Transcatheter Aortic Valve Implantation With the New Balloon-Expandable Sapien 3 Versus Sapien XT Valve System

A Propensity Score–Matched Single-Center Comparison

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Background—The new balloon-expandable Sapien 3 transcatheter heart valve (S3-THV) incorporates new features to reduce aortic regurgitation (AR) and vascular complications in transcatheter aortic valve implantation. Aim of this study is to compare the outcomes of the S3-THV with the preceding Sapien XT THV (SXT-THV) in patients who underwent transcatheter aortic valve implantation for symptomatic severe native aortic stenosis.

Methods and Results—Eligible patients were retrospectively identified in our institutional database and periprocedural clinical and imaging data were collected. Non-parsimonious one-to-many propensity score matching was performed to account for differences in baseline characteristics. Between November 2011 and December 2014, 167 patients underwent balloon-expandable transcatheter aortic valve implantation with either the S3-THV (n=49) or SXT-THV (n=118). Forty-four (89.8%) S3-THV patients were matched to 66 (55.9%) SXT-THV patients (mean age 80.3±8.4 and 80.5±7.8 years, median EuroSCORE 15.8 and 16.5%, respectively). In the S3-THV and SXT-THV groups, transfemoral approach (77.3% versus 78.8%) and postdilatation rates (15.9% versus 12.1%) were similar. Predischarge echocardiography demonstrated a lower incidence of ≥mild AR (15.9% versus 46.2%, *P*=0.003) for the S3-THV, despite reduced annulus area to prosthesis oversizing (8.2±5.1 versus 18.2±10.7%, *P*=0.001). Transfemoral access site–related life-threatening or major bleedings and vascular complications were absent in the S3-THV group (0% versus 7.7%, *P*=0.15). No differences were observed in pacemaker implantation rate (9.8% versus 8.8%, *P*=0.94) and 30-day mortality (both 5%).

Conclusions—In this retrospective, propensity score–matched analysis, the S3-THV performed superiorly to the SXT-THV, as demonstrated by improved valve patency and increased transfemoral access safety. **(*Circ Cardiovasc Interv*. 2015;8:e002408. DOI: 10.1161/CIRCINTERVENTIONS.115.002408.)**

Key Words: aortic regurgitation ■ aortic valve stenosis ■ transcatheter aortic valve implantation ■ vascular complications

Transcatheter aortic valve implantation (TAVI) has become a firmly established treatment option for symptomatic severe aortic stenosis (AS) in inoperable patients[1] and patients at high operative risk.[2,3] Although proven noninferior to surgical aortic valve replacement in terms of all-cause mortality, TAVI is associated with a higher incidence of postoperative aortic regurgitation (AR) and vascular complications.[2,3] Other non-negligible TAVI-related complications are cerebral embolic events and advanced conduction disturbances.[4] The extension of TAVI to lower risk populations requires minimization of these adverse events, partly depending on technological developments in transcatheter heart valves (THVs) and delivery systems.

Recently, the new balloon-expandable Sapien 3 THV (S3-THV; Edwards Lifesciences, Irvine, CA) has become commercially available.[5] The S3-THV embodies the next generation balloon-expandable valve of the Sapien valve family, building on the clinical experiences gained with the previous Sapien XT-THV (SXT-THV; Edwards Lifesciences). With its new features, including an outer annular sealing cuff, improved delivery system, and low crimped profile, the S3-THV is thought to achieve better results than the preceding SXT-THV.[5] Initial data from a multicenter registry prospectively evaluating the S3-THV looked promising, reporting low rates of AR, vascular complications, and stroke.[6] Comparative studies on the clinical outcomes of TAVI with the S3-THV and SXT-THV are currently scarce.

Aim of this study was to retrospectively compare the hemodynamic and clinical outcomes of TAVI with the S3-THV versus the SXT-THV in patients with symptomatic severe native AS.

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WHAT IS KNOWN

- The new Sapien 3 is designed to reduce aortic regurgitation and vascular complications after transcatheter aortic valve implantation, with its annular sealing cuff and lower delivery profile.
- Initial series suggest a higher pacemaker rate for the Sapien 3 compared with the preceding Sapien XT.

WHAT THE STUDY ADDS

- In this propensity score–matched analysis, the Sapien 3 performs better than the Sapien XT in terms of postoperative aortic regurgitation and vascular complications.
- Better valve patency was achieved with the Sapien 3, despite reduced oversizing, which may lower the risk of mechanical complications.
- A high implantation of the Sapien 3 is feasible and may provide similar pacemaker implantation rates compared with Sapien XT, compensating for the higher stent frame.

Methods

This is a retrospective single-center study. All patients who underwent TAVI for severe native AS at the University Medical Center Utrecht by means of S3-THV or SXT-THV implantation were identified in our institutional database and included in the study. Implantation of the SXT-THV had to be state-of-the-art, meaning performed with the Novaflex+ delivery system through an expandable sheath. Patients with bicuspid aortic valve anatomy or a degenerated surgical aortic valve were excluded from the study.

Patients were selected for TAVI based on Heart Team discussion involving at least one interventional cardiologist and one cardiac surgeon. Reasons to refrain from surgical aortic valve replacement included high operative risk (logistic EuroSCORE-I≥15%) and the presence of contraindications (eg, porcelain aorta, frailty, patent grafts in proximity of the sternum). Workup of TAVI candidates included transthoracic echocardiography (TTE), coronary angiography, thoracic and abdominal multislice computed tomography, and consultation of the geriatrics department.

Relevant periprocedural clinical and imaging data were collected and registered in a database. Follow-up was obtained using documentation of standard-of-care outpatient visits, and survival status was attained by interrogation of the Dutch municipal personal records database. Outcomes were registered in compliance with the Valve Academic Research Consortium 2 (VARC-2) criteria. Device success was defined accordingly as the proper implantation of the first valve prosthesis used, with intended performance of the valve (peak aortic flow velocity <3 m/s and no moderate or severe AR) and no procedural mortality. Vascular complications were documented for all procedural access sites, defined as any location traversed by a guidewire, a catheter, or a sheath during the procedure, including arteries, veins, left ventricular apex, and the aorta.

All patients gave informed consent for the TAVI procedure, and the study was performed under a waiver obtained from the institutional medical ethics committee (14–661/C).

Echocardiographic, Angiographic, and Multislice Computed Tomography Evaluation

All patients underwent TTE examination one day before TAVI and modified Simpson's biplane method or, in case of insufficient image quality, visually estimated and quantified in incremental steps of 5%. Prosthetic valve function was evaluated as recommended. Left ventricular outflow tract (LVOT) diameter measurements and Doppler velocity recordings for calculation of the effective orifice area were performed just beneath the ventricular margin of the prosthetic stent, as previously validated.[9] AR severity (both trans- and paraprosthetic) was assessed and classified by means of the integrative approach endorsed by the VARC-2 recommendations.[10]

Angiographic assessment of AR severity was performed according to the Sellers classification,[11] directly after valve implantation and after any countermeasures to address significant AR. Measurements of implantation depth and skewness of valve position were performed on angiographic images as previously described (see Figure in Data Supplement).[12] Implantation depth is presented both in percentages of stent frame height extending below the annulus plane and in millimeters. All measurements were performed by operators experienced in angiographic evaluations and independent from the procedure itself.

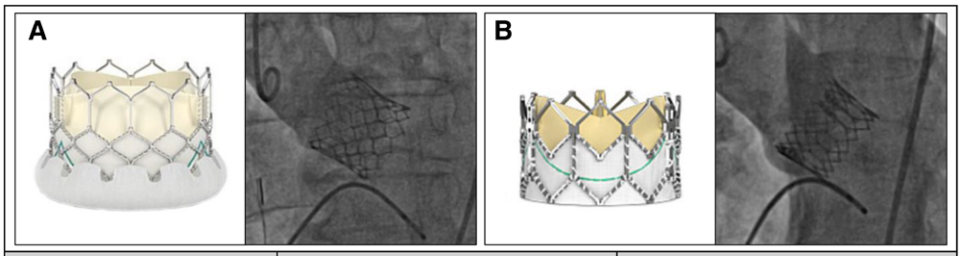
Preprocedural multislice computed tomography evaluation included measurement of the aortic annulus and aortic root dimensions and eligibility assessment of the TAVI access sites. Aortic annulus dimensions (minimum diameter, maximum diameter, perimeter, and area) were measured according to standard procedures using dedicated software (3Mensio; Pie Medical Imaging, Maastricht, The Netherlands). Valve prosthesis size was selected in accordance with the manufacturer's recommendations (Figure 1).

Valve Devices

The SXT-THV and its new iteration, S3-THV, are both balloon-expandable valves that consist of a trileaflet bovine pericardial valve sewn into a cobalt-chromium frame. The lower two-thirds of the frame are covered with an internal polyethylene terephthalate skirt. New feature to the S3 is the external polyethylene terephthalate sealing cuff designed to improve apposition with the aortic annulus and minimize paravalvular leakage. Other improvements to the S3-THV are the enhanced frame geometry that allows lower delivery profiles and the higher radial strength for better maintenance of circularity after deployment.[13] Both the SXT-THV and S3-THV valves are available in the sizes 23-mm, 26-mm, and 29-mm, whereas currently only the SXT-THV has a 20-mm version to accommodate small annuli. In the transfemoral approach, the SXT-THV and S3-THV valves are implanted with the NovaFlex+ and Commander delivery systems, respectively, introduced through expandable sheaths (eSheath; Edwards Lifesciences). In transapical or direct aortic procedures, the SXT-THV and S3-THV are deployed with the Ascendra and Certitude delivery systems, respectively. New refinement to the transfemoral S3-THV delivery system is a fine alignment wheel that allows small changes to prosthesis position without having to push or pull the whole delivery system, increasing positioning precision. Device characteristics and sizing charts for the SXT-THV and S3-THV are provided in Figure 1.

Implantation Procedure and Technique

Valve implantation was performed per transfemoral, transaortic, or transapical approach, in order of our institutional preference, depending on the presence of suitable access sites. Common access techniques were used. All transfemoral procedures involved a full percutaneous technique. Suture-mediated closure devices (Perclose ProGlide; Abbott Laboratories, Abbott Park, IL) were inserted into the femoral arteries to facilitate vascular closure. Conscious sedation was the default anesthetic method in transfemoral procedures; in surgical TAVI, general anesthesia was instituted. Fluoroscopic guidance was used to guide prosthesis positioning and deployment, whereas intraprocedural imaging support was accounted for by intracardiac echocardiography in the transfemoral and transesophageal echocardiography in surgical TAVI procedures. After routine predilatation to prepare the device landing zone, valve implantation was performed under rapid ventricu-



	SAPIEN 3			SAPIEN XT		
Prosthesis diameter	23-mm	26-mm	29-mm	23-mm	26-mm	29-mm
Prosthesis height, mm	18.0	20.0	22.5	14.3	17.2	19.1
Transfemoral sheath size	14-F	14-F	16-F	16-F	18-F	20-F
Transapical sheath size	18-F	18-F	21-F	24-F	24-F	26-F
Native annulus size on TEE, mm	18-22	21-25	24-28	18-21	22-24	25-27
Native annulus area, mm^2	338-430	430-546	540-680	314-415	415-530	530-660
Area derived diameter, mm	20.7-23.4	23.4-26.4	26.2-29.5	20.0-23.0	23.0-26.0	26.0-29.0

Figure 1. Device characteristics and sizing recommendations for the Sapien 3 (**A**) and Sapien XT (**B**).

during one slow inflation (5–10 s). Prosthesis position and function and patency of the coronary ostia were evaluated with angiography and intracardiac echocardiography or transesophageal echocardiography. Significant aortic regurgitation was addressed by postdilatation or second valve implantation, at discretion of the operator.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics software version 20 (IBM Corp., Armonk, NY) and R version 2.12.0 (http://www.r-project.org). Continuous variables are presented as means±standard deviation or medians [interquartile range], as considered appropriate, and categorical variables as counts and percentages. Comparison of continuous variables between groups was performed with the Student's *t* test or Mann–Whitney test, depending on data distribution. Categorical variables were compared using Chi-square or Fisher's Exact test, as considered appropriate. Two-tailed *P* values <0.05 were considered statistically significant.

Propensity score matching was performed to adjust for differences in baseline characteristics between the S3-THV and the SXT-THV groups. The propensity score, reflecting the propensity of being treated with the S3-THV, was calculated by means of nonparsimonious binary logistic regression, including the following baseline features: age, sex, body mass index, hypertension, diabetes mellitus, glomerular filtration rate, coronary artery disease, peripheral artery disease, cerebrovascular disease, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, atrial fibrillation, chronic obstructive pulmonary disease, pulmonary hypertension, porcelain aorta, left ventricular ejection fraction, mean transaortic pressure gradient, baseline moderate to severe AR, and procedural access. The 2 groups were matched on the logit of the propensity score (caliper set to 0.20) using a greedy, nearest neighbor, one (S3-THV) to many (SXT-THV) matching algorithm. Balance diagnostics were performed by inspection of the weighted standardized mean differences (*d*) (<0.20 indicating adequate balance) as previously devised.[14] In the absence of expert consensus on the estimation of treatment effects in propensity score matching, the 2 matched groups were handled as unpaired independent groups.[15] Although all reported values for the matched control group represent unweighted data for transparency purposes, all statistical analyses were weighted for the number of matches.

Results

Between November 2011 and December 2014, out of 253 [illegible] received a balloon-expandable valve. One SXT-THV patient was excluded because of degenerated surgical valve disease, leaving 167 patients for further analysis. Forty-nine (29.3%) patients received a S3-THV (which was introduced in February 2014) and 118 (70.7%) a SXT-THV. Baseline characteristics, procedural features, and outcomes of the total population are provided in Tables I–III in the Data Supplement. The overall S3 and SXT-THV groups were comparable with respect to logistic EuroSCORE (median 15.8% versus 16.0%, *P*=0.899) and comorbidities. In the S3-THV group, there was a trend toward a lower incidence of renal impairment (49% versus 63%, *P*=0.088) and atrial fibrillation (25% versus 39%, *P*=0.084), with significantly lower left ventricular ejection fraction (48.5±12.4 versus 52.7±12.2%, *P*=0.043).

By means of one-to-many propensity score matching, 44 (89.8%) S3-THV patients were matched to 66 (55.9%) SXT-THV patients (1.5 matches per S3-THV patient on average). Baseline characteristics were well balanced, whereas imaging data showed differences between the matched groups (see Table 1). Aortic annuli were larger in the S3-THV group, demonstrated by the significantly larger diameter and area measurements on multislice computed tomography (all *P*<0.05). For each prosthesis size (23-mm, 26-mm, and 29-mm), larger annuli were treated with the S3-THV, with significantly lower percentage area and mean diameter oversizing (Figure 2A and 2B).

The majority of S3- and SXT-THV patients were treated with transfemoral TAVI (77.3% and 78.8%) under local anesthesia. The S3-THV was implanted higher (ie, more aortic), indicated by the lesser percentage of stent frame height extending below the annulus plane (20.0±11.9 versus 31.0±11.7%, *P*<0.001) and lower implantation depth (4.0±2.2 versus 5.3±2.1 mm, *P*<0.001). Skewness of final valve position was smaller for the S3-THV (3.5±3.2 versus 5.3±3.8%, *P*=0.034). The incidence of postdilatation was comparable among the groups: 15.9% for the S3-THV and 12.1% for the SXT-THV (*P*=0.55). An overview of procedural features is provided in Table 2.

Table 1. Baseline Clinical Characteristics and Imaging Data

	Sapien 3 (n=44)	Sapien XT (n=66)	Weighted *d*	Weighted *p*
Age, y	80.3±8.4	80.5±7.8	0.002	0.99
Male sex	19 (43.2)	26 (39.4)	0.043	0.83
BMI, kg/m^2	25.5±4.0	25.6±3.8	–0.096	0.99
BSA, m^2	1.82±0.20	1.80±0.18	0.109	0.61
Logistic EuroSCORE, %	15.8 [9.9–23.4]	16.5 [11.4–22.2]	–0.070	0.90
NYHA class III/IV	22 (50.0)	42 (63.6)	–0.163	0.28
Recent cardiac decompensation (within 3 mo)	10 (22.7)	15 (22.7)	0.000	1.00
Diabetes mellitus	14 (31.8)	23 (34.8)	0.000	1.00
Hypertension	26 (59.1)	39 (59.1)	0.000	1.00
COPD	10 (22.7)	14 (21.2)	0.038	0.80
Glomerular filtration rate, mL/min	63.6±22.3	64.5±22.5	–0.039	0.86
Renal impairment (GFR <60 mL/min)	23 (52.3)	30 (45.5)	0.163	0.29
Dialysis	0	0		
Cerebrovascular disease	10 (22.7)	15(22.7)	0.000	1.00
Peripheral artery disease	14 (31.8)	18 (27.2)	0.045	0.76
Coronary artery disease	23 (52.3)	33 (50.0)	0.048	0.75
Prior myocardial infarction	5 (11.4)	13 (19.7)	–0.168	0.26
Prior PCI	16 (36.4)	23 (34.8)	0.034	0.82
Prior CABG	6 (13.6)	8 (12.1)	0.000	1.00
Prior BAV	0	3 (4.5)	–0.197	0.49
Atrial fibrillation	11 (25.0)	19 (28.8)	0.038	0.80
First degree atrioventricular block*	7/41 (17.1)	6/57 (10.5)	0.136	0.38
Right bundle branch block*	2/41 (4.9)	4/57 (7.0)	–0.122	1.00
Left bundle branch block*	3/41 (7.3)	5/57 (8.8)	–0.039	0.80
Prior pacemaker implantation	3 (6.8)	9 (13.6)	–0.160	0.48
Pulmonary hypertension	4 (9.1)	4 (6.1)	–0.074	0.68
Porcelain aorta	4 (9.1)	10 (15.2)	–0.094	0.74
Echocardiography data				
LVEF, %	50.0±11.4	49.6±13.0	0.023	0.63
Moderate to severe left ventricular dysfunction†	10 (22.7)	16 (24.2)	–0.066	0.67
Peak aortic gradient, mm Hg	65.4±21.3	68.6±21.4	–0.174	0.42
Mean aortic gradient, mm Hg	38.9±15.0	40.7±15.0	–0.191	0.50
Indexed aortic valve area, cm^2/m^2	0.41±0.11	0.38±0.09	0.434	0.081
Systolic pressure of pulmonary artery, mm Hg‡	38.8±14.3	41.6±11.2	–0.149	0.57
Moderate or severe aortic regurgitation	5 (11.4)	9 (13.6)	–0.041	0.78
Moderate or severe mitral regurgitation	11 (25.0)	14 (21.2)	0.066	0.80
Multislice computed tomography data				
Aortic annulus minor diameter, mm	22.0±2.6	21.0±2.0	0.480	0.038
Aortic annulus major diameter, mm	27.7±2.8	26.6±2.2	0.560	0.011
Aortic annulus mean diameter, mm	24.8±2.1	23.8±2.0	0.459	0.045
Eccentricity index§	0.21 [0.16–0.23]	0.21 [0.19–0.24]	–0.212	0.36
Aortic annulus area, mm^2	486±76	445±71	0.519	0.023
Aortic annulus area derived diameter, mm	24.8±2.0	23.7±1.9	0.520	0.023

BAV indicates balloon aortic valvuloplasty; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and PCI, percutaneous coronary intervention.

*As a percentage of patients without prior pacemaker implantation.

†Defined as left ventricular ejection fraction ≤40%.

‡Presented for 100 patients (n=46 for SXT and n=30 for S3).

§Calculated as 1-(minor diameter/major diameter), where an index of 1.00 indicates a perfect circular shape.

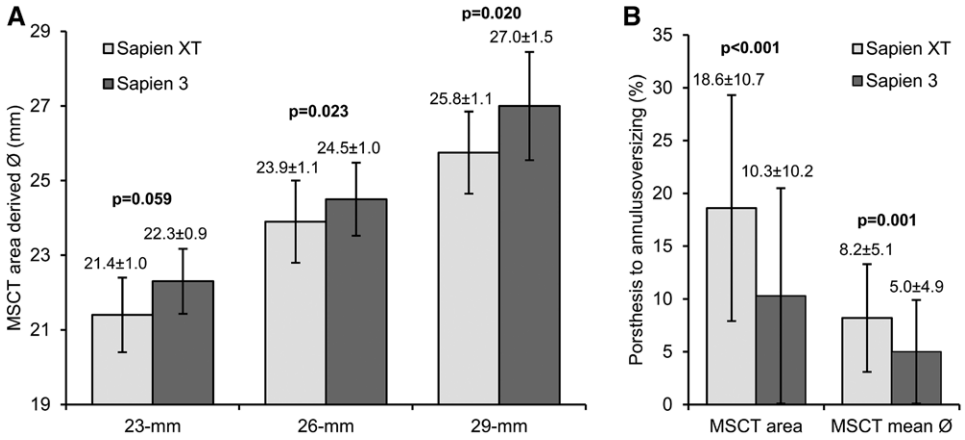


Figure 2. Sizing data for Sapien 3 and Sapien XT prostheses. Area-derived aortic annulus diameter of the treated valves presented per prosthesis type and size (**A**). Percentage oversizing with respect to the aortic annulus area and the mean diameter for both prosthesis types (**B**). Data are presented as mean±SD. MSCT indicates multi-slice computed tomography.

versus 15.1%, *P*=0.080) in the S3-THV group (Figure 3A). On final angiography, a significant difference in AR grade was observed, with lower Grade 1+ (13.6% versus 34.8%, *P*=0.002) and Grade 2+ AR (0% versus 6.1%, *P*=0.148) for the S3-THV (Figure 3B). No cases of grade 3 AR were recorded in any group. One case of coronary obstruction occurred in the S3-THV group (not because of the device, but because of compression of a diseased ostium of the right coronary artery by the deployment balloon), successfully treated with immediate PCI with stenting. Emergency surgery was required in one SXT-THV patient because of cardiac tamponade not resolved by subxiphoid pericardiocentesis.

All patients in the S3-THV and 65 (98.5%) in the SXT-THV group underwent predischarge TTE. Peak and mean aortic transvalvular pressure gradients decreased significantly in both groups (both *P*<0.001), with no cases of residual stenosis.

Table 2. Procedural Features

	Sapien 3 (n=44)	Sapien XT (n=66)	Weighted *p*
Procedural access*			0.95
Transfemoral	34 (77.3)	52 (78.8)	
Transapical/transaortic	10 (22.7)	14 (21.2)	
General anesthesia	12 (27.3)	15 (22.7)	0.76
Use of cardiopulmonary bypass	0	0	
Predilatation	43 (97.3)	66 (100)	1.00
Implanted prosthesis size			0.82
23-mm	8 (18.2)	18 (27.3)	
26-mm	24 (54.5)	32 (48.5)	
29-mm	12 (27.3)	16 (24.2)	
Deployment balloon underfilling (by 1 cc)	0	3 (4.5)	0.49
Stent frame height extending below annulus plane, %	20.0±11.9	31.0±11.7	<0.001
Prosthesis implantation depth, mm	4.0±2.2	5.3±2.1	<0.001
Skewness of prosthesis final position, %†	3.5±3.2	5.3±3.8	0.034
Post-dilatation	7 (15.9)	8 (12.1)	0.55
Balloon area to prosthesis nominal area ratio	0.92 [0.92–0.92]	0.92 [0.92–1.00]	0.43
Second valve implantation	0	0	
Valve malpositioning	0	0	
Coronary artery obstruction	1 (2.3)	0	1.00
Conversion to cardiac surgery	0	1 (1.5)	1.00
Intraprocedural death	0	0	
Fluoroscopy time, min	12.8 [10.0–14.6]	15.1 [12.0–18.3]	0.045
Contrast volume, mL	130 [120–150]	150 [125–180]	0.024
Acute device success	44 (100)	62 (93.9)	0.32

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