Original Article

Midterm Clinical Outcomes after Isolated Surgical and Transcatheter Aortic Valve Replacement in Low-Risk Patients with Aortic Stenosis

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Purpose: This study aimed to compare the clinical outcomes of isolated surgical aortic valve replacement (SAVR) and transfemoral (TF)-transcatheter aortic valve replacement (TAVR) in low-risk aortic stenosis (AS) patients.
Methods: A total of 696 low-risk (Society of Thoracic Surgeons score <4%) AS patients underwent isolated SAVR or TF-TAVR at five centers. After 1:1 propensity score matching, 159 pairs were identified. Early and follow-up events, including cardiac mortality and major adverse cardiac and cerebrovascular events (MACCE: all-cause mortality, heart failure admission, reoperation, prosthetic valve endocarditis, and stroke), were compared.
Results: Baseline characteristics are similar between the matched groups. There were no 30-day cardiac mortalities in either group. All-cause mortality and MACCE at 30 days did not differ. During 5-year follow-up (median 3.1 [range 0–7.2] years), the incidence of cardiac mortality (1.3% vs. 18.9%; adjusted hazard ratio [aHR], 8.89; 95% confidence interval [CI], 2.68–29.53; *P* <0.001), all-cause mortality (4.2% vs. 33.9%; aHR, 8.56; 95% CI, 3.41–21.45; *P* <0.001), and MACCE (25.1% vs. 47.0%; aHR, 2.36; 95% CI, 1.54–3.63; *P* <0.001) were lower in the SAVR group than in the TAVR group.
Conclusions: Isolated SAVR demonstrated better outcomes in low-risk AS patients. TAVR in this subset should be chosen carefully.

Keywords: surgical aortic valve replacement, aortic stenosis, transcatheter aortic valve replacement

Abbreviations

ACTIVIST	=	Accelerating Conventional and Transcatheter Integration in Valvular Intervention STrategy
AS	=	aortic stenosis
CI	=	confidence interval
EOAI	=	effective orifice area index
HR	=	hazard ratio
IQR	=	interquartile range
LV	=	left ventricular
LVDd	=	left ventricular end-diastolic diameter
LVEF	=	left ventricular ejection fraction
MACCE	=	major adverse cardiac and cerebrovascular events
PPI	=	permanent pacemaker implantation

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PVE = prosthetic valve endocarditis
PVL = paravalvular leak
SAVR = surgical aortic valve replacement
SMD = standardized mean difference
STS = Society of Thoracic Surgeons
TAVR = transcatheter aortic valve replacement
TF = transfemoral
TR = tricuspid regurgitation

Introduction

Transcatheter aortic valve replacement (TAVR) has led to a significant paradigm shift in the treatment of aortic stenosis (AS). TAVR, a method for aortic valve replacement in patients with AS, is now indicated alongside surgical aortic valve replacement (SAVR). Recent industry-sponsored prospective randomized controlled trials have demonstrated a short-term non-inferiority of TAVR to SAVR,[1,2] and midterm outcomes[3] among patients at low risk of surgery. Consequently, both the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend TAVR for low-risk patients, as well as SAVR.[4,5]

However, these randomized controlled trials targeting low-risk patients have limitations, including a certain number of patients who required concomitant procedures (PARTNER 3: 26.4%, Evolut Low-Risk Trial: 26.3%) or had a history of cardiac surgery (Evolut Low-Risk Trial: 2.1%) in the SAVR group. SAVR with concomitant surgeries represents a cohort with different prognoses compared to isolated SAVR,[6] and second-time cardiac surgeries carry a higher risk than first-time procedures.[7] On the other hand, in the TAVR group, most patients underwent the transfemoral (TF) approach (PARTNER 3: 100%, Evolut Low-Risk Trial: 99.0%). Hence, there is uncertainty when comparing isolated SAVR and TF-TAVR, which is considered the largest subset.

This study aimed to compare midterm clinical outcomes after isolated SAVR and TF-TAVR in low-risk patients with AS using data from the ACTIVIST (Accelerating Conventional and Transcatheter Integration in Valvular Intervention STrategy) registry.

Materials and Methods

Data source

The ACTIVIST registry is a retrospective, multicenter registry of all patients who underwent isolated SAVR or TAVR for severe AS at five centers in Japan. Appropriate clinical indications for SAVR or TAVR are determined by a team that includes cardiovascular surgeons and cardiologists. Isolated SAVR was performed in patients requiring intervention only for severe AS. Patients requiring concomitant surgery for other comorbidities (e.g., coronary artery bypass grafting, aortic surgeries, Maze procedures, and other valve surgeries) were excluded from this registry. Because it is based on the Japan Adult Cardiovascular Surgery Database, definitions of these comorbidities in the present study are available online at http://www.jacvsd.umin.jp.

A total of 2428 consecutive patients with severe AS undergoing isolated SAVR or TAVR at these centers between January 2016 and December 2021 were enrolled. The inclusion criterion was scheduled isolated SAVR or TF-TAVR performed in surgically low-risk patients between 65 and 89 years of age with a Society of Thoracic Surgeons (STS) score <4%. Exclusion criteria included history of previous cardiovascular surgery, aortic annular enlargement procedures, preoperative use of an assist device such as extracorporeal membrane oxygenation or intra-aortic balloon pump, infective endocarditis, hemodialysis patients, malignant disease, and cirrhosis.

Echocardiography data were extracted at three-time points: (1) baseline before surgery, (2) at discharge after aortic valve surgery, and (3) one year after surgery. After discharge, outpatient follow-up was conducted every six months to one year. Patients who could not attend the outpatient clinic were followed up by telephone as needed.

Ethical statement

This study was conducted in accordance with the principles of the latest Declaration of Helsinki. The Clinical Research Ethics Committee of Osaka University Hospital approved this study and the publication of its data (Approval No.: 20222 (T2), Approval Date: December 15, 2021). Written informed consent was obtained from all participants.

Endpoints

Clinical events were defined according to the criteria of the Valve Academic Research Consortium-3.[8]

After matching, the baseline characteristics were compared between the isolated SAVR and TF-TAVR groups. Events during the 30 days post-procedure and up to five years of follow-up, including cardiac death, major adverse cardiac and cerebrovascular events (MACCE: all-cause mortality, heart failure admission, reoperation,

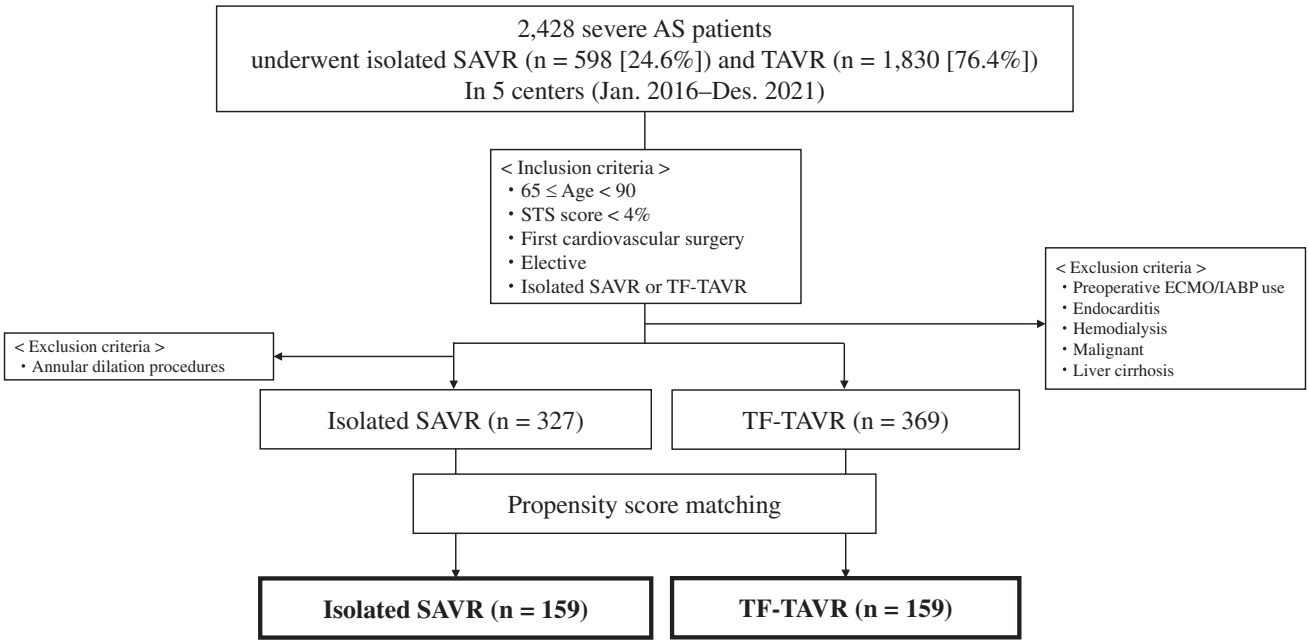

Fig. 1 Study flowchart of included patients. AS: aortic stenosis; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; STS: Society of Thoracic Surgeons; TF: transfemoral; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump

prosthetic valve endocarditis [PVE], and stroke), permanent pacemaker implantation (PPI), and paravalvular leak (PVL), were assessed for between-group differences.

Statistical analysis

Continuous variables were presented as medians (interquartile range [IQR]) and categorical variables as frequencies (%). Fisher's exact probability test was used for categorical variables compared between independent groups. The Wilcoxon rank-sum test was performed for continuous variables compared between independent groups. Propensity score matching (1:1 matching, nearest neighbor matching without replacement) was adjusted for significant differences in baseline covariates and potential confounders that could lead to biased estimates between the SAVR and TAVR groups. The propensity score for each patient was calculated by non-parsimonious multivariable logistic regression with the procedure as the endpoint (1 for the SAVR group and 0 for the TAVR group). Variables including the STS Predicted Risk of Mortality, age, gender, body mass index, insulin-dependent diabetes, estimated glomerular filtration rate, hypertension, chronic obstructive pulmonary disease, immunosuppressive drug use, peripheral artery disease, history of stroke, history of coronary artery disease, New York Heart Association functional class, history of atrial fibrillation/atrial flutter, albumin level, left ventricular ejection fraction (LVEF), aortic bicuspid valve, and mean aortic pressure gradient were included in the propensity-score calculation. Matching was performed using a caliper width set at 0.2 of the standard deviation of the pooled logit propensity score. In addition, the balance of the baseline characteristic distribution between the two groups was assessed by evaluating the standardized mean difference (SMD). Time-to-event was evaluated using Kaplan–Meier estimates and compared using the log-rank test. In the matched cohort, midterm endpoint risk was assessed as the hazard ratios (HRs) adjusted for factors with an SMD exceeding 10% by the Cox proportional hazard model. Statistical significance was two-tailed for all comparisons, with $P < 0.05$ considered significant. All analyses were performed using the R software version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population

The study flowchart is shown in **Fig. 1**, and baseline characteristics of the entire cohort before and after matching are shown in **Table 1**. Before matching, there were 327 patients in the isolated SAVR group and 369 in the TF-TAVR group. Those in the TAVR group had significantly higher STS scores than those in the SAVR

Table 1 Pre-match and post-match preoperative characteristics

Characteristics	Before matching				After matching			
	SAVR (n = 327)	TAVR (n = 369)	SMD	*P* value	SAVR (n = 159)	TAVR (n = 159)	SMD	*P* value
STS score (%)	2.15 (1.35–2.75)	3.04 (2.40–3.56)	–0.988	<0.001	2.61 (2.02–3.21)	2.78 (2.04–3.38)	–0.165	0.182
Age ≥80	72 (22.0)	269 (72.9)	1.18	<0.001	69 (43.4)	76 (47.8)	0.088	0.500
Male sex	149 (45.6)	181 (49.1)	0.070	0.400	73 (45.9)	73 (47.8)	0.000	>0.900
BMI (kg/m^2)	23.9 (21.9–26.3)	23.3 (20.5–25.6)	0.237	0.002	23.3 (21.6–26.3)	23.3 (20.7–25.9)	0.076	0.415
DM (insulin)	12 (3.7)	9 (2.4)	0.072	0.400	7 (4.4)	7 (4.4)	0.000	>0.900
eGFR <60 (mL/min/1.73 m^2)	173 (52.9)	220 (59.6)	0.136	0.079	92 (57.9)	98 (61.6)	0.077	0.600
Hypertension	237 (72.5)	268 (72.6)	0.003	>0.900	119 (74.8)	114 (71.7)	0.071	0.600
COPD ≥ moderate	12 (3.7)	19 (5.1)	0.072	0.400	8 (5.0)	11 (6.9)	0.080	0.600
Immunosuppressants	9 (2.8)	18 (4.9)	0.111	0.200	8 (5.0)	9 (5.7)	0.028	>0.900
Peripheral artery disease	13 (4.0)	19 (5.1)	0.056	0.500	7 (4.4)	8 (5.0)	0.030	>0.900
Cerebrovascular disease	24 (7.3)	42 (11.4)	0.139	0.071	16 (10.1)	16 (10.1)	0.000	>0.900
Coronary artery disease	23 (7.0)	49 (13.3)	0.208	0.008	13 (8.2)	20 (12.6)	0.145	0.300
NYHA ≥III	24 (7.3)	55 (14.9)	0.242	0.002	19 (11.9)	21 (13.2)	0.038	0.900
Af/AFL	31 (9.5)	39 (10.6)	0.036	0.700	17 (10.7)	21 (13.2)	0.078	0.600
Alb <3.5 (g/dL)	18 (5.5)	66 (17.9)	0.393	<0.001	17 (10.7)	19 (11.9)	0.040	0.900
LVEF (%)	69 (64–73)	67 (61–73)	0.163	0.060	68 (62–73)	68 (63–74)	–0.051	0.546
Bicuspid aortic valve	73 (22.3)	17 (4.6)	0.537	<0.001	16 (10.1)	16 (10.1)	0.000	>0.900
Mean PG (mmHg)	50 (41–62)	47 (40–57)	0.244	0.006	46 (39–57)	48 (40–58)	–0.019	0.503

Results are expressed as the median (interquartile range) for quantitative data and n (%) for categorical data.

P value: Wilcoxon for continuous; Fisher's exact test for categorical.

SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; SMD: standardized mean difference; STS: Society of Thoracic Surgeons; BMI: body mass index; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; Af: atrial fibrillation; AFL: atrial flutter; Alb: albumin; LVEF: left ventricular ejection fraction; PG: pressure gradient

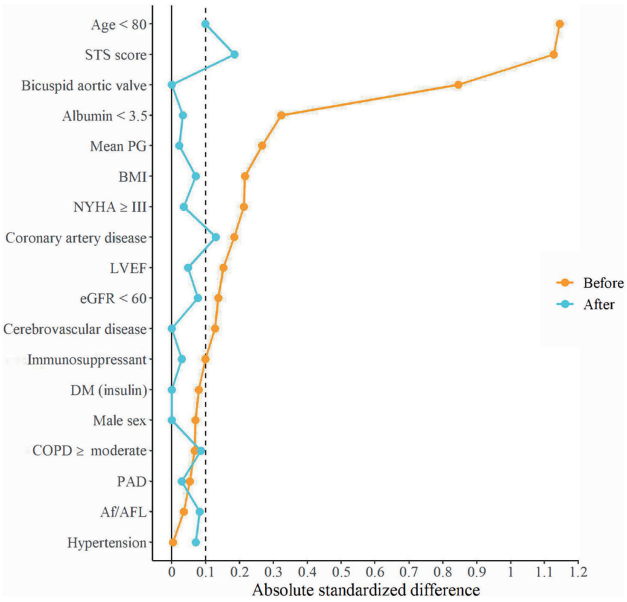

Fig. 2 Standardized differences between patients who underwent surgical aortic valve replacement and transcatheter aortic valve replacement before and after propensity score matching. STS: Society of Thoracic Surgeons; PG: pressure gradient; BMI: body mass index; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; PAD: peripheral artery disease; Af: atrial fibrillation; AFL: atrial flutter

group (3.04 [2.40–3.56] vs. 2.15 [1.35–2.75], *P* <0.001), were older (Age ≥80: 72.9% vs. 22.0%, *P* <0.001), had lower albumin levels (serum albumin <3.5 g/dL: 17.9% vs. 5.5%, *P* <0.001), and less frequent aortic bicuspid valves (4.6% vs. 22.3%, *P* <0.001). Propensity score matching identified 159 pairs as appropriate comparators (median age: 79 [76–82] years, male sex: 45.9%, median STS score: 2.70 [2.04–3.28]% in the total matched cohort), with no statistically significant differences in the baseline variables (**Fig. 2**).

Operative data and discharge echocardiography

The surgical details are presented in **Table 2**. In the matched cohort, the majority of the patients who underwent SAVR used stented bioprostheses (79.9%), while sutureless valves were used in 18.9% of the cases. Balloon-expandable valves (57.9%) were utilized more frequently than self-expandable valves (42.1%) in the TAVR group.

Postoperative echocardiography results indicated that the TAVR group had a higher LVEF (69.0 [63.0–73.0] vs. 65.0 [59.0–70.0], *P* <0.001) and greater effective orifice area index (EOAI) (1.05 [0.92–1.31] vs. 0.91 [0.82–1.01], *P* <0.001). Conversely, PVL ≥mild and ≥moderate were significantly higher in the TAVR group (35.2% vs. 1.3%, *P* <0.001; 5.0% vs. 0.0%, *P* = 0.003, respectively; **Table 2**).

Short-term outcomes and 1-year follow-up echocardiography data

Short-term results are presented in **Table 3**. In the matched cohort, there were no 30-day cardiac deaths in either group and no significant differences in MACCE or PPI between the SAVR and TAVR groups (MACCE: 1.3% vs. 1.9%, *P* = 1.000; PPI: 4.4% vs. 7.5%, *P* = 0.344) were observed. Echocardiography conducted one year after surgery revealed that the TAVR group exhibited a higher LVEF (70.0 [64.0–75.0]% vs. 68.0 [63.0–73.0]%, *P* = 0.032) and greater EOAI (1.09 [0.89–1.25] cm^2/m^2 vs. 1.01 [0.86–1.16] cm^2/m^2, *P* = 0.019). Conversely, PVL ≥mild and ≥moderate were significantly more common in the TAVR group at one year postoperatively (38.4% vs. 4.4%, *P* <0.001; 7.5% vs. 1.9%, *P* = 0.018, respectively).

Midterm main outcomes

The matched cohort had a median follow-up period of 3.1 (IQR: 1.8–4.3) (range: 0–7.2) years, with the Kaplan–Meier curves shown in **Fig. 3** (pre-matching curve in **Fig. 4**). Adjusted HRs were calculated using the Cox proportional hazards model to adjust for confounding preoperative background factors—STS score and prior coronary artery disease—with a post-matching SMD of ≥0.1 (**Table 4**). At the 5-year follow-up period, there was a significantly lower incidence of cardiac mortality in the SAVR group than in the TF-TAVR group (1.3% vs. 18.9%; adjusted HR, 8.89; 95% confidence interval [CI], 2.68–29.53; *P* <0.001). Similarly, the incidence of MACCE (25.1% vs. 47.0%; adjusted HR, 2.36; 95% CI, 1.54–3.63; *P* <0.001) and all-cause mortality (4.2% vs. 33.9%; adjusted HR, 8.56; 95% CI, 3.41–21.45; *P* <0.001) was significantly lower in the SAVR than in the TAVR groups. There was no significant difference between the SAVR and TAVR groups regarding PPI incidence (8.2% vs. 7.7%; adjusted HR, 1.26; 95% CI, 0.57–2.81; *P* = 0.572). The type of prosthetic valve (balloon-expandable or self-expandable) used in TAVR was not associated with cardiac mortality, MACCE, or all-cause mortality during the follow-up period (**Supplementary Tables S1–S3**: all supplementary files are available online).

Table 2 Operative data and discharge echocardiography results before and after propensity score matching

Operative data and discharge outcomes	Before matching			After matching		
	SAVR (n = 327)	TAVR (n = 369)	*P* value	SAVR (n = 159)	TAVR (n = 159)	*P* value
Operative data						
CPB time (min)	137.0 (112.8–164.3)	–	–	135.5 (117.0–164.0)	–	–
Aortic cross-clamp time (min)	95.0 (78.0–111.0)	–	–	95.0 (78.0–110.0)	–	–
Surgical prosthetic valve data						
Stented bioprosthesis	270 (82.6)	–	–	127 (79.9)	–	–
Sutureless valve	51 (15.6)	–	–	30 (18.9)	–	–
Mechanical valve	6 (1.8)	–	–	2 (1.3)	–	–
Transcatheter prosthetic valve data						
Self-expandable	–	150 (40.6)	–	–	67 (42.1)	–
Balloon-expandable	–	219 (59.4)	–	–	92 (57.9)	–
Valve size (mm)	21 (21–23)	26 (23–26)	<0.001	21 (21–23)	26 (23–26)	<0.001
Discharge echocardiogram						
LVEF (%)	65.0 (59.0–70.0)	68 (62–72)	<0.001	65.0 (59.0–70.0)	69.0 (63.0–73.0)	<0.001
Mean PG (mmHg)	11.0 (9.0–14.0)	10.0 (7.0–13.0)	<0.001	11.0 (9.0–14.0)	10.0 (7.0–13.0)	0.001
EOAI (cm^2/m^2)	0.93 (0.81–1.10)	1.08 (0.94–1.32)	<0.001	0.91 (0.82–1.01)	1.05 (0.92–1.31)	<0.001
PVL grade ≥ mild	8 (2.5)	139 (37.9)	<0.001	2 (1.3)	56 (35.2)	<0.001
PVL grade ≥ moderate	0 (0)	15 (4.1)	<0.001	0 (0.0)	8 (5.0)	0.003

Results are expressed as the median (interquartile range) for quantitative data and n (%) for categorical data.
P value: Wilcoxon for continuous; Fisher's exact test for categorical.
SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; CPB: cardiopulmonary bypass; LVEF: left ventricular ejection fraction; PG: pressure gradient; EOAI: effective orifice area index; PVL: paravalvular leak

Table 3 Short-term outcomes and 1-year follow-up echocardiography results before and after propensity score matching

Outcomes and follow-up results	Before matching			After matching		
	SAVR (n = 327)	TAVR (n = 369)	*P* value	SAVR (n = 159)	TAVR (n = 159)	*P* value
30-day Outcomes						
Cardiac mortality	0 (0)	0 (0)	1.000	0 (0.0)	0 (0.0)	1.000
MACCE	3 (0.9)	5 (1.4)	0.729	2 (1.3)	3 (1.9)	1.000
All-cause mortality	0 (0)	1 (0.3)	0.346	0 (0.0)	1 (0.6)	1.000
Heart failure admission	0 (0)	2 (0.5)	1.000	0 (0.0)	1 (0.6)	1.000
Reoperation	0 (0)	1 (0.3)	1.000	0 (0.0)	1 (0.6)	1.000
PVE	0 (0)	0 (0)	1.000	0 (0.0)	0 (0.0)	1.000
Stroke	3 (0.9)	0 (0)	0.103	2 (1.3)	0 (0.0)	0.498
PPI	12 (3.7)	24 (6.5)	0.122	7 (4.4)	12 (7.5)	0.344
1-year follow-up echocardiogram						
LVEF (%)	68.0 (64.0–72.0)	69.6 (64.0–74.0)	0.014	68.0 (63.0–73.0)	70.0 (64.0–75.0)	0.032
Mean PG (mmHg)	10.0 (7.0–13.0)	9.0 (6.0–13.0)	0.194	10.0 (7.0–13.0)	9.0 (6.0–13.0)	0.338
EOAI (cm^2/m^2)	0.99 (0.86–1.14)	1.10 (0.90–1.28)	<0.001	1.01 (0.86–1.16)	1.09 (0.89–1.25)	0.019
PVL grade ≥ mild	11 (3.9)	130 (40.5)	<0.001	7 (4.4)	61 (38.4)	<0.001
PVL grade ≥ moderate	3 (1.1)	21 (6.5)	<0.001	3 (1.9)	12 (7.5)	0.018

Results are expressed as the median (interquartile range) for quantitative data and n (%) for categorical data.
P value: Wilcoxon for continuous; Fisher's exact test for categorical.
SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; MACCE: major adverse cardiac and cerebrovascular events; PVE: prosthetic valve endocarditis; PPI: permanent pacemaker implantation; LVEF: left ventricular ejection fraction; PG: pressure gradient; EOAI: effective orifice area index; PVL: paravalvular leak

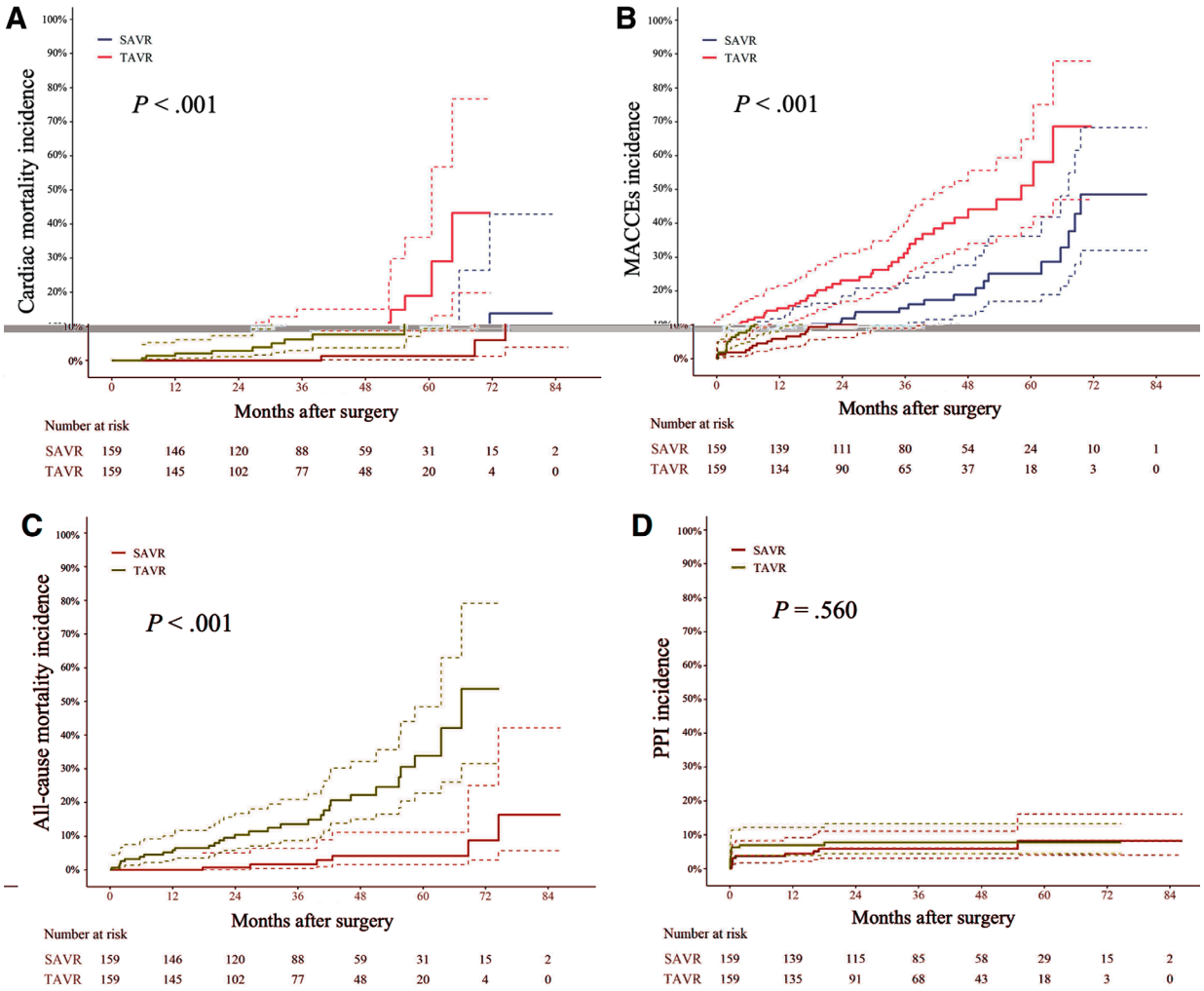

Fig. 3 Main outcomes in the propensity-score-matched cohort. Kaplan–Meier curves for cumulative incidence of cardiac mortality (**A**), MACCEs (**B**), all-cause mortality (**C**), and PPI (**D**). SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; MACCE: major adverse cardiac and cerebrovascular events; PPI: permanent pacemaker implantation

Midterm outcomes of each MACCE

Kaplan–Meier curves for each MACCE in the matched cohort are shown in **Fig. 5** (before matching curves are shown in **Fig. 6**). HRs for each MACCE were similarly adjusted for STS score and prior coronary artery disease (**Table 4**). At the 5-year follow-up period, reoperation rates (0.0% vs. 3.1%, log-rank $P = 0.038$) were significantly lower in the SAVR group than in the TAVR group. The details of reoperation procedures are shown in **Supplementary Table S4**. There were no significant differences between the two groups regarding heart failure hospitalizations, PVE, or stroke.

Discussion

This study compared isolated SAVR with TF-TAVR for 65- to 89-year-old, low-surgical-risk (STS score <4%) patients with severe AS without previous cardiac surgery in a Japanese multicenter retrospective registry propensity-score-matched study. The major finding was that the rate of cardiac mortality was significantly lower with SAVR than with the TAVR group during the 5-year follow-up period after propensity score-matching. In addition, patients who underwent SAVR had a significantly lower incidence of MACCE, including all-cause mortality and reoperation, and PVL than those who underwent TAVR in the matched cohort.

The results of our study showed that there was no mortality within 30 days postoperatively in patients with low-risk severe AS who underwent isolated SAVR, and their 5-year mortality rate was 4.2%. This compares favorably with the results of other low-risk prospective studies in the SAVR group (30-day mortality: 0.8%–1.1%, 5-year mortality rate: 8.2%).[4–6] This may be because the SAVR

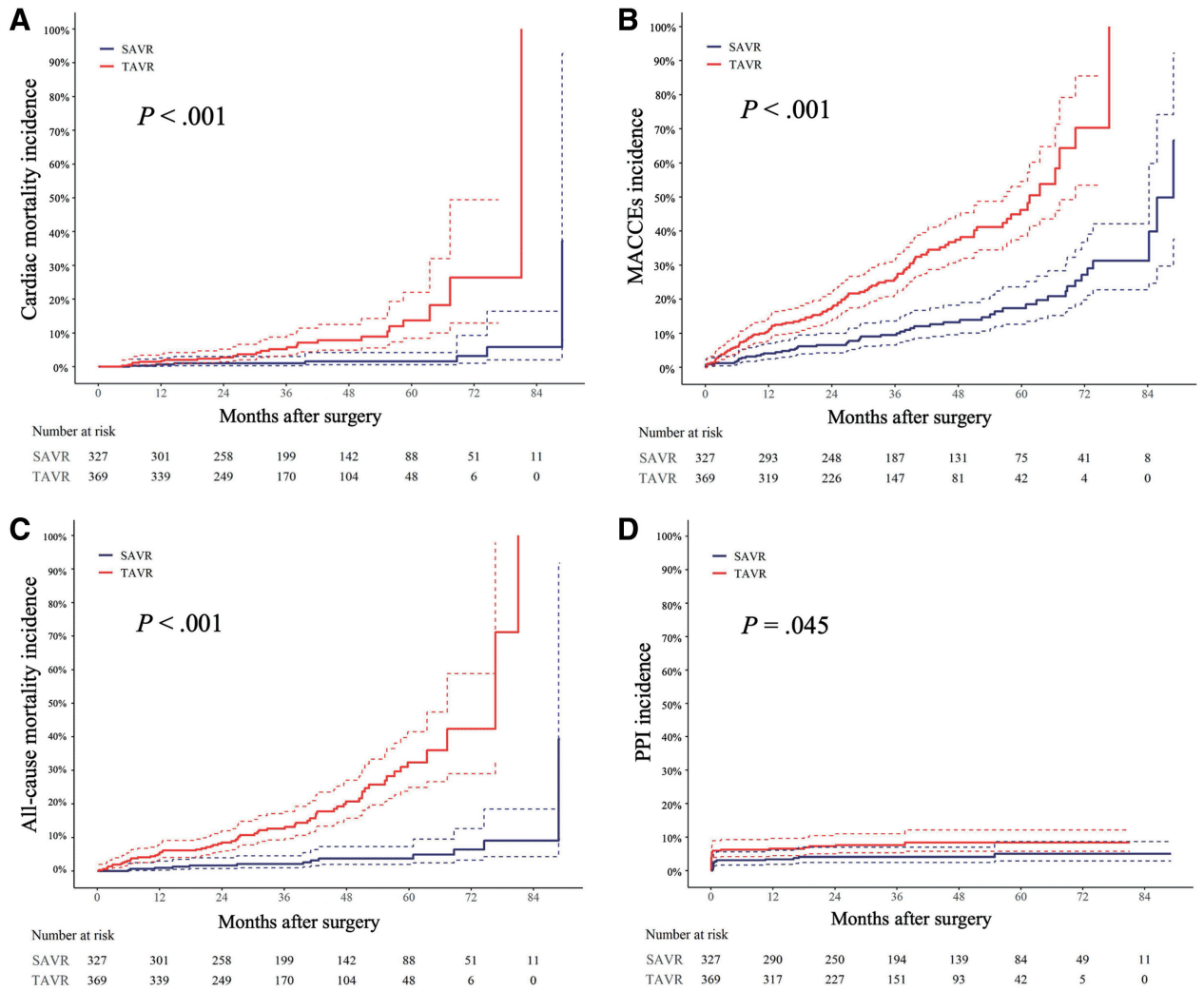

Fig. 4 Main outcomes before propensity score matching. Kaplan–Meier curves for cumulative incidence of cardiac mortality (**A**), MACCEs (**B**), all-cause mortality (**C**), and PPI (**D**). SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; MACCE: major adverse cardiac and cerebrovascular events; PPI: permanent pacemaker implantation

Table 4 Five-year outcomes in the propensity-score-matched cohort

Outcomes	SAVR (n = 159)		TAVR (n = 159)		Crude HR (95% CI)	*P* value	Adjusted HR (95% CI)*	*P* value
	No. events	Rate (%/5 years)	No. events	Rate (%/5 years)				
Cardiac mortality	3	1.3	13	18.9	8.99 (2.65–30.48)	<0.001	8.89 (2.68–29.53)	<0.001
All-MACCE	31	25.1	52	47.0	2.25 (1.47–3.44)	<0.001	2.36 (1.54–3.63)	<0.001
All-cause mortality	6	4.2	30	33.9	7.65 (3.11–18.81)	<0.001	8.56 (3.41–21.45)	<0.001
Heart failure admission	19	16.6	23	27.0	1.55 (0.85–2.85)	0.156	1.63 (0.89–2.99)	0.116
Reoperation	0	0.0	4	3.1	Inf		Inf	
PVE	2	1.3	5	5.1	2.75 (0.50–14.96)	0.242	2.40 (0.42–13.79)	0.327
Stroke	7	4.9	5	5.4	1.06 (0.32–3.46)	0.922	1.05 (0.33–3.32)	0.935
PPI	10	8.2	12	7.7	1.29 (0.57–2.90)	0.546	1.26 (0.57–2.81)	0.572

*Adjusted with STS score and history of coronary artery disease.

Results are expressed as the median (interquartile range) for quantitative data and n (%) for categorical data.

P value: Multivariable-adjusted Cox proportional hazards models.

SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; HR: hazard ratio; CI: confidence interval; PVL: paravalvular leak; MACCE: major adverse cardiac and cerebrovascular events; PVE: prosthetic valve endocarditis; PPI: permanent pacemaker implantation; STS: Society of Thoracic Surgeons

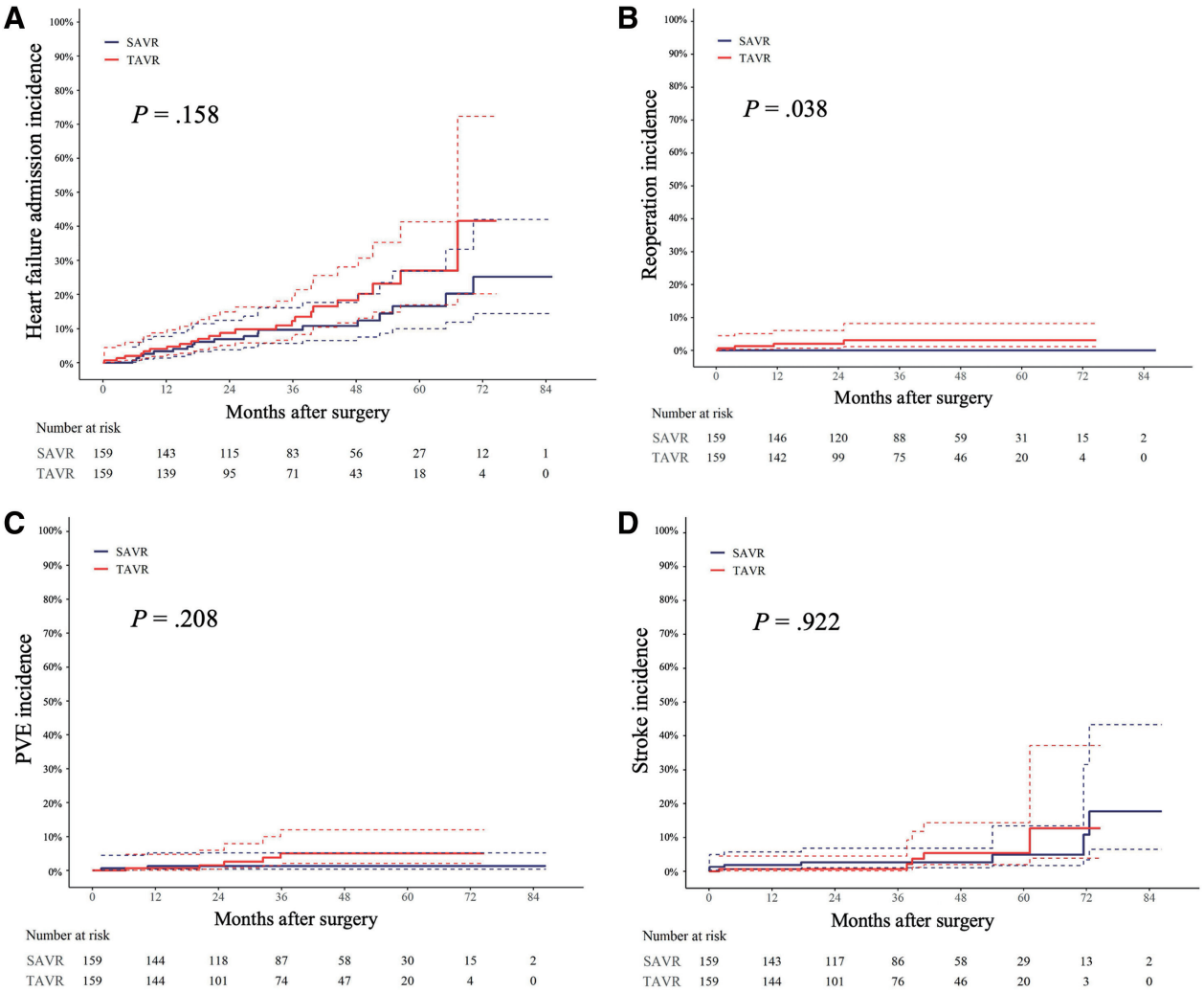

Fig. 5 MACCE outcomes for each group in the propensity-score-matched cohort. Kaplan–Meier curves for cumulative incidence of heart failure admission (**A**), reoperation (**B**), PVE (**C**), and Stroke (**D**). SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; PVE: prosthetic valve endocarditis; MACCE: major adverse cardiac and cerebrovascular events

groups in these prospective studies included patients with concomitant surgeries and had a history of cardiovascular surgery. Recent studies have implicated cardiac damage as a prognostic factor in patients with AS.[9–11] Isolated SAVR, specifically for severe AS, which is the only cause of cardiac damage, leads to an improved prognosis. Conversely, when concomitant surgery is required, cardiac damage could arise due to comorbidities as well as AS, and the preoperative heart is considered to have suffered severe damage not only because of AS alone. In addition, patients with severe AS who have a history of previous cardiac surgery might have suffered multiple cardiac damages, including those from previous cardiac diseases, besides AS. Because of this difference in the degree of preoperative cardiac damage, patients undergoing concomitant surgery and those with a history of previous cardiac surgery may have different long-term outcomes as well as different perioperative risks compared to patients undergoing isolated SAVR for the first time. Given these disparities in preoperative cardiac damage, caution is warranted when interpreting the results of the SAVR group in previously reported low-risk trials. On the other hand, the higher mortality rate in the TF-TAVR group in the current study, which is more than that in the previously reported low-risk trial (1 year: 5.8%, 5 years: 33.9%), is partly due to the higher median age of the current cohort (79 [IQR: 76–82] years) than the low-risk trial cohort (mean age: 73–74 years).[1–3] The trend of reducing the age indication for TAVR is evident in various guidelines, reflecting the implications of these results. However, in clinical practice, the choice between SAVR and TAVR often presents a dilemma, especially

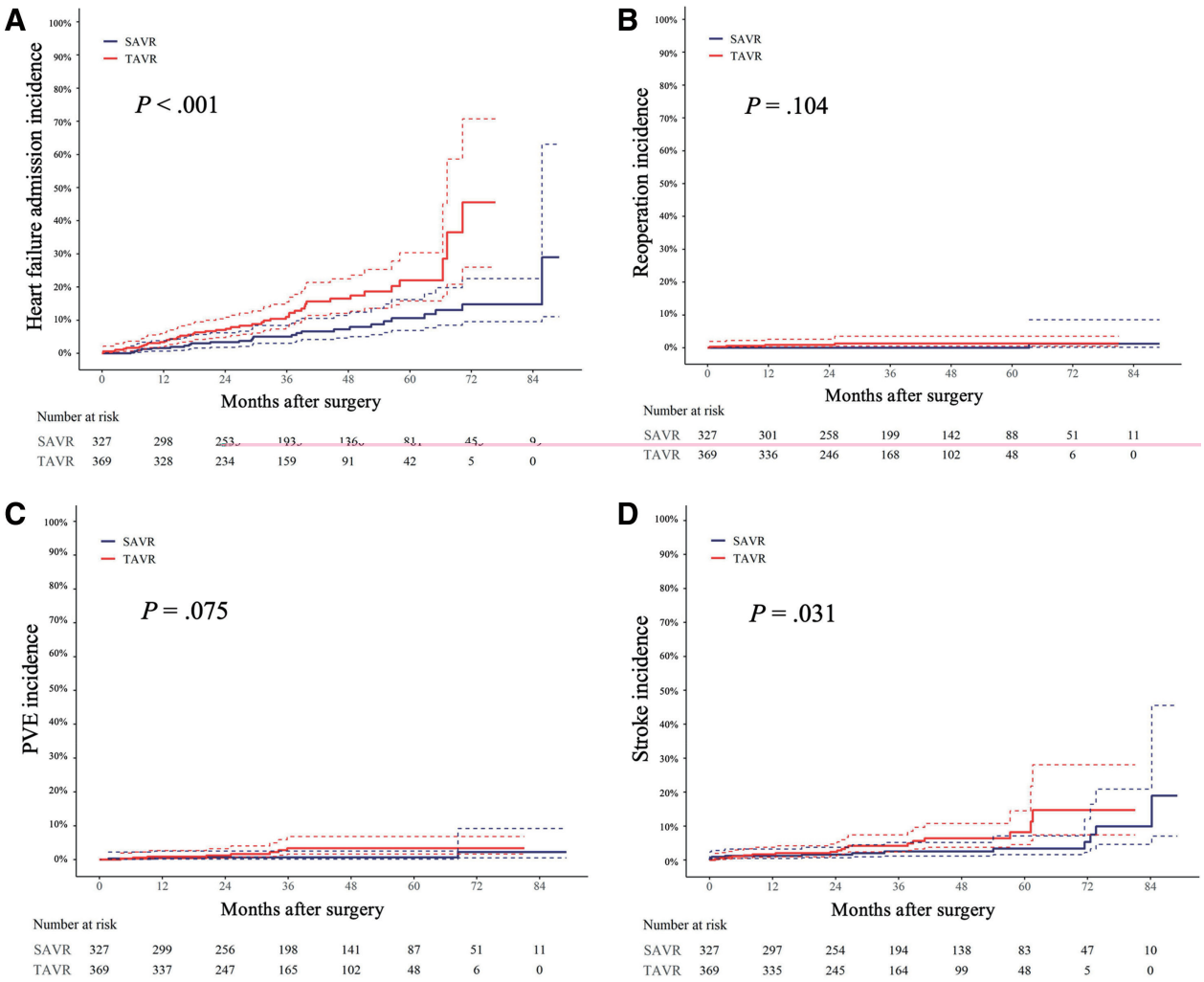

Fig. 6 MACCE outcomes for each group before propensity score matching. Kaplan–Meier curves for cumulative incidence of heart failure admission (**A**), reoperation (**B**), PVE (**C**), and Stroke (**D**). SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; CI: confidence interval; PVE: prosthetic valve endocarditis; MACCE: major adverse cardiac and cerebrovascular events

for low-risk patients around the age of 80. The outcomes of the SAVR and TAVR groups in the present study reflect the performance of isolated SAVR and TF-TAVR, which are commonly encountered in clinical settings for patients around the age of 80. The data provide a clinically relevant, real-world perspective, offering valuable insights for clinicians.

The lower mortality rate observed in isolated SAVR than in the TF-TAVR group may be related to the high incidence of PVL in the TAVR group. To assess the impact of PVL ≥moderate and PVL ≥mild on cardiac mortality, MACCE, and all-cause mortality, each HR was further adjusted by PVL ≥moderate or PVL ≥mild (**Table 5**). Adjusted HRs for cardiac mortality, MACCE, and all-cause mortality decreased with adjustment by PVL ≥moderate. And those adjusted HRs of PVL ≥moderate were: 12.58 (95% CI, 3.86–41.02; P <0.001), 4.41 (95% CI, 2.33–8.34; P <0.001), and 6.23 (95% CI, 1.69–23.06; P = 0.006), respectively. Adjustment by PVL ≥mild also showed a similar reduction in those HRs, although HR of PVL ≥mild itself was not significant. TAVR has made notable advancements in the degree and incidence of PVL with various device improvements, especially in the incidence of PVL ≥moderate, which has decreased significantly. However, the incidence of PVL ≥mild is still 14.5–29.1%.[12,13] Not only PVL ≥moderate but also PVL ≥mild cannot be ignored as factors affecting postoperative left ventricular (LV) remodeling[11] and long-term outcomes.[14] Consistent with previous findings, the significant HR of PVL ≥moderate for cardiac death and MACCE suggests its involvement in the incidence of these two adverse outcomes. Similarly, the adjusted

Table 5 Five-year outcomes in the propensity-score-matched cohort with an adjusted hazard ratio of paravalvular leak

Outcomes	SAVR (n = 159)		TAVR (n = 159)		Crude HR (95% CI), *P* value	Adjusted HR (95% CI), *P* value *1	Adjusted HR (95% CI), *P* value *2	Adjusted HR (95% CI) of PVL ≥moderate, *P* value *3	Adjusted HR (95% CI), *P* value *4	Adjusted HR (95% CI) of PVL ≥mild, *P* value *5
	No. events	Rate (%/5 years)	No. events	Rate (%/5 years)						
Cardiac mortality	3	1.3	13	18.9	8.99 (2.65–30.48), *P* <0.001	8.89 (2.68–29.53), *P* <0.001	7.50 (2.15–26.09), *P* = 0.002	12.58 (3.86–41.02), *P* <0.001	6.23 (1.69–23.06), *P* = 0.006	2.33 (0.78–7.00), *P* = 0.131
All-MACCE	31	25.1	52	47.0	2.25 (1.47–3.44), *P* <0.001	2.36 (1.54–3.63), *P* <0.001	2.28 (1.49–3.48), *P* <0.001	4.41 (2.33–8.34), *P* <0.001	2.17 (1.40–3.35), *P* <0.001	1.30 (0.77–2.19), *P* = 0.322
All-cause mortality	6	4.2	30	33.9	7.65 (3.11–18.81), *P* <0.001	8.56 (3.41–21.45), *P* <0.001	7.68 (3.01–19.58), *P* <0.001	4.12 (1.70–10.03), *P* = 0.002	6.97 (2.66–18.26), *P* <0.001	1.69 (0.85–3.39), *P* = 0.137
Heart failure admission	19	16.6	23	27.0	1.55 (0.85–2.85), *P* = 0.156	1.63 (0.89–2.99), *P* = 0.116				
Reoperation	0	0.0	4	3.1	Inf	Inf				
PVE	2	1.3	5	5.1	2.75 (0.50–14.96), *P* = 0.242	2.40 (0.42–13.79), *P* = 0.327				
Stroke	7	4.9	5	5.4	1.06 (0.32–3.46), *P* = 0.922	1.05 (0.33–3.32), *P* = 0.935				
PPI	10	8.2	12	7.7	1.29 (0.57–2.90), *P* = 0.546	1.26 (0.57–2.81), *P* = 0.572				

*1: Adjusted with STS score and history of coronary artery disease.

*2: Adjusted with STS score, history of coronary artery disease, and PVL ≥moderate.

*3: Hazard ratio of "PVL ≥moderate" in *2 analysis.

*4: Adjusted with STS score, history of coronary artery disease, and PVL ≥mild.

*5: Hazard ratio of "PVL ≥mild" in *4 analysis.

Results are expressed as median (interquartile range) for quantitative and n (%) for categorical.

P value: Multivariable-adjusted Cox proportional hazards models.

SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; HR: hazard ratio; CI: confidence interval; PVL: paravalvular leak; MACCE: major adverse cardiac and cerebrovascular events; PVE: prosthetic valve endocarditis; PPI: permanent pacemaker implantation; STS: Society of Thoracic Surgeons

HRs for cardiac death and MACCE decreased when adjusted by PVL ≥mild, suggesting its involvement in the occurrence of the events. Moreover, cardiac damage is correlated with LV mass, and post-aortic valve intervention LV mass regression is associated with prognosis.[11] Particularly, SAVR results in greater LV mass regression 1 year after aortic valve intervention than TAVR, with PVL being suggested as a contributing factor.[11] Therefore, the matched cohort was divided into two groups based on postoperative echocardiographic findings: PVL ≥ mild vs. PVL < mild. The PVL ≥ mild group tended to have larger left ventricular end-diastolic diameter (LVDd), higher frequency of tricuspid regurgitation (TR) ≥ mild, and larger LV mass index on postoperative echocardiography (**Supplementary Table S5**). Regarding the 1-year follow-up echocardiography, although the number of patients decreased, the PVL ≥ mild group still showed a tendency toward larger LVDd and larger LV mass index, indicating a worse cardiac condition (**Supplementary Table S6**). It is plausible to infer that postoperative PVL inhibited LV mass regression and deteriorated long-term outcomes, as observed in prior studies. The detailed mechanisms behind the improvement in LV mass regression after aortic valve intervention and the involvement of PVL in LV mass regression remain unclear and should be explored in future research endeavors.

While the STS score is reported to reflect long-term prognosis,[15,16] it is fundamentally an evaluation of perioperative performance. In recent low-risk trials, including the present study,[1–5] the STS score has been used for patient stratification. However, in actual cardiac surgery, stratifying patients based on the STS score to determine the treatment approach is difficult. Regardless of the decision for surgery, patient-specific discussions led by a heart team, which includes experienced cardiac surgeons, become even more crucial. Based on the findings of this study, isolated SAVR for low-risk patients with severe AS is suggested to avoid cardiac mortality and MACCE, potentially improving long-term outcomes. High-quality aortic valve therapy that not only avoids PVL and PPI but also considers the possibility of additional interventions is believed to contribute to the improvement in prognosis and lifetime management for patients with severe AS.

This study has several limitations. First, it is not a prospective intervention study. In addition, being a multicenter observational study introduces the possibility of unmeasured or unmatched confounding factors. Specifically, frailty assessment in this study only included albumin levels, lacking evaluation of physical functions such as clinical frailty score and walking speed. Frailty is an important factor that influences the decision-making process for the surgical approach, and there is a possibility that the bias introduced by the heart team's selection of the surgical approach has not been fully eliminated. To resolve the above, further long-term follow-up studies with a larger number of patients and prospective trials of isolated SAVR vs. TF-TAVR are needed. Nevertheless, no studies are comparing the results of isolated SAVR vs. TF-TAVR in surgically low-risk patients with severe AS. Therefore, the findings of this study will have a significant impact on treatment choices for severe AS.

Conclusion

In low-risk patients (STS score <4%) with severe AS aged 65–89 years, isolated SAVR demonstrated a significant reduction in the incidence of cardiac death, MACCE (including all-cause mortality), and PVL. These findings suggest that for individuals in this age population who do not require intervention other than severe AS, isolated SAVR stands out as a viable treatment option. TAVR should be chosen carefully in this subset.

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Declarations

Ethics approval statement

Osaka University Hospital Clinical Research Ethics Committee approved this study and publication of data

(approval number: 20222(T2); approval date: December 15, 2021).

Informed consent statement

Informed consent was obtained from the patients.

Funding statement

None declared.

Data availability statement

The authors declare that all data in this article are available within the article.

Author contributions

KH wrote the manuscript. KM revised the manuscript. All statistical analyses were performed by KP (a biostatistician). KH, KM, KY, and AK collected the data. KS and SM supervised and validated the manuscript.

Disclosure statement

The authors declare that they have no conflict of interest.

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