Long-term outcome of isolated mitral valve repair versus replacement for degenerative mitral regurgitation in propensity-matched patients

Takashi Kakuta, MD,[a] Defen Peng, PhD,[a,b] Matthew S. Yong, MD, PhD,[a] Peter Skarsgard, MD,[a] Richard Cook, MD,[a] and Jian Ye, MD[a]

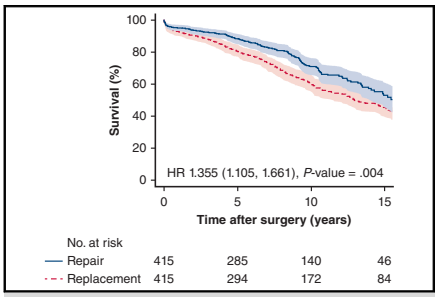
ABSTRACT

Objective: This study was performed to investigate the long-term outcomes in patients with degenerative mitral regurgitation (MR) undergoing mitral valve repair (MVr) versus mitral valve replacement (MVR) without concomitant surgeries.

Methods: The study cohort comprised 1493 patients with degenerative MR who were treated with isolated mitral valve surgery between January 2000 and December 2017 in a large multicenter (5 hospitals) registry of the Province of British Columbia, Canada, including 991 with repair and 502 with replacement. A propensity-matched comparison and risk-adjusted model were used to analyze the outcomes.

Results: After propensity matching (415 matched pairs), the 30-day mortalities were 2.4% and 3.6% in the MVr and MVR groups respectively (odds ratio [OR], 1.500; 95% confidence interval [CI], 0.674-3.339; $P = .32$). The MVR group had significantly greater rates of prolonged inotrope usage >24 hours ($P = .024$), prolonged ventilation ($P = .039$), and blood transfusion ($P = .023$). The respective 1-, 5-, 10-, and 15-year survival rates were 95.7%, 88.8%, 71.4%, and 53.3% in the MVr group, and 93.0%, 81.6%, 61.3%, and 46.0% in the MVR group (hazard ratio [HR], 1.355; 95% CI, 1.105-1.661; $P = .004$). A multivariable analysis revealed that MVR was an independent risk factor for 30-day mortality (OR, 2.270; 95% CI, 1.089-4.732; $P = .029$) and long-term mortality (HR, 1.417; 95% CI, 1.161-1.729; $P < .001$). The HR of MVR over MVr remained consistently greater than 1.0 across all ages.

Conclusions: MVr is associated with lower postoperative morbidity and better long-term survival compared with MVR in patients undergoing isolated mitral valve surgery for degenerative MR. The benefit of MVr appears age-independent. (JTCVS Open 2024;17:84-97)



Long-term survival following isolated MVr versus MVR in propensity-matched patients.

CENTRAL MESSAGE

MVr is associated with better long-term survival compared with MVR in propensity-matched patients undergoing mitral surgery without concomitant procedures, for degenerative mitral regurgitation.

PERSPECTIVE

This study was performed to investigate the long-term outcomes in patients undergoing MVr versus MVR without concomitant surgeries. MVr is associated with better long-term survival compared with MVR in propensity-matched patients with degenerative mitral regurgitation. The benefit appeared consistent across all ages. These findings provide strong evidence supporting the current recommendations.

From the [a]Division of Cardiovascular Surgery, St Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; and [b]Centre for Cardiovascular Innovation, University of British Columbia, Vancouver, British Columbia, Canada.

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Current address of Dr Kakuta: Department of Cardiovascular Surgery, Tohoku University Graduate School of Medicine, Aoba-ku, Sendai, Japan.

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Address for reprints: Jian Ye, MD, Division of Cardiovascular Surgery, St Paul's Hospital, University of British Columbia, 1081 Burrard St, Vancouver, British Columbia, Canada V6Z 1Y6 (E-mail: jye@providencehealth.bc.ca).

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Abbreviations and Acronyms
CI = confidence interval
CPB = cardiopulmonary bypass
HR = hazard ratio
LVEF = left ventricular ejection fraction
MR = mitral regurgitation
MV = mitral valve
MVr = mitral valve repair
MVR = mitral valve replacement
OR = odds ratio

Current American Heart Association/American College of Cardiology and European Society of Cardiology guidelines strongly recommend mitral valve repair (MVr) as the preferred surgical method to treat severe degenerative mitral regurgitation (MR) rather than mitral valve replacement (MVR).[1-3] This recommendation is based in part on studies showing an advantage of MVr, particularly in short- or long-term mortality compared with MVR.[4-8] Similarly, recent meta-analyses of previous studies have shown the superiority of MVr.[9] Subsequently, the use of MVr has steadily increased over the past decade with an acceptable repair failure rate of 6.4%, as shown in the recent US nationwide data.[10]

However, the evidence supporting the guidelines is derived largely from studies that include patients undergoing mitral valve (MV) surgery with other concomitant surgery, such as coronary artery bypass grafting, other valve surgery, or arrhythmia correction surgery, even in the prospective multinational registry study or the largest database study.[4-8,11-13] Several reports required significant statistical adjustment to control for differences related to the concomitant procedures. However, concomitant disease and procedure detail, such as the severity of coronary artery disease, number of coronary anastomoses, severity of other valve disease, or success rate of arrhythmia correction surgery, could not be adjusted. Therefore, the reported differences in outcomes for MVr and MVR, particularly in long-term survival, could have been affected by concomitant heart disease and surgery. One report by Gillinov and colleagues[14] compared outcomes of isolated mitral surgery (MVr vs MVR) in a relatively large cohort using propensity score matching analysis, but this study has the limitation of its single-institutional retrospective nature, and it failed to show the superiority of MVr in long-term survival despite better short-term outcomes.

Thus, this study was performed to investigate the long-term outcomes in patients with degenerative MR undergoing only MVr or MVR without any concomitant surgery using a large multicenter cardiac surgery registry in the Province of British Columbia, Canada.

METHODS

Ethics Statement

The study was approved by the Clinical Research Ethics Board of University of British Columbia (reference number: H17-03009, approval date: November 27, 2017). Informed consent was not required, given the retrospective nature of the review and the deidentified nature of the records.

Data Source and Study Population

The database used to conduct the study was the British Columbia Provincial Cardiac Surgery Registry, which prospectively documents all cardiac procedures in the province, where data submission to the database in mandatory. Patients were included from all 5 hospitals in the province of British Columbia where adult cardiac surgery is performed. Demographics, socioeconomic factors, chronic conditions, operative characteristics, 30-day morbidity and mortality, long-term mortality, and reoperation were included in the provider user files. Every consecutive patient with MVr or MVR without any concomitant surgery between January 2000 and December 2017 was identified from the provincial cardiac registry with prospective data collection. Patients were excluded if they were aged younger than 19 years, had nondegenerative MV etiology or infective endocarditis, or had any concomitant surgery. Consequently, the study cohort comprised 1493 patients who presented with degenerative MR and were treated with isolated MV surgery: 991 with repair, and 502 with replacement.

Statistical Analysis

Missing data. Missing data at baseline were infrequent (<1% for most variables); however, body mass index, hemoglobin, creatinine, and left ventricular ejection fraction (LVEF) were missing in 2.6%, 9.7%, 5.8%, and 1.5% of patients, respectively. To avoid losing observations in the statistical analysis, the multiple imputation approach under the assumption of "missing at random" was performed, and the number of imputations to be performed was specified as 5 for higher accuracy. The missing observations at baseline were filled with averages of 5 imputed values.

Statistical analysis before propensity score matching. Continuous variables were reported as mean ± standard deviation or median (25th to 75th interquartile range) and examined with Student *t* test or Wilcoxon rank sum test, except for survivals, which were reported as mean ± standard error. Categorical variables were presented as frequency (percentage) and examined with the χ^2 test or Fisher exact test between patients with repair and replacement. The relationship between short-term mortality and repair/replacement was analyzed using a logistic regression model. Kaplan–Meier methods were used to examine survival by the categorical factors studied. Categorical predictors of outcomes were individually tested for equality of survival with a log-rank test. The relationship between long-term mortality and repair/replacement was explored with Cox proportional hazards regression model as well. The proportional hazards assumption of the Cox regressions was tested using both graphical and time-dependent approaches. The traditional covariates adjustment method was conducted to control for potentially confounding variables in the Cox regression model. Covariate, which did not satisfy the proportional hazards assumption, was used as a time-dependent variable in the extended Cox regression model. A subdistribution hazard model considering death as a competing risk was conducted to explore how repair/replacement affects redo isolated MV surgery. Multivariable regression analyses were based on the results of the single-factor and the Akaike information criterion. Model fit statistics were compared at each step until the minimum Akaike information criterion was achieved.

Propensity score matching. A propensity-matched comparison was used to control for potentially confounding variables because of the significant differences in baseline characteristics and risk factors between repair and replacement undergoing isolated MV surgery. A logistic regression based on demographic and risk factors was used to generate a

propensity score for each patient with repair or replacement. The 32 variables were used in the propensity matching analysis, including age, sex, body mass index, creatinine level, hemoglobin, Canadian Cardiovascular Society class, New York Heart Association class, LVEF, emergency surgery, previous myocardial infarction, congestive heart failure, active endocarditis, hypertension, pulmonary hypertension, family history of coronary artery disease, dyslipidemia, preoperative arrhythmia, preoperative intra-aortic balloon pump, peripheral vascular disease, chronic obstructive pulmonary disease, preoperative ventilation, cerebral vascular accident/transient ischemic attach, acute renal failure, chronic renal failure, dialysis, diabetes, history of peptic ulcer/gastrointestinal bleeding history, malignant disease <5 years, smoking within 1 month, history of drug abuse, previous percutaneous coronary intervention, and previous open-heart surgery. Pairs of patients with repair or replacement were derived using greedy one-to-one matching with an absolute difference between the propensity scores of 0.20. After propensity matching, the McNemar test or conditional logistic model was used for the analysis of categorical variables, paired *t* test for normally distributed continuous variables, and Wilcoxon signed rank sum test for non-normally distributed continuous variables. The quality of the match was also assessed by using the standardized mean difference, by which an absolute standardized difference of >10% is suggested to represent a meaningful covariate imbalance. In addition, a robust variance estimator was used to account for the clustering within matched sets when using the logistic regression model or Cox proportional hazards model to regress the short-term/long-term outcomes on repair/replacement.

The conventional 5% level of significance was used as a nominal reporting level, and all reported *P*-values were 2-tailed. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute) and R software, version 4.2.3 (R Foundation for Statistical Computing).

RESULTS

Baseline Characteristics

Of 1493 patients, 1003 (67.2%) were male and the overall median age was 65 (56.0, 74.0) years. In general, patients who underwent MVr were younger with fewer comorbidities relative to patients who underwent MVR (Table 1). The patients who underwent MVr were also more likely to be male, had lower New York Heart Association class, greater LVEF, and less frequency of urgent surgery relative to the MVR group. Regarding comorbidities, the MVr group less frequently had previous myocardial infarction, chronic heart failure, pulmonary hypertension, preoperative arrhythmia, peripheral vessel disease, chronic obstructive pulmonary disease, cerebrovascular accidents, chronic renal failure, dialysis, diabetes, smoking history, and previous open-heart surgery compared with the MVR group (Table 1). However, following propensity-matching, no significant differences were observed in 32 baseline characteristics between the 2 groups with a median age of 70 years in both groups (Table 2).

In-Hospital Outcomes

The median follow-up time was 10.4 (5.7, 15.1) years (maximum 20.5 years). A total of 434 deaths were observed within the follow-up time period, of which 38 occurred within 30 days (overall 30-day mortality 2.5%) and 71 occurred within 1 year. Forty-seven patients (3.1%) required redo MV surgery.

In nonmatched and matched patients, pump time and aortic crossclamping time were similar between the MVr and MVR groups (Table 3 and Table E1). The overall incidence of permanent pacemaker implantation was quite low (1.5%) following either MVr or MVR and was not different between the 2 groups ($P = .57$) (Table E1). In matched patients, the MVR group had significantly greater incidences of prolonged inotrope usage >24 hours ($P = .024$), prolonged ventilation ($P = .039$), acute renal failure requiring dialysis, postoperative hemorrhage/tamponade, and use of blood products (red blood cells, plasma, and cryoprecipitate) (Table 3).

In unmatched patients, the observed 30-day mortalities were 1.1% and 5.4% in the MVr and MVR groups, respectively (odds ratio, 5.064; 95% confidence interval [CI], 2.491-10.296; $P < .001$). After matching, the 30-day mortalities were 2.4% and 3.6% in the MVr and MVR groups, respectively (odds ratio, 1.500; 95% CI, 0.674-3.339; $P = .32$) (Table 4).

Long-Term Outcomes

Before matching, the respective 1-, 5-, 10- and 15-year survival rates were 97.9 ± 0.5%, 93.2 ± 0.8%, 81.5 ± 1.5%, and 67.7 ± 2.4% in the MVr group and 90.0 ± 1.3%, 77.9 ± 1.9%, 57.9 ± 2.4%, and 42.8 ± 2.7% in the MVR group (log rank test $P < .001$) (Figure 1, *A*). After matching, the respective 1-, 5-, 10-, and 15-year survival rates were 95.7 ± 1.0%, 88.8 ± 1.6%, 71.4 ± 2.7%, and 53.3 ± 3.9% in the MVr group and 93.0 ± 1.3%, 81.6 ± 1.9%, 61.3 ± 2.6%, and 46.0 ± 3.0% in the MVR group, which was still significantly different between the 2 groups (hazard ratio [HR], 1.355; 95% CI, 1.105-1.661; $P = .004$) (Table 4, Figure 1, *B*). In unmatched patients, the freedom from MV reoperation was 98.0 ± 0.5% at 5 years and 97.1 ± 0.6% at 10 years in the MVr group and 98.0 ± 0.6% at 5 years and 95.2 ± 1.2% at 10 years in the MVR group (log rank test $P = .15$) (Figure 2, *A*). After matching, there was still no significant difference in the freedom from reoperation at 10 years between the MVr and MVR groups (96.6 ± 1.1% and 95.2 ± 1.2%, respectively, HR, 1.498; 95% CI, 0.713-3.146; $P = .29$) (Table 4, Figure 2, *B*).

Risk Factors for 30-Day Mortality and Reduced Long-Term Survival

A multivariable logistic regression analysis revealed that risk factors for 30-day mortality were MVR, older age, longer pump time, and reduced LVEF (≤50%) (Table E2). These factors were also confirmed to be independent risks for 1-year mortality and reduced long-term survival. Additional independent risk factors for reduced long-term survival included preoperative creatinine level, peripheral vascular disease, chronic obstructive pulmonary disease,

TABLE 1. Baseline characteristics (unmatched)

Variable	All n = 1493	Repair n = 991	Replacement n = 502	*P* value	SMD
Surgery age, y	65.0 (56.0, 74.0)	63.0 (54.0, 71.0)	71.0 (62.0, 78.0)	<.001	57.57
Sex (male)	1003 (67.2)	692 (69.8)	311 (62.0)	.002	−16.67
BMI, kg/m^2	25.6 (22.9, 28.4)	25.6 (23.0, 28.1)	25.5 (22.8, 28.8)	.74	6.15
Creatinine, μmol/L	87.3 (75.0, 102.0)	86.0 (73.0, 98.0)	91.0 (78.0, 110.0)	<.001	23.87
Hemoglobin, g/L	139.0 (129.0, 149.0)	141.0 (131.0, 150.0)	135.9 (124.0,146.0)	<.001	−35.16
CCS class				.21	7.79
None	1283 (85.9)	858 (86.6)	425 (84.7)		
Class 1 or 2	146 (9.8)	97 (9.8)	49 (9.8)		
Class 3 or 4	64 (4.3)	36 (3.6)	28 (5.6)		
NYHA class				<.001	47.13
None or class I	265 (17.7)	215 (21.7)	50 (10.0)		
Class II	546 (36.6)	395 (39.9)	151 (30.1)		
Class III	501 (33.6)	290 (29.3)	211 (42.0)		
Class IV	181 (12.1)	91 (9.2)	90 (17.9)		
LVEF (≤50%)	437 (29.3)	243 (24.5)	194 (38.6)	<.001	−30.74
Emergency or priority I for surgery	115 (7.7)	63 (6.4)	52 (10.4)	.006	14.50
Previous MI	76 (5.1)	35 (3.5)	41 (8.2)	<.001	19.85
CHF	894 (59.9)	528 (53.3)	366 (72.9)	<.001	41.55
Active endocarditis	8 (0.5)	4 (0.4)	4 (0.8)	.45	5.09
Hypertension	748 (50.1)	468 (47.2)	280 (55.8)	.002	17.17
Pulmonary hypertension	579 (38.8)	336 (33.9)	243 (48.4)	<.001	29.79
Family history of CAD	227 (15.2)	163 (16.4)	64 (12.7)	.06	−10.49
Dyslipidemia	462 (30.9)	282 (28.5)	180 (35.9)	.003	15.89
Preoperative arrhythmia	367 (24.6)	171 (17.3)	196 (39.0)	<.001	49.94
Preoperative IABP	7 (0.5)	3 (0.3)	4 (0.8)	.23	6.69
PVD	65 (4.4)	34 (3.4)	31 (6.2)	.014	12.86
COPD	252 (16.9)	144 (14.5)	108 (21.5)	<.001	18.24
Preoperative ventilation/ Intubation	19 (1.3)	7 (0.7)	12 (2.4)	.006	13.67
CVA/TIA	131 (8.8)	65 (6.6)	66 (13.1)	<.001	22.24
Renal failure—acute	21 (1.4)	13 (1.3)	8 (1.6)	.66	2.36
Renal failure—chronic	62 (4.2)	21 (2.1)	41 (8.2)	<.001	27.64
Dialysis	17 (1.1)	5 (0.5)	12 (2.4)	.001	15.84
Diabetes	140 (9.4)	68 (6.9)	72 (14.3)	<.001	24.48
Peptic ulcer, GI bleed history	71 (4.8)	40 (4.0)	31 (6.2)	.07	9.73
Malignant disease controlled <5 y	106 (7.1)	64 (6.5)	42 (8.4)	.18	7.29
Smoking history—smoker or d/c <1 mo	91 (6.1)	71 (7.2)	20 (4.0)	.015	−13.90
History of drug abuse	18 (1.2)	12 (1.2)	6 (1.2)	.98	−0.14
PCI	51 (3.4)	28 (2.8)	23 (4.6)	.08	9.31
Previous open-heart surgery	49 (3.3)	11 (1.1)	38 (7.6)	<.001	32.11

Values shown as median (interquartile range) or n (%). *SMD*, Standardized mean difference; *BMI*, body mass index; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *LVEF*, left ventricular ejection fraction; *MI*, myocardial infarction; *CHF*, congestive heart failure; *CAD*, coronary artery disease; *IABP*, intra-aortic balloon pump; *PVD*, peripheral vascular disease; *COPD*, chronic obstructive pulmonary disease; *CVA/TIA*, cerebrovascular accident/transient ischemic attack; *GI*, gastrointestinal; *d/c*, discontinued; *PCI*, percutaneous coronary intervention.

TABLE 2. Baseline characteristics (matched)

Variable	All n = 830	Repair n = 415	Replacement n = 415	*P* value	SMD
Surgery age, y	70.0 (61.0, 76.0)	70.0 (61.0, 76.0)	70.0 (60.0, 77.0)	.95	−0.41
Sex (male)	382 (42.9)	192 (43.1)	190 (42.7)	.61	−0.91
BMI, kg/m^2	25.6 (22.9, 28.6)	25.6 (23.0, 28.5)	25.4 (22.8, 28.7)	.80	−1.76
Creatinine, μmol/L	89.0 (76.0, 104.0)	89.0 (75.0, 104.0)	88.0 (77.0, 104.0)	.65	−3.12
Hemoglobin, g/L	136.0 (126.0, 147.0)	136.0 (126.0, 147.0)	136.0 (127.0, 147.0)	.58	3.81
CCS class				.93	−0.95
None	714 (86.0)	357 (86.0)	357 (86.0)		
Class 1 or 2	74 (8.9)	36 (8.7)	38 (9.2)		
Class 3 or 4	42 (5.1)	22 (5.3)	20 (4.8)		
NYHA class				.93	−2.79
None or class I	89 (10.7)	42 (10.1)	47 (11.3)		
Class II	277 (33.4)	138 (33.3)	139 (33.5)		
Class III	345 (41.6)	176 (42.4)	169 (40.7)		
Class IV	119 (14.3)	59 (14.2)	60 (14.5)		
LVEF (≤50%)	270 (32.5)	133 (32.0)	137 (33.0)	.77	−2.06
Emergency or priority I for surgery	81 (9.8)	43 (10.4)	38 (9.2)	.56	−4.06
Previous MI	52 (6.3)	25 (6)	27 (6.5)	.77	1.99
CHF	581 (70.0)	295 (71.1)	286 (68.9)	.47	−4.73
Active endocarditis	5 (0.6)	3 (0.7)	2 (0.5)	.65	−3.11
Hypertension	452 (54.5)	234 (56.4)	218 (52.5)	.26	−7.75
Pulmonary hypertension	362 (43.6)	179 (43.1)	183 (44.1)	.76	1.94
Family history of CAD	116 (14.0)	61 (14.7)	55 (13.3)	.56	−4.17
Dyslipidemia	278 (33.5)	143 (34.5)	135 (32.5)	.57	−4.09
Preoperative arrhythmia	261 (31.4)	130 (31.3)	131 (31.6)	.93	0.52
Preoperative IABP	6 (0.7)	3 (0.7)	3 (0.7)	.99	0.00
PVD	37 (4.5)	22 (5.3)	15 (3.6)	.25	−8.18
COPD	159 (19.2)	83 (20.0)	76 (18.3)	.55	−4.29
Preoperative ventilation/ intubation	13 (1.6)	7 (1.7)	6 (1.4)	.78	−1.94
CVA/TIA	83 (10.0)	41 (9.9)	42 (10.1)	.91	0.80
Renal failure—acute	16 (1.9)	9 (2.2)	7 (1.7)	.62	−3.51
Renal failure—chronic	30 (3.6)	16 (3.9)	14 (3.4)	.69	−2.58
Dialysis	9 (1.1)	5 (1.2)	4 (1.0)	.74	−2.33
Diabetes	90 (10.8)	47 (11.3)	43 (10.4)	.65	−3.10
Peptic ulcer, GI bleed history	47 (5.7)	23 (5.5)	24 (5.8)	.88	1.04
Malignant disease controlled <5 y	76 (9.2)	40 (9.6)	36 (8.7)	.63	−3.34
Smoking history preoperative smoker or d/c <1 mo	35 (4.2)	17 (4.1)	18 (4.3)	.86	1.20
History of drug abuse	11 (1.3)	6 (1.4)	5 (1.2)	.76	−2.11
PCI	36 (4.3)	19 (4.6)	17 (4.1)	.72	−2.37
Previous open-heart surgery	26 (3.1)	11 (2.7)	15 (3.6)	.29	5.54

Values shown as median (interquartile range), or n (%). *SMD*, Standardized mean difference; *BMI*, body mass index; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *LVEF*, left ventricular ejection fraction; *MI*, myocardial infarction; *CHF*, congestive heart failure; *CAD*, coronary artery disease; *IABP*, intra-aortic balloon pump; *PVD*, peripheral vascular disease; *COPD*, chronic obstructive pulmonary disease; *CVA/TIA*, cerebrovascular accident/transient ischemic attack; *GI*, gastrointestinal; *d/c*, discontinued; *PCI*, percutaneous coronary intervention.

TABLE 3. Intraoperative and postop complications (matched)

Variable	All n = 830	Repair n = 415	Replacement n = 415	*P* value
Pump time, min	120.0 (91.0, 157.0)	120.0 (90.0, 154.0)	123.0 (93.0, 161.0)	.29
Clamp time, min	95.0 (70.0, 125.0)	95.0 (70.0, 123.5)	95.0 (72.0, 128.0)	.41
Duration of operation, h	4.8 (3.9, 5.8)	4.8 (3.9, 5.8)	4.7 (3.9, 5.7)	.31
Duration of skin open, h	3.5 (2.8, 4.4)	3.5 (2.7, 4.4)	3.5 (2.8, 4.4)	.50
Creatinine—post, μmol/L	84.0 (70.0, 100.0)	83.0 (69.5, 98.0)	86.0 (70.0, 101.0)	.46
Creatinine—post, highest, μmol/L	95.0 (79.0, 120.0)	93.0 (77.0, 118.0)	97.0 (80.0, 122.0)	.10
Prosthetic valve endocarditis	1 (0.1)	1 (0.2)	0 (0.0)	<.001
Insertion of permanent pacemaker	20 (2.4)	11 (2.7)	9 (2.2)	.65
Postoperative hemorrhage/ tamponade	21 (2.5)	5 (1.2)	16 (3.9)	.016
Arrhythmia—cardiac arrest	7 (0.8)	3 (0.7)	4 (1.0)	.71
Arrhythmia—atrial	377 (45.4)	182 (43.9)	195 (47.0)	.36
Arrhythmia—heart block	47 (5.7)	20 (4.8)	27 (6.5)	.30
Valvular thromboembolism/ thrombosis	0 (0.0)	0 (0.0)	0 (0.0)	–
Inotropes >24 h	35 (4.2)	11 (2.7)	24 (5.8)	.024
CVA	14 (1.7)	5 (1.2)	9 (2.2)	.29
Acute failure requiring dialysis	17 (2.0)	4 (1.0)	13 (3.1)	.029
Acute failure without dialysis	29 (3.5)	15 (3.6)	14 (3.4)	.84
Peptic ulcer/GI bleed	7 (0.8)	2 (0.5)	5 (1.2)	.26
Prolonged ventilation	21 (2.5)	6 (1.4)	15 (3.6)	.039
Red blood cells	252 (30.4)	111 (26.7)	141 (34.0)	.023
Plasma	177 (21.3)	71 (17.1)	106 (25.5)	.003
Cryoprecipitate	17 (2.0)	2 (0.5)	15 (3.6)	.002
Platelets	155 (18.7)	67 (16.1)	88 (21.2)	.06

Values shown as median (interquartile range), or n (%). Calculation based on complete observations. *CVA*, Cerebrovascular accident/transient ischemic attack; *GI*, gastrointestinal.

preoperative arrhythmia, diabetes, and previous open-heart surgery (Tables E3 and E4).

Factors Affecting Redo MV Surgery

The multivariable subdistribution hazard model showed that the factors affecting redo MV surgery were age (years) (HR, 0.97; 95% CI, 0.951-0.99; $P = .004$) and LVEF ≤50% (HR, 2.090; 95% CI, 1.151-3.796; $P = .016$). MV replacement or repair was not significantly associated with the incidence of redo MV surgery (replacement vs repair, HR, 1.462; 95% CI, 0.762-2.806; $P = .25$) (Table E5).

Association Between the HRs of Replacement and Age

The HR of MVR versus MVr for long-term survival did not change significantly with age. Furthermore, the HR remained consistently greater than 1.00 across all ages, as shown in Figure E1.

DISCUSSION

Several previous studies have reported better outcomes after MVr compared with MVR[4-9,11-13]; however, the majority of these studies included patients undergoing MV surgery with or without concomitant surgery. The current study is valuable not only because of its large sample size with propensity matching and long-term outcomes but also because of its clean patient cohort with a single-valve etiology (degenerative MR) undergoing a single MV procedure without any concomitant surgical procedure. The results of our study demonstrate that patients undergoing MVr alone for degenerative MR have significantly lower postoperative morbidity, better long-term survival, and a similar rate of reoperation compared with

TABLE 4. Univariate/multivariable regression analysis on outcomes

Outcomes	Replacement vs repair		
	Unmatched	Adjusted*	Matched
30-d mortality			
Odds ratio (95% CI)	5.064 (2.491-10.296)	2.270 (1.089-4.732)	1.500 (0.674-3.339)
P value	<.001	.029	.32
1-y mortality			
Odds ratio (95% CI)	5.110 (3.032-8.609)	2.495 (1.432-4.349)	1.647 (0.902-3.009)
P value	<.001	.001	.10
Long-term mortality			
Hazard ratio (95% CI)	2.559 (2.112-3.101)	1.417 (1.161-1.729)	1.355 (1.105-1.661)
P value	<.001	<.001	.004
Redo operation			
Hazard ratio (95% CI)	1.325 (0.745-2.355)	1.462 (0.762-2.806)	1.498 (0.713-3.146)
P value	.34	.25	.29

*See adjusted models shown in Tables E2-E5.

patients undergoing MVR alone (Figure 3). Our study also suggests that the survival benefit of MVr versus MVR is persistent across all ages.

Outcomes of isolated MVr versus MVR using propensity score matching analysis have been previously described by Gillinov and collegues[14] in one report, which failed to show a superiority of MVr in long-term survival relative to MVR although MVr had better short-term outcomes than did MVR. To our knowledge, the current report is the first to demonstrate the superiority of MVr not only in short-term outcomes (postoperative morbidities) but also in long-term survival, in patients with degenerative MR undergoing isolated MV surgery.

There are several important differences between the report by Gillinov and collegues[14] and the current report. In Gillinov and collegues,[14] notwithstanding that the Cleveland Clinic has been a leader in MV repair for decades, the study period of 1985-2005 could be considered an early era for MV repair, before the maturation of the field and many of the repair techniques such as the use of chordal replacement. The current study considers a contemporary period from 2000-2017. In regard to the study cohort, Gillinov and collegues[14] contained 195 matched pairs and included a median follow-up of 2.6 years. The current study contains 415 matched pairs with a median follow-up of 10.4 years. In addition, in Gillinov and collegues,[14] concomitant tricuspid

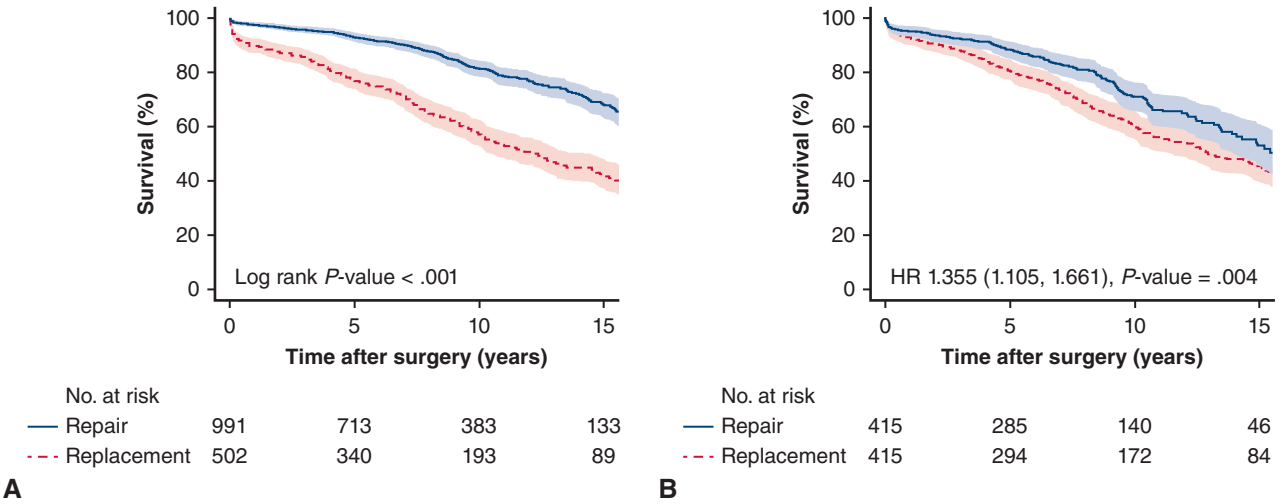

FIGURE 1. Long-term survival rate following MVr or MVR in unmatched (A) and matched (B) patients. Before matching (A), the respective 1-, 5-, 10-, and 15-year survival rates were 97.9 ± 0.5%, 93.2 ± 0.8%, 81.5 ± 1.5%, and 67.7 ± 2.4% in the MVr group and 90.0 ± 1.3%, 77.9 ± 1.9%, 57.9 ± 2.4%, and 42.8 ± 2.7% in the MVR group (log rank test $P < .001$). After matching (B), the respective 1-, 5-, 10-, and 15-year survival rates were 95.7 ± 1.0%, 88.8 ± 1.6%, 71.4 ± 2.7%, and 53.3 ± 3.9% in the MVr group, and 93.0 ± 1.3%, 81.6 ± 1.9%, 61.3 ± 2.6%, and 46.0 ± 3.0% in the MVR group, which still showed significant difference between the 2 groups (hazard ratio, 1.355; 95% confidence interval, 1.105-1.661; $P = .004$). 95% confidence intervals were shown via *shading*. *HR*, Hazard ratio; *MVr*, mitral valve repair; *MVR*, mitral valve replacement.

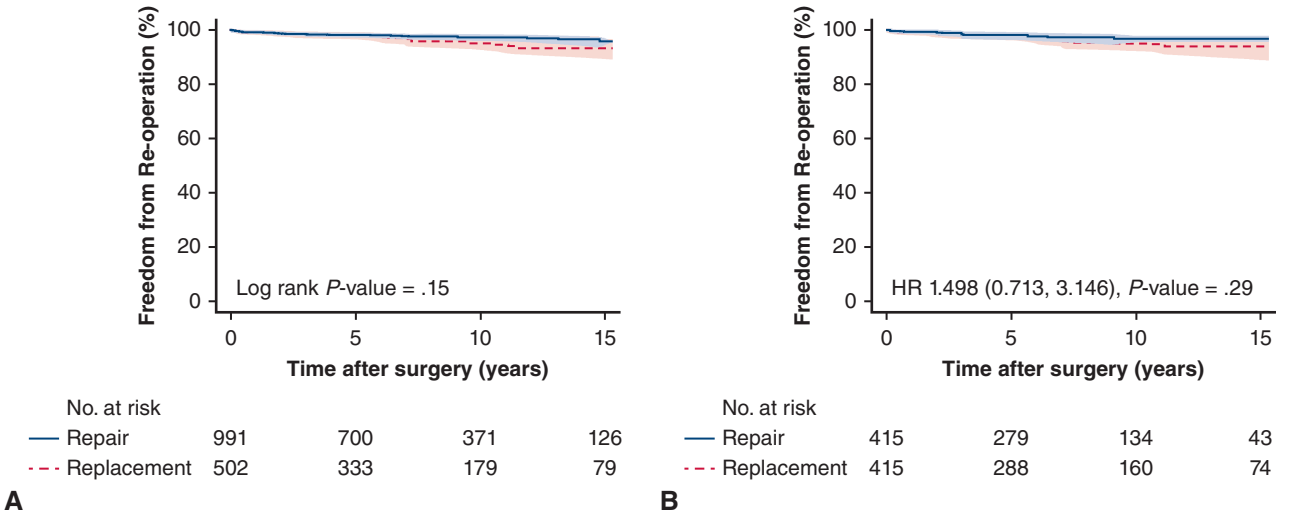

FIGURE 2. Freedom rate from mitral valve reintervention following MVr or MVR in unmatched (A) and matched (B) patients. In unmatched patients (A), the freedom rate from mitral valve reoperation was 98.0 ± 0.5% at 5 years and 97.1 ± 0.6% at 10 years in the MVr group, respectively, whereas that was 98.0 ± 0.6% and 95.2 ± 1.2% in the MVR group, respectively (log rank test $P = .15$). After matching (B), there was still no significant difference in the freedom rate from reoperation at 10 years between the MVr and MVR groups (96.6 ± 1.1% and 95.2 ± 1.2%, hazard ratio, 1.498; 95% confidence interval, 0.713-3.146; $P = .29$). 95% confidence intervals were shown via *shading*. *HR*, Hazard ratio; *MVr*, mitral valve repair; *MVR*, mitral valve replacement.

valve repair and ablation for atrial fibrillation were not excluded from the analysis nor included in propensity score matching, whereas in the current report, all concomitant cardiac procedures were excluded from the analysis.

The current study shows that the incidence of MV reintervention following either MVr or MVR is very low, with no significant difference between the MVr and MVR groups, which is consistent with other findings.[14] The long-term durability of MVr, with freedom from reoperation over 95% at 15 years, is on par with other leading mitral surgery centers.[15]

A previous study has shown that the benefit of MVr on survival decreases with advancing age.[4] However, in our study, the survival benefit of MVr over MVR is not affected by age, which is supported by the persistent HR of MVR versus MVr of greater than 1.0 across all ages. This is consistent with a recent meta-analysis.[9]

Our study also demonstrates that MVR is an independent risk factor for 30-day mortality, which is consistent with other studies showing MVR in elderly patients is a risk factor for short-term mortality, which may be due to a relatively greater incidence of complications with MVR compared with MVr.[16,17] Although some centers may still prefer MVR in the elderly to avoid the potential risk of repair failure, our study highlights the importance of considering MVr as the primary choice for degenerative MR regardless of age, given the finding of fewer postoperative complications, long-term survival benefit, and similar freedom from MV reintervention with MVr versus MVR. However, durable repair is important as failed repairs reduce its benefit compared with chordal sparing replacement in the elderly.[17]

Our study identifies many independent risk factors for short-term and long-term outcomes following isolated MV surgery in patients with degenerative MR. Our findings on risk factors align with those in other studies.[18,19] One study identified 6 significant predictors of long-term mortality after MV surgery, which included age, hemoglobin level, MVR, renal function, left atrial size, and left end-systolic diameter. Other recent studies have indicated that chronic obstructive pulmonary disease, peripheral artery disease, liver disease, and a history of cerebrovascular accidents are also risk factors for mortality following MV surgery.[13,20] Of all the risk factors in our study, only MVR, age and cardiopulmonary bypass (CPB) time are the risk factors for all 30-day, 1-year and long-term mortalities, which further supports that MVr should be considered as the primary choice for degenerative MR. Interestingly, emergency surgery, peripheral vascular disease, and chronic obstructive pulmonary disease are not independent risk factors for 30-day mortality, although they are risk factors for 1-year and long-term mortality. Another interesting finding in our study is that CPB time is an independent risk factor for 30-day and 1-year mortalities and long-term mortality after MV surgery. We are not aware of another study to suggest a positive relationship between CPB time and mortality after 30 days, although the relationship between crossclamp time and in-hospital mortality or morbidities has previously been described in studies using large databases.[21,22]

In addition to our large sample size with a single etiology of MV disease and isolated MV surgery without any concomitant cardiac procedures, propensity score matching including 32 variables allowed us to minimize the

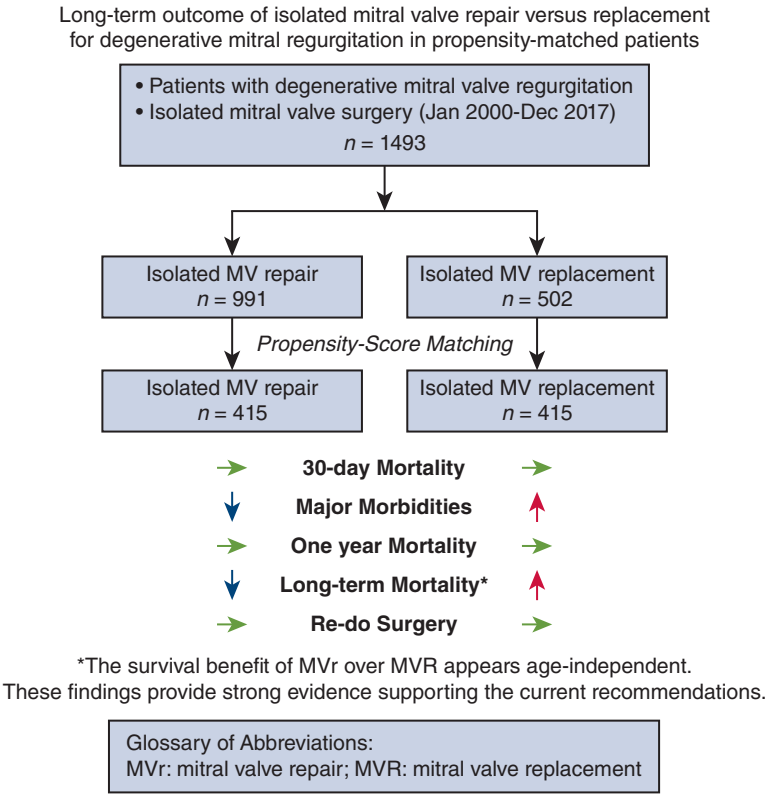

FIGURE 3. Study summary. Patients undergoing isolated MVr for degenerative mitral regurgitation have significantly lower postoperative morbidities, better long-term survival, and a similar rate of MV reoperation compared with patients undergoing isolated MRV. *MV*, Mitral valve; *MVr*, mitral valve repair; *MVR*, mitral valve replacement.

consequences of the lack of randomization and to obtain well-balanced treatment groups, leading to minimization of selection bias in comparing outcomes of MVr with MVR. Our data strengthen the evidence for MVr as the optimal treatment for patients with degenerative MR.

Limitations

This study is associated with the limitations inherent in any retrospective study. The database used in this study does not provide MVr technical detail. Consequently, we were not able to study the association between variables of valve repair technique and long-term survival. We were also unable to perform subgroup analysis on the outcomes of mechanical valves or tissue valves versus valve repair because of small sample sizes of subgroups after propensity score matching. Furthermore, the detail on chordal preservation in MVR was also not well documented in the registry, which cannot be considered in the analysis in the present study. We were not able to collect center specific information from the registry, or to collect detailed information on individual surgeon from the registry because these are quite sensitive information. Therefore, we were not able to explore center- or surgeon-level effect. Nonvalve repair surgeons were probably not able to perform complex MV repair and did not have a choice to repair.

CONCLUSIONS

MVr is associated with significantly fewer postoperative morbidities and better long-term survival compared with MVR in patients undergoing MV surgery alone for degenerative MR. Our findings strongly support MVr as the primary choice for the treatment of degenerative MR in patients regardless of age.

Conflict of Interest Statement

Dr Ye is a consultant to Edwards Lifesciences and JC Medical Inc. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: mitral valve repair, mitral valve replacement, degenerative mitral valve disease, isolated mitral valve surgery, propensity score matching

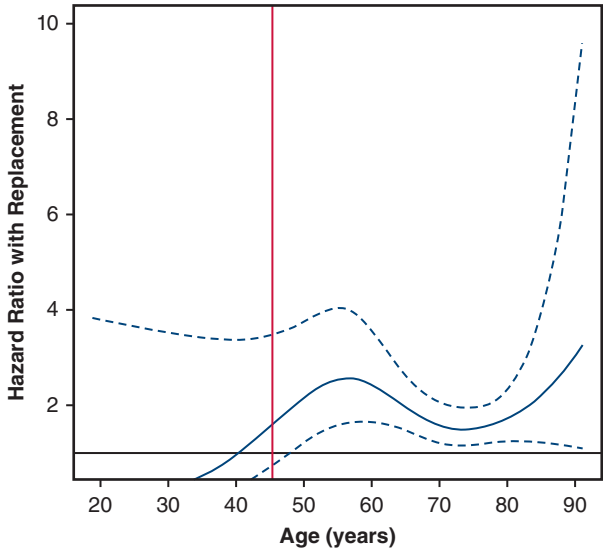

FIGURE E1. A hazard ratio of mitral valve replacement over repair across all ages. The hazard ratio of mitral valve replacement over mitral valve repair remained consistently greater than 1.0 across all ages. 95% confidence intervals are denoted with *hashed lines*.

TABLE E1. Intraoperative and postoperative complications (unmatched)

Variable	All n = 1493	Repair n = 991	Replacement n = 502	*P* value
Pump time, min	120.0 (92.0, 160.0)	120.0 (91.0, 158.5)	122.0 (92.0, 162.0)	.34
Clamp time, min	96.0 (71.0, 128.0)	97.0 (71.0, 128.0)	94.0 (71.0, 129.0)	.86
Duration of operation, h	4.8 (3.9, 5.8)	4.9 (4.0, 5.9)	4.7 (3.9, 5.8)	.26
Duration of skin open, h	3.5 (2.8, 4.4)	3.5 (2.7, 4.4)	3.5 (2.8, 4.5)	.49
Creatinine—post, μmol/L	83.0 (69.0, 97.0)	81.0 (68.0, 94.0)	87.0 (72.0, 106.0)	<.001
Creatinine—post, highest, μmol/L	92.0 (77.0, 113.0)	90.0 (75.0, 107.0)	100.0 (82.0, 130.0)	<.001
Prosthetic valve endocarditis	2 (0.1)	1 (0.1)	1 (0.2)	.99
Insertion of permanent pacemaker	23 (1.5)	14 (1.4)	9 (1.8)	.57
Postoperative hemorrhage/tamponade	28 (1.9)	10 (1.0)	18 (3.6)	<.001
Arrhythmia—cardiac arrest	8 (0.5)	4 (0.4)	4 (0.8)	.45
Arrhythmia—atrial	583 (39.0)	346 (34.9)	237 (47.2)	<.001
Arrhythmia—heart block	70 (4.7)	39 (3.9)	31 (6.2)	.05
Valvular thromboembolism/thrombosis	0 (0.0)	0 (0.0)	0 (0.0)	–
Inotropes >24 h	46 (3.1)	18 (1.8)	28 (5.6)	<.001
CVA	18 (1.2)	7 (0.7)	11 (2.2)	.013
Acute failure requiring dialysis	34 (2.3)	11 (1.1)	23 (4.6)	<.001
Acute failure without dialysis	37 (2.5)	15 (1.5)	22 (4.4)	<.001
Peptic ulcer/GI bleed	10 (0.7)	3 (0.3)	7 (1.4)	.036
Prolonged ventilation	34 (2.3)	9 (0.9)	25 (5.0)	<.001
Red blood cells	378 (25.3)	194 (19.6)	184 (36.7)	<.001
Plasma	293 (19.6)	154 (15.5)	139 (27.7)	<.001
Cryoprecipitate	26 (1.7)	8 (0.8)	18 (3.6)	<.001
Platelets	256 (17.1)	146 (14.7)	110 (21.9)	<.001

Values shown as median (interquartile range), or n (%). Calculation based on complete observations. *CVA*, Cerebrovascular accident; *GI*, gastrointestinal.

TABLE E2. Risk factors affecting 30-day mortality

Variable	Univariate analysis		Multivariable analysis*	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Replacement vs repair	5.064 (2.491-10.30)	<.001	2.270 (1.089-4.732)	.029
Age, y	1.103 (1.062-1.145)	<.001	1.088 (1.045-1.132)	<.001
Pump time, min	1.009 (1.004-1.013)	<.001	1.009 (1.004-1.014)	<.001
LVEF (≤50%)	3.415 (1.790-6.514)	<.001	2.802 (1.425-5.512)	.003

CI, Confidence interval; *LVEF*, left ventricular ejection fraction. *Hosmer and Lemeshow goodness-of-fit test $P = .29$, c statistic = 0.84.

TABLE E3. Risk factors affecting 1-year mortality

Variable	Univariate analysis		Multivariable analysis*	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Replacement vs repair	5.110 (3.032-8.609)	<.001	2.495 (1.432-4.349)	.001
Age, y	1.079 (1.052-1.107)	<.001	1.063 (1.033-1.094)	<.001
Pump time, min	1.007 (1.003- 1.011)	<.001	1.007 (1.003-1.011)	<.001
LVEF (≤50%)	3.743 (2.306-6.074)	<.001	2.623 (1.553-4.429)	<.001
Emergency or priority I for surgery	3.954 (2.196-7.121)	<.001	3.071 (1.585-5.947)	<.001
PVD	6.716 (3.528-12.78)	<.001	4.054 (1.958-8.392)	<.001
COPD	3.077 (1.866-5.074)	<.001	1.938 (1.110-3.382)	.020

CI, Confidence interval; *LVEF*, left ventricular ejection fraction; *PVD*, peripheral vascular disease; *COPD*, chronic obstructive pulmonary disease. *Hosmer and Lemeshow goodness-of-fit test $P = .83$, c statistic = 0.83.

TABLE E4. Risk factors affecting long-term mortality

Variable	Univariate analysis		Multivariable analysis	
	Hazards ratio (95% CI)	*P* value	Hazards ratio (95% CI)	*P* value
Replacement vs repair	2.559 (2.112-3.101)	<.001	1.424 (1.168-1.736)	<.001
Age, y	1.086 (1.074-1.098)	<.001	1.075 (1.062-1.088)	<.001
Pump time, min	1.004 (1.002-1.006)	<.001	1.004 (1.002-1.006)	<.001
Pump time × log (follow-up time)*	0.998 (0.997-0.999)	<.001	0.999 (0.998-1.000)	.003
LVEF (≤50%)	1.942 (1.602-2.354)	<.001	1.433 (1.173-1.751)	<.001
Creatinine, μmol/L	1.002 (1.001-1.003)	<.001	1.002 (1.001-1.003)	<.001
PVD	2.742 (1.857-4.048)	<.001	1.733 (1.238-2.426)	.001
COPD	2.236 (1.785-2.801)	<.001	1.752 (1.387-2.215)	<.001
Preoperative arrhythmia	2.482 (2.040-3.019)	<.001	1.400 (1.137-1.725)	.002
Diabetes	2.392 (1.820-3.143)	<.001	1.604 (1.184-2.173)	.002
Previous open-heart surgery	3.542 (2.297-5.463)	<.001	2.027 (1.399-2.935)	<.001

CI, Confidence interval; *LVEF*, left ventricular ejection fraction; *PVD*, peripheral vascular disease; *COPD*, chronic obstructive pulmonary disease. *Pump time did not satisfy proportional hazard assumption; accordingly, it was set as a time-dependent variable in the model fitting.

TABLE E5. Risk factors affecting redo surgery*

Variable	Univariate analysis		Multivariable analysis	
	Hazards ratio (95% CI)	*P* value	Hazards ratio (95% CI)	*P* value
Replacement vs repair	1.325 (0.745-2.355)	.34	1.462 (0.762-2.806)	.25
Age, y	0.974 (0.955-0.993)	.007	0.970 (0.951-0.990)	.004
LVEF (≤50%)	2.136 (1.205-3.789)	.009	2.090 (1.151-3.796)	.016

CI, Confidence interval; *LVEF*, left ventricular ejection fraction. *Death was treated as competing risks.