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ORIGINAL STUDIES

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Real world outcomes using 20 mm balloon expandable SAPIEN 3/ultra valves compared to larger valves (23, 26, and 29 mm)–a propensity matched analysis

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Abstract

Objective/Background: Small balloon expandable valves have higher echocardiographic transvalvular gradients and rates of prosthesis-patient mismatch (PPM) compared to larger valves. However, the impact of these echocardiographic findings on clinical outcomes is unknown. We sought to determine the clinical outcomes of 20 mm SAPIEN 3 (S3 BEV) compared to larger S3 BEV in relation to echocardiographic hemodynamics.

Methods: Using the STS/ACC transcatheter valve registry, we performed a propensity-matched comparison of patients undergoing treatment of native aortic valve stenosis using transfemoral, balloon-expandable implantation of 20 mm and ≥ 23 mm S3 BEVs. Baseline and procedure characteristics, echocardiographic variables and survival were analyzed. Multivariable logistic regression was used to identify predictors of 1-year mortality.

Results: After propensity matching of the 20 mm and ≥ 23 mm SAPIEN 3 valves, 3,931 pairs with comparable baseline characteristics were identified. Small valves were associated with significantly higher echocardiographic gradients at discharge (15.7 ± 7.1 mmHg vs. 11.7 ± 5.5 mmHg, $p < 0.0001$) and severe PPM rates (21.5% vs. 9.7%, $p < 0.0001$). There was no significant difference in 1-year all-cause mortality (20 mm: 13.0% vs. ≥23 mm: 12.7%, $p = 0.72$) or other major adverse event rates and outcomes between the two cohorts. Based on a multivariable analysis, elevated discharge mean gradient (>20 mmHg), severe PPM and the use of 20 mm versus ≥23 mm were not independent predictors of 1-year mortality.

Conclusion: SAPIEN 3 20 mm valves were associated with higher echocardiographic gradients, and severe PPM rates compared to larger valves but these factors were not associated with significant differences in 1-year all-cause mortality or rehospitalization.

KEYWORDS
structural heart disease, transcatheter aortic valve replacement, TVT registry

Statistical analyses were performed by Edwards Lifesciences. The views or opinions presented here do not represent those of the American College of Cardiology, the Society of Thoracic Surgeons, or the STS/ACC TVT Registry.

1 | INTRODUCTION

Treatment of patients with severe aortic stenosis and small annuli has remained a surgical challenge for which transcatheter options have become an acceptable alternative.[1,2] These patients can be treated either with 20 mm balloon expandable valves or 23–26 mm self-expanding valves. Retrospective registries have demonstrated higher echo gradients in smaller (≤23 mm) balloon expandable valves accompanied by higher rates of prosthesis-patient mismatch (PPM)[3,4] compared to the self-expanding valve, which have led some operators to utilize echocardiographic valve hemodynamics when choosing transcatheter heart valves. However, more recent studies shown no significant differences in transcatheter valve hemodynamics between self-expanding and balloon-expandable valves implanted into small annuli[5] and adverse outcomes associated with PPM are not consistently associated with balloon-expandable valves.[6-8] In fact, outcomes from large registries have suggested that despite differences in valve hemodynamics, there may be a survival benefit to the balloon-expandable platform.[9,10] Nonetheless, a prior Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry™ report demonstrated a 12.1% rate of severe PPM that was associated with a 1.19 adjusted hazard ratio for 1-year mortality.[11] Given the known increase in PPM in patients with small aortic annuli in trials,[6,12] we sought to describe the real-world experience of using the 20 mm SAPIEN 3 valves in a large population using data accumulated via the STS/ACC TVT Registry™ (TVT Registry).

2 | METHODS

The TVT Registry is a collaborative clinical registry developed by the STS and the ACC in response to the Centers for Medicare and Medicaid Services national coverage decision (May 2012) requirement for national registry participation of all United States transcatheter aortic valve replacement (TAVR) centers. The TVT Registry uses standardized definitions and collates participant-reported data, which includes clinical information such as patient demographics, comorbidities, functional status, quality of life indexes, and procedural details and outcomes from consecutive patients undergoing TAVR using commercially approved devices.[11] The TVT Registry protocol was granted a waiver of informed consent by Advarra© and Duke University Institutional Review Boards.

The SAPIEN 3 20 mm transcatheter heart valve (THV) was commercially approved in June 2015. This analysis is based on patients who underwent transfemoral native TAVR using the SAPIEN 3 or SAPIEN 3 Ultra and included in the TVT Registry between June 2015 and January 2020. All patients in the study cohort were linked to CMS claims data, in addition to the follow-up obtained from the TVT Registry.

Standardized definitions of adverse events and outcomes were based on VARC-2. Procedural, in-hospital, 30-day and 1-year outcomes were derived from the TVT Registry. PPM was classified based on discharge echocardiographic effective orifice area (EOA), calculated using the continuity equation. In non-obese (BMI < 30 kg/m^2) patients, PPM was defined as non-significant if EOAi was >0.85cm^2/m^2, moderate if >0.65 cm^2/m^2 and ≤ 0.85 cm^2/m^2, and severe if ≤0.65 cm^2/m^2. In obese patients (BMI ≥30 kg/m^2), non-significant if EOAi >0.70cm^2/m^2, moderate if >0.55 cm^2/m^2 and ≤ 0.70 cm^2/m^2, and severe if ≤0.55 cm^2/m^2.[2,13]

The 20 mm patients were propensity matched with patients receiving ≥23 mm Edwards SAPIEN 3 valves using 25 covariates (Table S1). Missing baseline values were imputed using the Markov-Chain Monte Carlo method prior to modeling. The balance between the cohorts was determined by calculating standardized differences for which a difference of less than 0.10 was considered to suggest a good balance.

Baseline characteristics were compared between 20 mm and ≥ 23 mm SAPIEN 3 valves. Subsequently, the SAPIEN 3 20 mm patients were compared to a propensity matched cohort of patients that received ≥23 mm SAPIEN 3 valves with respect to baseline characteristics, procedural variables, complications, echocardiographic parameters, 30-day and 1-year outcomes. Categorical variables were compared using the Chi-squared test or Fisher's exact test while continuous variables utilized the *t*-test. Statistical significance was determined using 95% confidence intervals. Time to death survival was assessed using the Kaplan–Meier method and statistical significance with log-rank test. All *P* values were 2-sided, and $p < 0.05$ was considered significant for all tests. In addition, multivariable analysis was also performed to identify independent predictors of 1-year mortality in patients with TAVR in native valve via transfemoral access. Baseline characteristics with p value of <0.1 in the univariable analysis were included in the multivariable model which included 35 covariates (Table S2). Proportional-hazards assumption was confirmed through testing based on Kolmogorov-type *Supremum Test*. A Cox regression model was used with stepwise selection, which consisted of entering in the model covariates with $p \leq 0.10$ and removing covariates with $p > 0.10$. Additional multivariable analyses were performed to assess the independent impact of discharge hemodynamics (trans-valvular echo gradient and the presence of severe PPM), moderate/severe paravalvular leak (PVL) and need for new pacemaker implant on 1-year mortality. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina).

3 | RESULTS

From June 2015 until January 2020, 145,917 patients underwent TAVR with SAPIEN 3 and SAPIEN 3 Ultra and were enrolled in the TVT Registry (Figure 1). Patients who had TAVR with either alternative access or underwent valve-in-valve (ViV) procedure were excluded. Among the remaining 132,730 patients, 3,932 underwent native TAVR with SAPIEN 3 20 mm valves and 128,798 with SAPIEN 3 ≥ 23 mm valves.

There were several differences in patients receiving 20 mm and ≥ 23 mm SAPIEN 3 valves (Table S3). Patients receiving 20 mm valves were almost all women (96.4% vs. 46.3%, p value <0.0001). They

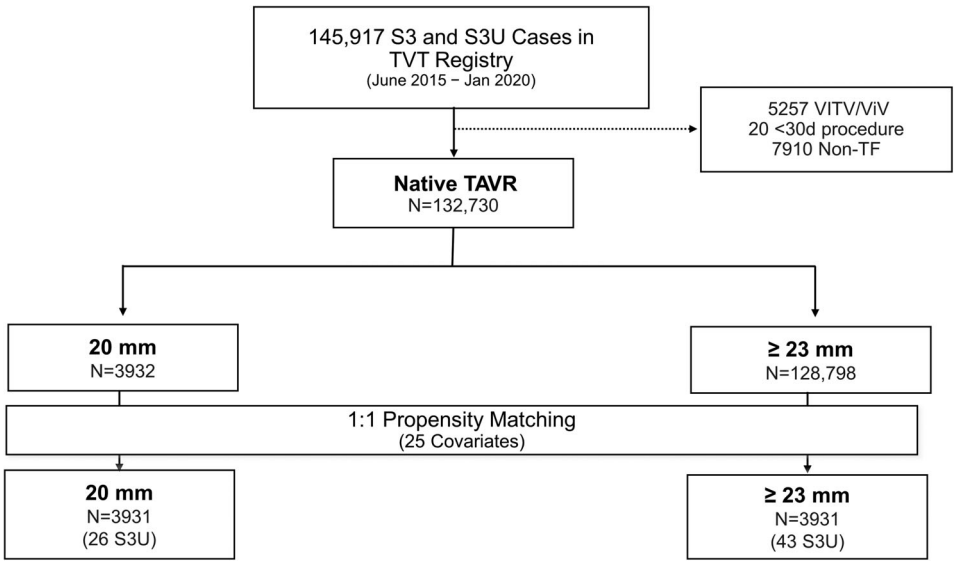

FIGURE 1 Flow chart of the study population. S3, SAPIEN 3; S3U, SAPIEN 3 Ultra; TAVR, transcatheter aortic valve replacement; TVT, transcatheter valve therapy; VITV, valve in transcatheter valve; ViV, valve-in-(surgical) valve; Non-TF, non-transfemoral

were slightly older and have higher surgical risk scores (7.1 ± 4.8% vs. 5.8 ± 4.4%, p value <0.0001). Propensity-matching resulted in 3931 pairs with comparable baseline characteristics (Table 1).

The procedural variables for the propensity matched 20 mm and ≥ 23 mm S3 cohorts are similar with some minor differences (Table S4). The 20 mm valves were associated with lower rates of conscious sedation (47.1% vs. 53.9%, $p < 0.0001$), and slightly longer procedure time (98.2 ± 51 vs. 92.6 ± 49 min, $p < 0.0001$). A lower rate of device success (94.7% vs. 97.2%, $p < 0.0001$) was observed in the 20 mm cohort associated with higher rates of moderate–severe paravalvular leak (PVL) and elevated post-procedure echo gradients. There were no differences with respect to device implantation success, conversion to open heart surgery, coronary obstruction or annulus rupture.

As depicted by Table 2, the rate of severe PPM was significantly higher (21.5% vs. 9.7%, $p < 0.0001$), associated with the higher mean gradients observed in the 20 mm cohort (15.7 vs. 11.7 mmHg, $p < 0.0001$). The rate of moderate/severe PVL was significantly higher in the 20 mm valve cohort at discharge, 30-days and 1-year (Table 2).

The in-hospital and 30-day outcomes of the propensity matched cohorts had minor differences (Table 3). The most significant difference noted was in permanent pacemaker implantation (4.3% vs. 8.5% at 30 days, $p < 0.0001$). The 30-day stroke rate was slightly higher in the 20 mm valve patients (2.5% vs. 1.9%, $p = 0.05$), however the rate of any readmission was lower (7.9% vs. 9.2%, $p = 0.04$).

At 1-year, there were no differences in death, stroke, any readmissions or valve related readmissions between patients receiving 20 mm and ≥ 23 mm SAPIEN 3 valves (Table 4). Symptom burden was the same between cohorts as the reported NYHA III/IV and self-reported KCCQ scores were undistinguishable (Table 4). There were slightly higher rates of valve re-intervention of the 20 mm (1.1% vs. 0.6%, $p = 0.03$) and the 1-year pacemaker rate was significantly lower (5.2% vs. 9.4%, $p < 0.0001$) compared to the ≥23 mm cohort. Kaplan–Meier analysis showed the survival curves comparing 20 mm and ≥ 23 mm valves were identical out to 1 year (Figure 2(A)). Even when excluding patients with moderate/severe PVL, no differences in survival were seen at 1 year (20 mm 12.3% vs. ≥23 mm 12.1%, $p = 0.248$, HR: 1.04 [95% CI: 0.97, 1.11]).

Independent predictors of 1-year mortality were identified using logistic regression. Most of the covariates chosen were statistically significant independent predictors of mortality but only some were truly clinically relevant such as the atrial fibrillation/flutter, patients on dialysis, severe chronic lung disease, immunocompromised status, and moderate–severe tricuspid insufficiency (Table S5). Moderate/severe PVL at discharge was associated with increased mortality at 1 year (Figure S1(A)). Interestingly, moderate/severe PVL and severe PPM did not appear to interact, severe PPM was still found to have neutral effect on mortality when included in the same multivariable analysis as moderate/severe PVL (HR 1.04 [0.94, 1.15], $p = 0.44$). The need for new pacemaker was also associated with increased mortality at 1 year (Figure S1(B)). The presence of severe PPM at discharge was not associated with 1-year all-cause mortality (Figure S1(C)). Concern for the possibility of the interaction of obesity resulting in overestimation of PPM prompted the use of BMI adjusted PPM definitions and the rate of severe PPM was recalculated at 16.4% (20 mm) versus 6.8% (≥23 mm), $p < 0.0001$. Multivariable analysis showed that the presence of BMI adjusted severe PPM was not associated with increased 1-year all-cause mortality (HR Severe vs. non-Severe 1.04 [0.94, 1.16], $p = 0.436$).

Interestingly, elevated discharge echo transvalvular mean pressure gradient was associated with lower all-cause mortality at 1 year (Figure S1(D)). Based on the multivariable analyses moderate/severe PVL and new pacemaker implant at discharge were independent predictors of increased 1-year all-cause mortality (Figure 2(B)). Elevated discharge mean gradient (≥ 20 mmHg), severe PPM and the use of 20 mm vs. ≥23 mm were not independent predictors of 1-year mortality (Figure 2(B)).

TABLE 1 Propensity adjusted baseline characteristics

	20 mm ($n = 3,931$)	≥23 mm ($n = 3,931$)	p value
Age (years)	81.9 ± 8.26	81.9 ± 8.16	0.89
STS risk score (%)	7.0 ± 4.78	7.1 ± 5.49	0.41
Male	142 (3.6)	142 (3.6)	1.0
NYHA III/IV	2,815 (72.2)	2,813 (72.3)	0.94
BMI (kg/m^2)	27.2 ± 6.72	27.0 ± 6.20	0.3
PAD	858 (21.8)	852 (21.7)	0.87
Carotid stenosis	984 (25.0)	971 (24.7)	0.73
Atrial fibrillation/flutter	1,083(27.6)	1,119 (28.5)	0.37
Prior stroke	412 (10.5)	409 (10.4)	0.91
Chronic lung disease	1,283 (32.6)	1,338 (34.0)	0.19
Prior PCI	991 (25.2)	970 (24.7)	0.58
Prior CABG	357(9.1)	348 (8.9)	0.72
Porcelain aorta	143 (3.6)	133 (3.4)	0.54
GFR (ml/min/1.73 m^2)	58.3 ± 23.86	58.3 ± 23.32	0.97
KCCQ	47.0 ± 24.73	46.4 ± 24.61	0.29

Note: Data presented as mean ± *SD* or No. of patients (%).
Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; GFR, glomerular filtration rate; KCCQ, Kansas City Cardiomyopathy Questionnaire; No, number; NYHA, New York Heart Association; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; *SD*, standard deviation; STS, Society of Thoracic Surgeons.

4 | DISCUSSION

The results of our study are as follows: (1) the vast majority of patients receiving SAPIEN 3 20 mm valves are women; (2) compared to implantation of ≥23 mm SAPIEN 3 valves, implantation of a 20 mm SAPIEN 3 valve was associated with greater rates of moderate–severe PVL, lower incidence of new pacemakers, higher echocardiographic gradients, and greater incidence of severe PPM; (3) on multivariable analysis, severe PPM, an echocardiographic gradient >20 mmHg, or the use of a 20 mm SAPIEN 3 valve were not predictors of increased 1-year mortality. Furthermore, hospital readmissions, symptoms and quality of life at 1 year were similar in both cohorts.

Relevance of PPM is predominantly described in the surgical literature. Meta-analysis of surgical studies found consistently higher hazard ratios for all-cause mortality for any PPM and severe PPM.[14] Examination of the Corevalve US Pivotal High Risk study comparing SAVR to TAVR showed severe PPM to independently predict mortality.[15] Investigators observed that patients with smaller annuli more frequently manifested severe PPM in the surgical cohort than the Corevalve/Evolut THV cohort. Moreover, in patients with small annulus, the rate of all-cause mortality was twice as high for patients with severe PPM, suggesting that PPM played a role in mortality. A follow-up Corevalve study, SURTAVI study showed no differences in TAVR or SAVR patient survival treated for small annuli despite the higher rates of severe PPM in the surgical population.[12]

The evidence for PPM in TAVR stems from the TVT Registry report describing a 12.1% rate of severe PPM that was associated with a 1.19 adjusted hazard ratio for 1-year mortality.[11] Although the multi-variate analysis identified valves ≤23 mm in diameter as a predictor of mortality, only 40% of patients in the severe PPM subgroup had valve diameters ≤23 mm. With a mean BSA of 1.98 m^2 (1.8–2.17), it is difficult to reconcile that 26 mm valves could cause severe PPM. Both our 20 mm SAPIEN study and the prior TVT Registry report assessed for PPM at discharge echocardiography. One difference is that the prior TVT Registry publication includes valve-in-valve procedures and alternative access in contrast to our 100% native valve, transfemoral TAVR cohort.

PPM has been shown to have overall neutral impact on mortality in PARTNER pivotal studies. Severe PPM was found in 20% and 14% of the randomized and non-randomized TAVR cohorts respectively.[6] There was no overall correlation with severe PPM and survival in the randomized cohort, in fact there appeared to have a slight survival advantage associated with severe PPM at 2 years. Similarly, PPM had no significant association with death in the PARTNER II study.[7] An analysis to re-stratify patients with PPM according to either echocardiographic or CT defined parameters to improve prognostication was performed in PARTNER II. TTE and CT defined PPM was discrepant, the rate of moderate and severe PPM in the TAVR population was 36% and 9% when characterized by TTE, while CT classified 18% and 6% of the same patients respectively. This suggests discordance between hemodynamic and anatomic assessment of PPM and may highlight a liability in hemodynamic assessments of valve area given the absence of increased mortality with the diagnosis of severe PPM.

The most recent pivotal study comparing the SAPIEN 3 valve to SAVR also demonstrated overall neutral impact of severe PPM on mortality.[8] The rate of severe PPM was 4.6% and 6.3% in the TAVR and SAVR cohort, respectively. As a collective, PPM was not associated with the composite endpoint of death, stroke or

TABLE 2 Propensity adjusted echocardiographic outcomes

	20 mm ($n = 3,931$)	≥23 mm ($n = 3,931$)	p value
Discharge			
Severe PPM	626 (21.5)	288 (9.7)	<0.0001
Mean gradient (mmHg)	15.7 ± 7.09	11.7 ± 5.54	<0.0001
Mean gradient ≥20 mmHg	822 (23.4)	258 (7.4)	<0.0001
Paravalvular leak			
None	2,205 (71.1)	2,625 (82.1)	<0.0001
Mild	815 (26.3)	539 (16.9)	<0.0001
Moderate	77 (2.5)	33 (1.0)	<0.0001
Severe	4 (0.1)	1 (0.03)	0.21
Moderate/severe	81 (2.6)	34 (1.1)	<0.0001
30-day			
Mean gradient	16.8 ± 6.51	12.1 ± 5.34	<0.0001
LVEF (%)	63.1 ± 8.35	61.3 ± 8.81	<0.0001
Paravalvular leak			
None	1,468 (57.8)	2018 (76.3)	<0.0001
Mild	936 (36.9)	587 (22.2)	<0.0001
Moderate	127 (5.0)	40 (1.5)	<0.0001
Severe	7 (0.3)	1 (0.04)	0.04
Moderate/severe	134 (5.3)	41 (1.5)	<0.0001
1-year			
Mean gradient	18.9 ± 7.70	13.0 ± 6.42	<0.0001
LVEF (%)	63.2 ± 8.19	61.4 ± 8.55	<0.0001
Paravalvular leak			
None	756 (58.7)	923 (77.9)	<0.0001
Mild	442 (34.3)	232 (19.6)	<0.0001
Moderate	85 (6.6)	30 (2.5)	<0.0001
Severe	5 (0.4)	0 (0.0)	0.06
Moderate/severe	90 (7.0)	30 (2.5)	<0.0001

Note: Data presented as mean ± *SD* or No. of patients (%).
Abbreviations: LVEF, left ventricular ejection fraction; No, number; PPM, prosthesis-patient mismatch; *SD*, standard deviation.

rehospitalization. However, when analyzing the impact of severe PPM on women only, a 3.67-fold increase in mortality at 1-year was observed[8] potentially due to smaller surgical valve sizes in women. In contradistinction, our analysis of the TVT Registry SAPIEN 3 20 mm data was comprised almost entirely of women and those with severe PPM had similar outcomes to the entire cohort.

Continued controversy exists over the why differences in mean gradients and valve areas favoring one valve type would result in long-term outcomes that favor the valve with reportedly higher gradients and smaller valve areas. Deharo et al.[10] used the French administrative hospital-discharge database to propensity match >10,000 pairs of patients and showed that the newest iteration of balloon-expandable transcatheter valve was associated with a lower yearly incidence of all-cause death, cardiovascular death, and rehospitalization for heart failure compared to the self-expanding valve. Similar results were found by van Belle et al.[9] with increased 2-year mortality associated with the self-expanding valve as well as a higher risk of ≥ moderate PVL. This discordance in hemodynamics and outcomes raises important issues about the flow characteristics of the SAPIEN 3 valve, which might result in an overestimation of transaortic gradient compared to invasive gradients[16] or an underestimation in true valve area by echocardiography.[17]

A glaring concern is the relatively high rate of PVL seen in 20 mm valve patients. The significantly higher 5.3% rate of 30-day moderate–severe PVL is concerning, especially when compared to the 1.5% rate of the ≥23 mm cohort. Furthermore, moderate–severe PVL was associated with a two-fold increase in all-cause mortality at 1-year (Figure S1(A)). Further analysis of the rates of moderate/severe PVL at 30-day post-TAVR, demonstrated that the difference in the rates in patients implanted with small versus large valves decreased yearly (from 7.1% in 2015 to 1.4% in 2019) (Figure S2(A)). We hypothesize this decrease in PVL rates is related to an increase in CT based

TABLE 3 Propensity Adjusted In-Hospital and 30-Day Outcomes

	20 mm ($n = 3,931$)	≥23 mm ($n = 3,931$)	p value
In-hospital outcomes			
All-cause mortality	64 (1.6)	76 (1.9)	0.31
Cardiac death	34 (0.9)	38 (1.0)	0.64
Stroke	74 (1.9)	60 (1.5)	0.22
Aortic valve re-intervention	28 (0.7)	18 (0.5)	0.14
Major vascular complication	72 (1.8)	56 (1.4)	0.15
New requirement for dialysis	20 (0.5)	20 (0.5)	1
New onset of atrial fibrillation	68 (1.7)	74 (1.9)	0.61
New pacemaker	149 (3.8)	277 (7.0)	<0.0001
30-day outcomes			
All-cause mortality	105 (2.8)	99 (2.6)	0.69
Cardiac death	38 (1.0)	42 (1.1)	0.64
O:E	0.38	0.35	
Stroke	98 (2.5)	72 (1.9)	0.05
Aortic valve re-intervention	28 (0.7)	19 (0.5)	0.19
Life-threatening bleeding	7 (0.2)	8 (0.2)	0.79
Major vascular complication	79 (2.0)	62 (1.6)	0.15
New requirement for dialysis	21 (0.6)	21 (0.6)	0.99
New pacemaker	165 (4.3)	324 (8.5)	<0.0001
Any readmission	292 (7.9)	339 (9.2)	0.04
Valve related readmission	25 (0.7)	21 (0.6)	0.57
NYHA III/IV	277 (9.2)	242 (7.9)	0.07
KCCQ	75.1 ± 21.60	74.5 ± 22.31	0.32

Note: Data presented as mean ± *SD* or No. of patients (%).
Abbreviations: NYHA, New York Heart Association; KCCQ, Kansas City Cardiomyopathy Questionnaire; No, number; PPM, prosthesis-patient mismatch; *SD*, standard deviation.

TABLE 4 Propensity adjusted 1 year outcomes

	20 mm ($n = 3,931$)	≥23 mm ($n = 3,931$)	p value
All-cause mortality	405 (13.0)	362 (12.7)	0.72
Cardiac death	76 (2.3)	69 (2.2)	0.78
Stroke	146 (4.3)	117 (3.7)	0.14
Aortic valve re-intervention	39 (1.1)	21 (0.6)	0.03
Life-threatening bleeding	12 (0.4)	13 (0.4)	0.76
Major vascular complication	84 (2.2)	68 (1.8)	0.21
New requirement for dialysis	27 (0.8)	26 (0.8)	0.96
New pacemaker	190 (5.2)	349 (9.4)	<0.0001
Any readmission	806 (26.4)	784 (26.9)	0.31
Valve related readmission	62 (2.0)	49 (1.7)	0.38
NYHA III/IV	138 (8.3)	100 (6.9)	0.12
KCCQ	78.6 ± 20.84	77.9 ± 21.13	0.33

Note: Data presented as mean ± *SD* or No. of patients (%).
Abbreviations: NYHA, New York Heart Association; KCCQ, Kansas City Cardiomyopathy Questionnaire; No, number; PPM, prosthesis-patient mismatch; *SD*, standard deviation.

valve sizing (Figure S2(B)). Improvement in valve sizing, implantation technique and possibly alternative valve selection may explain improved PVL rates (Figure S2(B)).

One interesting observation was the improved survival in patients with higher gradients. A potential explanation for this phenomenon is that patients with lower gradients include a group with low-flow,

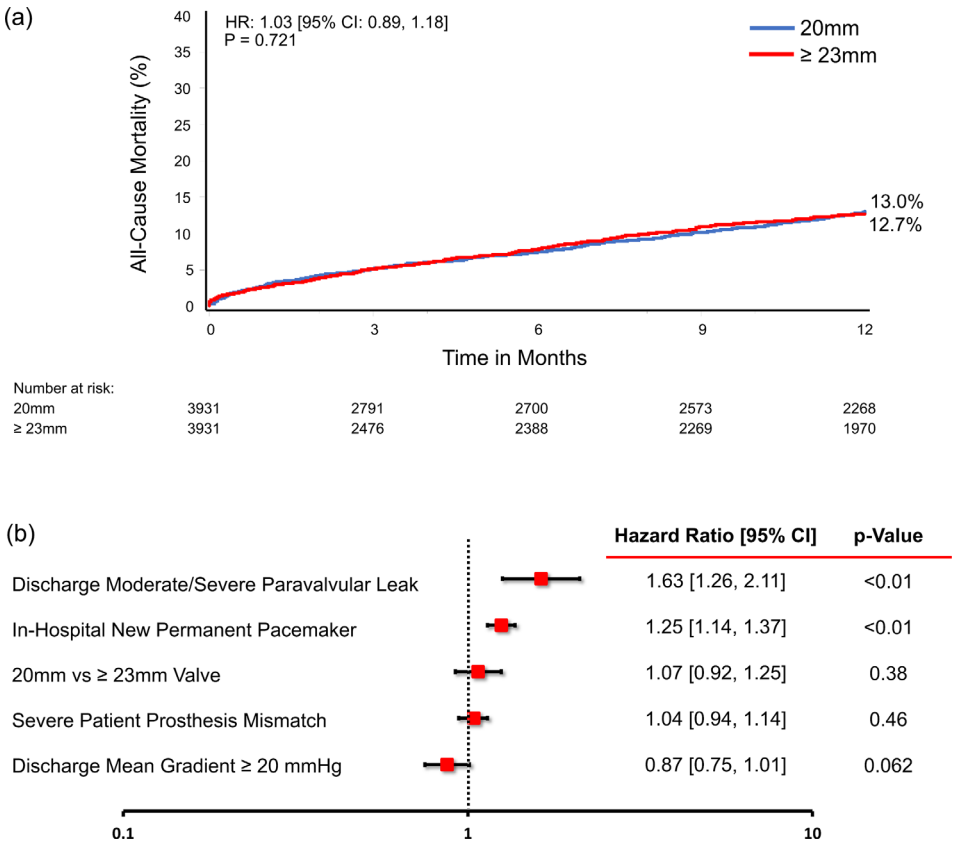

FIGURE 2 Kaplan–Meier estimate of 1-year all-cause mortality by valve size (A) and adjusted independent predictors of mortality at 1 year (B) [Color figure can be viewed at wileyonlinelibrary.com]

low-gradient aortic valve stenosis with lower stroke volume, which is known to be associated with decreased survival. From a retrospective analysis of a Corevalve study, low-gradient normal LVEF patients were found to have a 1 year all-cause mortality of 21% with only a 11.5% rate of cardiovascular mortality.[18] The TOPAS-TAVI study enrolled patients with low-flow, low-gradient aortic valve stenosis with reduced ejection fraction and similarly had high rates of all-cause death but less cardiac mortality (all cause death 32.3%, cardiac death 17.6%).[19] Both the Corevalve extended registry and TOPAS-TAVI reported stroke volume indexes of 34.6 ± 8.9 ml/m^2 and 32.9 ± 10.1 ml/m^2 respectively. It is possible that the low gradients post-procedure in our TVT Registry analysis include a group of patients with lower stroke volume with a higher risk of non-cardiac death.[20] With prospective studies using comprehensive echocardiographic assessment including stroke volume, investigators may someday better understand the prognostic relevance of elevated mean gradient following TAVR.

4.1 | Limitations

This is a retrospective analysis of a clinical registry and outcomes are corroborated by Medicare claims data. As such, the conclusions drawn are hypothesis gathering only. Nevertheless, the robustness of the propensity-matching does give more weight to the comparisons drawn between 20 mm and ≥ 23 mm valves. Although comparisons between the two cohorts were stronger with use of propensity matching, it reduced the sample size and limited the ability to identify mortality predictors, Unfortunately, patient level CT data are not available to corroborate our claims about CT sizing and all of the echocardiographic data is self-reported. In the TVT Registry database, EOA required to estimate PPM is available at discharge only and not at 30-day echocardiography, therefore PPM may have been assessed while the patient was potentially in a low-flow state from recent valve implantation. Additionally, the data are short-term and the impact of higher gradients or PPM may require more time to develop.

5 | CONCLUSION

This analysis demonstrates the safety and effectiveness of the Edwards SAPIEN 20 mm THV relative to its larger counterparts. Despite slightly higher gradients and higher rates of PPM, patients have identical symptom relief and survival at 12 months. While PVL rates were higher with SAPIEN 3 20 mm valves, we attribute this to a valve sizing learning curve and with improvement with CT utilization, the SAPIEN 3 PVL appeared to improve. The findings suggest that echocardiographic PPM may not influence outcomes and more research is needed to better understand the discrepancies in valve prosthesis size and echocardiographically measured EOA. Furthermore, longer follow up will be needed to better understand the impact of higher gradients and PPM on TAVR patients as the effect of such variables may not be detected this early in their clinical course.

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CONFLICT OF INTEREST

Marvin H. Eng is a clinical proctor for Medtronic and Edwards Lifesciences. Rebecca T. Hahn reports speaker fees from Boston Scientific Corporation, Baylis Medical, Edwards Lifesciences and Medtronic; consulting fees for Abbott Structural, Edwards Lifesciences, Gore Associates, Medtronic, Navigate and Philips Healthcare; non-financial support from 3mensio; equity with Navigate; and is Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she receives no direct industry compensation. Dee Dee Wang, MD has received research grant support from Boston Scientific; and is a consultant for Edwards Lifesciences, Boston Scientific, and Materialise. Dr. William W. O'Neill has received grant support from Edwards Lifesciences and Abiomed. James Lee and Mackram Eleid have no relevant disclosures.

DATA AVAILABILITY STATEMENT

Data restricted to third party and cannot be shared

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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