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Mid-term results of mitral valve replacement and repair: current clinical experience, technical aspects, and risk factor analysis

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Abstract

Aim: We evaluated the short- and mid-term results of mitral valve replacement (MVR) and mitral valve repair (MV-repair).

Methods: In total, 168 patients (mean age 67 ± 11 years) underwent MVR (n = 104) and MV-repair (n = 64). To treat posterior leaflet disease, MV-repair techniques included triangular or quadrangular resection (n = 38), P1-P2 plication (n = 4), side-to side P1-P2 (n = 1), posterior-medial commissure-plasty (n = 1), and annuloplasty (n = 20). A prosthetic ring was implanted in all patients. In the presence of degenerative disease involving the anterior leaflet, extensive myxomatous and/or prolapsing pathology of the entire valve, and/or rheumatic and endocarditis degeneration, surgical orientation was to perform MVR directly. When possible, the sub-valvular apparatus with its papillary muscle was partially preserved. The mean follow-up was 38 ± 22 months.

Results: Operative mortality (0.96% *vs.* 1.56%) and six-year survival (94% *vs.* 100%) were similar in MVR and MV-repair. The only independent predictor of late survival was advanced age at the operation (79.2 years *vs.* 66.4 years; P = 0.012). Freedom from redo-operation was 100%. Partial preservation of the sub-valvular apparatus with its papillary muscle during MVR allowed postoperatively a better left ventricular function with similar values achieved with MV-repair (P = 0.05), and it was a protective factor against the development of left ventricular

dysfunction during follow-up (P = 0.01).

Conclusion: MVR and MV-repair are associated with satisfactory results in the short and medium term. MV-repair to treat posterior leaflet disease is associated with a stable and long-lasting result; MVR allows equally satisfactory results in the presence of more extensive and more complex mitral valve disease. Partial preservation of the sub-valvular apparatus favors a better left ventricular systolic function.

Keywords: Mitral valve repair, mitral valve replacement, mitral valve surgery and late survival

INTRODUCTION

Mitral valve surgery is currently the treatment of choice for severe mitral regurgitation, based on replacement or repair of the native valve, and depending on the type of valve disease and its etiology.

In particular, mitral valve repair (MV-repair) in comparison with mitral valve replacement (MVR) has become the procedure of choice for treating the degenerative isolated mitral regurgitation, thanks to its proven advantages in terms of lower operative mortality, improved survival, better preservation of left ventricular function, and fewer valve prosthesis-related complications, including thromboembolism, anticoagulation-related bleeding events, and prosthetic valve dysfunction[1-3].

However, in current practice, patients with severe mitral insufficiency are older and often, in addition to presenting an endocarditic or rheumatic etiology, suffer from complex degenerative pathology of the mitral valve. Therefore, the choice of the surgeon must be based not only on trying to repair the valve but also, and above all, on the basis of the patient's preoperative clinical conditions, taking into account that a reparative intervention in the presence of complex pathology can lengthen the time of surgery or increase the risk of re-intervention if the repair fails. These latter aspects can negatively influence the short-term result, especially in older patients with greater co-morbidity[4].

The aim of the study was to evaluate the mid-term results of mitral surgery based on the experience of our center, focusing the analysis on the clinical characteristics of patients undergoing MVR in comparison with MV-repair, analyzing surgical choices and several technical aspects during the replacement or repair that led to replace the valve instead of repairing it. We also investigated risk factors for short-term complications and mid-term outcomes during a six-year follow-up period.

METHODS

Between January 2015 and November 2020, at the Cardiac Surgery Division of the Tor Vergata University Hospital, 168 patients (83 males, 85 females; mean age 67 ± 11 years, range 26-84 years) underwent mitral valve surgery: 104 patients underwent MVR and 64 patients MV-repair. Preoperative New York Heart Association (NYHA) class mean value was 2.7 ± 0.9. Overall, 114 patients (68%) were in NYHA functional class III-IV; 51 patients (30%) were in chronic atrial fibrillation; 81 patients (48%) were ≥ 70 years old. Preoperative characteristics of MVR and MV-repair groups of patients are reported in Table 1.

Inclusion criteria of the study considered all consecutive patients undergoing MVR or MV-repair as isolated surgical procedure (n = 87) or associated with tricuspid valve annuloplasty with the use of modified De Vega technique and/or other procedures, i.e., closure of patent foramen ovale and ligation or exclusion of the left auricle (n = 81). Major indications for mitral valve surgery were severe regurgitation (n = 139) (83%) and steno-insufficiency (n = 29) (17%), in accordance with the European Guidelines[5,6]. Degenerative

Table 1. Preoperative characteristics

Characteristics	MVR (*n* = 104)	MV-repair (*n* = 64)	*P*-value
Age, years	66.8 ± 11	67.1 ± 11	0.88
Sex (male), *n* (%)	44 (42)	39 (61)	0.02
NYHA class III-IV, *n* (%)	71 (68)	43 (67)	0.88
NYHA class, mean value	2.7 ± 0.9	2.6 ± 0.8	0.53
Mitral valve disease, *n* (%):			< 0.0001
Severe regurgitation	75 (72)	64 (100)	
Mixed pathology	29 (28)	0	
Mitral valve etiology, *n* (%):			< 0.0001
Degenerative	52 (50)	31 (48.4)	
Deg., anterior and/or post. leaflet's flail	16 (15.4)	33 (51.5)	
Rheumatic	25 (24)	0	
Endocarditis	11 (10.6)	0	
Chronic atrial fibrillation, *n* (%)	34 (33)	17 (16)	0.40
Smoking habit, *n* (%)	41 (39.4)	31 (48.4)	0.25
Diabetes mellitus, *n* (%)	19 (18)	11 (17)	0.86
Hyperlipidemia, *n* (%)	30 (29)	20 (31)	0.74
Hypertension, *n* (%)	70 (67)	34 (53)	0.41
Chronic pulmonary disease, *n* (%)	4 (3.8)	2 (3.1)	0.81
Previous stroke or TIA, *n* (%)	8 (7.6)	0	0.02
BMI > 30, *n* (%)	21 (20)	10 (15.6)	0.46
Redo operation, *n* (%)	7 (6.7)	0	0.03

BMI: Body mass index; TIA: transient ischemic attack.

etiology with or without leaflet(s) flail was found in 132 patients (78.6%) [Table 1]. The other mitral valve procedures performed in association with aortic valve replacement, coronary artery bypass grafting, or concomitant procedures on ascending aorta were excluded from our study. The study was approved by the Institutional Review Board of Tor Vergata University Hospital. All patients gave informed surgical consent. The study was retrospective by design.

Definitions and data analysis

Operative mortality included death in hospital after operation at any time or within 30 days after discharge. Postoperative low cardiac output syndrome associated with renal dysfunction was defined as cardiac index value less than 2.0 L/min/m^2 with or without renal impairment requiring the inotropic support by means of epinephrine or norepinephrine, with or without the infusion of levosimendan, for a postoperative period greater than 48 h. We analyzed the incidence of postoperative major cardiac and non-cardiac complications, as well as the need for re-exploration for bleeding and permanent pacemaker implantation.

The follow-up was performed by clinical evaluation of the patients and trans-thoracic echocardiograms, at 38 ± 22 (range 2-78, median 37) months after surgery. Adverse events were classified according to the definitions established by the Society of Thoracic Surgeons and the American Association for Thoracic Surgery "Guidelines for reporting morbidity and mortality and cardiac valve interventions"[7]. Follow-up was closed on 31 July 2021 and was 98% complete; two patients were lost. Trans-thoracic echocardiographic data were recorded in the preoperative period, at discharge, and during follow-up. Mitral and tricuspid valve regurgitation was classified as none (0/4+), trivial (1+/4), mild to moderate (2+/4), moderate to severe (3+/4), and severe (4+/4). Peak and mean mitral valve gradients, left ventricular ejection fraction, end-diastolic and end-systolic diameters, septum and posterior wall thickness, and pulmonary arterial pressure were evaluated in accordance with the guidelines of the American Society of Echocardiography[8,9].

Surgical approach and technical aspects

Surgery was performed through a complete sternotomy in all patients. Once cardiopulmonary bypass was started, after ascending aorta cross-clamping, cardiac arrest was achieved using 600 mL of antegrade warm blood cardioplegia as first dose, followed by 400 mL doses administered every 20-25 min or St. Thomas cold crystalloid solution at 10 mL/kg as first dose, followed by 5 mL/kg doses, administered every 30-35 min, into the aortic root[10]. After left atrium atriotomy, MVR was performed following the excision of the mitral leaflets. When possible, or when not excessively retracted or calcified, the sub-valvular apparatus with its papillary muscle was partially preserved, in order to better preserve the left ventricular systolic function, with almost complete maintenance of the posterior mitral leaflet. Prosthetic valve implantation was performed using double-needled 2-0 synthetic sutures and Teflon pledgets passed in supra-annular position. As for repair surgery, as it is used in most centers, we employed transesophageal Doppler echocardiography to better evaluate the mechanism of mitral disease before starting cardiopulmonary bypass and immediately after performing the repair technique to assess the final result. MV-repair was achieved with the use of the following techniques[11]: triangular or quadrangular resection (n = 38), P1-P2 plication (n = 4), and side-to side P1-P2 (n = 1) for the treatment of degenerative pathology of the posterior leaflet, posterior-medial commissure-plasty (n = 1), and annuloplasty without resection (n = 20) in the other repair cases. A prosthetic complete (n = 41) or C- (n = 23) ring was implanted in all patients.

On the contrary, in the presence of degenerative complex pathology, involving the anterior leaflet, i.e., extensive myxomatous and/or prolapsing pathology of the entire valve and steno-insufficiency, surgical orientation was to perform the replacement of the native valve directly. In the case of infectious etiology as well, surgical orientation was that of the valve replacement, as was the case when the leaflets were primarily damaged or fissured or to avoid, if the repair had been carried out, the potential risk of leaving a still infected valve tissue.

Statistical analysis

Statistical analysis was performed with the use of Stat View 4.5 (SAS Institute Inc., Abacus Concepts, Berkeley, CA). Contingency table raw data, using the Chi-squared or Fisher's exact test for categorical variables and the unpaired Student's t-test for continuous variables, were calculated to perform the comparisons of MVR with MV-repair groups of patients. The following preoperative variables were analyzed: age, sex, NYHA class, cardiac rhythm, body mass index, co-morbidity (i.e., smoking habit, diabetes mellitus dyslipidemia, arterial hypertension, chronic obstructive pulmonary disease, and peripheral vascular disease), the need for redo operation, and the pathology and the etiology of mitral valve disease. Echocardiographic measurements included left ventricular ejection fraction (LVEF), end-systolic and end-diastolic diameters, left atrium size, septum and posterior wall thickness, function and annulus diameter of the tricuspid valve, and systolic pulmonary artery pressure. Perioperative collected variables included cardiopulmonary bypass and aortic cross-clamp times, sizes of ring and valve prostheses implanted, combined procedures, and the development of postoperative complications. Late survival, i.e., not including in-hospital deaths, freedom from late cardiac death, and prosthetic valve-related events were calculated by means of the Kaplan-Meier method and were expressed as mean values of percentage plus or minus one standard deviation. The Mantel-Cox Log-rank test was used to compare the curves of freedom from events among patients undergoing MVR and those undergoing MV-repair. The Cox proportional hazards method was used to evaluate the influence of variables on time to death. Univariate analysis of preoperative and perioperative variables considered as potential risk factors for late results was performed, and the variables that reached a P-value less than 0.1 were included in the multivariate logistic regression analysis. All continuous values were expressed as mean plus or minus one standard deviation of the mean. The calculated echocardiographic parameters in the postoperative period and during the follow-up were compared with the preoperative ones. The P-values less than 0.05 were considered statistically significant.

RESULTS

Preoperative characteristics of MVR and MV-repair groups of patients are reported in Tables 1 and 2. The main preoperative differences among the two groups, i.e., MVR *vs.* MV-repair, of patients were found to be disease and etiology of the mitral valve dysfunction ($P < 0.0001$, for both comparisons). As compared with MV-repair, MVR group presented a more advanced degree of pathology, as evidenced by the higher incidence of reoperation and impaired cardiac function detected by echocardiography, i.e., larger left atrium size, higher pulmonary tension values, and steno-insufficiency of the mitral valve. Patients who underwent MVR with biological valve prostheses were significantly older (74 ± 7 years) than those who underwent MVR with mechanical prostheses (60 ± 9 years) and MV-Repair (67 ± 11 years) ($P < 0.0001$, for all comparisons). There were no statistically significant differences among the intraoperative analyzed variables and postoperative cardiac and major non-cardiac complications in the two groups of patients [Table 3]. MV-repair patients experienced a shorter postoperative length of stay. Operative mortality was 1.2% or two patients [Table 3]. A 72-year-old male patient died from perioperative myocardial infarction and low output cardiac syndrome, and a 67-year-old male patient died from intraoperative hemorrhagic infarction of the left ventricle at the weaning from cardiopulmonary bypass. Postoperative low cardiac output syndrome occurred in 36 patients (21%): in the logistic regression analysis, preoperative lower value of the left ventricular ejection fraction, more severe tricuspid regurgitation, and longer time of cardiopulmonary bypass were independent predictors of this complication [Table 4].

Using the same statistical analysis, surgical re-exploration for bleeding occurred in 11 patients (6.5%): preoperative greater left atrium enlargement (HR = 1.9; $P = 0.05$) and longer aortic cross-clamp time (HR = 2.1; $P = 0.03$) were independent predictors. Respiratory failure occurred in 14 patients (8.3%): chronic obstructive pulmonary disease (HR = 1.8; $P = 0.06$), peripheral vascular disease (HR = 2.0; $P = 0.04$), and longer time of cardiopulmonary bypass (HR = 2.1; $P = 0.03$) were independent predictors.

Postoperative echocardiography showed a similar improvement of the examined parameters in both groups of patients in comparison with preoperative data, with the exception of the postoperative left ventricular ejection fraction, which was better preserved in the MV-repair group compared with the MVR group ($P < 0.01$) [Table 5]. However, in patients undergoing MVR in which it was possible to partially preserve the sub-valvular apparatus with the posterior papillary muscle compared to its complete resection, the ejection fraction value was better preserved (57.7% ± 4.1%), with a mean value similar to that observed in MV-repair (57.3% ± 5.6%), and slightly significantly higher in comparison to the complete resection (53.6% ± 8.6%) ($P = 0.05$) [Table 5]. At discharge, no para-prosthesis leaks were detected in the entire patient population; in the MV-repair group, residual mitral regurgitation was absent in 32 patients (not including one death) (51.5%), trivial in 30 (47%), and mild in 1 case (1.5%).

Survival and freedom from major cardiovascular events

During follow-up, there were five deaths out of 164 patients (3%). One patient died from sudden death at 12 months following cardiac operation; three patients died from non-cardiac causes: one male patient died at 2 months from SARS-CoV-2-related respiratory infection; one female patient died at 36 months from respiratory infection; and one male patient died from non-prosthetic valve-related neurological damage. Another male patient at 12 months died from likely prosthetic valve-related ischemic stroke. At six years, actuarial survival was 96% ± 2.0%, freedom from late cardiac death was 99% ± 1.0%, and freedom from prosthetic valve thromboembolism was 99% ± 1.0%. In the Cox regression analysis, the only independent predictor for reduced survival was more advanced age at the operation [Table 4]. No case of prosthetic valve thrombosis, endocarditis, or major hemorrhage occurred during the follow-up. In the Mantel-Cox test, the type of operation, MVR *vs.* MV-repair, did not affect late mortality [Figure 1]. Late survival was reduced in

Table 2. Preoperative echocardiographic variables

Variable	MVR (*n* = 104)	MV-repair (*n* = 64)	*P*-value
LV ejection fraction, %	58.8 ± 6.3	57.5 ± 6.7	0.24
Mitral regurgitation grade (1-4/4+), mean	3.6 ± 0.9	3.8 ± 0.61	0.18
Medium trans mitral valve gradient, mmHg	7.9 ± 5.1	3.6 ± 1.9	0.0006
Tricuspid regurgitation grade (1-4/4+), mean	1.9 ± 1.1	1.7 ± 1.1	0.30
Tricuspid annulus, mm	38.7 ± 4.43	37.1 ± 5.7	0.19
Systolic pulmonary art. pressure, mmHg	42 ± 17	36 ± 9.5	0.01
Left atrium diameter, mm	53.7 ± 10	48.8 ± 8.8	0.03
LV end-diastolic diameter, mm	51.6 ± 7.1	52.6 ± 8.5	0.45
LV end-systolic diameter, mm	35.7 ± 7.6	35.1 ± 6.7	0.60
Interventricular septal thickness, mm	11.3 ± 1.4	11.5 ± 2.0	0.44
Posterior wall thickness, mm	10.9 ± 1.5	11.1 ± 1.8	0.51

LV: Left ventricular.

Table 3. Intraoperative and postoperative analyzed variables

Variable	MVR (*n* = 104)	MV-repair (*n* = 64)	*P*-value
Cardiopulmonary bypass, min	99.0 ± 29	91.7 ± 30	0.12
Aortic cross-clamp, min	92.3 ± 29	84.6 ± 18	0.06
Tricuspid valve repair, *n* (%)	42 (40)	26 (41)	> 0.99
Prosthetic valve annulus size, mm	27.7 ± 2.2	31.7 ± 2.5	< 0.0001
Other procedures, *n* (%)	16 (15)	6 (9)	0.26
Blood/crystalloid cardioplegia, *n/n*	34/70	13/51	0.09
Low cardiac output syndrome with or without renal dysfunction, *n* (%)	26 (25)	10 (16)	0.15
Perioperative myocardial infarction, *n* (%)	0	1 (1.56)	> 0.99
Surgical re-exploration for bleeding, *n* (%)	9 (8.7)	2 (3.1)	0.16
Pulmonary complications, *n* (%)	11 (10.6)	3 (4.7)	0.18
Stroke (ischemic), *n* (%)	1 (1.0)	0	> 0.90
Diffuse brain injury, *n* (%)	1 (1.0)	0	> 0.90
Permanent pacemaker implantation, *n* (%)	5 (4.8)	3 (4.7)	> 0.99
Operative mortality, *n* (%)	1 (0.96)	1 (1.56)	0.72
Stay in postoperative unit, days	3.9 ± 6.2	1.9 ± 1.5	0.01
Total stay in hospital, days	19.9 ± 13	15.6 ± 6.5	0.01

Table 4. Independent risk factors for postoperative low cardiac output syndrome (multivariate analysis)

Variable	Hazard ratio	95%CI	*P*-value
Longer CPB time (114 min *vs.* 91 min)	2.9	1.01-1.06	0.003
Preoperative tricuspid regurgitation (2.3 *vs.* 1.7/4)	2.5	1.14-2.68	0.01
Preoperative left ventricular ejection fraction	-2.6	0.85-0.97	0.01
Longer aortic cross-clamp time (100 min *vs.* 86 min)			0.69
MVR with mechanical prosthesis			0.22
MVR with biological prosthesis			0.06

CPB: Cardiopulmonary by-pass; MVR: mitral valve replacement.

patients undergoing MVR with biological prostheses compared to those undergoing MVR with mechanical prostheses or MV-repair ($P = 0.001$) [Figure 2]; however, this difference, as identified in the Cox regression analysis, was primarily related to the advanced age of the patients who had implanted biological valve

Table 5. Postoperative echocardiographic variables

Variable	MVR (*n* = 104)	MV-repair (*n* = 64)	*P*-value
LV ejection fraction, %	54.0 ± 8.3	57.3 ± 5.6	< 0.01
Mitral regurgitation grade (1-4+/4), mean	0.4 ± 0.5	0.5 ± 0.5	0.06
Medium trans mitral valve gradient, mmHg	3.7 ± 1.5	3.4 ± 1.4	0.27
Tricuspid regurgitation grade (1-4+/4), mean	0.9 ± 0.7	0.7 ± 0.6	0.15
Systolic pulmonary art. pressure, mmHg	33 ± 7.8	30 ± 6.3	0.04
LV end-diastolic diameter, mm	53.0 ± 7.0	52.4 ± 5.9	0.73
LV end-systolic diameter, mm	37.3 ± 8.0	36.5 ± 6.7	0.73
LV ejection fraction following partial preservation of sub-valvular apparatus and its papillary muscle during MVR (*n* = 19), %	57.7 ± 4.1*	-	
LV ejection fraction following complete resection of sub-valvular apparatus during MVR (*n* = 85), %	53.6 ± 8.6*	-	

**P*-value = 0.05 (partial preservation *vs.* complete resection, ANOVA test for repeated measures). LV: Left ventricular.

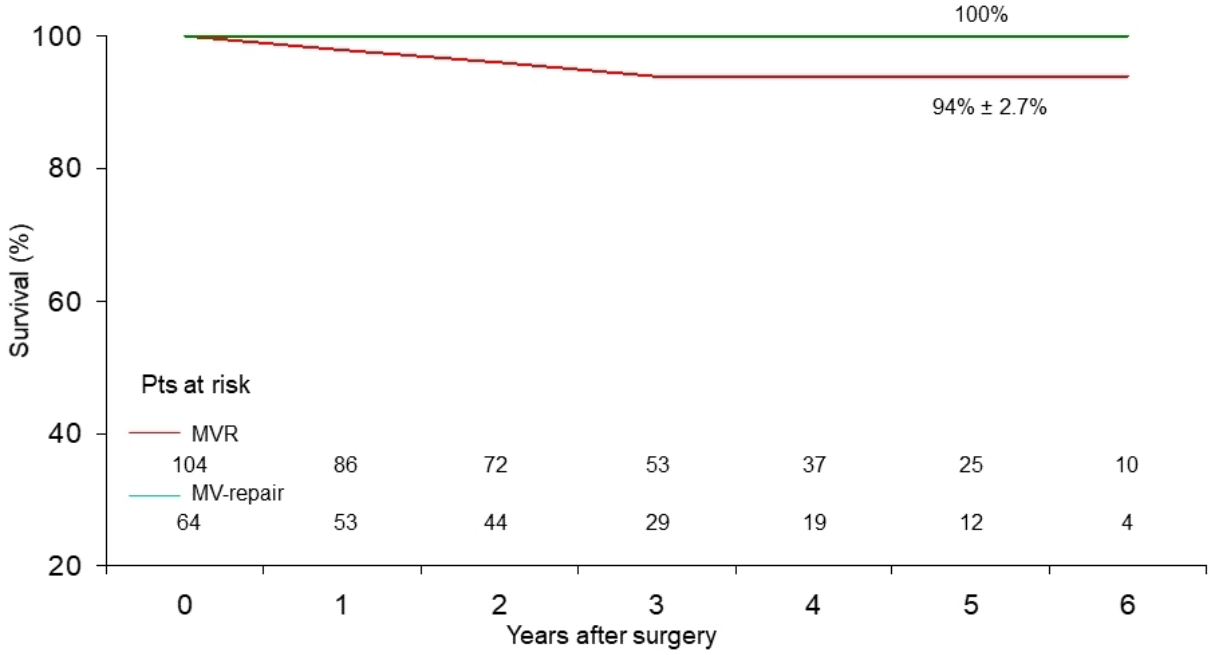

Figure 1. Survival after mitral valve replacement (MVR) *vs.* mitral valve repair (MV-repair) surgery (mean follow-up, 38 ± 22 months).

prostheses.

Clinical status during follow-up

NYHA functional class significantly improved in comparison with preoperative value (1.4 ± 0.6 *vs.* 2.7 ± 0.9; $P < 0.0001$); 155 (97%) out of 159 survived patients were in NYHA class I-II. Echocardiographic evaluation during follow-up showed a satisfactory left ventricular function expressed as LVEF greater than 50% in 116 (77%) out of 151 examined patients. Overall, mean values of NYHA functional class (1.6 ± 0.6 *vs.* 1.4 ± 0.5; $P = 0.03$), residual mitral regurgitation grade (1.0 ± 0.5/4+ *vs.* 0.9 ± 0.6/4+; $P = 0.18$), and LVEF (54.9 ± 5.9 *vs.* 56.3 ± 5.6; $P = 0.15$) were similar in MVR *vs.* MV-repair patients. No para-prosthetic valvular leak was detected. As found in the postoperative period, even during the follow-up, in patients in whom it was possible during MVR to partially preserve the sub-valvular apparatus with the posterior papillary muscle, the mean value of LVEF remained higher in comparison with those undergoing its complete

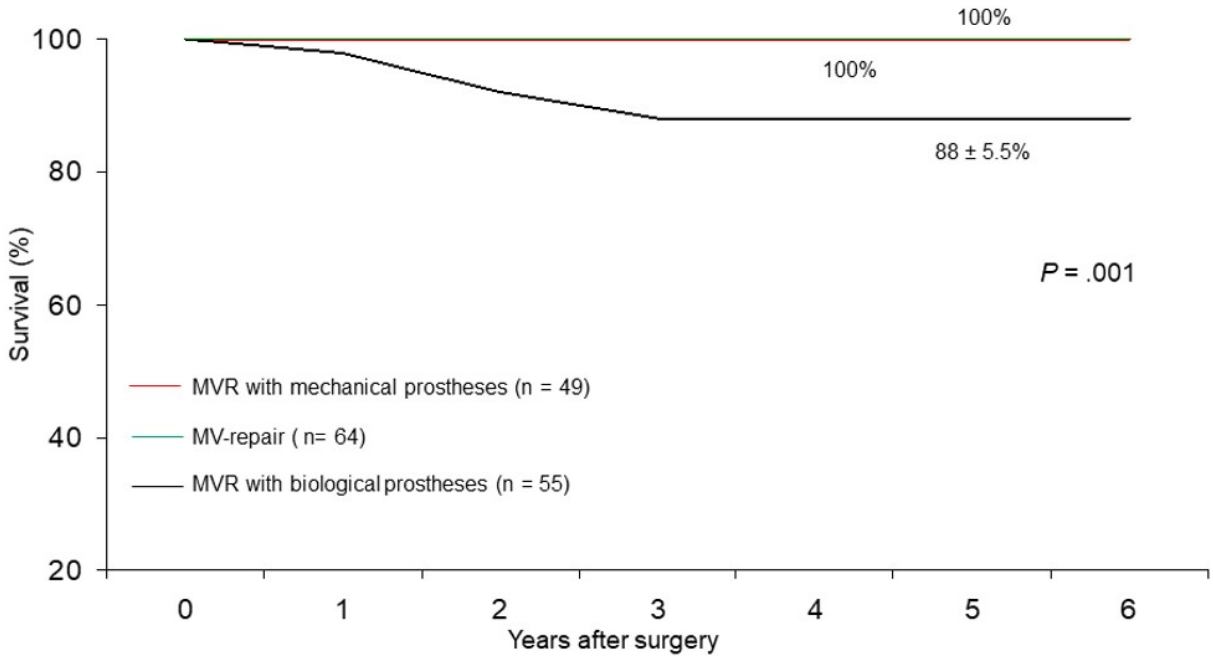

Figure 2. Survival in patients who underwent MVR with mechanical valve prostheses (*n* = 49), MV-repair (*n* = 64), and MVR with biological prostheses (*n* = 55) (Mantel-Cox Log rank test).

resection (57.4% *vs.* 54.4%; $P = 0.07$). In the logistic regression analysis, the following were independent risk factors for reduced left ventricular function expressed by a LVEF value ≤ 50%: a preoperative lower value of left ventricular ejection fraction (HR = 3.1; $P = 0.001$), a greater left atrium enlargement (HR = 2.1; $P = 0.03$), and the development of postoperative low cardiac output syndrome (HR = 2.4; $P = 0.01$). Partial preservation of papillary muscle in the course of MVR was identified as protective factor against the reduced left ventricular function only in the univariate analysis ($P = 0.01$).

Other analyzed results of the two surgical procedures of the postoperative period and during the follow-up are reported in the Supplementary Materials [Supplementary Figures 1-4].

DISCUSSION

Mitral surgery allows for the correction of severe mitral pathology by means of replacement or repair with an acceptable operative risk. In our study, the observed mortality was lower than 2% in both groups of patients. If it is also indicated early, i.e., before symptoms of heart failure onset, marked ventricular dilation, and reduced LVEF, it has been shown to improve long-term survival compared to medical therapy[12-15]. Degenerative disease is the most frequent etiology of mitral valve dysfunction in western countries, representing 60%-70%, i.e., 78.6% in our series, of mitral valves operated on. It is characterized by morphological changes mediated through glycosylaminoglycan and extracellular matrix alterations that can result in connective tissue disorder and, consequently, in significant dysfunction of the mitral valve. The degenerative disease can present itself in different ranges of presentation, i.e., isolated prolapse with or without flail of a single leaflet scallop, most often P2; bi-leaflet or exclusively anterior prolapse with excessive leaflet tissue; and annular dilation. Most cases of mitral valve insufficiency by degenerative disease can be repaired with current surgical techniques, and MV-repair represents the gold standard in this subset of patients. MV-repair is generally achieved by means of annuloplasty with a prosthetic ring to restore a normal annular geometry, increase leaflet coaptation, reduce tension on suture lines, and prevent future

dilatation. Leaflet resection with or without chordal procedure for the correction of the posterior leaflet prolapse is straightforward, and the long-term results are excellent, with a freedom from reoperation rate about 90% (range from 89.2% to 94%) following the repair at ten years of follow-up. The survival rate is very satisfactory in the long-term follow-up, ranging from 59% to 87%, depending on the average age of patients undergoing repair at surgery time[12,16,17]. Anterior leaflet and bi-leaflet prolapse are more difficult to repair, can require more complex techniques, and long-term results may not be as good as those for repair of prolapse of the posterior leaflet[12,13]. The advantages of repair over replacement are undoubtedly related to lower operative mortality, improved preservation of left ventricular systolic function, and greater late freedom from related prosthetic valves events. However, most published scientific papers comparing reparative versus replacement surgery are retrospective, and patients undergoing mitral repair were younger, with fewer co-morbidities. Moreover, with regard to the durability of repairs, it is important to note the proper standard for durability comparison is with mechanical valve replacement, as biological prostheses are known to be associated with limited durability in mitral position, with reoperation rate markedly increasing within ten years from the operation. Recently, an important multicenter study, the MIDA Database, after propensity matched score (2:1; MV-repair = 410, MVR = 205) showed that MV-repair compared with MVR for the treatment of mitral degenerative disease with leaflet flail was associated with lower operative mortality (0.2% *vs.* 4.4%; $P < 0.001$) and better survival at 10 (78% *vs.* 58%) and 20 years (46% *vs.* 23%) ($P < 0.001$)[18]. However, the greater benefit of the repair was evident in patients with posterior leaflet prolapse (78% of cases) compared with bi-leaflet (2%) or anterior leaflet (20%) prolapse, i.e., in the presence of a more complex pathology[18]. For these reasons, even today in current practice, especially in the presence of an older population and with different comorbidities, most surgeons perceive a reduction in the benefit of MV-repair in comparison with MVR and are hesitant to return to the operative room for an eventual unsuccessful repair. Indeed, the incidence of reoperation after MV-repair surgery is reported in the literature to be higher after anterior leaflet repair than posterior flap repair (28% *vs.* 11% at 15 years; $P = 0.0006$)[13].

For this reason, as well as based on our five-year experience on mitral surgery in a center of medium to high volume mitral procedures per year, we believe that valve repair is more effective for the treatment of degenerative pathology of the posterior leaflet rather than the anterior leaflet.

Obviously, the risk of structural valve deterioration of the biological prosthetic valves should be evaluated beyond the five-year follow-up period; however, to reduce the risk of a reoperation, in our center, we generally adopted the policy of implanting the biological prostheses in mitral position in patients of 70 years of age.

In our analysis of the results, we found that MVR and MV-repair gave results statistically similar in terms of both operative mortality (0.96% *vs.* 1.56%) [Table 3] and late survival (94% *vs.* 100%) [Figure 1] and late overall event-free survival, at least in the medium-term follow-up. Even in the population of older patients undergoing MVR with biological prostheses, six-year survival was satisfactory, with an incidence of prosthesis-related serious adverse events of 3.6%, not including non-cardiac related deaths. The postoperative complications rate was higher in the MVR group [Table 3], but this difference, as well as being not statistically significant, was likely related to a worse preoperative clinical presentation [Tables 1 and 2]. The only independent risk factor for reduced survival during follow-up was the most advanced age at surgery and not the type of mitral procedure [Table 6]. In fact, similar medium-term results were observed both in the MV-repair group in which the etiology was only degenerative, mainly of the posterior leaflet, and in the MVR group, in which there were cases affected by degenerative disease involving the entire valve, rheumatic and endocarditic etiology, with more complex and difficult pathologies

Table 6. Independent risk factors for late survival (multivariate analysis)

Variable	Hazard ratio	95%CI	*P*-value
Age at operation (79.2 years *vs.* 66.4 years)	1.3	1.07-1.67	0.012
Mitral valve surgery (replacement *vs.* repair)			0.158

liable for a possible repair.

A final aspect examined in our retrospective study, considered in the light of data presented in the literature, was that concerning the left ventricular function[19,20]. In the postoperative period, we clearly found that a lower preoperative LVEF was predictive of a higher risk of low cardiac output syndrome [Table 4]. Moreover, as also reported in the literature, we observed a better value of LVEF in the postoperative period and during follow-up in the MV-repair group in comparison with MVR [Table 5]. However, what emerged from our data is that, if the mitral valve was replaced with the partial preservation of its sub-valvular apparatus and papillary muscle, the ejection fraction value was higher than in patients in which it was completely removed, with values similar to those found in patients undergoing MV-repair, both in the postoperative period and during the follow-up [Supplementary Figures 1-4]. This testifies that primitively the impact on the left ventricular function depended on the possibility of being able to preserve the sub-valvular apparatus and not on the type of intervention, repair *vs.* replacement, "per se". Similarly, during the follow-up, we observed that a protective factor against the development of left ventricular dysfunction, i.e., LVEF value less than 50%, was the partial preservation of the sub-valvular apparatus.

The main limitations of our study are related to its retrospective nature, the medium-sized population sample operated on in a single center, and the medium- and non-long-term follow-up.

In conclusion, in current clinical practice, as in the case of the experience of our center, both MVR and MV-repair are associated with satisfactory results during short- and medium-term follow-up. The repair techniques for degenerative pathology of the posterior leaflet are associated with stable and long-lasting results; MVR allows equally good results to be obtained in cases of more extensive and more complex mitral valve disease. Partial preservation of the sub-valvular apparatus favors a better left ventricular systolic function.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study: Nardi P, Pisano C, Ruvolo G
Made contributions to perform data analysis and interpretation: Nardi P
Data acquisition, provided administrative, technical and material support: Bassano C, Bertoldo F, Salvati AC, Ferrante MS, Buioni D, Altieri C, Farinaccio A

Availability of data and materials

Surgical and Clinical Data Base of the Tor Vergata Polyclinic, Rome, Viale Oxford 81, 00133. Echographic data acquisition and interpretation: Altieri C.

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None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

The study was conducted according to the Declaration of Helsinki, and approved by the Independent Ethics Committee of the Tor Vergata University Polyclinic on 24 November 2021.

Consent for publication

Not applicable.

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REFERENCES

1. Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL. Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. *Circulation* 1995;91:1022-8. DOI PubMed
2. Gillinov AM, Blackstone EH, Nowicki ER, et al. Valve repair versus valve replacement for degenerative mitral valve disease. *J Thorac Cardiovasc Surg* 2008;135:885-93, 893.e1-2. DOI PubMed
3. Daneshmand MA, Milano CA, Rankin JS, et al. Mitral valve repair for degenerative disease: a 20-year experience. *Ann Thorac Surg* 2009;88:1828-37. DOI PubMed
4. Mick SL, Keshavamurthy S, Gillinov AM. Mitral valve repair versus replacement. *Ann Cardiothorac Surg* 2015;4:230-7. DOI PubMed PMC
5. Vahanian A, Alfieri O, Andreotti F, et al; Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC), European Association for Cardio-Thoracic Surgery (EACTS). Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J* 2012;33:2451-96. DOI PubMed
6. Vahanian A, Beyersdorf F, Praz F, et al; ESC/EACTS Scientific Document Group, ESC Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2021:ehab395. DOI PubMed
7. Akins CW, Miller DC, Turina MI, et al; Councils of the American Association for Thoracic Surgery, Society of Thoracic Surgeons, European Assoication for Cardio-Thoracic Surgery, Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity. Guidelines for reporting mortality and morbidity after cardiac valve interventions. *J Thorac Cardiovasc Surg* 2008;135:732-8. DOI PubMed
8. Lang RM, Bierig M, Devereux RB, et al; American Society of Echocardiography's Nomenclature and Standards Committee, Task Force on Chamber Quantification, American College of Cardiology Echocardiography Committee, American Heart Association, European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006;7:79-108. DOI PubMed
9. Zoghbi W. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and doppler echocardiography. *J Am Soc Echocardiogr* 2003;16:777-802. DOI PubMed
10. Nardi P, Vacirca SR, Russo M, et al. Cold crystalloid versus warm blood cardioplegia in patients undergoing aortic valve replacement. *J Thorac Dis* 2018;10:1490-9. DOI PubMed PMC
11. Schubert SA, Mehaffey JH, Charles EJ, Kron IL. Mitral valve repair: the French correction versus the American correction. *Surg Clin North Am* 2017;97:867-88. DOI PubMed PMC
12. McNeely CA, Vassileva CM. Long-term outcomes of mitral valve repair versus replacement for degenerative disease: a systematic review. *Curr Cardiol Rev* 2015;11:157-62. DOI PubMed PMC
13. Mohty D, Orszulak TA, Schaff HV, Avierinos JF, Tajik JA, Enriquez-Sarano M. Very long-term survival and durability of mitral valve repair for mitral valve prolapse. *Circulation* 2001;104:I1-7. DOI PubMed
14. Ling LH, Enriquez-Sarano M, Seward JB, et al. Early surgery in patients with mitral regurgitation due to flail leaflets: a long-term outcome study. *Circulation* 1997;96:1819-25. DOI PubMed
15. Nardi P, Pellegrino A, Scafuri A, et al. Survival and durability of mitral valve repair surgery for degenerative mitral valve disease. *J Card Surg* 2011;26:360-6. DOI PubMed
16. Suri RM, Schaff HV, Dearani JA, et al. Survival advantage and improved durability of mitral repair for leaflet prolapse subsets in the current era. *Ann Thorac Surg* 2006;82:819-26. DOI PubMed
17. Gardner MA, Hossack KF, Smith IR. Long-term results following repair for degenerative mitral regurgitation - analysis of factors influencing durability. *Heart Lung Circ* 2019;28:1852-65. DOI PubMed
18. Lazam S, Vanoverschelde JL, Tribouilloy C, et al; MIDA (Mitral Regurgitation International Database) Investigators. Twenty-year outcome after mitral repair versus replacement for severe degenerative mitral regurgitation: analysis of a large, prospective, multicenter, international registry. *Circulation* 2017;135:410-22. DOI PubMed

19. Hannan EL, Samadashvili Z, Smith CR, et al. Mitral valve repair versus replacement for patients with preserved left ventricular function without heart failure symptoms. *J Thorac Cardiovasc Surg* 2019;157:1432-9.e2. DOI PubMed
20. Suri RM, Schaff HV, Dearani JA, et al. Recovery of left ventricular function after surgical correction of mitral regurgitation caused by leaflet prolapse. *J Thorac Cardiovasc Surg* 2009;137:1071-6. DOI PubMed