Comparative Outcomes of Balloon-Expandable S3 Versus Self-Expanding Evolut Bioprostheses for Transcatheter Aortic Valve Implantation

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To date, comparisons between the balloon-expandable Edwards Sapien S3 (S3) versus the self-expanding Evolut R or PRO (Evolut) valves have been limited with respect to procedural outcomes. We aim to compare the safety, efficacy, and procedural efficiency of the S3 versus the Medtronic Evolut bioprostheses in patients who underwent transcatheter aortic valve implantation for severe aortic stenosis. Retrospective analysis was performed of all consecutive transcatheter aortic valve implantation procedures performed through the transfemoral approach with either S3 or Evolut at our hospital between September 2015 and January 2019. A total of 581 patients were included. There were no significant differences between S3 (n = 452) and Evolut (n = 129) concerning in-hospital or 30-day safety outcomes. S3 was associated with significantly shorter fluoroscopy times, lower fluoroscopy Air Kerma, and higher contrast use. S3 had lower postprocedure aortic valve area (1.71 ± 0.45 vs 1.84 ± 0.50 cm^2, p = 0.004), larger peak gradient at 30 days (10.7 ± 3.8 vs 7.0 ± 3.2 mm Hg, p <0.001), and lower aortic regurgitation (AR) rates postprocedure (47% vs 33%, p = 0.024) and at 30 days (50% vs 33%, p = 0.008), driven by mild AR. Device type was an independent predictor of AR postprocedure and at 30 days. Patients with ≥mild AR were more likely to have had Evolut valves (odds ratio = 2.94, p <0.001), especially in larger valves (>26 mm). Severe prosthesis-patient mismatch was higher in S3 (14.8% vs 7.9%, p <0.001). In conclusion, S3 is associated with less radiation exposure, higher contrast use, and lower incidence of AR at 30 days. Alternately, S3 has a higher transaortic gradient at 30 days, and higher levels of severe prosthesis-patient mismatch. **(Am J Cardiol 2019;124:1621−1629)**

Transcatheter aortic valve implantation (TAVI) is the treatment of choice for patients with severe, symptomatic aortic stenosis and prohibitive surgical risk, and an alternative to conventional surgical aortic valve replacement (SAVR) in patients with high, intermediate, and most recently low surgical risk.[1] The improvement in TAVI safety and efficacy has been largely related to technological improvements in valve design. The balloon-expandable S3 (Edwards LifeSciences, Irvine, CA) and the self-expanding Evolut valve (Evolut R and Evolut Pro, Medtronic, Minneapolis, MN) are the predominant devices used in the United States recently. Intrinsic differences between these 2 devices include inherent implications of balloon-expandable versus self-expanding valve deployment, the availability of prosthesis skirts to enable better valve sealing, and prosthesis placement in an annular versus supra-annular position. These differences are proposed as the basis for possible superiority of either device with respect to the incidence of procedural complications, hemodynamic improvements, incidence of paravalvular aortic regurgitation (AR), and prosthesis-patient mismatch (PPM).[2–7] To date, head-to-head comparisons between S3 and Evolut have been limited. The aim of our study is to describe the differences between S3 and Evolut with respect to in-hospital and 30-day clinical outcomes, procedural efficiency and hemodynamics, AR, and PPM.

Methods

This is a retrospective, observational study conducted at an 890-bed tertiary-care medical center, Hartford Hospital, in Hartford, Connecticut. The Institutional Review Board (Assurance #FWA000000601) approved the study as it met the criteria for a waiver of the requirement to obtain informed consent.

From a total cohort of 1,060 TAVI procedures performed between September 2012 and January 2019, 581 consecutive patients treated with S3, Evolut R, or Evolut PRO underwent retrospective analysis. Patients who underwent nonfemoral access, valve-in-valve cases in patients who previously underwent SAVR, and patients with incomplete records submitted to the Society of

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Thoracic Surgeons/American College of Cardiology (STS/ACC) Transcatheter Valve Therapy (TVT) Registry were excluded from the analysis. Final comparisons were made between 452 S3 patients and 129 Evolut patients (72 Evolut R, 57 Evolut PRO). All reported outcomes conformed to the Valve Academic Research Consortium (VARC-2) definitions.[8,9]

All patients underwent evaluation by a multidisciplinary valve committee with a preprocedure review of catheterization, echocardiographic, and multislice computed tomography data to document the severity of aortic stenosis and suitability for TAVI. Baseline STS-predicted risk of 30-day mortality (STS-PROM), as well as incremental risk assessment based upon functional assessment including patient frailty, severe pulmonary and hepatic disease, porcelain aorta, and hostile mediastinum, was determined for all patients. Patients were classified as extreme-risk (≥50% probability of death or serious irreversible complication), high-risk (STS-PROM >8 with <50% probability of death) or intermediate-risk (STS-PROM ≥4 and ≤8). Valve choice for each patient was made by the treating cardiothoracic surgeon and interventional cardiologist.

Procedures were performed in a hybrid catheterization laboratory using conscious sedation or general anesthesia. Transthoracic echocardiographic monitoring was used in conscious sedation, and transesophageal for general anesthesia cases. Standard techniques for implantation of the S3 (20, 23, 26, 29 mm), Evolut R (23, 26, 29, 34 mm), and Evolut PRO (23, 26, 29 mm) valves were employed in patients with annular diameters between 18 and 30 mm. Patients with a baseline AV area <0.7 cm^2 underwent balloon valvuloplasty before prosthesis insertion. Postdilation was performed in all patients who demonstrated >mild AR by echocardiography or aortography. Maximal balloon diameters for postdilation was determined by pre-TAVI CTA annular measurements, with a limit of 20% oversizing for S3 and the mean of the aortic annular diameter for Evolut.

Baseline demographics, previous cardiac history and risk factors, pre-TAVI catheterization, echocardiographic and radiographic findings, STS and incremental surgical risk, functional characteristics, and procedural characteristics were compared between the S3 and Evolut valve cohorts. Follow-up outcome measures included in-hospital and 30-day mortality, in-hospital and 30-day TIA/stroke, composite bleeding and vascular complications, cardiac arrest, conduction disturbance requiring permanent pacemaker placement, conversion to open heart surgery, a new requirement for dialysis, and coronary compression or obstruction. Follow-up echocardiographic comparisons included in-hospital (within 24 hours postprocedure) and 30-day left ventricular ejection fraction (LVEF), aortic valve (AV) area, AV mean gradient, AV peak velocity, and incidence of AR graded as none, trace, mild, moderate, or severe. Based on the discharge echocardiographic effective valve area indexed to body surface area, PPM was calculated for all patients and was classified as none (>0.85 cm^2/m^2), moderate (0.65 to 0.85 cm^2/m^2), or severe (<0.65 cm^2/m^2). Variables and all echocardiographic measurements were as defined by the STS/ACC TVT Registry data dictionary.[10]

Continuous variables are expressed as mean ± SD or median (interquartile range) and were compared with a Student's *t* test or the Mann-Whitney U test, respectively. Categorical variables were analyzed using the chi-square test or Fisher's exact test. Post hoc Bonferroni corrections were applied to adjust for multiple comparisons. Event rates were generated using the Kaplan-Meier method, and log-rank tests were used for group comparisons. Propensity matching of S3 and Evolut was performed subanalysis to eliminate baseline differences in body surface area, annulus diameter, and STS risk score. Binary logistic regression was performed by entering predictors and potential confounders of ≥mild AR at 30 days using a $p < 0.15$ cutoff. All effects were considered significant at $p < 0.05$. The statistical analyses were performed with SPSS 21.0 (SPSS, Chicago, IL).

Results

Baseline demographics and clinical characteristics of 452 S3 patients and 129 Evolut patients (72 Evolut R, 57 Evolut PRO) are shown in Table 1. The S3 group had a higher BSA, as well as a lower STS score. Nonetheless, the distribution of individual risk categories (e.g., intermediate, high, and inoperable), determined by STS-PROM plus incremental risk assessment, was comparable between the 2 cohorts. The 2 groups were otherwise well matched for demographic parameters. There were no significant differences between the S3 and Evolut groups concerning baseline echocardiographic measurements including LVEF, AV area, AV mean gradient, peak AV velocity, or degree of AR. The S3 group had a slightly larger aortic annulus diameter.

Table 2 lists in-hospital and 30-day outcomes for the study cohorts. There were no differences between S3 and Evolut with respect to in-hospital mortality or 30-day mortality. Device implantation was successful in all patients. There were no significant differences in the rates of TIA or strokes in-hospital or at 30 days between the 2 groups. Similarly, there were no significant differences concerning composite bleeding/vascular complications, need for dialysis, or the need for implantation of a permanent pacemaker.

Table 3 lists the procedural characteristic for the study groups. There was no difference between the 2 cohorts concerning the use of conscious sedation, procedure duration, valve embolization, cardiac arrest during the procedure, coronary obstruction, or conversion to SAVR. S3 procedures were associated with shorter fluoroscopy times, lower Air Kerma, and higher contrast use. The need for valve postdilation was lower in the S3 group compared with Evolut. There was no difference between the 2 groups concerning valve embolization, cardiac arrest during the procedure, coronary obstruction, or conversion to SAVR.

As summarized in Table 4, there were no significant differences between the 2 groups with respect to postprocedural and 30-day follow-up LVEF. Postprocedure, calculated AV area was significantly lower for the S3 group. Postprocedure mean AV gradient was not significantly different between the S3 and Evolut groups. At 30 days, however, S3 patients had a higher mean gradient.

Table 1
Baseline demographics and clinical characteristics of the groups

Variable	Sapien 3 (n = 452)	Evolut R/Pro (n = 129)	p Value
Age (y)	81.3 ± 8.2	82.0 ± 7.8	0.410
Women	200 (44%)	62 (48%)	0.443
Body surface area (m^2)	1.90 ± 0.25	1.83 ± 0.25	0.005
Body mass index (kg/m^2)	28.38 ± 6.27	27.36 ± 5.52	0.097
White	438 (97%)	124 (96%)	0.661
Hypertension	409 (90%)	117 (91%)	0.942
Diabetes mellitus	139 (31%)	41 (32%)	0.823
Smoker (current or within 1 year)	16 (4%)	9 (7%)	0.090
Previous myocardial infarction	110 (24%)	25 (19%)	0.240
Previous percutaneous intervention	109 (24%)	21 (16%)	0.060
Previous coronary bypass	77 (17%)	29 (22%)	0.158
Atrial fibrillation/flutter	334 (74%)	102 (79%)	0.260
Previous stroke	45 (10%)	13 (10%)	0.968
Previous transient ischemic attack	39 (9%)	6 (5%)	0.136
End stage renal disease requiring dialysis	11 (35)	3 (2%)	0.843
Chronic lung disease	#N/A	#N/A	0.647
No-Mild	296 (67%)	76 (63%)	
Moderate	59 (13%)	17 (14%)	
Severe	90 (20%)	29 (24%)	
Forced expiratory volume in one second (% predicted)	71.2 ± 23.6	72.1 ± 27.3	0.723
Diffusing capacity of the lungs for carbon monoxide (% predicted)	74.3 ± 22.1	70.1 ± 21.2	0.085
Creatinine (mg/dL)	1.31 ± 1.24	1.39 ± 1.13	0.520
Hemoglobin (g/dL)	11.64 ± 2.13	11.56 ± 1.71	0.683
International normalized ratio	1.10 ± 0.18	1.08 ± 0.24	0.458
Albumin (g/dL)	3.77 ± 0.45	3.70 ± 0.59	0.137
Society of Thoracic Surgeons Risk Score (%)	9.91 ± 7.09	13.04 ± 9.07	<0.001
Intermediate risk	123 (27%)	27 (21%)	
High risk	238 (53%)	65 (50%)	
Inoperable/extreme risk	91 (20%)	37 (29%)	
Kansas City Cardiomyopathy Questionnaire 12	50.05 ± 2.07	46.49 ± 24.77	0.161
Aortic valve annulus size (mm)	24.85 ± 2.47	24.03 ± 2.59	0.001
Aortic valve peak velocity (m/s)	4.14 ± 0.66	4.12 ± 0.61	0.693
Aortic valve peak gradient (mm Hg)	70.55 ± 22.35	70.16 ± 20.94	0.865
Mitral valve regurgitation	#N/A	#N/A	0.876
None	12 (4%)	3 (3%)	
Trace/trivial	46 (16%)	19 (19%)	
Mild	134 (48%)	51 (50%)	
Moderate	75 (27%)	23 (23%)	
Severe	12 (4%)	5 (5%)	
Aortic regurgitation	#N/A	#N/A	0.406
None	91 (21%)	26 (21%)	
Trace/trivial	83 (19%)	32 (26%)	
Mild	197 (45%)	51 (41%)	
Moderate	59 (13%)	15 (12%)	
Severe	11 (2%)	1 (1%)	
Number narrowed coronary arteries	#N/A916	#N/A	0.919
None	97 (21%)	27 (21%)	
1	78 (17%)	18 (14%)	
≥2	274 (60%)	83 (64%)	
Left main stenosis ≥50%	36 (8%)	13 (10%)	0.446
Proximal left anterior descending stenosis ≥70%	86 (19%)	26 (20%)	0.774
Heart failure prior 2 weeks	254 (56%)	82 (64%)	0.135
New York Heart Association Class (within 2 weeks)	#N/A	#N/A	0.476
I	32 (7%)	15 (12%)	
II to III	330 (73%)	88 (69%)	
IV	83 (18%)	25 (19%)	

Values are number (%), mean ± SD, unless otherwise indicated.

Table 2
In-hospital and 30-day clinical outcomes

Variable	Sapien 3 (n = 452)	Evolut R/Pro (n = 129)	p Value
In-hospital mortality	4 (0.9%)	1 (0.8%)	0.91
30-day mortality	5 (1.1%)	3 (2.3%)	0.29
In-hospital transient ischemic attack/stroke	7 (1.6%)	3 (2.3%)	0.46
30-day transient ischemic attack/stroke	8 (1.8%)	3 (2.3%)	0.71
Composite bleed/vascular compromise*	55 (12.2%)	17 (13.3%)	0.75
Need for dialysis	1 (0.2%)	0 (0%)	0.99
Need for permanent pacemaker	71 (15.8%)	27 (21.1%)	0.16

* The composite outcome of bleed/vascular adverse events as defined by the STS/ACC TVT Registry's Adverse Event Definitions v2.0.

Table 3
Procedural characteristics

Variable	Sapien 3 (n = 452)	Evolut R/Pro (n = 129)	p Value
Conscious sedation	361 (80%)	95 (74%)	0.431
Procedure duration (min)	84.5 ± 39.2	84.3 ± 29.8	0.940
Contrast volume (mL)	101.6 ± 42.1	91.3 ± 47.7	0.018
Fluoroscopy time (min)	22.1 ± 7.2	25.3 ± 24.9	0.019
Dose area product (mGy.cm2)	42,493 ± 41,074	45,297 ± 38,798	0.493
Air Kerma (mGy)	868.19 ± 892.08	1,316 ± 1,223	<0.001
Valve postdilation	113 (25.0%)	45 (34.9%)	0.033
Valve embolization	1(0.8%)	0 (0%)	0.221
Cardiac arrest	10 (2.2%)	1(0.8%)	0.470
Coronary obstruction	1 (0.2%)	0 (0%)	0.332
Conversion to surgical aortic valve replacement	0 (0%)	0 (0%)	-

Values are number (%) or mean ± SD, unless otherwise indicated.

Table 4
Comparison of short-term echocardiographic data

Variable	S3 (n = 452)	Evolut R/Pro (n = 129)	p Value
Left ventricular ejection fraction (%)			
Preprocedure	54.8 ± 15.3	55.5 ± 14.7	0.638
30-day	55.7 ± 12.5	56.1 ± 1.8	0.781
Aortic valve mean gradient (mm Hg)			
Preprocedure	41.96 ± 13.91	41.57 ± 12.48	0.772
Postprocedure	7.73 ± 15.06	6.78 ± 12.74	0.721
30-day	10.68 ± 3.77	6.98 ± 3.24	<0.001
Aortic valve area (cm^2)			
Preprocedure	0.70 ± 0.27	0.73 ± 0.24	0.255
Postprocedure	1.71 ± 0.45	1.84 ± 0.50	0.004
Postprocedure aortic regurgitation			<0.001
None	211 (47%)	43 (33%)	0.024
Trace/trivial	141 (32%)	34 (26%)	0.868
Mild	89 (20%)	49 (38%)	<0.001
Moderate	6 (1%)	3 (2%)	0.999
Severe	0 (0%)	0 (0%)	-
30-day aortic regurgitation		<0.001	
None	205 (50%)	33 (33%)	0.008
Trace/trivial	94 (23%)	18 (18%)	0.999
Mild	100 (25%)	44 (44%)	0.008
Moderate	9 (2%)	6 (6%)	0.188
Severe	0 (0%)	0 (0%)	-
Prosthesis-patient mismatch (cm^2/m^2)			
None (>0.85)	239 (53.7%)	86 (68.3%)	0.011
Moderate (0.65 to 0.85)	140 (31.5%)	30 (23.8%)	0.073
Severe (<0.65)	66 (14.8%)	10 (7.9%)	0.035

Values are number (%), mean ± SD, unless otherwise indicated.

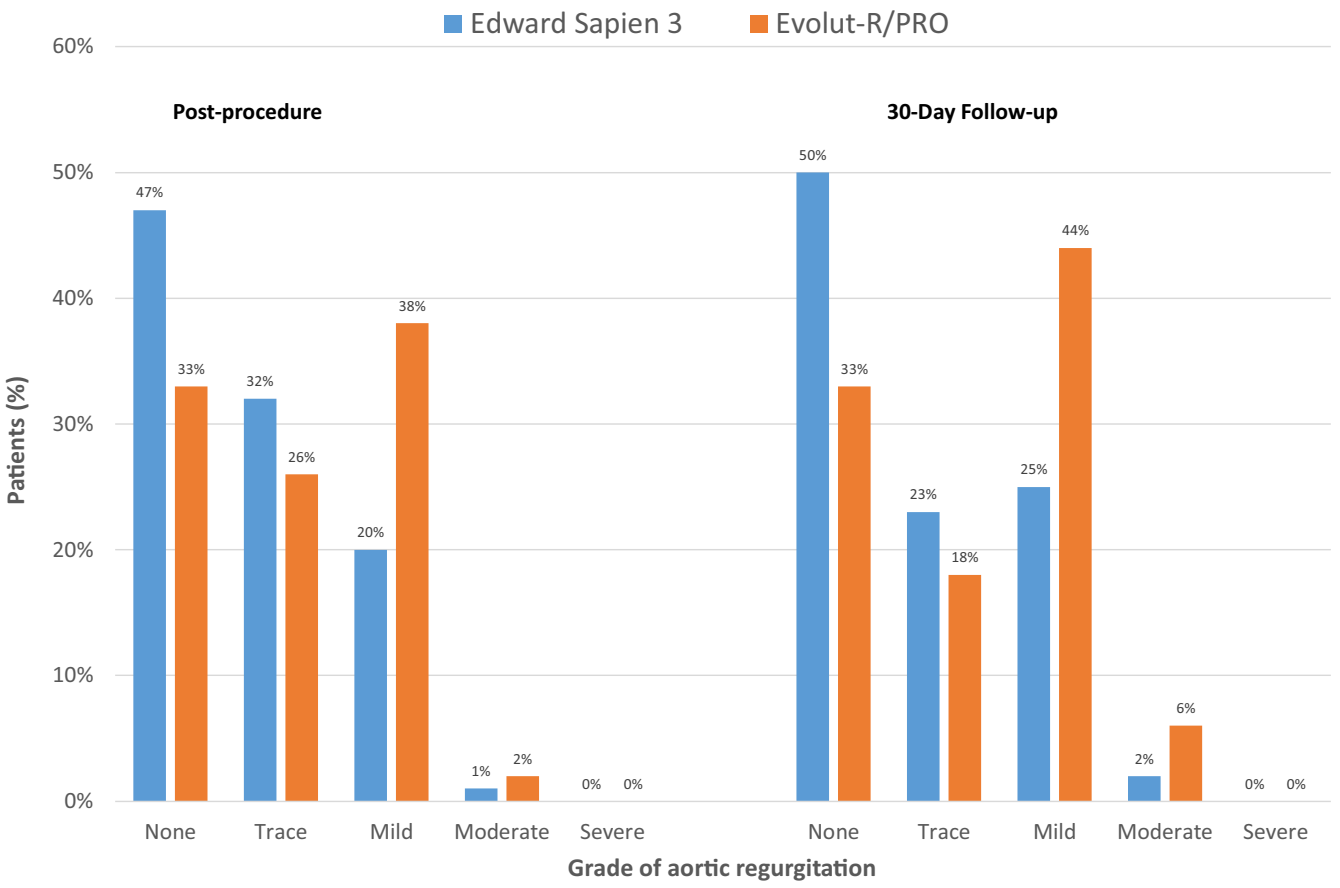

Figure 1. Postprocedure and 30-day rate of aortic regurgitation of different severities stratified by device type. In both postprocedure and 30-day follow-up, the S3 group had a significantly higher degree of freedom from any AR and a significantly lower incidence of mild AR ($p < 0.05$).

Postprocedure and 30-day rate of AR stratified by device type are illustrated in Figure 1. Postprocedure, the S3 group had a higher degree of freedom from any AR (47% vs 33%, $p < 0.024$), and a lower incidence of mild AR (20% vs 38%, $p < 0.001$). These findings were also present at 30 days, where the freedom from any degree of AR was higher in the S3 group (50% vs 33%, $p = 0.008$), with lower rates of mild AR at 30 days (25% vs 44%, $p = 0.008$). There was no difference in the incidence of moderate AR between the 2 groups, and there were no cases of severe AR in either cohort.

PPM was absent in 57% of the total population, 53.7% of S3 and 68.3% of Evolut patients ($p = 0.011$). S3 patients had a trend in higher incidence of moderate PPM and significantly higher incidence of severe PPM. As shown in Figure 2, subgroup analysis of PPM performed according to the valve size, irrespective of the valve type, revealed higher rates of PPM with sizes ≤23 mm compared with >23 mm (54.1% vs 39.7%, $p = 0.003$).

Univariate predictors of ≥mild AR at 30 days included age, higher BMI, higher BSA, previous HF, diabetes, PPM <0.85 cm^2/m^2, previous PCI, and Evolut use. Based upon multivariate logistic regression, BMI, diabetes, PPM ≤0.85 cm^2/m^2, and Evolut use were found to be significant independent predictors. Results of this regression analysis are listed in Table 5, where device type was the most significant predictor of ≥mild AR at 30 days.

Subgroup analyses by valve type were analyzed for significant predictors of ≥mild AR at 30 days, the S3 cohort did not reveal a relation between valve size (S3 >26 mm vs S3 ≤26 mm) and incidence of ≥mild AR (odds ratio [OR] = 0.75, $p = 0.637$). This was also true for the Evolut valves (>26 mm vs ≤26 mm; OR = 0.54, $p = 0.465$). However, in the subgroup analysis by valve size, Evolut had a higher incidence of ≥mild AR at 30 days compared with S3 in smaller valve sizes (Evolut ≤26 mm vs S3 ≤26 mm; OR = 2.72, $p = 0.017$), and was more pronounced in larger valves (Evolut >26 mm vs S3 >26 mm; OR = 3.33, $p = 0.002$). Figure 3 illustrates the differences in the incidence of ≥mild AR between the valve types and sizes.

In a subgroup analysis of Evolut R and Evolut PRO, Evolut R was more likely to have ≥mild AR than both the S3 (OR = 5.3 [2.6 to 10.6], $p < 0.001$), and the Evolut PRO (OR = 4.5 [1.7 to 11.8], $p = 0.002$). However, there was no significant difference in the likelihood of ≥mild AR between S3 and Evolut-PRO (OR = 1.2 [0.5 to 2.7], $p = 0.70$).

To remove potential baseline confounders, patients receiving S3 and Evolut valves were matched 1:1 for BSA, STS-risk score, and annular diameter. This yielded 113 patients in each group and resulted in similar differences between the S3 and Evolut outcomes (Table S1 and Figure S1 in Supplement). The propensity-matched subset of S3

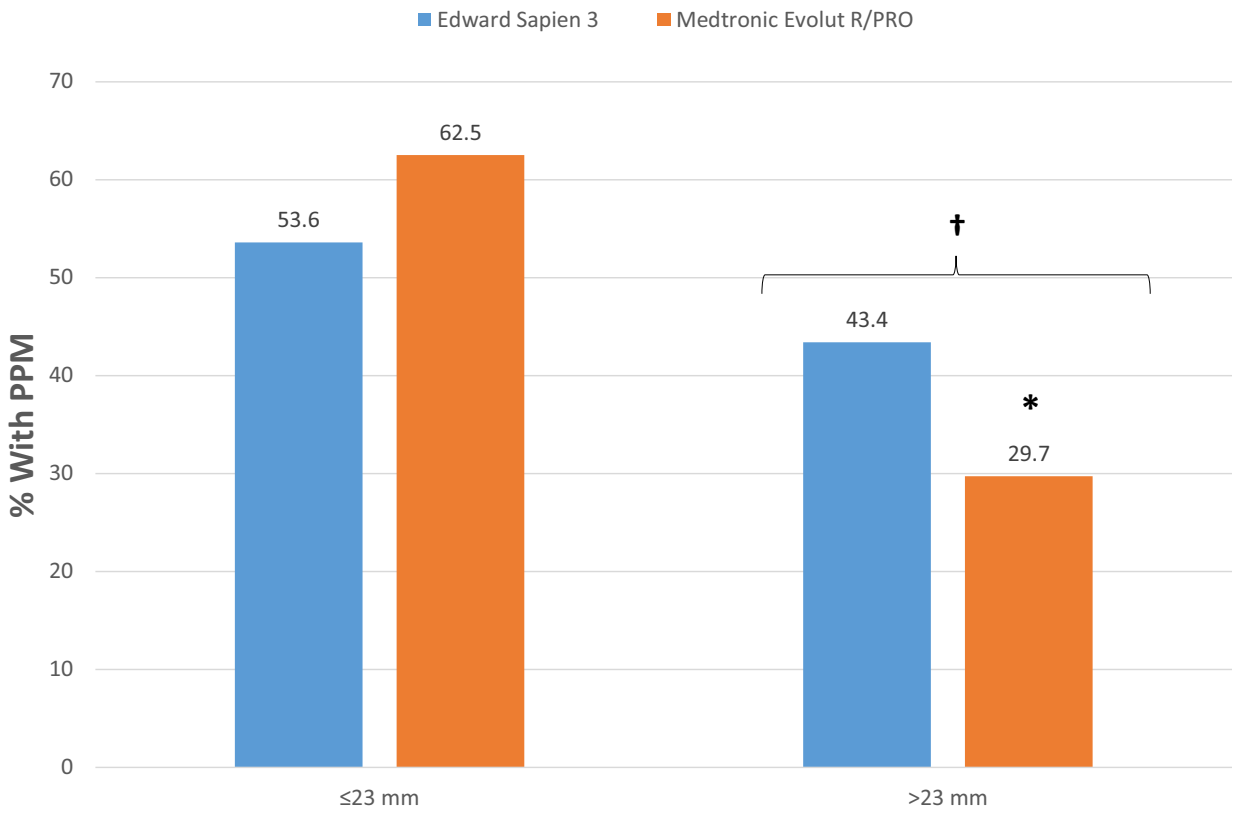

Figure 2. Differences in incidence of patient-prosthesis mismatch (PPM) stratified by device types and sizes. *Valves >23 mm, regardless of valve type, have significantly lower incidence of PPM in comparison with valves ≤23 mm ($p < 0.05$). †In valves >23 mm, Medtronic Evolut R/PRO has significantly lower incidence of PPM (≤0.85 cm^2/m^2) than Edward Sapien 3 ($p < 0.05$).

and Evolut revealed that the Evolut cohort displayed more AR both postprocedure and at 30 days.

Discussion

This retrospective study has demonstrated significant differences in procedural characteristics and hemodynamic outcomes in TAVI patients treated with either the balloon-expandable S3 or the self-expanding Evolut valve. Valve choice was the most significant independent predictor of AR. Studies of earlier generation valves revealed that valve type plays a significant role in device success due to a significantly lower rate post-TAVI AR.[4,11,12] Therefore, modifications in the design of newer valves were to reduce post-TAVI AR. The Evolut R design includes a skirt extending at the in-flow aspect of the valve. The Evolut PRO design adds a porcine pericardial tissue wrap around the outer sealing zone of its frame. Similarly, the S3 design includes an outer skirt to occlude any residual cavity between the native annulus and the prosthetic valve. Several studies showed that these changes resulted in a reduction of AR and higher device success rates compared with earlier devices.[5,13]

Studies comparing S3 and Evolut concerning post-TAVI AR have been limited and variable.[14–16] Ben-Shoshan et al showed no significant difference in the incidence of moderate or severe AR between S3 and Evolut R,[16] as did the recently reported SOLVE-TAVI trial at 30-day follow-up.[15] These observations are in contrast with a smaller study of 144 patients by Enriquez-Rodriguez that demonstrated that S3 was associated with a lower rate of moderate and severe AR compared with Evolut R.[14] The authors of this study partially attributed the increased rate of AR in the Evolut group due to more Evolut patients requiring >26 mm valve sizes. As documented in our study, differences in AR between S3 and Evolut were most prominent in larger annuli.

Differences between S3 and Evolut AR in the present study were driven primarily by a higher incidence of no AR and a lower incidence of mild AR in the S3 group. There was no significant difference in moderate AR, and severe AR was absent in both cohorts. Although some reports had suggested that mild post-TAVI AR is usually benign,[17,18] other studies have shown that even mild AR is considered an adverse prognostic indicator.[19–21] A previous meta-analysis showed that mild AR was significantly associated with increased mortality in an overall pooled analysis.[2] Furthermore, in a recently published study from the Japanese OCEAN-TAVI registry including 1,572 patients, a significant increase in the incidence of heart failure rehospitalization was demonstrated in patients with that had mild AR post-TAVI compared with patients with none or trivial.[21]

We found that Evolut PRO has a lower likelihood for developing AR compared with Evolut R, with similar incidence as the S3. This may be due to the improved seal in Evolut PRO, which is more similar to the S3, with the pericardial tissue wrap located on the outer part of the frame.

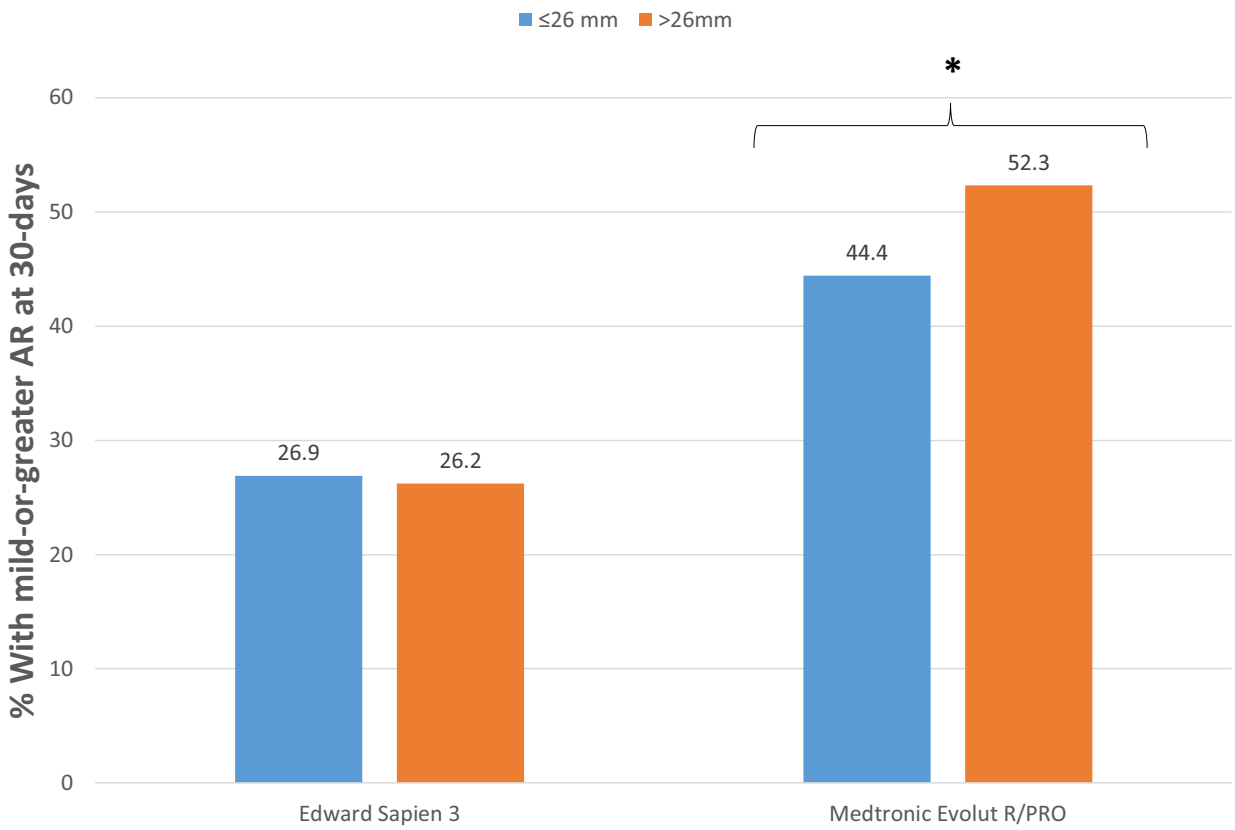

Figure 3. Differences in incidence of ≥mild AR at 30 days stratified by device types and sizes. *When including all valve sizes, Evolut R/PRO valves has a significantly higher incidence of ≥mild AR in comparison with Edward Sapien 3 ($p < 0.05$).

This is in agreement with a previous study that showed a significant improvement in Evolut PRO over the Evolut R concerning AR rates.[22]

The impact of mild AR post-TAVI will depend on whether AR worsens, stabilizes, or improves with time. Some studies found a higher progression of AR to moderate and severe with worse symptoms in patients with mild AR compared with no AR post-TAVI.[23] Although it is postulated that AR may lessen with time with self-expanding bioprostheses, there was no improvement observed in the present study in Evolut patients between discharge and 30 days. Therefore, longer follow-up studies are needed to determine the long-term impact of AR.

Table 5
Predictors of mild-or-greater aortic regurgitation at 30-day follow-up

Variable	Odds ratio	CI	p Value
Age (y)	1.00	0.97-1.03	0.837
Body mass index (kg/m^2)	0.94	0.89-0.99	0.038
Body surface area (m^2)	0.99	0.23-4.25	0.989
Heart failure (prior 2 weeks)	0.73	0.47-1.13	0.154
Diabetes mellitus	0.47	0.28-0.80	0.006
Patient-prosthesis mismatch ≤0.85 (cm^2/m^2)	1.74	1.09-2.78	0.021
Prior percutaneous intervention	0.68	0.38-1.21	0.189
Device type: Evolut R/Pro*	2.94	1.67-5.16	<0.001
Device size: ≤26 mm†	1.13	0.66-1.93	0.662

* In comparison with S3.
† In comparison with >26 mm.

We document a 43.1% incidence of PPM in the entire study population, including severe PPM in 13.3%. This is consistent with previous literature in terms of a higher rate of PPM in new-generation devices.[24,25] It is postulated that the use of an outer skirt can result in a reduced subannular orifice, leading to an increased prosthetic AV gradient and higher incidence of PPM. Our study agrees with previous reports in that the severe PPM rate is significantly higher in S3 compared with the Evolut valve. Abdelghani et al reported an incidence of moderate and severe PPM for S3 were 33.1% and 14.7%, compared with 23.3% and 3.5% for Evolut R/PRO.[25] The supra-annular location of the self-expanding prosthesis has been postulated to result in a larger effective valve orifice area. Support for this concept is provided by Jiaihawi et al who demonstrated that optimal positioning of a self-expanding prosthesis with reduced left ventricular depth was associated with a reduction in moderate/severe PPM from 48% to 15%. Regardless of valve type, we also found that rates of PPM are higher in smaller valves, in agreement with previous studies that have demonstrated that valve size ≤23 mm is a predictor for severe PPM.[26]

The long-term impact of PPM post-TAVI remains controversial. A recent report by Herrmann et al demonstrated that patients with severe PPM had increased late mortality and heart failure rehospitalization, whereas those with moderate PPM had outcomes that were not statistically significant from patients without PPM.[26]

The results of the present study demonstrate that the higher incidence of AR in Evolut compared with S3 is

exaggerated in patients with larger valve annuli. Studies on older-generation valves have historically shown that balloon-expandable valves were associated with less AR than self-expanding valves in patients with large annuli.[27] The present study suggests that this observation is also true for new-generation valves. Conversely, Evolut had a lower incidence of PPM, which was compounded in smaller valve sizes. It has been shown that Evolut R was associated with a decreased rate of PPM than with S3 only in small annuli.[27] Therefore, our results highlight the importance of considering the annulus size when choosing the valve type to mitigate AR and PPM.

The present study is the largest to compare the incidence of post-TAVI AR in S3 versus Evolut newer generation valves, and is the first study to focus on ≥mild rather than moderate/severe AR. One of the reasons is that recent studies using newer generation valves, including ours, have shown that the rates of moderate/severe AR are becoming increasingly low,[14,15] and more studies are recognizing the significance of residual mild AR post-TAVI. Although additional studies are required to determine the long-term consequences of mild AR and PPM, our observations highlight the need for future improvements in TAVI prostheses as the procedure is extended to low-risk patients, where long-term valve durability and AR progression may have late clinical consequences. Finally, our study is the first to examine the effect of valve annular size on AR and PPM within the 2 new-generation valve types, highlighting the importance of an individualized approach to choosing the type of valve.

Our study is limited by its single-center observational nature and needs a multicenter, randomized controlled trial for validation. Although patients were not randomized, we demonstrated well-matched cohorts, ensuring that any significant baseline differences were not confounders for ≥mild AR at 30 days by multivariate logistic regression analysis and by a propensity-matched subanalysis. Our data were limited by what was readily available in the STS/ACC TVT registry, which did not collect data on known offenders for developing AR, such as the CT-derived mean Agatston calcium score,[2,3] and implantation depth from the noncoronary cusp.[2,3,6,7]

In summary, despite similar short-term clinical outcomes, the S3 valve was associated with less radiation dose and fluoroscopy time, but higher contrast use. It had lower rates of ≥mild AR, at the cost of a lower AV area and a higher mean AV gradient on short-term follow-up, and a higher incidence of severe PPM compared with Evolut. The disparity in incidence of ≥mild AR is compounded in larger valves, whereas PPM was worse with smaller valve sizes regardless of valve type. Hence, the choice of valve type should take into consideration the annular size to balance AR and PPM, where Evolut theoretically may be better suited for smaller valves, while S3 for larger ones. These results encourage validation with large randomized controlled trials with long-term follow-up, focusing on the long-term implications of mild AR and severe PPM.

Disclosures

There are no relationships with industry.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.08.014.

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