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Article

Efficacy of Double Valve Replacement/Repair in Patients with Reduced Left Ventricular Ejection Fractions

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Abstract

Introduction: A reduced left ventricular ejection fraction (LVEF) is a known risk factor for double valve replacement or aortic valve replacement in combination with concomitant mitral valve repair (DVR) and is associated with high morbidity and mortality rates. In this study, we sought to analyze the 30-day mortality and long-term survival rates of patients with reduced LVEFs. **Methods**: A multicenter, retrospective, observational cohort study of patients who underwent DVR was performed at four centers from January 2016 to December 2021. LVEFs were categorized as 41%–50% (n = 120) or ≤40% (n = 58). For the effects of risk factors on 30-day mortality, binary logistic regression was performed. Survival rates were assessed with the Kaplan–Meier method. **Results**: A total of 178 patients who underwent DVR were included in this study, of whom 67.42% (n = 120) had LVEFs ranging from 41–50% and 32.58% (n = 58) had LVEFs ≤40%. More mechanical valves and tricuspid valve-forming rings were applied in the LVEF ≤40% group (68.97% versus 53.33%, p = 0.047; 31.03% versus 10.83%, p = 0.001). The 30-day mortality rates of DVR patients with LVEFs ranging from 41–50% and ≤40% were 8.33% and 17.24%, respectively (p = 0.078). During the follow-up period, there were no significant differences in long-term survival (log rank p = 0.75). On multivariable logistic regression analysis, age >65 years [odds ratio (OR): 5.559, 95% confidence interval (CI): 1.668–18.524, p = 0.005] and cardiopulmonary bypass (CPB) duration >200 min (OR: 5.031, 95% CI: 1.773–14.277, p = 0.002) were significantly associated with the likelihood of 30-day mortality. **Conclusions**: Although the differences in 30-day mortality and long-term survival rates between DVR patients with LVEFs ranging from 41–50% and ≤40% were not statistically significant in our cohort, an age >65 years and a CPB duration >200 min were predictors of 30-day mortality.

Keywords

heart valve disease; mortality; heart failure; ventricular ejection fraction

Introduction

The number of double valve replacement/repair (DVR) procedures performed exceed that of valve replacement procedures by 10% in developed countries and by approximately 20%–50% in developing countries. DVR is associated with severe postoperative mortality [1–4]. Additionally, the incidence of complications of the DVR procedure is relatively higher than that of isolated aortic valve or mitral valve replacement. Some studies have shown that DVR is a safe and feasible option for double-valve surgery [5–7]. DVR in patients with left ventricular dysfunction may further increase surgical risk, and many surgeons are hesitant to perform DVR among those patients despite the potential benefits.

A reduced left ventricular ejection fraction (LVEF) is an independent risk factor for postoperative complications among patients undergoing surgery. For those undergoing cardiac surgery, a reduced LVEF is known to increase the risks of postoperative adverse events and a poor prognosis [8–10]. These studies involved mainly aortic valve and coronary artery disease in patients with low ejection fractions. However, few studies have evaluated the mortality and complication rates of DVR in patients with reduced LVEFs [11]. Therefore, the aim of our study was to evaluate postoperative short- and long-term changes in patients with reduced LVEFs, as reflected by changes in complication and mortality rates, as well as the ranges of preoperative LVEFs in patients who underwent DVR. This information may help determine whether patients with severely reduced LVEFs should be considered for DVR.

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Table 1. Patient demographics and clinical characteristics.

	LVEF 41–50% (n = 120)	LVEF ≤40% (n = 58)	*p* value
Age, years	58.09 ± 9.49	57.55 ± 10.47	0.707
Gender, men, n (%)	68 (56.67)	30 (51.72)	0.534
BMI (kg/m^2)	23.34 ± 3.63	21.62 ± 3.09	0.006*
Smoke, n (%)	37 (30.83)	18 (31.03)	0.978
Alcohol, n (%)	21 (17.50)	8 (13.79)	0.530
Hypertension, n (%)	41 (34.17)	9 (15.52)	0.009*
Diabetes, n (%)	8 (6.67)	5 (8.62)	0.871
COPD, n (%)	2 (1.67)	2 (3.45)	0.832
AF, n (%)	62 (51.67)	36 (62.07)	0.006*
eGFR (mL/min/1.73 m^2)	80.85 ± 20.53	82.00 ± 22.51	0.735
LAD/BSA (mm/m^2)	29.27 ± 5.38	30.87 ± 6.28	0.079
LVESD/BSA (mm/m^2)	25.87 ± 4.27	30.12 ± 4.79	<0.001*
LVEDD/BSA (mm/m^2)	33.82 ± 5.03	36.99 ± 5.57	<0.001*
LVEF (%)	46.78 ± 2.93	37.37 ± 3.82	<0.001*
NYHA classification (%)			
II–III	77 (64.17)	16 (27.59)	<0.001*
III–IV	43 (35.83)	42 (72.41)	<0.001*
RHD, n (%)	67 (55.83)	45 (77.59)	0.005*
DHD, n (%)	42 (35.00)	11 (18.97)	0.028*
IE, n (%)	11 (9.17)	2 (3.45)	0.286
AV disease, n (%)			
Stenosis	18 (15.00)	12 (20.69)	0.342
Regurgitation	64 (53.33)	29 (50.00)	0.676
Mixed lesion	38 (31.67)	17 (29.31)	0.750
Deformity	5 (4.17)	3 (5.17)	1.000
MV disease, n (%)			
Stenosis	20 (16.67)	10 (17.24)	0.924
Regurgitation	62 (51.67)	21 (36.21)	0.053
Mixed lesion	38 (31.67)	27 (46.55)	0.053
TR, n (%)	45 (37.50)	38 (75.52)	<0.001*

* $p < 0.05$; eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (https://www.kidney.org/professionals/KDOQI/gfr_calculator). BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; AF, Atrial fibrillation; LAD, Left atrial dimension; LVESD, Left ventricular end-systolic dimension; LVEDD, Left ventricular end-diastolic dimension; BSA, body surface area; LVEF, Left ventricular ejection fraction; NYHA, New York Heart Association; RHD, Rheumatic heart disease; DHD, Degenerative heart disease; IE, Infectious endocarditis; AV, Aortic valve; MV, Mitral valve; TR, tricuspid regurgitation.

Methods

Patient Population

We retrospectively included 816 patients who underwent DVR for aortic and mitral disease at four centers from January 2016 to December 2021. Patients who underwent coronary artery bypass grafts, aortic dissection, or congenital heart disease surgery were excluded. Individuals with a preoperative LVEF <50% were included. Finally, 120 patients with LVEFs ranging from 41–50% and 58 patients with LVEFs ≤40% were enrolled.

The study was approved by the institutional review board at each site. All patients provided written informed consent.

Data Collection

All perioperative data were collected in a predefined form. Preoperative variables included age, sex, body mass index (BMI), body surface area (BSA), the presence of comorbidities, echocardiography data, and valvular pathology characteristics. The surgical details were described in our previous study [12]. The intraoperative variables included the type of surgical procedure, cardiopulmonary bypass (CPB) time, and clamping time. Postoperative variables included blood transfusion, intensive care unit stay,

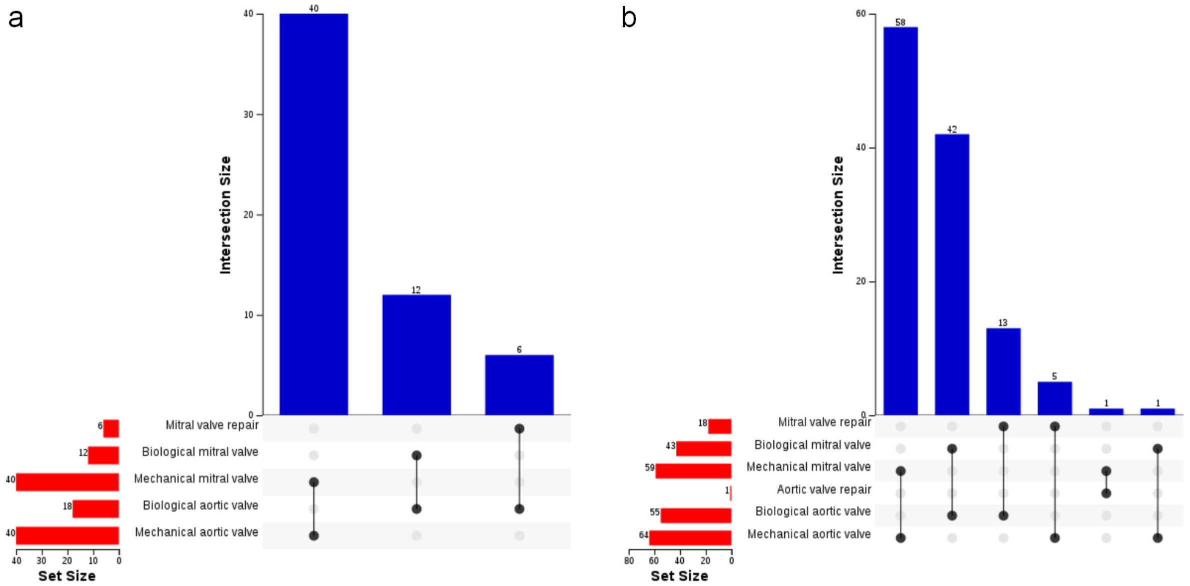

Fig. 1. The surgical combinations of left ventricular ejection fraction (LVEF) ≤40% and 41–50% are presented in (a,b), respectively.

hospital stay, echocardiography data, and 30-day mortality. During long-term follow-up (>30 days, up to 2500 days), the surviving patients and their relatives were interviewed by telephone or in outpatient charts.

Statistical Analysis

The statistical methods used were described in our previous study [13]. To study the effects of risk factors on 30-day mortality, binary logistic regression was performed, adjusted for variables with tolerance >0.1 or variance inflation factor <10, avoiding collinearity. Statistical analysis was performed via SPSS (version 25.0; IBM Corp., Armonk, NY, USA). A two-tailed p value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

A detailed overview of the patient characteristics is shown in Table 1. Compared with the patients in the LVEF 41–50% group, the patients in the LVEF ≤40% group had a lower BMI (21.62 ± 3.09 kg/m^2 versus 23.34 ± 3.63 kg/m^2, p = 0.006), a higher prevalence of AF (62.07% versus 51.67%, p = 0.006), a higher LVESD/BSA ratio (30.12 ± 4.79 mm/m^2 versus 25.87 ± 4.27 mm/m^2, p < 0.001) and a higher LVEDD/BSA ratio (36.99 ± 5.57 mm/m^2 versus 33.82 ± 5.03 mm/m^2, p < 0.001). Valvular pathology with RHD was more prevalent (77.59% versus 55.83%, p = 0.005), and TR was much more common (75.52% versus 37.50%, p < 0.001).

Surgical Details

The surgical details are summarized in Table 2. More mechanical valves were used for the mitral (68.97% versus 49.17%, p = 0.013) and aortic (68.97% versus 53.33%, p = 0.047) valves in patients with LVEFs ≤40%. The definitions of DVR, including the four surgical combinations, are presented in Fig. 1. The details of the subgroups are shown in **Supplementary Table 1**. In addition, a greater percentage of patients in the tricuspid valve-forming ring use group than in the LVEF 41–50% group (31.03% versus 10.83%, p = 0.001). No statistically significant differences were found between the two groups in terms of DeVage tricuspid annuloplasty, LAA amputation, Cox-Maze IV, CPB duration, or clamping time.

Early and Late Outcomes

Table 3 shows the postoperative characteristics of the two groups. Compared with those in the LVEF 41–50% group, individuals with a LVEF ≤40% had more RBC infusions (2 [IQR 0.75, 4.63] versus 2 [IQR 0, 4], p = 0.008), longer ICU stays (4 [IQR 2.75, 5] versus 3 [IQR 2, 4], p = 0.015), and higher ratios of LVESD/BSA (24.66 ± 5.86 mm/m^2 versus 21.63 ± 4.43 mm/m^2, p = 0.004) and LVEDD/BSA (31.91 ± 5.74 mm/m^2 versus 29.18 ± 4.11 mm/m^2, p = 0.006). Although the 30-day mortality in the LVEF ≤40% group was greater, there was no significant difference between the two groups (17.24% versus 8.33%, p = 0.078).

The details of the univariate and multivariate logistic regression models of 30-day mortality were analyzed and are shown in Table 4. Univariate logistic regression

Table 2. Surgical details.

	LVEF 41–50% (n = 120)	LVEF ≤40% (n = 58)	*p* value
Mitral valve repair, n (%)	18 (15.00)	6 (10.34)	0.394
Mechanical mitral valve, n (%)	59 (49.17)	40 (68.97)	0.013*
Biological mitral valve, n (%)	43 (35.83)	12 (20.69)	0.040*
Aortic valve repair, n (%)	1 (0.83)	-	-
Mechanical aortic valve, n (%)	64 (53.33)	40 (68.97)	0.047*
Biological aortic valve, n (%)	55 (45.83)	18 (31.03)	0.060
DeVega tricuspid annuloplasty, n (%)	32 (26.67)	20 (34.48)	0.282
Tricuspid valve forming ring, n (%)	13 (10.83)	18 (31.03)	0.001*
LAA amputated, n (%)	53 (44.17)	24 (41.38)	0.725
Cox Maze IV, n (%)	55 (45.83)	26 (44.83)	0.900
CPB duration (min)	172.30 ± 54.37	176.05 ± 50.42	0.662
Clamping time (min)	114.97 ± 26.02	116.81 ± 30.13	0.675

* $p < 0.05$; LAA, Left atrial appendage; CPB, Cardiopulmonary bypass; RBC, Red blood cell.

Table 3. Postoperative characteristics.

	LVEF 41–50% (n = 120)	LVEF ≤40% (n = 58)	*p* value
RBC infusion (Unit)	2 (0, 4)	2 (0.75, 4.63)	0.008*
Duration of intensive care unit (days)	3 (2, 4)	4 (2.75, 5)	0.015*
Hospital stay (days)	13 (8.25, 18)	13 (10.75, 20.00)	0.950
LAD/BSA (mm/m^2)	23.87 ± 4.45	24.30 ± 5.64	0.622
LVESD/BSA (mm/m^2)	21.63 ± 4.43	24.66 ± 5.86	0.004*
LVEDD/BSA (mm/m^2)	29.18 ± 4.11	31.91 ± 5.74	0.006*
LVEF (%)	49.20 ± 7.72	45.87 ± 9.80	0.051
30-Day mortality, n (%)	10 (8.33)	10 (17.24)	0.078

* $p < 0.05$; RBC, Red blood cell; LAD, Left atrial dimension; LVESD, Left ventricular end systolic dimension; LVEDD, Left ventricular end diastolic dimension; BSA, body surface area; LVEF, Left ventricular ejection fraction.

revealed that age >65 years (OR: 4.779, 95% CI: 1.665–13.714, p = 0.004), perioperative AF (OR: 3.707, 95% CI: 1.187–11.583, p = 0.024), TR (OR: 3.010, 95% CI: 1.100–8.236, p = 0.032), and CPB duration >200 min (OR: 5.186, 95% CI: 1.965–13.686, p = 0.001) were positively related to 30-day mortality. In a multivariable model, age >65 years (OR: 5.559, 95% CI: 1.668–18.524, p = 0.005) and CPB duration >200 min (OR: 5.031, 95% CI: 1.773–14.277, p = 0.002) were associated with the likelihood of 30-day mortality.

During follow-up after discharge (median time: 1440.5 days, IQR: 906.5–1935.5 days, maximum: 2501 days), 6 patients were lost to follow-up (1 in the LVEF ≤40% group, 5 in the LVEF 41–50% group), and 12 patients passed away (4 in the LVEF ≤40% group, 8 in the LVEF 41–50% group). As shown in Fig. 2, Kaplan–Meier analysis revealed that there were no differences in long-term survival between the two groups (log rank p = 0.75).

Discussion

In the present retrospective cohort study, we found that although the 30-day mortality rate of DVR patients with LVEFs ≤40% was higher than that of non-DVR patients, the difference was not statistically significant. The univariate logistic regression model revealed that age ≥65 years, perioperative AF, TR, and a CPB duration >200 min were associated with increased 30-day mortality. On multivariate analysis, age ≥65 years and a CPB duration >200 min contributed to 4.559- and 4.031-fold increases in 30-day mortality, respectively. However, owing to the small sample size in our study, it is necessary to observe the short- and long-term survival of a larger cohort of patients with reduced LVEFs.

Surgeons are careful when operating on patients with reduced LVEFs. Pieri M and colleagues reported that the overall perioperative mortality rate was 5.6% in a cohort of 781 patients with preoperative LVEFs ≤40%. The surgical procedures include CABG, mitral valve surgery, and aortic valve surgery [14]. In our study, the 30-day mortality rate of DVR patients with LVEFs ≤40% was 17.24%. It is not surprising that DVR patients suffer from more complex and worsening heart function. Thus, when operating on patients with reduced LVEFs, the challenge is to identify those who will benefit from DVR to decrease the 30-day mortality rate as much as possible. A few studies have evaluated 30-day mortality and long-term survival in DVR patients

Table 4. Univariate and Multivariate Analyses of 30-Day Mortality.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age >65 years	4.779 (1.665–13.714)	0.004*	5.559 (1.668–18.524)	0.005*
BMI ≤21.5 kg/m^2	2.107 (0.824–5.386)	0.120		
Perioperative AF	3.707 (1.187–11.583)	0.024*	3.297 (0.944–11.509)	0.061
Perioperative LVEF ≤40%	2.292 (0.895–5.866)	0.084		
TR	3.010 (1.100–8.236)	0.032*	2.241 (0.737–6.820)	0.155
CPB duration >200 min	5.186 (1.965–13.686)	0.001*	5.031 (1.773–14.277)	0.002*
Clamping time >120 min	1.005 (0.389–2.598)	0.991		

* $p < 0.05$, OR, Odds ratio; CI, Confidence interval; BMI, Body Mass Index; AF, Atrial fibrillation; LVEF, Left ventricular ejection fraction; TR, tricuspid regurgitation; CPB, Cardiopulmonary bypass.

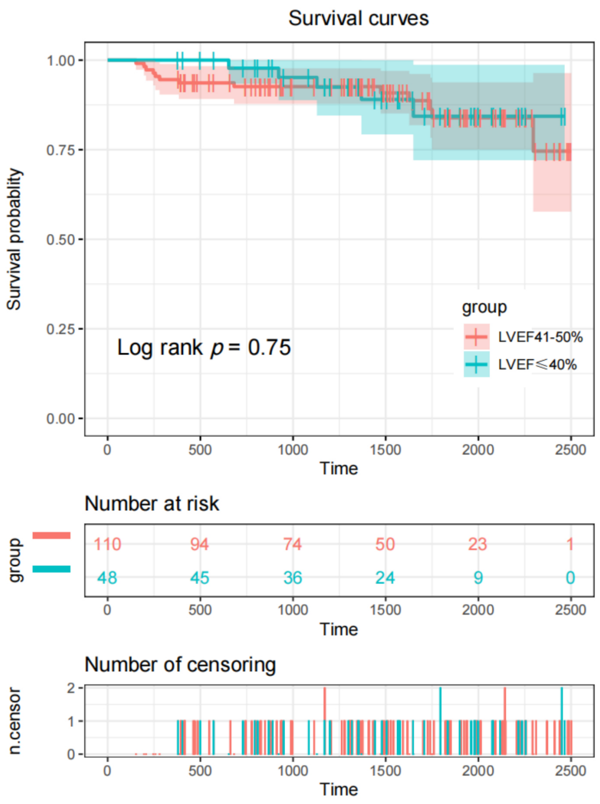

Fig. 2. Kaplan–Meier survival curves of patients who underwent double valve replacement/repair with LVEFs ≤40% and >40% to 50%, respectively.

with reduced LVEFs. Although statistically significant differences in 30-day mortality and long-term survival were not detected in our study, the method by which to identify risk factors related to 30-day mortality in DVR patients with reduced LVEFs was helpful.

As a risk factor in cardiac surgery, age has become a matter of great concern in treatment decision-making and survival [15,16]. Compared with the characteristics of DVR patients in Euro-American populations, a lower BMI is a feature of DVR patients (aged ≥60 years) in China [17]. This means that these patients would suffer from a much higher risk of mortality. Moreover, most of the patients who were lost to follow-up were older than 65 years in our study. Thus, we performed Kaplan–Meier analysis for patients with reduced LVEFs, including patients aged >65 years who were lost to follow-up, to obtain a survival curve that was close to reality.

DVR procedures are technically more complex than isolated valve operations and usually require prolonged CPB durations and aortic cross-clamping times. The operation itself calls for detailed planning but should not be a barrier to the decision for surgical intervention. The mean CPB duration and cross-clamping time ranged from 98.5 to 176 min and from 66.3 to 129 min, respectively [18–22]. In our study, the mean CPB duration and aortic cross-clamping time were 161.30 min and 115.55 min, respectively, which are similar to the results of previous studies. DVR patients need a longer CPB time to achieve better recovery of cardiac function, even with a shorter aortic cross-clamping time [7]. Our data support this viewpoint. In contrast to patients who were still alive within 30 days, patients who died within 30 days experienced longer CPB and clamping times. Logistic regression analysis revealed that a longer CPB duration was an independent risk factor for death within 30 days. Therefore, this result indicates that the 30-day mortality of DVR is commonly related to the operation itself, which is reflected by the CPB duration and aortic cross-clamping time, even with a worse preoperative condition.

AF is a known risk factor associated with increased mortality after cardiac surgery. Univariate logistic regression analysis revealed a 2.7-fold increase in 30-day mortality after DVR in patients with preoperative AF with a reduced LVEF. In addition to cardiac surgery, in a study cohort that included 8,635,758 patients who underwent noncardiac surgery, Prasada S *et al*. [23] reported that preoperative AF was associated with a greater risk of 30-day mortality, heart failure, and stroke. In our 30-day mortality cohort, 16 patients (80%) had preoperative AF. However, we did not perform AF ablation because of the increased surgical risk of concomitant ablation at the time of DVR. In a retrospective study of 238 patients with AF, Tong G *et al*. [19] reported no increase in the perioperative mortality or morbidity of AF ablation in DVR patients. In addition, a report from Petersen J *et al*. [24] failed to show a relationship between old age and AF ablation during cardiac surgery. In that study, the mean patient age was 68.4 ± 9.07 years. These patients were much older than the patients in our cohort were. These results are encouraging. More concomitant AF ablations will be considered for DVR patients in our future studies.

Several limitations exist in this study. First, the relatively small sample size limits the statistical power to detect significant differences. Second, the retrospective nature of the study introduces bias related to the selection of patients and the accuracy of the recorded data. A prospective study is needed to address the limitations of the current retrospective design.

Conclusions

Although the difference was not statistically significant, the rate of 30-day mortality was higher in patients with LVEFs $\leq$40%. However, factors such as age $>$65 years and a CPB duration $>$200 min contributed significantly to 30-day mortality. We suggest that this information is critical for assessing the risk of death when considering operation options for DVR patients with reduced LVEFs.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

GZS—Writing, Statistics and Draft. XXP and WW—Design, Reviewing. XPY, YYJ, WZ, MC, PSW and HYW—Data collection. YXP—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 accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was reviewed 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.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7837.

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