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Original Article

Redo mitral valve replacement for initially rheumatic heart disease: In-hospital outcomes and operative risk prediction

Mohamed Amr[1], Elsayed Fayad[1], Yasser Kamal[2]

[1] Department of Cardiothoracic Surgery, Faculty of Medicine, Suez Canal University, Egypt

[2] Department of Cardiothoracic Surgery, Faculty of Medicine, Minia University, El-Menya, Egypt

Abstract

Background: Redo mitral valve replacement (redo-MVR) remains a challenge despite advances in surgical techniques. Little is known about the outcomes of redo-MVR in patients with rheumatic heart disease. We aimed to evaluate the in-hospital outcomes and associated risk factors for mortality and morbidity after re-operative mitral valve replacement in patients with initial rheumatic heart disease.

Methods: This retrospective cohort study included 214 patients, 96 males (44.9%) and 118 females (55.1%), who underwent redo-MVR between January 2015 and December 2020. The mean age was 41.87±11.7 years. European Heart Surgery Risk Assessment System II (EuroSCORE II), Age, Creatinine, Ejection Fraction (ACEF) scores were used for risk stratification. The primary endpoints were in-hospital mortality, major morbidity (renal failure, prolonged ventilation, stroke, reoperation, or deep sternal wound infection), and the composite outcome of mortality and/or morbidity).

Results: Major morbidities occurred in 31.8% of patients, and the in-hospital mortality rate was 19.6%. Predictors of mortality were New York Heart Association class (NYHA) III/IV (OR: 5.4; p< 0.001), cardiogenic shock (OR: 13.74, p<0.001), low left ventricular ejection fraction (LVEF) (OR: 4.36; p= 0.01), and perioperative intra-aortic balloon pump (OR: 6.79; p= 0.01). The significant predictors of mortality and/or major morbidity were NYHA III/IV (OR: 2.39; p<0.001), low LVEF (OR: 4.44; p= 0.001), active endocarditis (OR: 2.4; p=0.04), and perioperative IABP (OR: 3.88; p= 0.045). EuroSCORE II had better accuracy than the ACEF score to predict adverse outcomes (AUC: 0.70 [95% CI: 0.63-0.78] versus 0.58 [95% CI: 0.50-0.66], p= 0.01).

Conclusion: Advanced NYHA class and low LVEF could be associated with poor outcomes after redo-MVR in patients with primary surgery for rheumatic mitral valve disease. EuroSCORE II is a helpful tool for risk stratification during redo-MVR.

KEYWORDS

Mitral valve surgery; Rheumatic heart disease; Reoperation; Predictors; EuroSCORE II

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Introduction

Valvular rheumatic heart disease remains a significant public health concern in developing countries with high morbidity and mortality [1]. Redo valve surgery for patients with initial rheumatic heart disease is an ongoing clinical issue because of the young age of the patients, progressive nature of the disease, thrombogenicity of the prosthetic valves, and degeneration of the bioprosthetic valves [2]. Mitral valve reoperations carry higher risks of adverse outcomes than primary operations [3].

Corresponding author: Mohamed Amr Doctor2001eg@yahoo.com

Estimation of the perioperative risk factors associated with increased operative risk after cardiac surgery is an important issue to determine the proper timing of surgery, decision-making, and allocation of hospital resources [4].

Therefore, this study aimed to evaluate in-hospital outcomes after redo-MVR in patients with previous mitral valve surgery for rheumatic heart disease and identify perioperative risk factors associated with in-hospital mortality and morbidity in this group of patients.

Patients and Methods

This retrospective multicenter cohort study included adult patients with prior mitral valve surgery (replacement or repair) for rheumatic heart disease who underwent redo-MVR between January 2015 and December 2020. We excluded prior double mitral and aortic valve replacement, prior cardiac surgery rather than mitral valve surgery, prior mitral valve surgery for degenerative and ischemic etiologies, redo mitral valve repair, and patients aged <18 years old. Based on the previously reported incidence of redo-MVR to be 9.8% [5], the calculated minimum sample size was 136 patients at a 95% confidence level and 5% margin of error.

Data collection and study endpoints

The collected data included: preoperative demographic features, clinical risk factors, operative risk scores (EuroSCORE II and Age, Creatinine, Ejection Fraction (ACEF) score), interval to reoperation, hemodynamic pathology, operation priority, operation sequence, indications of reoperation, number of valve procedures, additional valve procedures, durations of cardio-pulmonary bypass (CPB) and aortic cross-clamp, postoperative low cardiac output syndrome, perioperative insertion of intra-aortic balloon pump (IABP), any postoperative complication, duration of mechanical ventilation, duration of ICU stay, and duration of hospital stay. The primary endpoints of outcome were in-hospital mortality, major morbidity, and unfavorable outcome. In-hospital mortality was defined as death during the hospital stay or within 30 days after surgery. Major morbidity was defined following the Society of Thoracic Surgeons (STS) criteria [6], including renal failure, prolonged ventilation, stroke, reoperation, or deep sternal wound infection. The unfavorable outcome was defined as a composite of mortality and/or morbidity.

Table 1: Preoperative demographic and clinical characteristics of 214 patients who underwent redo-mitral valve replacement. Continuous data were presented as mean and SD and categorical data as numbers and percentages

Variables	Redo-mitral (n=214)
Age (years)	41.87±11.70
Female gender	118 (55.1%)
BMI (kg/m2)	26.25±4.71
NYHA class III/IV	96 (45%)
Smokers	6 (2.8%)
Peripheral vascular disease	2 (0.9%)
Cerebrovascular disease	10 (4.7%)
Chronic pulmonary disease	2 (0.9%)
Diabetes Mellitus	28(13.1%)
Cardiogenic shock	20 (9.3%)
Renal failure on dialysis	2(1.9%)
Ejection fraction (%)	57.30±6.52
Pulmonary hypertension	92 (43%)
Perioperative IABP	14 (6.5%)
Euroscore II (%)	7.4±7
ACEF score (%)	2.5±1.2

BMI: Body mass index. IABP: Intra-aortic balloon pump. ACEF score: Age, Creatinine, and Ejection Fraction score

Surgical technique

Femoral vessels were exposed as a routine before re-sternotomy. Operations were performed through median sternotomy incision using an oscillating saw. After the release of the pericardial adhesions, cardiopulmonary bypass was established with aorto-bicaval cannulation. Myocardial protection was achieved using antegrade cold blood cardioplegia and moderate hypothermia (30-32◦C). The left atrium was approached via the inter-atrial groove or trans-septal. After evaluation of the previous prosthetic valve, the sewing ring was freed by sharp dissection with a scalpel. Careful debridement of pannus and annular calcifications was performed. The prosthetic valve was inserted with interrupted pledget 2-0 Ethibond sutures. Temporary pacing

wires were inserted. When the hemodynamic variables were satisfactory, cardiopulmonary bypass was weaned off, followed by wound closure as usual.

Table 2: Preoperative extent and severity of mitral valve disease indicated for reoperation. Continuous data were presented as mean and SD and categorical data as numbers and percentages.

Variables	Redo-mitral (n=214)
Interval to reoperation (years)	7.81±5.45
Previous mitral valve procedure:	
Replacement (Mechanical valve)	158 (73.83%)
Replacement (Bioprosthesis)	26 (12.14%)
Repair	30 (14.01%)
Hemodynamic pathology:	
Regurgitation	144 (67.3%)
Stenosis	58 (27.1%)
Mixed	12 (5.6%)
Operation priority:	
Elective	88 (41.1%)
Urgent	40 (18.7%)
Emergent	80 (37.4%)
Salvage	6 (2.8%)
Operation sequence:	
Second	208 (97.2%)
Third	6 (2.8%)
Indications of reoperation:	
Prosthetic valve thrombosis	66 (30.8%)
Active endocarditis	52 (24.3%)
Structural deterioration	40 (18.7%)
Failed prior repair	30 (14%)
Paraprosthetic leak/dehiscence	26 (12.1%)
Number of valve procedures:	
One	190 (88.8%)
Two	22 (10.3%)
Three	2 (0.9%)
Additional valve procedures:	
Aortic	8 (3.7%)
Tricuspid	14 (6.5%)
Aortic + Tricuspid	2 (0.9%)

Statistical analysis

The statistical analysis was performed using IBM-SPSS Advanced Statistics version 20.0 (IBM Corp- Armonk, NY, USA) and R software version 4.1.1, 2021-08-10 (R Foundation for Statistical Computing). Quantitative data were expressed as mean ± SD, whereas the categorical data were expressed as number and percent. Univariable comparisons were performed using Student's t-test for quantitative data and Chi-square test for categorical data. Variables associated with adverse outcomes in the univariable analysis were included in the multivariable analysis using binary logistic regression to determine independent predictors of mortality and morbidity. The odds ratio (OR) and its 95% confidence interval (95% CI) were estimated for each risk factor. Receiver Operating Characteristic (ROC) curve was used to estimate the diagnostic accuracy of the scoring systems by calculating the area under the curve (AUC). DeLong's test was used to compare the AUC of each two ROC curves. A P-value of less than 0.05 was considered statistically significant.

Results

Baseline data

The study included 214 reoperations for mitral valve replacement after previous mitral valve surgery. Ninety-three patients (43.4%) were transferred from outside hospitals. There were 96 male (44.9%) and 118 female (55.1%) patients, and the mean age was 41.87±11.7 years (range: 19–70 years). Ninety-six patients (45%) were in NYHA class III-IV. The mean values of EuroSCORE II and ACEF score's predicted mortality were 7.4±7% and 2.5±1.2%, respectively. Preoperative demographic and clinical characteristics are presented in Table 1. The mean time interval to mitral reoperation was 7.81±5.45 years.

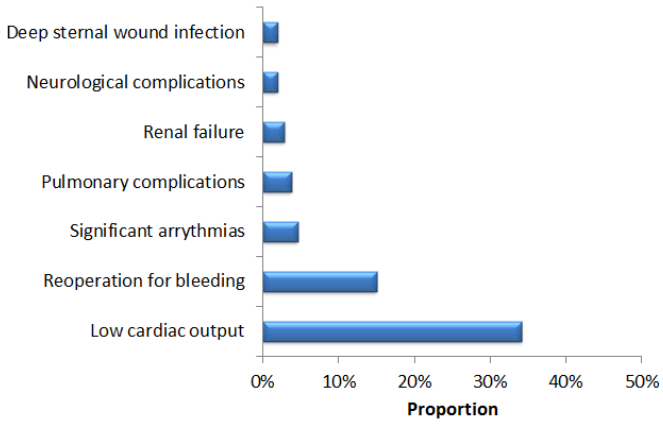

Figure 1: Proportions of postoperative complications after redo-mitral valve replacement

Operative data

The priority of operation was elective in 88 patients (41.1%) and non-elective (urgent,

Table 3: Comparison of postoperative outcome in accordance to priority of reoperation. Continuous data were presented as mean and SD and categorical data as numbers and percentages

Variables	Total (n=214)	Elective (n=88)	Non-elective (n=126)	P-value
Mortality	42 (19.6%)	8 (9.1%)	34 (27%)	0.001
Major morbidity	68 (31.8%)	18 (20.5%)	50 (39.7%)	0.003
Unfavorable outcome	78 (36.4%)	20 (22.7%)	58 (46%)	<0.001

emergent, or salvage) in 126 patients (58.9%). The indications of mitral valve reoperation were prosthetic valve thrombosis (30.8%), active endocarditis (24.3%), structural deterioration (18.7%), failed prior repair (14%), and periprosthetic leak/dehiscence (12.1%). Preoperative characteristics of prosthetic mitral valve disease are presented in Table 2. CPB and aortic cross-clamp mean duration were 106.49±43.46 min and 69.30±29.97 min, respectively.

Postoperative data

Postoperative complications included: low cardiac output syndrome (34.1%), reoperation for bleeding or cardiac arrest (15%), significant arrhythmias including supraventricular arrhythmias and heart block (4.6%), pulmonary complications including re-intubation and pneumonia (3.7%), renal failure (2.8%), neurological complications (1.9%), and deep sternal wound infection (1.9%). Proportions of postoperative complications are presented in Figure 1. The mean duration of mechanical ventilation, ICU stay, and hospital stay were 24.55±28.65 hours, 68.75±76.06 hours, and 10.79±6.79 days, respectively. Major morbidities (renal failure, prolonged ventilation >24 hours, stroke, reoperation, or deep sternal wound infection) occurred in 68 patients (31.8%). The mortality rate was 19.6% (n = 42). The causes of in-hospital mortality were cardiac (n = 19), multi-organ dysfunction (n = 12), sepsis (n = 6) and respiratory failure (n = 5). Unfavorable outcomes (a composite of mortality and/or major morbidity) occurred in 78 patients (36.4%).

The study included 126 patients (58.8%) who underwent non-elective operations (urgent/emergent/salvage) versus 88 patients (41.2%) who had elective operations. Non-elective operations were associated with significantly higher proportions of mortality, major morbidity, and unfavorable outcome (mortality and/or major morbidity) than elective operations (Table 3).

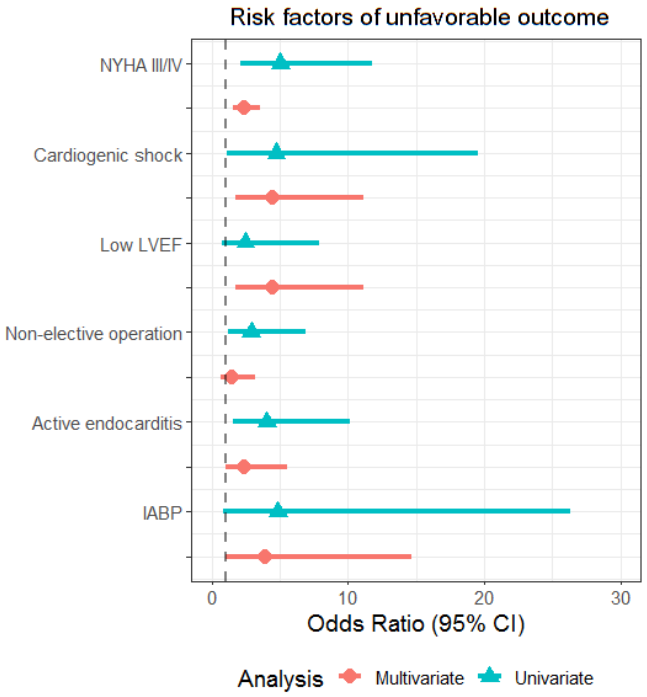

Figure 2: Univariable and multivariable odds ratio and its 95% confidence interval (95% CI) of preoperative risk factors for prediction of unfavorable outcome (mortality and/or morbidity) after redo-mitral valve replacement

Outcome's predictors:

On univariable analysis, the mortality rate was significantly higher in patients with NYHA class III/IV, cardiogenic shock, low LVEF, non-elective operation, active endocarditis, and perioperative IABP. On multivariable analysis, the independent predictors of mortality were NYHA III/IV, cardiogenic shock, low LVEF, and perioperative IABP. Major morbidity was higher in NYHA class III/IV patients, low LVEF, non-elective operation, and active endocarditis. On multivariate analysis, the predictors of major morbidity were NYHA class III/IV, low LVEF, and active endocarditis. Overall, the significant predictors of unfavorable outcome

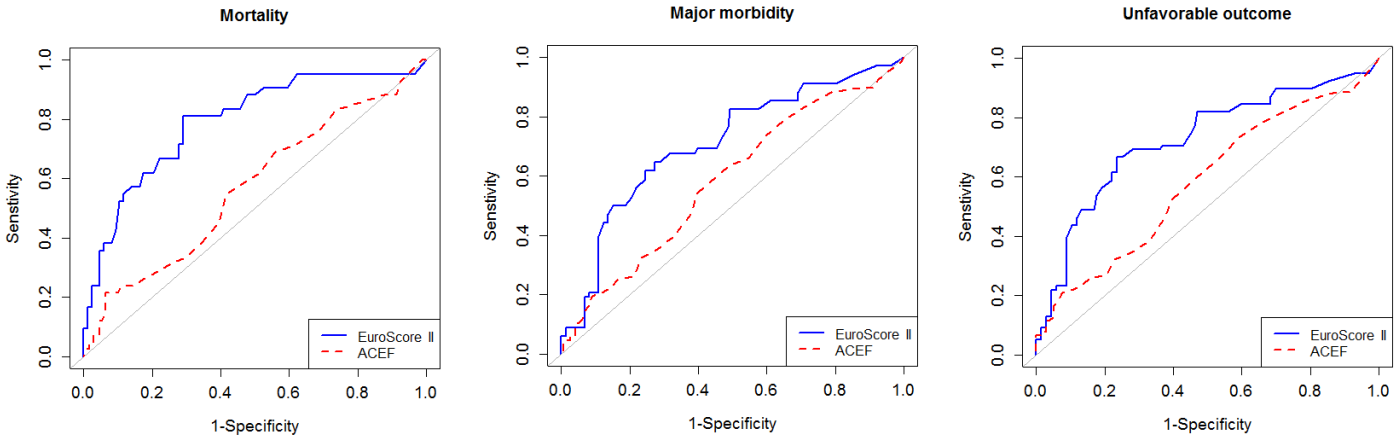

Figure 3: Receiver Operating Characteristics (ROC) curves demonstrating the accuracy of the risk scoring systems (EuroSCORE II and ACEF score) for prediction of in-hospital mortality, major morbidity, and unfavorable outcome (composite of mortality and/or major)

(mortality and/or major morbidity) were NYHA III/IV, low LVEF, active endocarditis, and perioperative IABP. Univariable and multivariable determinants of in-hospital postoperative outcomes are presented in Table 4 and Figure 2.

Receiver Operating Characteristic (ROC) curves demonstrated that EuroSCORE II and ACEF scores had a statistically significant difference of their AUC from the cutoff point of 50% to predict adverse outcomes. The accuracy of EuroSCORE II was higher than ACEF score for prediction of in-hospital mortality (AUC: 0.79 [95% CI: 0.71-0.87] versus 0.56 [95% CI: 0.47-0.66]), major morbidity (AUC: 0.70 [95% CI: 0.63-0.78] versus 0.58 [95% CI: 0.50-0.66]), and unfavorable outcome (AUC: 0.72 [95% CI: 0.65-0.79] versus 0.58 [95% CI: 0.50-0.66]) after redo-mitral valve replacement (Figure 3). The comparison of the AUC of both scoring systems by DeLong's test for two ROC curves revealed significant differences between both scores for prediction of mortality ($P < 0.001$), major morbidity ($P = 0.01$), and unfavorable outcome ($P = 0.004$).

Discussion

Many of the rheumatic heart disease (RHD) patients who undergo mitral valve surgery are young with a long life expectancy; thus, some may require reoperation for valve-related complications or structural deterioration [2]. However, scant data exists in the literature regarding the specific outcome evaluation after redo-mitral valve replacement in this group of patients. In the contemporary literature, re-operative mitral valve surgery remains a surgical challenge due to higher preoperative risk factors that lead to higher rates of in-hospital mortality and postoperative complications [5, 7].

In our series of redo-mitral valve replacements, most of the patients were female (55.1%) and had a mean age of 41.87±11.7 years, which can be explained by young age and frequent female gender RHD surgery patients. The indications of mitral valve reoperation in our series were prosthetic valve thrombosis (30.8%) followed by active endocarditis (24.3%), structural deterioration (18.7%), failed prior repair (14%), and periprosthetic leak/dehiscence (12.1%). The high proportion of patients with previous mechanical valve replacement (73.83%) could explain the inclusion of many reoperations for prosthetic valve complications.

The most common indication for redo mitral valve surgery differs between studies in literature, but most of these indications are related to prosthetic valve complications. Other investigators reported the most common indication of redo mitral surgery to be prosthetic valve endocarditis [8], prosthetic valve dysfunction [9], or paravalvular leakage [10]. Similar to our findings, Kumar and coworkers [2] reported that valve thrombosis and infective endocarditis were the most frequent indications for reoperation following mitral valve replacement. Kothari and colleagues [11] reported

Table 4: Univariate and multivariate preoperative determinants of postoperative in-hospital outcome

Risk factors	Univariable				Multivariable			
	OR	95% CI		*P-value*	OR	95% CI		*P-value*
		Lower	Upper			Lower	Upper	
Mortality:								
NYHA III/IV	11.20	4.46	28.08	<0.001	5.40	2.81	10.37	**<0.001**
Cardiogenic shock	13.83	4.90	39.01	<0.001	13.74	3.55	53.11	**<0.001**
Low LVEF	3.800	1.719	8.398	0.001	4.36	1.35	14.01	**0.01**
Non-elective operation	3.69	1.61	8.44	0.001	1.48	0.43	5.10	0.52
Active Endocarditis	5.20	2.52	10.72	<0.001	2.84	0.94	8.55	0.06
Perioperative IABP	6.51	2.12	19.97	0.001	6.79	1.40	32.87	**0.01**
Major morbidity:								
NYHA III/IV	4.01	2.17	7.40	<0.001	1.783	1.22	2.60	**0.003**
Low LVEF	3.929	1.840	8.389	<0.001	3.465	1.49	8.02	**0.004**
Non-elective operation	2.55	1.36	4.79	0.003	1.287	0.59	2.77	0.52
Active Endocarditis	4.45	2.30	8.60	<0.001	3.167	1.42	7.06	**0.005**
Unfavorable outcome:								
NYHA III/IV	5.03	2.14	11.81	<0.001	2.39	1.61	3.56	**<0.001**
Cardiogenic shock	4.740	1.149	19.55	0.001	2.48	0.78	7.86	0.12
Low LVEF	4.060	1.878	8.776	<0.001	4.44	1.77	11.13	**0.001**
Non-elective operation	2.90	1.22	6.86	<0.001	1.44	0.65	3.17	0.36
Active Endocarditis	4.03	1.59	10.18	<0.001	2.40	1.03	5.58	**0.041**
Perioperative IABP	4.853	0.89	26.33	0.005	3.88	1.02	14.68	**0.045**

OR: odds ratio; CI: confidence interval. LVEF: Left ventricular ejection fraction. IABP: Intra-aortic balloon pump. *Significant predictor

thrombosis and pannus formation as the most common cause of redo mitral surgery for mechanical prostheses. A direct relationship between prosthetic valve thrombosis and adherence to oral anticoagulant therapy has been stated that can be affected by awareness, availability, and follow-up of medication after primary operation [11].

The most common postoperative complication in our series was low cardiac output (34.1%), followed by reoperation for bleeding or cardiac arrest (15%) and significant arrhythmias (4.6%). Major morbidities (renal failure, prolonged ventilation, stroke, reoperation, or deep sternal wound infection) occurred in 68 patients (31.8%). Other investigators reported high frequencies of bleeding and low cardiac output after re-operative mitral surgery, which were also the major causes of early mortality [2]. Moreover, Mehaffey and colleagues [5] reported that redo mitral patients had a higher complications rate than patients with primary operations, including major morbidity (34.7 vs. 26.8%, p<0.0001) attributed to higher rates of prolonged ventilation, renal failure, and reoperation. The occurrence of major complications after redo operations via median sternotomy is an important issue as it can result in high in-hospital mortality rates. Thus, the current practice still recommends improvements in critical care medicine, perioperative myocardial protection, blood conservation protocols, and less-invasive alternatives to re-sternotomy [3].

The mean ICU and hospital stay duration in our series were 68.75±76.06 hours and 10.79±6.79 days, respectively. These findings are constant with other studies in the literature, which showed a mean hospital stay ranges from 6.2 to 17.2 days and ICU stay from 18 hours to 13.5 days [7]. In the current era of less-invasive techniques, the right mini-thoracotomy is an attractive alternative to median sternotomy for mitral reoperations to reduce hospital and ICU stay duration and minimize morbidity and mortality. However, the available evidence for the superiority of the mini-thoracotomy approach is limited with low quality [12].

The mortality rate was 19.6% (n = 42). Our mortality rate is constant with the reported perioperative mortality rates of 4.2% to 29.2% after re-sternotomy [2, 8, 11, 13, 14]. The variation in the range of mortality rates could be explained by differences in the choice of surgical approaches (re-sternotomy or right thoracotomy), times of redo surgery, indications of reoperation, and preoperative risk factors. The relatively high rate of in-hospital mortality in our series could be explained by high frequencies of preoperative NYHA III/IV class and non-elective priority of reoperations, which was associated with significantly higher mortality and major morbidity rates than elective reoperations.

In our series, advanced NYHA class, cardiogenic shock, low LVEF (<50%), and perioperative IABP were significant independent predictors of in-hospital mortality. Moreover, we found advanced NYHA class, low LVEF, non-elective operation, and active endocarditis as significant predictors of major morbidity. Also, multivariate analysis revealed that advanced NYHA class, low LVEF, active endocarditis, and perioperative IABP were significant predictors of unfavorable outcome (a composite of mortality and/or major morbidity) after redo-mitral valve replacement. Other studies in the literature have identified advanced NYHA class, low preoperative LVEF, cardiogenic shock, and preoperative IABP [3, 5, 14] as significant independent predictors of mortality after redo-mitral surgery. Additional reported predictors in previous studies included non-elective priority (urgent or emergent) [3, 5], active endocarditis [3], pulmonary hypertension [15], old age [16], and female gender [14]. Most of these factors are well known and included in the commonly used risk scoring systems that estimate the operative risk of cardiac surgery. Generally, the association of impaired systolic function deteriorated dyspnea status, and active endocarditis with poor outcome after redo surgery indicates the importance of early identification and management of prosthetic mitral valve complications.

In our series, EuroSCORE II and ACEF score could predict adverse outcomes after redo-MVR, while EuroSCORE II had significantly higher accuracy than ACEF score. There are many risk scoring systems for predicting outcomes after primary cardiac surgery; however, the literature did not validate these scores in redo surgery. EuroSCORE II is a widely used tool, but the inclusion of many non-significant risk factors led to the development of the ACEF score, which includes three risk factors, only making it more simplified [17]. Both EuroSCORE II and ACEF scores have been identified as good useful predictors of operative mortality after primary mitral valve surgery with a better discriminative power (higher AUC on ROC curve) for EuroSCORE II [18]. Our findings confirmed the superior accuracy of EuroSCORE II in redo-MVR; however, identification of more specific factors for younger patients with initially rheumatic heart disease should be considered in future studies.

Study limitations

Our multicenter study is potentially limited by: retrospective nature and inherent selection bias, absence of data related to long-term outcome, calculation of EuroSCORE II and ACEF score from prospectively collected factors in the medical records, and datasets with susceptible data collection bias. Although multicenter studies have advantages of reproducibility and generalizability, differences in the indication criteria and the surgical techniques, even minor, may be associated with interpretation bias, which may be overcome in future prospective studies.

Conclusion

Redo-MVR could be performed safely with acceptable in-hospital outcomes in rheumatic heart disease patients. Multiple preoperative risk factors, particularly advanced NYHA class and low LVEF, could have affected the outcomes. Risk stratification of adverse outcomes after redo-MVR is crucial. The currently available EuroSCORE II has good accuracy for predicting in-hospital mortality and major morbidity in this group of patients.

Conflict of interest: Authors declare no conflict of interest.

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