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의학박사 학위논문

대동맥판막 및 승모판막 치환술 시
판막유형 선택의 기준 연령 조사를 위한
국민건강보험공단 자료를 활용한 국가 코호트 연구

**A Nationwide Cohort Study to Explore
Reference-Ages for Selecting Prosthesis Types
for Heart Valve Replacement**

울산대학교 대학원

의학과

옥유정

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이 논문을 의학박사학위 논문으로 제출함

2022년 8월

울산대학교 대학원

의학과

옥유정

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Abstract

Background: Estimated life expectancy is the main determinant to select prosthetic types in heart valve replacement surgeries, with patient's age being the only objectifiable figure that can be used as a reference-indicator, however, there still are not enough data to suggest optimal age-cutoffs. This study sought to explore the age-dependent survival-hazard functions of the prosthesis-type in aortic valve replacement (AVR) or/and mitral valve replacement (MVR) using a national administrative claims database.

Methods: From the Korean National Health Insurance Service database, the data of 24,374 patients who underwent AVR or/and MVR from 2003 to 2018 were retrieved (11993 AVR; 8911 MVR; 3470 AVR+MVR). In the inverse-probability-weighted cohort, an age-stratified analysis was conducted to compare the risk of mortality, reoperation, thromboembolism, and bleeding between mechanical and biologic prostheses.

Results: Following AVR, bio-prosthesis was associated with significantly greater risks of mortality than those of mechanical prosthesis in patients aged <55 years (adjusted hazard ratio [aHR], 2.18; P=0.002) and 55 to 64 years (aHR, 1.29; P=0.037), but the risk of mortality reversed in patients aged \geq 65 years (aHR, 0.77; P=0.001). For MVR, the risk of mortality was also greater with bio-prosthesis in patients aged 55 to 69 years (aHR, 1.22; P=0.016), but there was no difference for patients \geq 70 years (P=0.687). The risk of reoperation was consistently higher with bio-prosthesis regardless of valve position in all age strata; however, the risks of thromboembolism and bleeding were higher in elderly patients after mechanical AVR, with no differences after MVR in all age strata.

Conclusions: Compared to bioprosthetic valve replacement, the long-term survival benefit associated with a mechanical prosthesis persisted until 65 years of age in AVR, and 70 years in MVR.

Key words: aortic valve replacement, mitral valve replacement, biologic prosthesis, mechanical prosthesis, age

Abstract word count: 276

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Introduction

Prosthetic valve replacement is the gold standard for the treatment of severe, symptomatic valvular heart disease (1). The choice of prosthesis type (biologic vs. mechanical) is influenced by several factors, including the patient's age, lifestyle, and preference, and the trade-off dynamics between the risks associated with anticoagulation and the potential for re-intervention (2-4). The individual patient's value and desire may be the backbone of the shared decision-making process for the prosthesis choice; however, the patient's age is the only objectifiable figure that medical-care providers can present as a reference-indicator among several factors that can influence the decision.

The latest American and European guidelines for valvular heart disease have suggested an age-criteria for biologic or mechanical prosthesis according to valve position (aortic or mitral) in the form of Class 2a recommendations (5, 6). Owing to the lack of sufficiently powered randomized trials, recent large registry-type observational studies have been the major basic evidence for these practice guidelines (7-10). Despite the substantial overlap of based evidences, these two practice guidelines have taken different positions with regards to the selection of prosthesis type, with a more forward stance on the use of bio-prosthesis in the American College of Cardiology/American Heart Association (ACC/AHA) guidelines (5, 6). The ACC/AHA guidelines flexibly individualize the choice of either a mechanical or bioprosthetic aortic valve replacement (AVR) for patients 50 to 65 years of age, whereas the guidelines from the European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) recommends mechanical prosthesis up to 60 years of age in AVR. The age-criteria disaccord between these authoritative guidelines leaves this issue to remain uncertain and arbitrary.

Therefore, the accumulation of real-world experiences based on a sufficiently large-sized cohort may help shape a balanced perspective on this issue. In this regard, this study aimed to compare the nationwide outcomes of mechanical versus bio-prosthesis for aortic- or mitral-valve replacement, using the national administrative database of the National Health Insurance Service (NHIS) linked with real-time vital status information derived from Statistics Korea (11-13).

Methods

Data Sources

The Republic of Korea has a national, mandatory healthcare insurance system called the NHIS that is a single-payer program covering 97% of the Korean population (52 million in 2019) (12). The NHIS has established a public nationwide claims database (National Health Information Database) that includes the socio-demographics, vital statistics, national health screening data (such as health behaviors and laboratory tests), and healthcare data with diagnosis, procedures, and prescriptions (11). Diagnosis was coded according to the International Classification of Disease, 10th Revision (ICD-10). Since the National Health Insurance program is compulsory for all Korean citizens and the NHIS is the sole payer of this program, complete long-term follow-up of all the patients is feasible, even if the patient receives subsequent treatment at another hospital, regardless of the region (14). This study was approved by the institutional review board of Asan Medical Center, Seoul, Korea, and exempting the study from requiring individual patients' consents. All of the data from the NHIS were anonymized before being provided to the authors (IRB number: 2020-0588).

All baseline comorbidities of this cohort were identified by extracting ICD-10 codes which were recorded twice or more individually within 1 year of surgery (Supplementary Table 1). A history of operative profiles was also identified by extracting the conforming NHIS claim codes for each patient (Supplementary Table 2). We included the institution volume for cardiac surgery, and health screening data for inclusive comparisons. Charlson comorbidity index and CHA2DS2-VASc score were assessed from the baseline comorbidities.

Study Population

This study included patients (>40 and ≤80 years) who underwent AVR or mitral valve replacement (MVR) between January 2003 and December 2018. The exclusion criteria for patients were as follows: (A) redo aortic/mitral valve surgery, (B) concomitant pulmonic/tricuspid valve replacement, (C) concomitant aorta surgery, (D) preoperative mechanical circulatory support or mechanical ventilation, (E) concomitant aortic/mitral valve repair, (F) simultaneous AVR and MVR with different types of prostheses, and (G) concomitant cardiac tumor surgery (Figure 1). In this study, patients who received isolated AVR or MVR as well as those who received both AVR and MVR simultaneously (double valve replacement, DVR) were designated as the subject of investigation.

An age-stratified analysis was conducted. For the cases of AVR and DVR, patients were subcategorized by age into 40 to 54 years, 55 to 64 years, and 65 to 79 years; and for MVR, they were subcategorized into 40 to 54 years, 55 to 69 years, and 70 to 79 years. The age strata for AVR and DVR were chosen

to be consistent with recommendations from previous randomized trials and relevant studies. For the analysis of MVR, the age strata were chosen not only considering the available guidelines and previous studies, but also the result of exploratory analyses on age-dependent survival-hazard functions performed at the beginning of this study.

Study Endpoints

Intravenous The primary endpoint was all-cause mortality during the follow-up period after receiving the prosthetic valves. The secondary endpoints were the valve-related events including the incidence of reoperation, systemic thromboembolism (including ischemic stroke), and major bleeding (including hemorrhagic stroke) (Supplementary Table 3).

Data on vital status were compiled and linked with data from Statistics Korea, through one-by-one match up using the personal ID number. Statistics Korea maintains death and survival information of all legitimate residents of South Korea on a real-time basis. Ischemic stroke event was defined as having both an ICD-10 diagnostic code and an NHIS claims code for brain image studies (computed tomography or magnetic resonance image) at the hospital. Major bleeding was defined as (A) hemorrhagic stroke diagnosed with brain image studies, (B) gastrointestinal bleeding, or (C) hemorrhagic events that occurred in unclassified sites (e.g., extracranial, intraocular, intra-articular, and hemothorax) requiring hospitalization.

Statistical analysis

Categorical variables were compared using the χ^2 test and are presented as frequencies and percentages. Continuous variables, expressed as mean \pm standard deviation, were compared using the Student's t-test.

To reduce the potential treatment-selection bias, the inverse probability of treatment weighting (IPTW) method was used based on the propensity score. The propensity scores were estimated with a logistic regression model incorporating all the baseline variables listed in Table 1. The adjustment with IPTW was performed based on the trimmed stabilized weight with robust standard errors, and the baseline profiles were well-balanced with most of the covariates having standardized mean differences of <10%. To assess the age-dependent effects of prosthesis type on mortality, a Cox proportional-hazards model was fit with the use of an interaction term for the age and prosthesis types in the IPTW-adjusted cohort. Linear, quadratic, natural spline, and restricted cubic spline models with the number of knots (3, 4 or 5 knots) function were considered and compared based on the Akaike information criterion. The linear model was chosen as the most suitable.

After inter-group adjustment with the IPTW method, the Cox proportional hazard model was used to compare the risk of all-cause mortality between the mechanical and bioprosthetic groups. The proportional hazards assumption was assessed using the Schoenfeld residual, which yielded no evidence to suggest rejecting the assumption about the long-term outcomes. The risk of time-related outcomes such as reoperation, systemic thromboembolism, and major bleeding events after prosthetic valve replacement were also evaluated after adjustment with the IPTW method, with all-cause mortality as a competing risk (15). Sub-distribution hazards were estimated with the method of Fine and Gray.

For further assessments, subgroup analyses were performed in various baseline risk-groups to compare the outcomes between the mechanical and biologic prosthetic valve replacement in the middle age group (55 to 64 years of age in AVR and 55 to 70 years of age in MVR). For these comparisons, separate IPTW-adjusted cohorts were generated to involve each of the subgroups in an effort to efficiently adjust for selection bias in the relatively small sample within each subgroup.

All reported P-values were two-tailed, and P-values < 0.05 were considered statistically significant. R software, version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) and the SAS Enterprise Guide software version 7.1 (SAS Institute, Inc., Cary, NC) were used for statistical analyses.

Results

Patient characteristics

Among the 39,851 patients who underwent at least one left-sided prosthetic heart valve replacement between 2003 and 2018 in South Korea, a total of 24,374 patients were included in this study after applying the exclusion criteria (Figure 1). AVR/MVR were performed in 11,993 and 8,911 patients, respectively, and 3,470 patients received both aortic and mitral prosthetic valves (DVR). Distributions of patients undergoing valve replacements depending on age are shown in Figure 2.

Baseline and operative characteristics of patients are summarized in Table 1. After adjustment with the IPTW method, most of the covariates in the cases of AVR and MVR were well-balanced between the patients who received biologic versus mechanical prosthesis, throughout the all-age strata (Supplementary Table 4-9). However, in the cases of DVR, there were limitations in obtaining an evenly balanced cohort except for the older age group (>65 years) even after adjustment with the IPTW method because of the relatively small-sized cohort and eccentric use of prosthesis type across age strata (Supplementary Table 10-12).

The number of patients who received bio-prostheses has largely increased through the study period regardless of valve position. For AVR, the use of bio-prostheses increased from 9.8% in the first quartile (2002-2005) to 43.2% in the last quartile (2014-2018) ($P<0.001$); and for MVR, the proportion of bio-prosthesis increased from 16.3% in the first quartile to 35.3% in the last quartile ($P<0.001$).

Mortality after Valve Replacement Surgery

The spline curve of Figure 3 displays the age-dependent relative hazards of bioprosthesis compared to mechanical prosthesis in each valve position. Patient's age was examined as a continuous variable in the IPTW-adjusted cohort. The central adjusted hazard ratio (aHR) line nearly touches the baseline (hazard ratio=1.0) at around 65 years of age for AVR (Figure 3A) while around 70 years for MVR (Figure 3B), suggesting that the survival benefit of mechanical prosthesis may persist to a higher age for the cases of MVR than for those of AVR.

Similarly, in the stratified analysis of AVR according to age strata, the risks of long-term mortality were significantly higher with bio-prosthesis in both the 40 to 54 years (aHR, 2.19; 95% confidence interval [CI], 1.32-3.63; $P=0.002$) and 55 to 64 years (aHR, 1.29; 95% CI, 1.02-1.63; $P=0.04$) age groups, whereas bio-prosthesis was associated with a lower mortality in patients aged 65 to 79 years (aHR, 0.77; 95% CI, 0.66-0.90; $P=0.001$) (Table 2 and Figure 4A).

In cases of MVR, receiving a bio-prosthesis was associated with a significantly higher long-term mortality than receiving a mechanical prosthesis in the age group of 55 to 69 years (aHR, 1.22; 95% CI, 1.04-1.44; P=0.016). However, long-term mortality did not differ between the valve types in patients aged 40 to 54 years (aHR, 1.15; 95% CI, 0.65-2.03; P=0.63) and 65 to 79 years (aHR, 1.06; 95% CI, 0.79-1.42; P=0.69) (Table 3 and Figure 4B). In patients who received both aortic and mitral prostheses, receiving a bio-prosthesis was associated with higher mortality (aHR, 2.02; 95% CI, 1.28-3.19; P=0.002) than receiving a mechanical prosthesis in the age group of 55 to 64 years (Table 4 and Figure 4C), with no significant difference in the other age groups.

Results for all-cause mortality and cardiac mortality were identical in all cohorts except for the <55 years of age group in MVR. There was no significant difference in overall mortality in patients with MVR <55 years of age, but rather a higher risk of mechanical valve in cardiac mortality and a higher risk of tissue valve in non-cardiac death (Supplementary Table 13).

Complications after Valve Replacement Surgery

Reoperation

The cumulative incidence of reoperation was significantly higher in the bio-prosthesis group throughout all age strata regardless of valve position (Table 2-4). The relative hazard of reoperation with bio-prosthesis was more prominent in MVR and DVR (Table 3 and 4). Among the middle age group patients (MVR, 55 to 69 years; DVR, 55 to 64 years) who received bioprosthetic valve replacement, the aHR for reoperation was 7.75 (95% CI, 5.14-11.69; P<0.001) following MVR and 7.13 (95% CI, 3.26-13.18; P<0.001) following DVR, in agreement with significant differences in survival in this age group.

Systemic thromboembolism and Major bleeding

In AVR, the cumulative incidence of systemic thromboembolism was significantly higher with mechanical prosthesis in older age groups (55 to 64 years and 65 to 79 years), but this was not the case in younger patients aged <55 years (Table 2). However, the risk of major bleeding was greater with mechanical AVR only in patients older than 65 years. In the cases of MVR and DVR, there were no differences in the risks of thromboembolism and major bleeding in all age strata (Table 3 and 4).

Subgroup Analyses According to the Risk Profiles

Subgroup risk analyses was conducted for the middle age group (55 to 64 years of age in AVR and 55 to 69 years of age in MVR) (Figure 5). Survival benefits by the mechanical prosthesis were

consistently observed in most of the subgroups (Supplementary Table 14 and 15), and there were no subgroups that benefitted by the use of bio-prostheses in this age group regardless of valve position. Charlson comorbidity index was solely identified as a significant effect modifier in the comparison between mitral biologic and mechanical prostheses (P for interaction=0.04), with a significant survival benefit with mechanical prosthesis in patients with Charlson comorbidity index <2 (hazard ratio, 1.49; 95% CI, 1.16-1.92; P=0.002).

Discussion

In this nationwide analysis over 16 years, the long-term outcomes after receiving either mechanical or biologic prosthesis in aortic- or mitral-valve replacement were evaluated after stratification of the recipient's age group. The survival benefit of mechanical prosthesis as compared to bio-prosthesis was seen up to the age of 65 years in AVR and from 55 to 69 years in MVR. Prosthetic AVR with mechanical prosthesis was associated with lower risks of reoperation throughout all age strata, but greater risks of thromboembolism and bleeding in elderly patients. Likewise, in the cases of MVR and DVR, the risks of reoperation were also greater with bio-prosthesis throughout all age strata, with no differences in the risks of thromboembolism and major bleeding in all age strata. There is a difference in the number of cases accompanied by atrial fibrillation in each patient group (around 5% in the AVR group, around 30-40% in the MVR/DVR group), and the proportion of concomitant ablation also differs (around 5% in the AVR group, over 40% in MVR group, over 30% in DVR group) (Table 1). This suggests that anti-coagulation managements were continued in a significant number of patients who used tissue valves in the MVR/DVR group, and this likely offset the difference in the cumulative incidence of thromboembolism and bleeding in patient with mechanical valve in MVR/DVR group.

Previous studies comparing mechanical versus bioprosthetic AVR have shown discordant results (3, 16, 17). State-wide cohort studies in both New York and California showed no differences in mortality of patients aged 50 to 69 years and 55 to 64 years, respectively (3, 16). However, in a similar analysis with Swedish nationwide registry data involving 1,099 matched-pairs of patients, those aged 50 to 69 years who received mechanical AVR had better long-term survival than those with bio-prostheses (17). The authors attributed the difference between their results and those of the study in New York to the high-quality anticoagulation management in Sweden. A similar explanation may be applied to our findings. In South Korea, the NHIS is mandatory for all legitimate residents and covers almost all major medical practices except for cosmetic procedures or surgeries. Therefore, all expenses related to heart surgery and postoperative anticoagulation management are provided to the insured without significant financial burden. In addition to this, the high population density and high accessibility to medical facilities in Korea may have contributed to high-quality anticoagulation management with very low rates of follow-up losses. In the AVR group, cardiac death had a higher risk for tissue valves, apart from the high rates of mechanical valve-related thromboembolism and bleeding events in patients younger than 65 years of age. This can explain the superiority of valve-related or anticoagulation-related complications management due to the high follow up rate.

In the practice guidelines, the first line of the "prosthetic valve selection" chapter explains the shared decision-making process based on the values and desires of "informed patients" (5). Informed patients

may decide prosthesis types considering the trade-off between the risks of re-intervention and of life-long anticoagulation, based on their value and preference. Although the decision-making process is basically grounded in the patient's desire, an important piece of information offered to patients may be the comparative outcomes of mechanical versus bio-prosthesis in the specific age group that they belong to. Recently, large-sized registry-type data comparable to that of national-level study were analyzed to compare the long-term outcomes after prosthetic AVR or MVR (2, 3, 16). With the use of sophisticated statistical methods, the analyses of a propensity-matched population of patients 50 to 69 years of age who underwent AVR or MVR in New York showed no significant differences in mortality between the two prosthesis types (2, 16). This result was the decisive evidence that the 2017 ACC/AHA focused update lower the age limit for bio-prosthesis, from 60 to 50 years (18). However, a larger-sized cohort study challenged the result of the former study and the 2017 ACC/AHA guideline. This statewide cohort study in California conducted a comparative analysis of the long-term outcomes after mechanical or bioprosthetic valve replacement in 9,942 patients who underwent AVR and 15,505 patients who underwent MVR (3). In this study, the benefit of a mechanical prosthesis remained up to 70 years of age in the mitral position, though the benefit in the aortic position disappeared by 55 years of age. This result brought out the amendment of the ACC/AHA guideline wherein the 2020 ACC/AHA guideline raised the lowest age limit for bioprosthetic MVR from 50 to 65 years (5). However, unlike the ACC/AHA guideline that relaxed the eligibility of bioprosthetic AVR from 50 years of age, the ESC/EACTS guideline still maintains a conservative stance on the use of bio-prostheses with an age limit of 65 and 70 years in aortic- and mitral-valve replacement, respectively (6).

If the value, lifestyle, and preference of the informed patient is the backbone for the choice of prosthetic valve type, the information offered to patients by the medical-care provider may be the cornerstone of the decision. This information should be simple, uncomplicated, and unbiased. The fact that the two most credible and authoritative guidelines in the clinical field provide contradictory recommendations will lead patients as well as medical-care providers to be troubled and indecisive. The ESC/EACTS joint committee judges that there is insufficient high-quality evidence to lower the age cut-off of prosthesis selection at this time (6). Due to the lack of compelling or indisputable evidence on this issue at present, we believe that our current research may be of value in making shared decision between patients and practitioners.

Limitations and Strengths

There In this study, patients who simultaneously received both AVR and MVR were analyzed together for the first time, albeit not to a satisfactory level of statistical power. Due to the eccentric use of prosthesis in patients aged <65 years in this setting, inter-group baseline profile imbalance and selection bias could not be effectively overcome. Therefore, the prominent inter-group divergence of mortality in patients aged 55 to 64 years should be interpreted with caution. Nevertheless, the multiplied risk of reoperation in bioprosthetic double valve replacement compared to that in mechanical prosthesis throughout all the age strata may have noticeable implications.

This study was based on a claims-administrative database for obtaining baseline profiles and outcomes rather than a clinical database. Thus, it may be subject to coding errors and omissions or misclassifications, along with important variables including clinical details such as echocardiography data. As in most retrospective observational studies, treatment not being randomized between groups was a limitation. Despite the use of robust IPTW methods to account for differences between groups, unmeasured confounding factors can still bias the results of the analysis.

In treating valvular heart disease, it has been recognized that there are potential inter-racial or inter-ethnic differences in baseline profile, management, and outcomes (19, 20). In particular, it has been continuously suggested that the target INR (international normalized ratio) after mechanical valve replacement in the Asian population may be different from that of the Western population (21-23). Existing evidence regarding prosthetic valve type selection is primarily grounded on the results of the Western population, with a lack of race-oriented evidence. Since this study was conducted primarily among East Asian populations, the results may not be generalizable to other races, but has a potentially stronger race-specific implication for the East Asian population.

Conclusion

In this nationwide comparison between mechanical and biologic prostheses in aortic- or mitral- valve replacement, the survival benefit up to 65 years of age in the aortic position and 55 to 69 years in MVR was observed with a mechanical prosthesis. The risk of reoperation was greater with bio-prostheses regardless of valve position in all age strata, but it also had a protective effect against thromboembolism or major bleeding after AVR in elderly patients. However, there were no significant differences in the risk of thromboembolism or major bleeding after MVR and DVR in all age strata.

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None.

Compliance with Ethical Standards**Conflict of Interest**

The authors declare that they have no conflicts of interest.

Ethical Approval

This study was approved by the review board at the participating institution.

Informed Consent

For this type of study formal consent is not required.

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Table 1. Baseline and operative characteristics according to the types of prostheses before Inverse Probability Weighting.

Variable	Aortic Valve Replacement				Mitral Valve Replacement				Aortic + Mitral Valve Replacement			
	Mechanical	Biological	P-value	SMD	Mechanical	Biological	SMD	Mechanical	Biological	SMD		
	prosthesis (n = 4825)	prosthesis (n = 7168)			prosthesis (n = 5957)	prosthesis (n = 2954)		prosthesis (n = 2463)	prosthesis (n = 1007)			
Baseline Demographics												
Age, years	57.5±8.0	70.7±6.0	<0.001	1.857	55.2±8.0	68.7±7.2	<0.001	1.77	55.0±7.8	69.3±6.8	<0.001	1.95
Female	1691 (35.0)	3200 (44.6)	<0.001	0.197	350 (58.9)	198(67.2)	<0.001	0.173	1395 (56.6)	595 (59.1)	0.19	0.05
Baseline Comorbidities												
Atrial fibrillation	277 (5.7)	456 (6.4)	0.16	0.026	2242 (37.6)	1204 (40.8)	<0.001	0.064	870 (35.3)	363 (36.0)	0.69	0.015
Hypertension	2563 (53.1)	5154 (71.9)	<0.001	0.396	2909 (48.8)	1954 (66.1)	0.064	0.356	127 0 (51.6)	665 (66.0)	<0.001	0.297
Diabetes mellitus	933 (19.3)	2267 (31.6)	<0.001	0.285	818 (13.7)	811 (27.5)	0.36	0.344	313 (12.7)	237 (23.5)	<0.001	0.284
Dyslipidemia	768 (15.9)	1862 (26.0)	<0.001	0.249	722 (12.1)	533 (18.0)	0.34	0.166	284 (11.5)	189 (18.8)	<0.001	0.203
Chronic kidney disease	200 (4.1)	406 (5.7)	<0.001	0.07	126 (2.1)	148 (5.0)	0.17	0.157	65 (2.6)	50 (5.0)	0.001	0.122
Dialysis	152 (3.2)	235 (3.3)	0.70	0.007	66 (1.1)	80 (2.7)	0.16	0.117	41 (1.7)	33 (3.1)	0.003	0.104
Stroke, TIA or SE	373 (7.7)	954 (13.3)	<0.001	0.183	841 (14.1)	530 (17.9)	0.12	0.104	290 (11.8)	161 (16.0)	0.001	0.122
Ischemic heart disease	1611 (33.4)	3233 (45.1)	<0.001	0.242	1215 (20.4)	917 (31.0)	0.10	0.245	561 (22.8)	319 (31.7)	<0.001	0.201
Myocardial infarction	130 (2.7)	290 (4.0)	<0.001	0.075	149 (2.5)	109 (3.7)	0.25	0.069	60 (2.4)	31 (3.1)	0.28	0.039
Previous PCI	168 (3.5)	550 (7.7)	<0.001	0.183	92 (1.5)	126 (4.3)	0.069	0.163	37 (1.5)	42 (4.2)	<0.001	0.161
Congestive heart failure	1213 (25.1)	2285 (31.9)	<0.001	0.15	2365 (39.7)	1519 (51.4)	0.16	0.237	1042 (42.3)	504 (50.0)	<0.001	0.156
Anemia	438 (9.1)	909 (12.7)	<0.001	0.116	486 (8.2)	403 (13.6)	0.24	0.177	203 (8.2)	134(13.3)	<0.001	0.164
Chronic obstructive pulmonary disease	160 (3.3)	520 (7.3)	<0.001	0.177	180 (3.0)	216 7.3)	0.18	0.195	67 (2.7)	70 (7.0)	<0.001	0.198
Asthma	518 (10.7)	1253 (17.5)	<0.001	0.195	817 (13.7)	605 (20.5)	0.20	0.18	288 (11.7)	224 (22.2)	<0.001	0.284
Peripheral vascular disease	256 (5.3)	629 (8.8)	<0.001	0.136	263 (4.4)	209 (7.1)	0.18	0.115	106 (4.3)	69 (6.9)	0.002	0.111
Previous cardiac surgery	19 (0.4)	43 (0.6)	0.12	0.029	23 (0.4)	22 (0.7)	0.12	0.048	3 (0.1)	6 (0.6)	0.02	0.079
Previous cancer	227 (4.7)	683 (9.5)	<0.001	0.188	200 (3.4)	209 (7.1)	0.048	0.168	68 (2.8)	70 (7.0)	<0.001	0.196

Charlson comorbidity index			<0.001	0.399			0.17	0.488			<0.001	0.449
0	1557 (32.3)	1232 (17.2)	<0.001	0.459	1617 (27.1)	376 (12.7)	0.49	0.507	686 (27.9)	168 (16.7)	<0.001	0.474
1	1293 (26.8)	1549 (21.6)			1700 (28.5)	668 (22.6)	0.51		781 (31.7)	225 (22.3)		
2	837 (17.3)	1479 (20.6)			1196 (20.1)	628 (21.3)			463 (18.8)	210 (20.9)		
≥ 3	728 (15.1)	1761 (24.6)			1051 (17.6)	798 (27.0)			395 (16.0)	260 (25.8)		
≥ 5	410 (8.5)	1147 (16.0)			393 (6.6)	484 (16.4)			138 (5.6)	144 (14.3)		
Year of surgery			<0.001	0.39			<0.001	0.286			<0.001	0.365
2002 to 2005	1024 (21.2)	701 (9.8)			1604 (26.9)	481 (16.3)			734 (29.8)	173 (17.2)		
2006 to 2009	1125 (23.3)	1369 (19.1)			1461 (24.5)	720 (24.4)			628 (25.5)	220 (21.8)		
2010 to 2013	1255 (26.0)	2001 (27.9)			1325 (22.2)	711 (24.1)			509 (20.7)	252 (25.0)		
2014 to 2018	1421 (29.5)	3097 (43.2)			1567 (26.3)	1042 (35.3)			592 (24.0)	362 (35.9)		
Cumulative hospital volume for cardiac surgery			<0.001	0.156			<0.001	0.291			<0.001	0.255
< 250 cases	1255 (26.0)	1923 (26.8)			1789 (30.0)	1014 (34.3)			511 (20.7)	278 (27.6)		
250 to 1000 cases	1313 (27.2)	2009 (28.0)			1549 (26.0)	968 (32.8)			668 (27.1)	298 (29.6)		
1000 to 3000 cases	1275 (26.4)	2181 (30.4)			1628 (27.3)	733 (24.8)			841 (34.1)	327 (32.5)		
≥ 3000 cases	982 (20.4)	1055 (14.7)			991 (16.6)	239 (8.1)			443 (18.0)	104 (10.3)		
Infective endocarditis	697 (14.4)	692 (9.7)	<0.001	0.148	775 (13.0)	484 (16.4)	<0.001	0.095	363 (14.7)	205 (20.4)	<0.001	0.148
Congestive heart failure	1242 (25.7)	2017 (28.1)	0.004	0.054	2145 (36.0)	1275 (43.2)	<0.001	0.147	945 (38.4)	462 (45.9)	<0.001	0.153
Health Screening Data												
Body Mass Index, kg/m ²	24.4±3.2	24.3±3.3	0.16	0.031	23.6±3.2	23.5±3.3	0.34	0.028	23.3±3.0	23.2±3.2	0.85	0.009
< 18.5	49 (1.0)	138 (1.9)			124 (2.1)	75 (2.5)			59 (2.4)	40 (4.0)		
≥ 18.5 and < 23	1046 (21.7)	1636 (22.8)			1419 (23.8)	755 (25.6)			597 (24.2)	248 (24.6)		
≥ 23 and < 25	818 (17.0)	1266 (17.7)			824 (13.8)	430 (14.6)			381 (15.5)	175 (17.4)		
≥ 25 and < 30	1168 (24.2)	1840 (25.7)			966 (16.2)	500 (16.9)			346 (14.0)	133 (13.2)		
≥ 30	164 (3.4)	261 (3.6)			119 (2.0)	64 (2.2)			30 (1.2)	16 (1.6)		
Not available	1580 (32.7)	2027 (28.3)			2505 (42.1)	1130 (38.3)			1050 (42.6)	395 (39.2)		
Systolic blood pressure, mmHg	126.5±17.0	129.9±17.3	<0.001	0.2	119.3±16.2	124.3±16.8	<0.001	0.305	119.9±15.8	124.8±17.9	<0.001	0.292

< 120	1024 (21.2)	1280 (17.9)		0.171	1712 (28.7)	658 (22.3)		0.243	672 (27.3)	209 (20.8)		0.243
≥ 120 and < 140	1536 (31.8)	2465 (34.4)			1375 (23.1)	836 (28.3)			587 (23.8)	291 (28.9)		
≥ 140	685 (14.2)	1381 (19.3)			365 (6.1)	326 (11.0)			153 (6.2)	112 (11.1)		
Not available	1580 (32.7)	2042 (28.5)			2505 (42.1)	1134 (38.4)			1051 (42.7)	395 (39.2)		
Diastolic blood pressure, mmHg	78.89±11.1	75.8±11.1	0.71	0.0008	74.3±11.2	75.3±11.1	0.002	0.089	72.4±10.6	73.4±10.9	0.061	0.09
< 80	1762 (36.5)	2900 (40.5)		0.105	2191 (36.8)	1061 (35.9)		0.115	961 (39.0)	390 (38.7)		0.108
≥ 80 and < 90	1074 (22.3)	1554 (21.7)			937 (15.7)	544 (18.4)			354 (14.4)	165 (16.4)		
≥ 90	409 (8.5)	672 (9.4)			324 (5.4)	215 (7.3)			97 (3.9)	57 (5.7)		
Not available	1580 (32.7)	2042 (28.5)			2505 (42.1)	1134 (38.4)			1051 (42.7)	395 (39.2)		
Smoking			<0.001	0.224			<0.001	0.195			0.003	0.142
Never smoker	1771 (36.7)	3344 (46.7)			2383 (40.0)	1426 (48.3)			973 (39.5)	459 (45.6)		
Previous smoker	717 (14.9)	1000 (14.0)			455 (7.6)	191 (6.5)			211 (8.6)	80 (7.9)		
Current smoker	712 (14.8)	704 (9.8)			541 (9.1)	164 (5.6)			203 (8.2)	58 (5.8)		
Not available	1625 (33.7)	2120 (29.6)			2578 (43.3)	1173 (39.7)			1076 (43.7)	410 (40.7)		
Alcohol use			<0.001	0.337			<0.001	0.254			<0.001	0.303
None	1358 (28.1)	3072 (42.9)			1560 (26.2)	1092 (38.0)			608 (24.7)	371 (36.8)		
Mild-to-moderate	1662 (34.4)	1664 (23.2)			1712 (28.7)	621 (21.0)			729 (29.6)	200 (19.9)		
Heavy	187 (3.9)	314 (4.4)			114 (1.9)	64 (2.2)			53 (2.2)	27 (2.7)		
Not available	1618 (33.5)	2118 (29.5)			2571 (43.2)	1177 (39.8)			1073 (43.6)	409 (40.6)		
Creatinine, mg/dL			<0.001	0.247			<0.001	0.176			<0.001	0.196
≤ 1.5	2157 (44.7)	3954 (55.2)			2191 (36.8)	1254 (42.5)			845 (34.3)	433 (43.0)		
> 1.5	84 (1.7)	229 (3.2)			56 (0.9)	73 (2.5)			26 (1.1)	18 (1.8)		
Not available	2584 (53.6)	2985 (41.6)			3710 (62.3)	1627 (55.1)			1592 (64.6)	556 (55.2)		
eGFR, mL/min/1.73m ²			<0.001	0.292			<0.001	0.274			<0.001	0.281
≥ 60	1586 (32.9)	2595 (36.2)			1529 (25.7)	753 (25.5)			597 (24.2)	266 (26.4)		
< 60	211 (4.4)	814 (11.4)			229 (3.8)	320 (10.8)			101 (4.1)	111 (11.0)		
Not available	3028 (62.8)	3759 (52.4)			4199 (70.5)	1881 (63.7)			1765 (71.7)	630 (62.6)		

Concomitant Procedure

Tricuspid valve repair	164 (3.4)	181 (2.5)	0.052	2450 (41.1)	1299 (44.0)	0.058	959 (38.9)	365 (36.2)	0.056
Coronary arterial bypass grafting	450 (9.3)	1275 (17.8)	0.249	269 (4.5)	298 (10.1)	0.215	67 (2.7)	62 (2.7)	0.167
Surgical ablation for Atrial fibrillation	207 (4.3)	358 (5.0)	0.033	2622 (44.0)	1237 (41.9)	0.043	973 (39.5)	367 (36.4)	0.063

Values are n (%), or mean ± standard deviation.

SMD, standardized mean difference; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention;

eGFR, estimated glomerular filtration rate.

Table 2. Between-Group Differences in Clinical Outcomes among Recipients of Mechanical and Biologic Aortic Valve Prostheses using competing risk analyses.

	Crude				IPTW-adjusted			
	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P-value	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P-value
Age < 55 (N=1804)	1654	150			1654	150		
Death	185	32	2.79 (1.91-4.07)	<0.001	186	30	2.18 (1.32-3.63)	0.002
Valve related events								
Reoperation	35	11	4.58 (2.32-9.04)	<0.001	35	9	3.27 (1.49-7.19)	0.003
Thromboembolism	118	6	0.73 (0.32-1.67)	0.459	117	4	0.45 (0.16-1.24)	0.124
Major bleeding	35	6	2.52 (1.07-5.95)	0.035	35	5	1.74 (0.58-5.24)	0.327
55 ≤ Age ≤ 64 (N=3000)	2227	773			2227	773		
Death	324	141	1.58 (1.29-1.93)	<0.001	324	137	1.29 (1.02-1.63)	0.037
Valve related events								
Reoperation	37	27	2.62 (1.58-4.33)	<0.001	35	32	2.77 (1.56-4.91)	<0.001
Thromboembolism	177	35	0.66 (0.46-0.95)	0.026	173	34	0.56 (0.37-0.85)	0.006
Major bleeding	76	14	0.62 (0.35-1.10)	0.103	74	14	0.54 (0.28-1.03)	0.062
Age ≥ 65 (N=7189)	944	6245			944	6245		
Death	313	1846	1.14 (1.01-1.28)	0.040	363	1834	0.77 (0.66-0.90)	0.001
Valve related events								
Reoperation	9	93	1.87 (0.93-3.74)	0.077	5	103	3.11 (1.30-7.45)	0.011
Thromboembolism	108	366	0.61 (0.49-0.75)	<0.001	109	375	0.55 (0.41-0.73)	0.000
Major bleeding	56	89	0.29 (0.21-0.40)	<0.001	38	90	0.39 (0.25-0.60)	0.000

IPTW, Inverse-probability-of-treatment weighting; HR, Hazard ratio; CI, Confidence interval.

Table 3. Between-Group Differences in Clinical Outcomes among Recipients of Mechanical and Biologic Mitral Valve Prostheses using competing risk analyses.

	Crude				IPTW-adjusted			
	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P- value	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P-value
Age < 55 (N=2937)	2783	154			2783	154		
Death	290	29	2.01 (1.43-3.06)	<0.001	301	17	1.15 (0.65-2.03)	0.626
Valve related events								
Reoperation	63	23	7.64 (4.77-12.23)	<0.001	16	1	4.69 (2.53-8.66)	<0.001
Thromboembolism	200	6	0.58 (0.26-1.30)	0.186	201	8	0.81 (0.27-2.50)	0.719
Major bleeding	102	3	0.57 (0.18-1.82)	0.346	101	3	0.63 (0.10-3.93)	0.624
55 ≤ Age ≤ 69 (N=4231)	2999	1232			2999	1232		
Death	613	393	1.77 (1.56-2.01)	<0.001	692	334	1.22 (1.04-1.44)	0.016
Valve related events								
Reoperation	45	91	5.27 (3.68-7.56)	<0.001	43	126	7.75 (5.14-11.69)	<0.001
Thromboembolism	267	103	0.95 (0.76-1.19)	0.667	266	107	0.99 (0.73-1.34)	0.934
Major bleeding	126	61	1.20 (0.89-1.63)	0.241	136	62	1.12 (0.75-1.68)	0.575
Age ≥ 70 (N=1743)	175	1568			175	1568		
Death	82	652	0.99 (0.78-1.24)	0.900	71	662	1.06 (0.79-1.42)	0.687
Valve related events								
Reoperation	0	53	Infinity	<0.001	0	54	Infinity	<0.001
Thromboembolism	11	155	1.81 (0.99-3.33)	0.055	9	157	2.18 (0.92-5.20)	0.078
Major bleeding	7	59	1.04 (0.48-2.25)	0.927	5	59	1.33 (0.51-3.48)	0.557

IPTW, Inverse-probability-of-treatment weighting; HR, Hazard ratio; CI, Confidence interval.

Table 4. Between-Group Differences in Clinical Outcomes among Recipients of Mechanical and Biologic Aortic + Mitral Valve Prostheses using competing risk analyses.

	Crude				IPTW-adjusted			
	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P-value	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P-value
Age < 55 (N=1206)	1163	43			1163	43		
Death	131	12	2.97 (1.65-5.38)	<0.001	135	8	1.64 (0.66-4.05)	0.284
Valve related events								
Reoperation	31	8	8.35 (3.89-17.92)	<0.001	31	6	5.62 (1.82-17.35)	0.003
Thromboembolism	89	4	1.37 (0.49-3.82)	0.550	88	3	1.05 (0.26-4.30)	0.950
Major bleeding	51	1	0.54 (0.07-3.97)	0.541	51	1	0.39 (0.05-3.02)	0.369
55 ≤ Age ≤ 64 (N=1130)	996	134			996	134		
Death	187	50	2.20 (1.61-3.00)	<0.001	190	46	2.02 (1.28-3.19)	0.002
Valve related events								
Reoperation	30	22	5.75 (3.35-9.86)	<0.001	30	26	7.13 (3.86-13.18)	<0.001
Thromboembolism	99	4	0.28 (0.10-0.75)	0.011	99	4	0.25 (0.08-0.78)	0.017
Major bleeding	53	11	1.53 (0.79-2.96)	0.203	53	12	1.75 (0.77-3.95)	0.180
Age ≥ 65 (N=1134)	304	830			304	830		
Death	110	336	1.22 (0.98-1.51)	0.070	119	331	0.95 (0.71-1.28)	0.750
Valve related events								
Reoperation	5	43	3.29 (1.29-8.38)	0.013	3	53	6.65 (2.27-19.50)	0.001
Thromboembolism	34	58	0.62 (0.41-0.94)	0.025	31	56	0.65 (0.36-1.14)	0.131
Major bleeding	11	21	0.70 (0.34-1.46)	0.341	6	19	1.22 (0.56-2.65)	0.618

IPTW, Inverse-probability-of-treatment weighting; HR, Hazard ratio; CI, Confidence interval.

Figure 1. Patient Inclusion Flow Diagram.

AVR, aortic valve replacement; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MVR, mitral valve replacement; NHIS, National Health Insurance Service; PVR, pulmonary valve replacement; TVR, tricuspid valve replacement.

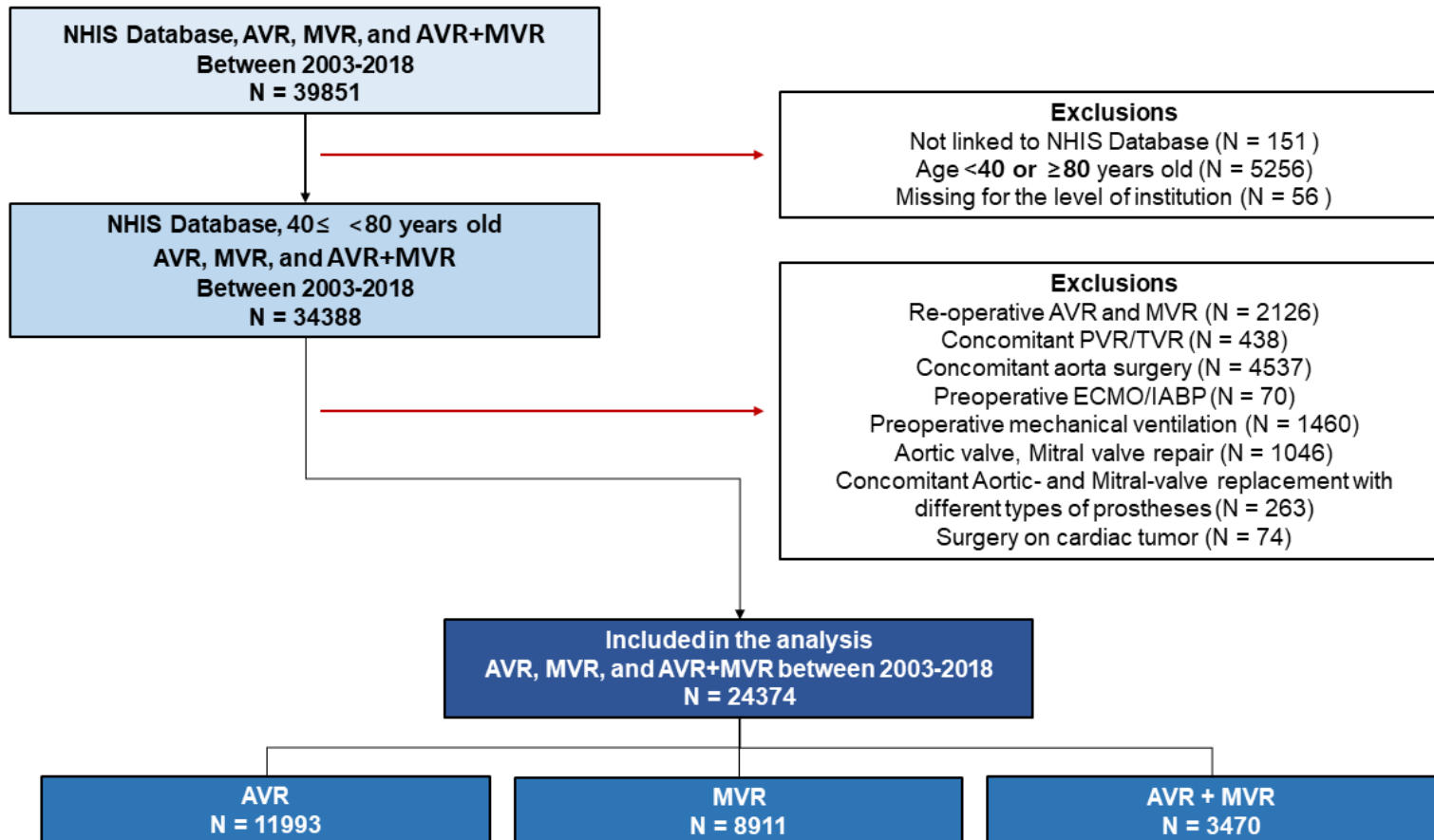


Figure 2. Distributions of patients undergoing valve replacements depending on age strata.

In (A) aortic valve replacement, (B) mitral valve replacement, and (C) simultaneous aortic- and mitral-valve replacement.

AVR, aortic valve replacement; MVR, mitral valve replacement.

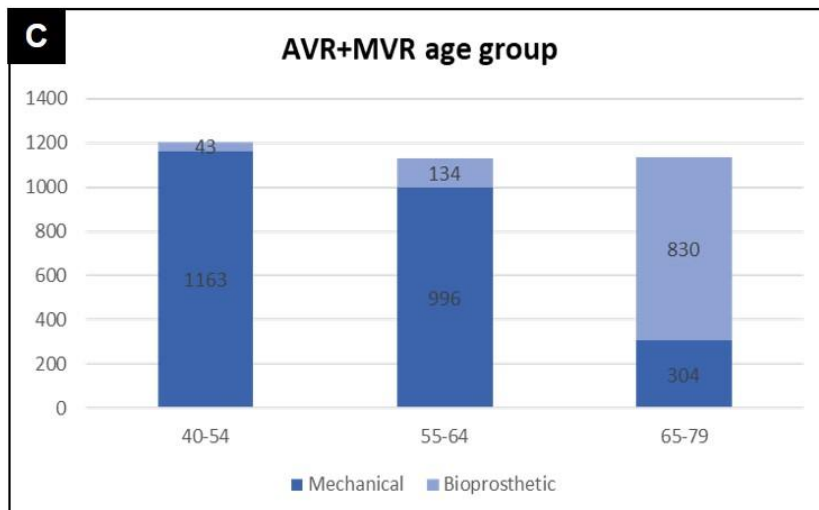
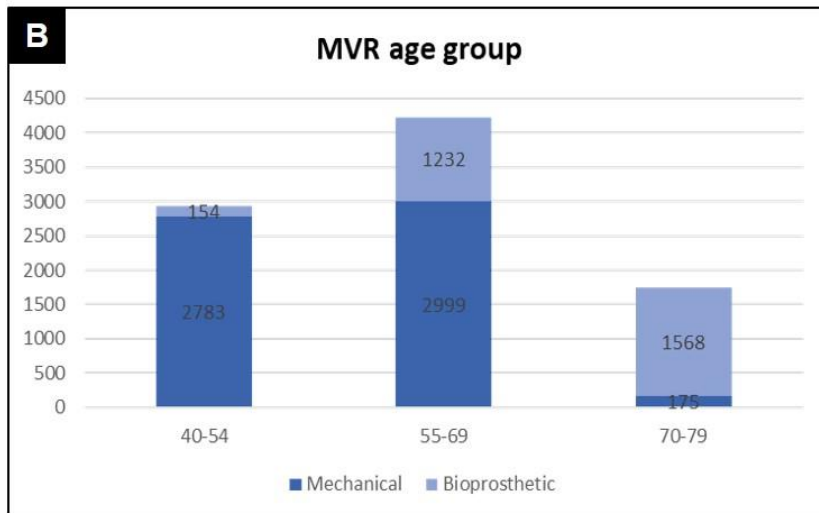
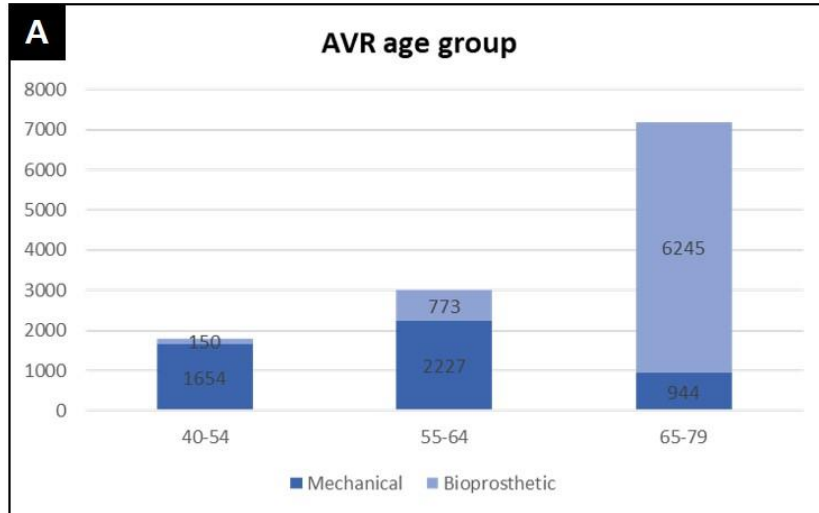


Figure 3. The age-dependent relative hazards of bioprosthesis compared to mechanical prosthesis in (A) aortic and in (B) mitral position.

The central solid lines represent the adjusted hazard ratio, and the dashed lines represent the 95% confidence intervals. The horizontal line at 1.00 denotes no difference between bioprosthesis versus mechanical prosthesis.

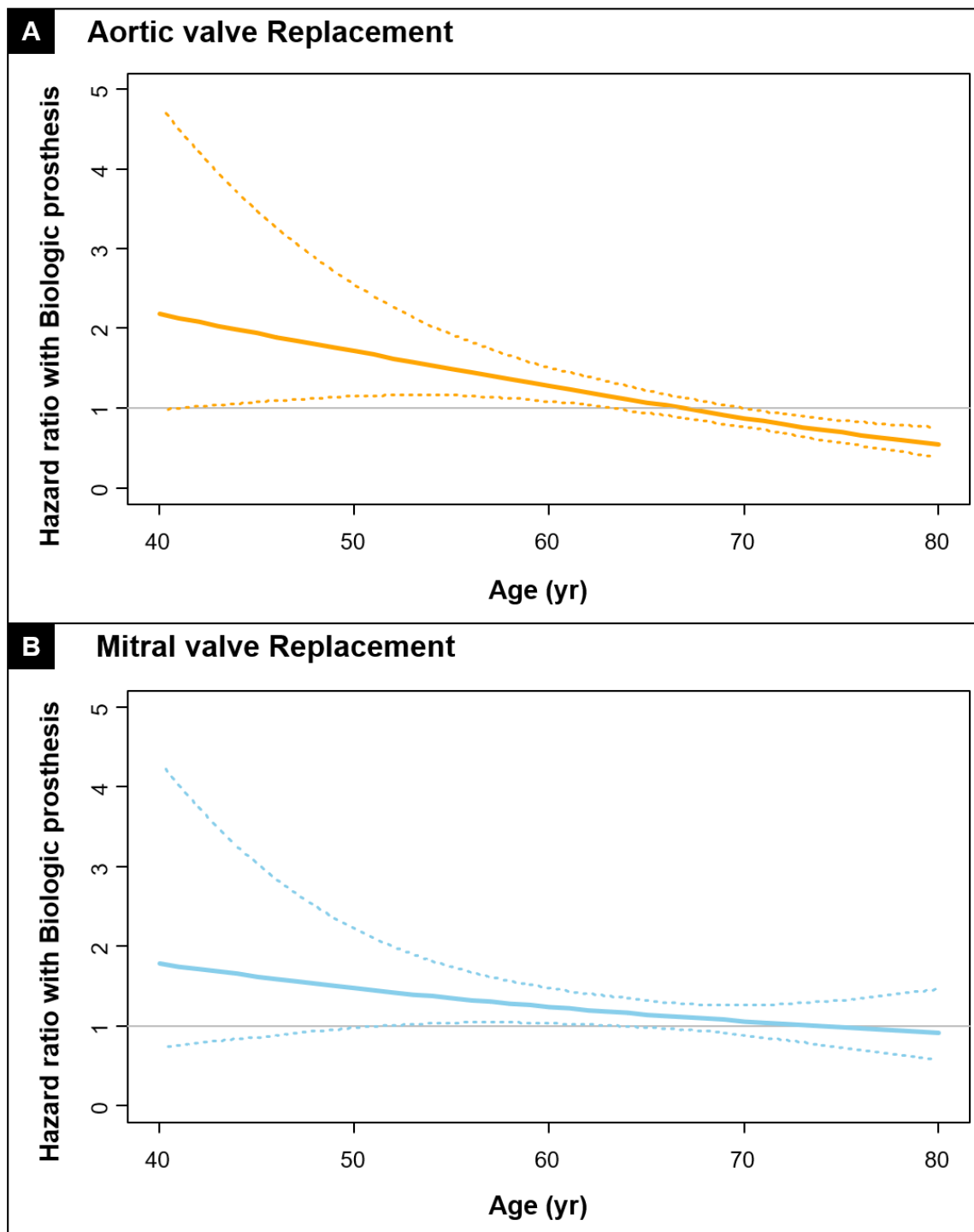


Figure 4. The adjusted risks of mortality of bioprosthesis according to age strata in (A) AVR, (B) MVR, and (C) DVR.

AVR, aortic valve replacement; MVR, mitral valve replacement; DVR, double valve replacement.

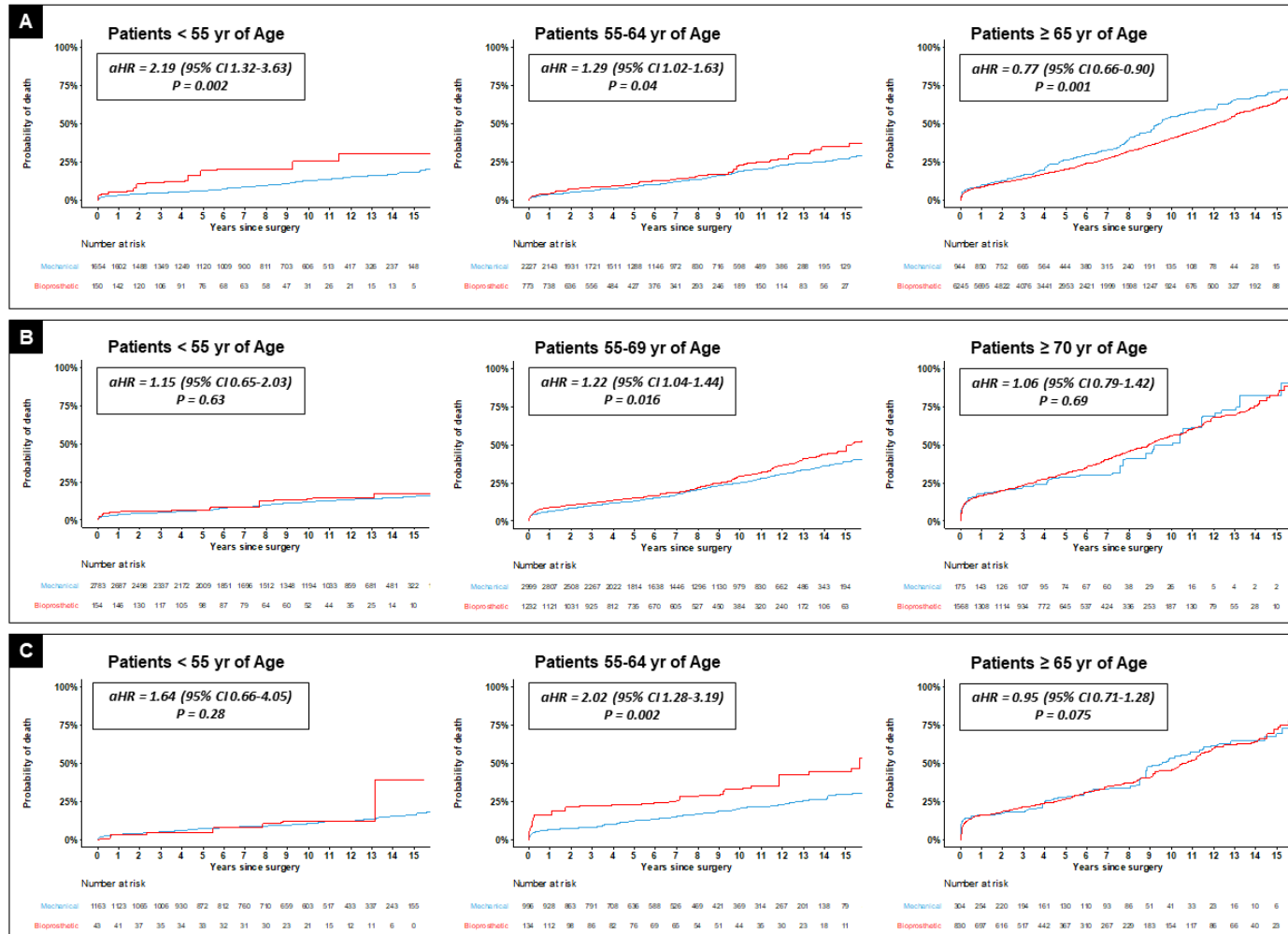
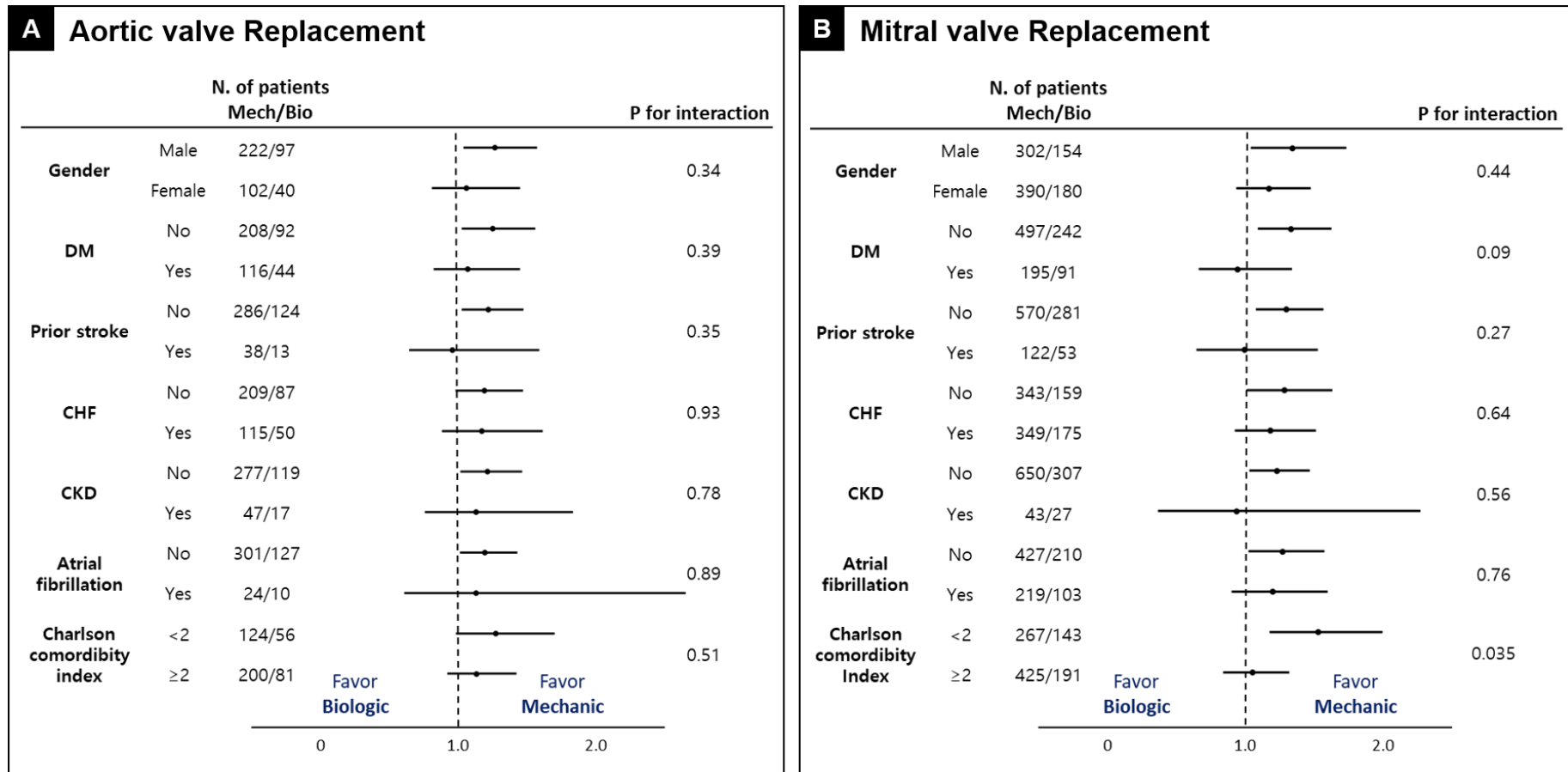


Figure 5. Adjusted risks for mortality according to various subgroups in the middle age group.

(A) Aortic valve replacement in 55 to 64 years of age, and (B) Mitral valve replacement in 55 to 69 years of age
 CHF, congestive heart failure; CKD, chronic kidney disease; DM, diabetes mellitus.



Supplementary Table 1. Definition of baseline comorbidities.

Comorbidities	ICD-10 codes / NHIS claim code	Number of diagnosis (Admission or outpatient clinic)
Atrial fibrillation	I48 / -	≥ 2
Hypertension	I10-I13, I15 / -	≥ 3
Diabetes mellitus	E10-E14 / -	≥ 3
Dyslipidemia	E78 / -	≥ 3
Chronic kidney disease	N18 / -	≥ 2
Dialysis	- / O701-O708	≥ 2
Ischemic stroke	I63, I64, I67.8-9 / -	≥ 2
Transient ischemic attack	G45 / -	≥ 2
Thromboembolism	I74 / -	≥ 2
Ischemic heart disease	I20-I25 / -	≥ 2
Myocardial infarction	I21-I23 / -	≥ 2
Previous PCI	I20-I25 / M6551-6554, M6561-M6567, M6571, M6572, M6634, M6638	≥ 1
Congestive heart failure	I50, I42, I11.0, I13.0, I13.2 / -	≥ 2
Anemia	D50-D64 / -	≥ 2
COPD	J44 / -	≥ 2
Asthma	J45 / -	≥ 2
Peripheral vascular disease	I70.1, I70.2, I70.8, I70.9, I73 / -	≥ 2
Previous cardiac surgery	O1660, O1671, O1672, O1680, O1701-O1705, O1710, O1711, O1721-O1723, O1730, O1740, O1750, O1760, O1770, O1781-	Admission only ≥ 1

	O1783, O1791-O1793, O1794-O1800, O1800, O1810, O1821-O1826, O1830, O1840, O1851, O1852, O1861, O1873-O1875, O1878, O1879, O0881-O0883, O1940, O1950, O1960, O1970, O1981, O1982, O2001, O2004, O2006, O2007, O1640, O1641, OA640, OA641, O1648, OA648, O1649, OA649, O1647, OA647, O2031-O2033		
Previous cancer	C00-C97 / -		≥ 1
Mode of valve disease			
Aortic valve			
Bicuspid aortic valve	Q23.1, Q23.8-9		≥ 1
Aortic stenosis	I06.0, I35.0, Q23.0		≥ 1
Aortic regurgitation	I06.1, I35.1, Q23.1		≥ 1
Combined	I06.2, I35.2		≥ 1
Others, NOS	I06.8-9, I35.8-9		≥ 1
Mitral valve			
Mitral stenosis	I05.0, I34.0, Q23.2		≥ 1
Mitral regurgitation	I05.1, I34.1, Q23.3		≥ 1
Combined	I05.2, I34.2		≥ 1
Others, NOS	I05.8-9, I34.8-9		≥ 1
Endocarditis	I33, I38, I39.0-1, I39.4, I39.8		≥ 1
Congestive heart failure	I50.0		≥ 1

PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; NOS, not otherwise specified

Supplementary Table 2. Definition of operative profiles.

Operative profiles	NHIS claim code
<i>Procedure</i>	
AVR	O1793, O1799
MVR	O1792
<i>Prosthesis</i>	
Mechanical valve	G2011025, G2011002, G2011007, G2011011, G2011012, G2011021, G2011129, G2011034, G2011029
Biological valve	G2001034, G2001102, G2001321, G2001002, G2001134, G2001203, G2001234, G2001003, G2001103, G2001121, G2001221, G2001021, G2001007, G2301002, G2301034
<i>Concomitant procedure</i>	
TV repair	O1781
CABG	O1640, O1641, O1647-O1649, OA640, OA641, OA647-OA649
Surgical ablation	O2006

AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 3. Definition of clinical outcomes.

Comorbidities	ICD-10 codes	Additional diagnosis
Ischemic stroke	I63, I64	Hospitalization, brain imaging (CT or MRI)
Systemic thromboembolism	I74	Hospitalization, imaging (CT or MRI)
Major bleeding	I85.0, K22.1, K22.8, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.0, K31.8, K55.2, K57.0, K57.1- K57.5, K57.8, K57.9, K62.5, K66.1, K92.0, K92.1, K92.2, D62, H05.2, H35.6, H43.1, J94.2, M25.0, R04	Hospitalization
Hemorrhagic stroke	I60-I62	Hospitalization, brain imaging (CT or MRI)

Supplementary Table 4. Baseline and operative characteristics according to the types of prostheses in 40 to 54 years of age undergoing aortic valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n=1654)	Biological prosthesis (n=150)	p-value	SMD	Mechanical prosthesis (n=1654)	Biological prosthesis (n=150)	SMD
<i>Baseline Demographics</i>							
Age, years	48.6±4.1	49.3±4.3	0.033	0.177	48.6±4.1	48.4±4.3	0.055
Female	506 (30.6)	38 (25.3)	0.179	0.117	498.1 (30.1)	41.9 (27.9)	0.049
<i>Baseline conditions</i>							
Atrial fibrillation	51 (3.1)	2 (1.3)	0.313	0.119	48.7 (2.9)	3.6 (2.4)	0.035
Hypertension	641 (38.8)	62 (41.3)	0.535	0.053	640.6 (38.7)	49.2 (32.8)	0.124
Diabetes mellitus	178 (10.8)	20 (13.3)	0.335	0.079	181.4 (11.0)	18.5 (12.3)	0.042
Dyslipidemia	169 (10.2)	18 (12.0)	0.493	0.057	169.5 (10.2)	15.5 (10.3)	0.003
Chronic kidney disease	59 (3.6)	14 (9.3)	0.001	0.236	66.4 (4.0)	4.6 (3.1)	0.051
Dialysis	55 (3.3)	14 (9.3)	<0.001	0.249	63.3 (3.8)	7.7 (5.1)	0.062
Stroke, TIA or SE	87 (5.3)	7 (4.7)	0.754	0.027	88 (5.3)	13.9 (9.3)	0.153
Ischemic heart disease	384 (23.2)	25 (16.7)	0.067	0.164	375.4 (22.7)	30.5 (20.3)	0.058
Myocardial infarction	26 (1.6)	1 (0.7)	0.721	0.086	24.8 (1.5)	0.7 (0.5)	0.109
Previous PCI	25 (1.5)	3 (2.0)	0.502	0.037	24.9 (1.5)	1.1 (0.7)	0.076
Congestive heart failure	379 (22.9)	36 (24.0)	0.762	0.026	380.8 (23.0)	33.4 (22.3)	0.018
Anemia	164 (9.9)	30 (20.0)	<0.001	0.286	175 (10.6)	17 (11.3)	0.024
COPD	28 (1.7)	1 (0.7)	0.507	0.095	26.2 (1.6)	0.2 (0.1)	0.158
Asthma	114 (6.9)	12 (8.0)	0.610	0.042	115.7 (7.0)	10.2 (6.8)	0.006
Peripheral vascular disease	62 (3.7)	2 (1.3)	0.126	0.154	58.7 (3.5)	2.3 (1.5)	0.13
Previous cardiac surgery	3 (0.2)	0 (0.0)	1.000	0.06	2.8 (0.2)	0 (0.0)	0.058
Previous cancer	42 (2.5)	12 (8.0)	0.001	0.246	49.2 (3.0)	6 (4.0)	0.055

<i>Charlson comorbidity index</i>			0.020	0.252			0.001
0	683 (41.3)	55 (36.7)	0.004	0.286	675.4 (40.8)	50.7 (33.8)	0.192
1	467 (28.2)	34 (22.7)			462.1 (27.9)	53.3 (35.5)	
2	253 (15.3)	25 (16.7)			255 (15.4)	25.4 (16.9)	
≥ 3	169 (10.2)	18 (12.0)			170.2 (10.3)	12.7 (8.5)	
≥ 5	82 (5.0)	18 (12.0)			91.4 (5.5)	7.8 (5.2)	
<i>Years of Surgery</i>			<0.001	0.472			0.166
2002~2005	398 (24.1)	18 (12.0)			381.7 (23.1)	28.5 (19.0)	
2006~2009	415 (25.1)	25 (16.7)			402.5 (24.3)	31.2 (20.8)	
2010~2013	405 (24.5)	40 (26.7)			407.2 (24.6)	38.7 (25.8)	
2014~2018	436 (26.4)	67 (44.7)			462.7 (28.0)	51.7 (34.5)	
<i>Cumulative hospital volume for cardiac surgery</i>							
<250 cases	424 (25.6)	40 (26.7)	0.032	0.253	426.9 (25.8)	41.6 (27.7)	0.15
250-1000 cases	423 (25.6)	53 (35.3)			434.9 (26.3)	47.1 (31.4)	
1000-3000 cases	498 (30.1)	38 (25.3)			492 (29.7)	39.1 (26.1)	
≥3000 cases	309 (18.7)	19 (12.7)			300.2 (18.1)	22.1 (14.7)	
<i>Mode of valve diseases</i>							
Bicuspid aortic valve	239 (14.4)	30 (20.0)	0.068	0.147	247.5 (15.0)	25.8 (17.2)	0.061
Aortic stenosis	774 (46.8)	66 (44.0)	0.511	0.056	770.5(46.6)	61.7 (41.1)	0.109
Aortic regurgitation	1107 (66.9)	102 (68.0)	0.789	0.023	1108.9 (67.0)	105.7 (70.5)	0.073
Combined	311 (18.8)	24 (16.0)	0.398	0.074	306.7 (18.5)	28.1 (18.7)	0.006
Others, NOS	476 (28.8)	36 (24.0)	0.214	0.109	468.6 (28.3)	40.8 (27.2)	0.025
Endocarditis	325 (19.6)	46 (30.7)	0.001	0.256	339.3 (20.5)	35.1 (23.4)	0.07
Congestive heart failure	423 (25.6)	43 (28.7)	0.407	0.07	428.2 (25.9)	42.6 (28.4)	0.056
<i>Health Screening Data</i>							
Height, m	165.3±8.7	165.8±7.1	0.586	0.055	165.4±8.7	165.1±6.9	0.039
Weight, kg	66.5±11.9	65.7±12.4	0.550	0.065	66.4±11.9	65.1±11.2	0.11

BMI, kg/m ²	24.2±3.3	23.8±3.5	0.247	0.124	24.2±3.3	23.8±3.0	0.122
< 18.5	19 (1.1)	6 (4.0)	0.071	0.22	24 (1.5)	3.1 (2.1)	0.126
≥ 18.5 and < 23	354 (24.1)	35 (23.3)			357.1 (21.6)	35.3 (23.5)	
≥ 23 and < 25	244 (14.8)	18 (12.0)			240.6 (14.5)	24.1 (16.1)	
≥ 25 and < 30	339 (20.5)	25 (16.7)			332.7 (20.1)	23.9 (15.9)	
≥ 30	50 (3.0)	5 (3.3)			50.2 (3.0)	3.9 (2.6)	
Not available	648 (39.2)	61 (40.7)			649.3 (39.3)	59.9 (39.9)	
Systolic blood pressure, mmHg	124.9±17.6	123.6 (14.6)	0.423	0.082	124.8 (17.6)	125.5±15.4	0.041
< 120	369 (22.3)	34 (22.7)	0.932	0.058	369.5 (22.3)	32.5 (21.7)	0.056
≥ 120 and < 140	443 (26.8)	40 (26.7)			443.1 (26.8)	37.9 (25.3)	
≥ 140	194 (11.7)	15 (10.0)			192.1 (11.6)	19.7 (13.1)	
Not available	648 (39.2)	61 (40.7)			649.3 (39.3)	59.9 (39.9)	
Diastolic blood pressure, mmHg	75.6±11.6	74.2±11.2	0.264	0.125	75.5±11.7	74.7±11.4	0.063
< 80	554 (33.5)	51 (34)	0.901	0.067	555.9 (33.6)	49.1 (32.7)	0.051
≥ 80 and < 90	326 (19.7)	29 (19.2)			325.2 (19.7)	31.4 (20.9)	
≥ 90	126 (7.6)	9 (6.0)			123.6 (7.5)	9.7 (6.5)	
Not available	648 (39.2)	61 (40.7)			649.3 (39.3)	59.9 (39.9)	
Smoking			0.862	0.074			0.116
Never smoker	484 (29.3)	40 (26.7)			480.6(29.1)	37.3 (24.9)	
Previous smoker	226 (13.7)	19 (12.7)			226 (13.7)	25.3 (16.9)	
Current smoker	284 (17.2)	28 (18.7)			285.5 (17.3)	26.7 (17.8)	
Not available	660 (39.9)	63 (42.0)			661.8 (40.0)	60.7 (40.5)	
Alcohol use			0.853	0.076			0.037

None	322 (19.5)	30 (20.0)			323.6 (19.6)	30.2 (20.1)	
Mild-to-moderate	619 (37.4)	51 (34.0)			614.7 (37.2)	54.8 (36.5)	
Heavy	56 (3.4)	6 (4.0)			56.6 (3.4)	4.3 (2.9)	
Not available	657 (39.7)	63 (42.0)			659.1 (39.8)	60.7 (40.5)	
Creatinine, mg/dL			0.005	0.225			0.174
<= 1.5	630 (38.1)	6 (43.3)			639.9 (38.7)	61 (40.7)	
> 1.5	19 (1.1)	6 (4.0)			20.4 (1.2)	5.6 (3.7)	
Not available	1005 (60.8)	79 (52.7)			993.6 (60.1)	83.3 (55.5)	
eGFR, mL/min/1.73m ²			0.021	0.201			0.111
≥ 60	503 (30.4)	52 (34.7)			514.8 (31.1)	49.6 (33.1)	
< 60	29 (1.8)	7 (4.7)			30.9 (1.9)	5.2 (3.5)	
Not available	1122 (67.8)	91 (60.7)			1108.2 (67.0)	95.3 (63.5)	
Concomitant Procedure							
TV repair	44 (2.7)	3 (2.0)	0.793	0.044	43(2.6)	2 (1.3)	0.09
CABG	88 (5.3)	6 (4.0)	0.486	0.063	85.9 (5.2)	7.9 (5.3)	0.004
Surgical ablation for Atrial fibrillation	49 (3.0)	4 (2.7)	1.000	0.018	49 (3.0)	6.1 (4.1)	0.06

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 5. Baseline and operative characteristics according to the types of prostheses in 55 to 64 years of age undergoing aortic valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n = 2227)	Biological prosthesis (n = 773)	p-value	SMD	Mechanical prosthesis (n = 2227)	Biological prosthesis (n = 773)	SMD
<i>Baseline Demographics</i>							
Age, years	59.5±2.8	61.3±2.5	<0.001	0.675	60.0±2.8	60.1±2.8	0.046
Female	790 (35.5)	289 (37.4)	0.34	0.04	801.1 (36.0)	289.2 (37.4)	0.03
<i>Baseline Comorbidities</i>							
Atrial fibrillation	128 (5.7)	31 (4.0)	0.063	0.081	118.2 (5.3)	41 (5.3)	<0.001
Hypertension	1277 (57.3)	478 (61.8)	0.029	0.092	1293.8 (58.1)	439.7 (56.9)	0.024
Diabetes mellitus	500 (22.5)	192 (24.8)	0.175	0.056	512.7 (23.0)	177.4 (22.9)	0.002
Dyslipidemia	406 (18.2)	172 (22.3)	0.015	0.1	438.4 (19.7)	160.6 (20.8)	0.027
Chronic kidney disease	97 (4.4)	61 (7.9)	<0.001	0.148	113.9 (5.1)	42.3 (5.5)	0.016
Dialysis	69 (3.1)	49 (6.3)	<0.001	0.153	85.3 (3.8)	34.5 (4.5)	0.032
Stroke, TIA or SE	173 (7.8)	55 (7.1)	0.555	0.025	170.4 (7.7)	57.9 (7.5)	0.006
Ischemic heart disease	813 (36.5)	282 (36.5)	0.99	0.001	810.4 (36.4)	273 (35.3)	0.022
Myocardial infarction	70 (3.1)	28 (3.6)	0.519	0.026	72.5 (3.3)	19.9 (2.6)	0.041
Previous PCI	91 (4.1)	38 (4.9)	0.327	0.04	99.2 (4.5)	30.2 (3.9)	0.027
Congestive heart failure	536 (24.1)	213 (27.6)	0.054	0.08	563.1 (25.3)	202.7 (2.62)	0.022
Anemia	176 (7.9)	93 (12.0)	0.001	0.138	199.7 (9.0)	71.9 (9.3)	0.012
COPD	76 (3.4)	34 (4.4)	0.209	0.051	83.6 (3.8)	30.1 (3.9)	0.007
Asthma	251 (11.3)	95 (12.3)	0.445	0.032	260 (11.7)	97.3 (12.6)	0.028
Peripheral vascular disease	115 (5.2)	56 (7.2)	0.032	0.086	124.8 (5.6)	38.5 (5.0)	0.028

Previous cardiac surgery	12 (0.5)	1 (0.1)	0.204517	0.071	9.2 (0.4)	0.4 (0.1)	0.076
Previous cancer	112 (5.0)	70 (9.1)	<0.001	0.158	134 (6.0)	49.4 (6.4)	0.016
Charlson comorbidity index			<0.001	0.173			0.028
0	682 (30.6)	181 (23.4)	<0.001	0.19	640.3 (28.8)	215.1 (27.8)	0.039
1	580 (26.0)	192 (24.8)			576.7 (25.9)	201.4 (26.1)	
2	390 (17.5)	153 (19.8)			393.7 (17.7)	130.5 (16.9)	
≥ 3	378 (17.0)	162 (21.0)			406.1 (18.2)	148.9 (19.3)	
≥ 5	197 (8.8)	85 (11.0)			210.3 (9.4)	77.1 (10.0)	
Years of Surgery			<0.001	0.352			0.08
2002~2005	430 (19.3)	95 (12.3)			386.7 (17.4)	117.6 (15.2)	
2006~2009	496 (22.3)	149 (19.3)			481.6 (21.6)	177.1 (22.9)	
2010~2013	594 (26.7)	157 (20.3)			553.9 (24.9)	179.5 (23.2)	
2014~2018	707 (31.7)	372 (48.1)			804.8 (36.1)	298.8 (38.7)	
hospital volumes			0.002	0.163			0.093
<250	551 (24.7)	188 (24.3)			559.9 (25.1)	203.7 (26.4)	
250-1000	611 (27.4)	248 (32.1)			646.3 (29.0)	248.2 (32.1)	
1000-3000	610 (27.4)	223 (28.8)			602.8 (27.1)	196.3 (25.4)	
≥3000	455 (20.4)	114 (14.7)			417.9 (18.8)	124.8 (16.1)	
Mode of valve diseases							
Bicuspid aortic valve	307 (13.8)	100 (12.9)	0.553	0.025	300.8 (13.5)	109.7 (14.2)	0.02
Aortic stenosis	1471 (66.1)	528 (68.3)	0.253	0.048	1487.9 (66.8)	535.2 (69.2)	0.052
Aortic regurgitation	1138 (51.1)	352 (45.5)	0.008	0.112	1099.6 (49.4)	362.0 (46.8)	0.051
Combined	436 (19.6)	154 (19.9)	0.836	0.009	433 (19.4)	137.9 (17.8)	0.041
Others, NOS	602 (27.0)	208 (26.9)	0.947	0.003	596.1 (26.8)	201.8 (26.1)	0.015
Endocarditis	275 (12.3)	113 (14.6)	0.105	0.066	285.3 (12.8)	100.4 (13.0)	0.005

Congestive heart failure	537 (24.1)	205 (26.5)	0.181	0.055	557.9 (25.1)	200.1 (25.9)	0.019
Health Screening Data							
Height, m	162.4±8.3	161.5±8.4	0.029	0.108	162.3 (8.26)	161.61 (8.41)	0.083
Weight, kg	65.0±10.8	63.9±10.6	0.042	0.101	64.7±10.7	64.1±11.0	0.06
BMI, kg/m ²	24.6±3.2	24.5±3.4	0.494	0.033	24.5±3.2	24.5±3.6	0.004
< 18.5	19 (0.9)	16 (2.1)	0.074	0.123	31.6 (1.4)	10.9 (1.4)	0.065
≥ 18.5 and < 23	481 (21.6)	161 (20.8)			479.1 (21.5)	183.5 (23.7)	
≥ 23 and < 25	403 (18.1)	150 (19.4)			413.2 (18.6)	136.5 (17.7)	
≥ 25 and < 30	572 (25.7)	208 (26.9)			570.6 (25.6)	192.6 (34.9)	
≥ 30	87 (3.9)	25 (3.2)			84.5 (3.8)	34 (4.4)	
Not available	665 (29.9)	213 (27.6)			647.9 (29.1)	215.5 (27.9)	
Systolic blood pressure, mmHg	126.2±16.2	127.6±17.1	0.09	0.082	126.5±16.3	126.6±16.7	0.006
< 120	480 (21.6)	172 (22.3)	0.249	0.084	483.8 (21.7)	170.6 (22.1)	0.029
≥ 120 and < 140	775 (34.8)	261 (33.8)			774.4 (34.8)	276.5 (35.8)	
≥ 140	307 (13.8)	127 (16.4)			320.8 (14.4)	110.4 (14.3)	
Not available	665 (29.9)	213 (27.6)			647.9 (29.1)	215.5 (27.9)	
Diastolic blood pressure, mmHg	75.9±10.7	75.49 (10.9)	0.484	0.034	75.7±10.7	75.9±10.5	0.016
< 80	849 (38.1)	312 (40.4)	0.618	0.056	864.6 (38.8)	303.5 (39.3)	0.032
≥ 80 and < 90	531 (23.8)	185 (23.9)			537.6 (24.1)	194.2 (25.1)	
≥ 90	182 (8.2)	63 (8.2)			176.9 (7.9)	59.8 (7.7)	
Not available	665 (29.9)	213 (27.6)			647.9 (29.1)	215.5 (27.9)	
Smoking			0.666	0.053			0.038
Never smoker	874 (39.2)	316 (40.9)			880.6 (39.5)	318.5 (41.2)	

Previous smoker	341 (15.3)	118 (15.3)			338.2 (15.2)	113.4 (14.7)	
Current smoker	336 (15.1)	122 (15.8)			349.2 (15.7)	122.2 (15.8)	
Not available	676 (30.4)	217 (28.1)			659 (29.6)	218.9 (28.3)	
Alcohol use			0.007	0.145			0.036
None	703 (31.6)	290 (37.5)			734.8 (33.0)	266.8 (34.5)	
Mild-to-moderate	753 (33.8)	226 (29.2)			728.9 (32.7)	251.9 (32.6)	
Heavy	98 (4.4)	42 (5.4)			108.2 (4.9)	37.3 (4.8)	
Not available	673 (30.2)	215 (27.8)			655 (29.4)	217 (28.1)	
Creatinine, mg/dL			0.001	0.162			0.05
<= 1.5	1072 (48.1)	432 (55.69)			1114.1 (50.0)	404.5 (52.3)	
> 1.5	48 (2.2)	19 (2.5)			50.3 (2.3)	14.6 (1.9)	
Not available	1107 (49.7)	322 (41.7)			1062.6 (47.7)	353.9 (45.8)	
eGFR, mL/min/1.73m ²			<0.001	0.207			0.058
≥ 60	784 (35.2)	337 (43.6)			834.9 (37.5)	311.2 (40.3)	
< 60	107 (4.8)	51 (6.6)			118.9 (5.3)	41.5 (5.4)	
Not available	1336 (60.0)	385 (49.8)			1273.2 (57.2)	420.3 (54.4)	
Concomitant Procedure							
TV valvuloplasty	71 (3.2)	12 (1.6)	0.017	0.108	60.8 (2.7)	16.5 (2.1)	0.039
CABG	229 (10.3)	93 (12.0)	0.176	0.056	236.3 (10.6)	77.6 (10.0)	0.019
Atrial fibrillation							
For surgical ablation	103 (4.6)	25 (3.2)	0.099	0.072	96.2 (4.3)	37.9 (4.9)	0.027

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 6. Baseline and operative characteristics according to the types of prostheses in 65 to 79 years of age undergoing aortic valve replacement.

	Unadjusted				IPTW		
	Mechanical	Biological	p-value	SMD	Mechanical	Biological	SMD
	prosthesis (n = 944)	prosthesis (n = 6245)			prosthesis (n = 944)	prosthesis (n = 6245)	
<i>Baseline Demographics</i>							
Age, years	68.5±3.3	72.3±4.0	<0.001	1.063	71.2±4.0	71.8±4.1	0.162
Female	395 (41.8)	2873 (46.0)	0.017	0.084	421 (44.6)	2839 (45.5)	0.017
<i>Baseline conditions</i>							
Atrial fibrillation	98 (10.4)	423 (6.8)	<0.001	0.129	85 (9.0)	451 (7.2)	0.065
Hypertension	645 (68.3)	4614 (73.9)	<0.001	0.123	692 (73.3)	4570 (73.2)	0.004
Diabetes mellitus	255 (27.0)	2055 (32.9)	<0.001	0.129	293 (31.0)	2005 (32.1)	0.024
Dyslipidemia	193 (20.4)	1672 (26.8)	<0.001	0.149	259 (27.4)	1614 (25.8)	0.036
Chronic kidney disease	44(4.7)	331 (5.3)	0.41	0.029	53 (5.6)	325 (5.2)	0.016
Dialysis	28 (3.0)	172 (2.8)	0.712	0.013	40 (4.2)	174 (2.8)	0.077
Stroke, TIA or SE	113 (12.0)	892 (14.3)	0.056	0.069	131 (13.9)	871 (13.9)	0.003
Ischemic heart disease	414 (43.9)	2926 (46.9)	0.085	0.06	452 (47.8)	2896 (46.6)	0.029
Myocardial infarction	34 (3.6)	261 (4.2)	0.404	0.03	57 (6.0)	259 (4.2)	0.085
Previous PCI	52 (5.5)	509 (8.2)	0.005	0.105	78 (8.3)	488 (7.8)	0.018
Congestive heart failure	298 (31.6)	2036 (32.6)	0.527	0.022	321 (34.0)	2033 (32.6)	0.029
Anemia	98 (10.4)	786 (12.6)	0.055	0.069	132 (14.0)	772 (12.4)	0.048
COPD	56 (5.9)	485 (7.8)	0.046	0.073	67 (7.1)	470 (7.5)	0.017
Asthma	153 (16.2)	1146 (18.4)	0.111	0.057	187 (19.8)	1131 (18.1)	0.043

Peripheral vascular disease	79 (8.4)	571 (9.1)	0.439	0.027	95 (10.1)	567 (9.1)	0.034
Previous cardiac surgery	4 (0.4)	42 (0.7)	0.372	0.034	3 (0.3)	40 (0.6)	0.045
Previous cancer	73 (7.7)	601 (9.6)	0.063	0.067	83 (8.8)	586 (9.4)	0.021
Charlson comorbidity index			<0.001	0.159			0.036
0	192 (20.3)	996 (15.9)	<0.001	0.208	143 (15.1)	1034 (16.6)	0.05
1	246 (26.1)	1323 (21.2)			206 (21.8)	1358 (21.7)	
2	194 (20.6)	1301 (20.8)			205 (21.8)	1302 (20.8)	
≥ 3	181 (19.2)	1581 (25.3)			226 (23.9)	1529 (24.5)	
≥ 5	131 (13.9)	1044 (16.7)			165 (17.4)	1022 (16.4)	
Years of Surgery			<0.001	0.381			0.111
2002~2005	196 (20.8)	588 (9.4)			125 (13.2)	684 (11.0)	
2006~2009	214 (22.7)	1195 (19.1)			209 (22.1)	1223 (19.6)	
2010~2013	256 (27.1)	1804 (28.9)			264 (28.0)	1786 (28.6)	
2014~2018	278 (29.4)	2658 (42.6)			346 (36.6)	2552 (40.9)	
Cumulative hospital volume for cardiac surgery			<0.001	0.338			0.196
<250 cases	280 (29.7)	1695 (27.1)			310.8 (32.9)	1724.7(27.6)	
250-1000 cases	279 (29.6)	1708 (27.3)			296.8 (31.4)	1731.7 (27.7)	
1000-3000 cases	167 (17.7)	1920 (30.7)			202.4 (21.4)	1811.7 (29.0)	
≥3000 cases	218 (23.1)	922 (14.8)			134 (14.2)	976.9 (15.6)	
Mode of valve diseases							
Bicuspid aortic valve	76 (8.1)	387 (6.2)	0.031	0.072	58.4 (0.9)	404 (6.5)	0.012
Aortic stenosis	708 (75.0)	4973 (79.6)	0.001	0.111	750.6 (12.0)	4936 (79.0)	0.011
Aortic regurgitation	366 (38.8)	1921 (30.8)	<0.001	0.169	309 (4.9)	1999 (32.0)	0.016
Combined	206 (21.8)	1201 (19.2)	0.062	0.064	187.5 (3.0)	1218 (19.5)	0.009

Others, NOS	267 (28.3)	1652 (26.5)	0.236	0.041	244.6 (3.9)	1662 (26.6)	0.016
Endocarditis	97 (10.3)	533 (8.5)	0.078	0.06	91.9 (1.5)	549 (8.8)	0.033
Congestive heart failure	282 (29.9)	1769 (28.3)	0.327	0.034	296.1 (4.7)	1795 (28.7)	0.057
<i>Health Screening Data</i>							
Height, m	160.1±3.4	158.8±8.6	<0.001	0.161	159.2±8.7	158.9 (8.62)	0.031
Weight, kg	62.7±10.0	61.4±10.0	0.001	0.135	61.5±10.2	61.5±10.0	0.006
BMI, kg/m ²	24.4±3.0	24.3±3.3	0.488	0.028	24.2±3.0	24.3±3.2	0.047
< 18.5	11 (1.2)	116 (1.9)			16.9 (1.8)	110.2 (1.8)	0.097
≥ 18.5 and < 23	211 (22.4)	1440 (23.1)			240.4 (25.5)	1444.2 (23.1)	
≥ 23 and < 25	171 (18.1)	1098 (17.6)			146.3 (15.5)	1102.3 (17.7)	
≥ 25 and < 30	257 (27.2)	1607 (25.7)			235.4 (24.9)	1616 (25.9)	
≥ 30	27 (2.9)	231 (3.7)			24.7 (2.6)	222.4 (3.6)	
Not available	267 (28.3)	1753 (28.1)			280.4 (29.7)	1750 (28.0)	
Systolic blood pressure, mmHg	129.5±17.3	130.3±17.3	0.227	0.05	129.8±17.3	130.2±17.3	0.022
< 120	175 (18.5)	1074 (17.2)	0.772	0.037	157.6(16.7)	1084.1 (17.4)	0.037
≥ 120 and < 140	318 (33.7)	2164 (34.7)			326.7 (34.6)	2157.2 (34.5)	
≥ 140	184 (19.5)	1239 (19.8)			179.3 (19.0)	1240.1 (19.9)	
Not available	267 (28.3)	1768 (28.3)			280.4 (29.7)	1763.6 (28.2)	
Diastolic blood pressure, mmHg	76.2±11.3	75.8±11.1	0.4	0.035	75.5±11.5	75.9±11.2	0.037
< 80	359 (38.0)	2537 (40.6)	0.353	0.063	378.7 (40.1)	2516.4 (40.3)	0.038
≥ 80 and < 90	217 (23.0)	1340 (21.5)			199.2 (21.1)	1351.6 (21.6)	
≥ 90	101 (10.7)	600 (9.6)			85.7 (9.1)	613.3 (9.8)	
Not available	267 (28.3)	1768 (28.3)			280.4 (29.7)	1763.6 (28.2)	

Smoking			0.091	0.088			0.046
Never smoker	413 (43.8)	2988 (47.8)			429.2 (45.5)	2958.5 (47.4)	
Previous smoker	150 (15.9)	863 (13.8)			138.7 (14.7)	884 (14.2)	
Current smoker	92 (9.7)	554 (8.9)			80.8 (8.6)	558 (8.9)	
Not available	289 (30.6)	1840 (29.5)			295.2 (31.3)	1844.5 (29.5)	
Alcohol use			<0.001	0.222			0.114
None	333 (35.3)	2752 (44.1)			358.2 (37.9)	2677.6 (42.9)	
Mild-to-moderate	290 (30.7)	1387 (22.2)			256.8 (27.2)	1465.1 (23.5)	
Heavy	33 (3.5)	266 (4.3)			35 (3.7)	259.1 (4.1)	
Not available	288 (30.5)	1840 (29.5)			294 (31.1)	1843.2 (29.5)	
Creatinine, mg/dL			<0.001	0.187			0.123
≤ 1.5	455 (48.2)	3457 (55.4)			456 (48.3)	3393.9 (54.3)	
> 1.5	17 (1.8)	204 (3.3)			29.9 (3.2)	198.7 (3.2)	
Not available	472 (50.0)	2584 (41.4)			458.1 (48.5)	2652.4 (42.5)	
eGFR, mL/min/1.73m ²			<0.001	0.18			0.095
≥ 60	299 (31.7)	2206 (35.3)			294.9 (31.2)	2168.4 (34.7)	
< 60	75 (7.9)	756 (12.1)			98.2 (10.4)	725.4 (11.6)	
Not available	570 (60.4)	3283 (52.6)			550.9 (58.4)	3351.2 (53.7)	
Concomitant Procedure							
TV repair	49 (5.2)	166 (2.7)	<0.001	0.131	35.6 (3.8)	189.8 (3.0)	0.041
CABG	133 (14.1)	1176 (18.8)	<0.001	0.128	160.7 (17.0)	1136.9 (18.2)	0.031
Surgical ablation for Atrial fibrillation	55 (5.8)	329 (5.3)	0.477	0.024	49.2 (5.2)	334.4 (5.4)	0.007

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 7. Baseline and operative characteristics according to the types of prostheses in 40 to 54 years of age undergoing mitral valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n = 2783)	Biological prosthesis (n = 154)	p-value	SMD	Mechanical prosthesis (n = 2783)	Biological prosthesis (n = 154)	SMD
<i>Baseline Demographics</i>							
Age, years	48.1±4.1	48.1±4	0.873	0.013	48.1±4.1	47.9±3.9	0.051
Female	1560 (56.1)	82 (53.2)	0.495	0.056	1557.6 (56.0)	87.1 (56.6)	0.012
<i>Baseline conditions</i>							
Atrial fibrillation	853 (30.7)	36 (23.4)	0.056	0.164	843.4 (30.3)	39.8 (25.8)	0.099
Hypertension	1089 (39.1)	69 (44.8)	0.161	0.115	1094.7 (39.3)	55.2 (35.8)	0.072
Diabetes mellitus	226 (8.1)	23 (14.9)	0.003	0.215	232.4 (8.4)	11.4 (7.4)	0.035
Dyslipidemia	231 (8.3)	11 (7.1)	0.611	0.043	226.2 (8.1)	13.2 (8.6)	0.016
Chronic kidney disease	56 (2.0)	17 (11.0)	<0.001	0.372	65.7 (2.4)	4.4 (2.9)	0.03
Dialysis	30 (1.1)	16 (10.4)	<0.001	0.409	40 (1.4)	3.1 (2.0)	0.046
Stroke, TIA or SE	332 (11.9)	18 (11.7)	0.928	0.007	332.9 (12.0)	25.7 (16.7)	0.136
Ischemic heart disease	419 (15.1)	26 (16.9)	0.538	0.05	421.5 (15.1)	23.5 (15.3)	0.003
Myocardial infarction	56 (2.0)	6 (3.9)	0.138	0.111	58 (2.1)	2.4 (1.6)	0.04
Previous PCI	24 (0.9)	3 (1.9)	0.166	0.092	24.8 (0.9)	0.7 (0.5)	0.056
Congestive heart failure	913 (32.8)	45 (29.2)	0.356	0.078	907.1 (32.6)	39.9 (25.9)	0.147
Anemia	249 (8.9)	36 (23.4)	<0.001	0.4	265 (9.5)	12.6 (8.2)	0.047
COPD	47 (1.7)	3 (1.9)	0.745	0.019	47.5 (1.7)	4.7 (3.1)	0.089
Asthma	289 (10.4)	17 (11.0)	0.796	0.021	289.4 (10.4)	16.6 (10.8)	0.012
Peripheral vascular disease	90 (3.2)	8 (5.2)	0.187	0.098	92.6 (3.3)	4.5 (2.9)	0.025

Previous cardiac surgery	11 (0.4)	0 (0.0)	1.000	0.089	10.4 (0.4)	0 (0.0)	0.087
Previous cancer	69 (2.5)	8 (5.2)	0.061	0.142	72.3 (2.6)	5.4 (3.5)	0.053
Charlson comorbidity index			<0.001	0.431			0.082
0	972 (34.9)	41 (26.6)	<0.001	0.444	961.1 (34.5)	46.8 (30.4)	0.126
1	837 (30.1)	35 (22.7)			826.3 (29.7)	46 (29.9)	
2	512 (18.4)	34 (22.1)			519.9 (18.7)	35.5 (23.1)	
≥ 3	361 (13.0)	21 (13.6)			363 (13.0)	18.6 (12.1)	
≥ 5	101 (3.6)	23 (14.9)			112.7 (4.0)	7.1 (4.6)	
Years of Surgery			0.001	0.366			0.293
2002~2005	802 (28.8)	24 (15.6)			782.6 (28.1)	27.6 (17.9)	
2006~2009	725 (26.1)	55 (35.7)			740.3 (26.6)	40.6 (26.4)	
2010~2013	624 (22.4)	30 (19.5)			620.9 (22.3)	34.3 (22.3)	
2014~2018	632 (22.7)	45 (29.2)			639.2 (23.0)	51.5 (33.4)	
Cumulative hospital volume for cardiac surgery			<0.001	0.719			0.198
<250 cases	974 (35.0)	39 (25.3)			960.4 (34.5)	52.5 (34.1)	
250-1000 cases	609 (21.9)	83 (53.9)			654.7 (23.5)	48.6 (31.6)	
1000-3000 cases	1200 (43.1)	32 (20.8)			1167.9 (42.0)	52.9 (34.4)	
≥3000 cases							
Mode of valve diseases							
Mitral stenosis	2382 (85.6)	119 (77.3)	0.005	0.215	2371 (85.2)	120 (77.9)	0.189
Mitral regurgitation	544 (19.5)	30 (19.5)	0.984	0.002	545 (19.6)	29 (18.6)	0.025
Combined	798 (28.7)	37 (24.0)	0.213	0.106	791 (28.4)	39 (25.6)	0.064
Others, NOS	1241 (44.6)	57 (37.0)	0.065	0.155	1230 (44.2)	67 (43.7)	0.01
Endocarditis	419 (15.1)	52 (33.8)	<0.001	0.446	444 (16.0)	32 (20.5)	0.117

Congestive heart failure	881 (31.7)	58 (37.7)	0.12	0.126	889 (31.9)	37 (24.2)	0.172
Health Screening Data							
Height, m	162.7±8.6	163.3±8.5	0.598	0.062	162.75 (8.62)	163.8±9.4	0.113
Weight, kg	62.3±11.0	62.3±11.2	0.994	0.001	62.3±11.0	63±11.2	0.065
BMI, kg/m ²	23.5±3.2	23.3±3.3	0.654	0.052	23.4±3.2	23.4±3.0	0.017
< 18.5	55 (2.0)	4 (2.6)	0.847	0.119	55.8 (2.0)	2.6 (1.7)	0.091
≥ 18.5 and < 23	631 (22.7)	32 (20.8)			628.4 (22.6)	38.2 (24.8)	
≥ 23 and < 25	340 (12.2)	21 (13.6)			340.5 (12.2)	21.9 (14.2)	
≥ 25 and < 30	389 (14.0)	17 (11.0)			386.2 (13.9)	20.2 (13.1)	
≥ 30	42 (1.5)	3 (1.9)			42.4 (1.5)	2 (1.3)	
Not available	1326 (47.6)	77 (50.0)			1329.7 (47.8)	69 (44.8)	
Systolic blood pressure, mmHg	117.4±16.1	122.5±18.3	0.007	0.298	117.6±118.4	118.4±14.5	0.048
< 120	810 (29.1)	38 (24.7)	0.477	0.127	804.1 (28.9)	50.5 (32.8)	0.101
≥ 120 and < 140	523 (18.8)	29 (18.8)			522.2 (18.8)	26.1 (16.9)	
≥ 140	124 (4.5)	10 (6.5)			127 (4.6)	8.4 (5.5)	
Not available	1326 (47.6)	77 (50.0)			1329.7 (47.8)	69 (44.8)	
Diastolic blood pressure, mmHg	73.7±11.6	75.8±12.9	0.135	0.166	73.8±11.7	73.3±11.7	0.047
< 80	956 (34.4)	45 (29.2)			949.1 (34.1)	57.7 (37.5)	0.089
≥ 80 and < 90	378 (13.6)	23 (14.9)			379.5 (13.6)	22 (14.3)	
≥ 90	123 (4.4)	9 (5.8)			124.8 (4.5)	5.3 (3.4)	
Not available	1326 (47.6)	77 (50.0)			1329.7 (47.8)	69 (44.8)	
Smoking			0.828	0.078			0.115
Never smoker	941 (33.8)	47 (30.5)			936.7 (33.7)	52.4 (34.0)	

Previous smoker	189 (6.8)	10 (6.5)			188.3 (6.8)	14.8 (9.6)	
Current smoker	288 (10.3)	18 (11.7)			289.6 (10.4)	17 (11.0)	
Not available	1365 (49.0)	79 (51.3)			1368.4 (49.2)	69.8 (45.3)	
Alcohol use			0.685	0.106			0.086
None	557 (20.0)	26 (16.9)			550.2 (19.8)	34 (22.1)	
Mild-to-moderate	807 (29.0)	47 (30.5)			811.1 (29.1)	45.9 (29.8)	
Heavy	59 (2.1)	2 (1.3)			57.9 (2.1)	4.2 (2.7)	
Not available	1360 (48.9)	79 (51.3)			1363.7 (49.0)	69.8 (45.3)	
Creatinine, mg/dL			<0.001	0.227			0.107
<= 1.5	884 (31.8)	42 (27.3)			878.6 (31.6)	56.4 (36.6)	
> 1.5	20 (0.7)	6 (3.9)			21.4 (0.8)	1 (0.6)	
Not available	1879 (67.5)	106 (68.8)			1882.9 (67.7)	96.6 (62.7)	
eGFR, mL/min/1.73m ²			0.026	0.172			0.161
≥ 60	648 (23.3)	33 (21.4)			646.3 (23.2)	42.1 (27.3)	
< 60	45 (1.6)	7 (4.5)			45.5 (1.6)	5.5 (3.6)	
Not available	2090 (75.1)	114 (74.0)			2091.3 (75.1)	106.5 (69.2)	
Concomitant Procedure							
TV repair	987 (35.5)	47 (30.5)	0.211	0.105	980.1 (35.2)	44.5 (28.9)	0.135
CABG	75 (2.7)	5 (3.2)	0.610	0.033	75.2 (2.7)	2.4 (1.6)	0.082
Surgical ablation for Atrial fibrillation	1182 (42.5)	60 (39.0)	0.391	0.072	1178.9 (42.4)	69.2 (44.9)	0.052

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 8. Baseline and operative characteristics according to the types of prostheses in 55 to 69 years of age undergoing mitral valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n = 2999)	Biological prosthesis (n = 1232)	p-value	SMD	Mechanical prosthesis (n = 2999)	Biological prosthesis (n = 1232)	SMD
<i>Baseline Demographics</i>							
Age, years	60.8±3.9	64.9±3.6	<0.001	1.077	62.0±4.3	62.3±4.2	0.077
Female	1840 (61.4)	804 (65.3)	0.017	0.081	1868 (62.3)	773 (62.8)	0.01
<i>Baseline conditions</i>							
Atrial fibrillation	1305 (43.5)	457 (37.1)	<0.001	0.131	1258 (42.0)	493 (40.0)	0.04
Hypertension	1691 (56.4)	742 (60.2)	0.022	0.078	1731 (57.7)	720 (58.2)	0.015
Diabetes mellitus	539 (18.0)	300 (24.4)	<0.001	0.157	609 (20.3)	279 (22.6)	0.057
Dyslipidemia	464 (15.5)	189 (15.3)	0.915	0.004	470 (15.7)	207 (16.8)	0.032
Chronic kidney disease	63 (2.1)	55 (4.5)	<0.001	0.133	83 (2.8)	46 (3.8)	0.055
Dialysis	35 (1.2)	35 (2.8)	<0.001	0.12	49 (1.6)	27 (2.2)	0.042
Stroke, TIA or SE	480 (16.0)	210 (17.0)	0.405	0.028	493 (16.4)	212 (17.2)	0.021
Ischemic heart disease	728 (24.3)	342 (27.8)	0.018	0.079	745 (24.8)	310 (25.1)	0.007
Myocardial infarction	84 (2.8)	42 (3.4)	0.29	0.035	94 (3.1)	38 (3.0)	0.006
Previous PCI	60 (2.0)	40 (3.2)	0.015	0.078	69 (2.3)	25 (2.0)	0.017
Congestive heart failure	1351 (45.0)	613 (49.8)	0.005	0.094	1392 (46.4)	593 (48.2)	0.035
Anemia	213 (7.1)	145 (11.8)	<0.001	0.16	261 (8.7)	105 (8.5)	0.006
COPD	117 (3.9)	75 (6.1)	0.002	0.1	133 (4.4)	51 (4.1)	0.015
Asthma	487 (16.2)	236 (19.2)	0.022	0.076	511 (17.0)	218 (17.7)	0.016
Peripheral vascular disease	155 (5.2)	79 (6.4)	0.108	0.053	172 (5.7)	71 (5.8)	0.002

Previous cardiac surgery	10 (0.3)	8 (0.6)	0.151	0.045	11 (0.4)	4 (0.3)	0.012
Previous cancer	124 (4.1)	70 (5.7)	0.029	0.072	139 (4.6)	57 (4.6)	<0.001
Charlson comorbidity index			<0.001	0.241			0.072
0	6189 (20.6)	174 (14.1)	<0.001	0.238	557 (18.6)	197 (16.0)	0.083
1	838 (27.9)	311 (25.2)			806 (26.9)	330 (26.8)	
2	640 (21.3)	277 (22.5)			650 (21.7)	266 (21.6)	
≥ 3	637 (21.2)	294 (23.9)			664 (22.2)	286 (23.2)	
≥ 5	266 (8.9)	176 (14.3)			321 (10.7)	153 (12.4)	
Years of Surgery			0.032	0.1			0.007
2002~2005	763 (25.4)	278 (22.6)			731 (24.4)	299 (24.3)	
2006~2009	694 (23.1)	331 (26.9)			731 (24.4)	300 (24.3)	
2010~2013	662 (22.1)	255 (20.7)			642 (21.4)	267 (21.7)	
2014~2018	880 (29.3)	368 (29.9)			895 (29.8)	366 (29.7)	
Cumulative hospital volume for cardiac surgery			<0.001	0.297			0.136
<250 cases	1011 (33.7)	505 (41.0)			1080 (36.0)	473 (38.4)	
250-1000 cases	630 (21.0)	344 (27.9)			703 (23.4)	337 (27.3)	
1000-3000 cases	1358 (45.3)	383 (31.1)			1217 (40.6)	422 (34.2)	
≥3000 cases							
Mode of valve diseases							
Mitral stenosis	2598 (86.6)	1020 (82.8)	0.001	0.107	2568 (85.6)	1046 (84.9)	0.021
Mitral regurgitation	531 (17.7)	273 (22.2)	0.001	0.112	555 (18.5)	232 (18.8)	0.008
Combined	885 (29.5)	291 (23.6)	<0.001	0.134	844 (28.1)	355 (28.8)	0.015
Others, NOS	1369 (45.6)	453 (36.8)	<0.001	0.181	1312 (43.7)	549 (44.5)	0.016
Endocarditis	328 (10.9)	203 (16.5)	<0.001	0.162	371 (12.4)	160 (13.0)	0.019

Congestive heart failure	1176 (39.2)	513 (41.6)	0.143	0.049	1196 (39.9)	512 (41.5)	0.034
Health Screening Data							
Height, m	159.4±8.4	157.6 (8.1)	<0.001	0.211	159.1±8.5	158.1±8.3	0.121
Weight, kg	60.4±10.5	58.2±9.9	<0.001	0.22	59.9±10.5	59.0±10.3	0.086
BMI, kg/m ²	23.7±3.2	23.4±3.3	0.013	0.107	23.6±3.2	23.6±3.4	0.009
< 18.5	64 (2.1)	36 (2.9)	0.12	0.1	74.9 (2.5)	31.7 (2.6)	0.038
≥ 18.5 and < 23	748 (24.9)	320 (26.0)			761 (25.4)	310 (25.2)	
≥ 23 and < 25	470 (15.7)	189 (15.3)			460 (15.3)	182 (14.8)	
≥ 25 and < 30	547 (18.2)	188 (15.3)			518 (17.3)	202 (16.4)	
≥ 30	71 (2.4)	24 (1.9)			69 (2.3)	27 (2.2)	
Not available	1099 (36.6)	475 (38.6)			1116 (37.2)	479 (38.8)	
Systolic blood pressure, mmHg	120.6±16.3	122.6±17.3	0.005	0.124	121.4±16.8	121.9±17.2	0.026
< 120	868 (28.9)	305 (24.8)	0.009	0.114	828 (27.6)	322 (26.1)	0.043
≥ 120 and < 140	803 (26.8)	330 (26.8)			794 (26.5)	318 (25.8)	
≥ 140	229 (7.6)	121 (9.8)			261 (8.7)	112 (9.1)	
Not available	1099 (36.6)	476 (38.6)			1116 (37.2)	479 (38.9)	
Diastolic blood pressure, mmHg	74.8±10.9	75.4±11.2	0.194	0.056	75.1±11.0	75.3±11.1	0.015
< 80	1172(39.1)	440 (35.7)	0.158	0.077	1134 (37.8)	446 (36.12)	0.04
≥ 80 and < 90	531 (17.7)	221 (17.9)			536 (17.9)	216 (17.5)	
≥ 90	197 (6.6)	95 (7.7)			212 (7.1)	91 (7.4)	
Not available	1099 (36.6)	476 (38.6)			1116 (37.2)	479 (38.9)	
Smoking			0.011	0.115			0.072
Never smoker	1366 (45.5)	565 (45.9)			1371 (45.7)	572 (46.4)	

Previous smoker	254 (8.5)	76 (6.2)			230 (7.7)	77 (6.3)	
Current smoker	246 (8.2)	83 (6.7)			231 (7.7)	82 (6.7)	
Not available	1133 (37.8)	508 (41.2)			1167 (28.9)	501 (40.6)	
Alcohol use			0.007	0.119			0.042
None	939 (31.3)	394 (32.0)			937 (31.2)	379 (30.7)	
Mild-to-moderate	875 (29.2)	299 (24.3)			836 (27.9)	326 (26.4)	
Heavy	54 (1.8)	29 (2.4)			59 (2.0)	27 (2.2)	
Not available	1131 (37.7)	510 (41.4)			1167 (38.9)	501 (40.7)	
Creatinine, mg/dL			0.001	0.119			0.06
<= 1.5	1237 (41.2)	472 (38.2)			1207 (40.2)	462 (37.5)	
> 1.5	34 (1.1)	32 (2.6)			44 (1.5)	22 (1.8)	
Not available	1728 (57.6)	728 (59.1)			1748 (58.3)	748 (60.7)	
eGFR, mL/min/1.73m ²			<0.001	0.161			0.072
≥ 60	842 (28.1)	296 (24.0)			816 (27.2)	299 (24.2)	
< 60	164 (5.5)	114 (9.3)			189 (6.3)	88 (7.1)	
Not available	1993 (66.5)	8227 (66.7)			1994 (66.5)	846 (68.6)	
Concomitant Procedure							
TV repair	1385 (46.2)	526 (42.7)	0.038	0.07	1330 (44.4)	513 (41.6)	0.055
CABG	176 (5.9)	100 (8.1)	0.007	0.088	201 (6.7)	82 (6.6)	0.004
Surgical ablation for Atrial fibrillation	1388 (46.3)	552 (44.8)	0.381	0.03	1353 (45.1)	544 (44.2)	0.019

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 9. Baseline and operative characteristics according to the types of prostheses in 70 to 79 years of age undergoing mitral valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n = 175)	Biological prosthesis (n = 1568)	p-value	SMD	Mechanical prosthesis (n = 175)	Biological prosthesis (n = 1568)	SMD
<i>Baseline Demographics</i>							
Age, years	72.5±2.3	73.7±2.7	<0.001	0.451	73.2±2.5	73.6±5.7	0.131
Female	107 (61.1)	1099 (70.1)	0.015	0.189	124.5 (71.1)	1086.9 (69.3)	0.04
<i>Baseline conditions</i>							
Atrial fibrillation	84 (48.0)	711 (45.3)	0.504	0.053	70.9 (40.5)	713.3 (45.5)	0.1
Hypertension	129 (73.7)	1143 (72.9)	0.817	0.019	138.3 (79.0)	1146.4 (73.1)	0.139
Diabetes mellitus	53 (30.3)	488 (31.1)	0.82	0.018	54.2 (31.0)	485.8 (31.0)	<0.001
Dyslipidemia	27 (15.4)	333 (21.2)	0.072	0.151	32.6 (18.6)	325.1 (20.7)	0.053
Chronic kidney disease	7 (4.0)	76 (4.8)	0.618	0.041	5.8 (3.3)	74.8 (4.8)	0.075
Dialysis	1 (0.6)	29 (1.8)	0.355	0.117	1.4 (0.8)	27 (1.7)	0.082
Stroke, TIA or SE	29 (16.6)	302 (19.3)	0.39	0.07	31.2 (17.8)	297.9 (19.0)	0.03
Ischemic heart disease	68 (38.9)	549 (35.0)	0.313	0.08	65 (37.1)	554.4 (35.4)	0.038
Myocardial infarction	9 (5.1)	61 (3.9)	0.423	0.06	9.4 (5.4)	63.4 (4.0)	0.064
Previous PCI	8 (4.6)	83 (5.3)	0.684	0.033	11.5 (6.6)	81.3 (5.2)	0.058
Congestive heart failure	101 (57.7)	861 (54.9)	0.479	0.057	98.3 (56.2)	866.3 (55.2)	0.018
Anemia	24 (13.7)	222 (14.2)	0.873	0.013	22.4 (12.8)	221.6 (14.1)	0.039
COPD	16 (9.1)	138 (8.8)	0.88	0.012	24.1 (13.8)	139.9 (8.9)	0.153
Asthma	41 (23.4)	352 (22.4)	0.769	0.023	48.2 (27.5)	356.3 (22.7)	0.112
Peripheral vascular disease	18 (10.3)	122 (7.8)	0.247	0.087	11.8 (6.7)	124.8 (8.0)	0.047

Previous cardiac surgery	2 (1.1)	14 (0.9)	0.671	0.025	0.7 (0.4)	14.1 (0.9)	0.062
Previous cancer	7 (4.0)	131 (8.4)	0.043	0.182	13.9 (7.9)	124.3 (7.9)	0.002
Charlson comorbidity index			0.384	0.075			0.008
0	27 (15.4)	161 (10.3)	0.044	0.248	19.5 (11.1)	168.1 (10.7)	0.19
1	25 (14.3)	322 (20.5)			27.5 (15.7)	311.3 (19.9)	
2	44 (25.1)	317 (20.2)			38.9 (22.2)	325 (20.7)	
≥ 3	53 (30.3)	483 (30.8)			65.6 (37.5)	483.9 (30.9)	
≥ 5	26 (14.9)	285 (18.2)			23.6 (13.5)	279.6 (17.8)	
Years of Surgery			<0.001	0.327			0.074
2002~2005	39 (22.3)	179 (11.4)			19.5 (11.1)	197.6 (12.6)	
2006~2009	42 (24.0)	334 (21.3)			42.5 (24.3)	339 (21.6)	
2010~2013	39 (22.3)	426 (27.2)			47.1 (26.9)	418 (26.7)	
2014~2018	55 (31.4)	629 (40.1)			65.9 (37.7)	613.4 (39.1)	
Cumulative hospital volume for cardiac surgery			0.953	0.025			0.152
<250 cases	73 (41.7)	635 (40.5)			63.6 (36.3)	633.7 (40.4)	
250-1000 cases	41 (23.4)	376 (24.0)			36.1 (20.6)	375.5 (23.9)	
1000-3000 cases	61 (34.9)	557 (35.5)			75.3 (43.0)	558.9 (35.6)	
≥3000 cases							
Mode of valve diseases							
Mitral stenosis	147 (84.0)	1348 (86.0)	0.479	0.055	151 (86.4)	1345 (85.8)	0.018
Mitral regurgitation	28 (16.0)	327 (20.9)	0.13	0.125	34 (19.3)	318 (20.3)	0.025
Combined	57 (32.6)	306 (19.5)	<0.001	0.301	38 (21.7)	328 (20.9)	0.019
Others, NOS	82 (46.9)	522 (33.3)	<0.001	0.28	67 (38.1)	546 (34.8)	0.067
Endocarditis	28 (16.0)	229 (14.6)	0.621	0.039	26 (15.0)	230 (14.7)	0.009

Congestive heart failure	88 (50.3)	704 (44.9)	0.175	0.108	83 (47.7)	713 (45.4)	0.045
Health Screening Data							
Height, m	156.6±8.1	156.1±8.5	0.621	0.054	154.8±7.4	156.2±8.5	0.168
Weight, kg	58.3±11.1	57.7±9.8	0.632	0.049	56.6±9.3	57.7±9.8	0.122
BMI, kg/m ²	23.7±3.5	23.6±3.3	0.966	0.004	23.5±3.0	23.6±3.3	0.036
< 18.5	5 (2.9)	35 (2.2)	0.099	0.252	3.1 (1.8)	35.8 (2.3)	0.098
≥ 18.5 and < 23	40 (22.9)	403 (25.7)			43.1 (24.6)	399.1 (25.5)	
≥ 23 and < 25	14 (8.0)	220 (14.0)			25.1 (14.3)	210.9 (13.5)	
≥ 25 and < 30	30 (17.1)	295 (18.8)			30.5 (17.4)	292.7 (18.7)	
≥ 30	6 (3.4)	37 (2.4)			2.5 (1.4)	37.2 (2.4)	
Not available	80 (45.7)	578 (36.9)			70.7 (40.4)	592.2 (37.8)	
Systolic blood pressure, mmHg	122.2±13.8	125.7±16.1	0.043	0.231	126.1±14.7	125.5 (16.1)	0.042
< 120	34 (19.4)	315 (20.1)	0.056	0.231	30.2 (17.3)	313.7 (20.0)	0.085
≥ 120 and < 140	49 (28.0)	477 (30.4)			51 (29.1)	472.2 (30.1)	
≥ 140	12 (6.9)	195 (12.4)			23.1 (13.2)	187 (11.9)	
Not available	80 (45.7)	581 (37.1)			70.7 (40.4)	595.1 (38.0)	
Diastolic blood pressure, mmHg	73.6±8.9	75.2±10.8	0.104	0.161	74.8±10.0	75.0±10.8	0.021
< 80	63 (36.0)	576 (36.7)	0.024	0.273	63 (36.2)	574 (36.6)	0.08
≥ 80 and < 90	28 (16.0)	300 (19.1)			32 (18.5)	295 (18.8)	
≥ 90	4 (2.3)	111 (7.1)			9 (5.0)	104 (6.6)	
Not available	80 (45.7)	581 (37.1)			71 (40.4)	595 (38.0)	
Smoking			0.165	0.179			0.086
Never smoker	76 (43.4)	814 (51.9)			88 (50.4)	802 (51.2)	

Previous smoker	12 (6.9)	105 (6.7)			9 (4.9)	104 (6.7)	
Current smoker	7 (4.0)	63 (4.0)			8 (4.3)	62 (4.0)	
Not available	80 (45.7)	586 (37.4)			71 (40.4)	599 (38.2)	
Alcohol use			0.104	0.21			0.052
None	64 (36.6)	672(42.9)			73 (41.7)	661 (42.2)	
Mild-to-moderate	30 (17.1)	275 (17.5)			28 (15.9)	275 (17.5)	
Heavy	1 (0.6)	33 (2.1)			4 (2.1)	31 (2.0)	
Not available	80 (45.7)	588 (37.5)			71 (40.4)	601 (38.3)	
Creatinine, mg/dL			0.094	0.178			0.11
<= 1.5	70 (40.0)	740 (47.2)			80 (45.4)	727 (46.4)	
> 1.5	2 (1.1)	35 (2.2)			2 (0.9)	33 (2.1)	
Not available	103 (58.9)	793 (50.6)			94 (53.8)	807 (51.5)	
eGFR, mL/min/1.73m ²			0.29	0.128			0.095
≥ 60	39 (22.3)	424 (27.0)			47 (27.0)	416 (26.5)	
< 60	20 (11.4)	199 (12.7)			17 (9.5)	195 (12.4)	
Not available	116 (66.3)	945 (60.3)			111 (63.5)	957 (61.0)	
Concomitant Procedure							
TV repair	78 (44.6)	726 (46.3)	0.663	0.035	85 (48.5)	725 (46.3)	0.045
CABG	18 (10.3)	193 (12.3)	0.436	0.064	20 (11.3)	190 (12.1)	0.028
Surgical ablation for Atrial fibrillation	52 (29.7)	625 (39.9)	0.009	0.214	73 (41.5)	609 (38.7)	0.054

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass graftin

Supplementary Table 10. Baseline and operative characteristics according to the types of prostheses in 40 to 54 years of age undergoing aortic and mitral valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n = 1163)	Biological prosthesis (n = 43)	p-value	SMD	Mechanical prosthesis (n = 1163)	Biological prosthesis (n = 43)	SMD
<i>Baseline Demographics</i>							
Age, years	48.1±4.1	49.0±4.0	0.167	0.217	48.2±4.1	47.8±4.4	0.085
Female	658 (56.6)	18 (41.9)	0.056	0.298	652.1 (56.1)	23.6 (54.9)	0.025
<i>Baseline conditions</i>							
Atrial fibrillation	354 (30.4)	5 (11.6)	0.008	0.474	346.6 (29.8)	12.4 (28.8)	0.021
Hypertension	500 (43.0)	14 (32.6)	0.174	0.216	496.2 (42.7)	18.2 (42.3)	0.005
Diabetes mellitus	78 (6.7)	3 (7.0)	0.763	0.011	77.5 (6.7)	5 (11.6)	0.176
Dyslipidemia	94 (8.1)	1 (2.3)	0.248	0.261	90.8 (7.8)	0.1 (0.2)	0.401
Chronic kidney disease	19 (1.6)	4 (9.3)	0.008	0.342	21.4 (1.8)	0.4 (0.9)	0.078
Dialysis	13 (1.1)	4 (9.3)	0.002	0.375	15.6 (1.3)	0.4 (0.9)	0.039
Stroke, TIA or SE	99 (8.5)	3 (7.0)	1.000	0.057	97.8 (8.4)	1.5 (3.5)	0.208
Ischemic heart disease	226 (19.4)	4 (9.3)	0.097	0.292	222.4 (19.1)	7.8 (18.1)	0.025
Myocardial infarction	21 (1.8)	0 (0.0)	1.000	0.192	20.3 (1.7)	0 (0.0)	0.188
Previous PCI	11 (0.9)	0 (0.0)	1.000	0.138	10.6 (0.9)	0 (0.0)	0.136
Congestive heart failure	431 (37.1)	13 (30.2)	0.362	0.145	426.8 (36.7)	10.1 (23.5)	0.293
Anemia	90 (7.7)	6 (14.0)	0.146	0.201	92.6 (8.0)	4.2 (9.8)	0.064
COPD	18 (1.5)	1 (2.3)	0.501	0.056	17.8 (1.5)	0.1 (0.2)	0.141
Asthma	114 (9.8)	4 (9.3)	1.000	0.017	113.6 (9.8)	3.1 (7.2)	0.088
Peripheral vascular disease	34 (2.9)	0 (0.0)	0.630	0.245	32.8 (2.8)	0 (0.0)	0.241

Previous cardiac surgery	0 (0.0)	1 (2.3)	0.036	0.218	0 (0.0)	0.1 (0.2)	0.051
Previous cancer	17 (1.5)	1 (2.3)	0.482	0.063	17.2 (1.5)	0.2 (0.5)	0.113
Charlson comorbidity index			0.560	0.192			0.103
0	430 (37.0)	15 (34.9)	0.426	0.249	430 (37.0)	19.5 (45.3)	0.293
1	383 (32.9)	14 (32.6)			382.7 (32.9)	9.5 (22.1)	
2	185 (15.9)	5 (11.6)			184.4 (15.9)	8 (18.6)	
≥ 3	136 (11.7)	6 (14.0)			136.4 (11.7)	5.7 (13.3)	
≥ 5	29 (2.5)	3 (7.0)			29.5 (2.5)	0.3 (0.7)	
Years of Surgery			0.733	0.176			0.167
2002~2005	398 (34.2)	12 (27.9)			394.8 (33.9)	11.5 (26.7)	
2006~2009	334 (28.7)	15 (34.9)			336.9 (29.0)	14.9 (34.7)	
2010~2013	216 (18.6)	7 (16.3)			215.9 (18.6)	8.2 (19.1)	
2014~2018	215 (18.5)	9 (20.9)			215.4 (18.5)	8.4 (19.5)	
Cumulative hospital volume for cardiac surgery (AVR)			<0.001	0.81			0.501
<250	237 (20.4)	11 (25.6)			238.9 (20.5)	11.9 (27.7)	
250-1000	319 (27.4)	24 (55.8)			331.1 (28.5)	17.2 (40.0)	
1000-3000	416 (35.8)	7 (16.3)			407.7 (35.1)	12.5 (29.1)	
≥3000	191 (16.4)	1 (2.3)			185.4 (15.9)	1.4 (3.3)	
Cumulative hospital volume for cardiac surgery (MVR)			<0.001	0.813			0.399
<250	290 (24.9)	12 (27.9)			291.1 (25.0)	12.8 (29.8)	
250-1000	266 (22.9)	23 (53.5)			278.9 (24.0)	16.2 (37.7)	
1000-3000	607 (52.2)	8 (18.6)			593 (51.0)	13.9 (32.3)	
≥3000							

<i>Mode of valve diseases</i>							
<i>Aortic valve disease</i>							
Bicuspid aortic valve	12 (1.0)	0 (0.0)	1.000	0.144	11.6 (1.0)	0 (0.0)	0.142
Aortic stenosis	412 (35.4)	8 (18.6)	0.023	0.386	405.9 (34.9)	16.1 (37.4)	0.052
Aortic regurgitation	611 (52.5)	24 (55.8)	0.673	0.066	611.6 (52.6)	21.3 (49.5)	0.063
Combined	310 (26.7)	9 (20.9)	0.403	0.135	308.5 (26.5)	10.2 (23.7)	0.067
Others, NOS	362 (31.1)	11 (25.6)	0.440	0.123	360.1 (31.0)	11.4 (26.5)	0.1
<i>Mitral valve disease</i>							
Mitral stenosis	895 (77.0)	27 (62.8)	0.032	0.312	888.5 (76.4)	32.9 (76.5)	0.002
Mitral regurgitation	153 (13.2)	9 (20.9)	0.142	0.208	156.4 (13.4)	6.1 (14.2)	0.019
Combined	355 (30.5)	8 (18.6)	0.094	0.28	351.7 (30.2)	13.3 (30.9)	0.016
Others, NOS	506 (43.5)	11 (25.6)	0.020	0.384	499.3 (42.9)	18.1 (42.1)	0.019
Endocarditis	174 (15.0)	17 (39.5)	<0.001	0.574	184.6 (15.9)	8.2 (19.1)	0.085
Congestive heart failure	433 (37.2)	19 (44.2)	0.355	0.142	437.4 (37.6)	19.9 (46.3)	0.178
<i>Health Screening Data</i>							
Height, m	162.5±8.6	162.9±8.6	0.830	0.049	162.5±7.9	165.9±9.7	0.38
Weight, kg	61.4±11.0	63.5±11.0	0.410	0.173	61.5±10.8	64.4±11.6	0.259
BMI, kg/m ²	23.2±3.2	23.9±3.2	0.488	0.181	23.2 (3.22)	23.3±3.1	0.028
< 18.5	29 (2.5)	1 (2.3)	0.075	0.519	28.8 (2.5)	1.1 (2.6)	0.646
≥ 18.5 and < 23	283 (24.3)	7 (16.3)			281.3 (24.2)	6.2 (14.4)	
≥ 23 and < 25	151 (13.0)	9 (20.9)			151.1 (13.0)	12.8 (29.8)	
≥ 25 and < 30	144 (12.4)	1 (2.3)			142.6 (12.3)	0.4 (0.9)	
≥ 30	16 (1.4)	2 (4.7)			15.8 (1.4)	0.7 (1.6)	
Not available	540 (46.4)	23 (53.5)			543.4 (46.7)	21.7 (50.5)	

Systolic blood pressure, mmHg	118.3±16.1	118.8±16.1	0.913	0.029	118.3±15.7	118.3±18.4	0.001
< 120	325 (27.9)	10 (23.3)	0.639	0.2	323.1 (27.8)	9.2 (21.4)	0.185
≥ 120 and < 140	244 (21.0)	7 (16.3)			242.2 (20.8)	10.8 (25.1)	
≥ 140	54 (4.6)	3 (7.0)			54.3 (4.7)	1.3 (3.0)	
Not available	540 (46.4)	23 (53.5)			543.4 (46.7)	21.7 (50.5)	
Diastolic blood pressure, mmHg	72.0±11.6	72.7±11.6	0.778	0.06	72.0±10.8	72.9±10.4	0.081
< 80	430 (37.0)	13 (30.2)	0.130	0.336	428.3(36.8)	13.1 (30.5)	0.134
≥ 80 and < 90	151 (13.0)	3 (7.0)			149.6 (12.9)	6.4 (14.9)	
≥ 90	42 (3.6)	4 (9.3)			41.7 (3.6)	1.7 (4.0)	
Not available	540 (46.4)	23 (53.5)			543.4 (46.7)	21.7 (50.5)	
Smoking			0.355	0.29			0.312
Never smoker	416 (35.8)	10 (23.3)			412.7 (35.5)	11.6 (27.0)	
Previous smoker	85 (7.3)	4 (9.3)			85 (7.3)	6.8(15.8)	
Current smoker	110 (9.5)	6 (14.0)			110.1 (9.5)	2.9 (6.7)	
Not available	552 (47.5)	23 (53.5)			555.2 (47.7)	21.7 (50.5)	
Alcohol use			0.446	0.282			0.289
None	217 (18.7)	4 (9.3)			214.7 (18.5)	4.5 (10.5)	
Mild-to-moderate	374 (32.2)	14 (32.6)			372.9 (32.1)	16.2 (37.7)	
Heavy	21 (1.8)	1 (2.3)			21.2 (1.8)	0.1 (0.2)	
Not available	551 (47.4)	24 (55.8)			554.3 (47.7)	22.2 (51.6)	
Creatinine, mg/dL			0.125	0.241			0.042
≤ 1.5	337 (29.0)	9 (20.9)			334.9 (28.8)	12.6 (29.3)	
> 1.5	5 (0.4)	1 (2.3)			4.8 (0.4)	0.1 (0.2)	

Not available	821 (70.6)	33 (76.7)			823.3 (70.8)	30.3 (70.5)	
eGFR, mL/min/1.73m ²			0.750	0.123			0.239
≥ 60	245 (21.1)	7 (16.3)			242.9 (20.9)	6.6 (15.3)	
< 60	25 (2.1)	1 (2.3)			25.2 (2.2)	0.1 (0.2)	
Not available	893 (76.8)	35 (81.4)			894.9 (76.9)	36.3 (84.4)	
Concomitant Procedure							
TV repair	421 (36.2)	13 (30.2)	0.423	0.127	418.2 (36.0)	12.3(28.6)	0.158
CABG	16 (1.4)	4 (9.3)	0.004	0.358	17.5 (1.5)	0.5 (1.2)	0.031
Surgical ablation for Atrial fibrillation	451 (38.8)	7 (16.3)	0.003	0.521	441.8 (38.0)	10.7 (24.9)	0.286

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 11. Baseline and operative characteristics according to the types of prostheses in 55 to 64 years of age undergoing aortic and mitral valve replacement.

	Unadjusted				IPTW		
	Mechanical prosthesis (n = 996)	Biological prosthesis (n = 134)	p-value	SMD	Mechanical prosthesis (n = 996)	Biological prosthesis (n = 134)	SMD
<i>Baseline Demographics</i>							
Age, years	59.2±2.8	60.7±2.9	<0.001	0.527	59.4±2.8	59.7±3.2	0.114
Female	565 (56.7)	72 (53.7)	0.512	0.06	561.7 (56.4)	73.3 (54.7)	0.034
<i>Baseline conditions</i>							
Atrial fibrillation	378 (38.0)	41 (30.6)	0.098	0.155	370.3 (37.2)	49 (36.6)	0.013
Hypertension	567 (56.9)	74 (55.2)	0.709	0.034	565.3 (56.8)	70.9 (52.9)	0.077
Diabetes mellitus	168 (16.9)	28 (20.9)	0.248	0.103	173.4 (17.4)	22.1 (16.5)	0.025
Dyslipidemia	143 (14.4)	20 (14.9)	0.861	0.016	144.6 (14.5)	21.4 (16.0)	0.041
Chronic kidney disease	32 (3.2)	12 (9.0)	0.001	0.242	36.9 (3.7)	4.9 (3.7)	0.001
Dialysis	22 (2.2)	9 (6.7)	0.007252	0.22	25.7 (2.6)	3.6 (2.7)	0.008
Stroke, TIA or SE	145 (14.6)	23 (17.2)	0.426	0.071	148.9 (14.9)	18.9 (14.1)	0.023
Ischemic heart disease	244 (24.5)	41 (30.6)	0.127	0.137	250.1 (25.1)	31.8 (23.7)	0.032
Myocardial infarction	27 (2.7)	6 (4.5)	0.268987	0.095	28.9 (2.9)	3.7 (2.8)	0.01
Previous PCI	16 (1.6)	5 (3.7)	0.092545	0.132	17.8 (1.8)	2.2 (1.6)	0.011
Congestive heart failure	448 (45.0)	58 (43.3)	0.711	0.034	447.6 (44.9)	59.1 (44.1)	0.016
Anemia	77 (7.7)	29 (21.6)	<0.001	0.401	89.3 (9.0)	11.1 (8.3)	0.024
COPD	35 (3.5)	3 (2.2)	0.611456	0.076	33.1 (3.3)	1.7 (1.3)	0.139
Asthma	123 (12.3)	21 (15.7)	0.279	0.096	127.1 (12.8)	14.8 (11.0)	0.052

Peripheral vascular disease	48 (4.8)	9 (6.7)	0.346	0.081	49.6 (5.0)	5.6 (4.2)	0.038
Previous cardiac surgery	2 (0.2)	0 (0.0)	1	0.063	1.8 (0.2)	0 (0.0)	0.06
Previous cancer	35 (3.5)	10 (7.5)	0.028	0.174	39.6 (4.0)	8.5 (6.3)	0.107
Charlson comorbidity index			0.025	0.274			0.053
0	221 (22.2)	33 (24.6)	0.002	0.389	224.5 (22.5)	36 (26.9)	0.224
1	308 (30.9)	22 (16.4)			290.5 (29.2)	26.5 (19.8)	
2	206 (20.7)	28 (20.9)			207.3 (20.8)	31.4 (23.4)	
≥ 3	187 (18.8)	32 (23.9)			190 (19.1)	28.8 (21.5)	
≥ 5	74 (7.4)	19 (14.2)			83.7 (8.4)	11.4 (8.5)	
Years of Surgery			0.176	0.214			0.114
2002~2005	268 (26.9)	38 (28.4)			269.9 (27.1)	43.2 (32.2)	
2006~2009	235 (23.6)	39 (29.1)			239.2 (24.0)	30.5 (22.8)	
2010~2013	227 (22.80)	20 (14.9)			217.3 (21.8)	27.2 (20.3)	
2014~2018	266 (26.7)	37 (27.6)			269.6 (27.1)	33 (24.6)	
Cumulative hospital volume for cardiac surgery (AVR)			<0.001	0.459			0.244
<250	208 (20.9)	40 (29.9)			214.5 (21.5)	26.7 (19.9)	
250-1000	267 (26.8)	46 (34.3)			281.6 (28.3)	52.8 (39.4)	
1000-3000	338 (33.9)	41 (30.6)			331.7 (33.3)	35.2 (26.3)	
≥3000	183 (18.4)	7 (5.2)			168.3 (16.9)	19.3 (14.4)	
Cumulative hospital volume for cardiac surgery (MVR)			0.002	0.337			0.256
<250	254 (25.5)	45 (33.6)			258.7 (26.0)	32.4 (24.2)	
250-1000	221 (22.2)	41 (30.6)			237.4 (23.8)	47.1 (35.1)	
1000-3000	521 (52.3)	48 (35.8)			499.9 (50.2)	54.5 (40.7)	

≥ 3000							
<i>Mode of valve diseases</i>							
<i>Aortic valve disease</i>							
Bicuspid aortic valve	20 (2.0)	2 (1.5)	1	0.039	19.3 (1.9)	1.1 (0.8)	0.097
Aortic stenosis	429 (43.1)	44 (32.8)	0.024	0.212	419.4 (42.1)	51.1 (38.1)	0.081
Aortic regurgitation	464 (46.6)	66 (49.3)	0.561	0.053	467.1 (46.9)	64.8 (48.4)	0.029
Combined	269 (27.0)	34 (25.4)	0.688	0.037	265.9 (26.7)	34.8 (26.0)	0.017
Others, NOS	314 (31.5)	36 (26.9)	0.273	0.103	306.4 (30.8)	35.3 (26.3)	0.098
<i>Mitral valve disease</i>							
Mitral stenosis	770 (77.3)	89 (66.4)	0.006	0.244	756.5 (76.0)	94.6 (70.6)	0.121
Mitral regurgitation	140 (14.1)	13 (9.7)	0.167	0.135	135.3 (13.6)	17.8 (13.3)	0.01
Combined	288 (28.9)	41 (30.6)	0.688	0.037	294.3 (29.5)	43.5 (32.5)	0.064
Others, NOS	425 (42.7)	53 (39.6)	0.493	0.063	424 (42.6)	55.3 (41.3)	0.026
Endocarditis	156 (15.7)	33 (24.6)	0.009	0.225	170.2 (17.1)	27.3 (20.4)	0.085
Congestive heart failure	391 (39.3)	56 (41.8)	0.573	0.052	394 (39.6)	59.4 (44.3)	0.097
<i>Health Screening Data</i>							
Height, m	159.7 \pm 7.9	160.1 \pm 7.1	0.673	0.054	159.7 \pm 7.9	159.3 \pm 7.5	0.055
Weight, kg	59.9 \pm 9.8	58.2 \pm 9.5	0.15	0.179	59.7 \pm 9.9	58.0 \pm 8.0	0.185
BMI, kg/m ²	23.4 \pm 2.8	22.7 \pm 3.3	0.041	0.236	23.3 \pm 2.9	22.9 \pm 3.3	0.123
< 18.5	21 (2.1)	7 (5.2)	0.057	0.295	24.2 (2.4)	6.3 (4.7)	0.353
≥ 18.5 and < 23	238 (23.9)	37 (27.6)			243 (24.4)	31.4 (23.4)	
≥ 23 and < 25	170 (17.1)	13 (9.7)			159.2 (16.0)	8.1 (6.0)	
≥ 25 and < 30	154 (15.5)	16 (11.9)			153.3 (15.4)	23.2 (17.3)	
≥ 30	12 (1.2)	2 (1.5)			11.6 (1.2)	0.9 (0.7)	
Not available	401 (40.3)	59 (44.0)			404.7 (40.6)	64.1 (47.8)	

Systolic blood pressure, mmHg	120.3±15.8	124.7±15.8	0.023	0.278	120.9±16.2	124.0±15.4	0.194
< 120	271 (27.2)	22 (16.4)	0.057	0.269	260.9 (26.2)	30 (22.4)	0.271
≥ 120 and < 140	252 (25.3)	42 (31.3)			255.2 (25.6)	23.4 (17.5)	
≥ 140	71 (7.1)	11 (8.2)			74.2 (7.4)	16.5 (12.3)	
Not available	402 (40.4)	59 (44.0)			405.6 (40.7)	64.1 (47.8)	
Diastolic blood pressure, mmHg	72.4±10.3	75.2±9.0	0.024	0.291	72.8 (10.62)	74.3±9.4	0.141
< 80	407 (40.9)	41 (30.6)	0.104	0.23	393.2 (39.5)	40.3 (30.1)	0.205
≥ 80 and < 90	148 (14.9)	27 (20.1)			156 (15.7)	22.2 (16.6)	
≥ 90	39 (3.9)	7 (5.2)			41.2 (4.1)	7.5 (5.6)	
Not available	402 (40.4)	59 (44.0)			405.6 (40.7)	64.1 (47.8)	
Smoking			0.355	0.182			0.162
Never smoker	420 (42.2)	58 (43.3)			421.7 (42.3)	50 (37.3)	
Previous smoker	98 (9.8)	7 (5.2)			93 (9.3)	9.1 (6.8)	
Current smoker	72 (7.2)	9 (6.7)			71.8 (7.2)	10.6 (7.9)	
Not available	406 (40.8)	60 (44.8)			409.5 (41.1)	64.3 (48.0)	
Alcohol use			0.388	0.151			0.222
None	275 (27.6)	32 (23.9)			271.5 (27.3)	32 (23.9)	
Mild-to-moderate	292 (29.3)	36 (26.9)			286 (28.7)	29.9 (22.3)	
Heavy	25 (2.5)	6 (4.5)			30.7 (3.1)	7.8 (5.8)	
Not available	404 (40.6)	60 (44.8)			407.7 (40.9)	64.3 (48.0)	
Creatinine, mg/dL			0.045	0.236			0.129
≤ 1.5	367 (36.8)	35 (26.1)			359 (36.0)	41.7 (31.1)	
> 1.5	14 (1.4)	3 (2.2)			13.8 (1.4)	0.9 (0.7)	

Not available	615 (61.7)	96 (71.6)			623.2 (62.6)	91.4 (68.2)	
eGFR, mL/min/1.73m ²			0.208	0.17			0.079
≥ 60	263 (26.4)	26 (19.4)			258.8 (26.0)	30.5 (22.8)	
< 60	39 (3.9)	5 (3.7)			37.6 (3.8)	5.9 (4.4)	
Not available	694 (69.7)	103 (76.9)			699.6 (70.2)	97.6 (72.8)	
Concomitant Procedure							
TV repair	406 (40.8)	58 (43.3)	0.578	0.051	405.4 (40.7)	48.6 (36.3)	0.091
CABG	37 (3.7)	5 (3.7)	1	0.001	37.5 (3.8)	6.6 (4.9)	0.056
Surgical ablation for Atrial fibrillation	406 (40.8)	54 (40.3)	0.918	0.009	405.5 (40.7)	50.3 (37.5)	0.065

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 12. Baseline and operative characteristics according to the types of prostheses in 65 to 79 years of age undergoing aortic and mitral valve replacement.

	Unadjusted				IPTW		
	Mechanical	Biological	p-value	SMD	Mechanical	Biological	SMD
	prosthesis (n = 304)	prosthesis (n = 830)			prosthesis (n = 304)	prosthesis (n = 830)	
<i>Baseline Demographics</i>							
Age, years	67.7±2.7	71.7±3.8	<0.001	1.235	69.8±3.4	70.7±3.9	0.247
Female	172 (56.6)	505 (60.8)	0.195	0.087	188.5 (62.0)	505.2 (60.9)	0.024
<i>Baseline conditions</i>							
Atrial fibrillation	138(45.4)	317 (38.2)	0.028	0.146	114.7 (37.7)	331.5 (39.9)	0.045
Hypertension	203 (66.8)	577 (69.5)	0.377	0.059	217.1 (71.4)	569.4 (68.6)	0.062
Diabetes mellitus	67 (22.0)	206 (24.8)	0.332	0.066	77.8 (25.6)	198.2 (23.9)	0.04
Dyslipidemia	47 (15.5)	168 (20.2)	0.069	0.125	62.9 (20.7)	160.6 (19.3)	0.033
Chronic kidney disease	14 (4.6)	34 (4.1)	0.706	0.025	14 (4.6)	33.1 (4.0)	0.03
Dialysis	6 (2.0)	20 (2.4)	0.664	0.03	9.3 (3.1)	18.4 (2.2)	0.053
Stroke, TIA or SE	46 (15.1)	135 (16.3)	0.644	0.031	41 (13.5)	134 (16.1)	0.075
Ischemic heart disease	91 (29.9)	274 (33.0)	0.326	0.066	97.3 (32.0)	259.5 (31.3)	0.016
Myocardial infarction	12 (3.9)	25 (3.0)	0.432	0.051	16.1 (5.3)	29.4 (3.5)	0.085
Previous PCI	10 (3.3)	37 (4.5)	0.382	0.061	14.7 (4.8)	34 (4.1)	0.035
Congestive heart failure	163 (53.6)	433 (52.2)	0.665	0.029	174.7 (57.5)	438 (52.8)	0.094
Anemia	36 (11.8)	99 (11.9)	0.969	0.003	31.7 (10.4)	98.8 (11.9)	0.047
COPD	14 (4.6)	66 (8.0)	0.051	0.138	13.5 (4.4)	57.4 (6.9)	0.106
Asthma	51 (16.8)	199 (24.0)	0.010	0.179	56.2 (18.5)	188.6 (22.7)	0.105

Peripheral vascular disease	24 (7.9)	60 (70.2)	0.705	0.025	25 (8.2)	57.7 (7.0)	0.048
Previous cardiac surgery	1 (0.3)	5 (0.6)	1.000	0.04	0.9 (0.3)	4.8 (0.6)	0.044
Previous cancer	16 (5.3)	59 (7.1)	0.268	0.077	22.1 (7.3)	55 (6.6)	0.025
Charlson comorbidity index			0.292	0.089			0.004
0	35 (11.5)	120 (14.5)	0.071	0.197	36.4 (12.0)	116.4 (14.0)	0.14
1	90 (29.6)	189 (22.8)			72 (23.7)	194.2 (23.4)	
2	72 (23.7)	177 (21.3)			82 (27.0)	185.8 (22.4)	
≥ 3	72 (23.7)	222 (26.7)			68.3 (22.5)	219.9 (26.5)	
≥ 5	35 (11.5)	122 (14.7)			45.3 (14.9)	113.8 (13.7)	
Years of Surgery			0.017	0.21			0.036
2002~2005	68 (22.4)	123 (14.8)			52.1 (17.1)	138.5 (16.7)	
2006~2009	59 (19.4)	166 (20.2)			63.2 (20.8)	169 (20.4)	
2010~2013	66 (21.7)	225 (27.1)			81.1 (26.7)	214.6 (25.9)	
2014~2018	111 (36.5)	316 (38.1)			107.6 (35.4)	308 (37.1)	
Cumulative hospital volume for cardiac surgery (AVR)			<0.001	0.309			0.076
<250	66 (21.7)	227 (27.3)			81.9 (26.9)	222.6 (26.8)	
250-1000	82 (27.0)	228 (27.5)			81.8 (26.9)	225.9 (27.2)	
1000-3000	87 (28.6)	279 (33.6)			89.6 (29.5)	264 (31.78)	
≥3000	69 (22.7)	96 (11.6)			50.6 (16.6)	117.5 (14.2)	
Cumulative hospital volume for cardiac surgery (MVR)			0.007	0.216			0.074
<250	74 (24.3)	283 (34.1)			89.9 (29.6)	268.5 (32.3)	
250-1000	74 (24.3)	172 (20.7)			73.8 (24.3)	179.9 (21.7)	
1000-3000	156 (51.3)	375 (45.2)			140.2 (46.1)	381.5 (46.0)	

≥ 3000							
<i>Mode of valve diseases</i>							
<i>Aortic valve disease</i>							
Bicuspid aortic valve	8 (2.6)	8 (1.0)	0.046	0.126	4.7 (1.5)	9.4 (1.1)	0.035
Aortic stenosis	165 (54.3)	417 (50.2)	0.228	0.081	164.4 (54.1)	427 (51.4)	0.053
Aortic regurgitation	124 (40.8)	343 (41.3)	0.871	0.011	119.1 (39.2)	349.4 (42.1)	0.059
Combined	83 (27.3)	184 (22.2)	0.071	0.119	83.8 (27.6)	192.7 (23.2)	0.1
Others, NOS	99 (32.6)	222 (26.7)	0.054	0.128	92.2 (30.3)	227.7 (27.4)	0.064
<i>Mitral valve disease</i>							
Mitral stenosis	237 (78.0)	608 (73.3)	0.107	0.11	225.6 (74.2)	620.1 (74.7)	0.011
Mitral regurgitation	36 (11.8)	84 (10.1)	0.404	0.055	26.2 (8.6)	86.9 (10.5)	0.063
Combined	98 (32.2)	209 (25.2)	0.018	0.156	108.7 (35.87)	232.7 (28.0)	0.166
Others, NOS	143 (47.0)	292 (35.2)	<0.001	0.243	140.3 (46.2)	326 (39.3)	0.139
Endocarditis	33 (10.9)	155 (18.7)	0.002	0.222	40.3 (13.3)	135.7 (16.3)	0.087
Congestive heart failure	121 (39.8)	387 (46.6)	0.041	0.138	144.8 (47.6)	372.4 (44.9)	0.055
<i>Health Screening Data</i>							
Height, m	159.2±8.5	157.3±8.6	0.008	0.226	158.9±8.4	157.5±8.5	0.165
Weight, kg	58.7±9.2	57.7±9.5	0.209	0.106	58.6±9.7	57.7±9.3	0.097
BMI, kg/m ²	23.1±3.0	23.3±3.1	0.537	0.053	23.1±2.8	23.2±3.1	0.031
< 18.5	9 (3.0)	32 (3.9)	0.770	0.111	11.4 (3.8)	30.1 (3.6)	0.097
≥ 18.5 and < 23	76 (25.0)	204 (24.6)			82.1 (27.0)	207.6 (25.0)	
≥ 23 and < 25	60 (19.7)	153 (18.4)			54.1 (17.8)	152.7 (18.4)	
≥ 25 and < 30	48 (15.8)	116 (14.0)			44.9 (14.8)	117.8 (14.2)	
≥ 30	2 (0.7)	12 (1.4)			1.3 (0.4)	9.5 (1.1)	
Not available	109 (35.9)	313 (37.7)			110.2 (36.3)	312.2 (37.6)	

Systolic blood pressure, mmHg	123.9±15.6	125.1±18.0	0.371	0.073	124.8±14.8	124.6±17.6	0.013
< 120	76 (25.0)	177 (21.3)	0.400	0.116	69.2 (22.8)	188.3 (22.7)	0.034
≥ 120 and < 140	91 (29.9)	242 (29.2)			91.4 (30.1)	238.4 (28.7)	
≥ 140	28 (9.2)	98 (11.8)			33.2 (10.9)	91.1 (11.0)	
Not available	109 (35.9)	313 (37.7)			110.2 (36.3)	312.2 (37.6)	
Diastolic blood pressure, mmHg	73.8±11.0	73.2±11.1	0.500	0.057	73.8 (10.4)	73.3±10.9	0.044
< 80	124 (40.8)	336 (40.5)	0.876	0.055	121.6 (40.0)	337.1 (40.6)	0.049
≥ 80 and < 90	55 (18.1)	135 (16.3)			55.4 (18.2)	137.6 (16.6)	
≥ 90	16 (5.3)	46 (5.5)			16.7 (5.5)	43 (5.2)	
Not available	109 (35.9)	313 (37.7)			110.2 (36.3)	312.2 (37.6)	
Smoking			0.658	0.083			0.071
Never smoker	137 (45.1)	391 (47.1)			150.3 (49.4)	391.4 (47.2)	
Previous smoker	28 (9.2)	69 (8.3)			25.9 (8.5)	68.2 (8.2)	
Current smoker	21 (6.9)	43 (5.2)			12 (3.9)	43.3 (5.2)	
Not available	118 (38.8)	327 (39.4)			115.8 (38.1)	327.1 (39.4)	
Alcohol use			0.772	0.07			0.076
None	116 (38.2)	335 (40.4)			126.7 (41.7)	329.5 (39.7)	
Mild-to-moderate	63 (20.7)	150 (18.1)			57.1 (18.8)	155.2 (18.7)	
Heavy	7 (2.3)	20 (2.4)			4.4 (1.4)	19.6 (2.4)	
Not available	118 (38.8)	325 (39.2)			115.8 (38.1)	325.6 (39.2)	
Creatinine, mg/dL			0.791	0.044			0.188
≤ 1.5	141 (46.4)	389 (46.9)			138 (45.4)	387.7 (46.7)	
> 1.5	7 (2.3)	14 (1.7)			14.1 (4.6)	11.9 (1.4)	

Not available	156 (51.3)	427 (51.4)			151.9 (50.0)	430.5 (51.9)	
eGFR, mL/min/1.73m ²			0.917	0.028			0.056
≥ 60	89 (29.3)	233 (28.1)			80.4 (26.4)	237.1 (28.6)	
< 60	37 (12.2)	105 (12.7)			38.3 (12.6)	94.1 (11.3)	
Not available	178 (58.6)	492 (59.3)			185.3 (61.0)	498.7 (60.1)	
Concomitant Procedure							
TV repair	132 (43.4)	294 (35.4)	0.014	0.164	123.2 (40.5)	310.9 (37.5)	0.063
CABG	14 (4.6)	53 (6.4)	0.260	0.078	25.6 (8.4)	53.6 (6.5)	0.075
Surgical ablation for Atrial fibrillation	116 (38.2)	306 (36.9)	0.690	0.027	115 (37.8)	311.9 (37.6)	0.005

Values are n (%), or mean ± standard deviation, unless otherwise indicated. IPTW, inverse-probability-of-treatment weighting; SMD, standardized mean difference; BMI, body mass index; TIA, transient ischemic attack; SE, systemic embolization; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; DOAC, direct oral anticoagulant; AVR, aortic valve replacement; MVR, mitral valve replacement; MV, mitral valve; TV, tricuspid valve; CABG, coronary artery bypass grafting

Supplementary Table 13. Between-Group Differences of Mortality among Recipients of Mechanical and Biologic Prostheses using competing risk analyses.

	Crude		IPTW-adjusted				
	HR (95% CI)	P-value	Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P-value	
AVR	Age < 55 (N=1206)		1654	150			
	Death	2.79 (1.91-4.07)	<0.001	186	30	2.18 (1.32-3.63)	0.002
	Cardiac death	3.23(2.01-5.20)	<0.001	93	15	1.99(1.07-3.68)	0.029
	Non-cardiac death	1.82(0.97-3.42)	0.062	93	15	2.17(0.97-4.83)	0.058
	55 ≤ Age ≤64 (N=1130)			2227	773		
	Death	1.58 (1.29-1.93)	<0.001	324	137	1.29 (1.02-1.63)	0.037
	Cardiac death	1.74(1.32-2.29)	<0.001	150	73	1.48(1.06-2.06)	0.022
	Non-cardiac death	1.32(0.99-1.75)	0.059	174	63	1.08(0.78-1.51)	0.637
	Age ≥ 65 (N=1134)			944	6245		
	Death	1.14 (1.01-1.28)	0.040	363	1834	0.77 (0.66-0.90)	0.001
	Cardiac death	0.92(0.78-1.10)	0.363	188	814	0.67(0.53-0.84)	0.001
	Non-cardiac death	1.25(1.06-1.47)	0.010	175	1020	0.95(0.76-1.20)	0.689
MVR	Age < 55 (N=2937)		2783	154			
	Death	2.01 (1.43-3.06)	<0.001	301	17	1.15 (0.65-2.03)	0.626
	Cardiac death	0.68 (0.30-1.55)	0.358	170	3	0.34 (0.14-0.84)	0.020
	Non-cardiac death	3.97 (2.52-6.26)	<0.001	131	14	2.29 (1.17-4.46)	0.015
	55 ≤ Age ≤69 (N=4231)			2999	1232		
	Death	1.77 (1.56-2.01)	<0.001	692	334	1.22 (1.04-1.44)	0.016
	Cardiac death	1.78 (1.50-2.10)	<0.001	385	194	1.25 (1.01-1.55)	0.041
	Non-cardiac death	1.52 (1.25-1.85)	<0.001	307	140	1.13 (0.88-1.45)	0.331

AVR+MVR	Age ≥ 70 (N=1743)			175	1568		
	Death	0.99 (0.78-1.24)	0.900	71	662	1.06 (0.79-1.42)	0.687
	Cardiac death	0.94 (0.70-1.25)	0.664	43	427	1.14 (0.77-1.68)	0.509
	Non-cardiac death	1.00 (0.68-1.44)	0.972	28	235	0.93 (0.58-1.49)	0.747
	Age < 55 (N=1206)			1163	43		
	Death	2.97 (1.65-5.38)	<0.001	135	8	1.64 (0.66-4.05)	0.284
	Cardiac death	2.91 (1.41-6.01)	0.004	86	6	2.01(0.68-5.91)	0.206
	Non-cardiac death	2.54 (0.92-7.00)	0.071	49	1	0.88 (0.21-3.63)	0.857
	55 ≤ Age ≤64 (N=1130)			996	134		
	Death	2.20 (1.61-3.00)	<0.001	190	46	2.02 (1.28-3.19)	0.002
	Cardiac death	1.64 (1.08-2.51)	0.022	121	31	2.06 (1.17-3.64)	0.013
	Non-cardiac death	2.75 (1.72-4.38)	<0.001	69	15	1.62 (0.84-3.14)	0.149
	Age ≥ 65 (N=1134)			304	830		
	Death	1.22 (0.98-1.51)	0.070	119	331	0.95 (0.71-1.28)	0.750
	Cardiac death	1.17 (0.89-1.54)	0.253	79	218	0.96 (0.65-1.43)	0.842
	Non-cardiac death	1.14 (0.81-1.61)	0.456	40	113	1.00 (0.61-1.64)	0.993

IPTW, Inverse-probability-of-treatment weighting; HR, Hazard ratio; CI, Confidence interval.

Supplementary Table 14. Subgroup Analyses According to the Risk Profiles in all age groups undergoing aortic valve replacement (IPTW-adjusted).

		Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P value	P value for interaction
Age < 55 (N=1804)						
Sex type	Male	141	24	2.12 (1.20-3.74)	0.009	0.931
	Female	45	6	2.24 (0.78-6.42)	0.135	
Diabetes mellitus	No	142	22	2.21 (1.23-3.96)	0.008	0.674
	Yes	44	8	1.76 (0.72-4.29)	0.214	
Prior Stroke	No	172	24	2.03 (1.18-3.51)	0.011	0.864
	Yes	14	6	2.29 (0.65-7.99)	0.196	
Congestive heart failure	No	137	22	2.21 (1.23-3.96)	0.008	0.962
	Yes	49	8	2.15 (0.81-5.70)	0.125	
Chronic kidney disease	No	160	27	2.31 (1.34-3.99)	0.003	0.790
	Yes	26	3	2.67 (1.06-6.71)	0.037	
Atrial fibrillation	No	175	29	2.29 (1.37-3.83)	0.002	0.460
	Yes	11	1	0.78 (0.05-12.9)	0.863	
Charlson comorbidity index	<2	96	16	2.26 (1.11-4.58)	0.025	0.948
	≥2	90	14	2.18 (1.10-4.33)	0.026	
Dialysis	No	162	28	2.40 (1.41-4.10)	0.001	0.122
	Yes	24	2	0.72 (0.17-3.00)	0.655	
55 ≤ Age ≤64 (N=3000)						
Sex type	Male	222	97	1.40 (10.5-1.85)	0.020	0.342
	Female	102	40	1.09 (0.72-1.67)	0.682	
Diabetes mellitus	No	208	92	1.38 (1.04-1.83)	0.028	0.392
	Yes	116	44	1.11 (0.73-1.67)	0.630	
Prior Stroke	No	286	124	1.33 (1.04-1.71)	0.025	0.352
	Yes	38	13	0.94 (0.47-1.88)	0.855	
Congestive heart failure	No	209	87	1.29 (0.97-1.70)	0.079	0.931
	Yes	115	50	1.26 (0.82-1.92)	0.288	
Chronic kidney disease	No	277	119	1.32 (1.02-1.69)	0.032	0.781
	Yes	47	17	1.20 (0.64-2.24)	0.575	
Atrial fibrillation	No	301	127	1.29 (1.02-1.64)	0.036	0.891
	Yes	24	10	1.20 (0.41-3.46)	0.740	

Charlson comorbidity index	<2	124	56	1.41 (0.97-2.04)	0.069	0.505
	≥2	200	81	1.20 (0.88-1.63)	0.248	
Dialysis	No	281	119	1.31 (1.02-1.68)	0.036	0.469
	Yes	43	17	1.02 (0.54-1.91)	0.956	
Age ≥ 65 (N=7189)						
Sex type	Male	210	1106	0.83 (0.68-1.00)	0.046	0.354
	Female	153	728	0.71 (0.55-0.92)	0.009	
Diabetes mellitus	No	230	1188	0.81 (0.67-0.97)	0.022	0.413
	Yes	133	646	0.70 (0.53-0.93)	0.015	
Prior Stroke	No	293	1542	0.81 (0.68-0.96)	0.013	0.236
	Yes	69	292	0.63 (0.43-0.91)	0.015	
Congestive heart failure	No	230	1185	0.77 (0.63-0.93)	0.007	0.792
	Yes	132	649	0.80 (0.62-1.03)	0.081	
Chronic kidney disease	No	325	1662	0.79 (0.67-0.92)	0.003	0.348
	Yes	37	172	0.60 (0.35-1.02)	0.061	
Atrial fibrillation	No	335	1690	0.77 (0.65-0.90)	0.001	0.609
	Yes	28	143	0.89 (0.51-1.55)	0.683	
Charlson comorbidity index	<2	105	622	0.86 (0.67-1.12)	0.264	0.371
	≥2	257	1212	0.75 (0.62-0.90)	0.003	
Dialysis	No	327	1719	0.80 (0.69-0.94)	0.006	0.201
	Yes	35	115	0.54 (0.29-0.98)	0.042	

Supplementary Table 15. Subgroup Analyses According to the Risk Profiles in all age groups undergoing mitral valve replacement (IPTW-adjusted).

		Mechanical prosthesis	Biological prosthesis	HR (95% CI)	P value	P value for interaction
Age < 55 (N=2937)						
Sex type	Male	174	8	0.92 (0.39-2.18)	0.846	0.412
	Female	127	9	1.47 (0.71-3.07)	0.301	
Diabetes mellitus	No	237	14	1.17 (0.60-2.27)	0.642	0.775
	Yes	64	3	1.39 (0.51-3.79)	0.515	
Prior Stroke	No	263	15	1.22 (0.66-2.25)	0.527	0.550
	Yes	38	2	0.78 (0.21-2.92)	0.717	
Congestive heart failure	No	183	14	1.48 (0.78-2.82)	0.230	0.084
	Yes	118	2	0.53 (0.20-1.41)	0.202	
Chronic kidney disease	No	269	14	1.08 (0.57-2.05)	0.815	0.419
	Yes	32	3	1.89 (0.57-6.26)	0.298	
Atrial fibrillation	No	220	16	1.48 (0.82-2.65)	0.191	0.042
	Yes	82	1	0.17 (0.02-1.26)	0.083	
Charlson comorbidity index	<2	149	9	1.41 (0.57-3.48)	0.453	0.378
	≥2	152	8	0.86 (0.45-1.64)	0.642	
Dialysis	No	277	16	1.17 (0.64-2.14)	0.609	0.421
	Yes	24	1	0.70 (0.24-2.10)	0.527	
55 ≤ Age ≤69 (N=4231)						
Sex type	Male	302	154	1.32 (1.03-1.68)	0.027	0.439
	Female	390	180	1.16 (0.93-1.44)	0.182	
Diabetes mellitus	No	497	242	1.31 (1.08-1.58)	0.006	0.094
	Yes	195	91	0.94 (0.68-1.31)	0.731	
Prior Stroke	No	570	281	1.28 (1.07-1.53)	0.008	0.265
	Yes	122	53	0.99 (0.66-1.49)	0.971	
Congestive heart failure	No	343	159	1.26 (1.00-1.58)	0.046	0.641
	Yes	349	175	1.17 (0.93-1.47)	0.193	
Chronic kidney disease	No	650	307	1.21 (1.02-1.43)-	0.025	0.562
	Yes	43	27	0.94 (0.41-2.18)	0.885	
Atrial fibrillation	No	427	210	1.25 (1.02-1.53)	0.033	0.756
	Yes	265	124	1.18 (0.90-1.55)	0.224	

Charlson comorbidity index	<2	267	143	1.49 (1.16-1.92)	0.002	0.035
	≥2	425	191	1.05 (0.85-1.29)	0.682	
Dialysis	No	658	310	1.19 (1.01-1.41)	0.038	0.144
	Yes	34	24	1.87 (1.05-3.31)	0.033	
Age ≥ 70 (N=1743)						
Sex type	Male	24	212	0.98 (0.62-1.54)	0.936	0.704
	Female	47	450	1.10 (0.76-1.60)	0.617	
Diabetes mellitus	No	46	433	1.05 (0.74-1.49)	0.795	0.836
	Yes	25	230	1.12 (0.68-1.83)	0.661	
Prior Stroke	No	58	534	1.04 (0.75-1.44)	0.815	0.756
	Yes	13	128	1.17 (0.61-2.22)	0.641	
Congestive heart failure	No	46	286	0.68 (0.47-0.98)	0.038	0.001
	Yes	25	377	1.77 (1.16-2.70)	0.008	
Chronic kidney disease	No	67	615	1.06 (0.78-1.43)	0.721	0.477
	Yes	4	47	0.80 (0.40-1.61)	0.535	
Atrial fibrillation	No	43	397	1.16 (0.77-1.74)	0.483	0.443
	Yes	28	266	0.93 (0.64-1.36)	0.708	
Charlson comorbidity index	<2	22	182	0.77 (0.45-1.29)	0.318	0.136
	≥2	49	481	1.24 (0.87-1.75)	0.235	
Dialysis	No	70	640	1.05 (0.78-1.41)	0.742	0.558
	Yes	1	22	0.91 (0.61-1.34)	0.622	

Korean abstracts (국문요약)

서론: 예상 수명은 심장 판막 치환술에서 인공 판막 유형을 선택하는 주요 결정 요인이며, 환자의 연령이 참조 지표로 사용할 수 있는 유일한 객관적 수치이지만 최적의 연령 기준을 제안하기에는 아직 데이터가 충분하지 않다. 이 연구는 국가 행정 청구 데이터베이스를 사용하여 대동맥 판막 치환술 (AVR) 또는 승모판 치환술 (MVR)에서 인공 판막 유형의 연령 의존적 생존 위험 함수를 탐색하고자 하였다.

연구 방법: 국민건강보험공단 데이터베이스를 사용하여 2003년부터 2018년까지 AVR 또는 MVR을 시행한 환자 24,374 명의 데이터를 검색하였다 (11993 AVR; 8911 MVR; 3470 AVR+MVR). 역 확률 가중 코호트에서 기계판막과 조직판막 간의 사망률, 재수술, 혈전색전증 및 출혈의 위험을 비교하기 위해 연령 계층 분석을 수행하였다.

결과: AVR 후 55세 미만(adjusted hazard ratio [aHR], 2.18; P=0.002) 및 55~64세 환자 (aHR, 1.29; P=0.037)에서 조직판막은 기계판막보다 유의하게 더 큰 사망 위험이 있었으나, 65세 이상의 환자에서 사망률의 위험은 역전되었다(aHR, 0.77; P=0.001). MVR의 경우, 55세에서 69세 사이의 환자에서 조직판막의 사망 위험은 더 높았지만(aHR, 1.22; P=0.016), 70세 이상의 환자에서는 차이가 없었다(P=0.687). 재수술의 위험은 모든 연령층에서 판막 위치에 관계없이 조직판막에서 일관되게 더 높게 나타났다. 그러나 혈전색전증 및 출혈의 위험은 AVR에서는 기계판막을 사용한 고령 환자에서 더 높았으나, MVR에서는 모든 연령층에서 차이가 없었다.

결론: 조직 판막과 비교하여 기계 판막과 관련된 장기 생존 혜택은 AVR에서 65세, MVR에서 70세까지 지속되었다.