Mitral valve replacement versus repair for severe mitral regurgitation in patients with reduced left ventricular ejection fraction

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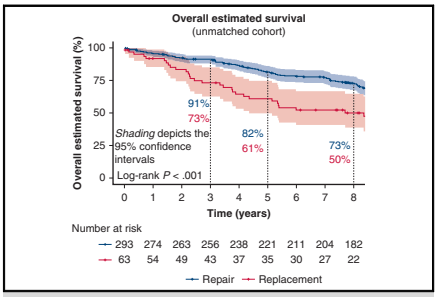
ABSTRACT

Objective: This study compares early and long-term outcomes following mitral valve (MV) repair and replacement in patients with mitral regurgitation (MR) and reduced left ventricular ejection fraction (LVEF).

Methods: Patients with primary or secondary MR and LVEF <50% who underwent MV replacement or repair (with/without atrial septal defect closure and/or atrial fibrillation ablation) between 2005 and 2017 at our center were retrospectively analyzed using unadjusted and propensity score matching techniques (42 pairs).

Results: A total of 356 patients with either primary (n = 162 [45.5%]) or secondary MR (n = 194 [54.5%]) and LVEF <50% underwent MV repair (n = 293 [82.3%]) or replacement (n = 63 [17.7%]) during the study period. In-hospital mortality was 0.3% (repair) and 1.6% (replacement) in the unmatched cohort ($P = .32$); there were no in-hospital deaths after matching. Estimated survival was 72.8% (repair) versus 50.1% (replacement) at 8 years in the unmatched ($P < .001$), and 64.3% (repair) versus 50.7% (replacement) in the matched groups ($P = .028$). Eight-year cumulative incidence of reoperation was 7.0% and 11.6% in unmatched ($P = .28$), and 9.9% and 12.7% in matched ($P = .69$) repair and replacement groups, respectively. Markedly reduced LVEF (<40%) was among the independent predictors of long-term mortality (hazard ratio, 1.7; 95% CI, 1.2-2.4; $P = .002$). In secondary MR, MV repair showed an 8-year survival benefit over replacement (65.1% vs 44.6%; $P = .002$), with no difference in reoperation rate (11.6% [repair] vs 17.0% [replacement]; $P = .11$).

Conclusions: MV repair performed in primary or secondary MR and reduced LVEF provides superior long-term results compared with replacement. Severe LV dysfunction is a significant predictor of reduced survival following MV surgery. (JTCVS Open 2024;22:191-207)



Estimated survival after mitral valve repair versus replacement in the unadjusted cohort.

CENTRAL MESSAGE

Mitral valve repair provides superior long-term results compared with replacement in patients with primary or secondary mitral regurgitation and reduced ejection fraction.

PERSPECTIVE

The optimal surgical strategy in patients with mitral regurgitation and reduced left ventricular ejection fraction remains debatable. Previous publications favor mitral valve replacement over repair in this specific patient subset. In this study, we observed that mitral valve repair provided a long-term survival benefit compared with mitral valve replacement.

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Abbreviations and Acronyms

LV = left ventricle/ventricular
LVAD = left ventricular assist device
LVEF = left ventricular ejection fraction
MR = mitral regurgitation
M-TEER = transcatheter edge-to-edge MV repair
MV = mitral valve
PSM = propensity score matching
SHR = subdistribution hazard ratio
SMR = secondary mitral regurgitation

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Mitral valve (MV) surgery in patients with mitral regurgitation (MR) and normal left ventricular ejection fraction (LVEF) offers excellent results.[1-3] However, for those patients presenting with MR and moderate to severe left ventricular (LV) systolic dysfunction, the long-term prognosis of the disease and outcomes after MV surgery are known to be poor.[4,5] Patients with MR and reduced LVEF represent a heterogeneous group with varying etiology and prognosis, depending on the severity of the accompanying heart failure. In addition, the long-term outcomes following MV surgery are closely related to the progression of ventricular dysfunction.[6] Although heart failure occurs during the natural course of advanced or untreated chronic primary MR, the underlying pathophysiological mechanisms of secondary MR (SMR) do not directly involve the MV leaflets. SMR is instead caused by LV and/or left atrial dysfunction, which causes LV remodeling and papillary muscle displacement in the case of ventricular SMR or annular dilation in the case of atrial SMR. The worse prognosis post-SMR surgery may be related to the fact that the underlying pathology is not addressed, in contrast to surgical treatment of primary MR.

Current guidelines recommend MV repair in preference to replacement in patients with primary MR, if a durable repair is possible and surgical risk is low (Class I, Level of evidence B).[7,8] However, there is scarce evidence in patients with reduced LVEF and primary MR, who oftentimes have an increased surgical risk, and their survival prognosis and symptomatic improvement postsurgery are less well defined. There is also limited evidence for the surgical treatment of SMR, with previous publications favoring MV replacement over repair in this specific-patient subset.[9,10] Furthermore, the emergence of transcatheter edge-to-edge MV repair (M-TEER) as a feasible and safe alternative in patients with MR and LV dysfunction at high surgical risk widens the spectrum of treatment options and increases the complexity of the decision-making process in this patient subset.[11,12]

Our group has previously reported encouraging long-term outcomes following MV repair in patients with reduced LVEF.[6] However, sparse data are available in the literature about the comparative results of MV repair and replacement in heart valve centers with expertise in MV repair. This study aims to compare the early and long-term outcomes following MV repair and replacement in patients with LVEF <50%.

MATERIALS AND METHODS

Ethical Statement

This research project was approved by the University of Leipzig (institutional review board No.: 476/19-ek; November 2019). Individual patient informed consent was waived due to the anonymous data management and the retrospective nature of this study.

Patient Cohort

Patients with LVEF <50% who underwent isolated MV repair or replacement (with optional atrial septal defect closure or ablation) for primary and secondary MR between 2005 and 2017 at the Leipzig Heart Center were included and retrospectively analyzed (Figure 1). Decision to perform the MV surgery was made according to the current guidelines, and repair was performed whenever possible. Patients with infective endocarditis, moderate or severe MV stenosis, and those requiring nonelective surgery were excluded from the analysis.

Surgical Techniques

Surgical exposure was performed using either median sternotomy or right minithoracotomy. At our center, isolated MV procedures are usually performed via right minithoracotomy. However, the final decision about the surgical access is based on the patient's surgical risk, the possibility of concomitant cardiac procedures, and the surgeon's experience and preferences.

Our minimally invasive MV repair technique has been described previously.[13] MV replacement was performed using horizontal mattress pledgeted sutures with the preservation of 1 or both leaflets. In the MV repair cohort, secondary MR was corrected using undersized ring annuloplasty, and optional subvalvular or MV leaflet repair techniques.

Study Outcomes and Definitions

The primary outcome was in-hospital mortality and estimated long-term survival. The secondary outcomes were early postoperative morbidity and long-term freedom from all-cause cardiac reoperation.

Heart failure was classified according to the European guidelines for the management of heart failure,[14] where heart failure with reduced LVEF was defined as symptomatic heart failure with LVEF ≤40%, and heart failure with mildly reduced LVEF was defined as symptomatic heart failure with LVEF 41% to 49%.

Follow-up

The follow-up of the discharged patients was performed using mailed questionnaires, telephone contact with the patient and/or family members, and consultation with the German National Vital Statistics Registry.

Statistical Analysis

Data were analyzed using R version 4.1.2. (R Foundation for Statistical Computing) and RStudio version 2021.09.0. Unmatched groups were

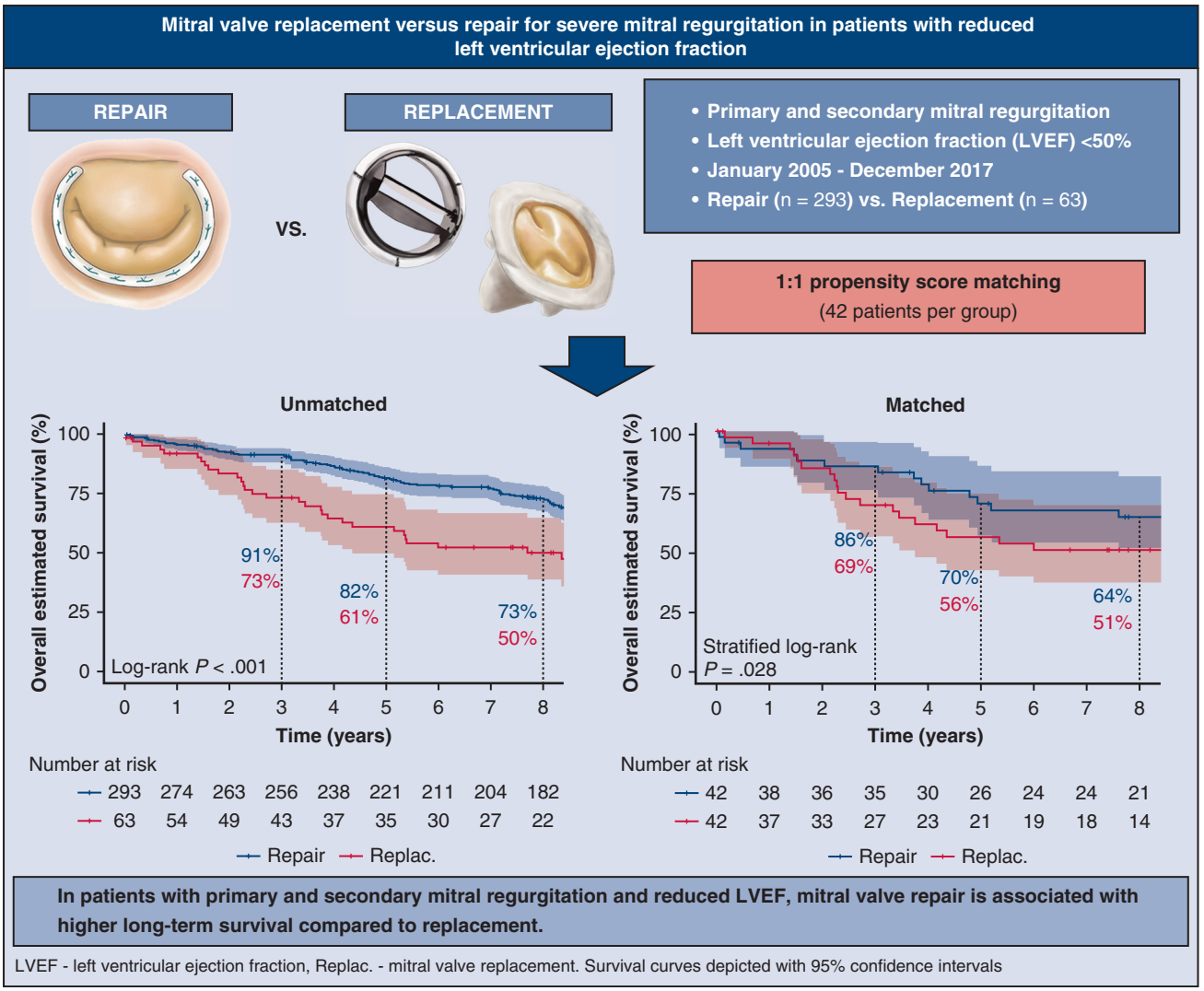

FIGURE 1. Summary of methods and main findings of the study.

compared using the Wilcoxon sum-rank test, 2-sided Fisher exact test, or χ^2 test. To adjust for clinical differences, propensity score matching (PSM) was performed in 1:1 fashion using the nearest neighbor method with a 0.2 caliper. The covariates used for PSM are displayed in Figure 2 and Figure E1. For comparison of the early outcomes between the matched groups, we used the Wilcoxon-signed rank and McNemar tests.

For late mortality, a time-to-event analysis using the Kaplan-Meier method was performed. In the matched cohort, a stratified log-rank test was used to evaluate the differences between the estimated survival curves. Cox proportional hazard model was used for the time-to-event analysis evaluating the hazard ratios (HRs) for predictors of late mortality based on the unmatched cohort. Variables were selected based on their clinical relevance and univariable Cox regression (the cutoff P value was set at <.2). Additionally, the type of MV intervention was added to this multivariate model to evaluate its effect on long-term mortality. In the matched cohort, the effect of the MV intervention type on late mortality was assessed using a Cox-proportional hazard model (incorporating a robust variance estimator) regressing the outcome on a single variable denoting the treatment type.

For the all-cause cardiac reoperations in the unmatched cohort, we used the Fine-Gray subdistribution hazard model (evaluating the subdistribution hazard ratio [SHR]) with mortality as a competing event regressing on a single variable denoting the treatment type. In the matched patients, both a clustered Fine-Gray subdistribution hazard model and a cause-specific hazard model with a robust variance estimator regressed on MV treatment type were used.

Secondary analysis using the above-described statistical methods was performed in a subgroup of patients with SMR in unadjusted and adjusted fashion (1:1 PSM using the nearest neighbor method with a 0.2 caliper)

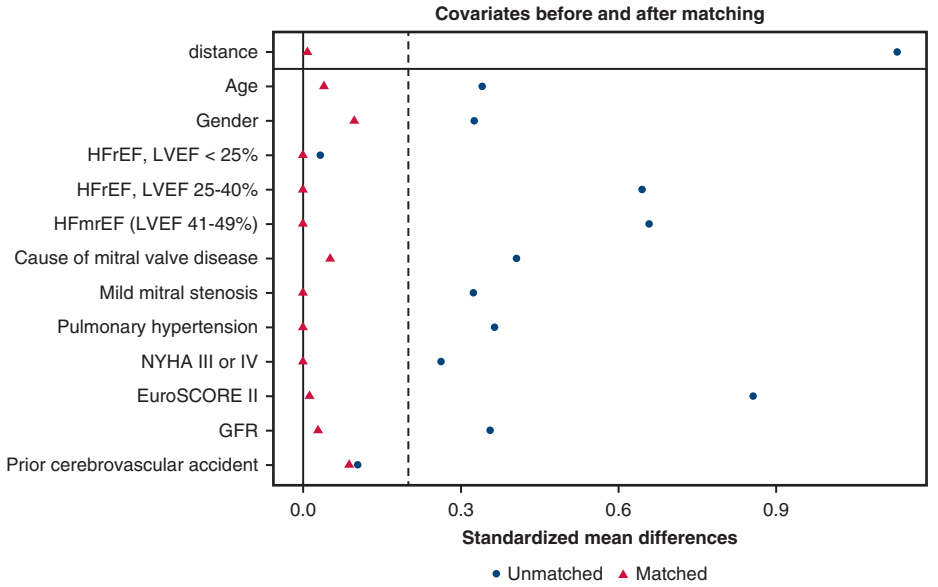

FIGURE 2. Covariates before and after propensity score matching. *HFrEF*, Heart failure with reduced ejection fraction; *LVEF*, left ventricular ejection fraction; *HFmrEF*, heart failure with mildly reduced ejection fraction; *NYHA*, New York Heart Association Heart; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *GFR*, glomerular filtration rate.

(Figure E2). There was nearly no missing data in the baseline and operative patient characteristics (<1% for 1 variable not relevant for matching or regression), thus no imputation was used.

RESULTS

Study Cohort

During the study period, a total of 356 patients with LVEF <50% underwent isolated MV repair (n = 293 [82.3%]) or replacement (n = 63 [17.7%]) for primary and secondary MR and were included in the analysis. Baseline patient characteristics stratified by type of MV intervention are depicted in Table 1. Patients undergoing MV replacement more frequently presented with severe pulmonary hypertension (n = 25 [39.7%] vs n = 64 [21.8%]; $P = .003$), higher mean European System for Cardiac Operative Risk Evaluation II score (7.6%; interquartile range [IQR], 4.4%-11.3% vs 2.6%; IQR, 1.5%-4.3%; $P < .001$), and lower LVEF (36.4% ± 6.4% vs 39.6% ± 7.6%; $P < .001$). Secondary MR was more frequent in the MV replacement group (n = 44 [69.8%]), whereas the prevalence of primary and secondary MR was similar in the MV repair group (143 [48.8%] and 150 [51.2%], respectively). Persistent atrial fibrillation was more common in the MV repair group (n = 151 [51.5%] vs n = 26 [41.3%]; $P = .001$). After PSM, all the baseline patient characteristics were comparable between the study groups (Table 1).

Intraoperative Data

In the MV replacement group, MV repair was initially attempted in 13 out of 63 (20.6%) cases (Table 2). Most patients in the MV repair group (n = 276 [94.2%]) underwent surgery via right minithoracotomy, whereas this access was used only in 10 (15.9%) patients undergoing MV replacement. Concomitant atrial fibrillation ablation was performed more often in the MV repair group (n = 123 [42.0%] vs n = 16 [25.4%]; $P = .014$).

Early Outcomes

There were 2 in-hospital deaths in the unadjusted cohort: 1 (1.6%) patient died after MV replacement due to multiorgan failure, the other patient died after MV repair (0.3%) due to postoperative stroke. Unadjusted analysis showed that MV replacement was associated with a higher rate of re-exploration due to major bleeding (n = 9 [14.3%] vs n = 14 [4.8%]; $P = .01$), more frequent acute renal injury requiring dialysis (n = 7 [11.1%] vs n = 9 [3.1%]; $P = .012$), and longer hospital stay (12.0 days; IQR, 9.0-21.0 days vs 10.0 days; IQR, 8.0-14.0 days; $P = .01$). After PSM, early postoperative complications occurred with similar frequency in both groups (Table 3).

Long-Term Outcomes

Follow-up was complete in 96% patients and was performed until January 2024. The mean follow-up duration was 9.2 ± 5.0 years.

All-cause late death. The estimated unadjusted long-term survival was significantly higher after MV repair with 72.8% ± 2.7% versus 50.1% ± 6.6% at 8 years (log-rank $P < .001$) (Figure 3, *A*).

Cox proportional hazard model built on the overall cohort data revealed that diabetes mellitus (HR, 2.1; 95% CI, 1.5-

TABLE 1. Patient baseline characteristics

Variable	Unmatched			Matched		
	MV replacement n = 63	MV repair n = 293	*P* value	MV replacement n = 42	MV repair n = 42	*P* value
Age (y)	66.6 ± 10.0	63.1 ± 11.8	.064	65.0 ± 9.6	64.6 ± 11.6	.86
Female	38 (60.3)	130 (44.4)	.021	23 (54.8)	25 (59.5)	.67
Body mass index	26.7 (24.5-29.3)	26.0 (23.0-29.2)	.18	27.0 (24.8-29.7)	26.5 (23.9-29.6)	.96
Body surface area (m^2)	1.88 ± 0.22	1.91 ± 0.24	.22	1.92 ± 0.19	1.87 ± 0.21	.44
Hyperlipidemia	33 (52.4)	133 (45.4)	.31	21 (50.0)	23 (54.8)	.64
Arterial hypertension	51 (81.0)	222 (75.8)	.38	35 (83.3)	35 (83.3)	1.00
Diabetes mellitus	21 (33.3)	71 (24.2)	.13	13 (31.0)	19 (45.2)	.20
Chronic obstructive pulmonary disease	4 (6.3)	19 (6.5)	1.00	2 (4.8)	5 (11.9)	.18
Peripheral arterial disease	6 (9.5)	17 (5.8)	.27	3 (7.1)	4 (9.5)	.71
Severe pulmonary hypertension	25 (39.7)	64 (21.8)	.003	15 (35.7)	15 (35.7)	1.00
Atrial fibrillation	26 (41.3)	151 (51.5)	.001	18 (42.9)	28 (66.7)	.06
Prior cerebrovascular incident	5 (7.9)	15 (5.1)	.37	5 (11.9)	6 (14.3)	.74
GFR (mL/minute/1.73 m^2)	72.0 (48.0-87.0)	73.2 (55.1-94.5)	.14	77.0 (57.8-90.8)	69.6 (44.9-87.0)	.66
Prior dialysis	2 (3.2)	2 (0.7)	.15	2 (4.8)	2 (4.8)	1.00
Prior myocardial infarction	10 (15.9)	39 (13.3)	.59	6 (14.3)	6 (14.3)	1.00
Prior pacemaker	10 (15.9)	24 (8.2)	.06	7 (16.7)	4 (9.5)	.32
Prior ICD	9 (14.3)	23 (7.9)	.14	7 (16.7)	6 (14.3)	.76
New York Heart Association functional class III or IV	42 (66.7)	159 (54.3)	.072	26 (61.9)	26 (61.9)	1.00
Cause of mitral valve disease						
Primary MR	19 (30.2)	143 (48.8)	.007	10 (23.8)	11 (26.2)	.78
Secondary MR	44 (69.8)	150 (51.2)		32 (76.2)	31 (73.8)	
Ischemic cardiomyopathy with MR	9 (14.3)	34 (11.6)	.57	5 (11.9)	7 (16.7)	.48
Dilated cardiomyopathy with MR	35 (55.5)	116 (39.6)		27 (64.3)	24 (57.1)	
Mild mitral valve stenosis	6 (9.5)	0	<.001	0	0	1.00
EuroSCORE II	7.6 (4.4-11.3)	2.6 (1.5-4.3)	<.001	5.8 (3.6-8.1)	6.0 (2.5-8.7)	0.94
Preoperative LVEF (%)	36.4 ± 6.4	39.6 ± 7.6	<.001	36.4 ± 5.7	35.9 ± 7.2	.73
HFrEF, of them:	48 (76.2)	141 (48.1)	<.001	33 (78.6)	33 (78.6)	1.00
LVEF <25%	2 (3.2)	11 (3.8)	1.00	1 (2.4)	1 (2.4)	1.00
LVEF 25%-40%	46 (73.0)	130 (44.4)	<.001	32 (76.2)	32 (76.2)	1.00
HFmrEF (LVEF 41%-49%)	15 (23.8)	152 (51.9)	<.001	9 (21.4)	9 (21.4)	1.00

Continuous values are expressed as mean ± SD or median (interquartile range). *MV*, Mitral valve; *GFR*, glomerular filtration rate; *ICD*, implantable cardioverter-defibrillator; *MR*, mitral regurgitation; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *LVEF*, left ventricular ejection fraction; *HFrEF*, heart failure with reduced ejection fraction; *HFmrEF*, heart failure with mildly reduced ejection fraction.

2.9; $P < .001$), LVEF ≤40% (HR, 1.7; 95% CI, 1.2-2.4; $P = .002$), reduced glomerular filtration rate (HR, 0.994; 95% CI, 0.989-0.999; $P = .03$), and New York Heart Association functional class III or IV (HR, 1.6; 95% CI, 1.2-2.2; $P = .003$) were preoperative predictors of long-term mortality after MV surgery (Figure 4). Moreover, adding the type of MV surgery in this regression model showed that MV replacement was associated with increased risk of long-term mortality (HR, 1.7; 95% CI, 1.2-2.5; $P = .005$).

Similarly, adjusted survival after MV repair and replacement was 64.3% ± 7.7% versus 50.7% ± 8.1% at 8 years, respectively (stratified log-rank $P = .028$) (Figure 3, *B*). However, the type of MV surgery was not associated with an increased risk of long-term mortality according to the Cox-proportional hazard model of the matched cohort (MV replacement: HR, 1.6; 95% CI, 0.9-2.7; $P = .11$).

All-cause cardiac reoperation. During the follow-up, cardiac reoperation for any cause was performed in 29 (8.1%) patients in the entire cohort, with 2 (0.6%) patients requiring more than one cardiac reoperation. In the MV repair group, 4 (1.4%) patients underwent heart transplantation (with prior implantation of left ventricular assist

TABLE 2. Operative characteristics

Variable	Unmatched			Matched		
	MV replacement (n = 63)	MV repair (n = 293)	*P* value	MV replacement (n = 42)	MV repair (n = 42)	*P* value
Cardiopulmonary bypass time (min)	115.0 (93.0-162.5)	114.0 (96.0-137.0)	.33	114.5 (88.8-151.3)	106.5 (95.3-127.8)	.25
Aortic crossclamp time (min)	65.0 (55.5-88.0)	65.0 (52.0-82.0)	.44	65.0 (55.3-88.0)	60.0 (51.5-78.0)	.31
MV ring model						
MiCardia Dynamic Annuloplasty Ring		1 (0.3)				
CE Physio Ring Model 4450		174 (59.4)				
Carpentier-MC-AIMR Eilogix Ring M. 4100		59 (20.1)				
SJM Rigid Saddle Ring RSAR		17 (5.8)				
Cosgrove-Edwards Annuloplasty Band Modell 4600		9 (3.1)				
CE Physio-II Ring Modell 5200		25 (8.5)				
SJM Attune Flexible Adjustable Ring		5 (1.7)				
Mitzral Solution		3 (1.0)				
MV prosthesis type						
Mechanical	11 (17.5)					
Biological	52 (82.5)					
MV prosthesis model						
CE S.A.V. - Mitral Model 6650	1 (1.6)					
CE Perimount-Plus-Mitral Model 6900P	5 (7.9)					
CE Perimount Magna Mitral Valve 7000TFX	1 (1.6)					
ATS Mitral Model 500	8 (12.7)					
SJM-Epic-Mitral Model EL-M	35 (55.6)					
SJM Mitral Modell MJ-501	3 (4.8)					
Medtronic Mosaic - Mitral Model 310	10 (15.9)					
Ring or valve size (mm)	30.6 ± 1.9	31.0 ± 3.4	.88	30.7 ± 1.9	30.2 ± 2.9	.35
Surgical approach						
Right minithoracotomy	10 (15.9)	276 (94.2)	**<.001**	5 (11.9)	40 (95.2)	**<.001**
Median sternotomy	53 (84.1)	17 (5.8)	**<.001**	37 (88.1)	2 (4.8)	**<.001**
Conversion to full sternotomy	1 (1.6)	3 (1.0)	.54	0	0	1.00
Concomitant procedures						
Atrial fibrillation ablation	16 (25.4)	123 (42.0)	**.014**	11 (26.2)	25 (59.5)	**.006**
ASD closure	9 (14.3)	27 (9.2)	.25	8 (19.0)	7 (16.7)	.78
Additional subvalvular repair	-	18 (6.1)	–	–	4 (9.5)	–

Continuous data values are presented as mean ± SD or median (interquartile range). Others are presented as n (%). *MV*, Mitral valve; *CE*, Carpentier-Edwards; *SJM*, St Jude Medical; *ASD*, atrial septal defect.

device [LVAD] in 1 (0.3%) case), another 6 (2.0%) patients underwent LVAD implantation. MV reoperation with valve replacement was performed in 11 (3.8%) patients and MV re-repair in 1 patient (0.3%).

In the MV replacement group, 1 patient (1.6%) underwent heart transplantation, and 3 (4.8%) patients required LVAD implantation. Repeated MV replacement was performed in 3 (4.8%) patients (with 1 patient requiring a second reoperation due to re-endocarditis).

In the unmatched cohort, no statistically significant difference was observed in the cumulative incidence of cardiac reoperation between the 2 groups (7.0% and 11.6% at 8 years after MV repair and replacement, respectively; SHR 1.6; 95% CI, 0.7-3.7; $P = .28$) after adjusting for death as a competing event (Figure 5, *A*). Similarly, there was no statistically significant difference in the cumulative incidence of cardiac reoperation between the matched groups (9.9% and 12.7% at 8 years after MV repair and replacement, respectively; SHR 1.3; 95% CI, 0.3 to 5.1; $P = .69$) (Figure 5, *B*). The type of MV surgery was not identified as a predictor of long-term cardiac reoperation according to cause-specific hazard model (HR, 1.4; 95% CI, 0.4-5.2; $P = .66$).

Subgroup analysis in patients with SMR. A total of 194 (54.5% of the overall cohort) patients with SMR (150 [77.3%] patients with MV repair and 44 [22.7%] cases of MV replacement) were analyzed. Of all the SMR patients, 151 (77.8%) presented with dilated cardiomyopathy. The

TABLE 3. Early outcomes

Variable	Unmatched			Matched		
	MV replacement (n = 63)	MV repair (n = 293)	*P* value	MV replacement (n = 42)	MV repair (n = 42)	*P* value
In-hospital mortality	1 (1.6)	1 (0.3)	.32	0	0	.00
Low cardiac output syndrome	4 (6.4)	8 (2.7)	.24	1 (2.4)	2 (4.8)	.56
Myocardial infarction	0	2 (0.7)	1.00	0	1 (2.4)	1.00
Stroke	1 (1.6)	8 (2.7)	1.00	0	1 (2.4)	1.00
Re-exploration due to bleeding	9 (14.3)	14 (4.8)	**.010**	6 (14.3)	6 (14.3)	1.00
Acute renal injury requiring dialysis	7 (11.1)	9 (3.1)	**.012**	3 (7.1)	2 (4.8)	.65
Respiratory failure	11 (17.5)	32 (10.9)	.15	8 (19.0)	7 (16.7)	.80
Sepsis	1 (1.6)	4 (1.4)	1.00	0	1 (2.4)	1.00
Pacemaker implantation	2 (3.2)	6 (2.0)	.64	1 (2.4)	0	1.00
Hospital stay (d)	12.0 (9.0-21.0)	10.0 (8.0-14.0)	**.011**	12.0 (9.0-20.8)	12.0 (10.0-20.3)	.88

Continuous data values are presented as median (interquartile range). Others are presented as n (%). *MV*, Mitral valve.

baseline characteristics before and after matching are depicted in Table E1. After PSM both groups were comparable. Unadjusted comparisons of the early postoperative outcomes showed lower rates of re-exploration for bleeding (9 [6.0%] vs 9 [20.5%]; $P = .007$) and acute renal injury requiring dialysis (6 [4.0%] vs 7 [15.9%]; $P = .011$) in the MV repair group. In the matched groups, these trends were still present; however, not statistically significant (Table E2). The risk factors of long-term mortality were common to those observed in the overall cohort analysis (Figure E3). Also here, MV replacement was associated with increased risk of long-term mortality (HR, 1.7; 95% CI, 1.1-2.7; $P = .023$). The estimated survival in the unmatched SMR patients was 65.1% ± 4.0% versus 44.6% ± 8.0% at 8 years in the repair versus replacement groups, respectively (log-rank $P = .002$) (Figure E4). In the matched SMR cohort, survival after MV repair versus replacement was 63.5% ± 9.3% versus 39.7% ± 9.6% at 8 years (stratified log-rank $P = .11$). There were no statistically significant differences in the cumulative rate of cardiac reoperations (after adjusting for death as a competing event) between the MV repair and replacement groups both in the unmatched (cumulative incidence of 11.6% vs 17.0% at 8 years, respectively; SHR, 1.4; 95% CI, 0.6-3.4; $P = .44$), and matched groups (cumulative incidence of 7.1% vs 18.0% at 8 years, respectively; SHR, 2.9; 95% CI, 0.7 to 12.1; $P = .15$) (Figure E5). There was also no significant effect of treatment type observed on the cause-specific hazards for reoperations (cause-specific HR, 3.2; 95% CI, 0.8-13.2; $P = .13$). Additional results for patients with nonischemic SMR are available in Tables E3 and E4 and Figure E6.

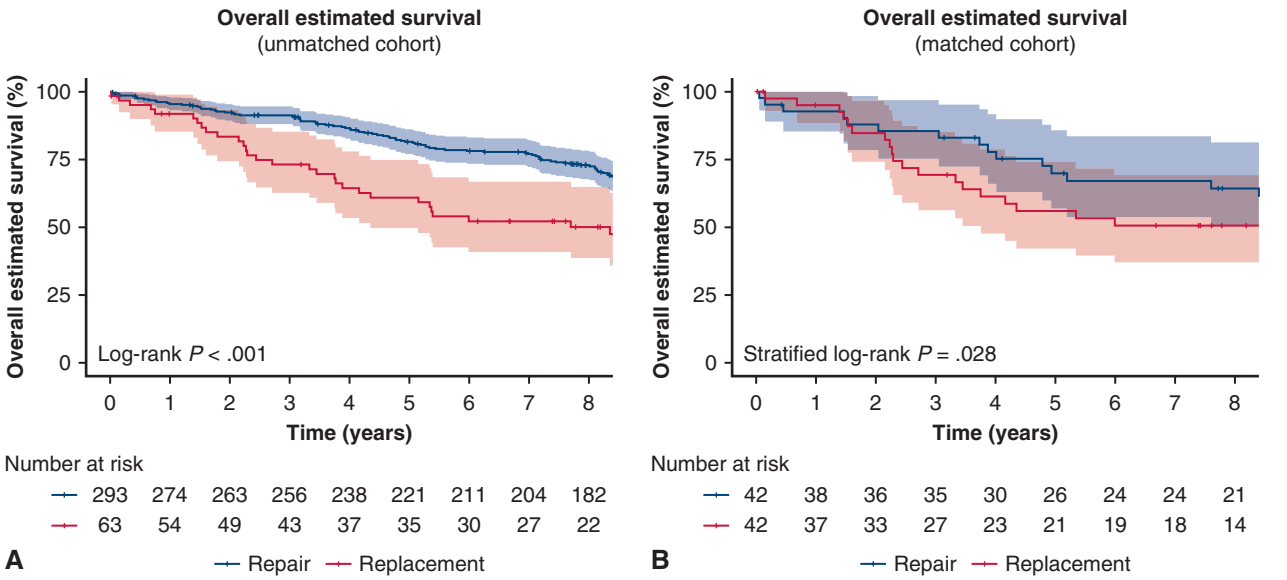

FIGURE 3. Kaplan-Meier curves for overall survival in the unmatched (A) and matched (B) cohorts. Overall survival was calculated starting with the procedure. Stratified log-rank test was used in the matched cohort to account for the matched nature of the data. *Shading* depicts the 95% CI.

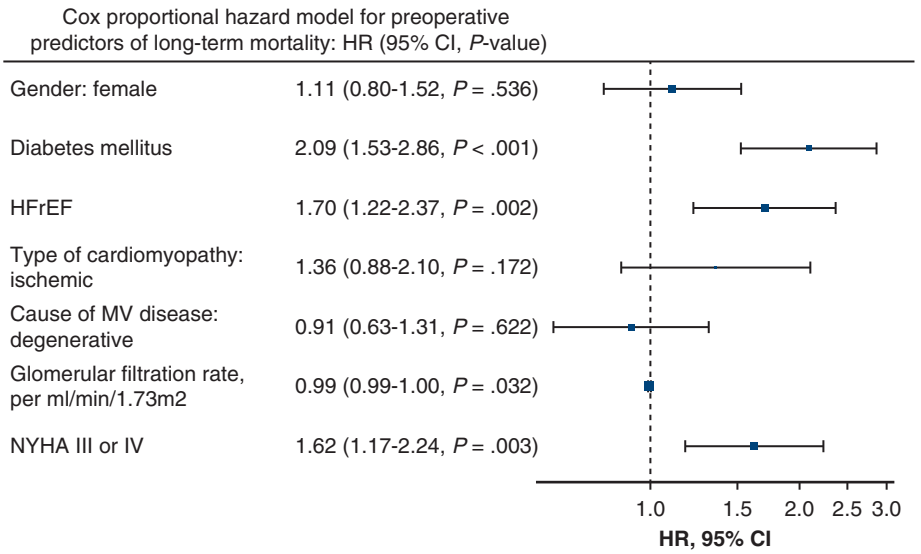

FIGURE 4. Cox proportional hazard model for predictors of long-term mortality. *HFrEF*, Heart failure with reduced ejection fraction; *MV*, mitral valve; *NYHA*, New York Heart Association.

DISCUSSION

In this study, we analyzed a cohort of 356 patients with primary and secondary MR and reduced LVEF who underwent MV surgery at a tertiary heart valve center during a 12-year period, with a focus on MV repair or replacement. Furthermore, a subanalysis of the main study outcomes among patients with SMR comparing both surgical strategies (repair vs replacement) was performed. The main results are:

- MV repair performed in patients with primary or secondary MR and reduced LVEF was associated with superior long-term survival compared with MV replacement in both unadjusted and matched cohorts.
- Similar trends were observed in the subgroup analysis of SMR cases, with MV repair providing improved long-term survival compared to MV replacement (unadjusted analysis).
- Both in the main and SMR study cohorts, no statistically significant difference was found between MV repair and replacement in terms of reoperation rates.
- Reduced LVEF was an independent predictor of long-term mortality after MV surgery in patients with primary and secondary MR.

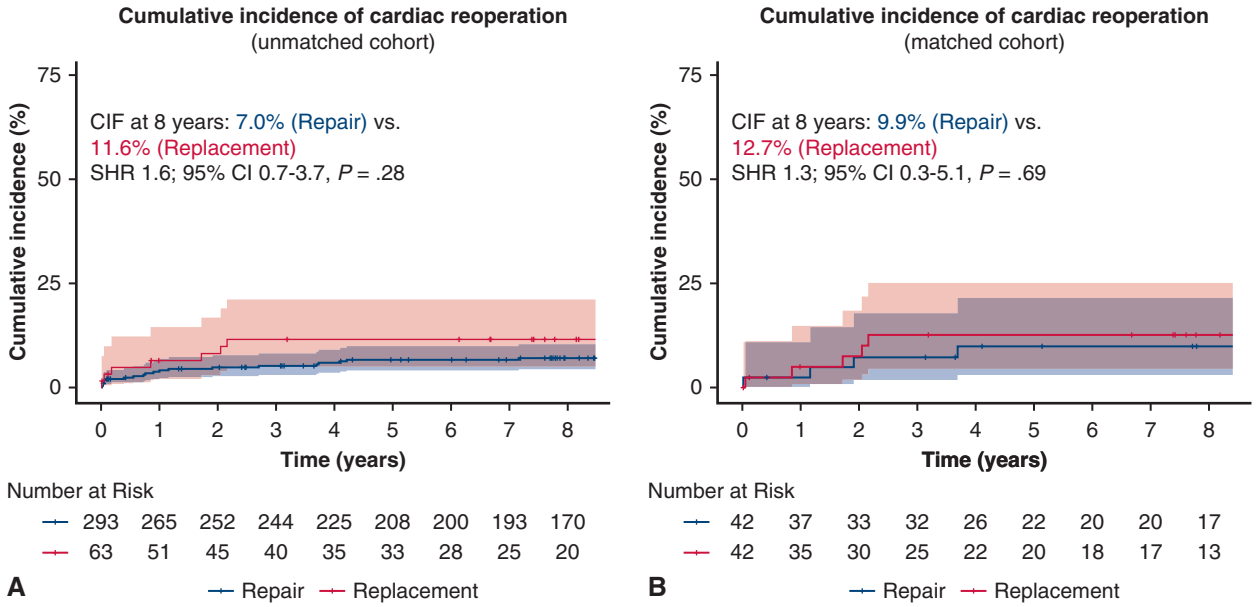

FIGURE 5. Cumulative incidence curves for all-cause reoperation (with death as a competing event) for the unmatched (A) and matched (B) cohorts. *CIF*, Cumulative incidence function; *SHR*, subdistribution hazard ratio. *Shading* depicts the 95% CI.

LV dysfunction and symptoms of heart failure are well-known risk factors for early and late mortality after both MV repair and replacement.[6-8,15,16] Although both surgical and M-TEER correction of MR are associated with some degree of LVEF reduction during the early postoperative period,[17-20] low preoperative LVEF has been reported as 1 of the predictors of significant LVEF decline after MR correction.[21,22] Previous studies have reported the rate of LV dysfunction reaching 18% to 20% in patients undergoing MV repair with normal preoperative LV function, and 23% in cases with reduced preoperative LVEF.[17,23] In patients with degenerative MR, a considerable number of retrospective studies have confirmed the benefits of MV repair over replacement, making it the gold standard of treatment in this group of patients.[3,15,24] In contrast to primary MR, treatment recommendations in SMR are based on limited and controversial data, and indications for surgery have been reduced since both MV repair and replacement failed to show any clear benefit in late survival of these patients.[25,26]

The results of the present study are encouraging because they confirm the safety and effectiveness of MV surgery in selected patients with reduced LVEF, and prove that MV repair can be performed with good results not only in primary but also in secondary MR. Because our cohort consisted of combined patients collective with degenerative and secondary MR, an additional subgroup analysis was performed among patients with SMR. In this subcategory, the vast majority of patients presented with dilated cardiomyopathy. The fact that only patients without indication for concomitant myocardial revascularization were included in the current analysis explains such a small number of cases with ischemic MR. Similar trends in early and late results with MV repair providing superior postoperative survival compared with MV replacement were observed also in this subcategory of patients.

To date, there has been no randomized trial involving MV surgery in patients with SMR and nonischemic cardiomyopathy. Limited evidence is available regarding ischemic MR with patients eligible for myocardial revascularization.[27-30] However, even these randomized trials did not confirm or were not designed to demonstrate a survival benefit of simultaneous MV and coronary bypass surgery. The main limitation of surgery in patients with SMR is that none of the available approaches is curative. For example, the most common technique used for MV repair in SMR is undersized annuloplasty. It is associated with a significant rate of recurrent MR, which can be as high as 25% at 1 year and 58% at 2 years.[30,31] This explains why some surgeons tend to favor MV replacement over repair. In the context of isolated MV surgery for SMR, current valvular heart disease guidelines suggest surgical intervention as a Class IIB recommendation (level of evidence B and C for the American[7] and the European[8] guidelines, respectively) with chordal-sparring mitral valve replacement considered as the preferred surgical option in the American guidelines, and repair whenever possible in the European ones.

The constantly emerging area of transcatheter techniques has opened a new perspective on the treatment of secondary MR in general and redefined the possible role of surgical treatment in this patient category. For instance, the rate of recurrent MR of 5% at 1 year in the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial, and even 17% in the MITRA-FR (Multicentre Study of Percutaneous Mitral Valve Repair using MitraClip Device in Patients With Severe Secondary Mitral Regurgitation) trial was surprisingly low compared with other publications.[11,12] When comparing the midterm results of these trials with the present study, the current results of both MV repair and replacement are surprisingly good. In the recently published 5-year outcomes of the COAPT trial,[32] the authors reported 57.3% cumulative incidence of all-cause death at 5 years after MitraClip (Abbott), which is higher than that observed in the current analysis of SMR patients (28.6% [repair] and 52.4% [replacement] in the matched SMR groups). In the MITRA-FR trial,[33] freedom from all-cause death at 2 years after successful device implantation was 75% ± 5% (compared with 93.3% ± 4.6% after MV repair and 82.2% ± 7.2% after MV replacement in the current adjusted SMR analysis). However, it should be noted that the patients in these trials and our study are not necessarily comparable, and that M-TEER could be an acceptable alternative in patients with high surgical risk and/or severely reduced LVEF.

It has been questioned whether or not MV repair with undersized annuloplasty alone is efficient enough in SMR.[26,34] The vast majority of patients with SMR in our study underwent isolated undersized annuloplasty without subvalvular reconstruction techniques and showed a lower rate of all-cause cardiac reoperation compared to MV replacement. Comparison of the current study results with those available in the literature is limited due to the differences in the preoperative patient characteristics, and should therefore be interpreted with caution. De Bonis and colleagues[35] reported higher operative mortality (12.7% vs 2.3%) and lower 2.5-year survival (73% ± 8% vs 92% ± 3%) in patients undergoing MV replacement compared with repair. Similarly, Calafiore and colleagues[36] reported improved 5-year survival in patients undergoing MV repair (87% ± 7%) compared with replacement (70% ± 10%). However, both of the above-mentioned studies included mostly patients with ischemic SMR with indication for concomitant coronary bypass grafting. The results of the Polish National Registry Data analysis, including 7633 patients with SMR (half of the cases with ischemic MR), showed that MV

repair was associated with a higher 5-year survival compared with MV replacement (71% vs 66%) and that MV replacement was the independent predictor of long-term mortality both in unadjusted and matched cohorts.[37]

The current analysis did not include any comparison between cases with atrial versus ventricular SMR, although atrial fibrillation was one of the variables used for PSM. Ring annuloplasty seems to be especially effective in patients with atrial MR compared with patients with ventricular SMR.[38]

Finally, similar to our previously published analysis, the degree of LV dysfunction was a significant marker of reduced survival both in the general cohort and in the subgroup of patients with SMR.[6] Therefore, in patients with severely reduced LVEF a multidisciplinary heart team discussion with a heart failure specialist is suggested to evaluate alternative treatment options such as M-TEER, ventricular assist device implantation, or heart transplantation.

Limitations

The major limitation of the present study is its retrospective nature with all the inherent limitations of such analyses. In addition, we compared 2 heterogeneous groups of patients, and although our statistical analysis was designed to account for the baseline differences, PSM resulted in small samples of patients. Therefore, the eventual lack of statistically significant difference does not necessarily mean that there is a lack of clinically significant difference, especially in comparisons showing clearly divergent results. In addition, intraoperative details such as surgical exposure or concomitant procedures were not used as covariates for PSM. Moreover, no extensive assessment of preoperative and postoperative echocardiographic measurements (including the rate and degree of recurrent MR) was available in this study. Possible selection bias due to the exclusion of cases with ischemic MR and indication for concomitant coronary bypass surgery, resulting in SMR being represented mostly by patients with nonischemic SMR, is also a limitation. Finally, no differentiation between the atrial and ventricular SMR was possible in this analysis because the current definition of atrial SMR excludes cases with reduced LVEF.[39]

CONCLUSIONS

MV repair performed in patients with primary or secondary MR and reduced LVEF provides superior long-term results compared with MV replacement. Severe LV dysfunction is a significant predictor of reduced survival following MV surgery.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/mitral-valve-replacement-versu-7186.

Conflict of Interest Statement

Dr Borger's hospital receives speakers' honoraria and/or consulting fees on his behalf from Edwards Lifesciences, Medtronic, Abbott, and CryoLife. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handing 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 regurgitation, heart failure, mitral valve repair, mitral valve replacement

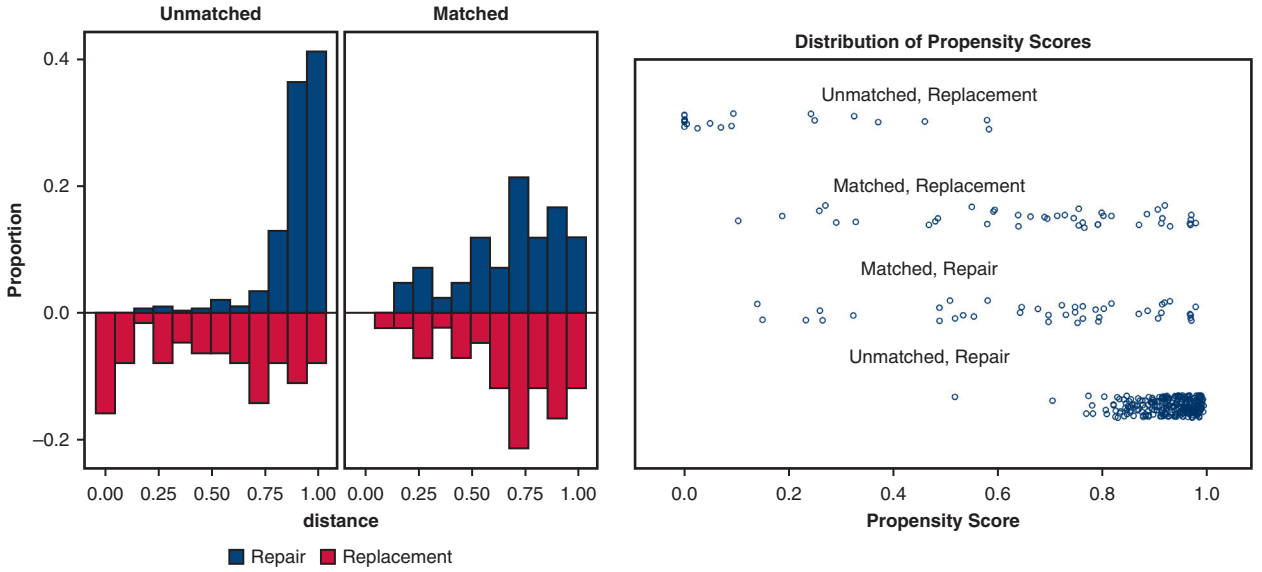

FIGURE E1. Distribution of propensity scores before and after matching (overall cohort).

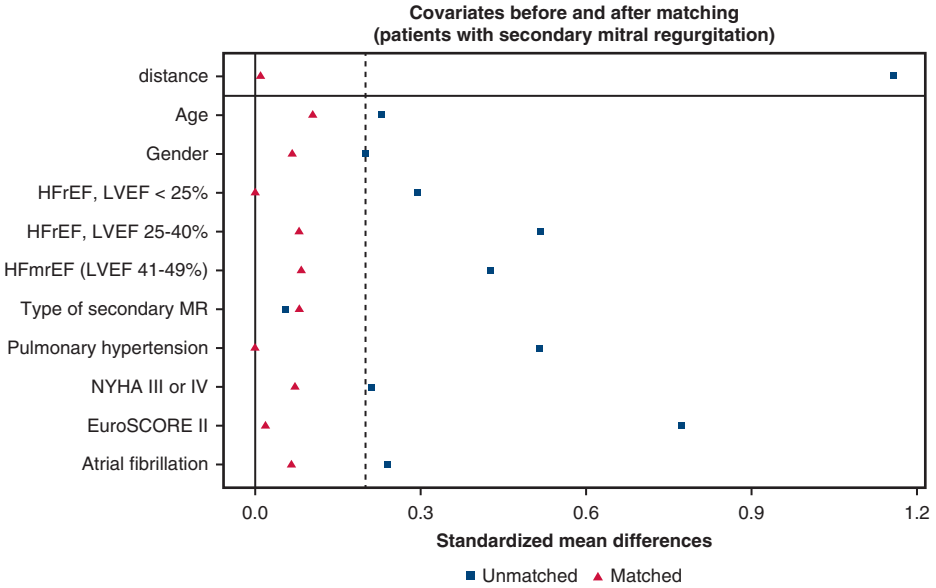

FIGURE E2. Subgroup analysis in patients with secondary mitral regurgitation: Covariates before and after propensity score matching. *HFrEF*, Heart failure with reduced ejection fraction; *LVEF*, left ventricular ejection fraction; *HFmrEF*, heart failure with mildly reduced ejection fraction; *MR*, mitral regurgitation; *NYHA*, New York Heart Association Heart; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation.

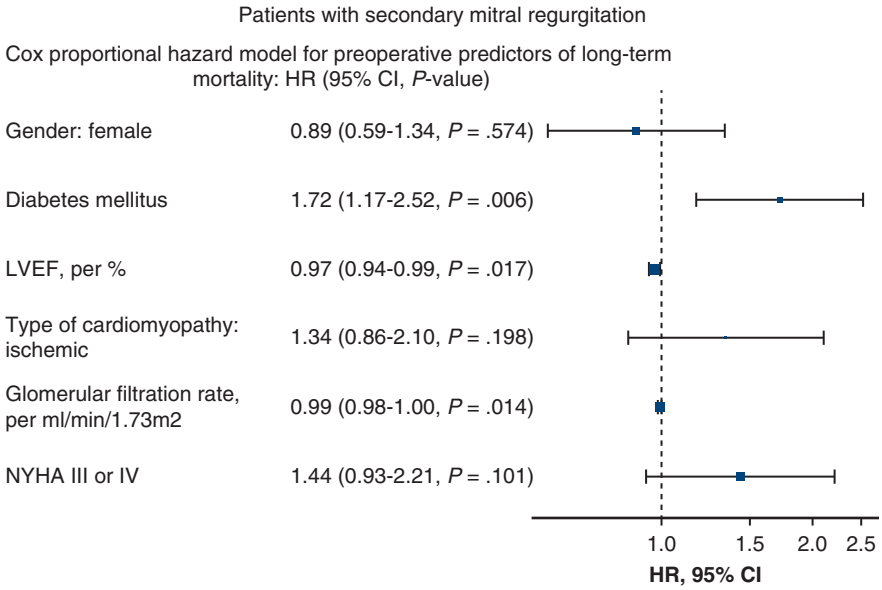

FIGURE E3. Cox proportional hazard model for predictors of long-term mortality in patients with secondary mitral regurgitation. *HR*, Hazard ratio; *CI,* confidence interval; *LVEF,* left ventricular ejection fraction; *NYHA,* New York Heart Association Heart failure classification.

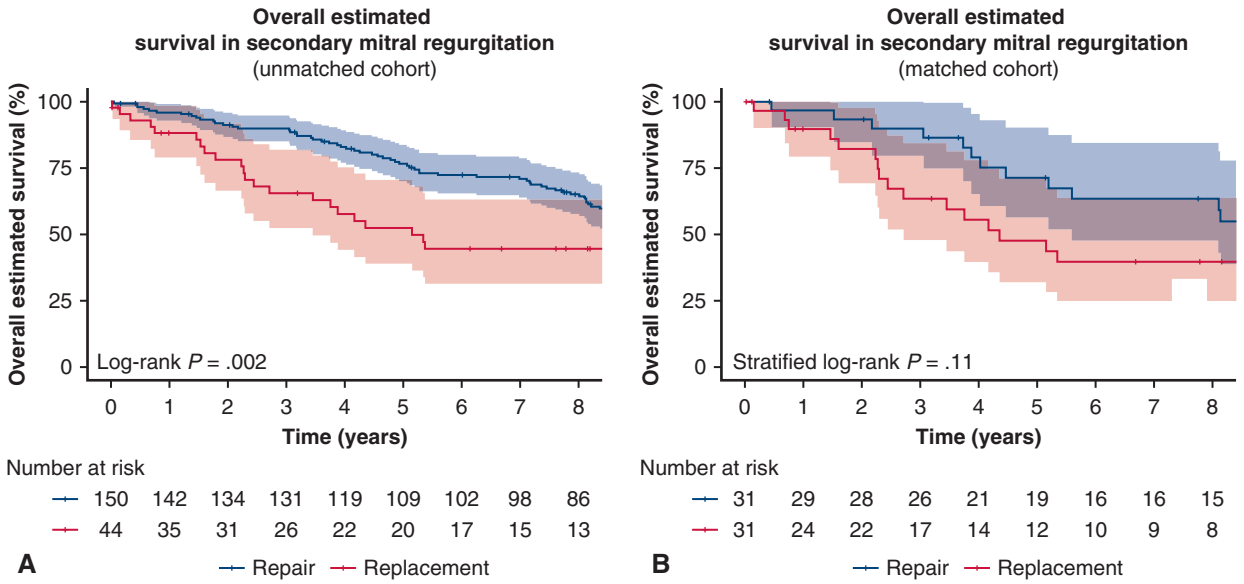

FIGURE E4. Kaplan-Meier curves for overall estimated survival in the unmatched (A) and matched (B) cohorts in patients with secondary mitral regurgitation. Overall survival was calculated starting with the procedure. Stratified log-rank test was used in the matched cohort to account for the matched nature of the data. *Shading* depicts the 95% confidence intervals.

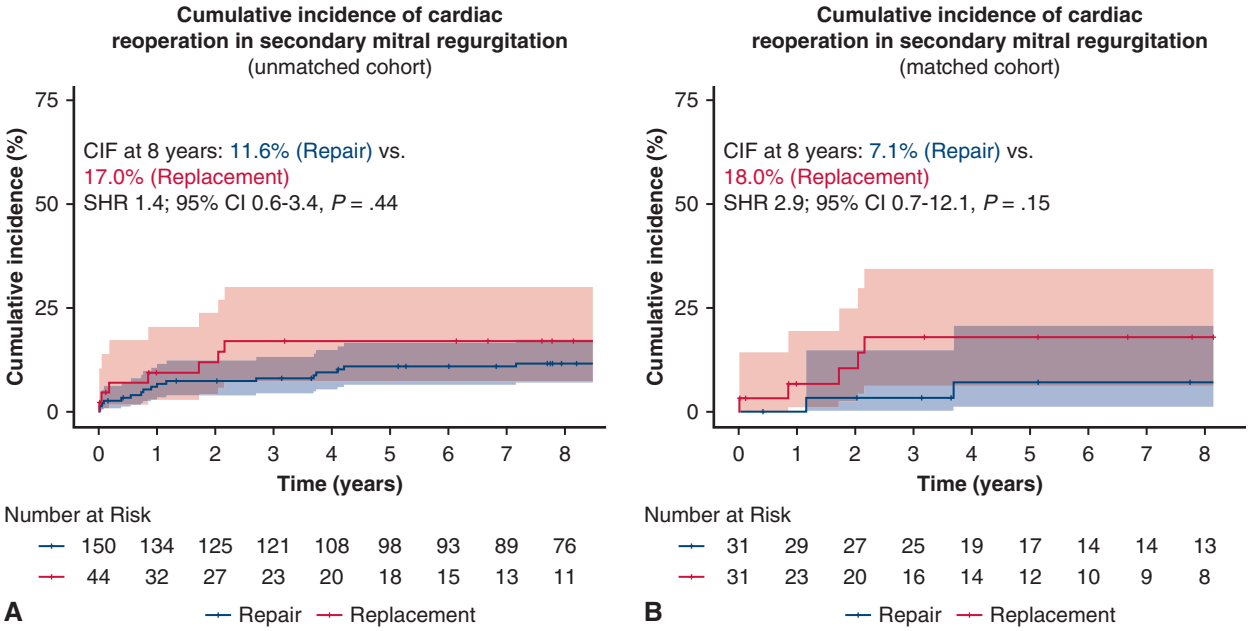

FIGURE E5. Cumulative incidence curves for all-cause reoperation (evaluated with death as a competing event) for the unmatched (A) and matched (B) cohorts in patients with secondary mitral regurgitation. *CIF*, Cumulative incidence function; *SHR*, subdistribution hazard ratio. *Shading* depicts the 95% CI.

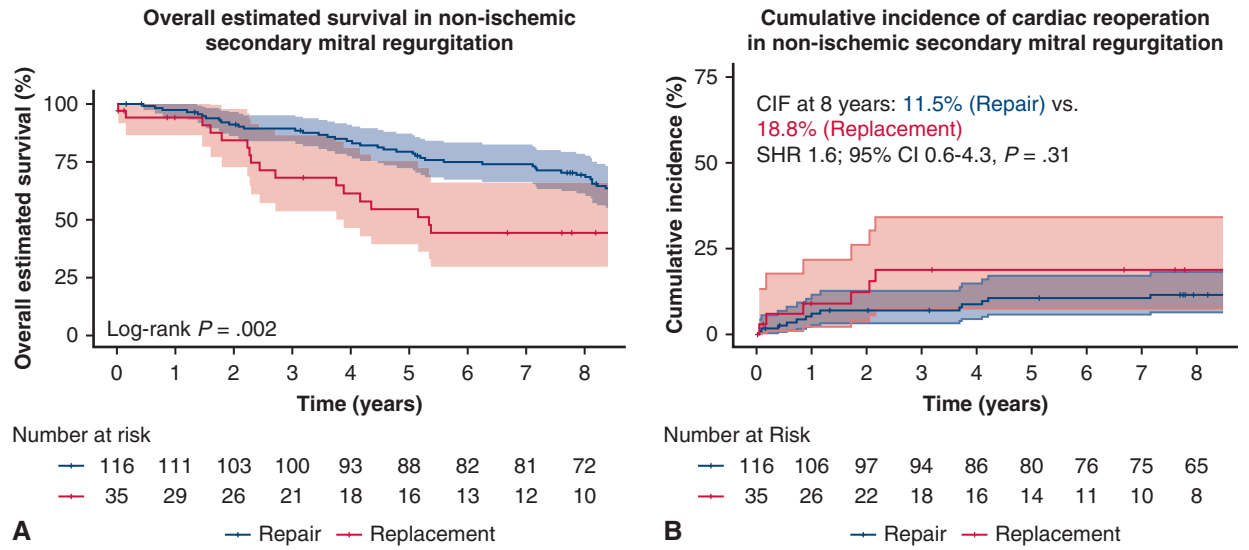

FIGURE E6. Kaplan-Meier curve for overall survival (A) and cumulative incidence curve for all-cause reoperation evaluated with death as a competing event (B) in patients with nonischemic secondary mitral regurgitation. *CIF*, Cumulative incidence function; *SHR*, subdistribution hazard ratio. Overall survival was calculated starting with the procedure. *Shading* depicts the 95% CI.

TABLE E1. Preoperative characteristics in patients with secondary (nonischemic and ischemic) mitral regurgitation (MR)

	Unmatched			Matched		
Patient preoperative characteristics	**MV replacement (n = 44)**	**MV repair (n = 150)**	***P* value**	**MV replacement (n = 31)**	**MV repair (n = 31)**	***P* value**
Nonischemic secondary MR	35 (79.5)	116 (77.3)	.88	25 (80.7)	26 (83.9)	.71
Ischemic secondary MR	9 (20.5)	34 (22.7)		6 (19.4)	5 (16.1)	
Age (y)	66.4 ± 9.1	64.3 ± 10.2	.20	65.6 ± 9.4	64.6 ± 12.2	.72
Female	28 (63.6)	81 (54.0)	.26	19 (61.3)	20 (64.5)	.74
Hyperlipidemia	28 (63.6)	80 (53.3)	.23	20 (64.5)	18 (58.1)	.59
Arterial hypertension	36 (81.8)	117 (78.0)	.59	27 (87.1)	22 (71.0)	.10
Diabetes mellitus	17 (38.6)	47 (31.3)	.36	11 (35.5)	12 (38.7)	.82
Chronic obstructive pulmonary disease	4 (9.1)	9 (6.0)	.50	1 (3.3)	3 (9.7)	.32
Peripheral arterial disease	1 (2.3)	8 (5.3)	.69	0	3 (9.7)	.23
Severe pulmonary hypertension	21 (47.7)	33 (22.0)	**<.001**	14 (45.2)	14 (45.2)	1.00
Atrial fibrillation	18 (40.9)	79 (52.7)	.23	18 (58.1)	19 (61.3)	.80
Prior stroke	4 (9.1)	11 (7.3)	.75	2 (6.4)	5 (16.1)	.26
GFR (mL/minute/1.73 m^2)	65.7 ± 28.7	73.6 ± 30.2	.12	72 (52.5-89.0)	53.2 (45.7-69.5)	.10
Prior pacemaker	9 (20.5)	16 (10.7)	.088	5 (16.1)	4 (12.9)	.71
Prior ICD	8 (18.2)	16 (10.7)	.20	6 (19.4)	4 (12.9)	.48
NYHA functional class III or IV	32 (72.7)	95 (63.3)	.25	22 (71.0)	23 (74.2)	.76
EuroSCORE II (%)	7.4 (4.8-10.7)	2.9 (1.7-4.8)	**<.001**	6.0 (4.2-8.1)	5.8 (2.7-7.8)	.66
Preoperative LVEF (%)	35.0 (30.0-40.0)	37.5 (31.3-44.0)	.077	35.1 ± 4.9	35.3 ± 6.9	.86
HFrEF, (LVEF ≤40%) of them:	36 (81.8)	98 (65.3)	**.037**	27 (87.1)	26 (83.9)	.65
LVEF <25%	1 (2.3)	10 (6.7)	.46	0	0	1.00
LVEF 25%-40%	35 (79.5)	88 (58.7)	**.011**	27 (87.1)	26 (83.9)	.65
HFmrEF, LVEF 41%-49%	8 (18.2)	52 (34.7)	**.042**	4 (12.9)	5 (16.1)	.65

Continuous data values are presented as mean ± SD or median (interquartile range). Other values are presented as n (%). *MV*, Mitral valve; *MR*, mitral regurgitation; *GFR*, glomerular filtration rate; *ICD*, implantable cardioverter-defibrillator; *NYHA*, New York Heart Association; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *LVEF*, left ventricular ejection fraction; *HFrEF*, heart failure with reduced ejection fraction; *HFmrEF*, heart failure with mildly reduced ejection fraction.

TABLE E2. Intraoperative data and early postoperative outcomes after mitral valve (MV) surgery in patients with secondary (ischemic and nonischemic) mitral regurgitation

	Unmatched			Matched		
Intra- and postoperative outcomes	**MV replacement (n = 44)**	**MV repair (n = 150)**	***P* value**	**MV replacement (n = 31)**	**MV repair (n = 31)**	***P* value**
Intraoperative data						
Right minithoracotomy	7 (15.9)	141 (94.0)	**<.001**	6 (19.4)	31 (100)	**<.001**
Atrial fibrillation ablation	11 (25.0)	61 (40.7)	.059	9 (29.0)	11 (35.5)	.59
ASD closure	7 (15.9)	13 (8.7)	.17	6 (19.4)	4 (12.9)	.48
Additional subvalvular repair	–	18 (12.0)	–	–	2 (6.5)	–
Postoperative outcomes						
In-hospital mortality	1 (2.3)	0	.23	0	0	1.00
Low cardiac output syndrome	4 (9.1)	6 (4.0)	.24	2 (6.5)	1 (3.2)	.56
Myocardial infarction	0	2 (1.3)	1.00	0	1 (3.2)	1.00
Stroke	1 (2.3)	5 (3.3)	1.00	0	1 (3.2)	1.00
Re-exploration due to bleeding	9 (20.5)	9 (6.0)	**.007**	5 (16.1)	4 (12.9)	.74
Acute renal injury requiring dialysis	7 (15.9)	6 (4.0)	**.011**	4 (12.9)	1 (3.2)	.18
Respiratory failure	10 (22.7)	19 (12.7)	.10	6 (19.4)	2 (6.5)	.16
Sepsis	1 (2.3)	4 (2.7)	1.0	0	0	1.00
Atrial fibrillation	16 (36.4)	63 (42.0)	.50	13 (41.9)	13 (41.9)	1.00
Pacemaker implantation	1 (2.3)	0	.23	0	0	1.00
Hospital stay (d)	13.0 (9.8-22.0)	12 (9.0-16.0)	.088	12.0 (10.0-21.0)	11.0 (8.0-15.0)	.16

Continuous data values are presented as median (interquartile range). Other values are presented as n (%). *MV*, Mitral valve; *ASD*, atrial septal defect.

TABLE E3. Preoperative characteristics in patients with secondary non-ischemic mitral regurgitation

Patient preoperative characteristics	**MV replacement (n = 35)**	**MV repair (n = 116)**	***P* value**
Age (y)	66.9 ± 8.3	63.7 ± 10.0	.056
Female	24 (68.6)	69 (59.5)	.33
Hyperlipidemia	20 (57.1)	51 (44.0)	.17
Arterial hypertension	28 (80.0)	86 (74.1)	.48
Diabetes mellitus	14 (40.0)	35 (30.2)	.28
Chronic obstructive pulmonary disease	3 (8.6)	8 (6.9)	.72
Peripheral arterial disease	0	5 (4.3)	.59
Severe pulmonary hypertension	17 (48.6)	23 (19.8)	**<.001**
Atrial fibrillation	14 (40.0)	64 (55.2)	.12
Prior stroke	3 (8.6)	7 (6.0)	.70
GFR (mL/minute/1.73 m^2)	69.7 ± 26.0	74.0 ± 30.3	.42
Prior pacemaker	7 (20.0)	11 (9.5)	.13
Prior ICD	6 (17.1)	14 (12.1)	.41
NYHA functional class III or IV	26 (74.3)	70 (60.3)	.13
EuroSCORE II (%)	7.2 (4.8-10.2)	2.9 (1.8-4.7)	**<.001**
Preoperative LVEF (%)	36.0 (31.0-40.0)	36.5 (30.8-44.0)	.47
HFrEF, LVEF ≤40% of them:	29 (82.9)	78 (67.2)	.075
LVEF <25%	1 (2.9)	10 (8.6)	.46
LVEF 25%-40%	28 (80.0)	68 (58.6)	**.021**
HFmrEF, LVEF 41%-49%	6 (17.1)	38 (32.8)	.091

Continuous data values are presented as mean ± SD or median (interquartile range). Others are presented as n (%). *MV*, Mitral valve; *GFR*, glomerular filtration rate; *ICD*, implantable cardioverter-defibrillator; *NYHA*, New York Heart Association; *EuroScore*, European System for Cardiac Operative Risk Evaluation; *HFrEF*, heart failure with reduced ejection fraction; *LVEF*, left ventricular ejection fraction; *HFmrEF*, heart failure with mildly reduced ejection fraction.

TABLE E4. Intraoperative data and early postoperative outcomes after mitral valve (MV) surgery in patients with secondary nonischemic mitral regurgitation

Intra- and postoperative outcomes	MV replacement (n = 35)	MV repair (n = 116)	*P* value
Intraoperative data			
Right minithoracotomy	4 (11.4)	109 (94.0)	**<.001**
Atrial fibrillation ablation	10 (28.6)	53 (45.7)	.072
ASD closure	5 (14.3)	11 (9.5)	.53
Additional subvalvular repair	–	11 (9.5)	–
Postoperative outcomes			
In-hospital mortality	1 (2.9)	0	.23
Low cardiac output syndrome	3 (8.6)	4 (3.4)	.35
Myocardial infarction	0	1 (0.9)	1.00
Stroke	1 (2.9)	3 (2.6)	1.00
Re-exploration due to bleeding	5 (14.3)	8 (6.9)	.18
Acute renal injury requiring dialysis	2 (5.7)	2 (1.7)	.23
Respiratory failure	7 (20.0)	12 (10.3)	.15
Sepsis	1 (2.9)	1 (0.9)	.41
Atrial fibrillation	13 (37.1)	48 (41.4)	.65
Pacemaker implantation	1 (2.9)	0	.23
Hospital stay (d)	12.0 (9.0-19.0)	11.0 (9.0-16.0)	.33

Continuous data values are presented as median (interquartile range). Others are presented as n (%). *ASD*, Atrial septal defect.