Heart Surgery Forum 2025; 28(4): E314–E326
doi: 10.59958/hsf.8277

Article

Morbidity and Mortality of Double Valve Replacement/Repair: A Cohort Study

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Submitted: 3 November 2024 Revised: 9 January 2025 Accepted: 14 March 2025 Published: 20 April 2025

Abstract

Background: Aortic and mitral valve replacement or aortic valve replacement with mitral valve repair (DVR) is often associated with a higher risk of morbidity and mortality. Therefore, this study aimed to review and analyze the outcomes of DVR to identify factors associated with morbidity and mortality. **Methods**: Few multicenter data are available on the clinical outcomes of concomitant DVR in China. In four centers, we performed a cohort study of 816 patients who underwent DVR between January 2016 and December 2021. The 30-day mortality and a 6.5-year follow-up were assessed. **Results**: A total of 722 patients were included in the final analysis. Overall, the median cardiopulmonary bypass (CPB) time and aortic cross-clamp time were 164.5 minutes and 111 minutes, respectively. The overall 30-day mortality was 5.0% (n = 36). After propensity score matching (PSM), logistic regression analysis showed that EuroSCORE II, preoperative ejection fraction (EF), and CPB duration were risk factors for death within 30 days. The median follow-up period was 1225.5 days. In total, 54 patients were lost during the follow-up; 61 patients died during the follow-up. Kaplan–Meier survival analysis revealed a cumulative survival rate of 86.0% at 6.5 years. Cox regression analysis identified ages $\geq$60 years and postoperative estimated glomerular filtration rates (eGFR) $\leq$65 mL/min/1.73 m^2 as independent late mortality factors. **Conclusions**: Patients undergoing DVR still have a high risk of mortality and morbidity at 30 days and during follow-up. These patients aged $\geq$60 years and postoperative eGFR $\leq$65 mL/min/1.73 m^2 are predictive of high mortality and poor prognosis during follow-up.

Keywords

heart valve disease; morbidity; mortality

Introduction

A steady increase in aortic and mitral valve replacement or aortic valve replacement with mitral valve repair (DVR) has been observed since the early 1960s [1]. Previous studies showed that in-hospital mortality in DVR ranges from 5% to 15%, and the survival rate at 10 years was reported between 50% and 70% [2]. The mortality rate for double valve replacement was 9.1% [3]. The early mortality rate for valve repair was 11.9% and 11.0% for replacement; survival ($\pm$ SD) in mitral valve repair with aortic valve replacement was 67 $\pm$ 11% and 81 $\pm$ 3% in double valve replacement at the five-year follow-up [4], Operative mortality rates for DVR were 3.6%. The 30-year survival rate of DVR was 37.5% [5]. Recently, morbidity and mortality have significantly decreased following the introduction of the manufacturing engineering of valve prostheses and safer surgical treatment of the disease [6,7]. However, the complications associated with DVR are usually multifactorial in etiology and depend on factors such as the patient's functional status, prosthetic valve type, and anticoagulation [8]. Moreover, these risk factors have been analyzed without propensity score matching (PSM), while confounders have reduced the credibility and reliability of the results [9]. Thus, the accurate risk factors associated with the morbidity and mortality of DVR have yet to be detected. Furthermore, the in-hospital mortality and long-term survival of DVR patients in China have not been well investigated. Thus, we used a cohort study design to review the experience of four centers with DVR. The annual volume of DVR operations at our four centers comprises more than 19 cases. Meanwhile, all four centers are high-volume categories based on the literature [10], meaning the quality of our valve procedures is reliable. The primary outcomes were mortality and morbidity at 30 days and during follow-up, and the secondary outcomes were factors that predict high mortality and poor prognosis during follow-up. We hypothesize that certain perioperative factors, such

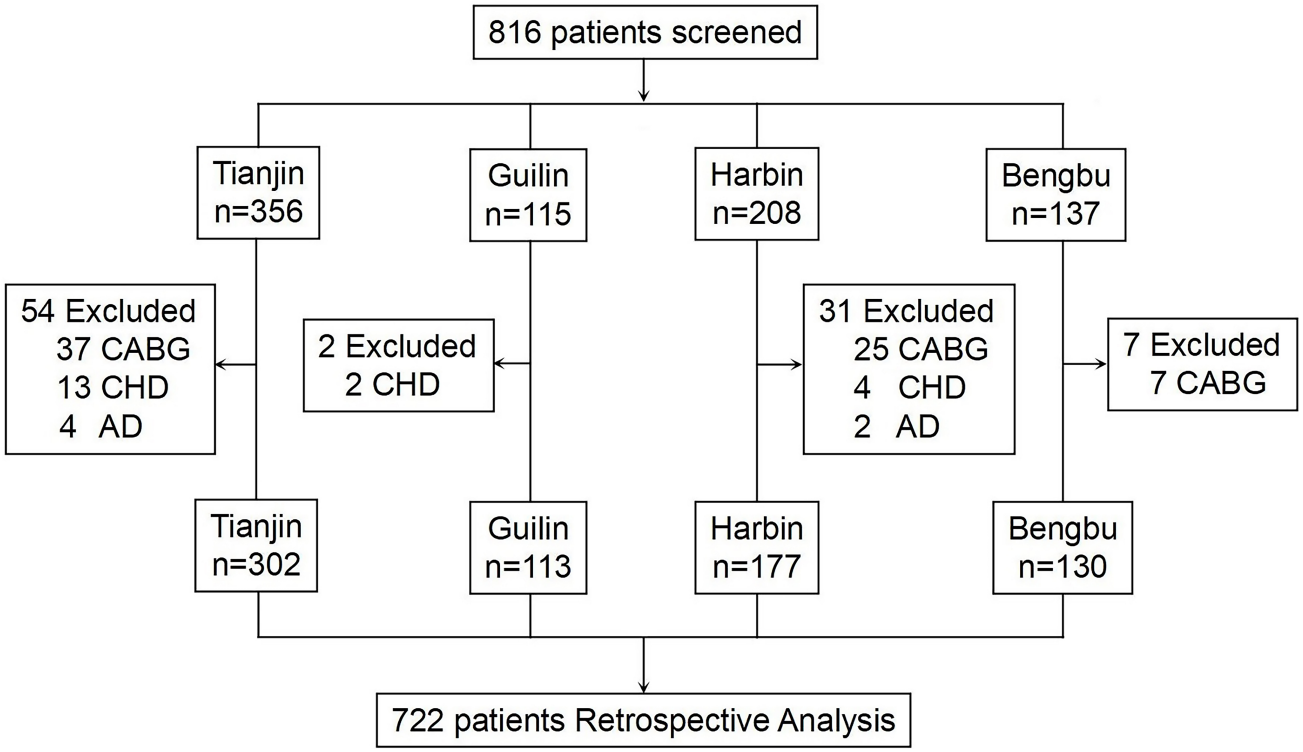

Fig. 1. Flow diagram of patient enrollment. CABG, coronary artery bypass grafts; CHD, congenital heart disease; AD, aortic dissection.

as age, lower ejection fraction (EF), cardiopulmonary bypass (CPB) duration, intensive care unit stay, and renal and liver functions, are independently associated with increased morbidity and mortality in DVR patients.

Methods

Patient Characteristics

From January 2016 to December 2021, 816 patients undergoing DVR for aortic and mitral disease were enrolled at four centers. Patients in the inclusion criteria ranged in age from 18 to 80 years. The indications for DVR were evaluated according to the guidelines for diagnosing and treating valvular heart disease. Patients with a history of heart valve surgery were included in the study. Each patient declared no previous active infections or severe comorbidities. DVR patients with coronary artery bypass grafts, aortic dissection, and congenital heart disease surgery were excluded. Preoperative, intraoperative, and postoperative data were collected. Patient data were collected through the hospital's electronic medical records and uniform electronic forms. The surviving patients and their relatives were interviewed by telephone or outpatient chart in June 2022 to assess survival and morbidity retrospectively.

Statistical Analysis

The applied statistical analysis procedures have been described previously [11]. Continuous variables are presented as the mean ± standard deviation, while categorical or integer variables are presented as numbers and percentages. The Student's *t*-test was used for normally distributed numerical variables to compare values between the two groups, and the Wilcoxon signed-rank test was for non-normally distributed data. One-way analysis of variance (ANOVA) or the Kruskal–Wallis test was used to compare more than two groups. When statistical significance was observed among groups, the method was used to compare between groups. Categorical or integer parameters were compared using Fisher's exact or chi-square tests. Other continuous variables are expressed as the median and interquartile (25th to 75th percentile) range and were compared using the Mann–Whitney U-test or Kruskal–Wallis test. To adjust for death cause bias within 30 days and in the follow-up, we conducted 1:1 PSM on the survival and death groups using the nearest neighbor caliper matching technique. These propensity scores were calculated using a multinomial logistic regression model. To further reduce the selection bias, we also included institutional experience in the model, which is defined by the annual volume of DVR operations at each of our four centers. The matching was performed within a caliper of 20% of the standard deviation of the propensity score to prevent bias from

Table 1. Demographics and perioperative characteristics of the DVR recipients stratified by centers.

Variable	Overall (n = 722)	Tianjin (n = 302)	Guilin (n = 113)	Harbin (n = 177)	Bengbu (n = 130)	*p*-value
Age, years	57.4 ± 9.3	59.4 ± 9.7	54.0 ± 9.1	55.7 ± 7.8	58.1 ± 9.5	<0.001*
Gender, men, n (%)	338 (46.8)	135 (44.7)	54 (47.8)	81 (45.8)	68 (52.3)	0.524
BMI (kg/m^2)	23.4 ± 3.7	24.1 ± 3.6	22.0 ± 3.7	23.4 ± 3.5	22.6 ± 3.5	<0.001*
BSA (m^2)	1.7 ± 0.2	1.7 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.7 ± 0.2	<0.001*
History of smoking, n (%)	185 (25.6)	87 (28.8)	26 (23.0)	45 (38.5)	27 (20.8)	0.305
Hypertension, n (%)	184 (25.5)	125 (41.4)	17 (15.0)	21 (11.9)	21 (16.2)	<0.001*
Diabetes mellitus, n (%)	55 (7.6)	27 (8.9)	4 (3.5)	11 (6.2)	13 (10.0)	0.176
History of stroke, n (%)	62 (8.6)	30 (9.9)	1 (0.9)	23 (13.0)	8 (6.2)	0.002*
COPD, n (%)	18 (2.5)	9 (3.0)	1 (0.9)	1 (0.6)	7 (5.4)	0.033*
History of valve surgery, n (%)	17 (2.4)	11 (3.6)	2 (1.8)	0 (0.0)	4 (3.1)	0.032*
ALT (U/L)	18.3 (13, 29.3)	18.80 (13, 30)	18.34 (11.7, 30.8)	19 (13, 32)	16 (13, 26)	0.363
AST (U/L)	21.5 (17.9, 29.2)	21 (17.2, 27.1)	23.4 (18.2, 31.2)	21 (17, 30)	22 (19, 30)	0.043*
Cr (μmol/L)	82.3 ± 26.2	80.2 ± 21.9	93.0 ± 37.3	87.3 ± 28.0	71.8 ± 16.8	<0.001*
eGFR (mL/min/1.73 m^2)	81.1 ± 21.8	85.6 ± 18.2	66.3 ± 23.4	72.1 ± 21.8	94.2 ± 16.6	<0.001*
AF, n (%)	389 (53.9)	169 (56.0)	48 (42.5)	109 (61.6)	63 (48.5)	0.007*
LAD (mm)	51.1 ± 9.4	51.5 ± 9.5	48.1 ± 7.9	53.1 ± 9.3	49.1 ± 9.7	<0.001*
EF (%)	55.6 ± 8.8	56.0 ± 8.5	55.0 ± 9.2	58.9 ± 8.4	50.6 ± 7.7	<0.001*
BNP (pg/mL)	1253 (509.1, 2900)	1166 (525.6, 2683)	1787 (493.2, 5211.5)	1559 (620, 3213)	1623.3 (742.2, 5555.3)	<0.001*
PaO_2 (mmHg)	89.0 (78.8, 103)	92.2 (81, 109)	87.3 (78.8, 97.9)	84 (76, 98)	87.2 (76.1, 112.1)	0.002*
EuroSCORE II	1.5 (1.1, 2.3)	1.7 (1.2, 2.7)	1.5 (1.3, 2.2)	1.0 (0.8, 1.3)	1.9 (1.4, 2.7)	<0.001*

*, $p < 0.05$; eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (https://www.kidney.org/professionals/KDOQI/gfr_calculator). DVR, aortic and mitral valve replacement or aortic valve replacement with mitral valve repair; BMI, body mass index; BSA, body surface area; COPD, chronic obstructive pulmonary disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; eGFR, estimated glomerular filtration rate; AF, atrial fibrillation; LAD, left atrial dimension; EF, ejection fraction; BNP, B-type natriuretic peptide; PaO_2, partial pressure of oxygen in arterial blood; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II. Numbers in brackets are interquartile ranges (IQRs).

distant matches. The matching was performed without replacement. Survival curves for the primary endpoint of all-cause mortalities were constructed using the Kaplan–Meier method. The Cox proportional hazards model was used to identify variables independently associated with mortality. All statistical procedures were performed using SPSS 25.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 9.0 (GraphPad Software Inc., La Jolla, CA, USA). A two-tailed *p*-value <0.05 was considered statistically significant.

Results

The characteristics of the study group are presented in Fig. 1. A total of 816 patients were screened, and 94 DVR patients with aortic dissection surgery (n = 6), coronary artery bypass graft (n = 69), and congenital heart disease surgery (n = 19) were excluded, meaning 722 patients were in the final analysis.

Preoperative Status

The demographics and perioperative characteristics of the DVR recipients stratified by centers are summarized in Table 1. There were 338 male and 384 female patients with a mean age of 57.4 ± 9.3 years. The mean body mass index (BMI) and body surface area (BSA) were 23.4 ± 3.7 kg/m^2 and 1.7 ± 0.2 m^2, respectively. A history of smoking and diabetes mellitus was observed in 185 (25.6%) patients and 55 (7.6%) patients, respectively. Hypertension and atrial fibrillation (AF) were observed in 184 (25.5%) patients and 389 (53.9%) patients, respectively.

Valvular Pathology

Overall, the etiology of the valve lesions was predominantly rheumatic (67.3%) and degenerative (22.9%). In particular, the majority of the patients at the Bengbu and Guilin centers had rheumatic valve disease (83.9% and

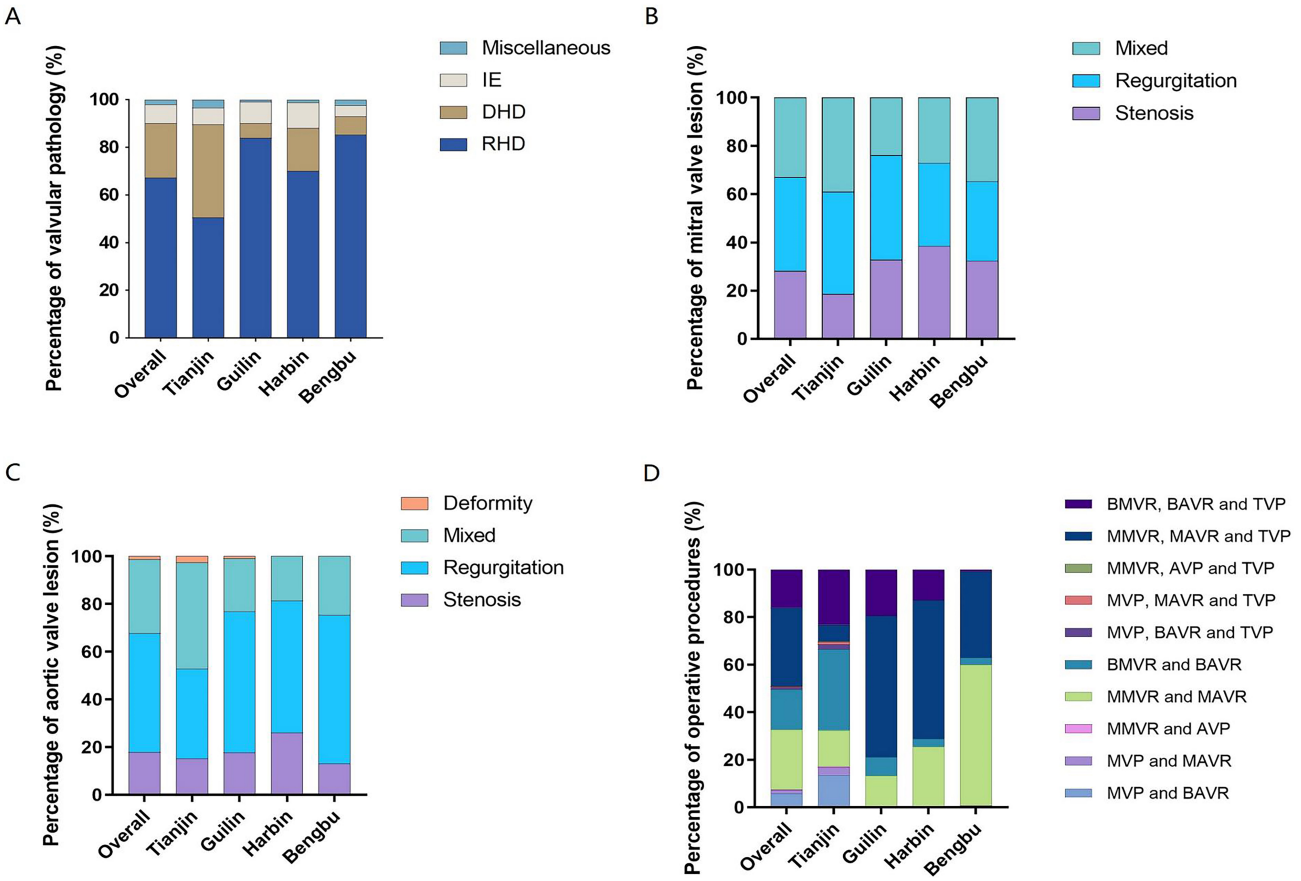

Fig. 2. Characteristics of operative procedures. (A) Valvular pathology. IE, infective endocarditis; DHD, degenerative heart disease; RHD, rheumatic heart disease. (B) Mitral valve lesion. (C) Aortic valve lesion. (D) Surgical methods. BMVR, biological prostheses in mitral valve replacement; BAVR, biological prostheses in aortic valve replacement; TVP, tricuspid valvuloplasty; MMVR, mechanical prostheses in mitral valve replacement; MAVR, mechanical prostheses in aortic valve replacement; AVP, aortic valvuloplasty; MVP, mitral valvuloplasty.

Table 2. Demographics and intraoperative characteristics of the DVR recipients stratified by centers.

Variable	Overall (n = 722)	Tianjin (n = 302)	Guilin (n = 113)	Harbin (n = 177)	Bengbu (n = 130)	*p*-value
CPB duration (min)	164.5 (135.0, 220.0)	146.0 (123.0, 170.0)	153.0 (129.0, 175.0)	245.0 (201.0, 283.5)	173.5 (148.8, 210.5)	<0.001*
Aortic cross-clamping time (min)	111.0 (92.0, 130.0)	108.0 (92.8, 127.0)	115.0 (100.0, 129.5)	102.0 (87.5, 122.0)	125.0 (101.0, 149.0)	<0.001*
AF ablation, n (%)	92 (12.7)	78 (25.9)	10 (8.9)	4 (2.3)	0 (0.0)	<0.001*
RBC transfusion (units)	2 (0, 4)	2 (0, 4)	1 (0, 2)	1 (0, 2)	2 (2, 4)	<0.001*

*, $p < 0.05$; CPB, cardiopulmonary bypass; RBC, red blood cell. Numbers in brackets are interquartile ranges (IQRs).

85.4%, respectively; Fig. 2A). For mitral valve lesions, the predominant lesion was regurgitation, which occurred in 38.9% of patients, followed by mixed mitral valve disease (33.0%) and mitral stenosis (28.1%) (Fig. 2B). Aortic valve lesions occurred from regurgitation in 360 patients (49.9%), mixed disease in 224 patients (31.0%), stenosis in 129 patients (17.9%), and bicuspid or quadricuspid aortic valves in nine patients (1.3%) (Fig. 2C).

Operative Procedures

The operative procedures are presented in Fig. 2D. Most patients (659, 91.3%) underwent double valve replacement. The double valves were replaced with mechanical prostheses in 421 patients and biological prostheses in 238 patients. Among these DVR patients, 354 had tricuspid valvuloplasty with tricuspid annuloplasty ring implantation or the modified De Vega technique.

Table 3. Postoperative characteristics of the DVR recipients stratified by centers.

Variable	Overall (n = 722)	Tianjin (n = 302)	Guilin (n = 113)	Harbin (n = 177)	Bengbu (n = 130)	*p*-value
Re-exploration for bleeding, n (%)	27 (3.7)	15 (5.0)	4 (3.5)	4 (2.3)	4 (3.1)	0.532
Re-exploration for any indication, n (%)	8 (1.1)	5 (1.7)	1 (0.9)	1 (0.6)	1 (0.8)	0.818
Mechanical ventilation >24 h, n (%)	271 (37.5)	77 (25.5)	33 (29.2)	134 (75.7)	27 (20.8)	<0.001*
Total drainage volume (mL)	920 (700, 1776.3)	1200 (947.5, 1800)	720 (560, 975)	875 (637.5, 1302.5)	637.5 (437.5, 942.5)	<0.001*
IABP, n (%)	8 (1.1)	8 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0.018*
ECMO, n (%)	2 (0.3)	1 (0.3)	1 (0.9)	0 (0.0)	0 (0.0)	0.469
RRT, n (%)	14 (2.0)	8 (2.7)	1 (0.9)	1 (0.6)	4 (3.1)	0.261
Cr (μmol/L)	92 (73.8, 120)	93 (76, 115)	128.4 (97.8, 161)	88 (68, 109.5)	77 (65, 103)	<0.001*
eGFR (mL/min/1.73 m^2)	71.0 ± 26.1	70.0 ± 22.2	51.2 ± 20.7	77.5 ± 26.4	80.5 ± 29.6	<0.001*
ALT (U/L)	29.9 (19.3, 52.2)	29.0 (19.1, 51.6)	34 (21.2, 53.1)	18 (12, 30.5)	25 (16, 47.3)	0.240
AST (U/L)	68.8 (43.7, 97.8)	79.3 (62.6, 107.9)	85.6 (69.2, 139.6)	30 (21.5, 46.5)	74.5 (40, 105.8)	<0.001*
BNP (pg/mL)	1733 (867.8, 4342)	1724 (881.6, 3551)	1598 (827.2, 5174)	1733 (887, 4390)	1731 (904.3, 3227)	0.861
Wound infection, n (%)	15 (2.1)	12 (4.0)	2 (1.8)	0 (0.0)	1 (0.8)	0.011*
Stroke, n (%)	13 (1.8)	7 (2.3)	0 (0.0)	1 (0.6)	5 (3.9)	0.066
Gastrointestinal bleeding, n (%)	4 (0.6)	2 (0.7)	0 (0.0)	1 (0.6)	1 (0.8)	1.000
LAD (mm)	42.8 ± 7.2	43.2 ± 6.8	40.4 ± 6.4	44.2 ± 8.3	40.1 ± 5.8	<0.001*
EF (%)	54.3 ± 8.3	52.7 ± 8.0	53.8 ± 10.2	57.9 ± 7.1	52.9 ± 7.8	<0.001*
Intensive care unit stay (days)	3 (2, 5)	2.5 (2, 4)	4 (3, 5)	3 (1, 6)	3 (2, 4)	<0.001*
Time from operation to discharge (days)	13 (10, 18)	11 (8, 17)	13 (10, 17)	15 (11, 20)	14 (11.8, 20)	<0.001*
Death within 30 days, n (%)	36 (5.0)	8 (2.7)	8 (7.1)	9 (5.1)	11 (8.5)	0.047
Lost to follow-up, n (%)	54 (7.9)	13 (4.4)	17 (16.2)	13 (7.7)	11 (9.2)	0.003*
AF recurrence, n (%)	27 (29.4)	25 (32.1)	0 (0.0)	2 (50.0)	-	0.039*
New onset AF, n (%)	23 (7.5)	7 (5.5)	5 (8.9)	6 (9.5)	5 (8.1)	0.659
Death within 5 years, n (%)	61 (9.7)	22 (7.8)	6 (6.8)	19 (12.3)	14 (13.0)	0.217
Follow-up (days)	1225.5 (717, 1697)	1320 (708.5, 1824)	1059 (544.5, 1686)	1196 (805, 1572)	1185 (704.5, 1581)	0.059

*, $p < 0.05$; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy. Numbers in brackets are interquartile ranges (IQRs).

Intraoperative Characteristics

Intraoperative data are summarized in Table 2. Overall, the median CPB time was 164.5 (135.0, 220.0) minutes, and the median aortic cross-clamp time was 111 (92.0, 130.0) minutes. The Cox maze IV procedure for AF ablation was performed in 92 (12.7%) patients. All the intraoperative variables analyzed significantly differed among groups ($p < 0.001$).

Postoperative Characteristics and Follow-up

Postoperative characteristics are summarized in Table 3. The variables of mechanical ventilation >24 hours, total drainage volume, intra-aortic balloon pump (IABP) application, renal function, wound infection, and cardiac function significantly differed among the four centers. Overall, the median length was 3 (2, 5) days for intensive care unit stays and 13 (10, 18) days from operation to discharge. The overall 30-day mortality was 5.0%.

Cause of Death Analysis

The causes of death are listed in Table 4. Early mortality occurred in 36 patients owing to the following events: low cardiac output (11 deaths), infections (8 deaths), multiorgan dysfunction syndrome (MODS) (8 deaths), ventricular fibrillation (5 deaths), left ventricle rupture (3 deaths), and stroke (1 death).

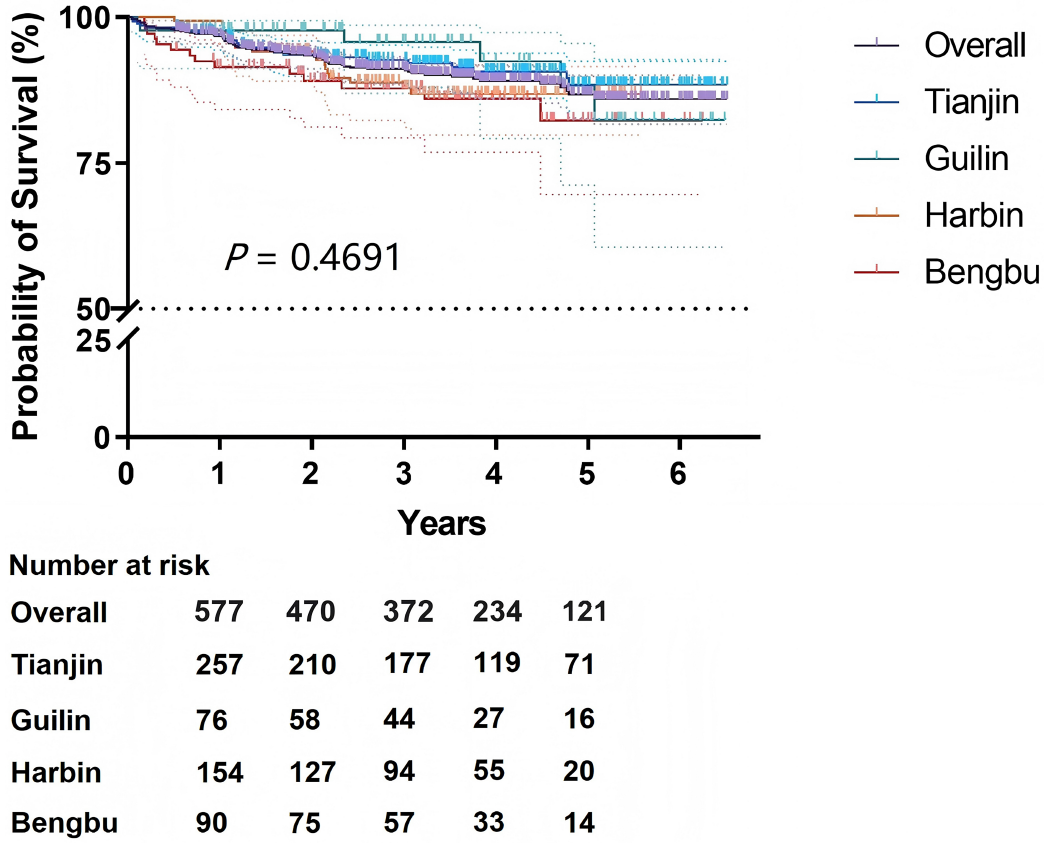

Fig. 3. Kaplan–Meier curves of the survival outcomes for DVR patients in the four assessed centers.

Table 4. Causes of death.

Causes	Overall (n = 97)	Tianjin (n = 30)	Guilin (n = 14)	Harbin (n = 28)	Bengbu (n = 25)
Death within 30 days					
Low cardiac output	11	-	4	5	2
Infection	8	2	1	4	1
MODS	8	4	-	-	4
Ventricular fibrillation	5	1	3	-	1
Left ventricle rupture	3	-	-	-	3
Stroke	1	1	-	-	-
Death in follow-up					
Stroke	28	9	1	10	8
Infection	10	1	1	4	4
Noncardiac death	9	6	-	2	1
Low cardiac output	5	2	3	-	-
MODS	5	3	-	2	-
Ventricular fibrillation	4	1	1	1	1

MODS, multi-organ dysfunction syndrome.

As shown in Table 5, after PSM, 36 patients in the death within 30 days group were successfully matched with 36 patients in the non-death within 30 days group in a 1:1 fashion. Perioperatively, the group experiencing death within 30 days had a lower PaO_2, a higher EuroSCORE II, and lower EF than the survival group ($p = 0.022$, 0.004, and <0.001, respectively). Intraoperatively, there were significant differences in CPB duration and aortic cross-clamping time ($p < 0.001$ and $p = 0.001$, respectively). Postoperatively, in the death within 30 days group, the intensive care unit stay and mechanical ventilation were increased ($p = 0.022$ and <0.001). The renal and liver function were also significantly worse.

Table 5. Characteristics of the DVR recipients stratified by death within 30 days.

Variable	Non-death within 30 days (n = 36)	Death within 30 days (n = 36)	*p*-value
Perioperative characteristic			
Age (years)	60.9 ± 7.8	61.8 ± 7.6	0.611
Gender, men, n (%)	18 (50.0)	17 (47.2)	0.814
BMI (kg/m^2)	22.0 ± 2.9	22.0 ± 4.0	0.679
BSA (m^2)	1.6 ± 0.2	1.6 ± 0.2	0.640
History of smoking, n (%)	8 (22.2)	9 (25.0)	0.781
Hypertension, n (%)	7 (19.4)	10 (27.8)	0.405
Diabetes mellitus, n (%)	7 (19.4)	6 (16.7)	0.759
History of stroke, n (%)	6 (16.7)	5 (13.9)	0.743
COPD, n (%)	1 (2.8)	2 (5.6)	1.000
AF, n (%)	21 (58.3)	20 (55.6)	0.812
History of valve surgery, n (%)	1 (2.8)	2 (5.6)	1.000
Cr (μmol/L)	79.2 ± 17.1	82.3 ± 36.9	0.652
eGFR (mL/min/1.73 m^2)	81.9 ± 19.3	81.5 ± 22.4	0.935
ALT (U/L)	17.2 (13.9, 35.5)	16.00 (12.0, 26.2)	0.257
AST (U/L)	24.1 ± 9.0	23.5 ± 7.3	0.794
BNP (pg/mL)	1093 (399.1, 2129.3)	880.1 (514.5, 3128.5)	0.770
PaO_2 (mmHg)	89.0 (81.7, 135.5)	81.80 (74.2, 91.2)	0.022*
EuroSCORE II	1.52 (1.2, 2.0)	2.0 (1.5, 6.5)	0.004*
LAD (mm)	52.5 ± 9.3	50.6 ± 8.7	0.376
EF (%)	54.4 ± 3.7	48.7 ± 5.1	<0.001*
Intraoperative characteristics			
Mechanical valve prosthesis, n (%)	27 (22.2)	28 (77.8)	0.781
Tricuspid valvuloplasty, n (%)	12 (33.3)	10 (27.8)	0.609
AF ablation, n (%)	1 (2.8)	1 (2.8)	1.000
CPB duration (min)	135 (110, 235)	238 (196, 243)	<0.001*
Aortic cross-clamping time (min)	83 (73, 159)	143 (132, 180)	0.001*
IABP, n (%)	0 (0.0)	1 (2.8)	1.000
ECMO, n (%)	0 (0.0)	0 (0.0)	-
RRT, n (%)	0 (0.0)	0 (0.0)	-
RBC transfusion (units)	2 (2, 3.5)	8 (8, 16)	0.439
Postoperative characteristics			
Intensive care unit stay (days)	2 (2, 5)	3.5 (2, 6)	0.022*
Mechanical ventilation >24 h, n (%)	14 (38.9)	32 (88.9)	<0.001*
Total drainage volume (mL)	967 (626.3, 1517.5)	965 (692.5, 1670)	0.776
IABP, n (%)	0 (0.0)	2 (5.6)	0.493
ECMO, n (%)	0 (0.0)	0 (0.0)	-
RRT, n (%)	1 (2.8)	7 (19.4)	0.055
Cr (μmol/L)	50 (50, 100)	192 (192, 297)	<0.001*
eGFR (mL/min/1.73 m^2)	102 (75, 102)	25 (14, 25)	<0.001*
ALT (U/L)	42 (29, 42)	240 (240, 4087)	0.033*
AST (U/L)	46 (29, 102)	324 (89, 324)	0.018*

*, $p < 0.05$; eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (https://www.kidney.org/professionals/KDOQI/gfr_calculator). Numbers in brackets are interquartile ranges (IQRs).

Univariate logistic regression analysis revealed that preoperative EuroSCORE II, EF, CPB duration, and aortic cross-clamping time were predictors of death within 30 days. We established two multivariate logistic regression models. EuroSCORE II (OR: 1.37, 95% CI: 1.02–1.84; $p = 0.034$), EF (OR: 0.69, 95% CI: 0.57–0.83; $p < 0.001$), and CPB duration (OR: 1.02, 95% CI: 1.00–1.03; $p = 0.023$) were positively related to the occurrence of death within 30 days (Table 6).

Table 6. Univariate and multivariate analyses of characteristics associated with death within 30 days.

	OR	95% CI		*p*-value
		Lower limit	Upper limit	
Univariate				
PaO_2	0.99	0.98	1.00	0.088
EuroSCORE II	1.50	1.13	1.98	0.005*
EF	0.69	0.57	0.82	<0.001*
CPB duration	1.11	1.01	1.03	<0.001*
Aortic cross-clamping time	1.02	1.01	1.04	0.003*
Multivariate model 1				
EuroSCORE II	1.37	1.02	1.84	0.034*
EF	0.69	0.57	0.83	<0.001*
Multivariate model 2				
CPB duration	1.02	1.00	1.03	0.023*
Aortic cross-clamping time	1.00	0.98	1.02	0.878

*, $p < 0.05$; 95% CI, 95% confidence interval; OR, odds ratio.

Follow-up

As shown in Table 3, during the follow-up following hospital discharge, the median follow-up period was 1225.5 (717, 1697) days. A total of 54 patients were lost during the follow-up, which was completed by the remaining 92.1% of patients (632/686). Using spot electrocardiogram (ECG) monitoring, 65 of the 92 patients (70.7%) underwent AF ablation and remained in sinus rhythm during the follow-up. Furthermore, 23 new-onset AF cases occurred in 308 patients receiving DVR procedures. Unfortunately, 61 patients died during follow-up. Of these, 28 patients died of stroke, 10 patients died of infection, nine patients died of noncardiac causes (six patients with cancer, two patients with gastrointestinal bleeding, and one patient with aspiration), five patients died of low cardiac output, five patients died of MODS, and four patients died of ventricular fibrillation (Table 4).

Following PSM, the 38 patients who died in the follow-up group were matched with 38 patients who survived in follow-up. Most of the baseline characteristics were balanced between the two groups, except for Cr, estimated glomerular filtration rate (eGFR), B-type natriuretic peptide (BNP), and left atrial dimension (LAD) ($p = 0.015$, 0.013, <0.001 and $p = 0.009$, respectively). Postoperatively, the Cr, eGFR, and LAD variables were poor in the death during the follow-up group ($p = 0.029$, = 0.017, and = 0.019, respectively) (Table 7).

The univariate and multivariate logistic regression analyses are summarized in Table 8. Preoperative Cr, eGFR, BNP, LAD, total drainage, and postoperative Cr, eGFR, and LAD were predictors of death during follow-up. Two multivariate logistic regression models were established: In Model 1, perioperative BNP (OR: 1.001, 95% CI: 1.001–1.002; $p = 0.002$) and perioperative LAD (OR: 1.133, 95% CI: 1.004–1.277; $p = 0.043$) were related to death during follow-up. In Model 2, a lower postoperative eGFR (OR: 1.027, 95% CI: 1.009–1.046; $p = 0.004$) negatively affected survival during follow-up. An increased postoperative LAD (OR: 1.073, 95% CI: 1.010–1.141; $p = 0.023$) was associated with death during follow-up. As determined by multivariate Cox regression analysis of risk factors, ages ≥60 years (HR: 2.39, 95% CI: 1.38–4.15; $p = 0.002$) and postoperative eGFR ≤65 mL/min/1.73 m^2 (HR: 2.59, 95% CI: 1.53–4.39; $p < 0.001$) remained independent predictors of death during follow-up (Table 9).

The Kaplan–Meier survival analysis revealed a cumulative survival rate of 86.0% (Fig. 3). The follow-up outcomes are summarized by age stratification in Fig. 4A. We found that patients younger than 60 years exhibited better survival curves than those older than 60 years ($p < 0.001$). When stratified by postoperative eGFR, the survival rate was significantly higher in the eGFR >65 mL/min/1.73 m^2 group ($p < 0.001$; Fig. 4B). Comparatively, valve lesion type, operative method, and the postoperative LAD exhibited no difference in long-term survival when stratified by AF (Fig. 4C–F).

Discussion

This study selected four centers according to their location in geographical regions (Northeast, Central, and South China), degree of urbanization (municipality, provincial capital, and midsize cities), and medical resource coverage. We summarized the DVR data to provide a more convincing and comprehensive understanding and to ensure that the results of this study represent the treatment status of DVR in China as realistically as possible.

Immune effector mechanisms lead to heart tissue damage, culminating in aortic and mitral valve dysfunctions. The progression of aortic valve stenosis includes angiogenesis, inflammation, and remodeling of the extracellular matrix, leading to osteogenesis in the aortic valve and reveal-

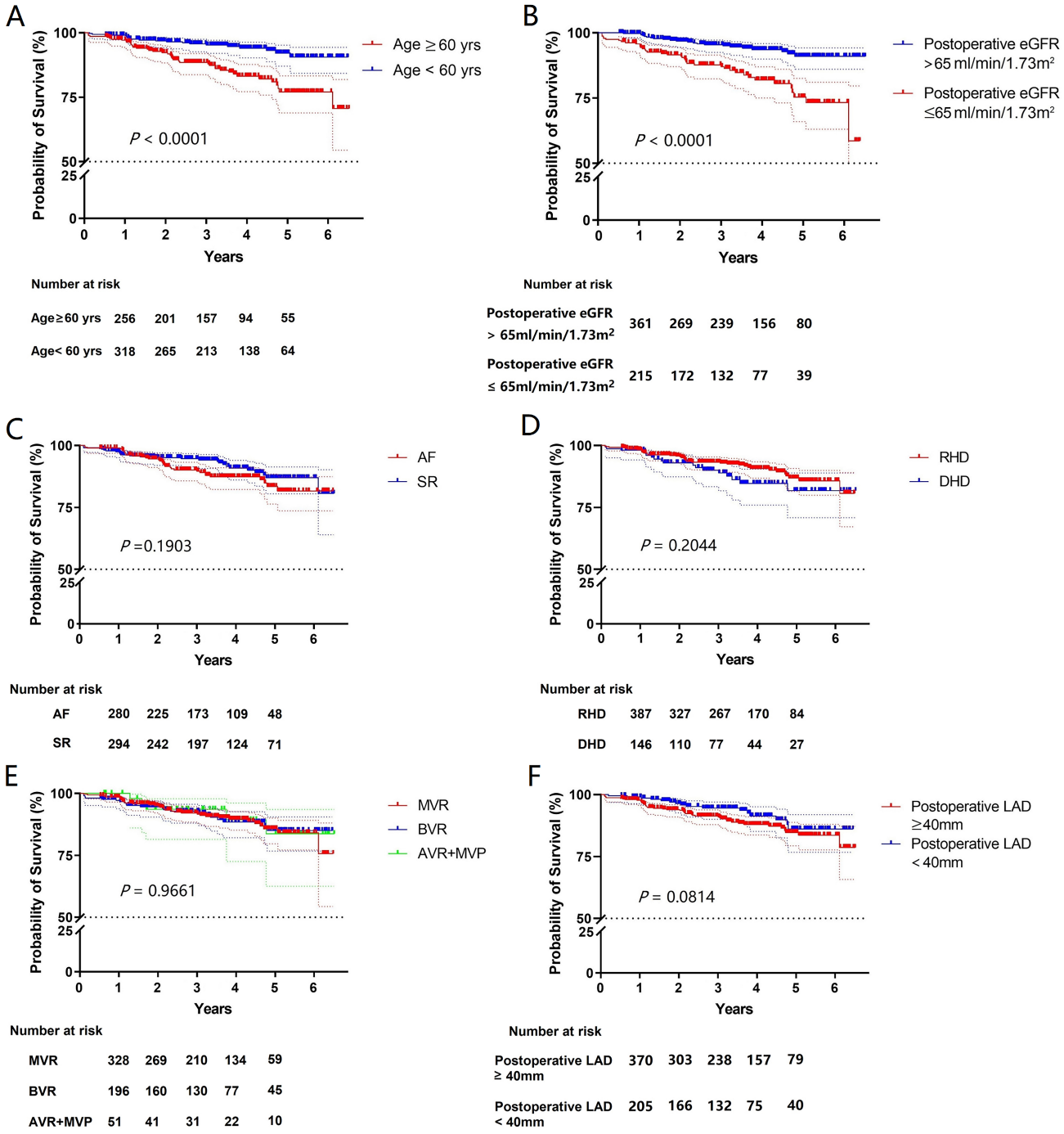

Fig. 4. Kaplan–Meier curves of the survival outcomes for DVR patients in different variables. Kaplan–Meier curves of (A) survival for ages ≥60 and <60 years. (B) Postoperative eGFR >65 mL/min/1.73 m^2 and ≤65 mL/min/1.73 m^2. (C) Survival curves for AF and SR; SR, sinus rhythm. (D) RHD and DHD. (E) MVR, BVR, and AVR + MVP; MVR, mechanical valve replacement; BVR, bioprosthetic valve replacement; AVR, aortic valve replacement. (F) Postoperative LAD ≥40 mm and <40 mm.

ing many mechanisms similar to atherosclerosis. Currently, no medical therapy has been shown to significantly prevent the development of calcific aortic valve stenosis or slow its progression. Thus, the only treatment available in symptomatic severe stenosis is percutaneous or surgical aortic valve replacement.

As a risk factor in cardiac surgery, age has become a concern for treatment decision-making and survival [12–14]. Compared with the characteristics of DVR patients in Euro–American populations, DVR patients in China (age ≥60 years) exhibited a smaller BSA and lower BMI [15,16]. Forgie K *et al.* [17] reported that compared with patients with normal weights, aortic valve replacement

Table 7. Characteristics of the DVR recipients stratified by death in follow-up.

Variable	Survival in follow-up (n = 38)	Death during follow-up (n = 38)	*p*-value
Perioperative characteristic			
Age (years)	56.5 ± 9.5	58.4 ± 11.2	0.435
Gender, men, n (%)	18 (47.4)	19 (50.0)	0.818
BMI (kg/m^2)	23.0 ± 3.9	23.8 ± 4.1	0.372
BSA (m^2)	1.6 ± 0.2	1.7 ± 0.2	0.284
History of smoking, n (%)	9 (23.7)	10 (26.3)	0.791
Hypertension, n (%)	9 (23.7)	16 (42.1)	0.071
Diabetes mellitus, n (%)	1 (2.6)	5 (13.2)	0.089
History of stroke, n (%)	1 (2.6)	4 (10.5)	0.165
COPD, n (%)	4 (10.5)	2 (5.3)	0.395
AF, n (%)	21 (55.3)	21 (55.3)	1.000
History of valve surgery, n (%)	0 (0.0)	0 (0.0)	-
Cr (μmol/L)	69 (62.8, 84.3)	88 (66.0, 111.0)	0.015*
eGFR (mL/min/1.73 m^2)	96 (79.0, 107.5)	78 (53.0, 97.0)	0.013*
ALT (U/L)	15 (12.0, 27.0)	19 (14.0, 24.0)	0.269
AST (U/L)	21.5 (19.0, 28.3)	22 (19.0, 28.0)	0.996
BNP (pg/mL)	521 (347.7, 783.0)	2163 (688.0, 4672.0)	<0.001*
PaO_2 (mmHg)	98.3 ± 30.3	95.8 ± 25.1	0.698
EuroSCORE II	1.9 (1.3, 2.6)	2 (1.2, 2.7)	0.490
LAD (mm)	48.8 ± 8.9	53.8 ± 8.5	0.009*
EF (%)	51.4 ± 9.1	55.00 ± 8.8	0.084
Intraoperative characteristics			
Mechanical valve prosthesis, n (%)	5 (13.2)	19 (50.0)	0.001*
Tricuspid valvuloplasty, n (%)	12 (31.6)	13 (34.2)	0.807
AF ablation, n (%)	3 (7.9)	3 (7.9)	1.000
CPB duration (min)	156.5 (128.0, 180.3)	175 (156.3, 197.3)	0.004*
Aortic cross-clamping time (min)	108 (91.8, 125.3)	125 (106.3, 140.0)	0.008*
IABP, n (%)	0 (0.0)	0 (0.0)	-
ECMO, n (%)	0 (0.0)	0 (0.0)	-
RBC transfusion (units)	2 (1.8, 4.0)	1.5 (0.0, 4.0)	0.060
Postoperative characteristics			
Intensive care unit stay (days)	3 (2.0, 4.0)	2.5 (2.0, 4.3)	0.536
Mechanical ventilation >24 h, n (%)	9 (23.7)	9 (23.7)	1.000
Total drainage volume (mL)	690 (487.5, 1200.0)	1445 (673.8, 1802.5)	0.001*
IABP, n (%)	0 (0.0)	0 (0.0)	-
ECMO, n (%)	0 (0.0)	0 (0.0)	-
RRT, n (%)	1 (2.6)	3 (7.9)	0.304
Cr (μmol/L)	77.5 (70.8, 93.2)	99.0 (75.8, 136.8)	0.029*
eGFR (mL/min/1.73 m^2)	90.0 (72.5, 101.0)	67.5 (48.8, 94.8)	0.017*
ALT (U/L)	22 (14.8, 34.3)	25 (18.0, 55.0)	0.109
AST (U/L)	57 (25.5, 88.0)	62 (40.0, 75.0)	0.433
Time from operation to discharge (days)	14 (11.0, 19.3)	16 (10.8, 30.8)	0.379
LAD (mm)	40.9 ± 4.9	44.1 ± 7.2	0.019*
EF (%)	53.3 ± 7.9	53.3 ± 8.6	0.992

*, $p < 0.05$; eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (https://www.kidney.org/professionals/KDOQI/gfr_calculator). Numbers in brackets are interquartile ranges (IQRs).

(AVR) patients (BMI <20 kg/m^2) were associated with an increased risk of all-cause mortality at the longest follow-up time point; this aligns with our observation. Moreover, most patients lost during the follow-up were older than 60 years; thus, the actual survival rate in our study of patients older than 60 years may be much worse.

Patients with chronic kidney disease (CKD) exhibit an increased risk of cardiovascular morbidity and mortal-

Table 8. Univariate and multivariate logistic regression analyses of characteristics associated with death in follow-up.

	OR	95% CI		*p*-value
		Lower limit	Upper limit	
Univariate				
Perioperative Cr	1.036	1.013	1.060	0.002*
Perioperative eGFR	1.035	1.014	1.056	0.001*
Perioperative BNP	1.001	1.001	1.002	0.001*
Perioperative LAD	1.090	1.012	1.174	0.023*
Total drainage	1.001	1.000	1.002	0.005*
Postoperative Cr	1.020	1.006	1.003	0.005*
Postoperative eGFR	0.972	0.955	0.989	0.001*
Postoperative LAD	1.074	1.002	1.137	0.013*
Multivariate model 1				
Perioperative BNP	1.001	1.001	1.002	0.002*
Perioperative LAD	1.133	1.004	1.277	0.043*
Multivariate model 2				
Postoperative eGFR	1.027	1.009	1.046	0.004*
Postoperative LAD	1.073	1.010	1.141	0.023*

*, $p < 0.05$.

Table 9. Univariate and multivariate Cox regression analyses of characteristics associated with death in follow-up.

	HR	95% CI		*p*-value
		Lower limit	Upper limit	
Univariate Cox regression				
Age ≥60 years	2.86	1.66	4.92	<0.001*
Postoperative AF	1.40	0.85	2.31	0.193
Rheumatic heart disease	1.48	0.81	2.72	0.159
TVP with annuloplasty ring	0.97	0.55	1.74	0.753
Postoperative eGFR ≤65 mL/min/1.73 m^2	3.55	2.10	6.02	<0.001*
Postoperative LAD ≥40 mm	1.52	0.90	2.58	0.081
Multivariate Cox regression				
Age ≥60 years	2.39	1.38	4.15	0.002*
Postoperative eGFR ≤65 mL/min/1.73 m^2	2.59	1.53	4.39	<0.001*

*, $p < 0.05$.

ity [18]. The characteristic of valve calcification caused by CKD is common and an important underlying mechanism of valve dysfunction and even death [19]. Hensen LCR and colleagues reported a cohort including 66 patients who had mitral and/or aortic valve calcium with a mean eGFR of 61 mL/min/1.73 m^2. During a median follow-up of 6 years, the patient population had a higher mortality profile than patients without calcium [20]. Nakazato T and coworkers [21] presented a study on the relationship between preoperative eGFR and cardiovascular morbidity in 210 patients who underwent mitral valve surgery. Nakazato T and coworkers [21] observed that an eGFR <60 mL/min/1.73 m^2 was an independent predictor of late major adverse cardiac events (MACEs). In our study, compared with that in survivors at follow-up, the prevalence of a reduced eGFR was high in patients who died during the follow-up, both preoperatively and postoperatively (Table 9). Moreover, the regression analysis data supported an association between postoperative eGFR ≤65 mL/min/1.73 m^2 and death during follow-up. Meanwhile, decreased long-term survival has also been shown in patients with postoperative eGFR ≤65 mL/min/1.73 m^2. In these patients, the impact of renal function deterioration on mortality in follow-up is unchangeable, even with improved heart function. Xhakollari L *et al*. [22] reported a significant association between mild to moderate impairment of renal function and echocardiographic markers of cardiac structure and diastolic function. Indeed, the interaction between the kidney and heart exists even in the early stages of renal impairment [23]. Based on this evidence, we speculate that despite improved cardiac function and morphology after DVR, the impact of preoperative impaired renal function might be irreversible and continuous. Finally, under the harmful interaction between cardiac and renal function, these patients with preoperative and postoperative low eGFR remained at risk of high mortality.

For patients, the DVR procedure aims to restore cardiac morphology and function, allowing for longer survival and improved quality of life. Theoretically, the long-term effect of mitral valve repair with aortic valve replacement is the best compared with mechanical or biological valve replacement [24,25]. The reason lies in preserving the mitral subvalvular apparatus and avoiding complications caused by anticoagulation. However, clinical evidence is more ambiguous, and no explicit guidelines exist on the choice of mitral valvuloplasty with aortic valve replacement (mitral valvuloplasty (MVP) + AVR). Saurav A *et al*. [26] performed a meta-analysis of MVP + AVR to compare the outcome of DVR. The 30-day mortality and follow-up mortality were significantly lower in the MVP + AVR group than in the DVR group [26]. An observational study by Egger ML and his colleague [27] reported that DVR and MVP + AVR are safe and feasible. However, Egger ML *et al*. [27] could not conclude the superiority of one surgical technique over the other, regardless of the 30-day mortality or overall mortality; these findings align with our results. In our study, the 30-day mortality and survival at follow-up of 61 degenerative heart disease patients undergoing MVP + AVR were similar to those undergoing DVR, including mechanical and biological valve replacement (Fig. 4E). These patients were also at risk of cardiac remodeling, renal dysfunction, prosthetic valve failure, and thromboembolic complications. In particular, MVP + AVR should not be performed in patients with rheumatic disease because of the higher incidence of mitral valve reoperation [26,28]. In general, because of the lack of clinical evidence supporting the recommendations for MVP + AVR, identifying patients suitable for this surgical method remains under investigation.

Conclusions

In summary, patients undergoing DVR still have a high risk of mortality and morbidity, both in the hospital and during follow-up. Patients aged $\geq$60 years and postoperative eGFR $\leq$65 mL/min/1.73 m^2 are predictive of high mortality and poor prognosis during the follow-up. To obtain better long-term outcomes, continuous surveillance of DVR patients is needed.

Availability of Data and Materials

The clinical data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

XXP—Writing, Statistics and Draft. WW and HYW—Design, Reviewing. GZS, WZ, and MC—Data collection. GW—Statistics and Draft. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be account able for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Bengbu Medical University (reference number: 2024[103]). All participants provided written informed consent, and the ethics committee approved the procedures.

Acknowledgment

Not applicable.

Funding

This work was supported by grants from Guangxi Medical and health key cultivation discipline construction project, Science foundation for outstanding youth of the first affiliated hospital of Bengbu medical college (2021byyfyjq02), Natural science foundation project of Bengbu medical college (2022byzd030), Graduate scientific research innovation program of Bengbu medical college (Byycx22096), Tianjin key medical discipline (specialty) construction project.

Conflict of Interest

The authors declare no conflict of interest.

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