Comparative Study - Retrospective Cohort

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Long-term outcomes of mitral valve replacement in dialysis patients: evidence from a nationwide database

Kelvin J. Yang, MD, MRes[a], Hsun-Yi Fu, MD[b], Chia-Jui Chang, MSc[c,d], Ting-Chuan Wang, PhD[e], Chih-Hsien Wang, MD, PhD[a], Nai-Kuan Chou, MD[a], I-Hui Wu, MD, PhD[a], Ron-Bin Hsu, MD, PhD[a], Shu-Chien Huang, MD, PhD[a], Hsi-Yu Yu, MD, PhD[a], Yih-Sharng Chen, MD, PhD[a], Nai-Hsin Chi, MD, PhD[a,*]

Background: To compare the late outcomes between mechanical and bioprostheses after isolated mitral valve replacement (MVR) in dialysis-dependent patients.

Methods: A nationwide propensity-matched retrospective cohort study was conducted involving dialysis patients who underwent primary mitral replacement between 2001 and 2018. Ten-year postoperative outcomes were compared between mitral bioprosthesis and mechanical prosthesis using the Cox proportional hazard model and restricted mean survival time (RMST).

Results: The all-cause mortality was 20.8 and 13.0 events per 100 person-years, with a 10-year RMST of 7.40 and 7.31 years for bioprosthesis and mechanical prosthesis, respectively. Major bleeding was the most common adverse event for both bioprosthesis and mechanical prosthesis, with an incidence rate of 19.5 and 19.1 events per 100 person-years, respectively. The incidence of valve reoperation was higher among those who received bioprosthesis (0.55 events per 100 person-years). After 1:1 matching, the all-cause mortality was 15.45 and 14.54 events per 100 person-years for bioprosthesis and mechanical prosthesis, respectively. The RMST at 10 years was comparable between the two groups after matching (5.10 years for bioprosthesis vs. 4.59 years for mechanical prosthesis), with an RMST difference of −0.03. Further, no difference was observed in the incidence of major adverse valve-related events between bioprosthesis and mechanical valves. However, bioprosthesis was associated with a higher incidence of mitral valve reoperation among all major adverse events (RMST difference −0.24 years, 95% CI −0.48 to −0.01, $P=0.047$).

Conclusions: This study found no association between valve selection and long-term survival outcomes in dialysis patients after MVR. However, bioprosthetic valves may be associated with a slightly higher incidence of reoperation, while other valve-related adverse events, including major bleeding and stroke, were comparable between the two types of prostheses.

Keywords: end-stage renal disease, hemodialysis, mitral valve, prosthetic valve, valve replacement

Introduction

The prevalence of end-stage renal disease (ESRD) in patients receiving renal replacement therapy (RRT) has risen dramatically due to improved survival, better access to RRT, increased prevalence of associated comorbidities, and exposure to environmental toxins[1]. The worldwide use of RRT is expected to exceed 5.4 million by 2030, with the greatest growth in East and Southeast Asia[2].

In ESRD patients on RRT, cardiovascular disease is responsible for ~40% of deaths. Valvular heart disease accounts for up to 20% of all cardiovascular deaths[3], with an estimated relative risk of 4–5-fold compared with that in the general population[4,5]. The progression of valvular heart disease in ESRD patients is also considerably higher because of secondary hyperparathyroidism and associated abnormal calcium/phosphate metabolism, which accelerates valvular calcification and degeneration[6].

[a]Department of Cardiovascular Surgery, National Taiwan University Hospital, Taipei, [b]Department of Cardiovascular Surgery, National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu, [c]Graduate Institute of Clinical Pharmacy, College of Medicine, National Taiwan University, [d]Department of Pharmacy, National Taiwan University Cancer Center and [e]Health Data Research Center, National Taiwan University, Taipei, Taiwan

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Surgery, National Taiwan University Hospital, No. 8, Chung-Shan S Road, Taipei, Taiwan. Tel.: +886 223 123 456, Ext. 65082, fax: +886 223 956 934. E-mail: chinaihsin@gmail.com (N.-H. Chi).

International Journal of Surgery (2023) 109:3778–3787

Received 30 May 2023; Accepted 4 August 2023

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/international-journal-of-surgery.

Published online 2 September 2023

http://dx.doi.org/10.1097/JS9.0000000000000684

The debate on the optimal type of prosthesis for valve replacement surgery in dialysis-dependent patients has been ongoing for decades, and a clear consensus is currently lacking in the most recent societal guideline[7,8]. Historically, mechanical prosthesis was recommended for valve replacement in dialysis-dependent patients by the 1998 American Heart Association (AHA)/American College of Cardiology (ACC) because bioprosthetic valves are prone to structural valve deterioration (SVD) in dialysis patients[9]. Numerous studies have shown comparable outcomes between the two types of prosthetic valves; however, most were single-center retrospective studies with a relatively small sample size and an unmatched heterogeneous cohort[10–14]. The most recent guidelines now recommend individualizing the selection of valve type through shared decision-making based on factors including age, risk of bleeding, life expectancy, patient preference, and comorbidities[7].

Using a nationwide population-based cohort, our study aimed to compare late outcomes between mechanical prosthesis and bioprosthesis after isolated mitral valve replacement (MVR) in dialysis-dependent patients.

HIGHLIGHTS

- The debate on the optimal type of prosthesis for valve replacement surgery in dialysis-dependent patients has been ongoing for decades and lacks strong evidence.
- Our study is a nationalwide population study aimed at investigating the optimal prosthetic valve choice in dialysis patients undergoing mitral valve replacement (MVR) surgery.
- Our study found no significant differences in terms of overall survival between bioprosthetic valves and mechanical valves in patients on hemodialysis undergoing MVR. However, bioprosthetic valves were associated with a higher reoperation incidence than that of mechanical valves.
- The choice of mitral prosthetic valve in dialysis patients would require shared decision-making and considerations of patient-related factors, including bleeding risk, life expectancy, compliance to anticoagulants, and comorbidities.

Methods

Our methods have been reported in line with the STROCSS criteria[15] (Supplemental Digital Content 1, http://links.lww.com/JS9/A941).

Data source

The source of our study data was the Taiwan National Health Insurance Research Database (NHIRD). The NHIRD is derived from Taiwan's National Health Insurance (NHI), an obligatory, government-operated, nationwide, single-payer health insurance program launched in 1995. Over 99% of the nation's 23.6 million population is currently covered by the program, and the NHI provides comprehensive financial coverage on almost all major surgical procedures. The NHIRD systemically collects clinical data, including demographics, diagnoses, procedures, and prescriptions, to enable continuous long-term tracking of claims from individual patients. Background on NHI and NHIRD has been previously described in the relevant literature[16–18]. This study was approved by the institutional review board.

Study population

All patients who underwent surgical valve replacement for the first time between 1 January 2001 and 31 December 2018, were identified from the NHIRD based on a combination of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) procedure codes. Patients with the following conditions were excluded from the study: (1) Those without a diagnosis of mitral valve disease; (2) concomitant valve replacement procedures other than the mitral valve; (3) age <18 years at the time of surgery; (4) in-hospital mortality during index admission for MVR; (5) missing important clinical information; (6) dialysis not conducted within one year of the index MVR procedure. The complete flow diagram of patient selection is depicted in Figure 1, and a list of complete clinical definitions, ICD diagnostic codes, and reimbursement codes are presented in Supplementary Tables 1 and 2 (Supplemental Digital Content 2, http://links.lww.com/JS9/A942).

Study outcomes

The primary outcome was all-cause mortality. Secondary outcomes were composite outcomes of major adverse prosthesis-related events (including major bleeding, ischemic stroke, mitral valve reoperation, endocarditis, and sudden cardiac death) and their components. Major bleeding events are defined as intracranial bleeding and any hemorrhagic events involving either the gastrointestinal/genitourinary/musculoskeletal systems requiring hospital re-admission. A death record was used to define mortality, and the occurrence of any major adverse prosthesis-related events was defined by the principal ICD diagnostic codes of the next emergency room or inpatient admission after the initial MVR. NHI reimbursement codes were used to identify patients who required reoperation. Patients were followed up until death or 31 June 2022, whichever came first.

Statistical analysis

Continuous variables are displayed as mean ± standard deviation (SD) or median and 25–75% interquartile range (IQR), depending on whether the variable was normally distributed, whereas categorical variables were presented as numbers and percentages. The homogeneity between the bioprosthesis and mechanical prosthesis groups was expressed as standardized mean difference (SMD), with a value of 0.1 or less indicating ideal balance and 0.1–0.2 as acceptable balance[19]. Next, matching using the propensity score (PS) was performed to equalize the potential prognostic factors in both groups. In our study, PS was the conditional probability for obtaining a mitral bioprosthesis for MVR and was derived from a logistic regression model, incorporating all baseline covariates listed in Table 1. After the PS was assigned to each covariate, 1:1 matching was formulated by implementing the greedy nearest neighbor matching algorithm without replacement with a caliper of 0.2 of the SD of the logit of the PS[20].

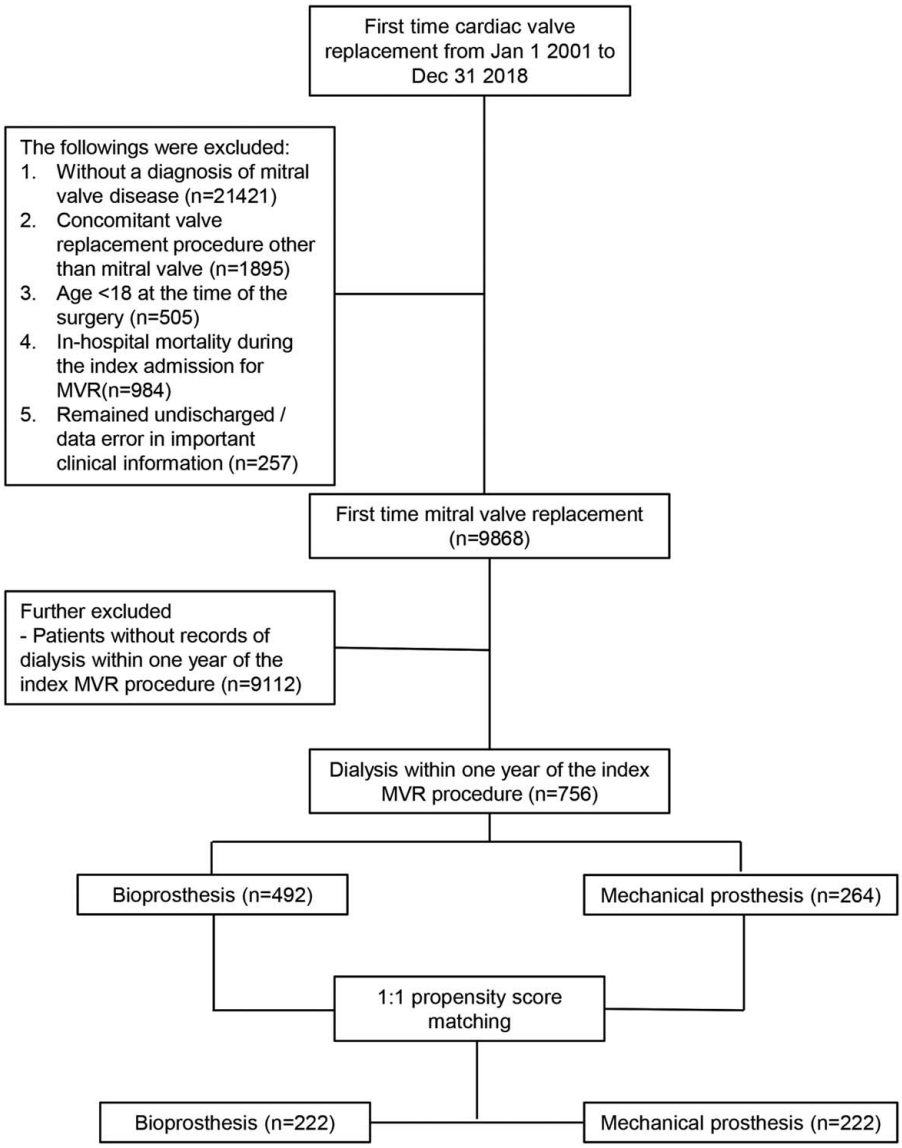

Figure 1. Flow diagram of the selection and matching of the study cohort. Patients who underwent first-time cardiac valve replacement between 2001 and 2018 in the National Health Insurance Research Database were screened for eligibility. A study cohort of 756 dialysis patients who received primary surgical mitral valve replacement was analyzed. Using propensity score matching, the long-term outcome was compared between 222 patients with a bioprosthesis and 222 patients with a mechanical valve. MVR, mitral valve replacement.

The incidence rates of all-cause mortality and major adverse prosthesis-related events were analyzed using a Poisson regression model. All-cause mortality and freedom from adverse events were modeled using the Kaplan–Meier method, and the log-rank test was applied to test for statistical significance. Statistical significance was set at $P < 0.05$. In addition, we compared the long-term outcomes at 10 years postoperative between the mitral bioprosthesis and mechanical prosthesis using the Cox proportional hazard model, and restricted mean survival time (RMST) was also calculated to address the effect of nonproportional hazards. RMST represents the average effect of the choice of prosthesis type over a prespecified follow-up period[21]. Finally, a subgroup analysis stratified by age, sex, urgency of the procedure, underlying valve pathology, and Charlson Comorbidity Index (CCI) was performed to evaluate the differential effect of prosthesis type on long-term outcomes. All statistical analyses were performed using the MedCalc statistical software version 20.118 (MedCalc Software, Ostend, Belgium).

Results

Patient demographics

A total of 756 dialysis-dependent patients who underwent MVR for the first time were identified from the NHIRD between January 2001 and December 2018. Bioprostheses were implanted in 492 (65.1%) patients, while the remaining 264 (34.9%) received mechanical prostheses (Figure 1). Substantial differences in demographics were observed between the two groups before matching. Those who received mitral bioprosthesis were significantly older, with 73.6% over the age of 60 when compared to 40.5% in

Table 1

Patient demographics before matching and after matching.

Patient demographics	Before matching				After matching			
	Bioprosthesis ($n=492$)	Mechanical prosthesis ($n=264$)	SMD	*P*	Bioprosthesis ($n=222$)	Mechanical prosthesis ($n=222$)	SMD	*P*
Age								
Mean (SD)	65.2520325 (10.98)	57.0681818 (11.13)	0.7400	< 0.0001	59.2612613 (10.52)	59.2072072 (10.28)	0.0052	0.9563
Specific age group								
> 60-year-old	362 (73.58%)	107 (40.53%)	0.7082	< 0.0001	118 (53.15%)	105 (47.30%)	0.1173	0.2172
Gender								
Male	241 (48.98%)	138 (52.27%)	− 0.0658	0.3886	112 (50.45%)	116 (52.25%)	− 0.0361	0.7041
Female	251 (51.02%)	126 (47.73)	0.0658		110 (49.55%)	106 (47.75%)	0.0361	
Year of surgery								
2001–2004	32 (6.50%)	36 (13.64%)	− 0.2387	< 0.0001	14 (6.31%)	29 (13.06%)	− 0.2300	0.0065
2005–2009	109 (22.15%)	84 (31.82%)	− 0.2190		55 (24.77%)	71 (31.98%)	− 0.1604	
2010–2014	197 (40.04%)	84 (31.82%)	0.1720		84 (37.84%)	76 (34.23%)	0.0751	
2015–2018	154 (31.30%)	60 (22.73%)	0.1940		69 (31.08%)	46 (20.72%)	0.2382	
Urgency of surgery	178 (36.18%)	71 (26.89%)	0.2008	0.0096	65 (29.28%)	61 (27.48%)	0.0400	0.6737
Mitral valve etiology								
Mitral stenosis	36 (7.32%)	37 (14.02%)	− 0.2183	0.0030	22 (9.91%)	28 (12.61%)	− 0.0856	0.3677
Mitral regurgitation	95 (19.31%)	33 (12.50%)	0.1870	0.0173	46 (20.72%)	28 (12.61%)	0.2189	0.0219
Combine stenosis regurgitation	24 (4.88%)	20 (7.58%)	− 0.1118	0.1310	11 (4.95%)	17 (7.66%)	− 0.1114	0.2414
Rheumatic mitral valve disease	86 (17.48%)	76 (28.79%)	− 0.2706	0.0003	39 (17.57%)	65 (29.28%)	− 0.2792	0.0036
Endocarditis	72 (14.63%)	39 (14.77%)	− 0.0039	0.9591	33 (14.86%)	32 (14.41%)	0.0127	0.8932
Others	255 (51.83%)	121 (45.83%)	0.1202	0.1160	109 (49.10%)	104 (46.85%)	0.0451	0.6348
Concomitant procedure during MVR								
Valve repair	194 (39.43%)	94 (35.61%)	0.0791	0.3019	89 (40.09%)	80 (36.04%)	0.0836	0.3790
CABG	184 (37.40%)	69 (26.14%)	0.2437	0.0018	77 (34.68%)	62 (27.93%)	0.1461	0.1248
PCI	18 (3.66%)	8 (3.03%)	0.0349	0.6514	7 (3.15%)	7 (3.15%)	0.0000	1.0000
Comorbidities within the past year								
Hypertension	388 (78.86%)	191 (72.35%)	0.1521	0.0438	169 (76.13%)	165 (74.32%)	0.0417	0.6601
Diabetes mellitus	255 (51.83%)	108 (40.91%)	0.2203	0.0042	102 (45.95%)	110 (49.55%)	− 0.0722	0.8488
Hyperlipidemia	150 (30.49%)	68 (25.76%)	0.1054	0.1711	64 (28.83%)	61 (27.48%)	0.0301	0.7516
Coronary artery disease	321 (65.24%)	147 (55.68%)	0.1965	0.0099	135 (60.81%)	134 (60.36%)	0.0092	0.9226
Prior myocardial infarction	87 (17.68%)	47 (17.80%)	− 0.0031	0.9671	41 (18.47%)	39 (17.57%)	0.0234	0.8049
Congestive heart failure	393 (79.88%)	204 (77.27%)	0.0635	0.4021	174 (78.38%)	173 (77.93%)	0.0109	0.9086
Cerebrovascular disease	76 (15.45%)	47 (17.80%)	− 0.0633	0.4028	35 (15.77%)	37 (16.67%)	− 0.0244	0.7968
Prior ischemic stroke	39 (7.93%)	20 (7.58%)	0.0131	0.8638	15 (6.76%)	17 (7.66%)	− 0.0348	0.7136
Peripheral artery disease	40 (8.13%)	19 (7.20%)	0.0351	0.6484	15 (6.76%)	13 (5.86%)	0.0371	0.6962
Atrial fibrillation	170 (34.55%)	98 (37.12%)	− 0.0536	0.4816	71 (31.98%)	80 (36.04%)	− 0.0857	0.3673
Prior major bleeding	107 (21.75%)	45 (17.05%)	0.1191	0.1241	36 (16.22%)	39 (17.57%)	− 0.0361	0.7040
Coagulopathy	14 (2.85%)	4 (1.52%)	0.0912	0.2527	3 (1.35%)	3 (1.35%)	0.0000	1.0000
Prior endocarditis	100 (20.33%)	61 (23.11%)	− 0.0675	0.3733	44 (19.82%)	48 (21.62%)	− 0.0445	0.6395
Chronic pulmonary disease	156 (31.71%)	94 (35.61%)	− 0.0826	0.2774	77 (34.68%)	78 (35.14%)	− 0.0094	0.9207
Rheumatic disease	22 (4.47%)	11 (4.17%)	0.0150	0.8449	5 (2.25%)	11 (4.95%)	− 0.1454	0.1266
Peptic ulcer	118 (23.98%)	56 (21.21%)	0.0663	0.3881	45 (20.27%)	50 (22.52%)	− 0.0549	0.5629
Liver disease	81 (16.46%)	52 (19.70)	− 0.0841	0.2656	38 (17.12%)	44 (19.82%)	− 0.0697	0.4631
Cancer	41 (8.33%)	14 (5.30%)	0.1204	0.1262	16 (7.21%)	14 (6.31%)	0.0359	0.7053
Osteoporosis	22 (4.47%)	7 (2.65%)	0.0983	0.2142	5 (2.25%)	6 (2.70%)	− 0.0290	0.7601
CCI distribution								
Mean (SD)	4.7947154 (2.33)	4.3295455 (2.35)	0.1987	0.0093	4.4954955 (2.47)	4.5495495 (2.35)	− 0.0224	0.8132
0	31 (6.30%)	30 (11.36)%)	0.0063	0.0708	24 (10.81%)	22 (9.91%)	0.0955	0.6326
1			− 0.1890				0.0000	
2	50 (10.16%)	29 (10.98)	− 0.0267		24 (10.81%)	19 (8.56%)	0.0762	
≥ 3	411 (83.54%)	205 (77.65%)	0.1492		174 (78.38%)	181 (81.53%)	− 0.0788	

Table 1

(*Continued*)

Patient demographics	Before matching				After matching			
	Bioprosthesis ($n=492$)	Mechanical prosthesis ($n=264$)	SMD	*P*	Bioprosthesis ($n=222$)	Mechanical prosthesis ($n=222$)	SMD	*P*
Medication within the past year								
NOAC	31 (6.30%)	4 (1.52%)	0.2489	0.3190	5 (2.25%)	3 (1.35%)	0.0678	0.4755
NSAID	393 (79.88%)	208 (78.79%)	0.0269	0.7234	175 (78.83%)	175 (78.83%)	0.0000	1.0000
PPI	399 (81.1%)	194 (73.48%)	0.1825	0.0152	175 (78.83%)	165 (74.32%)	0.1065	0.2625
H2 blocker	372 (75.61%)	202 (76.52%)	−0.0212	0.7813	162 (72.97%)	171 (77.03%)	−0.0937	0.3239
ACEI/ARB	386 (78.46%)	206 (78.03%)	0.0103	0.8925	168 (75.68%)	174 (78.38%)	−0.0643	0.4985
Beta blocker	409 (83.13%)	217 (82.2%)	0.0247	0.7458	192 (86.49%)	180 (81.08%)	0.1470	0.1223
Statin	201 (40.85%)	87 (32.95%)	0.1642	0.0330	89 (40.09%)	77 (34.68%)	0.1119	0.2392
Insulin	385 (78.25%)	199 (75.38%)	0.0681	0.3690	165 (74.32%)	166 (74.77%)	−0.0103	0.9132
Other hypoglycemic agent	215 (43.70%)	93 (35.23%)	0.1740	0.0238	78 (35.14%)	86 (38.74%)	−0.0747	0.4315

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CABG, coronary artery bypass; CCI, Charlson comorbidity index; MVR, mitral valve replacement; NOAC, non-vitamin K oral anticoagulants; NSAID, non-steroidal anti-inflammatory drugs; PCI, primary coronary intervention; PPI, proton pump inhibitors; SD, standard deviation; SMD, standardized mean difference.

patients who received mechanical prosthesis (mean age 65.3 ± 11.0 vs. 57.1 ± 11.1 years, SMD 0.74, $P < 0.0001$), and had more comorbidities, reflected by the higher CCI (mean CCI 4.79 ± 2.3 vs. 4.33 ± 2.4, SMD 0.20, $P = 0.0093$). Urgent surgery and concomitant coronary artery bypass grafting (CABG) were also more common in patients who received bioprosthesis. In terms of the underlying valve etiology, mitral regurgitation was the chief indication for MVR in the bioprosthesis group as opposed to rheumatic mitral stenosis in those with a mechanical prosthesis. The baseline characteristics of the patient cohort are shown in Table 1.

After 1:1 propensity score matching, 222 matched pairs were included in the analysis. Major discrepancies in baseline characteristics were balanced after matching; however, underlying valve etiology for MVR remained different between the two groups. The graphical distribution of PS in both patient groups is shown in Supplementary Figure 1 (Supplemental Digital Content 2, http://links.lww.com/JS9/A943).

Primary/secondary outcomes

Before matching, all-cause mortality was higher among dialysis-dependent patients who received MVR using bioprosthesis. The all-cause mortality was 20.8 and 13.0 events per 100 person-years [hazard ratio (HR) 1.52, 95% CI 1.26–1.84], with a 10-year RMST of 7.40 and 7.31 years (RMST difference −0.86, 95% CI −1.0 to −0.73) for bioprosthesis and mechanical prosthesis, respectively. For composite outcomes of major adverse valve-related events, the incidence rates were 50.1 events per 100 person-years in the bioprosthesis group and 40.1 events per 100 person-years in the mechanical prosthesis group (HR 1.12, 95% CI 0.95–1.31), with an RMST difference of −0.27 years (95% CI −0.42 to −0.11). When each component of the adverse events was analyzed, major bleeding was the most common adverse event that occurred after MVR in dialysis patients, with an incidence rate of 19.5 for bioprosthesis and 19.1 events per 100 person-years for mechanical prosthesis (HR 0.96, 95% CI 0.77–1.19), but there was no difference between the two groups. The incidence of valve reoperation was higher among those who received bioprosthesis (0.55 events per 100 person-years). In contrast, no patient required reoperation after MVR with mechanical valve (RMST difference −0.12, 95% CI −0.16 to −0.08). No significant difference was observed between the two groups in terms of ischemic stroke, reoperation rate, and endocarditis (Table 2).

After 1:1 matching using propensity score matching, the difference in all-cause mortality between the two groups of patients was no longer observed. The all-cause mortality was 15.45 and 14.54 events per 100 person-years (HR 1.05, 95% CI 0.83–1.33) for bioprosthesis and mechanical prosthesis, respectively. The RMST at 10 years was also comparable between the two groups after matching (5.10 years for bioprosthesis vs. 4.59 years for mechanical prosthesis), with an RMST difference of −0.03 (95% CI −0.77 to 0.72). Further, no difference was observed in the incidence of major adverse valve-related events (HR 0.94, 95% CI 0.77–1.15) between bioprosthesis and mechanical valve. However, among all major adverse events, bioprosthesis use was associated with a higher incidence of mitral valve reoperation after matching (RMST difference −0.24, 95% CI −0.48 to −0.01, $P = 0.047$). The Kaplan–Meier curves showing the long-term overall survival and adverse event-free survival of the matched cohort are shown in Figure 2.

Subgroup analysis

Long-term survival was comparable between the two types of prosthetic valves in both the young (18–59 years) and old (≥ 60 years) age groups. Prosthetic valve choice had no impact on long-term overall survival or adverse prosthesis-related events in different patient subgroups stratified by sex, the urgency of surgery, and CCI (Supplementary Tables 3–7, Supplemental Digital Content 2, http://links.lww.com/JS9/A942). However, we found a higher incidence of recurrent endocarditis in the mechanical valve group, in which initial MVR was performed to treat endocarditis. The estimated event-free survival time across 10 years of follow-up was significantly different between the two types of prosthetic valves (RMST at 10 years: 4.19 years, 95% CI 2.62–5.77 in bioprosthesis vs. 1.7 years, 95% CI 0.7–2.7 in mechanical valve), with an RMST difference of 2.49 years (95% CI 0.63–4.36).

Table 2

Primary and secondary outcomes in unmatched and matched dialysis-dependent cohorts undergoing mitral valve replacement.

	Pre-matching					Post-matching				
	Biological		Mechanical			Biological		Mechanical		
	Event no. (Incidence rate)	RMST at 10 years	Event no. (Incidence rate)	RMST at 10 years	HR (95% CI)	Event no. (Incidence rate)	RMST at 10 years	Event no. (Incidence rate)	RMST at 10 years	HR (95% CI)	RMST difference (95% CI)
All-cause mortality	339 (20.76)	7.4	164 (13.03)	8.27	1.52 (1.26–1.84)	135 (15.45)	5.1	147 (14.54)	5.13	1.05 (0.83–1.33)	−0.03 (−0.77 to 0.72)
Major adverse valve-related event	427 (50.08)	4.17	230 (40.07)	4.43	1.12 (0.95–1.31)	184 (40.27)	2.53	195 (41.16)	2.37	0.94 (0.77–1.15)	0.15 (−0.43 to 0.74)
Major bleeding	214 (19.47)	6.59	142 (19.05)	6.5	0.96 (0.77–1.19)	99 (16.63)	4.92	117 (19.27)	4.6	0.84 (0.65–1.1)	0.32 (−0.54 to 1.18)
Ischemic stroke	84 (5.79)	8.15	47 (4.27)	8.17	1.23 (0.86–1.77)	32 (4.03)	8.37	40 (4.56)	7.96	0.84 (0.53–1.34)	0.41 (−0.36 to 1.18)
Reoperation	9 (0.55)	9.82	0	9.95	n/a	5 (0.58)	9.76	0	10	n/a	−0.24 (−0.48 to −0.01)
Endocarditis	92 (6.59)	8.07	68 (6.89)	8.08	0.8 (0.58–1.1)	42 (5.78)	7.86	55 (6.9)	7.32	0.79 (0.52–1.18)	0.54 (−0.3 to 1.38)

HR, hazard ratio; RMST, restricted mean survival time.

Discussion

The selection of optimal prosthetic valves for dialysis patients has been an unresolved dilemma for cardiac surgeons in the past few decades. The potential risk of accelerated SVD had to be weighed against the risk of bleeding and thromboembolism when deciding on the appropriate prosthesis type in dialysis patients. Our study is the largest propensity-matched cohort to date, involving dialysis patients who underwent isolated MVR. The rationale for excluding the prosthetic aortic valve from our study and focusing exclusively on mitral prosthesis was based on the inherent differences in valve structure, mechanical load, and stress distribution[22]. For these reasons, bioprosthetic valves are expected to degenerate faster in the mitral position, which is also reflected by the latest guidelines in that mitral bioprosthesis is recommended for patients over the age of 65. Whereas for aortic prosthesis, either mechanical or bioprosthesis was recommended for patients between the age of 50–65[7]. This study demonstrated the following key findings: (1) overall, postoperative survival remains poor in dialysis patients undergoing MVR; (2) the bioprosthetic and mechanical valves exhibited no significant difference in terms of all-cause mortality or major adverse valve-related events during the 18-year study period; (3) a bioprosthetic valve is associated with higher incidence of reoperation; (4) in dialysis patients with preoperative endocarditis, MVR with a mechanical valve was associated with a higher incidence of recurrent endocarditis.

Contemporary guidelines/consensus

The early guidelines from the AHA/ACC in 1998 recommended mechanical valves as the prosthesis of choice in dialysis-dependent patients undergoing valve replacement because of concerns regarding the durability of bioprostheses based on early reports of calcification occurring in porcine bioprostheses in dialysis patients[9,23,24]. Possible mechanisms of bioprosthetic deterioration might involve derangement of calcium and phosphate metabolism, as well as immune-mediated reactions[25,26]. However, according to some reports that showed comparable clinical outcomes between the two types of prostheses, the AHA/ACC guidelines no longer provide specific recommendations for valve selection in this particular group of patients since 2006[27]. Instead, the most recent recommendation was that valve selection should be a shared decision-making process, and the choice should be individualized for each patient. In contrast, the early European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) guidelines in 2007/2012 recommended the placement of bioprosthetic valves over mechanical valves in dialysis patients based on poor long-term survival of ESRD patients relative to the durability of bioprosthesis[28,29]. The subsequent 2017 guidelines provided no explicit recommendation, whereas the most recent 2021 guidelines recommend using mechanical prostheses in patients at risk of accelerated SVD, such as hemodialysis[30]. Unfortunately, the controversy over the optimal prosthesis in dialysis patients remains, as most existing literature are mainly single-centered, retrospective studies, which are limited by their heterogeneous cohort and relatively small sample size.

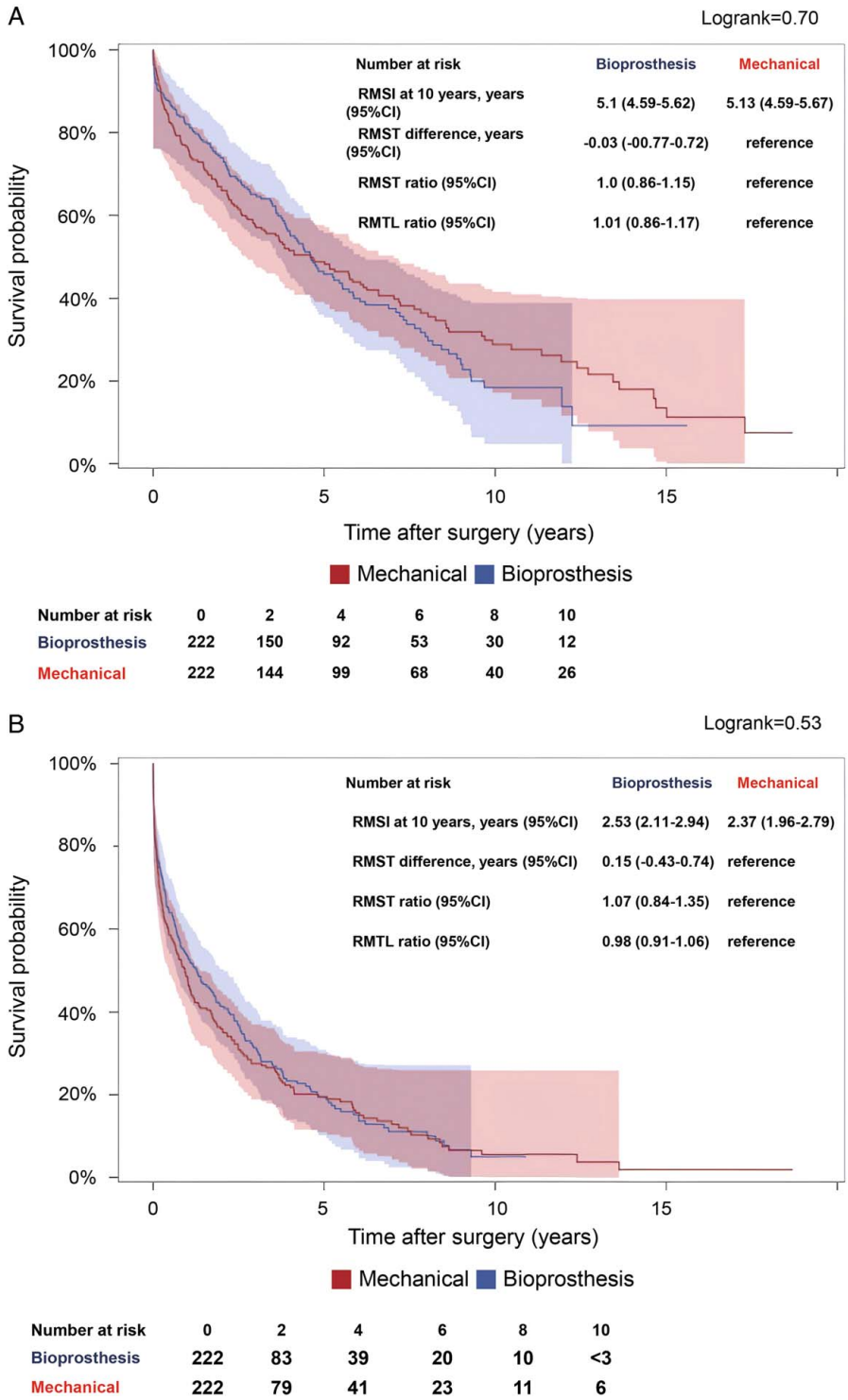

Figure 2. (A) Long-term survival among propensity-matched dialysis patients. The overall survival and estimated restricted mean survival time after primary surgical mitral valve replacement is depicted and compared between the two types of prosthetic valves. The group of patients who received a mechanical valve was the reference group. The numbers of patients at risk are included below each graph. (B) Major adverse event-free survival among propensity-matched dialysis patients. The major adverse event-free survival and estimated major adverse event-free survival days after primary surgical mitral valve replacement are depicted and compared between the two types of prosthetic valves. The group of patients who received a mechanical valve was the reference group. The numbers of patients at risk are included below each graph. CI, confidence interval; RMST, restricted mean survival time; RMTL, restricted mean time lost.

MVR in dialysis patients

There is currently a lack of studies specifically investigating the long-term impact of valve type after MVR in dialysis-dependent patients. Most studies included a mixture of aortic valve replacement (AVR) and MVR. The cohort numbers were either limited, or there was a significant discrepancy in the number of cases between the mechanical prosthesis and bioprosthesis. Nevertheless, most studies have reported relatively inferior survival outcomes in dialysis-dependent patients undergoing valve replacement surgery compared with those without ESRD. The 5-year survival of ESRD patients after valve replacement surgery is ~30–60%[10,31–33], with early studies reporting a survival as low as 15.9% at 6 years[34]. The difference in long-term survival between early and contemporary studies may reflect an improvement in the medical management of dialysis patients. Our study cohort also demonstrated poor long-term survival after MVR in dialysis patients, where the overall 5-year survival was ~48%, which was lower than that of non-dialysis patients from previous studies, ranging from 60% to over 80% at 10 years[35,36]. This result concords with a previous study in which only approximately half of the dialysis patients survived longer than 2 years after valve replacement surgery, even in those younger than 65 years old[37].

Over the last two decades, numerous retrospective studies have attempted to investigate the impact of prosthetic type on long-term survival outcomes in patients on dialysis, and most have found minimal differences in long-term survival[10–14]. One of the earliest studies by Brinkman *et al.*[34] from Emory University found that the type of valve prosthesis did not influence early or late mortality, but patients who received a mechanical prosthesis had a six-fold higher incidence of bleeding and stroke. Tourani *et al.*[14] from the same institution later found similar results, which showed similar long-term survival among 202 patients receiving bioprosthetic and mechanical valve replacements. Subgroup analysis revealed that prosthetic type did not impact postoperative morbidity and long-term survival in dialysis patients who received isolated MVR ($N = 49$). Recent studies by Manghelli *et al.*[31] reported 5-year survival rates of 23 and 33% for bioprosthetic and mechanical valves, respectively (with an overall 10-year survival of only 13%). A recent meta-analysis of 10 164 dialysis-dependent patients also found little difference in survival (HR 0.90, 95% CI 0.73–1.12) when MVR patients were excluded from the analysis, while mechanical valves exhibited superior long-term survival in dialysis patients undergoing isolated AVR[38].

In our study, RMST analysis was used to assess the effect of mitral prosthesis choice in patients undergoing dialysis. RMST is defined as the 'average time free from an event (e.g. death or postoperative morbidities) up until a specific timepoint,' and has been validated as an alternative measure of clinical effect which may also aid patient communications in real-life clinical practice[21]. During a 10-year follow-up, our dialysis patients survived an average of 5.10 years and 5.13 years after MVR for the bioprosthesis and mechanical prosthesis group, respectively, with no significant difference in RMST (– 0.03 years, 95% CI – 0.77 to 0.72). In addition to long-term survival, postoperative valve-related adverse events need to be taken into consideration when selecting prostheses for dialysis patients. Chief concerns for mechanical prostheses are the risk of bleeding and cerebral embolic events, while for bioprosthetic valves are the potential for accelerated prosthetic valve deterioration and reoperation. For dialysis patients receiving a mechanical prosthesis, the prevailing challenge is that these patients require frequent arteriovenous fistula access and are more prone to bleeding events[39]. The increased risk of bleeding may be attributed to inherent platelet dysfunction in ESRD patients, as well as the use of anticoagulants after mechanical valve replacement. Chi *et al.*[38] reported a significantly higher bleeding risk for mechanical prosthesis than in bioprosthetic valves, when the international normalized ratio (INR) exceeds 2.5. On the other hand, subtherapeutic INR values due to poor compliance with anticoagulation therapy are also problematic, as previous studies have reported a significantly lower rate of valve-related embolic events in patients with a bioprosthetic valve at 5 years (88.3% in mechanical prosthesis vs. 97.2% in bioprosthesis, $P = 0.007$)[10,12]. In our study, no overall difference in major bleeding and stroke were observed and the results were consistent after subgroup analysis in patients of different age groups/gender/surgical urgency/valvular pathology or CCI.

With regards to reoperations, our study found a slightly higher reoperation rate in the bioprosthesis group; however, the overall actual number was small, with only 5/222 (2.25%) in the bioprosthesis group and 0/222 (0%) in the mechanical group (freedom from reoperation at 5 years). Although a direct comparison may not be entirely appropriate, as most studies include both mitral and aortic prostheses, our results were consistent with prior studies showing a relatively low reoperation rate, with 5-year freedom from reoperation of ~98%[10]. It seems that dialysis patients are unlikely to benefit from the increased durability of mechanical prostheses, at least in the intermediate term.

Intending to identify a potential subgroup of dialysis patients who may benefit from the long durability of mechanical valves, Manghelli *et al.*[31] concluded in their study that diabetes mellitus, New York Heart Association (NYHA) class > III, and age were significant adverse predictors of 5-year survival. Ikeno *et al.* also demonstrated no difference in long-term survival between prosthetic valve types. However, they identified diabetic nephropathy, NYHA class III, and MVR as risk factors for late mortality[10]. In contrast, our subgroup analysis found no difference in survival and adverse valve-related events between prosthesis choices in different age groups, sex, the urgency of surgery, and comorbidity levels. The only subgroup of patients who may benefit from bioprosthesis over mechanical prosthesis is those who received MVR primarily for the treatment of endocarditis, as mechanical valves were associated with higher risk of prosthetic valve endocarditis. The high burden of dialysis-access-related bloodstream infection is a known risk factor for infective endocarditis. Additionally, dialysis has been reported as a risk factor for prosthetic valve endocarditis after valve replacement[40].

Limitations

Our study had several limitations that are inherent to retrospective observational studies. First, certain clinical parameters were not available from the NHIRD, such as laboratory data (e.g. international normalized ratio), New York Heart Association (NYHA) class, and left ventricular ejection fraction, which are important variables that might influence postoperative outcomes. Further, the lack of echocardiographic findings limits the evaluation of SVD of the bioprosthetic valve in cases of reoperation. In this study, PS matching was used to ensure that the two study

groups were balanced in terms of baseline characteristics. However, some discrepancies remained after matching, such as valve etiology, but a perfect matching between the two groups would ultimately result in a very small case number, and thus the study might be limited by uncontrolled variables and potential selection bias. In addition, our study was carried out over an extended period from 2001 to 2018; improvement in surgical techniques and iterations of prosthetic valves over time might also have an impact on surgical outcomes. Finally, although a slightly higher rate of reoperation was reported among those who received bioprosthesis, the relatively small number of events might result in decreased statistical power.

Conclusions

Our study consisted of one of the largest matched cohorts that compared the long-term outcomes associated with bioprosthetic and mechanical valves in dialysis-dependent patients undergoing a first-time single MVR. We did not find an association between valve selection and long-term survival outcomes in dialysis patients after MVR. However, bioprosthetic valves may be associated with a slightly higher incidence of reoperation, while other valve-related adverse events, including major bleeding and stroke, were comparable between the two types of prostheses.

Ethical approval

This study was approved by the ethical committee of the National Taiwan University Hospital, Institutional Review Board number: 202012072RIND, Date of IRB approval: 2021/03/16.

Consent

Informed consent was waived. Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

K.J.Y.: data curation, formal analysis, methodology, writing – original draft, and writing – review and editing; H.-Y.F.: methodology, validation, review, and editing; C.-J.C. and T.-C.W.: formal analysis, methodology, and software; C.-H.W., I.-H.W., S.-C.H., and H.-Y.Y.: validation, review, and editing; N.-K.C. and R.-B.H.: review and editing; Y.-S.C.: conceptualization, resources, review, and editing; N.-H.C.: conceptualization, methodology, resources, supervision, review, and editing.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Nai-Hsin Chi, No. 7, Chung-Shan S Road, Taipei, Taiwan; Tel: 886 2 23123456 ext. 65082, fax: 886 2 23956934; E-mail: chinaihsin@gmail.com

Data availability statement

Datasets generated during and/or analyzed during the current study are available upon reasonable request.

Provenance and peer review

Not applicable.

Presentation

Not applicable.

Acknowledgements

The authors thank the staff at the Seventh Core Laboratory, Department of Medical Research, National Taiwan University Hospital. The study data source is from the Health and Welfare Data Science Center, Ministry of Health and Welfare (HWDC, MOHM). The authors acknowledge the statistical assistance provided by the Health Data Research Center, National Taiwan University.

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