

Early Safety and Efficacy of Sapien 3 20 mm Transcatheter Heart Valve Implantation in Small Japanese Body Size

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) is effective in treating severe aortic stenosis in inoperable or high-risk surgical patients, however, the little is known about outcomes after Sapien 3 20 mm transcatheter heart valve (THV) implantation. The purpose of this study was to investigate the short term outcomes of Sapien 3 20 mm THV implantation in Japanese people with a small body size.

Methods: We retrospectively collected the hospital records of consecutive patients who underwent TAVI using the Sapien 3 20 mm THV between October 2016 and March 2017. Clinical and echocardiographic data from before and one week after TAVI were collected.

Results: Six Japanese patients (all female, mean age 89 ± 5 years, body surface area [BSA] $1.29 \pm 0.16\text{m}^2$) received a Sapien 3 20 mm THV. All the procedures were feasible and successful, and the 30-day mortality rate was 0%. The functional class and the echocardiographic findings significantly improved (aortic valve area, $0.5 \pm 0.1\text{cm}^2$ to $0.8 \pm 0.1\text{cm}^2$; mean pressure gradient, $55 \pm 15\text{mmHg}$ to $19 \pm 7\text{mmHg}$; $P = .043$, respectively). However, the values of the indexed effective orifice area in all patients after Sapien 3 20 mm THV implantation were less than $0.85\text{cm}^2/\text{m}^2$, suggesting prosthesis-patient mismatch (PPM).

Conclusions: The implantation of a Sapien 3 20 mm THV was safe and effective in high surgical risk elderly Japanese patients with a small body size. PPM after Sapien 3 20mm THV may be prevalent among Asians with small body sizes. Careful clinical follow-up will be necessary after Sapien 3 20 mm THV implantation.

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is an established treatment for inoperable or high-risk surgical patients with severe symptomatic aortic stenosis (AS). TAVI has been reported to improve hemodynamic aortic valve function and

survival, despite complications including paravalvular leak (PVL), vascular complication, and conduction disturbance [Meguro 2013; Smith 2011; Leon 2010]. Recently, the balloon-expandable Sapien 3 transcatheter heart valve (Sapien 3 THV, Edwards Lifescience, Irvine, CA), which was reported to reduce PVL and vascular complications, was approved and widely used to treat severe symptomatic AS [Webb 2014]. TAVI with Sapien 3 THV in intermediate-risk patients showed an association with lower rates of mortality, strokes, and regurgitation at one year [Thourani 2016].

Asian patients have a smaller body size, aortic root size, and vascular access diameter than European patients, which may be a potential risk for aortic root rupture, vascular complications, and residual THV pressure gradients [Watanabe 2015; Watanabe 2014]. The prevalence of Sapien 3 20 mm THV implantation is limited in European patients [Sawaya 2016]. Although a larger body size is reported to be associated with the prosthesis-patient mismatch (PPM), little is known about the association between PPM and a small body size [Pibarot 2014]. The purpose of this study was to describe the short term outcomes of Sapien 3 20 mm THV implantation and PPM in small Asian body size.

MATERIALS AND METHODS

Study Population

We retrospectively enrolled consecutive patients who underwent TAVI using the Sapien 3 20 mm THV at our institution between October 2016 and March 2017. Patients with severe symptomatic AS received TAVI if they were at high surgical risk, which was defined by a Society of Thoracic Surgery (STS) risk score above 8%. High surgical risk was also defined by being considered ineligible for open-chest cardiac surgery on the clinical consensus of a multidisciplinary heart team composed of cardiac surgeons, interventional cardiologists, imaging specialists, and anesthesiologists. Our institutional review board approved the study, and written informed consent was obtained.

Multi Detector Computed Tomography: Measurement and Procedure

Valve anatomy and annulus size were evaluated with multi-detector computed tomography (MDCT). The vascular access site was also assessed using MDCT, as previously described [Tops 2008]. The THV size and access site were

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Table 1. Patient Characteristics and MDCT Measurements

	Age, year	BMI, kg/m ²	BSA, m ²	STS score, %	Logistic EuroSCORE, %	NYHA class	Annulus area, mm ²	Coronary height, mm Left	Coronary height, mm Right	Minimum access diameter, mm	Area oversizing, %
1	92	15.4	0.98	8.6	16.1	4	319.0	10.0	12.4	5.3	2.7
2	92	21.5	1.34	10.7	27.0	4	305.0	13.3	11.4	6.0	7.0
3	91	22.5	1.38	5.9	10.7	3	302.9	11.7	13.1	5.8	7.7
4	85	22.0	1.32	11.4	29.8	3	320.0	13.8	15.7	5.5	2.4
5	91	23.5	1.40	8.2	38.8	3	298.4	11.5	15.5	5.1	9.0
6	80	20.4	1.30	8.2	22.2	4	321.5	9.6	13.0	5.5	2.0
Mean	89	20.9	1.29	8.8	24.1	4	311.1	11.7	13.5	5.5	5.1
SD	5	2.9	0.16	2.0	10.0	1	10.2	1.7	1.7	0.3	3.1

MDCT indicates multi-detector computed tomography; BMI, body mass index; BSA, Body surface area; STS, Society of Thoracic Surgery; NYHA, New York heart association; SD, standard deviation.

selected according to the MDCT measurement. The technical aspects of the TAVI procedure using the Sapien 3 system have been described in detail elsewhere [Binder 2012].

Data Collection and Study Endpoints

Clinical and echocardiographic data at baseline and during the TAVI procedure, and echocardiographic data one week after TAVI, were collected from the hospital records retrospectively. The device success, vascular complications, bleeding complications, PPM, and all-cause mortality rate at 30 days were assessed according to the Valve Academic Research Consortium 2 (VARC2) criteria [Kappetein 2012]. The severity of the PPM was also graded from the echocardiogram using the indexed effective orifice area (EOA), with absence defined as $>0.85 \text{ cm}^2/\text{m}^2$, moderate defined as ≥ 0.65 to $\leq 0.85 \text{ cm}^2/\text{m}^2$, and severe defined as $<0.65 \text{ cm}^2/\text{m}^2$.

Statistical Analysis

Data were described as mean with standard deviation (SD). To compare the echocardiographic findings before and after the TAVI, we used the Wilcoxon signed-rank test. All statistical analyses were done using SPSS Statistics version 19 (SPSS, Chicago, IL).

RESULTS

Between October 2016 and March 2017, six patients received Sapien 3 20 mm THV. In the same period, ten patients received a differently sized Sapien 3 THV or self-expanding THV in our institution. Those patients who underwent Sapien 3 20 mm THV implantation were all female and were found to have a small BSA and small body size in the assessment of the MDCT (Table 1).

Device success was achieved in all patients, and no patient died within 30 days (Table 2). Four patients received two units of red blood cell transfusion, indicating that 66% of patients had a major bleeding complication. All procedures for the

insertion and removal of 14 Fr e-sheaths from the femoral artery were performed by surgical cut down. None of the patients had vascular complications, though the minimum access diameter was small (Table 1). Coronary protection was required in two cases for the left coronary artery because of low coronary height or a bulky, calcified left coronary cusp leaflet, however, coronary occlusion did not occur. All patients were discharged from our hospital 18 ± 9 (range 9 - 33) days after the procedure without any symptom related to AS.

The echocardiographic findings of AS significantly improved after TAVI in all patients, and there were no moderate or higher amounts of aortic regurgitation (Table 2). However, the values of EOA in all patients were less than 1.0 cm^2 , and indexed EOA values were less than $0.85 \text{ cm}^2/\text{m}^2$, indicating that all patients had prosthetic aortic valve stenosis and PPM. Furthermore, four patients (66%) had severe PPM after TAVI.

DISCUSSION

We described our six initial cases of Sapien 3 20 mm THV in Japanese patients who had a small body size ($\text{BSA } 1.29 \pm 0.16 \text{ m}^2$), and a small annulus and vascular access diameter. All procedures were feasible and successful, and the 30-day mortality rate was 0%. The functional class and the echocardiographic findings improved, but PPM was seen in all patients.

Six out of sixteen patients (38%) with severe symptomatic AS were treated with the Sapien 3 20 mm THV in our institution during the study period. This was much higher than in previous studies in North America or European countries, where the Sapien 3 20 mm THV procedures were one of the effective treatment options in patients with failing small, surgical aortic bioprostheses [Puri 2017; Kodali 2016; Loyalka 2016; Sawaya 2016]. One reason for this is that Asian populations have a relatively smaller body size and a smaller aortic annulus size than American or European populations [Watanabe 2015]. Furthermore, since those cases were from

Table 2. Clinical Endpoints and Echocardiographic Findings

	Clinical endpoints			Before TAVI					After TAVI					
	Device success	30-day mortality	Hospital stay after TAVI, days	Peak velocity, m/s	Peak PG, mmHg	Mean PG, mmHg	AVA, cm ²	AVAI, cm ² /m ²	Peak velocity, m/s	Peak PG, mmHg	Mean PG, mmHg	EOA, cm ²	EOAi, cm ² /m ²	PVL grade
1	Yes	No	14	4.7	88	45	0.5	0.51	2.6	27	15	0.8	0.82	mild
2	Yes	No	22	5.0	100	71	0.6	0.45	2.3	22	11	0.8	0.60	no
3	Yes	No	33	4.0	65	42	0.6	0.43	3.3	43	24	0.9	0.65	mild
4	Yes	No	13	4.1	67	41	0.5	0.38	3.0	35	21	0.7	0.53	mild
5	Yes	No	9	4.7	87	59	0.5	0.36	2.7	30	15	0.9	0.64	no
6	Yes	No	18	5.3	111	73	0.4	0.31	3.7	55	30	0.8	0.61	mild
Mean			18	4.6	86	55	0.5	0.41	2.9	35	19	0.8	0.64	
SD			9	0.5	18	15	0.1	0.07	0.5	12	7	0.1	0.10	
P value									.043	.043	.043	.043	.043	

TAVI indicates Transcatheter aortic valve implantation; AVA, aortic valve area; AVAI, indexed aortic valve area; EOA, effective orifice area; EOAi, indexed effective orifice area; PG, pressure gradient; PVL, paravalvular leak; SD, standard deviation.

P value: Values were compared to those before TAVI with Wilcoxon signed-rank test.

our initial experience of TAVI, including procedures in the proctoring phase, they were restricted to inoperable or highly prohibited risk patients for surgical aortic valve replacement that were different from those in recent reports [Reardon 2017; Kodali 2016]. The six patients in this paper were all female, and the mean age (89 ± 5) was still higher than those in the early reports in American or European countries, though we used the same classical indication for TAVI [Leon 2010]. Thus, this may also lead to the high prevalence of small body sizes suitable for a Sapien 3 20 mm THV.

In this cohort, all six patients had PPM and four (66%) had severe PPM. Half of the patients had mild valvular stenosis after TAVI, which was defined as a residual mean pressure gradient ≥ 20 mmHg [Kappetein 2012]. Those rates of PPM and valvular stenosis after TAVI were higher than those in previous reports in North America or European countries [Pibarot 2014]. In our cohort, a smaller valve size, suitable for a Sapien 3 20 mm THV, may be the risk factor for the occurrence of PPM after TAVI. This may be the case even though body size was small ($BSA 1.29 \pm 0.16$ m²), contrary to previous reports, which suggested that a larger BSA and body mass index (BMI) were associated with the PPM [Pibarot 2014]. The results from previous studies are not applicable to our cohorts, because the BSA and BMI are quite different, and previous studies didn't include such small body sizes. The external sealing cuff is characteristic to Sapien 3 THV for effective sealing, and prevention of para-valvular regurgitation. This external sealing cuff may interfere with valve function and may also add to the increased rate of PPM [Theron 2017].

The consequences and clinical outcomes of having a small body size and PPM after TAVI is not well established yet. Some reports suggest that patients with PPM had a smaller

reduction of left ventricular mass and smaller improvement of NYHA functional class when compared with patients without PPM [Ewe 2011]. However, in meta-analyses, there were no statistically significant differences in late mortality between patients with and without PPM [Takagi 2015]. On the other hand, the results of TAVI in patients with failed bioprosthetic surgical valves were recently reported, and it was shown that the patients with small prosthetic surgical valves (≤ 21 mm in label size) had lower survival rates compared to patients with larger prosthetic surgical valves [Dvir 2014]. Thus, a smaller body size that is suitable for a Sapien 3 20 mm THV, such as that which is seen in Asian anatomy, might also contribute to the worsened prognosis after TAVI.

In our study, all patients (NYHA III/IV) could be discharged from our hospital directly to their own house. TAVI seemed to be a safe and effective treatment for the patients in this study, which were aged, of high surgical risk, and came to the hospital over a short period of time. Caution should be exercised for the extension of TAVI indication to low risk patients in the case of an anatomy suitable for a Sapien 3 THV for long term efficacy, though PPM after SAVR was reported to be more frequent than TAVI [Pibarot 2014].

STUDY LIMITATIONS

Our report was composed of only six retrospectively collected Japanese patients who were treated with a Sapien 3 THV. The number of patients was small, therefore it is difficult to generalize our data to all Sapien 3 THVs used in a small Asian body size. Despite this, we believe that our data will contribute to starting long-term observational studies after Sapien 3 20 mm THV implantation in Asians with a

small body size. Further investigation, such as multicenter registry data in Asian countries, is necessary to elucidate the long term efficacy and safety of the Sapien 3 THV 20 mm device in a small body size and the clinical consequences of a high PPM rate.

CONCLUSION

The implantation of the Sapien 3 20 mm THV was safe and effective in aged, high surgical risk Japanese patients with a small body size. The PPM after Sapien 3 20 mm THV implantation may be prevalent in small Asian body sizes. Larger case series will be necessary to generalize our findings and clarify the consequences of PPM.

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