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ORIGINAL ARTICLE
Valvular Heart Disease

Risk of Coronary Occlusion Due to Sinus Sequestration by Redo Transcatheter Aortic Valve Implantation in Japanese Patients With SAPIEN 3

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Background: Transcatheter aortic valve (TAV)-in-TAV is an attractive treatment for degenerated TAV. The risk of coronary artery occlusion due to sequestration of the sinus of Valsalva (SOV) in TAV-in-TAV has been reported, but the risk in Japanese patients is unknown. This study aimed to investigate the proportion of Japanese patients who are expected to experience difficulty with the second TAV implantation (TAVI) and evaluate the possibility of reducing the risk of coronary artery occlusion.

Methods and Results: Patients (n=308) with an implanted SAPIEN 3 were divided into 2 groups: a high-risk group, which included patients with a TAV–sinotubular junction (STJ) distance <2 mm and a risk plane above the STJ (n=121); and a low-risk group, which included all other patients (n=187). The preoperative SOV diameter, mean STJ diameter, and STJ height were significantly larger in the low-risk group (P<0.05). The cut-off value for predicting the risk of SOV sequestration due to TAV-in-TAV in the difference between the mean STJ diameter and area-derived annulus diameter was 3.0 mm (sensitivity 70%; specificity 68%; area under the curve 0.74).

Conclusions: Japanese patients may have a higher risk for sinus sequestration caused by TAV-in-TAV. The risk of sinus sequestration should be assessed before the first TAVI in young patients who are likely to require TAV-in-TAV, and whether TAVI is the best aortic valve therapy must be carefully decided.

Key Words: Aortic stenosis; TAV-in-TAV; Transcatheter aortic valve; Valve-in-valve

In recent years, the introduction of minimally invasive transcatheter aortic valve implantation (TAVI) has expanded the indications for the treatment of aortic valve stenosis. Traditionally, TAVI is initiated for older patients who are not eligible for open cardiac surgery.[1–3] However, improved TAVI outcomes have expanded the indication to low-risk patients, and TAVI in younger patients is expected to increase in the future.[4,5] Low-risk younger patient populations with long life expectancy who have undergone TAVI may have a degenerated transcatheter aortic valve (TAV).[6] A degenerated TAV may require reoperation, for which TAV-in-TAV may be an attractive treatment option.[7–9] Conversely, there is a risk of coronary artery occlusion caused by sinus sequestration with TAV-in-TAV (**Figure 1**), as reported in previous studies.[10–12] TAV-in-TAV is a risk factor for coronary artery occlusion caused by sinus sequestration, because the leaflet of the first TAV is completely pushed open by the second TAV, sealing the stent frame to the commissure level.[10,11] The combination of a low sinotubular junction (STJ) and a high TAV commissure increases the risk of coronary artery occlusion. The height of the STJ is reportedly lower and its diameter is smaller in Japanese than Western populations,[10] and whether the risk of coronary artery occlusion with the second TAVI is similar in Japanese patients is unknown. Therefore, the aim of this study was to evaluate the proportion of Japanese patients who are expected to have difficulty with TAV-in-TAV and investigate the possibility of reducing the risk of coronary artery occlusion caused by sinus sequestration using a previously TAV-implanted population.

Methods

Study Population and Design

The present single-center retrospective observational study enrolled consecutive patients with symptomatic severe aortic stenosis who had undergone transfemoral TAVI between 2013 and 2021 at Iwate Medical University Hospital (n=707). Patients with SAPIEN 3 (Edwards Lifesciences,

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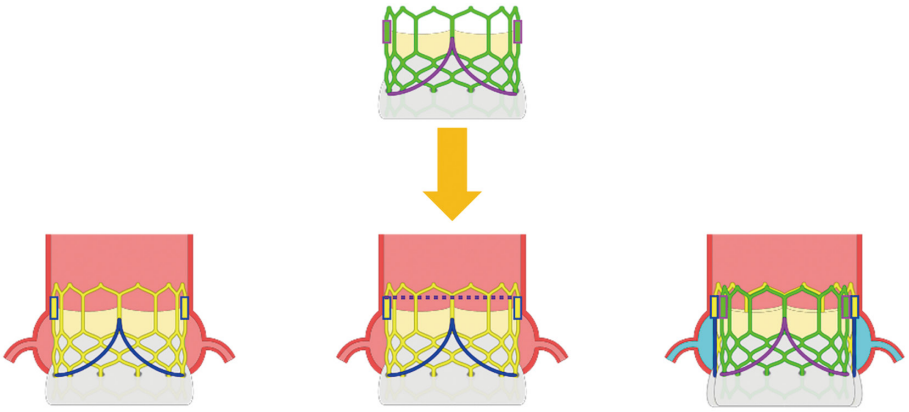

Figure 1. Mechanism of sinus of Valsalva (SOV) sequestration in transcatheter aortic valve (TAV)-in-TAV. By implanting a second TAV inside the first TAV, the first TAV leaflet is lifted up to form a cylinder. When the lifted TAV leaflet extends to the sinotubular junction, the SOV is completely sequestrated and blood flow to the coronary artery is interrupted.

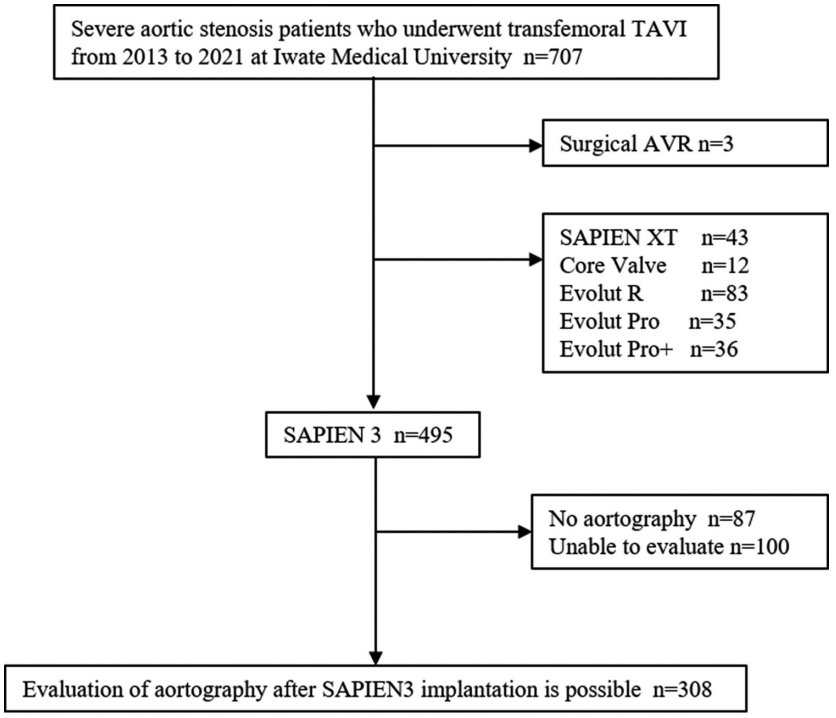

Figure 2. Patient recruitment flowchart. AVR, aortic valve replacement; TAVI, transcatheter aortic valve implantation.

Irvine, CA, USA) valve implantation (n=495) were included in the retrospective analysis. A total of 209 patients who had other valves implanted (SAPIEN XT, n=43; Core Valve, n=12; Evolut R, n=83; Evolut Pro, n=35; and Evolut Pro+, n=36), 3 patients who were converted to cardiac surgery, 87 patients who did not undergo aortography after TAVI due to chronic kidney disease, and 100 patients who underwent aortography but for whom a quantitative evaluation was difficult were excluded (**Figure 2**). No patients underwent emergency or urgent TAVI during the study period. The eligibility for TAVI was established based on the consensus of a multidisciplinary heart team.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Human Research Committee of Iwate Medical University (MH2022-146). Each patient provided written informed consent for data collection before TAVI.

Pre-TAVI Echocardiography and Computed Tomography (CT)

Echocardiographic parameters were measured preoperatively according to the American Society of Echocardiography guidelines.[13] The height of the annulus, the sinus of

Valsalva (SOV), STJ, and coronary arteries was analyzed on preoperative CT according to current guidelines.[14] STJ height was defined as the distance from the annulus plane to the lowest point of the STJ. The height of the coronary arteries was measured to the inferior border of each coronary artery ostium in the stretched multiplanar image.

Post-TAVI Aortography Analysis and Definitions

Immediately after SAPIEN 3 valve implantation, aortography was performed by setting the X-ray imaging angle at which the upper and lower edges of the SAPIEN 3 were aligned. As shown in **Figure 3**, valve height was measured from the top to the bottom of the stent frame edges on the left (*a*) and right (*b*) sides and from the lower sinus border to the bottom of the stent frame on the left (*c*) and right (*d*) sides, respectively. The mean implantation depth was calculated as a percentage of the total stent frame height as follows: $([c/a]+[d/b])/2\times100$ (**Figure 3**).

The risk plane (RP) was defined as the level at which the coronary catheter could not pass through after the TAV was implanted. The RP was the upper edge line of the lifted TAV, coinciding with the upper commissure tab attached to the SAPIEN 3 frame. The RP was drawn on the top edge of the commissure tab parallel to the line drawn from the left edge to the right edge at the top edge of the SAPIEN 3 frame (S3 topline; **Figure 4**). To evaluate the relationship between the TAV commissure and the height of the STJ, the height from the bottom edge of the STJ to the commissure tab line on aortography was measured. The distance from the left stent frame to the left STJ at the S3 topline level was defined as the distance between the TAV and the STJ (**Figure 4A**).

In the present study, it was assumed that after TAV-in-TAV the leaflets of the first TAV were completely pushed apart by the second TAV, sealing the stent frame circumferentially to the RP. Consequently, the TAV frame becomes a tubular closed structure, causing sinus sequestration and leading to coronary occlusion. Therefore, assuming this worst-case scenario, TAV-in-TAV is associated with a risk of coronary artery occlusion caused by sinus sequestration in the following cases:[10,11] (1) The RP is above the STJ; and (2) the distance between the TAV and STJ is <2.0 mm (6-Fr equivalent, the minimum distance a coronary catheter can enter the coronary ostium) at the left coronary sinus (**Figure 5**). Patients fulfilling both these conditions were assigned to the sinus sequestration high-risk group, whereas all other patients were assigned to the sinus sequestration low-risk group.

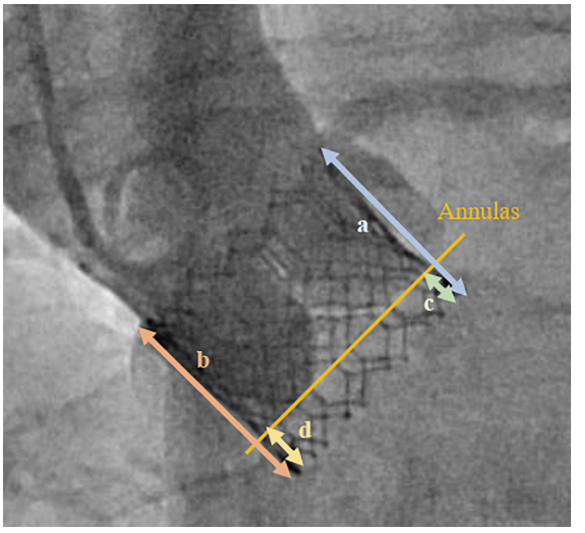

Figure 3. Implantation depth ratio. Valve height was measured from the top to the bottom of the stent frame edges on the left (*a*) and right (*b*) sides and from the lower sinus border to the bottom of the stent frame on the left (*c*) and right (*d*) sides, respectively. The mean implantation depth was calculated as a percentage of the total stent frame height as follows: $([c/a]+[d/b])/2\times100$.

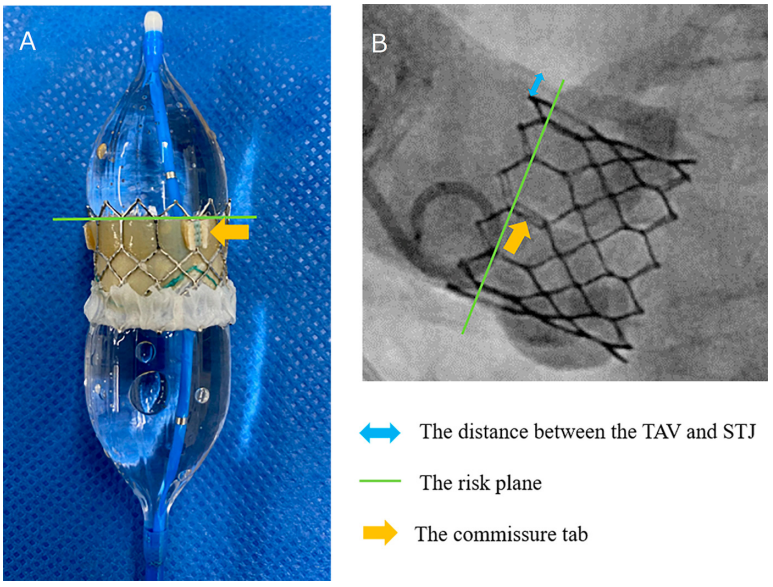

Figure 4. Measurement sites on aortography. (**A**) The risk plane (RP) was defined as the level at which the coronary catheter could not pass through after the transcatheter aortic valve (TAV) was implanted. The RP was the upper edge line of the lifted TAV, coinciding with the upper commissure tab attached to the SAPIEN 3 (S3) frame. The distance from the left stent frame to the left sinotubular junction (STJ) at the S3 topline level was defined as the distance between the TAV and STJ. (**B**) Relationship between the lifted TAV and the RP observed in vitro.

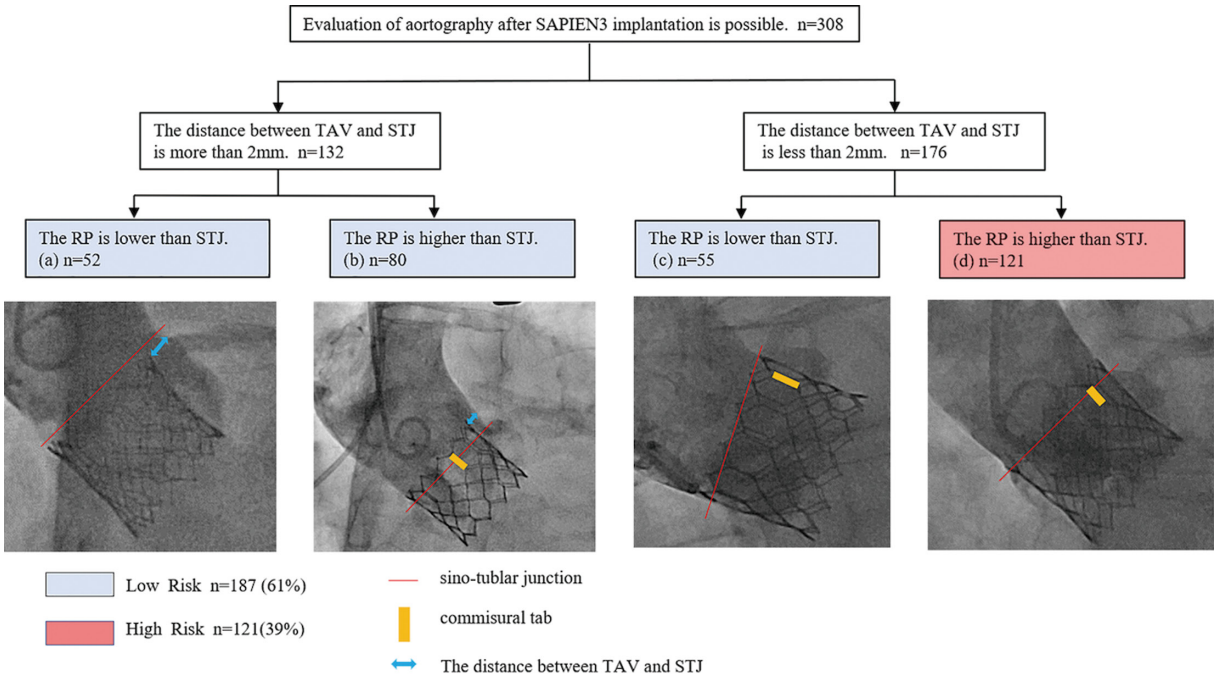

Figure 5. Flowchart showing categorization of patients into low- and high-risk categories based on aortography. Cases (a)–(c) were defined as the low-risk group for sinus sequestration with a high risk of preserving blood flow to the sinus of Valsalva even after transcatheter aortic valve (TAV)-in-TAV. Case (d) was defined as the high-risk group for sinus sequestration because the gap between the sinotubular junction (STJ) and the stent frame may be lost and the blood flow to sinus of Valsalva could be disrupted. RP, risk plane.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as the mean±SD or median and interquartile range, as appropriate. Qualitative variables are expressed as numbers and percentages. Normality was checked using the Shapiro-Wilk test. Differences between mean values were evaluated using paired and unpaired (for independent group comparisons) and Student's t-tests for normally distributed data. The Mann-Whitney or Wilcoxon signed-rank test was used to evaluate non-parametric data. The Chi-squared test was used for categorical variables, and Fisher's exact test was used for categorical variables with low frequencies (expected cell count <5). Pearson correlation coefficients were used to investigate the relationship between cardiac reverse remodeling parameters and baseline parameters. Receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated to assess the discriminative power of the STJ height, mean STJ diameter, or difference between the mean STJ diameter and the area-derived annulus diameter for CT-identified risk of coronary obstruction. Two-tailed $P<0.05$ was considered statistically significant.

Results

Relationship Between TAV and STJ

We identified 308 cases of TAVI performed at Iwate Medical University in which SAPIEN 3 was implanted and postimplantation aortoangiography evaluated STJ height and width, coronary artery entry height, and TAVI depth in the left coronary sinus. Patients were divided into 2 groups according to the distance between the TAV and STJ: ≥2 mm (n=132) and <2 mm (n=176). Among those with a distance between the TAV and STJ ≥2 mm, 52 had the RP lower than the STJ ("a"), and 80 had the RP higher than the STJ ("b"). Among those with a distance between the TAV and STJ <2 mm, 55 had the RP lower than the STJ ("c"), and 121 had the RP higher than the STJ ("d"). Cases (a)–(c) were defined as the low-risk group for sinus sequestration with a high risk of preserving blood flow to the SOV even after TAV-in-TAV. Case (d) was defined as the high-risk group for sinus sequestration because the gap between the STJ and the stent frame may be lost, and the blood flow to the SOV could be disrupted. The low- and high-risk groups consisted of 187 (61%) and 121 (39%) patients, respectively (**Figure 5**).

Baseline Characteristics

The baseline characteristics of the 2 groups are presented in **Table 1**. There were no significant differences in clinical characteristics between the 2 groups. The STJ diameter on preoperative echocardiography was significantly smaller in the high-risk group. On CT, the high-risk group had a significantly larger area-derived annulus diameter, larger SOV (left/right/non-coronary cusp), lower STJ height, smaller STJ (maximum/minimum/mean) diameter, and a smaller difference in the STJ and annulus diameter than the low-risk group. The characteristics of the first SAPIEN

Table 1. Baseline Characteristics Before the First TAVI According to Risk of the Valsalva Sinus Sequestration

	Low risk (n=187)	High risk (n=121)	P value
Clinical characteristics			
Age (years)	82.8±5.4	82.0±5.9	0.278
Male sex	77 (41)	38 (31)	0.083
Height (cm)	151.2±9.4	150.4±9.1	0.461
Weight (kg)	52.9±10.0	53.0±11.7	0.899
BSA (m^2)	1.5±0.2	1.5±0.2	0.810
STS score (%)	5.7±3.2	5.3±3.0	0.307
Clinical frailty scale	3.8±1.0	3.8±0.9	0.810
Hypertension	142 (76)	90 (74)	0.757
Dyslipidemia	82 (44)	54 (45)	0.893
Diabetes	57 (31)	38 (31)	0.864
Atrial fibrillation	45 (24)	21 (17)	0.161
Echocardiography			
LVEF (%)	63.7±9.7	63.3±9.5	0.685
Aortic valve area (cm^2)	0.7±0.2	0.7±0.2	0.480
Peak aortic valve velocity (m/s)	4.7±0.7	4.8±0.8	0.879
Mean pressure gradient (mmHg)	52.6±16.6	53.6±19.5	0.621
Aortic annular diameter (mm)	21.8±4.3	21.7±1.5	0.768
Sinus of Valsalva (mm)	24.4±3.1	23.4±2.5	0.002
LVDd (mm)	42.1±6.6	42.7±5.1	0.352
LVDs (mm)	26.7±6.8	27.5±6.2	0.299
IVST (mm)	14.3±2.2	14.0±2.1	0.172
PWT (mm)	13.3±2.0	13.2±1.7	0.777
Pre-TAVI CT			
Annular area (mm^2)	428.3±73.2	444.4±69.5	0.053
Mean annular diameter (mm)	21.2±7.1	22.8±5.6	0.031
STJ height (mm)	17.8±2.4	17.2±2.1	0.020
STJ diameter (mm)			
Maximum	27.8±2.7	26.5±2.4	<0.001
Minimum	26.8±2.6	25.4±2.3	<0.001
Mean	27.3±2.6	26.0±2.3	<0.001
STJ diameter–annular diameter (mm)	4.1±2.1	2.2±1.8	<0.001
Left coronary height (mm)	12.8±2.4	12.5±2.2	0.226
Left coronary sinus of Valsalva (mm)	31.4±3.0	30.2±2.5	<0.001
Right coronary sinus of Valsalva (mm)	30.5±3.2	29.4±2.5	0.001
Non-coronary sinus of Valsalva (mm)	32.1±3.1	31.0±2.8	0.001

Unless indicated otherwise, data are given as the mean±SD or n (%). BSA, body surface area; CT, computed tomography; IVST, interventricular septal thickness; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; PWT, posterior wall thickness; STJ, sinotubular junction; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.

3 valve implanted are presented in **Table 2**. The size of the implanted TAV was significantly different between the 2 groups. There were no significant differences in the size of the implanted TAV or the mean implantation depth ratio between the 2 groups.

ROC Curve Analysis for the Prediction of Sinus Sequestration at the Left Coronary Cusp Identified by CT

In SAPIEN 3, the cut-off values for predicting the risk of sinus sequestration were 17.6 mm for STJ height (sensitivity 52%; specificity 63%; AUC 0.58), 27.9 mm for mean STJ diameter (sensitivity 44%; specificity 82%; AUC 0.66), and 3.0 mm for the difference between the mean STJ diameter and the area-derived aortic valve diameter identified by CT (sensitivity 70%; specificity 68%; AUC 0.74; **Figure 6**).

Discussion

This study evaluated the risk of left coronary artery occlusion caused by sinus sequestration in TAV-in-TAV by analyzing post-TAVI aortography. The main findings of the study are as follows: (1) by using the valve to aorta and the height from the RP to the STJ to evaluate the risk of sinus sequestration at the second TAVI, 39% of patients with SAPIEN 3 were classified as being at high risk of sinus sequestration; and (2) a difference of >3 mm between the mean STJ and the area-derived annulus size measured by CT was suggested to be useful for predicting the risk of sinus sequestration at the second TAVI.

The indications for TAVI are gradually expanding, and TAVI for younger patients is increasing.[4,5] Biological valves

Table 2. Characteristics of the First SAPIEN 3 Valve Implanted

	Low risk (n=187)	High risk (n=121)	P value
Valve size (mm)			
20	13 (7)	1 (1)	0.044
23	89 (48)	55 (46)	
26	73 (40)	52 (43)	
29	12 (6)	13 (11)	
Implantation depth (mm)	3.4±1.2	3.5±1.2	0.267
Implantation depth ratio (%)			
91–100	7 (4)	1 (1)	0.576
81–90	53 (28)	38 (31)	
71–80	107 (57)	70 (58)	
61–70	10 (5)	5 (4)	

Unless indicated otherwise, data are given as the mean±SD or n (%).

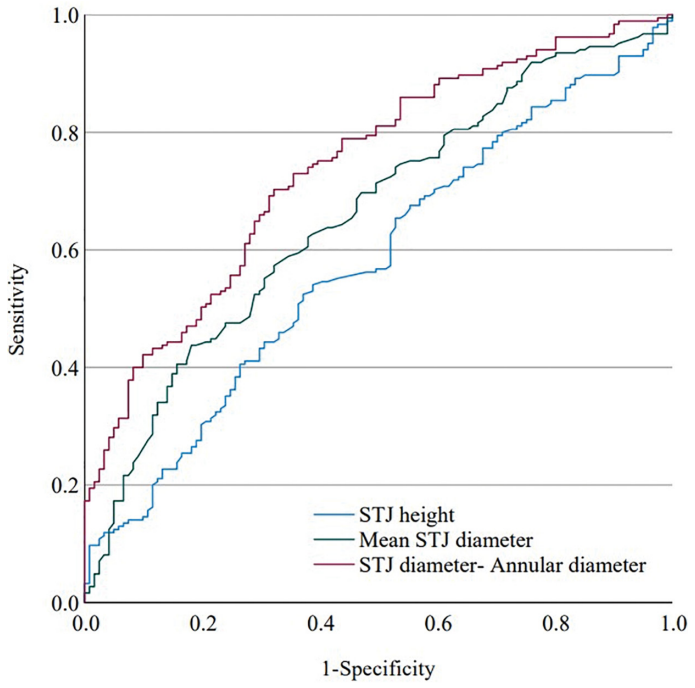

Figure 6. Receiver operating characteristic curve. The cut-off values for predicting the risk of computed tomography-identified sinus sequestration were 17.6mm for STJ height (sensitivity 52%; specificity 63%; area under the curve [AUC] 0.58), 27.9mm for the mean STJ diameter (sensitivity 44%; specificity 82%; AUC 0.66), and 3.0mm for the difference between the mean STJ diameter and the area-derived annulus diameter (sensitivity 70%; specificity 68%; AUC 0.74).

have a lifespan of 10–15 years, and treatment options for degenerated TAV will be of great interest in the future. Expectations are high for minimally invasive TAV-in-TAV for degenerated TAV. Conversely, sinus sequestration has been reported as a complication specific to TAV-in-TAV.[10,11] Most coronary arteries originate in the SOV, and the left coronary artery is specifically at risk of complete occlusion caused by SOV closure. The mechanism of left coronary artery occlusion caused by sinus sequestration is different from that of coronary artery occlusion in the first TAV.[15] Coronary artery occlusion in the second TAVI is caused by the first TAV remaining open and forming a cylinder.[10,11] In Western patients, the risk of sinus sequestration with TAV-in-TAV has been reported to be 45% for self-expanding valves, but only 2% for balloon-expandable valves.[10] In contrast, 39% of Japanese patients implanted with SAPIEN 3 in the present study had a high risk of sinus sequestration. The risk of sinus sequestration in TAV-in-TAV may be different in Japanese than Western patients.

There are two possible reasons for the difference in risk between Japanese and Western patients. First, STJ and SOV are known to be smaller in Japanese than Western populations,[16] and the anatomically smaller periaortic valve structures in Japanese people may have influenced the results of this study. Specifically, the small STJ diameter is a characteristic of Japanese people,[16] and the space between the expanded SAPIEN 3 and the aorta is often insufficient, which may be a major risk factor for sinus sequestration in TAV-in-TAV. The risk of TAV-in-TAV in Japanese patients has also been reported using similar criteria as in the present study.[17] In that study, the authors

validated the risk of TAV-in-TAV and found that TAV-in-TAV was not feasible for 48.2% of patients in the SAPIEN 3 series and approximately 80% of patients in the Evolut series.[17] The findings may reflect the risk of TAV-in-TAV in the Japanese population, which approximates the results in the present study.

Second, the recent trend of high-implantation techniques for TAV may influence the results. The risk of permanent pacemaker implantation after TAVI depends on deep TAVI.[18] In the present study, a high TAV was implanted in numerous cases to reduce the risk of permanent pacemaker implantation and to ensure a large effective orifice area. Conversely, a high initial TAV implantation increases the risk of sinus sequestration in the TAV-in-TAV by allowing the RP to reach the STJ line. A trade-off occurs between the risk of permanent pacemaker implantation and the risk of sinus sequestration in TAV-in-TAV. This present study includes more recent patients than studies on Western patients, which may be due to high implantation. In view of future TAV-in-TAV, a very high TAVI position may not be suitable for the small and low STJ of Japanese patients. Furthermore, more attention should be paid to the TAV position in patients with a short membrane septum, which increases the risk of PPI.

Predicting coronary artery occlusion risk caused by sinus sequestration is crucial for deciding the indication for TAV-in-TAV. A low STJ height and a small STJ diameter have been reported as risk factors for sinus sequestration.[10] However, we considered STJ data to insufficient for the prediction of coronary artery occlusion risk, because annulus and TAV size could affect SOV sequestration. Because the space between the TAV frame and STJ is required for SOV sequestration, we focused on the difference between STJ and annulus size to examine the risk of TAV-in-TAV. Eventually, we found that a difference of <3 mm between the mean STJ and the annulus size could be a better indicator of a high risk of sinus sequestration. Japanese patients may have an STJ that is smaller than the annulus. A relatively low STJ height and a small STJ diameter compared with the implanted TAV size appear to increase the risk of sinus sequestration. Therefore, in patients with aortic stenosis with a small difference between the mean STJ and the area-derived annulus size, surgical aortic valve replacement should be preferred to TAVI in young patients who will require TAV-in-TAV in the future.

The technique used in the first TAVI may also alter the risk of sinus sequestration with TAV-in-TAV. The implantation depth is an important factor in changing the risk of sinus sequestration. We predicted how much sinus sequestration could be avoided in a hypothetical scenario in which the TAV is implanted 10% deeper than the height of the implanted TAV. The height of the TAV frame, after expansion with the nominal volume, was defined as 15.5 for 20 mm, 18 for 23 mm, 20 for 26 mm, and 25.5 for 29 mm. Then, the 10% of each TAV height was 1.55 for 20 mm, 1.8 for 23 mm, 2 for 26 mm, and 2.55 or 29 mm. For the 10% deeper virtual TAVI, the risk in the high-risk group decreased from 7.1% to 0% for the 20-mm SAPIEN 3, from 38.2% to 25.7% for the 23-mm SAPIEN 3, from 41.6% to 30.4% for the 26-mm SAPIEN 3, and from 52.0% to 28.0% for the 29-mm SAPIEN 3. After considering 10% deeper virtual TAVI, the overall high-risk group was estimated to decrease from 39% to 12%. Herein, we validated the virtual implantation of a 10% deeper TAV, suggesting that it may reduce the risk of sinus sequestration in many cases, regardless of the valve size to be implanted. Meanwhile, a deeper TAV position leads to an increased risk of permanent pacemaker implantation. In older patients who would not need a second TAVI, a shallow implantation position may be preferred to avoid permanent pacemaker implantation; however, younger patients often have better atrioventricular conduction than older patients, and a relatively deep TAV may be considered for TAV-in-TAV. The optimal TAV valve implantation depth depends on the patient's age and STJ size and height. Predetermining the target depth of the TAV according to a patient's background is recommended. The height of TAV in young patients should be further investigated. The valve size can also influence the risk of sinus sequestration.

The choice of TAV size is particularly important in patients with borderline TAV sizes (330–350, 430–440, and 540–560 mm^2), as estimated from preoperative CT of the aortic valve orifice area. In cases with borderline TAV size, if avoiding prosthesis coronary artery occlusion risk patient mismatch or decreasing para-valvular leak is a priority, a larger TAV size may be a favorable option. In contrast, if the TAV is smaller, more space can be provided between the STJ and the TAV frame. In addition, overfilling implantation may shorten the TAV height, resulting in a lower height of the TAV commissure. In the case of borderline TAV size, a smaller TAV may reduce the risk of sinus sequestration caused by TAV-in-TAV. However, the relationship between TAV durability and oversized implantation is unclear. Circular TAV was suggested to increase durability;[19] however, the long-term outcomes of TAV implanted with overfilling remain to be investigated in future studies.

The availability of TAV-in-TAV has expanded the indications for TAVI in younger patients. However, the present study suggests that the risk of sinus sequestration by TAV-in-TAV in Japanese patients may be higher than that in Western patients. In young Japanese patients, the initial indication for TAVI should be determined by considering the possibility of future TAV-in-TAV. Although BASILICA (Bioprosthetic or Native Aortic Scallop Intentional Laceration to Prevent Iatrogenic Coronary Artery Obstruction) is a surgical procedure that uses an electrocautery scalpel to incise the leaflets of old biological valves to prevent coronary artery occlusion, studies have reported that it may not be a reliable method of preventing coronary artery occlusion.[20] BASILICA is not widely used, and the use of this device is not feasible at this stage. Therefore, preoperative evaluation of risk factors and preventing coronary artery occlusion caused by sinus sequestration are important.

This study has several limitations. First, this study was validated in a relatively small number of patients from a single center; hence, a larger sample size is needed to clarify sinus sequestration risk. Second, the study assumed that the first TAV leaflet opens up to the commissural level, which may overestimate the risk of sinus sequestration. Third, the risk of sinus sequestration was assessed with fluoroscopic images after TAVI, but there was no validation with CT. In cases where CT scans were measured postoperatively, a correlation between CT scan and angiographic measurements of the valve to aorta-distance was confirmed; however, similar validation by CT scans may be necessary. Because space essentially spreads in 3 dimensions, it is possible that some patients in the high-risk group have sufficient space to preserve coronary blood flow. Fourth,

only the risk of left coronary artery occlusion was evaluated because assessing the right coronary sinus on fluoroscopic images was difficult. In previous studies, the risk of sinus sequestration in SAPIEN 3 during TAV-in-TAV was entirely dependent on left coronary sinus sequestration.[10] Finally, the study population was limited to patients with SAPIEN 3 implantation; therefore, patients with other valve implantations were not included.

In conclusion, Japanese patients may have a higher risk for sinus sequestration caused by TAV-in-TAV. The risk of sinus sequestration should be assessed before the first TAVI in young patients who are likely to require TAV-in-TAV, and whether TAVI is the best aortic valve therapy must be carefully decided.

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IRB Information

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Human Research Committee of Iwate Medical University (MH2022-146). This study was approved by the Clinical Investigation Ethics Committee of the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (Reference no. UMIN000050294).

Data Availability

The deidentified participant data will not be shared.

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