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Clinical Research

Mechanical versus Bioprosthetic Aortic Valve Replacement in Patients Aged 50 to 70 Years

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Background: This study compared the outcomes of surgical aortic valve replacement (AVR) in patients aged 50 to 70 years based on the type of prosthetic valve used.
Methods: We compared patients who underwent mechanical AVR to those who underwent bioprosthetic AVR at our institution between January 2000 and March 2019. Competing risk analysis and the inverse probability of treatment weighting (IPTW) method based on propensity score were employed for comparisons.
Results: A total of 1,580 patients (984 patients with mechanical AVR; 596 patients with bioprosthetic AVR) were enrolled. There was no significant difference in early mortality between the mechanical AVR and bioprosthetic AVR groups (0.9% vs. 1.7%, p=0.177). After IPTW adjustment, the risk of all-cause mortality was significantly higher in the bioprosthetic AVR group than in the mechanical AVR group (hazard ratio [HR], 1.39; 95% confidence interval [CI], 1.07–1.80; p=0.014). Competing risk analysis revealed lower risks of stroke (sub-distributional hazard ratio [sHR], 0.44; 95% CI, 0.28–0.67; p<0.001) and anticoagulation-related bleeding (sHR, 0.35; 95% CI, 0.23–0.53; p<0.001) in the bioprosthetic AVR group. Conversely, the risk of aortic valve (AV) reintervention was higher in the bioprosthetic AVR group (sHR, 6.14; 95% CI, 3.17–11.93; p<0.001).
Conclusion: Among patients aged 50 to 70 years who underwent surgical AVR, those receiving mechanical valves showed better survival than those with bioprosthetic valves. The mechanical AVR group exhibited a higher risk of stroke and anticoagulation-related bleeding, while the bioprosthetic AVR group showed a higher risk of AV reintervention.

Keywords: Aortic valve replacement, Middle aged, Prosthetic valve, Mechanical valve, Bioprosthesis

Introduction

Aortic valve replacement (AVR) is the established treatment for severe aortic valve (AV) disease [1]. When performing AVR, the choice of prosthetic valve type should be based on the individual patient's clinical condition and preferences [2,3]. Among various factors, the patient's age is considered the most important. While a bioprosthetic valve is generally preferred for elderly patients with a shorter life expectancy and comorbidities that contraindicate long-term anticoagulation, a mechanical valve has traditionally been chosen for young patients due to its long-term durability.

However, there has been a recent increase in the use of bioprosthetic valves in relatively young patients [4]. This trend may be attributed to the anticipated option of a trans-catheter valve-in-valve procedure for cases of prosthetic valve failure [5]. The age threshold for the use of a mechanical valve is not clearly defined, as exemplified by the differing guidelines from Europe and the United States. The European guidelines recommend the use of a mechanical valve in patients aged <60 years [6], while the US guidelines advocate a more liberal use of bioprosthetic valves, leaving a gray zone between the ages of 50 and 65

years [7]. Moreover, the complexity surrounding the choice of prosthetic valves is further compounded by the recent favorable clinical outcomes of mechanical valves in this middle-aged group [8].

In this context, this study aimed to evaluate the early and long-term clinical outcomes of patients aged 50 to 70 years who underwent AVR, according to the type of prosthetic valve used.

Methods

Study cohort

We searched the Institutional Cardiac Surgery Database to identify patients aged 50 to 70 years who had undergone a first-time isolated surgical AVR without other concomitant valve surgery, using either a mechanical or bioprosthetic valve between January 2000 and March 2019. The following exclusion criteria were applied to yield a patient cohort with reasonable comparability: (1) a history of previous prosthetic valve replacement, (2) concomitant aortic root replacement, and (3) AVR due to infective endocarditis or acute type A aortic dissection (Fig. 1). Patients who underwent AVR with the following concomitant surgical procedures were included: coronary artery bypass grafting (CABG), ascending aorta or hemi-arch replacement, simple congenital heart defects repair, and surgical atrial fibrillation ablation.

The choice between a mechanical or bioprosthetic valve was primarily made by patients and their families following a thorough discussion with the operating surgeon. This decision considered the patient's comorbidities, their preference regarding the use of anticoagulation, and the risk of AV reintervention. The study protocol was approved by the institutional review board of Asan Medical Center (approval number: 2020-0122; date of approval: 2020-02-04). The requirement for informed patient consent was waived considering the retrospective nature of the study.

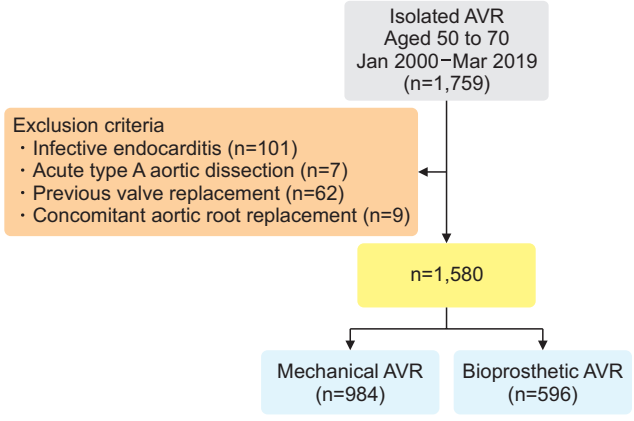

Fig. 1. Patient selection flow diagram for a study comparing prosthetic types. AVR, aortic valve replacement.

Outcomes of interest and clinical follow-up

The primary outcome of interest was all-cause mortality. The secondary outcomes of interest were early postoperative complications, stroke, anticoagulation-related bleeding, AV reintervention, operated valve endocarditis, and rehospitalization for cardiovascular causes. The definition of each outcome utilized the endpoint definitions from the Valve Academic Research Consortium 3 (VARC-3): Updated Endpoint Definitions for Aortic Valve Clinical Research for clear and homogenous reporting [7]. Clinical follow-up data were obtained until July 31, 2023. Vital status data were validated using the database of the National Health Insurance System of South Korea.

Statistical analysis

Continuous variables were expressed as means±standard deviations. Categorical variables were described as frequencies with percentages. Intergroup differences in the baseline characteristics were compared using Student t-tests for continuous variables and the chi-square test or Fisher exact test for categorical variables.

To address differences in the baseline and operative profiles between the mechanical and bioprosthetic AVR groups, inverse-probability-of-treatment weighting (IPTW) based on propensity score (PS) modeling was performed. The PS was defined as the probability of a patient undergoing AVR with a bioprosthetic valve based on their baseline and operative profiles. The PS was estimated using logistic regression analysis incorporating all covariates listed in Table 1 and Table 2 except cardiopulmonary bypass (CPB) time and aorta cross-clamping (ACC) time. The balance of the covariates was assessed by the standardized mean difference, with a difference of ≤10% considered an ideal balance, and a difference of ≤15% a reasonable balance [9].

For analysis of all-cause mortality, the IPTW-adjusted Cox proportional hazard model was utilized to compute hazard ratios (HRs) with 95% confidence intervals (CIs). The proportional hazard assumption was tested using Schoenfeld residuals. Other time-related secondary outcomes of interest were analyzed using a competing risk model including all-cause mortality as a competing risk. A

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Table 1. Baseline patient characteristics according to type of prosthetic valve used in AVR

Characteristic	Original				IPTW		
	Mechanical AVR (n=984)	Bioprosthetic AVR (n=596)	p-value	SMD (%)	Mechanical AVR (n=984)	Bioprosthetic AVR (n=596)	SMD (%)
Baseline demographics							
Age (yr)	59.8±5.2	65.5±4.0	<0.001	125.1	61.7±5.3	62.4±5.4	12.5
Female	376 (38.2)	236 (39.6)	0.621	2.8	38.1	39.0	1.9
Body mass index (kg/m^2)	24.6±3.2	24.5±3.3	0.565	3.0	24.5±3.1	24.4±3.2	4.2
Baseline comorbidities							
Hypertension	503 (51.1)	332 (55.7)	0.086	9.2	53.4	52.0	2.8
Diabetes mellitus	171 (17.4)	151 (25.3)	<0.001	19.5	19.5	18.5	2.5
Dyslipidemia	354 (36.0)	233 (39.1)	0.234	6.4	36.7	36.9	0.3
eGFR <30 mL/min/1.73 m^2	23 (2.3)	42 (7.0)	<0.001	22.4	3.9	3.9	<0.1
Dialysis	16 (1.6)	33 (5.5)	<0.001	21.2	2.4	3.1	4.3
Stroke or TIA	34 (3.5)	40 (6.7)	0.004	14.9	4.8	4.9	0.5
Coronary artery disease	160 (16.3)	141 (23.7)	<0.001	18.6	18.8	20.3	3.8
Previous PCI	35 (3.6)	39 (6.5)	0.009	13.7	4.0	4.1	0.6
Atrial fibrillation	86 (8.7)	52 (8.7)	1.000	0.1	8.6	7.7	3.3
Chronic lung disease	130 (13.2)	74 (12.4)	0.704	2.4	14.0	12.0	6.2
NYHA fc III or IV	204 (20.7)	127 (21.3)	0.834	1.4	21.1	18.8	5.7
Previous cardiac surgery	25 (2.5)	7 (1.2)	0.092	10.1	2.2	2.2	0.2
Hemoglobin (g/dL)	13.4±1.6	12.8±1.7	<0.001	35.2	13.2±1.7	13.0±1.6	9.3
AV pathology			0.002	18.3			2.8
Stenosis	589 (59.9)	379 (63.6)			61.5	62.7	
Insufficiency	256 (26.0)	112 (18.8)			24.2	23.7	
Steno-insufficiency	139 (14.1)	105 (17.6)			14.3	13.6	
Echocardiographic data							
Bicuspid AV	567 (57.6)	267 (44.8)	<0.001	25.9	53.5	51.5	4.0
Rheumatic pathology	75 (7.6)	40 (6.7)	0.565	3.5	7.5	7.0	1.7
LVEF (%)	57.3±11.6	57.8±11.9	0.404	4.3	57.6±11.3	58.2±11.3	5.0
LVESD (mm)	36.9±11.4	35.2±10.4	0.004	15.2	36.2±11.1	35.5±10.6	6.5
LVEDD (mm)	55.1±10.6	53.6±9.4	0.005	14.7	54.6±10.2	54.0±9.9	5.6
LA diameter (mm)	41.8±7.4	42.0±7.0	0.481	3.7	41.8±7.2	41.4±7.3	4.8
Peak RV-RA PG (mm Hg)	26.9±9.9	26.9±9.4	0.882	0.8	26.6±9.7	26.3±9.2	3.2
Significant MR[a]	32 (3.3)	23 (3.9)	0.620	3.3	3.5	3.2	1.7
Significant TR[b]	7 (0.7)	10 (1.7)	0.120	8.9	0.7	0.9	1.6

Values are presented as mean±standard deviation, number (%), or % unless otherwise indicated.
AVR, aortic valve replacement; IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; eGFR, estimated glomerular filtration rate; TIA, transient ischemic attack; PCI, percutaneous coronary intervention; NYHA fc, New York Heart Association functional class; AV, aortic valve; LVEF, left ventricle ejection fraction; LVESD, left ventricle end-systolic dimension; LVEDD, left ventricle end-diastolic dimension; LA, left atrium; RV, right ventricle; RA, right atrium; PG, pressure gradient; MR, mitral regurgitation; TR, tricuspid regurgitation.
[a]Moderate to severe mitral regurgitation. [b]Moderate to severe tricuspid regurgitation.

sub-distributional hazard function was generated using the Fine-Gray model. Early postoperative outcomes were evaluated using the logistic regression model. We further evaluated the impact of secondary outcomes on all-cause mortality by incorporating them as a time-varying covariate in the Cox regression model.

For further assessment, subgroup analyses for all-cause mortality using Cox models were conducted to evaluate the impact of prosthesis type based on the predetermined baseline and operative profiles. In addition, to reinforce the robustness of the original analyses, we conducted a sensitivity analysis of the association between mechanical versus bioprosthetic AVR and the primary and secondary outcomes of interest within a narrowed age range of 50 to 65 years.

For all statistical analyses, a p-value <0.05 indicated significance. Statistical analyses were performed using R ver. 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

Table 2. Operative profiles according to type of prosthetic valve used in AVR

Variable	Original				IPTW		
	Mechanical AVR (n=984)	Bioprosthetic AVR (n=596)	p-value	SMD (%)	Mechanical AVR (n=984)	Bioprosthetic AVR (n=596)	SMD (%)
Emergency or urgency	32 (3.2)	14 (2.3)	0.446	6.8	2.8	1.8	6.2
Minimally invasive approach	129 (13.1)	149 (25.0)	<0.001	30.6	17.8	23.2	13.4
CPB time (min)	123.5±55.1	114.3±45.7	0.001	18.2	124.4±54.8	114.9±47.6	18.5
ACC time (min)	77.7±33.7	73.7±30.3	0.018	12.5	78.0±33.7	75.7±32.8	6.7
Concomitant procedure							
CABG	135 (13.7)	113 (19.0)	0.007	14.2	15.2	15.3	0.1
Surgical AF ablation	36 (3.7)	29 (4.9)	0.298	6.0	4.1	4.4	1.2
Ascending aorta replacement	159 (16.2)	66 (11.1)	0.006	14.9	14.2	13.8	1.1
Congenital correction	26 (2.6)	15 (2.5)	1.000	0.8	2.9	4.2	6.8

Values are presented as number (%), %, or mean±standard deviation unless otherwise indicated.
AVR, aortic valve replacement; IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; CPB, cardiopulmonary bypass; ACC, aorta cross-clamping; CABG, coronary artery bypass grafting; AF, atrial fibrillation.

Results

Patient characteristics

Among the 1,759 patients who had undergone isolated AVR, 1,580 were selected and 179 were excluded. Mechanical and bioprosthetic valves were implanted in 984 (62.3%) and 596 (37.7%) patients, respectively (Fig. 1). The baseline characteristics according to prosthetic valve type are summarized in Table 1. Patients in the bioprosthetic AVR group were older than the mechanical AVR group and had a higher prevalence of diabetes mellitus, kidney disease, stroke, and coronary artery disease. Bicuspid AV, however, was more prevalent in the mechanical AVR group.

The operative profiles according to the type of prosthetic valve are summarized in Table 2. A minimally invasive approach was more frequently employed in the bioprosthetic AVR group than in the mechanical AVR group. In the bioprosthetic AVR group, sutureless or rapid deployment (RD) bioprostheses were implanted in 104 patients (Supplementary Table 1). CPB and ACC times were longer in the mechanical AVR group than in the bioprosthetic AVR group. Concomitant CABG was more frequently performed in the bioprosthetic AVR group, while ascending aorta replacement was more commonly performed in the mechanical AVR group.

After adjustments using IPTW, most baseline and operative profiles were well-balanced with the standardized differences <10% for almost all variables, indicating only small differences between the 2 groups (Tables 1, 2).

Clinical outcomes

The incidence of early and long-term clinical outcomes and risk analysis of the 2 groups are summarized in Table 3. Early mortality occurred in 9 (0.9%) and 10 (1.7%) patients in the mechanical and bioprosthetic AVR groups, respectively (p=0.177). The risks of early complications between the 2 groups were comparable in both the original and the IPTW-adjusted cohort.

During a median follow-up period of 9.1 years (interquartile range, 6.0 to 13.4 years), the observed (crude) incidence of all-cause death (2.0% per patient-year [PY] versus 3.6%/PY, p<0.001) and AV reintervention (0.5%/PY versus 0.9%/PY, p<0.001) was significantly higher in the bioprosthetic AVR group than in the mechanical AVR group (Table 3). Among the 76 patients who underwent AV reintervention, 7 (3.3%/PY) in the mechanical AVR group and 19 (13.4%/PY) in the bioprosthetic AVR group died during the follow-up period. In the time-varying Cox analysis, the occurrence of AV reintervention showed a significant association with the increased risk of all-cause mortality (HR, 2.12; 95% CI, 1.40–3.21; p<0.001). However, the incidence of stroke (1.3%/PY versus 0.9%/PY, p=0.025) and anticoagulation-related bleeding (1.5%/PY versus 0.8%/PY, p=0.004) was significantly higher in the mechanical AVR group than in the bioprosthetic AVR group.

After adjustment, the use of a bioprosthetic valve was associated with an increased risk of all-cause death (HR, 1.39; 95% CI, 1.07–1.80; p=0.014) and AV reintervention (sub-distributional HR [sHR], 6.14; 95% CI, 3.17–11.93; p<0.001) (Figs. 2B, 3D). However, using a bioprosthetic valve was associated with a significantly decreased risk of

Table 3. Clinical outcomes in mechanical AVR versus bioprosthetic AVR for patients aged 50 to 70 years (n=1,580)

Outcomes[a]	Original				IPTW			
	No. of events (rate)		OR or HR (95% CI)	p-value	No. of events (rate)		OR or HR/sHR (95% CI)	p-value
	Mechanical AVR (N=984)	Bioprosthetic AVR (N=596)			Mechanical AVR (N=984)	Bioprosthetic AVR (N=596)		
Early outcomes, no. (%)								
Early death	9 (0.9)	10 (1.7)	1.85 (0.75–4.58)	0.177	1.0	1.1	1.19 (0.42–3.33)	0.741
Bleeding requiring exploration	35 (3.6)	27 (4.5)	1.29 (0.77–2.15)	0.330	3.7	3.8	1.05 (0.60–1.83)	0.856
LCOS requiring MCS[b]	11 (1.1)	11 (1.8)	1.66 (0.72–3.86)	0.230	1.1	1.2	1.08 (0.40–2.87)	0.885
Stroke	25 (2.5)	22 (3.7)	1.47 (0.82–2.63)	0.190	2.7	2.7	1.01 (0.53–1.95)	0.966
New onset dialysis	10 (1.0)	6 (1.0)	0.99 (0.36–2.74)	0.985	1.3	0.6	0.48 (0.15–1.59)	0.233
Sternal wound infection	12 (1.2)	8 (1.3)	1.10 (0.45–2.71)	0.830	1.2	1.3	1.14 (0.45–2.90)	0.787
Overall outcomes, no. (%/PY)								
All-cause death	220 (2.0)	167 (3.6)	2.15 (1.74–2.64)	<0.001	2.3	2.9	1.39 (1.07–1.80)	0.014
Stroke	106 (1.3)	32 (0.9)	0.63 (0.43–0.94)	0.025	1.4	0.5	0.44 (0.28–0.67)	<0.001
Anticoagulation-related bleeding	119 (1.5)	31 (0.8)	0.55 (0.37–0.82)	0.004	1.5	0.6	0.35 (0.23–0.53)	<0.001
Operated valve endocarditis	22 (0.3)	14 (0.4)	1.28 (0.66–2.53)	0.464	0.2	0.4	1.31 (0.61–2.82)	0.486
AV reintervention	41 (0.5)	35 (0.9)	2.35 (1.48–3.74)	<0.001	0.4	0.8	6.14 (3.17–11.93)	<0.001
SVD	0	17 (0.5)			0.0	0.4		
Endocarditis	16 (0.2)	13 (0.3)			0.2	0.3		
Pannus	15 (0.2)	1 (0.0)			0.2	0.0		
Others	10 (0.1)	4 (0.1)			0.1	0.1		
Readmission due to cardiac cause	256 (3.6)	118 (3.5)	0.96 (0.77–1.20)	0.710	3.6	3.1	1.30 (0.86–1.97)	0.210

Values are presented as number (%) or number (% per patient-year) unless otherwise indicated. Early outcomes are presented as ORs. Overall outcomes are presented as HRs or sHRs.
AVR, aortic valve replacement; IPTW, inverse-probability-of-treatment weighting; OR, odds ratio; HR, hazard ratio; CI, confidence interval; sHR, sub-distributional hazard ratio; LCOS, low cardiac output syndrome; MCS, mechanical circulatory support; PY, patient-year; AV, aortic valve; SVD, structural valve deterioration.
[a]Outcomes captured using the primary diagnosis during a visit to the emergency department or using any primary or secondary diagnosis during hospitalization. [b]Included extracorporeal membrane oxygenation, intra-aortic balloon pump, and ventricular assist device.

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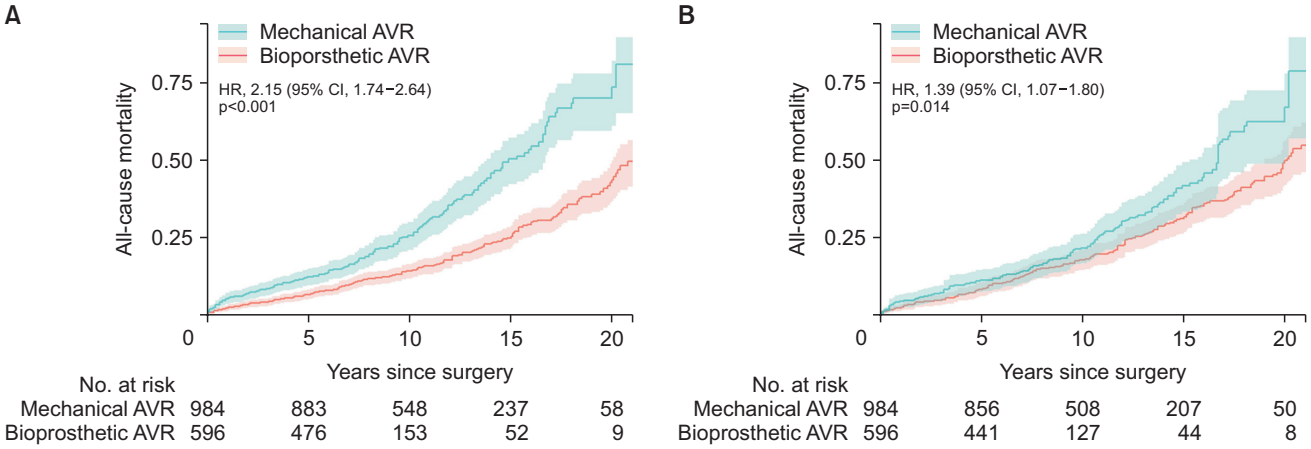

Fig. 2. All-cause mortality after mechanical aortic valve replacement (AVR) versus bioprosthetic AVR in the original cohort (A) and the inverse-probability-of-treatment weighting (IPTW)-adjusted cohort (B). HR, hazard ratio; CI, confidence interval.

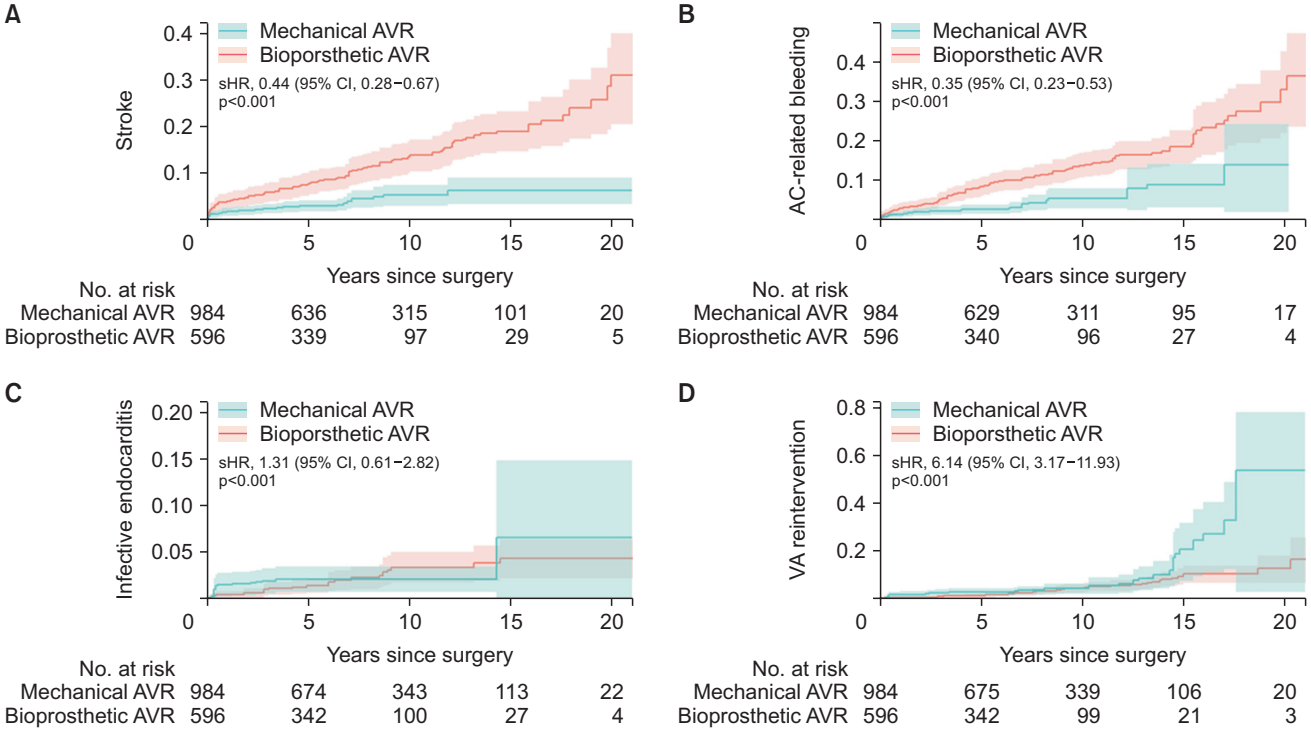

Fig. 3. Time-to-event curves for (A) stroke, (B) anticoagulation (AC)-related bleeding, (C) infective endocarditis, and (D) aortic valve (AV) reintervention in the inverse-probability-of-treatment weighting (IPTW)-adjusted cohorts for a comparison of mechanical and bioprosthetic aortic valve replacement (AVR). sHR, sub-distributional hazard ratio; CI, confidence interval.

stroke (sHR, 0.44; 95% CI, 0.28–0.67; p<0.001) and anticoagulation-related bleeding (sHR, 0.35; 95% CI, 0.23–0.53; p<0.001) (Fig. 3A, B). The risks of endocarditis and readmission due to cardiac causes were comparable between the 2 groups (Table 3).

Subgroup and sensitivity analysis

The impact of prosthetic valve type on all-cause mortality according to various subgroups is demonstrated in Fig. 4. The advantages of mechanical valves over bioprosthetic valves were consistently observed across the various clini-

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Subgroups	No. of patients (%)	HR (95% CI)	p-value	p for interaction
Age (yr)	1,580 (100.0)			0.112
50–60	580 (367)	2.06 (1.04–4.10)	0.039	
61–70	1,000 (63.3)	1.12 (0.86–1.46)	0.398	
Sex				0.454
Male	968 (61.3)	1.47 (1.05–2.07)	0.026	
Female	612 (38.7)	1.25 (0.84–1.86)	0.268	
Hypertension				0.561
No	745 (47.2)	1.46 (0.93–2.30)	0.100	
Yes	835 (52.8)	1.34 (0.99–1.83)	0.059	
Dyslipidemia				0.002
No	993 (62.8)	1.83 (1.34–2.49)	<0.001	
Yes	587 (37.2)	0.78 (0.50–1.20)	0.257	
eGFR (mL/min/1.73 m^2)				0.783
≥30	1,515 (95.9)	1.44 (1.09–1.89)	0.009	
<30	65 (4.1)	1.03 (0.51–2.08)	0.944	
Coronary artery disease				0.501
No	1,279 (80.9)	1.33 (1.00–1.77)	0.050	
Yes	301 (19.1)	1.48 (0.85–2.58)	0.164	
AV etiology				0.599
Stenosis	968 (61.3)	1.44 (1.03–2.02)	0.033	
Insufficiency	368 (23.3)	1.10 (0.63–1.92)	0.732	
Steno-insufficiency	244 (15.4)	1.77 (0.98–3.20)	0.060	
Minimally invasive approach				0.681
No	1,302 (82.4)	1.34 (1.03–1.75)	0.031	
Yes	278 (17.6)	2.77 (0.89–8.55)	0.077	
Concomitant CABG				0.089
No	1,332 (84.3)	1.23 (0.90–1.67)	0.197	
Yes	248 (15.7)	1.91 (1.19–3.07)	0.007	

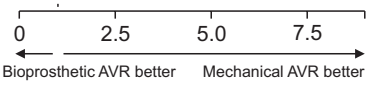

Fig. 4. Hazards of bioprosthetic aortic valve replacement (AVR) for all-cause mortality according to various subgroups in the inverse-probability-of-treatment weighting (IPTW)-adjusted cohort. HR, hazard ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; AV, aortic valve; CABG, coronary artery bypass grafting.

cal and surgical subgroups. Of note, the interaction between all-cause mortality risk and the dyslipidemia subgroup was found.

The results of sensitivity analysis for the baseline clinical and operative characteristics of patients aged 50 to 65 years are presented in Supplementary Tables 2 and 3. The overall outcomes in this cohort remained consistent with those observed in the original cohort (Supplementary Table 4).

Discussion

In this study, we observed that patients aged 50 to 70 years who underwent surgical AVR with a mechanical valve exhibited superior survival rates compared to those who received a bioprosthetic valve. Meanwhile, patients in the mechanical AVR group showed a lower risk of AV reintervention but a higher risk of stroke and anticoagulation-related bleeding than those in the bioprosthetic AVR group.

Among numerous studies comparing the clinical outcomes of mechanical and bioprosthetic AVR in middle-aged patients, some studies found that long-term survival was significantly greater with mechanical AVR than bioprosthetic AVR [3,8,10-17], whereas others found no significant survival difference [18-21]. The most recent meta-analysis, which included 22 publications and involved 32,298 patients, reported greater long-term survival with mechanical AVR than bioprosthetic AVR among individuals aged 50 to 70 years [13]. However, they also reported that when they reduced the upper limit of the age range to 65 years, the survival benefit of the mechanical valve disappeared. A nationwide cohort study in Korea also demonstrated that the long-term survival benefit associated with

mechanical prostheses versus bioprostheses persisted until the age of 65 years in AVR [8]. In alignment with these previous studies, our study showed a superior survival benefit associated with the use of mechanical valves compared to bioprosthetic valves, notably persisting within a subset of patients aged 50–65 years (Supplementary Table 4).

In the context of higher survival rates in the mechanical AVR group, the risk of each secondary outcome was analyzed. Our study reconfirmed the findings of previous studies that showed a higher risk of AV reintervention in patients who underwent bioprosthetic AVR [10,12,14,15,17,19,20,22-24] and an increased risk of bleeding related to long-term anticoagulation in those who underwent mechanical AVR [12,15,17,19-21] (Table 3, Fig. 3). Given the significant association between AV reintervention and an increased risk of all-cause mortality (HR, 2.12; 95% CI, 1.40–3.21; p<0.001), the notably higher incidence of AV reintervention (sHR, 6.14; 95% CI, 3.17–11.93; p<0.001) may have contributed to the increased risk of all-cause mortality in the bioprosthetic AVR group. Of note, we observed a sharp increase in AV reintervention starting approximately 15 years after bioprosthetic AVR (Fig. 3D), which aligns with previous studies that reported a durability of ≥15 years for bioprosthetic valves [25-27]. Consequently, the mean age at the time of AV reintervention was significantly higher in the bioprosthetic AVR group than the mechanical AVR group (72.8±6.4 years verse 67.3±7.0 years, p=0.001) with a higher incidence of early mortality (20.0% versus 7.3%).

In the present study, there was a significantly higher incidence of stroke associated with mechanical AVR (Fig. 3A). Among the comparative studies analyzing valve types in middle-aged AVR, only a few reported a significant difference in the occurrence of stroke [12,13,15,18,20,24,28-30]. Stroke is a devastating complication that may occur early or late after prosthetic valve replacement and results from embolism, intracranial hemorrhage, or both [31]. Considering the higher incidence of anticoagulation-related bleeding in our mechanical AVR group, stroke due to hemorrhage might have occurred more frequently in the mechanical AVR group than in the bioprosthetic AVR group. Notably, more patients underwent concomitant CABG in the bioprosthetic AVR group than in the mechanical AVR group. Since postoperative treatment of patients undergoing CABG includes antithrombotic medication, this difference might have affected the outcomes related to stroke risk or anticoagulation-bleeding. Nonetheless, the survival advantage favoring mechanical valves was observed across the subgroups with and without CABG (Fig. 4). In addition, a decreased risk of anticoagulation-related bleeding and stroke related to the use of bioprosthetic valves persisted within the subgroup of patients without concomitant CABG (Supplementary Tables 5–7).

A rising trend in the use of bioprosthetic valves in younger patients [4] was also mirrored in the increased use of these valves at our institution (Supplementary Fig. 1). Several factors have influenced this increase in the use of bioprosthetic valves: anticipated avoidance of anticoagulation, transcatheter valve-in-valve options in cases of structural valve degeneration, and the introduction of new technologies such as sutureless or RD prostheses [32]. Our institution has also witnessed a concurrent increase in the use of sutureless/RD prostheses, correlating with shorter ACC and CPB times, and a greater use of minimally invasive approaches within the bioprosthetic AVR group (Supplementary Table 1). However, our study found that mechanical valves offered superior long-term survival in patients aged between 50 and 70 years. Therefore, caution is warranted when selecting prosthetic valve types for individuals in this middle-aged group. Alternatively, transcatheter valve-in-valve interventions for bioprosthetic valve failure have shown lower procedure-related mortality and morbidity compared to reoperative surgical AVR [5]. This suggests a potential improvement in the long-term outcomes associated with bioprosthetic valves, prompting the need for further research in this area.

This study had several limitations. First, this was an observational retrospective study that primarily relied on IPTW and regression adjustment to address the concern of selection bias. Second, since this was a single-center study, caution is essential when applying the conclusions of this study to other centers. Finally, the enrollment period for this study was from 2000 to 2019, and it should be noted that there have been improvements in surgical techniques and overall patient care during this period. This should be considered when interpreting the results.

In conclusion, among patients aged 50 to 70 years who underwent surgical AVR, the use of mechanical valves was associated with lower all-cause mortality than bioprosthetic valves. However, the mechanical AVR group showed a higher risk of stroke and anticoagulation-related bleeding than the bioprosthetic AVR group. Conversely, the use of bioprosthetic valves correlated with an increased risk of AV reintervention.

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Conflict of interest

Joon Bum Kim is an associate editor and Ho Jin Kim is an editorial board member of the journal. Both were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflict of interest relevant to this article was reported.

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Supplementary materials

Supplementary materials can be found via https://doi.org/10.5090/jcs.23.143. **Supplementary Table 1**. Operative profiles in the bioprosthetic AVR group: conventional versus sutureless/RD valve. **Supplementary Table 2**. Baseline characteristics according to prosthetic valve type in patients aged 50 to 65 years. **Supplementary Table 3**. Operative profiles according to prosthetic valve type in AVR patients aged 50 to 65 years. **Supplementary Table 4**. Clinical outcomes of mechanical versus bioprosthetic AVR groups in patients aged 50 to 65 years. **Supplementary Table 5**. Baseline characteristics according to prosthetic valve type in patients without concomitant CABG. **Supplementary Table 6**. Operative profiles according to prosthetic valve type in patients without concomitant CABG. **Supplementary Table 7**. Clinical outcomes of mechanical versus bioprosthetic AVR groups in patients without concomitant CABG. **Supplementary Fig. 1**. Number of isolated aortic valve replacements (AVRs) per year in patients aged 50 to 70 years.

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