Received: 18 January 2024 | Revised: 18 August 2024 | Accepted: 5 September 2024

DOI: 10.1002/hsr2.70097

ORIGINAL RESEARCH

Health Science Reports Open Access WILEY

Clinical outcomes, hemodynamics, and leaflet thrombosis following transcatheter aortic valve replacement with novel intra-annular devices

Juri Iwata[1] | Kentaro Hayashida[1] | Akiyoshi Kajino[1] | Shingo Sakata[1] | Shohei Imaeda[1] | Toshinobu Ryuzaki[1] | Hikaru Tsuruta[1] | Hideyuki Shimizu[2] | Masaki Ieda[1]

[1]Department of Cardiology, Keio University School of Medicine, Tokyo, Japan

[2]Department of Cardiovascular Surgery, Keio University School of Medicine, Tokyo, Japan

Correspondence
Kentaro Hayashida, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.
Email: khayashidamd@gmail.com

Funding information
None

Abstract

Background: The indication of transcatheter aortic valve replacement (TAVR) is becoming more prevalent among younger and lower-risk patients. However, data on the latest intra-annular TAVR devices are limited. This study aims to compare the short-term clinical outcomes of two intra-annular transcatheter aortic valve replacement (TAVR) devices in Japan: SAPIEN 3 Ultra RESILIA (S3UR) and Navitor.

Methods: Of the 286 patients who underwent TAVR between May 2022 and October 2023 at our center, we enrolled 97 consecutive patients who received either S3UR or Navitor. We compared the intraprocedural invasive and echocardiographic hemodynamic assessment and post-procedural multidetector computed tomography (MDCT).

Results: The basic characteristics of the 97 patients (median age, 86 years [interquartile range, 81–89 years]) were similar. Technical success, defined by the Valve Academic Research Consortium, was achieved in all cases. Despite a smaller annulus, Navitor demonstrated decreased mean pressure gradient by TTE, 9.2 [7.3–13.6] mmHg versus 7.5 [5.9–9.5] mmHg, $p = 0.006$; but not by invasive measurement 5.1 [3.4–7.7] mmHg versus 5.3 [3.2–7.9] mmHg, $p = 0.986$). Discordance between echocardiographic and invasive assessment was more prominent with S3UR. However, severe prosthesis-patient mismatch was similarly noted between the two devices. Mild paravalvular leak (PVL) (24.5% vs. 54.5%, $p = 0.002$) was more frequent with the Navitor, despite no moderate-severe PVL in each group. The incidence of hypoattenuated leaflet thickening (HALT) detected by MDCT was similar between the two groups.

Conclusions: Both intra-annular valves demonstrated excellent hemodynamic performance with minimal PVL after TAVR. The incidence of HALT in both devices was comparable.

KEYWORDS
aortic stenosis, intra-annular, Navitor, SAPIEN 3 Ultra RESILIA, transcatheter aortic valve replacement

1 | INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has traditionally been performed for patients with symptomatic severe aortic stenosis (AS), who are at high surgical risk. However, advancements in devices and procedural techniques have expanded the indication of TAVR to include younger, lower-risk patients.[1–3] Nevertheless, clinical experience with these newer devices is limited, and few studies have compared their outcomes.

Intra-annular valves, which secure future coronary access, have shown advantages; however, some prior research suggests that they may be associated with higher rates of leaflet thrombosis and pressure gradients than supra-annular valves.[4,5] SAPIEN 3 Ultra RESILIA (S3UR) (Edwards Lifesciences) is the latest generation balloon-expandable valve with Ultra skirt™ designed to further reduce the risk of paravalvular leak (PVL) and RESILIA tissue™, which improves the durability of the bioprosthesis.[6–8] Moreover, Navitor (Abbott) represents the latest generation of intra-annular self-expandable valves, featuring NaviSeal™ to mitigate PVL. It boasts a highly flexible delivery system (FlexNav™) with an improved hydrophilic coating, allowing for the implantation of the bioprosthesis, even in patients with smaller vascular access.[9–11] Although these devices continue to evolve and gain wider acceptance, there remains a paucity of data regarding clinical experiences with these new devices, including leaflet thrombosis.

Therefore, we aimed to compare the short-term clinical outcomes, precise assessment of hemodynamic performance, and multidetector computed tomography (MDCT) analysis of leaflet thrombosis between S3UR and Navitor, the latest intra-annular TAVR devices.

2 | METHODS

2.1 | Study design and sample

Of the 286 patients who underwent TAVR between May 2022 and October 2023 at our center, 97 consecutive patients who received either S3UR or Navitor via the transfemoral approach and underwent post-procedural MDCT analysis were included in this study (Figure 1). The decision to proceed with TAVR was based on multidisciplinary discussions with the heart team. A total of 189 patients were excluded for various reasons, such as the use of other devices (Sapien 3; Evolut series), transcatheter aortic valve (TAV) in TAV, TAV in the surgical aortic valve, reduced renal function (estimated glomerular filtration rate (eGFR) < 20 mL/min/1.73 m^2), severe asthma, allergy to contrast, and a lack of postprocedural MDCT or effective orifice area (EOA) data through TTE. All 97 enrolled patients underwent TAVR using the transfemoral approach under local and monitored anesthesia. Baseline characteristics and clinical outcomes, including hemodynamic performance and

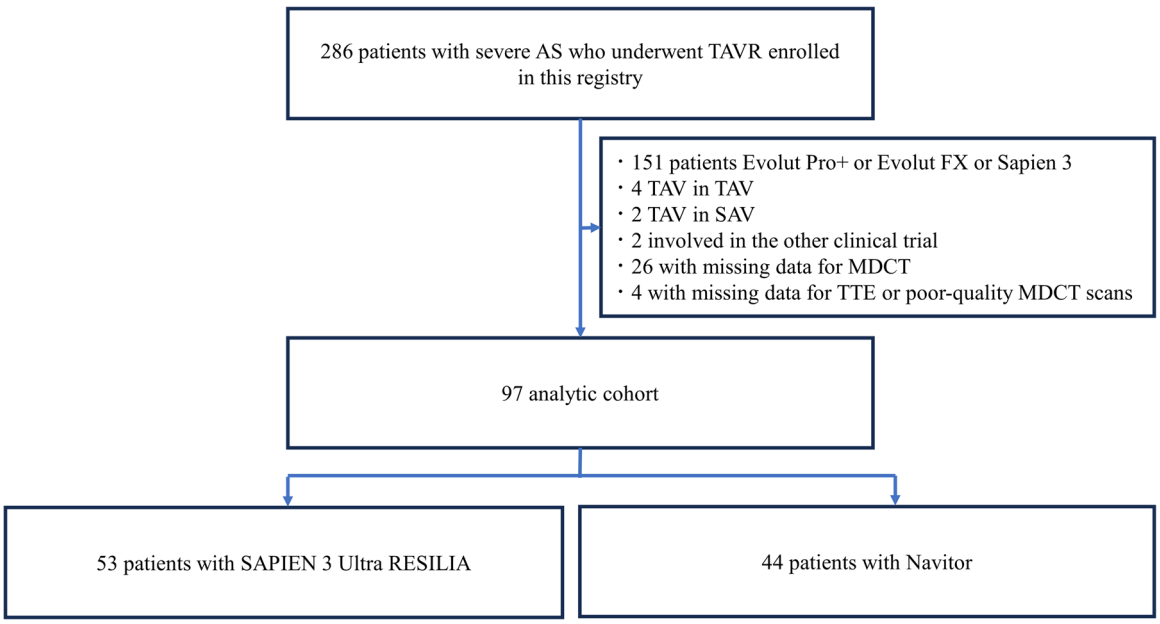

FIGURE 1 The Flowchart of the study population. AS, aortic stenosis; MDCT, multidetector computed tomography; SAV, surgical aortic valve; TAV, transcatheter aortic valve; TAVR, transcatheter aortic valve replacement; TTE, transthoracic echocardiography.

incidence and distribution of leaflet thrombosis on post-procedural MDCT within 2 days after the procedure, were compared between the two devices. The study protocol was approved by the Institutional Review Board and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from each patient, following the Ethical Guidelines for Medical and Health Research Involving Human Subjects and the Personal Information Protection Law in Japan.

2.2 | Postprocedural MDCT analysis and leaflet thrombosis

All post-procedural MDCT scans, utilizing contrast-enhanced electrocardiography-gated data, were performed within 1–2 days after the procedure and were independently evaluated by two experienced cardiologists (Drs. K. H. and J. I.). We used 3mensio Structural Heart software (Photron M&E Solutions Inc.) in our analysis. Hypoattenuated leaflet thickening (HALT) was measured during the diastolic phase at 75% of the R–R interval, enabling optimal leaflet imaging. HALT was also evaluated in the lateral and longitudinal directions on the aortic aspect of the leaflet on two-dimensional CT scanning and rated on a scale of 1–4 in accordance with the Valve Academic Research Consortium-3: VARC-3 criteria.[12]

2.3 | Postprocedural echocardiographic assessment

Postprocedural transthoracic echocardiography (TTE) was performed on the first postoperative day. A board-certified echocardiography team evaluated various parameters, including left ventricular ejection fraction, PVL severity, prosthetic valve function (including the EOA), and mean pressure gradient, using TTE. Moderate and severe prosthesis-patient mismatch (PPM) were defined as indexed EOA measurements, separated between patients with a body mass index (BMI) < 30 kg/m^2 (severe PPM iEOA <0.65 cm^2/m^2; moderate PPM 0.65 cm^2/m^2 ≦ iEOA ≦ 0.85 cm^2/m^2; and no PPM iEOA > 0.85 cm^2/m^2) and patients with BMI ≧ 30 kg/m^2 (severe PPM iEOA <0.55 cm^2/m^2; moderate PPM 0.55 cm^2/m^2 ≦ iEOA ≦ 0.70 cm^2/m^2; and no PPM iEOA > 0.70 cm^2/m^2).[13]

2.4 | Definitions of variables and outcomes

Laboratory tests were conducted preoperatively and on the first postoperative day. These tests included assessments of eGFR, albumin, hemoglobin, D-dimer, platelet, and brain natriuretic peptide level. The eGFR was calculated using the Modification of Diet in Renal Disease Equation for Japanese Patients, as recommended by the Japanese Society of Nephrology.[14] The technical success of VARC was defined as the absence of mortality, proper implantation of a single transcatheter valve, and freedom from device- or vascular-related complications.[12]

2.5 | Patient follow-up

All patients received a minimum of 24 h of observation in the intensive care unit following the TAVR procedure.

2.6 | Antithrombotic therapy

In general, post-TAVR patients without a baseline indication for oral anticoagulants (OAC) received single antiplatelet therapy, whereas those with other indications, such as atrial fibrillation, were administered.[15] In cases in which patients were deemed to be at high risk for antithrombotic therapy, no specific antithrombotic regimen was administered.[16]

2.7 | Statistical analysis

The baseline characteristics were compared between the S3UR and Navitor groups. Categorical variables are presented as numbers with relative percentages and were compared using the chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± standard or median (interquartile range [IQR]), and their comparisons were made using unpaired and paired Student's *t*-test or Mann–Whitney *U* test, depending on the distribution of data. Statistical significance was set at $p < 0.05$. IBM SPSS statistical software (version 29.0; International Business Machines Corp.) was used for all the statistical analyses.

3 | RESULTS

3.1 | Baseline patients and procedural characteristics

The baseline characteristics categorized by valve type are summarized in Table 1. Notably, baseline characteristics were similar between the S3UR and Navitor groups. However, the Navitor was more frequently used for patients with smaller annuli (annulus area, 387 [IQR: 362–455] cm^2 vs. 356 [317–405] cm^2, $p < 0.007$, perimeter, 71.1 [69.2–76.9] mm vs. 67.9 [65.0–72.4] mm, $p = 0.008$) or narrower vascular access than the S3UR (minimal lumen diameter (MLD) of right iliofemoral access, 6.3 [5.7–7.0] mm vs. 6.0 [4.9–6.5] mm, $p = 0.042$; MLD of left iliofemoral access, 6.0 [5.5–6.7] mm vs. 5.5 [4.9–6.2] mm, $p = 0.047$). All the patients had tricuspid valves, none had bicuspid valves.

3.2 | Procedural characteristics and postprocedural clinical outcomes

The procedural characteristics and postprocedural clinical outcomes are summarized in Tables 2 and 3, respectively. Notably, the VARC-

TABLE 1 Baseline characteristics.

	Overall *n* = 97	S3UR *n* = 53	Navitor *n* = 44	*p*
Age, year	86 [81–89]	85 [80–89]	87 [84–89]	0.088
BMI, kg/m²	21.8 [19.9-24.6]	22.1 [20.3–25.1]	21.8 [19.8–24.4]	0.577
Male	29 (29.9)	16 (30.2)	13 (29.5)	0.945
CFS ≧5	5 (5.2)	2 (3.8)	3 (6.8)	0.5
NYHA 3 or 4	11 (11.3)	7 (13.2)	4 (9.1)	0.524
Dyslipidemia	43 (44.3)	21 (39.6)	22 (50.0)	0.306
Diabetes mellitus	24 (24.7)	16 (30.2)	8 (18.2)	0.172
Hypertension	61 (62.9)	30 (56.6)	31 (70.5)	0.16
Coronary artery disease	25 (25.8)	13 (24.5)	12 (27.3)	0.758
Peripheral artery disease	7 (7.2)	6 (11.3)	1 (2.3)	0.086
COPD	8 (8.2)	5 (9.4)	3 (6.8)	0.641
Previous CABG	2 (2.1)	1 (1.9)	1 (2.3)	0.894
Previous PCI	10 (10.3)	3 (5.7)	7 (15.9)	0.098
Laboratory tests				
Hemoglobin, g/dL	11.4 [10.5–12.7]	11.1 [10.3–12.8]	11.7 [10.8–12.5]	0.406
eGFR, ml/min/1.73 m²	48.8 [34.1–60.0]	47.0 [26.0–61.5]	49.9 [41.0–58.0]	0.174
Albumin, g/dl	3.8 [3.5–4.1]	3.8 [3.5–4.0]	3.9 [3.6–4.2]	0.328
BNP, pg/ml	249 [109–464]	235 [112–509]	256 [106–394]	0.607
D-dimer, μg/ml	1.1 [0.7–2.2]	1.0 [0.55–2.3]	1.1 [0.82–1.9]	0.202
Platelet, 10^3/μl	180 [154–221]	185 [161–228]	174 [135–217]	0.176
Echocardiographic variables				
PFV, m/s	4.5 [4.2–5.1]	4.5 [4.2–5.0]	4.6 [4.1–5.1]	0.862
Mean pressure gradient, mmHg	42 [36–57]	41 [36–55]	45 [35–59]	0.392
AVA, cm²	0.61 [0.51–0.75]	0.64 [0.50–0.79]	0.60 [0.51–0.70]	0.447
Index AVA, cm²/m²	0.41 [0.35–0.50]	0.41 [0.35–0.51]	0.42 [0.36–0.49]	0.905
EF, % (Simpson)	64.9 [60.1–69.8]	63.3 [59.1–69.1]	67.1 [61.2–71.5]	0.152
AR ≦mild	92 (94.8)	50 (94.3)	42 (95.5)	0.805
Moderate ≦AR	5 (5.2)	3 (5.7)	2 (4.5)	
MR ≦mild	86 (88.7)	46 (86.8)	40 (90.9)	0.524
Mild-moderate ≦MR	11 (11.3)	7 (13.2)	4 (9.1)	
MDCT variables				
Area, mm²	376 [336–428]	387 [362–455]	356 [317–405]	0.007
Perimeter, mm	70.6 [66.5–75.2]	71.1 [69.2–76.9]	67.9 [65.0–72.4]	0.008
MLD of right iliofemoral access, mm	6.1 [5.5–6.9]	6.3 [5.7–7.0]	6.0 [4.9–6.5]	0.042
MLD of left iliofemoral access, mm	5.9 [5.1–6.6]	6.0 [5.5–6.7]	5.5 [4.9–6.2]	0.047
Electrocardiogram				
Af	19 (19.6)	14 (26.4)	5 (11.4)	0.063
CRBBB	11 (11.3)	8 (15.1)	3 (6.8)	0.201

TABLE 1 (Continued)

	Overall *n* = 97	S3UR *n* = 53	Navitor *n* = 44	*p*
CLBBB	4 (4.1)	2 (3.8)	2 (4.5)	0.849
STS score, %	5.1 [3.4-7.3]	5.9 [3.3-8.6]	4.7 [3.4-6.5]	0.21

Note: Values are *n* (%), or median (IQR).

Abbreviations: Af, atrial fibrillation; AR, aortic regurgitation; AVA, aortic valve area; BMI, body mass index; BNP, brain natriuretic peptide; CABG, coronary artery bypass grafting; CLBBB, complete left bundle branch block; CRBBB, complete right bundle branch block; CFS, clinical frailty scale; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; eGFR, estimated glomerular filtration rate; IQR, interquartile range; MR, mitral regurgitation; MDCT, multidetector computed tomography; MLD, minimal lumen diameter; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PFV, peak flow velocity; S3UR, SAPIEN 3 Ultra RESILIA; STS score, The Society of Thoracic Surgeons' score.

TABLE 2 Procedural characteristics.

	Overall *n* = 97	S3UR *n* = 53	Navitor *n* = 44	*p*
Valve size				
20 mm	2	2	-	
23 mm	51	36	15	
25 mm	19	-	19	
26 mm	13	13	-	
27 mm	8	-	8	
29 mm	4	2	2	
Urgency	2 (2.1)	2 (3.8)	0 (0)	0.193
Predilatation	49 (50.5)	6 (11.3)	44 (100)	<0.001
Postdilatation	8 (8.2)	6 (11.3)	2 (4.5)	0.227
Mean pressure gradient (invasive), mmHg	5.1 [3.4–7.7]	5.1 [3.4–7.7]	5.3 [3.2–7.9]	0.986

Note: Values are *n* (%), or median (IQR).

Abbreviations: IQR, interquartile range; S3UR, SAPIEN 3 Ultra RESILIA.

defined technical success was achieved in all cases. Importantly, no fatal complications including death, stroke, or heart failure were observed in either the S3UR or Navitor groups. Pre-dilation was more frequently performed with Navitor (11.3% vs. 100%, $p < 0.001$). Additionally, mild PVL was more frequently observed in the Navitor group (24.5% vs. 54.5%, $p = 0.002$), although no cases of moderate to severe PVL were detected in either group. Notably, permanent pacemaker implantation was more frequently required with Navitor than with S3UR (5.7% vs. 27.3%, $p = 0.003$), resulting in a longer hospital stay (6 [4–9] days vs. 11 [8–17] days, $p < 0.001$). In terms of mean pressure gradient improvement, the Navitor showed better results than the S3UR during TTE evaluation. However, no significant difference was observed in the pressure gradient measured using invasive hemodynamic assessment with catheters between the two groups during the procedure. Furthermore, the S3UR and Navitor demonstrated significantly better pressure gradient at the catheter than with TTE (catheters vs. TTE, 5.1 [3.4–7.7] mmHg vs. 9.2 [7.3–13.6] mmHg, $p < 0.001$; 5.3 [3.2–7.9] mmHg vs. 7.5 [5.9–9.5] mmHg, $p = 0.010$), indicating the presence of discordance (Figure 2). This discordance was more prominent with the S3UR than with the Navitor.

3.3 | MDCT analysis

A total of 28 patients (28.9%) experienced significant HALT (≧VARC-3 Grade 1). The incidence of HALT was statistically comparable between the S3UR and Navitor groups (22.6% vs. 36.4%, $p = 0.329$) (Table 4). Notably, HALT > 50% involvement, corresponding to a VARC criteria grade of ≥3, was observed at a low rate in both groups (3.8% vs. 6.8%, $p = 0.329$). Furthermore, no significant difference was observed in the incidence of HALT in each cusp (non-coronary, right coronary, and left coronary) in either group. The invasive and echocardiographic evaluations of hemodynamic performance with and without HALT are summarized in Table 5. Importantly, HALT was not associated with hemodynamic performance, as evaluated by invasive measurements and echocardiography,

TABLE 3 Postprocedural clinical outcomes.

	Overall *n* = 97	S3UR *n* = 53	Navitor *n* = 44	*p*
VARC-technical success	97 (100)	53 (100)	44 (100)	-
Death	0 (0)	0 (0)	0 (0)	-
Stroke	0 (0)	0 (0)	0 (0)	-
Heart failure	0 (0)	0 (0)	0 (0)	-
New PMI after the procedure	15 (15.5)	3 (5.7)	12 (27.3)	0.003
Hospital stay	8 [6–13]	6 [4–9]	11 [8–17]	<0.001
No antithrombotic therapy at discharge	36 (37.1)	21 (39.6)	15 (34.1)	0.575
Echocardiographic variables				
THV Vmax, m/s	2.1 [1.9–2.4]	2.1 [1.9–2.7]	2.0 [1.7–2.3]	0.016
Mean pressure gradient, mmHg	8.5 [6.3–11.0]	9.2 [7.3–13.6]	7.5 [5.9–9.5]	0.006
EOA, cm^2	1.60 [1.33–1.90]	1.51 [1.29–1.77]	1.80 [1.38–1.97]	0.009
Index EOA, cm^2/m^2	1.07 [0.91–1.27]	1.01 [0.86–1.19]	1.16 [0.99–1.44]	0.004
PPM				
No PPM	83 (85.6)	42 (79.2)	41 (93.2)	
Moderate PPM	11 (11.3)	10 (18.9)	1 (2.3)	
Severe PPM	3 (3.1)	1 (1.9)	2 (4.5)	0.085
PVL				
None or trivial PVL	60 (61.9)	40 (75.5)	20 (45.5)	-
Mild PVL	37 (38.1)	13 (24.5)	24 (54.5)	-
Moderate or severe PVL	0 (0)	0 (0)	0 (0)	0.002
Postprocedural laboratory data				
Hemoglobin, g/dL	10.5 [9.6–11.4]	10.5 [9.5–11.9]	10.6 [9.9-11.3]	0.679
D-dimer, μg/mL	3.5 [2.6–4.6]	3.1 [2.5–4.4]	3.7 [2.7-5.4]	0.28
Platelet, $10^3/\mu l$	131 [102–159]	136 [109–163]	119 [94-145]	0.04
BNP, pg/mL	288 [172–478]	277 [156–464]	312 [180-496]	0.268

Note: Values are *n* (%), or median (IQR).

Abbreviations: BNP, brain natriuretic peptide; EOA, effective orifice area; IQR, interquartile range; SPMI, pacemaker implantation; PPM, prosthesis-patient mismatch; PVL, paravalvular leak; S3UR, SAPIEN 3 Ultra RESILIA; THV, transcatheter heart valve; VARC, Valve Academic Research Consortium.

in either the S3UR or Navitor groups. No additional antithrombotic therapy was administered for the patients with HALT, due to the absence of hemodynamic deterioration.

4 | DISCUSSION

In this study, we demonstrated several key findings. (1) The 30-day clinical outcomes, including mortality, stroke, heart failure, and device technical success, were excellent in both groups. (2) The Navitor valve was associated with a lower pressure gradient on echocardiographic evaluations; however, the invasive hemodynamic assessments were similar. (3) S3UR was associated with a lower incidence of significant PVL and permanent pacemaker requirement. (4) The incidence of HALT was similar between both groups. To the best of our knowledge, this is the first report comparing the S3UR and Navitor, new intra-annular TAVR devices, with a complete data set of echocardiographic and invasive assessment of hemodynamic performance, and MDCT analysis of HALT.

The S3UR and Navitor showed improvements from each previous-generation valve to reduce PVL or vascular access complications, resulting in excellent 30-day outcomes in this study, consistent with previous Sapien 3 Ultra and Navitor studies.[6–11] However, data on the hemodynamic performance of recently developed intra-annular devices are limited. In our study, Navitor was associated with a significantly lower post-procedural pressure gradient on TTE

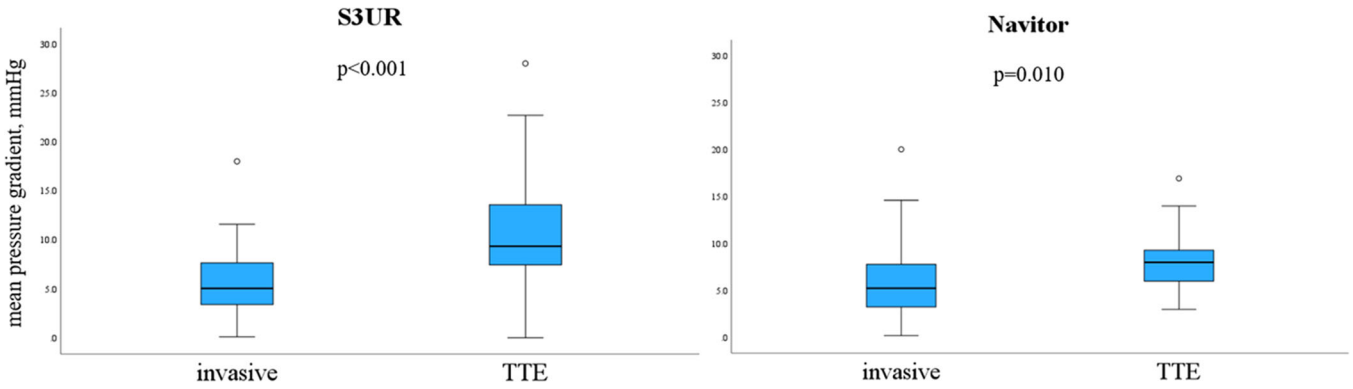

FIGURE 2 Discordance in each S3UR and Navitor. Discordance after TAVR for each valve is shown. The pressure gradient was lower with invasive measurements than with TTE and was more pronounced for S3UR. S3UR, SAPIEN 3 Ultra RESILIA; TAVR, transcatheter aortic valve replacement; TTE, transthoracic echocardiography.

TABLE 4 HALT with MDCT analysis.

	Overall *n* = 97	S3UR *n* = 53	Navitor *n* = 44	*p*
HALT	28 (28.9)	12 (22.6)	16 (36.4)	0.138
HALT < grade 2	23 (23.7)	10 (18.9)	13 (29.5)	0.329
HALT > grade 3	5 (5.2)	2 (3.8)	3 (6.8)	
HALT with NCC leaflet	4 (4.1)	3 (5.7)	1 (2.3)	0.118
HALT with RCC leaflet	10 (10.3)	3 (5.7)	7 (15.9)	
HALT with LCC leaflet	3 (3.1)	0 (0)	3 (6.8)	
HALT with multileaflet	11 (11.3)	6 (11.3)	5 (11.4)	
HALT with 1 leaflet	17 (17.5)	6 (11.3)	11 (25.0)	0.346
HALT with 2 leaflets	6 (6.2)	3 (5.7)	3 (6.8)	
HALT with 3 leaflets	5 (5.2)	3 (5.7)	2 (4.5)	

Note: Values are *n* (%).

Abbreviations: HALT, hypoattenuated leaflet thickening; LCC, left-coronary cusp; MDCT, multi-detector computed tomography; NCC, noncoronary cusp; RCC, right-coronary cusp; S3UR, SAPIEN 3 Ultra RESILIA.

despite the smaller aortic annulus in this group than that in the S3UR group. However, the incidence of moderate or severe PPM was low in both groups. Moreover, invasive measurements performed during the procedure demonstrated no significant difference in the pressure gradient between the two devices. Therefore, S3UR and Navitor demonstrate excellent hemodynamic performance, which may lead to favorable long-term outcomes.[17,18]

The pressure gradient typically appears higher in echocardiographic assessments than invasive measurement in most cases because of pressure recovery, a phenomenon commonly referred to as "discordance".[19,20] In this study, we also observed this phenomenon with both TAVR devices, and it was notably more pronounced with S3UR, which is consistent with the findings of a prior study.[20] Discordance should be noted, especially in the case of the S3UR, to prevent misinterpretation of the results obtained through TTE.

Both devices demonstrated favorable outcomes in reducing moderate to severe PVL. The use of Navitor was associated with a higher incidence of mild PVL in this study, probably because of patient selection; patients with LVOT calcification tended to be treated with self-expanding devices. Importantly, we previously reported that even mild PVL may impact heart failure rehospitalization in the contemporary TAVR era.[21] Therefore, mitigating mild PVL using new devices, particularly in low-risk patients, is crucial.

In this study, permanent pacemaker implantation was required more frequently with Navitor, possibly due to the need to avoid unexpected upward motion of the bioprosthesis. Currently, we have adopted the "distal opening technique" to mitigate the risk of non-uniform expansion and facilitate correct positioning.[22]

We observed periprocedural HALT (Grades 1–3) in 28.9% of cases, with significant HALT noted in 5.2% at 1–2 days after the procedure. This represents a higher incidence of HALT than that reported in our previous study using SAPIEN 3.[23] The reason for this is that S3UR and Navitor are novel valves that have not been analyzed previously, and therefore, the clinical outcomes in this study including the rate of early detected HALT are novel compared to previous studies. Moreover, no differences were observed in valve performance or early adverse events between patients with and without HALT. This study was performed in a single center and a limited number of cohorts, however, this fact was consistent with our previous study.[23] Given the current uncertainty regarding the clinical implications and natural history of HALT, long-term studies are necessary to determine how HALT and antithrombotic therapy may affect valve performance, durability, and the occurrence of thromboembolic events with S3UR and Navitor in the future.

5 | LIMITATIONS

This study had some limitations. First, it was a retrospective, observational, single-center study, and concomitant factors may have influenced the results. Second, the present study included a relatively limited number of patients undergoing TAVR with S3UR and Navitor,

TABLE 5 Comparison between with and without HALT in each valve.

	S3UR With HALT $n = 12$	Without HALT $n = 41$	p	Navitor With HALT $n = 16$	Without HALT $n = 28$	p
No antithrombotic therapy at discharge	7 (58.3)	25 (61.0)	0.869	11 (68.8)	18 (64.3)	0.764
Mean pressure gradient (invasive), mmHg	4.75 [2.95–6.48]	5.25 [3.5–7.85]	0.35	5.65 [3.2–7.0]	5.01[3.18–9.73]	0.728
Echocardiographic variables						
THV max velocity, m/s	2.23 [2.02–2.62]	2.14 [1.91–2.67]	0.45	2.0 [1.6–2.25]	2.02 [1.70–2.3]	0.687
Mean pressure gradient, mmHg	10.3 [9.32–13.6]	8.3 [7.0–13.6]	0.154	7.0 [5.9–9.0]	8.3 [5.33–11.0]	0.47
EOA, cm^2	1.37 [1.14–1.79]	1.56 [1.30–1.77]	0.344	1.7 [1.33–1.93]	1.82 [1.38–2.05]	0.323
Index EOA, cm^2/m^2	0.93 [0.78–1.20]	1.01 [0.87–1.19]	0.395	1.07 [1.0–1.39]	1.27 [0.99–1.48]	0.487
PPM						
No PPM	9 (75.0)	33 (80.5)	-	15 (93.8)	25 (89.3)	-
Moderate PPM	2 (16.7)	8 (19.5)	-	0 (0)	2 (7.1)	-
Severe PPM	1 (8.3)	0 (0)	0.174	1 (6.3)	1 (3.6)	0.515
PVL						
None or trivial PVL	11 (91.7)	29 (70.7)	-	10 (62.5)	10 (35.7)	-
Mild PVL	1 (8.3)	12 (30.8)	0.138	6 (37.5)	18 (64.3)	0.086
Postprocedural laboratory data						
Hemoglobin, g/dL	11.85 [10.63–12.8]	10.2 [9.35–11.2]	0.021	10.95 [10.33–12.1]	10.2 [9.53–11.1]	0.028
D-dimer, μg/mL	4.4 [2.12–6.50]	3.0 [2.45–4.3]	0.213	3.6 [2.5–5.6]	3.7 [2.8–5.05]	0.723
Platelet, $10^3/\mu L$	144 [125–202]	134 [105–160]	0.23	124 [101–143]	115 [87–161]	0.798
BNP, pg/mL	304 [178–598]	244 [128–464]	0.496	197 [160–335]	383 [234–507]	0.045

Note: Values are *n* (%), or median (IQR).

Abbreviations: BNP, brain natriuretic peptide; EOA, effective orifice area; HALT, hypoattenuated leaflet thickening; IQR, interquartile range; SPMI, pacemaker implantation; PPM, prosthesis-patient mismatch; PVL, paravalvular leak; S3UR, SAPIEN 3 Ultra RESILIA; THV, transcatheter heart valve.

with complete datasets, including TTE data, invasive hemodynamic assessment, and MDCT analysis. Further validation of the results is required through larger multicenter studies. We are currently conducting a multicenter study to confirm our findings, using data from the OCEAN-TAVI registry. Third, histopathological data were not obtained and the diagnosis of thrombosis relied solely on MDCT because of the subjectivity of several physicians. However, HALT was initially diagnosed using MDCT, and the patients in the current study had complete TTE and MDCT datasets to assess the impact of HALT on hemodynamic outcomes. Long-term follow-ups are necessary to confirm our findings.

6 | CONCLUSION

The latest intra-annular valves, S3UR and Navitor, demonstrated excellent hemodynamic performance, as confirmed by TTE and invasive measurements, with minimal PVL in the short-term after TAVR. Navitor use was associated with better hemodynamic performance on TTE and a higher incidence of permanent pacemaker requirement than S3UR use. The incidence of HALT in both valves was comparable. Therefore, long-term studies are warranted.

AUTHOR CONTRIBUTIONS

Juri Iwata: Conceptualization; data curation; formal analysis; investigation; project administration; writing—original draft; writing—review and editing. **Kentaro Hayashida**: Conceptualization; supervision. **Akiyoshi Kajino**: Conceptualization. **Shingo Sakata**: Conceptualization. **Shohei Imaeda**: Conceptualization. **Toshinobu Ryuzaki**: Conceptualization. **Hikaru Tsuruta**: Conceptualization. **Hideyuki Shimizu**: Supervision. **Masaki Ieda**: Supervision.

ACKNOWLEDGMENTS

The authors extend their gratitude to all the investigators who participated in this study.

CONFLICT OF INTEREST STATEMENT

Dr. Hayashida is a clinical proctor of Edwards Lifesciences, Medtronic, and Abbott. Dr. Shimizu is a clinical proctor at Edwards Life Sciences. The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study protocol was developed in accordance with the Declaration of Helsinki and approved by Keio University School of Medicine Ethics Committee: (UMIN000020423).

TRANSPARENCY STATEMENT

The lead author Kentaro Hayashida affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ORCID

Juri Iwata http://orcid.org/0000-0002-6809-5259
Kentaro Hayashida http://orcid.org/0000-0002-1750-1982

REFERENCES

1. Pibarot P, Salaun E, Dahou A, et al. Echocardiographic results of transcatheter versus surgical aortic valve replacement in low-risk patients: the PARTNER 3 trial. *Circulation*. 2020;141:1527-1537.
2. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med*. 2019;380:1706-1715.
3. Thyregod HGH, Ihlemann N, Jørgensen TH, et al. Five-year clinical and echocardiographic outcomes from the NOTION randomized clinical trial in patients at lower surgical risk. *Circulation*. 2019;139:2714-2723.
4. Scotti A, Fovino LN, Coisne A, et al. 10-Year impact of transcatheter aortic valve replacement leaflet design (intra- versus supra-annular) in mortality and hemodynamic performance. *Front Cardiovasc Med*. 2022;9:924958.
5. Nai Fovino L, Scotti A, Massussi M, et al. Incidence and feasibility of coronary access after transcatheter aortic valve replacement. *Catheter Cardiovasc Interv*. 2020;96:E535-E541.
6. Nazif TM, Cahill TJ, Daniels D, et al. Real-world experience with the SAPIEN 3 ultra transcatheter heart valve: a propensity-matched analysis from the United States. *Circ: Cardiovasc Interv*. 2021;14:e010543.
7. Cannata S, Gandolfo C, Ribichini FL, et al. One-year outcomes after transcatheter aortic valve implantation with the latest-generation SAPIEN balloon-expandable valve: the S3U registry. *EuroIntervention*. 2023;18:1418-1427.
8. Bavaria JE, Griffith B, Heimansohn DA, et al. Five-year outcomes of the COMMENCE trial investigating aortic valve replacement with RESILIA tissue. *Ann Thorac Surg*. 2023;115:1429-1436.
9. Eckel CE, Kim WK, Grothusen C, et al. Comparison of the new-generation self-expanding Navitor transcatheter heart valve with its predecessor, the Portico, in severe native aortic valve stenosis. *J Clin Med*. 2023;12:3999.
10. Reardon MJ, Chehab B, Smith D, et al. 30-Day clinical outcomes of a self-expanding transcatheter aortic valve. *JACC: Cardiovasc Interv*. 2023;16:681-689.
11. Sondergaard L, Walton AS, Worthley SG, et al. Thirty-day and one-year outcomes of the Navitor transcatheter heart valve in patients with aortic stenosis: the prospective, multicentre, global PORTICONG study. *EuroIntervention*. 2023;19:248-255.
12. Varc-3 Writing C, Genereux P, Piazza N, Alu MC, et al. Valve academic research consortium 3: updated endpoint definitions for aortic valve clinical research. *Eur Heart J*. 2021;42:1825-1857. doi:10.1093/eurheartj/ehaa799
13. Pibarot P, Dumesnil JG. Valve prosthesis–patient mismatch, 1978 to 2011. *J Am Coll Cardiol*. 2012;60:1136-1139.
14. Imai E, Horio M, Nitta K, et al. Modification of the modification of diet in renal disease (MDRD) study equation for Japan. *Am J Kidney Dis*. 2007;50:927-937.
15. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2021;43:561-632.
16. Kobari Y, Inohara T, Tsuruta H, et al. No antithrombotic therapy after transcatheter aortic valve replacement. *JACC: Cardiovasc Interv*. 2023;16:79-91.
17. Chen YH, Chang HH, Kuo CC, Leu HB, Lin SM. Impact of prosthesis-patient mismatch after transcatheter aortic valve replacement in asian patients. *Ann Thorac Surg*. 2022;114:1612-1619.
18. Miyasaka M, Tada N. Prosthesis–patient mismatch after transcatheter aortic valve implantation. *Cardiovasc Interv Ther*. 2022;37:615-625.
19. Hayashida K. Transcatheter valve treatment for a failed small surgical aortic valve. *J Am Coll Cardiol*. 2022;80:694-696.
20. Rodés-Cabau J, Abbas AE, Serra V, et al. Balloon- vs self-expanding valve systems for failed small surgical aortic valve bioprostheses. *J Am Coll Cardiol*. 2022;80:681-693.
21. Yoshijima N, Yanagisawa R, Hase H, et al. Update on the clinical impact of mild aortic regurgitation after transcatheter aortic valve implantation: insights from the Japanese multicenter OCEAN-TAVI registry. *Catheter Cardiovasc Interv*. 2020;95:35-44.
22. Kobari Y, Yamamoto M, Hayashida K. A novel technique to optimize implantation of the navitor valve in transcatheter aortic valve replacement. *Eur Heart J - Case Rep*. 2023;7:ytad480.
23. Yanagisawa R, Tanaka M, Yashima F, et al. Early and late leaflet thrombosis after transcatheter aortic valve replacement. *Circ: Cardiovasc Interv*. 2019;12:e007349.

How to cite this article: Iwata J, Hayashida K, Kajino A, et al. Clinical outcomes, hemodynamics, and leaflet thrombosis following transcatheter aortic valve replacement with novel intra-annular devices. *Health Sci Rep*. 2025;8:e70097. doi:10.1002/hsr2.70097