Clinical Outcomes of Isolated Redo Mitral Valve Replacement in Patients with Mitral Prosthetic Heart Valve Dysfunction

Ahmet Güner[1], Ersin Kadiroğulları[2], Taner İyigün[2], İsmail Gürbak[1], Burak Onan[1], Ünal Aydın[2], Mustafa Gürsoy[3], Mehmet Ertürk[1]

[1] Department of Cardiology, Mehmet Akif Ersoy Cardiothoracic and Vascular Surgery Training and Research Hospital, Istanbul, Turkey
[2] Department of Cardiovascular Surgery, Mehmet Akif Ersoy Cardiothoracic and Vascular Surgery Training and Research Hospital, Istanbul, Turkey
[3] Department of Cardiology, University of Izmir Katip Celebi, Atatürk Training and Research Hospital, Izmir, Turkey

ABSTRACT

Introduction: Redo mitral valve replacement (redo-MVR) represents a clinical challenge due to higher rates of peri-operative morbidity and mortality.

Patients and Methods: This retrospective study enrolled a total of 103 patients who underwent isolated redo-MVR due to prosthetic valve dysfunction. Patients who had an isolated bypass, low echocardiographic quality, history of repeated re-replacements (more than twice), paravalvular leak repair without preoperative and intraoperative transesophageal echocardiography examination, isolated congenital surgery or isolated open-heart surgical intervention (of any type) without a valve procedure at their first or later operations were excluded. The primary endpoint of the study was in-hospital death. Secondary endpoint included individual morbidity.

Results: A total of 103 patients (mean age: 50.7 ± 13.4 years; male: 58) who underwent isolated redo-MVR were enrolled in this study. The most common complaint of the patients at admission was obstruction or heart failure-related symptoms (80.6%) and the primary indication for redo-MVR was prosthetic valve thrombosis in 58 patients (56.3%). In-hospital mortality was 12.6% (13 patients). The postoperative complications included major bleeding (n= 11) postoperative infection [sepsis, mediastinitis, pneumonia, wound infection (n= 15)], low cardiac output syndrome (n= 10), acute kidney injury (n= 17), pericardial effusion with tamponade (n= 10), pleural effusion requiring hospitalization and drainage (n= 18), ischemic stroke (n= 4), fatal ventricular arrhythmia (n= 1), peripheral embolism (n= 1), moderate to severe paravalvular leak (n= 5). There was not any catastrophic heart laceration.

Conclusion: In-hospital mortality and complications of the isolated redo-MVR in our center are acceptable. With a well-defined protocol and appropriate patient selection, mortality in emergencies cases may be reduced.

Key Words: Echocardiography; prosthetic valve; valve surgery.

Mitral Protez Kalp Kapak Disfonksiyonlu Hastalarda İzole Redo Mitral Kapak Replasmanının Klinik Sonuçları

ÖZ

Giriş: Redo mitral kapak replasmanı (redo-MKR), daha yüksek perioperatif morbidite ve mortalite oranı nedeniyle zorlu bir klinik durum teşkil eder.

Hastalar ve Yöntem: Bu geriye dönük çalışmaya, protez kapak disfonksiyonu nedeniyle izole redo-MKR uygulanan toplam 103 hasta dahil edildi. İzole baypas yapılanlar, düşük ekokardiyografik pencereye sahip olanlar, tekrarlanan replasmanlar (ikiden fazla), preoperatif ve intraoperatif transözefageal ekokardiyografi muayenesi olmadan paravalvüler kaçak onarımı yapılanlar, izole konjenital cerrahi veya izole açık kalp cerrahi müdahalesi (herhangi bir tipte) kapak prosedürü olmaksızın olan hastalar ilk veya sonraki operasyonlarında hariç tutuldu. Çalışmanın birincil sonlanım noktası hastane içi ölüm idi. İkincil sonlanım noktası bireysel morbidite idi.

Bulgular: İzole redo-MKR uygulanan toplam 103 hasta (ortalama yaş: 50.7 ± 13.4 yıl; erkek: 58) bu çalışmaya dahil edilmiştir. Başvuru anında en sık muayene bulguları obstrüksiyon veya kalp yetersizliğine bağlı semptomlardı (%80.6) ve redo-MKR için birincil endikasyon 58 hastada (%56.3) protez kapak trombozuydu. Hastane içi mortalite %12.6 (13 hasta) idi. Postoperatif komplikasyonlar arasında majör kanama (n= 11), postoperatif enfeksiyon [sepsis, mediastinit, pnömoni, yara enfeksiyonu (n= 15)], düşük debi sendromu (n= 10), akut böbrek hasarı (n= 17), tamponad bulguları olan perikardiyal efüzyon (n= 10), hastanede yatış ve drenaj gerektiren plevral efüzyon (n= 18), iskemik inme (n= 4), ölümcül ventriküler aritmi (n= 1), periferik emboli (n= 1), orta-şiddetli paravalvüler kaçak (n= 5) yer almıştır. Ayrıca, cerrahi sırasında herhangi bir ölümcül kalp yaralanması gerçekleşmemiştir.

Sonuç: Merkezimizdeki izole redo-MKR'nin hastane içi mortalitesi ve komplikasyonları kabul edilebilir oranlardadır. İyi tanımlanmış bir protokol ve uygun hasta seçimi ile acil durumlarda mortalite azaltılabilir.

Anahtar Kelimeler: Ekokardiyografi; kapak cerrahisi; protez kapak.

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Correspondence

Ahmet Güner

E-mail: ahmetguner488@gmail.com
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INTRODUCTION

Redo valve surgery is a challenging intervention for cardiovascular surgeons due to its severe in-hospital morbidity and higher mortality than native valve surgery[1,2]. Mitral valve reoperations, especially re-sternotomy and naturally due to previous operations, may expose repeat valve operations to complications due to graft injuries, bleeding, and the presence of adhesions. This may lead to higher complications, especially in patients with vascular structures lying behind the sternum or with a previous history of chest wound infection and radiotherapy[1,2]. The most important complication in patients with valve replacement is prosthetic valve dysfunction (PVD) [3]. Despite the surgical improvement and increasing success rate of prosthetic valve replacements, several risk factors still pose a challenge for clinician. Therefore, understanding the risk factors affecting short-term or in-hospital mortality after replacing prosthetic valves is vital. Patients undergoing valvular reoperation present with various clinical projections of PVD, including prosthetic valve endocarditis (PVE), obstructive prosthetic valve thrombosis (PVT), obstructive pannus formation, and paravalvular leaks (PVLs)[4-6]. There is limited data on redo-valve surgery in our country[1,7]. Hence, in the present study, we aimed to investigate these risk factors for in-hospital mortality in patients who underwent isolated redo mitral valve replacement (redo-MVR).

PATIENTS and METHODS

Study Population

This retrospective study enrolled a total of 103 patients who underwent isolated redo-MVR due to PVDs between February 2011 and January 2021 in our hospital. The preoperative, perioperative, and postoperative data of the patients were retrieved from electronic database of the hospital. Besides, the missing demographic data of the patients were obtained by telephone interview. All patients who had previous isolated mechanical mitral valve surgeries were included in the study. Patients who had an isolated bypass, age < 18, low echocardiographic quality, history of repeated re-replacements (> 2), PVL repair without preoperative and intraoperative TEE examination, isolated congenital surgery or isolated open-heart surgical intervention (of any type) without a valve procedure at their first or later operations were excluded. Patients who underwent isolated redo-MVR other than all these exclusion criteria were included in the study. Moreover, patients who underwent Maze procedure for atrial fibrillation together with isolated redo-MVR were also included in the study. Coronary angiography was performed in all elective patients aged > 40 years, and cardiac catheterization was performed together with cardiac angiography in some of the patients. The flow chart for patient selection is summarized in Figure 1. This study was designed in accordance with the principles of the Declaration of Helsinki and was approved by the local Institutional Review Board (Ethics committee approval number: 2021/12).

Echocardiography

Detailed transthoracic echocardiography (TTE) evaluation was performed on all patients with Philips iE33 (Philips Medical Systems, Andover, Massachusetts) echocardiography devices. Standard parasternal long axis, short axis, apical 4- and 5- chambers views were measured in detail. Left atrial diameter, left ventricular end systolic and end diastolic diameters were measured and noted on the parasternal long axis view. The tricuspid annular plane systolic excursion was measured by placing a cursor on the lateral tricuspid annulus in the apical 4-chamber view. Left ventricular ejection fractions (LVEF) were measured by biplane Simpson method. Moreover, transesophageal echocardiography (TEE) examination was also performed all patients during the preoperative evaluation period. Cardiac structures and great arteries were evaluated in detail from different windows and images were recorded. Obstruction parameters were guided by Doppler echocardiographic parameters[8]. Thrombus, pannus, PVL, and vegetation have been described as cardiovascular imaging guidelines[8-11].

Surgical Technique

All patients were found suitable for general anesthesia after preoperative evaluation. The operation was performed under general anesthesia and a median re-sternotomy was utilized. Mediastinal adhesions were opened and cardiac and great vessels were exposed before systemic heparinization. Surgical intervention was performed using a standard cardiopulmonary bypass technique with central cannulation under moderate degree hypothermia. Myocardial protection was provided with antegrade intermittent or continuous retrograde isothermic blood cardioplegia solution. The previous prosthetic valve was checked and a decision was made for valve replacement. For replacement, previously implanted valve and sutures were removed, the mitral annulus was exposed and interrupted pledgeted sutures with pledgets on the left atrial side were used. Subsequently, a hotshot cardioplegia was delivered and the aortic cross-clamp was removed once the heart started beating. Once all parameters were satisfactory, cardiopulmonary bypass was weaned off and the sternum was closed[12].

Clinical Outcomes and Definition of Complications

The primary outcome measures of the study was in-hospital mortality. Secondary outcomes included individual morbidity rates. Postoperative complications included major bleeding, low cardiac output syndrome (LCOS), tamponade, pleural effusion

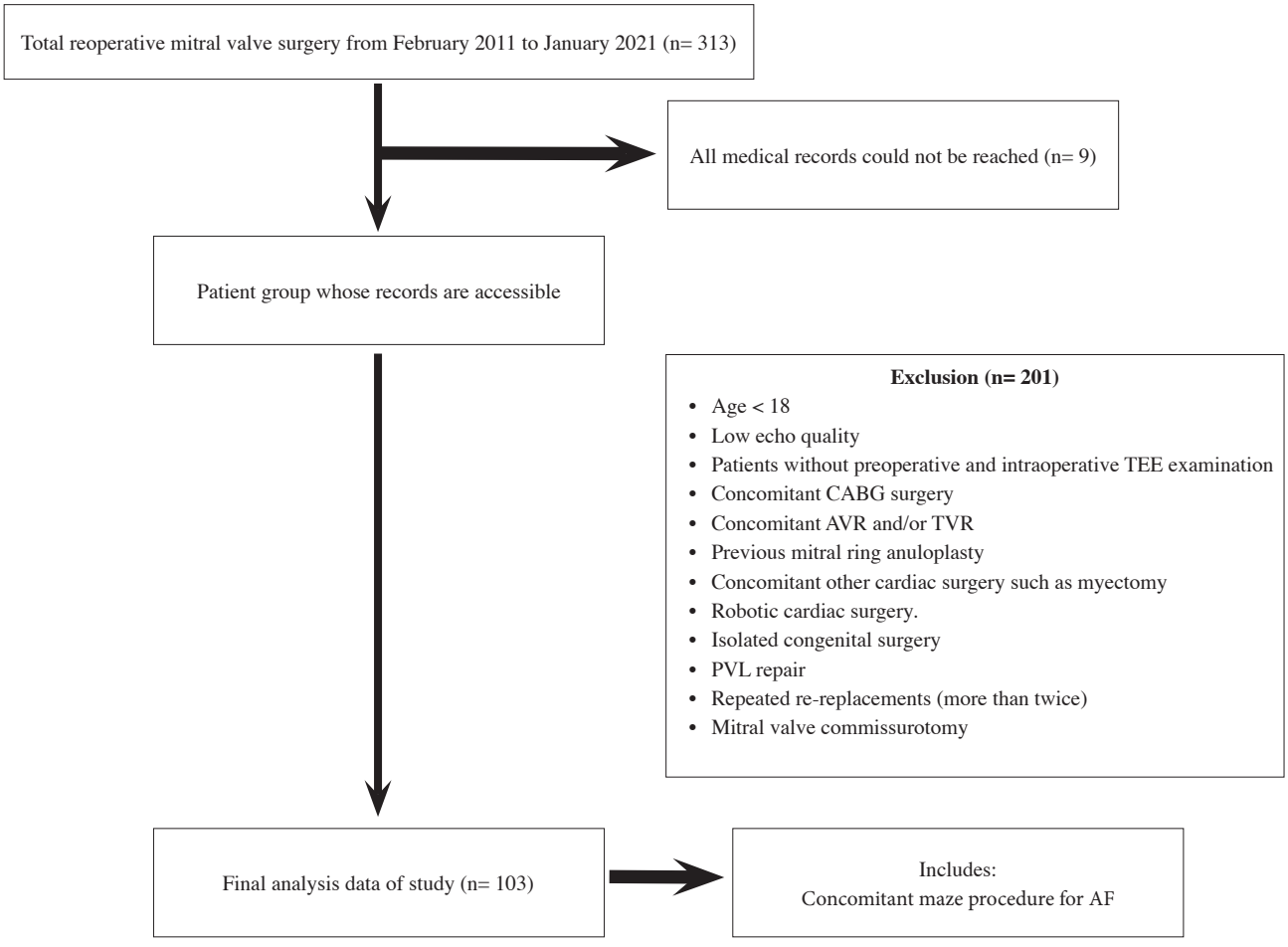

Figure 1. Flow chart for patient selection (AF: Atrial fibrillation, AVR: Aortic valve replacement, CABG: Coronary artery by-pass grafting, PVL: Paravalvular leak, TEE: Transesophageal echocardiography, TVR: Tricuspid valve replacement).

requiring drainage, sepsis, mediastinitis, pneumonia requiring antibiotic therapy, wound infection, acute kidney injury (AKI) requiring renal replacement therapy, ischemic stroke, heparin-induced thrombocytopenia and thrombosis syndrome (HITTs), peripheral embolism, and moderate to severe PVL. Ischemic stroke, in accordance with the latest definition; it was defined as an episode of neurological dysfunction due to cerebral, spinal, or retinal infarction[13]. The LCOS was defined as a requirement for inotropic support for > 24 hour[12]. Definitions of major bleeding, tamponade, AKI, pleural effusion requiring drainage, sepsis, mediastinitis, pneumonia and wound infection were made according to the latest updated literature and guideline to report morbidity and mortality after heart valve surgery[12,14]. Acute peripheral arterial thromboembolism is defined in accordance with the literature[15]. The clinical diagnosis of stroke was made by a neurologist. The diagnosis of thromboembolism induced acute limb ischemia was made by an experienced cardiologist or cardiovascular surgeon after detailed evaluation of coronary and peripheral angiographies.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp. Armonk, NY). The normality distribution of continuous variables was tested with the Kolmogorov-Smirnov test. Continuous variables with normal distribution were expressed as mean ± standard deviation while continuous variables without normal distribution were expressed as median (25^{th}-75^{th} percentiles). Categorical variables were expressed as frequencies and percentages. Continuous variables were compared using Student's t-test or the Mann-Whitney U test when applicable. Chi-square or Fisher exact test was used for comparison of categorical variables as appropriate. Correlational analyses were performed using Pearson's or Spearmen's correlation tests as appropriate. A logistic regression analysis was performed to identify any independent predictors of in-hospital mortality. A two-sided p value of < 0.05 was considered significant.

RESULTS

A total of 103 patients (mean age: 50.7 ± 13.4 years; male: 58) who underwent isolated redo-MVR were enrolled in this study. The patients who had previously underwent isolated MVR were selected. On the basis of data obtained from previous hospital records, various types of prothesis were used in various centers in the primary operations [CarboMedics (Austin, TX, USA) in 22, St. Jude (St. Paul, MN, USA) in 59, Sorin (Milan, Italy) in 11, and ATS (Minneapolis, MN, USA) in 10 patients], and most of the leaflets were bileaflet (95.1%). Preoperatively, 36 patients (35%) were in NYHA functional class III/IV, and 67 in class I/II (65%). The mean interval between primary operation and reoperation was 103.3 ± 88.1 months. The most common complaint of the patients at admission was obstruction or HF-related symptoms (80.6%), followed by embolism-related (6.8%) and other complaints. Indications for redo-MVR were PVT in 58 patients (56.3%), PVE in 24 patients (23.3%), PVL in 12 (13.6%), PVD due to obstructive pannus formation in seven (6.8%). Preoperative atrial fibrillation was present in 44 patients (42.7%). The laboratory findings and other demographic features are displayed in Table 1.

The valve area, mean and maximum gradients were 1.4 ± 0.6 cm^2, 26.8 ± 10.5 mmHg, and 14.6 ± 7.7 mmHg, respectively. In 36 patients (34.6%), stuck leaflet was detected by multimodality imaging (TTE, TEE and fluoroscopy). Other baseline echocardiographic findings of the patients are demostrated in Table 2.

The intraoperative and postoperative results of the patients are listed in Table 3. The cross-clamp time and total perfusion time were 96.8 ± 53.6 minutes and 142.5 ± 72.9 minutes, respectively. Elective surgery was performed in 71.8% of the patients, and 29 patients (28.2%) were operated under emergency conditions and the mean hospital stay time was 14.5 ± 16.8 days. In-hospital mortality was 12.6% (13 patients). The post-operative complications included major bleeding (n= 11) post-operative infection [sepsis, mediastinitis, pneumonia, wound infection (n= 15)], LCOS (n= 10), AKI with a need for renal replacement therapy (n= 17), pericardial effusion with tamponade (n= 10), pleural effusion requiring hospitalization and drainage (n= 18), ischemic stroke (n= 4), HITTs (n= 3), fatal ventricular arrhythmia (n= 1), peripheral embolism (n= 1), moderate to severe PVL (n= 5). There was not any catastrophic heart laceration. Totally, 13 patients died due to various causes: LCOS (n= 4), sepsis (n= 2), major bleeding (n= 3), tamponade (n= 2), acute kidney injury (n= 1) and fatal ventricular arrhythmia (n= 1).

Table 1. Comparison of mean scores of HLBS-II between groups

Variable	All patients (n= 103)
Age (years)	50.7 ± 13.4
Gender, n (%)	
Male	58 (56.3)
Female	45 (43.7)
BMI (kg/m^2)	26.3 ± 2.3
ETSVS (months)	103.3 ± 88.1
Heart rhythm, n (%)	
Sinus	59 (57.3)
AF	44 (42.7)
NYHA, n (%)	
I/II	67 (65)
III/IV	36 (35)
Chief complaint on admission, n (%)	
Obstruction or HF related symptoms	83 (80.6)
Embolism related symptoms	7 (6.8)
Syncope	3 (2.9)
Fever	5 (4.9)
History, n (%)	
HF	21 (20.4)
Stroke	10 (9.7)
TIA	6 (5.8)
HT	38 (36.9)
DM	12 (11.7)
CAD	15 (14.6)
Asthma/COPD	17 (16.5)
Previous PVT	27 (26.2)
Thyroid dysfunction	4 (3.8)
Smoking	23 (22.3)
Drugs, n (%)	
Warfarin	101 (98.1)
Acetylsalicylic acid	32 (31.1)
ACE-inh	35 (34)
ARB	4 (3.9)
Beta-blocker	71 (68.9)
Digoxin	9 (8.7)
CCB	7 (6.8)
Amiodarone	12 (11.6)
Diuretic	49 (47.5)
Statin	21 (20.4)
Usual warfarin dose (mg)	6.1 ± 3.7
Admission INR	2.1 ± 1.1
Leaflet satatus	
Monoleaflet	5 (4.9)
Bileaflet	98 (95.1)
Valve type, n (%)	
St. Jude medical	59 (57.3)
Sorin	11 (10.7)
Carbomedics	22 (21.4)
ATS	10 (9.7)
TRI	1 (1)

Table 1. Comparison of mean scores of HLBS-II between groups (continued)

Variable	All patients (n= 103)
Reoperation indication, n (%)	
PVT	58 (56.3)
PVE	24 (23.3)
PVL	12 (13.6)
Pannus formation	7 (6.8)
Blood work-up	
Glucose (mg/dL)	110.6 ± 35.4
Creatinine (mg/dL)	0.9 ± 0.4
AST (U/dL)	84.3 ± 409.3
White blood cell count (10^9/L)	5.52 ± 5.96
Hemoglobin (g/dL)	11.7 ± 2.2
Platelet (10^9/L)	262 ± 87.2
CRP (mg/dL)	20.1 ± 28.9
ESR (mm/hour)	44.1 ± 33.5

ACE-inh: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blocker, AF: Atrial fibrillation, AST: Aspartate aminotransferase, BMI: Body mass index, CAD: Coronary artery disease, CCB: Calcium channel blockers, COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, DM: Diabetes mellitus, ESR: Erythrocyte sedimentation rate, ETSVS: Elapsed time since valve surgery, HF: Heart failure, HT: Hypertension, INR: International normalized ratio, NYHA: New York Heart Association, PVT: Prosthetic valve thrombosis, PVL: Paravalvular leak, PVE: Prosthetic valve endocarditis, TIA: Transient ischemic attack.

Table 2. Baseline echocardiographic findings of the patients

Variable	All patients (n= 103)
Mitral (mean ± SD)	
Valve area (cm^2)	24 (23.3)
Max gradient (mmHg)	12 (13.6)
Mean gradient (mmHg)	7 (6.8)
Stuck leaflet, n (%)	36 (34.6)
LV ejection fraction (%)	53.3 ± 9.3
LVEDD (cm)	5.0 ± 0.6
LVESD (cm)	3.3 ± 0.7
LA diameter (cm)	4.7 ± 0.4
LA spontaneous ECHO contrast, n (%)	53 (51.4)
Estimated sPAP (mmHg)	47 ± 17.7
TAPSE (cm)	1.9 ± 0.2

LV: Left ventricle, LVEDD: Left ventricle end diastolic diameter, LVESD: Left ventricle endsystolic diameter, LA: Left atrium, sPAP: Systolic pulmonary artery pressure, TAPSE: Tricuspid annular plane systolic excursion, SD: Standart deviation.

Multiple logistic regression analysis was performed for statistically significant parameters in univariate analyzes for independent predictors of in-hospital mortality. Systolic pulmonary artery pressure (sPAP) (OR= 1.046; 95% CI: 1.007-1.086; p= 0.021) and emergency operation (OR= 20.037; 95% CI: 3.510-114.386; p= 0.001) were independent predictors of in-hospital mortality (Table 4).

Table 3. Intraoperative and postoperative results of the patients

Variable	All patients (n= 103)
Cross-clamp time (min)	96.8 ± 53.6
Total perfusion time (min)	142.5 ± 72.9
Reoperation surgery, n (%)	
Elective	74 (71.8)
Emergency	29 (28.2)
Valve replacement, n (%)	
Mechanical prosthetic	86 (83.5)
Bioprosthetic	17 (16.5)
Hospital stay (day)	14.5 ± 16.8
In-hospital mortality, n (%)	13 (12.6)
Complications, n (%)	
Major bleeding	11 (10.7)
LCOS	10 (9.7)
Tamponade	10 (9.7)
Pleural effusion requiring drainage	18 (17.5)
Fatal ventricular arrhythmia	1 (1)
Sepsis	2 (1.9)
Mediastinitis	1 (1)
Pneumonia	5 (4.9)
Wound infection	7 (6.8)
Acute kidney injury with a need for renal replacement therapy	17 (16.5)
Ischemic stroke	4 (3.9)
HITTs	3 (2.9)
Peripheral embolism	1 (1)
Moderate to severe PVL	5 (4.9)

LCOS: Low cardiac output syndrome, HITTs: Heparin-induced thrombocytopenia and thrombosis syndrome, PVL: Paravalvular leak.

Table 4. Regression analysis of potential predictor factors for in-hospital mortality

	Univariate analysis		Multivariable analysis	
Variables	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
NYHA III/IV	4.500 (1.281-15.812)	0.018	1.008 (0.385-2.641)	0.987
sPAP	1.036 (1.006-1.068)	0.019	1.046 (1.007-1.086)	0.021
PVE	5.010 (1.492-16.825)	0.009	2.764 (0.616-12.416)	0.185
Emergency operation	22.0 (4.474-108.17)	< 0.001	20.037 (3.510-114.386)	0.001

NYHA: New York Heart Association, PVE: Prosthetic valve endocarditis, sPAP: Systolic pulmonary artery pressure, CI: Confidence interval, OR: Odds ratio.

DISCUSSION

Two major findings of the current study are: I) in-hospital mortality and complication rates in patients who underwent isolated redo-MVR were consistent with the limited data reported in our country, II) sPAP and emergency operation were identified as independent predictors of in-hospital mortality.

In recent years, despite the great improvement in surgical outcomes after reoperations for valve replacement in parallel with technological advances, this type of surgery still poses an ongoing challenge for cardiac surgeons. Therefore, understanding the risk factors that affect operative and in-hospital mortality is vital for survival after replacement of prosthetic valves. There may be various indications for redo-MVR[1-3,7]. In patients with a mechanical valve, reoperation occurs due to valve thrombosis or pannus formation, PVL, and endocarditis[4,7,16,17]. Indications for redo-MVR in the present study were mechanical PVDs due to obstructive pannus formation, PVT, PVE and PVL.

Several investigators and different tertiary centers previously reported the clinical results and short and long-term mortality rates of reoperative mitral valve surgery. With advances in surgical technique and perioperative management, the mortality and morbidity risk associated with redo-MVR has decreased[18]. As patients continue to survive longer after their initial operation, the need for reoperative surgery is increasing[19]. According to a recent review, there was a reported 10% rise per year in the number of redo-MVR from 2002 to 2016(19). As experience with redo-MVR has grown, outcomes have become more favorable. Recent reports suggest that the risk of mortality now ranges from 4% to 11.1%[19,20]. However, it is known that low mortality rate and optimal results are obtained in cases of redo-MVR due to bioprosthetic structural valve deterioration. Although there is limited data on this field in our country, the operative and short-term mortality rates have been reported between 6.4% and 15.7%[1,7]. In the current study, the in-hospital mortality rate was 12.6%, and this rate may have been affected by the characteristics of more complex cases.

One of the significant mortality predictors of redo valve surgery is emergency operation[7,14,19-21]. Rizzoli et al have previously reported that emergent operation was a significant risk factor for early mortality[22]. Moreover, Akins et al reported a 2.5-fold increase in mortality risk in patients who underwent non-elective reoperative valve surgery in both aortic and mitral positions[23]. Recently, Kilic et al indicated that predictors of the composite outcome of mortality or major morbidity included cardiogenic shock, severe tricuspid regurgitation, urgent or emergent status, and concurrent coronary artery bypass grafting[14]. In the present study, emergency reoperation was found to be an independent predictor of in-hospital mortality.

High sPAP is a clinical and hemodynamic syndrome, usually caused by left-sided heart diseases[24]. In the current study, high sPAP was associated with 3-month mortality. This finding has been previously described in several papers regarding redo valve or mitral regurgitation surgery[24,25].

LIMITATIONS

This study has several limitations. First of all, this was a retrospective study and enrolled a relatively small patient population. Second, postoperative TEE was not performed in most of the patients. Hence, some TEE detectable PVDs such as PVL might have been underestimated. Third, the current data cover only the in-hospital results. Lastly high proportion of complicated cases might have partly influenced in-hospital mortality and morbidity.

CONCLUSION

In-hospital mortality and complications of the isolated redo-MVR in our center are acceptable compared with established data. With a well-defined protocol and appropriate patient selection, mortality in emergent cases may be reduced. Emergency operation and sPAP are independently associated with in-hospital mortality in redo-MVR patients.

Ethics Committee Approval: This study was approved by Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Institutional Ethics Comittee (2021/12).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - AG, EK; Analysis/Interpretation - EK, Tİ, İG; Data Collection - AG, Tİ, ÜA, BO; Writing - AG; Critical Revision - AG, BO, ME, MG; Statistical Analysis - AG, EK; Overall Responsibility - AG, ÜA, İG, BO, EK; Final Approval - All of Authors.

Conflict of Interest: The authors have no conflicts of interest to declare.

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