Myval, Sapien, RCT, COMPARE-TAVI 1

INTRODUCTION

Transcatheter aortic valve intervention (TAVI) is becoming the preferred treatment for severe symptomatic aortic stenosis, surpassing the use of surgical aortic valve replacement. While prosthesis-patient mismatch (PPM) is less common in TAVI,[1-3] the incidence still remains relatively high, with moderate and severe PPM occurring in one-third of subjects.[4,5] However, this may be overestimated due to limitations in the current PPM definition.

Predicted PPM may still be a consideration in future decision-making when selecting the appropriate valve prosthesis, although recent studies have questioned its significance, particularly in cases of moderate PPM.[6,7] In surgical aortic valve replacement, most studies have defined PPM by dividing the predicted effective orifice area (EOA) by the patient's body surface area. The EOA is the normal reference value for the model and size of the prosthetic valve, that is, from in vitro assessment. In contrast, TAVI studies have used the EOA measured by Doppler

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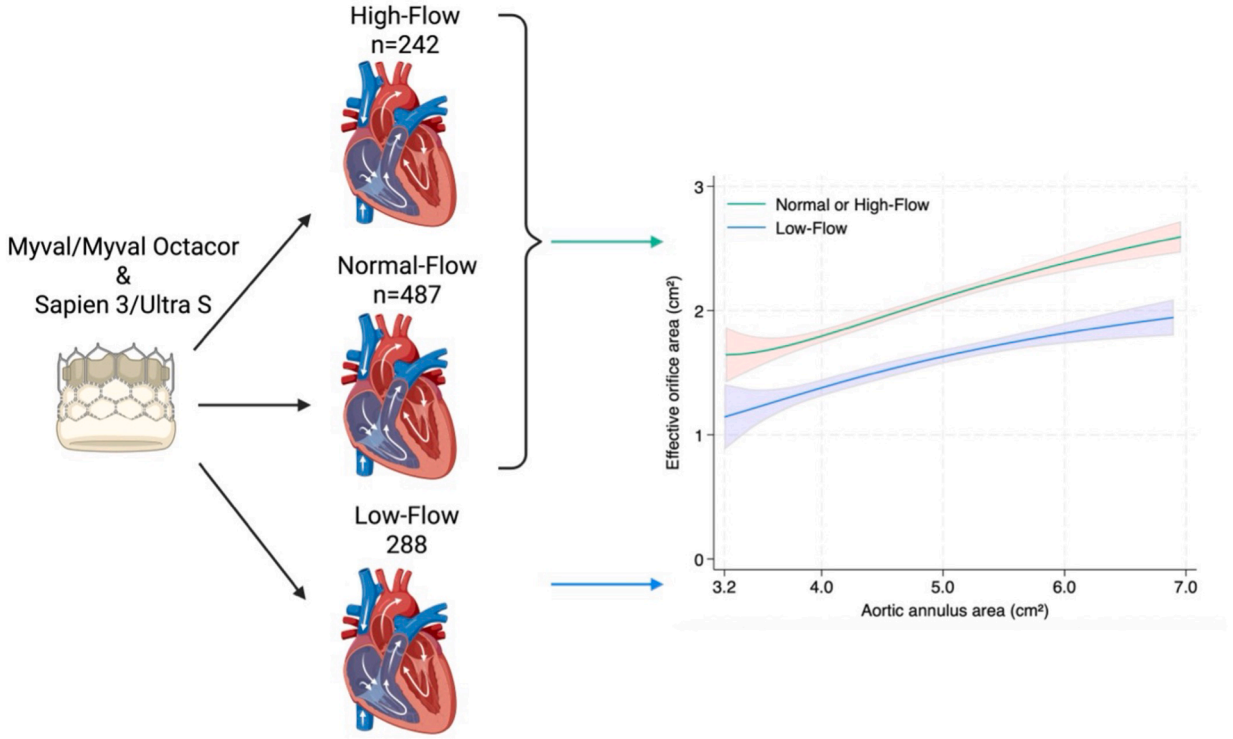

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Central Illustration Spline curve of EOA and aortic annulus area stratified by flow status. Created partially with BioRender.com.

echocardiography to calculate PPM. Recently it has become evident that utilizing echocardiography-based EOA after TAVI, may largely overestimate the occurrence of PPM.[8] Although many potential mechanisms may explain this pseudo-PPM condition, EOA is largely determined by the transvalvular flow, and a reduced stroke volume may lead to a lower EOA than the is expected for the EOA of a normal valve prosthesis.[8]

Thus, transthoracic echocardiographic Doppler-derived hemodynamic data for THVs during normal flow may be more ideally used as "expected EOA" when guiding treatment decisions. The COMPARE-TAVI 1 trial is a multicenter study in which all-comer patients scheduled for transfemoral TAVI were randomized 1:1 to receive either Sapien 3/Sapien 3 Ultra or Myval/Myval Octacor transcatheter heart valves (THVs). The aim of this COMPARE-TAVI 1 substudy was twofold:

1) To evaluate the impact of flow status on calculated EOA.
2) To establish EOA during normal flow as a reference for "expected EOA" for the balloon-expandable Myval and Sapien THV series.

METHODS

This substudy of the COMPARE-TAVI 1[9] trial focuses on calculated EOA measured from echocardiography performed 30 days after TAVI. In cases of missing values at 30 days, discharge data were used to supplement the analyses. Ethical approval was obtained as previously detailed.[9,10]

Patient Population and Core Laboratory

The COMPARE-TAVI 1 trial enrolled all-comer patients scheduled for transfemoral TAVI to treatment with Sapien 3/Sapien 3 Ultra (Edwards Lifesciences) or Myval/Myval Octacor (Meril Life Sciences) THVs from June 15, 2020, to November 2, 2023.[10]

A comprehensive transthoracic echocardiography was performed according to a prespecified core laboratory echocardiographic protocol using Vivid 9 (GE Healthcare) or EPIQ7 (Philips Professional Healthcare) machines, at baseline, at discharge, and 30 days after the procedure. All echocardiograms were digitally archived locally, deidentified, transferred in raw format, and, after quality approval, analyzed by an echocardiographic core laboratory based at the Department of Cardiology and Cardiology Research Group at Odense University Hospital, Odense, Denmark. Image acquisition and analysis were performed according to the American Society of Echocardiography standards for echocardiography core laboratories.[11]

Echocardiograms were assigned to 5 readers that included highly experienced research fellows and board-certified cardiologists with level III certification in echocardiography and were subsequently approved by the core lab director. Echocardiograms were analyzed using Viewpoint 6 (GE Healthcare) and Intellispace Cardiovascular

Abbreviations

AR = Aortic regurgitation

BMI = Body mass index

DVI = Doppler velocity index

EOA = Effective orifice area

EOAi = Effective orifice area indexed

LV = Left ventricular

PPM = Prosthesis-patient mismatch

SVi = Stroke volume index

TAVI = Transcatheter aortic valve intervention

THVs = Transcatheter heart valves

VARC-3 = Valve Academic Research Consortium 3

(Philips Healthcare Best) software. The core laboratory remained blinded during all echocardiographic measurements of the 2 balloon-expandable valves.

Echocardiographic Measurements for Balloon-Expandable Valves

Doppler values were calculated as the average of 3 cardiac cycles for patients with sinus rhythm and 5 cycles for atrial fibrillation with horizontal sweep of 100 cm/sec and a frame rate of minimum 60/sec. Left ventricular (LV) outflow tract diameter was measured from zoom mode in the parasternal long-axis view in early systole, from the outer edge to the outer edge at the prosthesis inflow edge, and the LV outflow tract pulsed-wave Doppler volume placed on the prosthesis inflow edge (Supplemental Figure 1). Left ventricular outflow tract cross-sectional area was calculated using the formula: $\pi \times$ ([LV outflow tract]cm/2)^2. Calculated EOA was estimated by quantitative Doppler ultrasound using the continuity equation. Peak and mean flow velocity across the valve were determined in the window where the highest velocity could be recorded using continuous-wave Doppler with the cursor aligned as parallel as possible to flow across the valve, utilizing multiple acoustic windows including apical, right parasternal, and suprasternal views. Peak and mean transvalvular gradients were estimated using the modified Bernoulli equation.[12] Doppler velocity index (DVI) was calculated as the ratio of the LV outlet tract velocity-time integral to the aortic valve velocity-time integral. Peak instantaneous and mean gradients across the aortic prosthesis were measured by continuous-wave Doppler, most from the apical window, but occasionally from the right parasternal location.

Left ventricular ejection fraction was calculated by the Simpson's biplane method from the apical 4-chamber and 2-chamber views. Stroke volume index (SVi) was calculated using pulsed-wave Doppler as the product of the LV outflow area and LV outflow tract time-velocity integral indexed to body surface area. Patients were stratified according to SVi into those with low flow (SVi <35 mL/m^2), normal flow (SVi 35-50 ml/m^2), and high flow (SVi>50 mL/m^2) as well as by sex.

The PPM was calculated using echocardiographic measurements of EOA indexed (EOAi) by body surface area. In accordance with Valve Academic Research Consortium 3 (VARC-3) criteria, PPM was defined as present if EOAi was ≤0.85 cm^2/m^2 for patients with body mass index (BMI) <30 or ≤0.70 cm^2/m^2 for those with BMI ≥30.[13]

Aortic regurgitation (AR) after the procedure was assessed using a multiparameter integrative approach, incorporating color and continuous-wave Doppler, visual assessment of jet origin and path, vena contracta width and area, pressure half-time, diastolic flow reversal in the descending aorta, and circumferential extent of paravalvular leak.[14] Grading was conducted according to a 5-class scheme as follows: none or trace; mild; mild to moderate; moderate; moderate to severe; severe. The 5-class grading was collapsed into the 3-class grading scheme recommended by the American Society of Echocardiography guidelines and the VARC-3 criteria.[13,15] We reported the incidence of total (paravalvular + transvalvular) AR.

STATISTICS

Complete case analyses were performed, including only measurements available at the 30-day follow-up. Discharge measurements were used to supplement missing data for calculated EOA, mean gradient, peak gradient, DVI, and valve size. The number of echocardiograms used for analysis is clearly detailed in the tables. Echocardiographic variables are investigated for normal distribution with histograms and reported as mean ± SD for each valve size. Body surface area was calculated using the Mosteller formula.

Spline plot calculated the EOA based on fractional polynomial estimates of the aortic annulus area, and valve sizes were presented, showing the mean and CIs for the low-, normal-, or high-flow groups. Violin plots were used to present the calculated EOA for each valve size, and main variables were stratified for sex. Differences in calculated EOA, transvalvular gradient, and distribution of patients across flow groups were compared between Myval and Sapien THVs.

Comparisons between the Myval and Myval Octacor valves were conducted for sizes 23 and 29 mm, as there were too few cases in sizes 20, 21.5, 30.5, and 32 mm for comparison.

Continuous variables were compared using Student's *t* test, as well as 1-way and 2-way analysis of variance to evaluate group differences and the interaction effects of sex, where appropriate. Categorical variables were analyzed using the chi-squared test. Multivariable linear regression was used to assess independent determinants of SVi. A P value <.05 was considered statistically significant. Statistical analyses were conducted using STATA/IC 18 (StataCorp).

RESULTS

In the COMPARE-TAVI 1 trial, 1,031 patients underwent randomization; 507 patients were treated with Myval THV series (Myval $n = 183$, Myval Octacor $n = 324$) and 523 with Sapien THV series (Sapien 3 $n = 402$, Sapien 3 Ultra $n = 121$). Due to missing 30-day data, discharge measurements were utilized for 27 cases of calculated EOA and DVI, 26 cases of SVi, 25 cases of AR, and 27 cases of aortic peak and mean gradients. Low flow was observed in 28.3% ($n = 288$), normal flow in 47.9% ($n = 487$), and high flow in 23.8% ($n = 242$) of patients, with no difference between the Myval and Sapien groups ($P = .643$). Baseline characteristics stratified by postprocedural flow are presented in Supplemental Table 1. In multivariable regression, atrial fibrillation and LV ejection fraction were independently associated with higher SVi, whereas peripheral vascular disease and PPM were associated with lower values (all $P < .05$). Prior to TAVI, 169 (16.4%) patients had low flow, low gradient (<35 mL/m^2 and mean transvalvular gradient <40 mm Hg), 137 (13.3%) had normal flow, low gradient (≥35 mL/m^2 and mean transvalvular gradient <40 mm Hg), 255 (24.7%) had low flow, high gradient (<35 mL/m^2 and mean transvalvular gradient ≥40 mm Hg), and 470 (45.6%) had normal flow, high gradient (≥35 mL/m^2 and mean transvalvular gradient ≥40 mm Hg).

HIGHLIGHTS

- Flow state strongly influences EOA and transvalvular gradients post-TAVI.
- Myval THVs showed lower gradients and higher EOA compared to Sapien THVs.
- Reference EOA values under normal flow may improve TAVI assessment and planning.

According to flow, PPM counts according to postprocedural measurements were 55 (20.2%), 38 (13.9%), 78 (28.6%), and 102 (37.4%; $P = .012$), respectively.

Patients received Myval/Myval Octacor THVs of various sizes, ranging from 20 to 32 mm. The mean calculated EOA across all Myval/Myval Octacor valve sizes was 1.99 ± 0.55 cm^2, and the aortic valve mean gradient was 9.46 ± 3.84 mm Hg (Table 1). In the Sapien 3/Sapien 3 Ultra THVs group, valve sizes ranged from 20 to 29 mm, of which size 29 mm was Sapien 3. The mean calculated EOA across all Sapien 3/Sapien valve sizes was 1.81 ± 0.56 cm^2, and the aortic valve mean gradient was 11.47 ± 4.47 mm Hg (Table 2, Supplemental Figure 2). Compared to Sapien THVs, Myval THVs exhibited overall a higher mean calculated EOA (<0.001) and lower mean gradients (<0.001).

Compared to normal flow in all patients, calculated EOA was significantly lower in low-flow patients across all valve sizes. Conversely, in high-flow patients, calculated EOA was significantly higher across all valve sizes, as well as overall ($P < .001$; Tables 1 and 2). The relation between flow and aortic annulus area is presented in the Central Illustration.

The calculated EOA directly correlated with flow (Figure 1) irrespective of platform (Figure 2). These differences were paralleled by a progressive decrease in mean gradients from the smallest to the largest valve size ($P < .001$; Tables 1 and 2). In low-flow patients, gradients were overall lower compared to normal flow, which was the case for both mean and peak gradients in both platforms. A sensitivity analysis limited to patients with data at 30 days is presented in Supplemental Figure 3, demonstrating consistent results with the main analysis.

The DVI averaged 0.55 ± 0.13 in Myval and 0.49 ± 0.12 in Sapien, showing no significant difference between the smallest and largest valve sizes. The DVI was significantly lower in low-flow patients across all valve sizes except 21.5 mm and 30.5 mm ($P < .001$). In contrast, high-flow patients had significantly higher DVI across almost all sizes ($P < .001$).

Differences in key hemodynamic performance between Myval and Myval Octacor valves were few (Table 3). Average calculated EOA for all sizes was similar for the Myval and Myval Octacor series ($P = .311$), although the Myval Octacor valve had a significantly larger calculated EOA in the 23 mm size ($P < .001$). The Myval Octacor valve also demonstrated lower mean ($P = .001$) and peak gradients ($P = .008$) compared to the Myval valve.

Compared to men, women received smaller prosthetic valves and had accordingly lower calculated EOA. After adjusting for differences in valve size, sex did not exhibit a significant effect on calculated EOA (Supplemental Figure 4 and 5). Overall female sex was associated with higher mean and peak gradients across prosthetic sizes; however, this difference was primarily driven by valve sizes with few observations and imbalanced group sizes between men and women. With the most commonly used prostheses, Myval (size, 23-29 mm) and Sapien (size 23-29 mm), women had lower gradients.

Aortic regurgitation was classified as none/trace in 64.4% ($n = 657$), mild in 34.2% ($n = 349$), and moderate/severe in 1.4% ($n = 14$) of cases (Figure 3). Aortic regurgitation increased with flow overall ($P = .003$), showing a visual trend in both platforms, while Myval demonstrated significantly higher AR than Sapien ($P < .001$). Excluding patients with moderate or severe AR yielded consistent results. Aortic regurgitation for the entire cohort in patients with normal flow versus low flow or high flow is presented in Supplemental Figure 6.

Effective orifice area stratified by flow status, BMI, and PPM is shown in Supplemental Figure 7, while Supplemental Figure 8 displays PPM stratified by flow status.

DISCUSSION

In the present study, we provide detailed insights into the hemodynamic performance of the Myval and Sapien THVs, particularly under varying flow states, valve sizes, and aortic annulus area and between sexes. These measurements provide valuable reference tables to guide the assessment of the expected performance postimplantation. The main findings include the following: (1) Low flow was associated with smaller calculated EOA and lower DVI, while high-flow conditions showed larger calculated EOA and higher DVI. (2) The Myval Octacor valve exhibited overall lower mean and peak gradients compared to the Myval valve. (3) Myval THVs exhibited overall lower mean and peak gradients compared to Sapien THVs. (4) Female sex demonstrated higher mean and peak gradients independent of valve size with Myval. Reference tables are essential tools for assessing the immediate and longitudinal function of an implanted valve of known size to normative core lab-assessed data and predicting the expected valve area in vivo before valve implantation.

Importantly, the flow and stroke volume across an implanted valve are paramount and largely affect measured transvalvular gradients, the calculated EOA and AR. Patients with low flow had lower measured gradients and calculated EOA and were more likely to be labeled as having PPM.[8] Indeed, we demonstrate that calculated EOA, DVI, and transvalvular gradients are largely determined by transvalvular flow, with low-flow patients experiencing significant lower values and high-flow patients presenting with higher gradients and calculated EOA. Conversely, significant residual AR may overstate calculated EOA by increasing SVi, emphasizing the need for careful interpretation. Aortic regurgitation may increase both LV outflow tract and aortic valve velocity-time integral, and DVI remains unchanged, thus yielding the same DVI and the same calculated EOA. However, in this all-comers study, low-flow and high-flow subgroups were more balanced, thus reducing their overall influence on the cohort. However, this may not extend to reference tables from studies using different inclusion criteria, which could influence the reported proportions. The EOA in the LANDMARK trial (2.02 cm^2) was more closely aligned with the normal-flow group in our study (2.00 cm^2), although the mean gradient across all valve sizes was lower in the LANDMARK trial compared to our findings (8.20 mm Hg vs 9.46 mm Hg).[16] Thus, it is essential that reported reference values also account for flow conditions across valves, to differentiate between PPM and pseudo-PPM. Although it is generally accepted that LV outflow tract velocity-time integral and aortic velocity-time integral change in parallel, in low-flow state conditions, stroke volume may not be sufficient to open a normal functioning prosthetic valve

Table 1 Effective orifice area, DVI, and gradients for all balloon-expandable Myval valves stratified by 30-day SVi postimplantation

	Valve iteration					
Prosthetic valve size	All flow	Normal flow	Low flow	Normal vs low flow *P* value	High-flow	Normal vs high-flow *P* value
EOA, cm^2	*P* < .001*					
20 mm	1.19 ± 0.17 (3)	1.19 ± 0.17 (3)	NA	NA	NA	NA
21.5 mm	1.50 ± 0.38 (23)	1.40 ± 0.22 (10)	1.14 ± 0.13 (6)	**.021**	1.94 ± 0.25 (7)	**<.001**
23 mm	1.79 ± 0.45 (97)	1.79 ± 0.35 (36)	1.40 ± 0.23 (28)	**<.001**	2.12 ± 0.42 (33)	**<.001**
24.5 mm	1.86 ± 0.47 (109)	1.87 ± 0.38 (53)	1.42 ± 0.26 (28)	**<.001**	2.28 ± 0.38 (28)	**<.001**
26 mm	2.09 ± 0.54 (141)	2.08 ± 0.44 (71)	1.78 ± 0.47 (41)	**.001**	2.53 ± 0.53 (29)	**<.001**
27.5 mm	2.15 ± 0.56 (66)	2.15 ± 0.40 (33)	1.83 ± 0.48 (22)	**.010**	2.78 ± 0.62 (11)	**<.001**
29 mm	2.33 ± 0.55 (50)	2.37 ± 0.46 (21)	1.94 ± 0.43 (16)	**.007**	2.77 ± 0.50 (13)	**.022**
30.5 mm	2.57 ± 0.70 (9)	2.88 ± 0.90 (4)	2.15 ± 0.50 (3)	.265	2.59 ± 0.07 (2)	.690
32 mm	2.58 ± (1)	NA	2.58 ± (1)	NA	NA	NA
All sizes	1.99 ± 0.55 (499)	2.00 ± 0.48 (231)	1.65 ± 0.46 (145)	**<.001**	2.38 ± 0.52 (123)	**<.001**
Mean gradient, mm Hg	*P* < .001*					
20 mm	20.47 ± 4.51 (3)	20.47 ± 4.51 (3)	NA	NA	NA	NA
21.5 mm	14.05 ± 5.47 (23)	15.91 ± 6.77 (10)	13.25 ± 3.03 (6)	.383	12.07 ± 4.72 (7)	.217
23 mm	10.11 ± 4.20 (98)	9.90 ± 3.96 (36)	9.30 ± 3.72 (28)	.535	10.75 ± 4.60 (33)	.415
24.5 mm	10.01 ± 3.39 (110)	10.28 ± 3.33 (53)	8.54 ± 3.19 (28)	**.027**	11.08 ± 3.33 (28)	.308
26 mm	8.91 ± 3.30 (142)	9.29 ± 2.84 (72)	7.27 ± 2.65 (41)	**<.001**	10.28 ± 4.24 (29)	.174
27.5 mm	8.31 ± 2.73 (66)	8.61 ± 2.70 (33)	7.33 ± 2.41 (22)	.079	9.39 ± 3.04 (11)	.428
29 mm	7.74 ± 2.90 (50)	7.80 ± 3.54 (21)	7.54 ± 2.38 (16)	.803	7.91 ± 2.51 (13)	.918
30.5 mm	7.85 ± 1.73 (9)	6.65 ± 2.59 (4)	8.13 ± 1.40 (3)	.416	7.80 ± 2.69 (2)	.638
32 mm	3.70 ± (1)	NA	3.70 ± (1)	NA	NA	NA
All sizes	9.46 ± 3.84 (502)	9.76 ± 3.93 (232)	8.19 ± 3.18 (145)	**<.001**	10.32 ± 3.97 (123)	.208
Peak gradient, mm Hg	*P* < .001					
20 mm	36.08 ± 6.95 (3)	36.08 ± 6.95 (3)	NA	NA	NA	NA
21.5 mm	24.09 ± 9.31 (23)	26.03 ± 10.77 (10)	24.01 ± 7.14 (6)	.691	21.39 ± 9.31 (7)	.371
23 mm	18.23 ± 7.80 (98)	18.05 ± 7.25 (36)	16.25 ± 6.68 (28)	.311	19.63 ± 8.74 (33)	.413
24.5 mm	18.02 ± 6.21 (110)	18.41 ± 6.14 (53)	15.81 ± 6.15 (28)	.073	19.71 ± 5.94 (28)	.366
26 mm	16.05 ± 6.11 (142)	16.90 ± 5.32 (72)	12.65 ± 4.72 (41)	**<.001**	18.78 ± 7.63 (29)	.162
27.5 mm	14.90 ± 5.09 (66)	15.26 ± 4.30 (33)	12.99 ± 5.16 (22)	.083	17.62 ± 6.03 (11)	.163
29 mm	13.14 ± 4.94 (50)	12.97 ± 6.02 (21)	12.51 ± 4.06 (16)	.791	14.18 ± 4.13 (13)	.530
30.5 mm	12.49 ± 3.48 (9)	11.3 ± 3.72 (4)	13.18 ± 3.02 (3)	.509	13.86 ± 5.11 (2)	.513
32 mm	6.76 ± (1)	NA	6.76 ± (1)	NA	NA	NA
All sizes	16.87 ± 6.97 (502)	17.38 ± 6.87 (232)	14.43 ± 6.00 (145)	**<.001**	18.70 ± 7.34 (123)	.094
DVI	*P* = .08*					
20 mm	0.43 ± 0.10 (3)	0.43 ± 0.10 (3)	NA	NA	NA	NA
21.5 mm	0.51 ± 0.13 (23)	0.49 ± 0.11 (10)	0.41 ± 0.06 (6)	.112	0.64 ± 0.10 (7)	**.011**
23 mm	0.55 ± 0.12 (97)	0.55 ± 0.12 (36)	0.46 ± 0.09 (28)	**.001**	0.63 ± 0.11 (33)	**.010**
24.5 mm	0.54 ± 0.12 (109)	0.54 ± 0.11 (53)	0.44 ± 0.08 (28)	**<.001**	0.62 ± 0.12 (28)	**.001**
26 mm	0.57 ± 0.13 (141)	0.57 ± 0.12 (71)	0.52 ± 0.13 (41)	**.024**	0.64 ± 0.13 (29)	**.015**
27.5 mm	0.53 ± 0.12 (66)	0.54 ± 0.10 (33)	0.47 ± 0.10 (22)	**.017**	0.64 ± 0.14 (11)	**.016**
29 mm	0.54 ± 0.11 (50)	0.54 ± 0.08 (21)	0.48 ± 0.10 (16)	**.026**	0.62 ± 0.11 (13)	**.018**
30.5 mm	0.60 ± 0.15 (9)	0.66 ± 0.20 (4)	0.53 ± 0.13 (3)	.371	0.57 ± 0.02 (2)	.578
32 mm	0.45 ± (1)	NA	0.45 ± (1)	NA	NA	NA
All sizes	0.55 ± 0.13 (499)	0.55 ± 0.11 (231)	0.47 ± 0.10 (141)	**<.001**	0.63 ± 0.12 (123)	**<.001**

Values are mean ± SD (*n*). This table shows the EOA, aortic mean and peak gradient for each balloon-expandable valve iteration by valve size implanted. Low flow is <35 mL/m^2, normal flow from ≥35 mL/m^2 to ≤50 mL/m^2, and high flow >50 mL/m^2. *P* values <.05 are written in bold, indicating significant differences between groups.

**P* value derived from 1-way analysis of variance analysis between variable and valve size.

Table 2 Effective orifice area, DVI, and gradients for all balloon-expandable Sapien valves stratified by 30-day SVi postimplantation

	Valve iteration					
Prosthetic valve size	All flow	Normal flow	Low flow	Normal vs low flow *P* value	High flow	Normal vs high flow *P* value
EOA, cm^2	**<0.001***					
20 mm	1.27 ± 0.60 (9)	1.17 ± 0.57 (6)	1.06 ± 0.004 (2)	.800	2.31 ± . (1)	NA
23 mm	1.56 ± 0.46 (167)	1.53 ± 0.40 (78)	1.26 ± 0.30 (41)	**<.001**	1.85 ± 0.50 (48)	**<.001**
26 mm	1.83 ± 0.47 (221)	1.84 ± 0.37 (109)	1.51 ± 0.42 (65)	**<.001**	2.23 ± 0.43 (47)	**<.001**
29 mm	2.18 ± 0.59 (120)	2.21 ± 0.47 (62)	1.73 ± 0.33 (35)	**<.001**	2.78 ± 0.66 (23)	**<.001**
All sizes	1.81 ± 0.56 (517)	1.82 ± 0.49 (255)	1.81 ± 0.56 (143)	**<.001**	2.18 ± 0.61 (119)	**<.001**
Mean gradient, mm Hg	**<0.001***					
20 mm	18.1 ± 4.44 (9)	17.88 ± 4.53 (6)	18.20 ± 4.44 (2)	.942	18.90 ± (1)	NA
23 mm	13.6 ± 4.98 (168)	13.42 ± 4.06 (78)	11.68 ± 4.98 (41)	**.043**	15.39 ± 5.54 (48)	**.023**
26 mm	10.8 ± 3.85 (221)	11.15 ± 3.93 (109)	9.57 ± 3.85 (65)	**.007**	11.79 ± 4.11 (47)	.360
29 mm	9.17 ± 2.73 (120)	9.13 ± 2.73 (62)	8.63 ± 2.49 (35)	.363	10.10 ± 3.21 (23)	.155
All sizes	11.47 ± 4.47 (518)	11.51 ± 4.13 (255)	10.06 ± 3.98 (143)	**<.001**	12.98 ± 5.06 (119)	**.003**
Peak gradient, mm Hg	**<0.001***					
20 mm	31.76 ± 8.08 (9)	31.76 ± 8.08 (6)	32.68 ± 15.76 (2)	.791	36.72 ± (1)	NA
23 mm	23.79 ± 8.76 (168)	23.79 ± 8.76 (78)	20.67 ± 8.08 (41)	.088	26.76 ± 9.38 (48)	**.013**
26 mm	19.04 ± 19.04 (221)	19.04 ± 19.04 (109)	16.47 ± 5.49 (65)	**<.001**	21.25 ± 6.99 (47)	.145
29 mm	16.53 ± 5.42 (120)	16.63 ± 4.80 (62)	15.36 ± 4.29 (35)	.196	18.04 ± 7.86 (23)	.318
All sizes	20.22 ± 7.75 (518)	20.21 ± 6.71 (255)	17.63 ± 6.77 (143)	**<.001**	23.00 ± 8.88 (119)	**<.001**
DVI	*P* = .85*					
20 mm	0.47 ± 0.21 (9)	0.43 ± 0.20 (6)	0.40 ± 0.09 (2)	.852	0.82 ± (1)	NA
23 mm	0.48 ± 0.12 (167)	0.47 ± 0.10 (78)	0.43 ± 0.11 (41)	**.044**	0.54 ± 0.13 (48)	**.002**
26 mm	0.49 ± 0.12 (221)	0.49 ± 0.10 (109)	0.42 ± 0.10 (65)	**<.001**	0.57 ± 0.13 (47)	**<.001**
29 mm	0.49 ± 0.11 (120)	0.50 ± 0.10 (62)	0.42 ± 0.07 (35)	**<.001**	0.59 ± 0.13 (23)	**.001**
All sizes	0.49 ± 0.12 (517)	0.49 ± 0.10 (255)	0.42 ± 0.10 (143)	**<.001**	0.56 ± 0.13 (119)	**<.001**

Values are mean ± SD (n). This table shows the EOA, aortic mean and peak gradient for each balloon-expandable valve iteration by valve size implanted. Low flow is <35 mL/m^2, normal flow from ≥35 mL/m^2 to ≤50 mL/m^2, and high flow >50 mL/m^2. *P* values <.05 are written in bold, indicating significant differences between groups.

**P* value derived from 1-way analysis of variance analysis between variable and valve size.

to its full extent, and EOAi may thus underestimate the opening of a valve that could be achieved during normal-flow conditions. This is a similar concept to pseudo-severe aortic stenosis in low-flow, low-gradient aortic stenosis where differentiation between severe and pseudo-severe aortic stenosis can be achieved by normalizing flow with the use of dobutamine.[17] Overall, the hemodynamic performance of Myval THV series was comparable to Sapien 3, Evolut R, and CoreValve.[18,19] Interestingly, the Myval Octacor valve may exhibit lower gradients than the Myval valve, suggesting potential advantages in some cases, although the comparison was not randomized.

Current valvular guidelines and VARC-3 criteria do not differentiate between sex when assessing severity of a native or a prosthetic

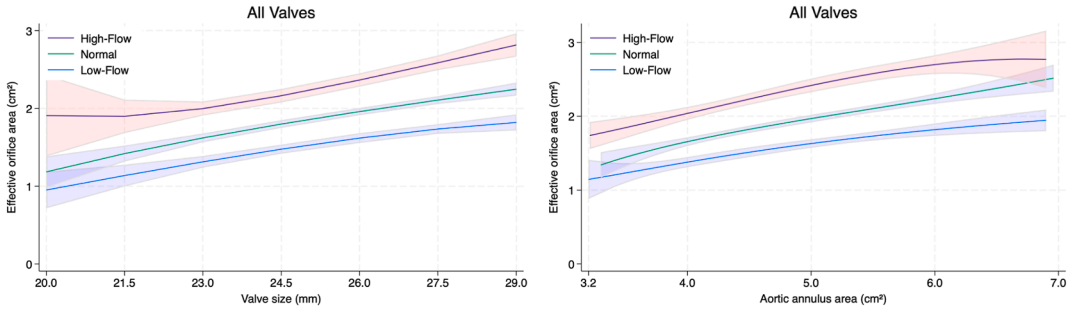

Figure 1 Spline curves for Myval and Sapien valves of EOA association with flow status, valve size (*left case*), and aortic annulus area (*right case*).

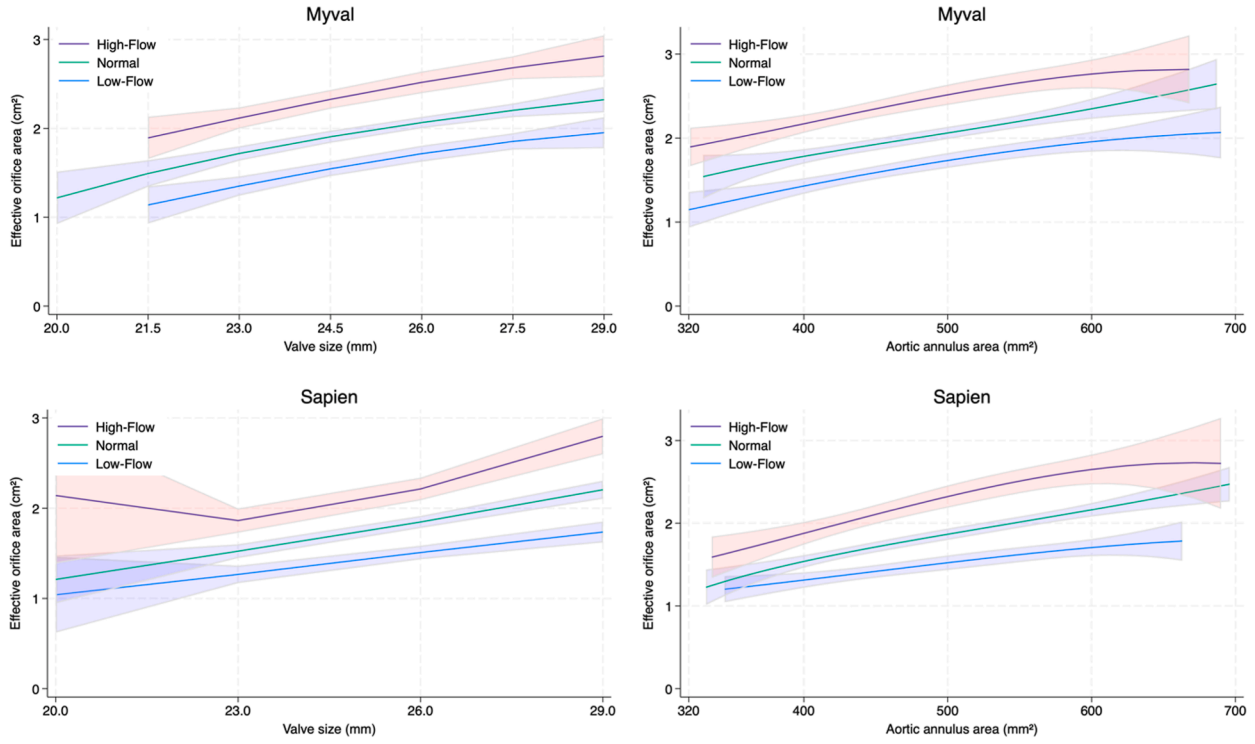

Figure 2 Spline curves for Myval valves of EOA association with flow status, valve size (*upper left case*), and aortic annulus area (*upper right case*) and Sapien valves of EOA association with flow status, valve size (*lower left case*), and aortic annulus area (*lower right case*).

valve.[13,20,21] Accordingly, the thresholds for EOA and transvalvular gradients are uniform in the assessment of severe aortic stenosis, PPM, and structural valve deterioration. However, the smaller body surface area requiring lower stroke volumes in female compared to male patients yields lower transvalvular peak velocities and mean gradients in patients with native aortic stenosis. In a recent paper including 927 patients with severe aortic stenosis, Ito *et al.*[22] demonstrated that, although the use of indexed parameters by body surface area was

Table 3 Effective orifice area, aortic gradients, and DVI by Myval valve prosthesis at 30 days stratified by valve size

	Valve iteration					
Prosthetic valve size	All sizes	23 mm	24.5 mm	26 mm	27.5 mm	29 mm
EOA, cm^2						
Myval	1.96 ± 0.57 (182)	1.53 ± 0.32 (27)	1.78 ± 0.51 (38)	2.16 ± 0.49 (54)	2.14 ± 0.62 (24)	2.35 ± 0.57 (23)
Myval Octacor	2.01 ± 0.54 (317)	1.89 ± 0.45 (70)	1.90 ± 0.44 (71)	2.04 ± 0.56 (87)	2.16 ± 0.53 (42)	2.32 ± 0.54 (27)
P value	.311	**<.001**	.198	.194	.903	.890
Mean gradient, mm Hg						
Myval	9.97 ± 4.13 (182)	11.40 ± 3.96 (27)	11.18 ± 3.95 (38)	8.78 ± 3.27 (54)	8.36 ± 2.60 (24)	8.12 ± 3.57 (23)
Myval Octacor	9.14 ± 3.62 (320)	9.61 ± 4.21 (71)	9.40 ± 2.90 (72)	8.99 ± 3.33 (88)	8.29 ± 2.83 (42)	7.42 ± 2.20 (27)
P value	**.001**	.059	**.008**	.708	.922	.398
Peak gradient, mm Hg						
Myval	17.97 ± 7.36 (182)	20.25 ± 6.90 (27)	20.25 ± 7.10 (38)	16.24 ± 6.36 (54)	15.18 ± 4.55 (24)	13.83 ± 5.90 (23)
Myval Octacor	16.25 ± 6.67 (320)	17.46 ± 8.03 (71)	16.84 ± 5.37 (72)	15.94 ± 5.99 (88)	14.74 ± 5.41 (42)	12.54 ± 3.97 (27)
P value	**.008**	.115	**.006**	.774	.734	.366
DVI						
Myval	0.55 ± 0.12 (182)	0.52 ± 0.09 (27)	0.53 ± 0.12 (38)	0.60 ± 0.12 (54)	0.54 ± 0.12 (24)	0.54 ± 0.11 (23)
Myval Octacor	0.55 ± 0.13 (317)	0.57 ± 0.13 (70)	0.54 ± 0.12 (71)	0.56 ± 0.14 (87)	0.53 ± 0.12 (42)	0.54 ± 0.11 (27)
P value	.897	.079	.695	.078	.755	.963

Values are mean ± SD (*n*). This table shows the EOA, aortic mean, and peak gradient for each balloon-expandable valve iteration by valve size implanted. *P* values <.05 are written in bold, indicating significant differences between groups.

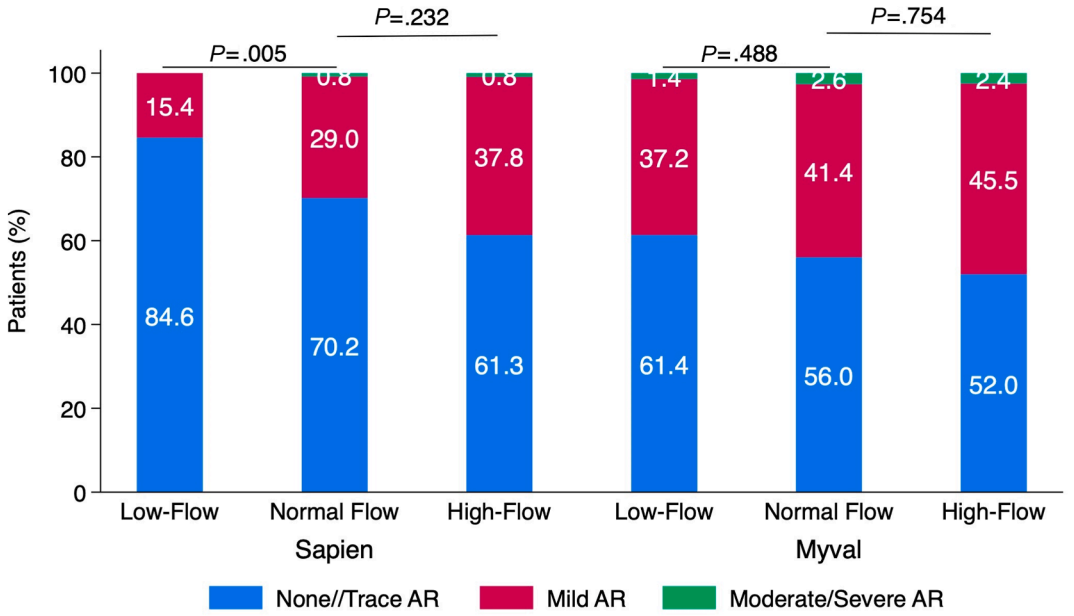

Figure 3 Aortic regurgitation for Sapien and Myval valves platforms in patients with normal flow versus low flow or high flow. In Sapien (n = 517), the distribution of SVi was low flow n = 143, normal flow n = 255, and high flow n = 119. In Myval Octacor (n = 500), the distribution of SVi was low flow n = 145, normal flow n = 232, and high flow n = 123. *AR*, Aortic regurgitation.

important in sex-related differences of aortic valve hemodynamics, women demonstrated lower gradients despite a low aortic valve area being the consequence of a lower stroke volume. We corroborate these findings and extend them as we demonstrate that women across a wide range of prosthesis sizes share calculated EOA and DVI with men but present with lower transvalvular gradients. This finding suggests that reference values also should be reported in a sex-specific manner.

LIMITATIONS

Several limitations warrant consideration. First, due to the limited sample size in patients receiving valve sizes 20 mm (n = 3), 21.5 mm (n = 23), 30.5 mm (n = 9), and 32 mm (n = 1), further confirmation is required. Second, although the number was limited, discharge measurements supplemented missing 30-day data, which could introduce bias. Third, the comparison between Myval and Myval Octacor patients was limited by the lack of randomization, which could have impacted outcomes. Fourth, these findings are based on hemodynamic measurements performed by the core laboratory and may not fully reflect values obtained at individual sites. However, these tables provide a reference for expected normal values as measured by the COMPARE-TAVI 1 core laboratory. Finally, the estimation of LV outflow tract cross-sectional area by two-dimensional echocardiography assumes circular geometry and relies on a single-plane measurement of the LV outflow tract diameter, which may result in inaccurate representation of the true anatomical area, particularly in cases of elliptical morphology.[23]

CONCLUSION

This study offers comprehensive analysis of the hemodynamic performance of Myval and Sapien THVs. We highlight the impact of flow state, valve size, and sex on valve evaluation. The calculated EOA presented for normal flow is proposed as a reference value to provide valuable information for assessing transcatheter valve function, supporting clinical decision-making, and optimizing preimplant planning for individualized patient care.

DATA SHARING STATEMENT

All study-related documents will be made available on request. Individual data collected for the study will be made available for collaborative pooled analyses provided relevant contracts and data sharing agreements are made. Only anonymized data will be shared. Any requests for data access should be directed to the sponsor at Aarhus University via email: chriterk@rm.dk.

REVIEW STATEMENT

Given her role as *JASE* Editor-in-Chief, Patricia A. Pellikka, MD, had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to guest editor Sheldon E. Litwin, MD.

CONFLICTS OF INTERESTS

C.J.T. reports lecture fees, proctor fees, and research grants from Edwards Lifesciences, Meril Life Sciences, Terumo, and Medtronic. P.H. reports lecture fees and proctor fees from Meril Life Sciences. E.H.C. reports previous proctoring or lecture fees from Boston, Edwards, Meril, and Abbott and research grants from Abbott. H.N. reports lecture fees and proctor fees from Edwards Lifesciences and Meril Life Sciences. F.U. reports proctor fees from Meril. The

remaining coauthors report no conflicts of interest with regard to this manuscript.

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Data management was provided by and REDCap was hosted by OPEN, Open Patient Data Explorative Network, Odense University Hospital, Region of Southern Denmark. For the main study (COMPARE-TAVI 1), data were hosted at Aarhus University Hospital in corolog.net. During the preparation of this work ChatGPT was occasionally used for grammar assistance. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.echo.2025.09.017.

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