Mitral Valve Repair in Patients With Low Left Ventricular Ejection Fractions*

Early and Late Results

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Study objectives: **This retrospective study was performed to examine the outcome of mitral valve repair (ie, mitral valvuloplasty [MVP]) in relation to preoperative low left ventricular ejection fraction (LVEF).**

Design and settings: **From our series of 338 consecutive patients who underwent MVP between 1983 and 2001, we compared the course of 302 patients with preoperative LVEF of > 35% (group I) to that of 36 patients with LVEF of ≤ 35% (group II).**

Results: **Preoperatively, group II patients were more likely to be associated with ischemic heart disease (IHD) [$p < 0.0002$], and to have undergone emergency surgery ($p < 0.02$) and concomitant coronary artery bypass graft surgery (CABG) [$p < 0.02$]. The perioperative mortality rate was 8% for group II and 2% for group I ($p < 0.03$). On multivariate analysis, predictors of increased operative mortality were emergent operation ($p < 0.001$) and preoperative New York Heart Association (NYHA) class IV ($p < 0.02$). Predictors of overall mortality (early and late) included emergency operation ($p < 0.02$), preoperative NYHA class IV ($p < 0.002$), and IHD ($p < 0.0001$). Postoperatively, 78% of patients from both groups were in NYHA class I/II. The 5-year rate of freedom from reoperation was 89%. The estimated overall 5-year survival rate (early and late) was 82% for group I and 54% for group II ($p < 0.02$), and when associated with prior CABG, prior myocardial infarction, or concomitant CABG, it was 0%, 37%, and 63%, respectively, in group II.**

Conclusions: **Good symptomatic relief and acceptable overall survival can be obtained in patients in both groups after they have undergone MVP, in the absence of serious comorbidities. Preoperative NYHA class IV and end-stage IHD increase early and late mortality, particularly in group II patients, in whom surgery may be a salvage effort only. Prognosis is dismal in group II patients who have previously undergone CABG. In chronic cases, an early referral for MVP electively before deterioration to end-stage heart disease would improve survival even in patients with low LVEF.** ***(CHEST 2004; 126:709–715)***

Key words: coronary artery bypass graft; end-stage heart disease; ischemic heart disease; left ventricular ejection fraction; low ejection fraction; mitral valve repair; mitral valvuloplasty; New York Heart Association functional class

Abbreviations: AF = atrial fibrillation; AP = annuloplasty; CABG = coronary artery bypass graft; IABP = intra-aortic balloon pump; IHD = ischemic heart disease; LV = left ventricle, ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MVP = mitral valvuloplasty; NYHA = New York Heart Association

Preoperative left ventricular ejection fraction (LVEF) has been shown to be an important prognostic indicator of outcome after mitral valve surgery.[1–5] The management of mitral regurgitation with preoperative low LVEF has been problematic.[5–8] Therefore, we retrospectively analyzed our experience with patients undergoing mitral valvuloplasty (MVP) to evaluate the influence of low LVEF on the outcome. We included only those patients in whom the preoperative LVEF had been recorded by angiography or echocardiography. Furthermore, unlike some other studies,[4,5] we also included patients who had undergone MVP with prior or concomitant coronary artery bypass graft (CABG) or with another valve operation.

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Patients and Methods

We studied 338 consecutive patients on our service at the Methodist Hospital who underwent mitral valve repair, either isolated or combined with other procedures, between 1983 and February 2001 by a single surgeon (G.M.L.). Patients ranged in age from 16 to 93 years (mean [± SD] age, 62 ± 15 years). The data were reviewed retrospectively (Tables 1, 2), and the patients were classified into the following two groups: (1) group I, with a preoperative LVEF of > 35% (302 patients; 89%); and (2) group II, with a preoperative LVEF of ≤ 35% (36 patients; 11%). Ischemic heart disease (IHD) included coronary artery disease, prior myocardial infarction (MI), prior CABG, and concomitant CABG.

Statistical Analysis

The database and its supporting programs were written in American National Standards Institute standard MUMPS language (M; Massachusetts General Hospital; Boston, MA [current version: DTM, version 6.4; InterSystems Corportation; Cambridge, MA]). Logistic and Cox regressions were performed with statistical software (BMDP Dynamic, version 7.0, SPSS Inc; Chicago, IL). χ^2 and t tests were performed using custom MUMPS code validated against BMDP. The univariate analysis was done using the χ^2 test for categoric variables and a pooled t test for continuous variables. The Kaplan-Meier method was used to estimate the long-term survival. The variables tested for the multivariate analysis included age, gender, LVEF of ≤ 35%, preoperative New York Heart Association (NYHA) class IV, IHD, non-sinus rhythm, leaflet pathology, emergency operation, and type of repair (as classified in Table 2). The risk factors were analyzed using a stepwise logistic regression for calculating the operative mortality, and the Cox regression was used to predict long-term survival.

Surgical Technique

The operative approach was a median sternotomy, using bicaval cannulation and ascending aortic return. Moderate systemic hypothermia and hemodilution were maintained during cardiopulmonary bypass. Crystalloid, high-potassium cardioplegia was used in all patients (antegrade until 1992, and retrograde [without adjunctive antegrade perfusion] beginning in 1993). Intraoperative transesophageal echocardiography has been an indispensable step in the use of MVP. After a precise diagnosis of the problem, MVP was performed using the surgical techniques listed in Table 2. Mitral regurgitation was the predominant finding in all patients, but only 16 (5%) had associated mitral stenosis (group I, 14 patients; group II, 2 patients). Repair (*ie*, resection/plication) involved neither leaflet in 221 patients (65%), both leaflets in 28 patients (8%), and a single leaflet in 89 patients (26%) [anterior leaflet, 24 patients (7%); posterior leaflet, 65 patients (19%)]. Chordal repair included chordal shortening in 1 patient, chordal transfer in 1 patient, and chordal replacement with polytetrafluoroethylene in 169 patients (anterior leaflet, 92 patients; posterior leaflet, 106 patients). The types of annuloplasty (AP) were as follows: Kay AP, 36 patients (11%); adjustable, flexible ring AP using a Puig-Massana ring, 208 patients (62%); and adjustable, flexible ring AP using other rings (including a St. Jude Medical Tailor ring), 94 patients (28%). A commissurotomy was performed in 16 patients (5%). Pericardial patches and other miscellaneous procedures were performed in some. Concomitant cardiac procedures were performed in 134 patients (40%) [CABG, 79 patients (23%); aortic valve replacement, 27 patients (8%); other procedures, 62 patients (18%)]. The mean (± SD) bypass time was 81 ± 29 min for group I and 99 ± 34 min for group II ($p < 0.004$). The mean aortic cross-clamp time was 61 ± 25 min for group I and 70 ± 22 min for group II (difference not significant). After repair, the systolic anterior motion of any severity was found in only four patients (small annulus and small left ventricular (LV) cavity, three patients; large posterior leaflet, one patient). Three patients improved intraoperatively by loosening the AP, and the condition of one patient resolved.

Table 1—*Patient Characteristics**

Characteristics	Patients, No. Total	Group I	Group II	p Value
Total	338 (100)	302	36	
Gender				
Male	167 (49)	144	23	
Female	171 (51)	158	13	
Age > 65 yr	163 (48)	143	20	
NYHA				
Non-class IV	273 (81)	248	25	
Class IV	65 (19)	54	11	
No IHD	210 (62)	198	12	< 0.0002
IHD	128 (38)	104	24	
Prior MI	56 (17)	40	16	< 0.0001
No prior MI	282 (83)	262	20	
Prior CABG	19 (6)	13	6	< 0.003
No prior CABG	319 (94)	289	30	
Concomitant CABG	79 (23)	65	14	< 0.02
No concomitant CABG	259 (77)	237	22	

*Values in parentheses are %.

Table 2—*Operative Profile**

Variables	Patients, No. Total	Group I	Group II	p Value
Elective operation	325 (96)	293	32	< 0.02
Emergency operation	13 (4)	9	4	
Leaflet repair ± AP	70 (21)	65	5	
Leaflet + chordal repair ± AP	47 (14)	46	1	< 0.003
Chordal repair ± AP	124 (37)	111	13	
Annuloplasty alone	97 (29)	80	17	

*Values in parentheses are %. ± = with or without.

Results

Preoperative rhythm was sinus/paced sinus in 171 patients (51%), atrial fibrillation (AF) or paced AF in 103 patients (30%), and other in 64 patients (19%). The mean LVEF values were 55 ± 13% for the entire cohort, 58 ± 10% for group I patients, and 30 ± 4% for group II patients. The values of LVEF utilized for this study were the last values recorded immediately prior to operation, therefore, some were after intensive medical therapy in the hospital. In group II patients, the LVEF was 26 to 35% in 27 patients, 21 to 25% in 7 patients, and 16 to 20% in 2 patients. An intra-aortic balloon pump (IABP) was required preoperatively in 17 patients (5%), of whom

9 were in NYHA class IV ($p < 0.0003$), 15 had IHD ($p < 0.0001$), and 5 underwent emergency surgery ($p < 0.0001$). The median age was 65 years (different not significant for groups I and II). There were 163 patients (48%) > 65 years of age, of whom 42 were in NYHA class IV ($p < 0.004$), 79 had IHD ($p < 0.0001$), 20 were in group II (difference not significant), and 7 underwent emergency surgery (difference not significant). The mitral valve pathology (not mutually exclusive) was myxomatous in 179 patients (53%), degenerative in 99 patients (29%), ischemic in 33 patients (10%), rheumatic in 28 patients (8%), and other (including endocarditis) in 33 patients (10%), and Barlow disease was present in 2 patients. Significantly more patients with IHD were in NYHA class IV (32 of 128 patients [25.0%] vs 33 of 210 patients [15.7%], respectively; $p < 0.04$).

Operative Mortality

Nine patients (2.6%) with multiple comorbidities died within 30 days of undergoing the operation (group I, 6 of 302 patients [2%]; group II, 3 of 36 patients [8%]; $p < 0.03$). Five patients were diabetic, and five patients were > 65 years old. Preoperatively, six patients were in NYHA class IV, five patients had prior MIs, four patients had undergone emergency surgery, three patients had endocarditis (one of whom had undergone a prior aortic valve replacement), one patient had experienced cardiac arrest and cerebral encephalopathy, and one patient had required an IABP. The intraoperative IABP was required in six patients. Concomitant CABG was performed in five patients. The cause of death was cited as multisystem failure in all. All three of the group II patients had been in NYHA class IV and had IHD, and the preoperative LVEF was 30% in one patient and was 21 to 25% in the other two patients. There was a significant increase in the mortality in patients in group II compared to those in group I who had prior MIs ($p < 0.008$) or had undergone concomitant CABG ($p < 0.001$). Tables 3 and 4 list the predictors of operative mortality by univariate and multivariate analysis, respectively.

Table 3—*Risk Factors for Operative Mortality: Univariate Analysis*

Risk Factor	p Value
Emergency operation	< 0.0001
Preoperative NYHA class IV	< 0.0003
Preoperative NYHA class IV + IHD	< 0.002
Prior MI	< 0.007
Concomitant CABG	< 0.04
Group II	< 0.03

Table 4—*Operative Mortality: Multivariate Analysis (Stepwise Logistic Regression Analysis)**

Risk Factor	OR (95% CL)	p Value
Emergency operation	5.9 (1.3, 26.9)	0.001
Preoperative NYHA class IV, status	17.2 (3.6, 83.2)	0.02

*CL = confidence limits; OR = odds ratio.

Long-term Results

Postoperatively, 78% patients were in NYHA class I/II in both groups. Mitral regurgitation was absent or mild in 96% of patients, and moderate in 4%. Follow-up was obtained by a questionnaire that was sent to the patients each year on the anniversary of their operation. It was 95% complete. The range of follow-up was 4 days (0.01 years) to 16 years (mean, 4.0 ± 3.0 years). For the overall group, the rate of freedom from reoperation at 5 years was 89%, and it was 77% for patients with preoperative NYHA class IV plus IHD. The overall long-term mortality rate includes the operative mortality rate from this study. The estimated overall 5-year survival rate was 79% for the entire cohort (338 patients) [Fig 1], 82% for group I and 54% for group II (Fig 2) [$p < 0.02$]. Various factors affecting long-term survival are listed in Tables 5, 6, 7, and 8. If the operative deaths are excluded, the 5-year survival rate was 81% for the operative survivors (329 patients), 84% for group I patients, and 59% for group II patients (difference not significant). Tables 9 and 10 list the independent predictors of long-term mortality for the entire cohort and for operative survivors, respectively, by multivariate analysis.

Discussion

The management of mitral regurgitation is problematic in patients with preoperative low LVEF, particularly when associated with IHD or end-stage heart failure. In some series on MVP,[2] the patients with low LVEF and IHD were excluded, and in some[9] the effect of LVEF has not been analyzed. Our study included patients with low LVEF, IHD, and NYHA class IV status. Some previous studies[10] on MVP defined low LVEF as an LVEF of < 50%, as opposed to the value of ≤ 35% used in our study.

Low LVEF, IHD, and Other Risk Factors for MVP

Kay and colleagues[1,2] and Rankin et al[11] have documented acceptable early and intermediate-term results of MVP in patients with ischemic mitral regurgitation. In this study, IHD was the most significant independent predictor of late mortality.

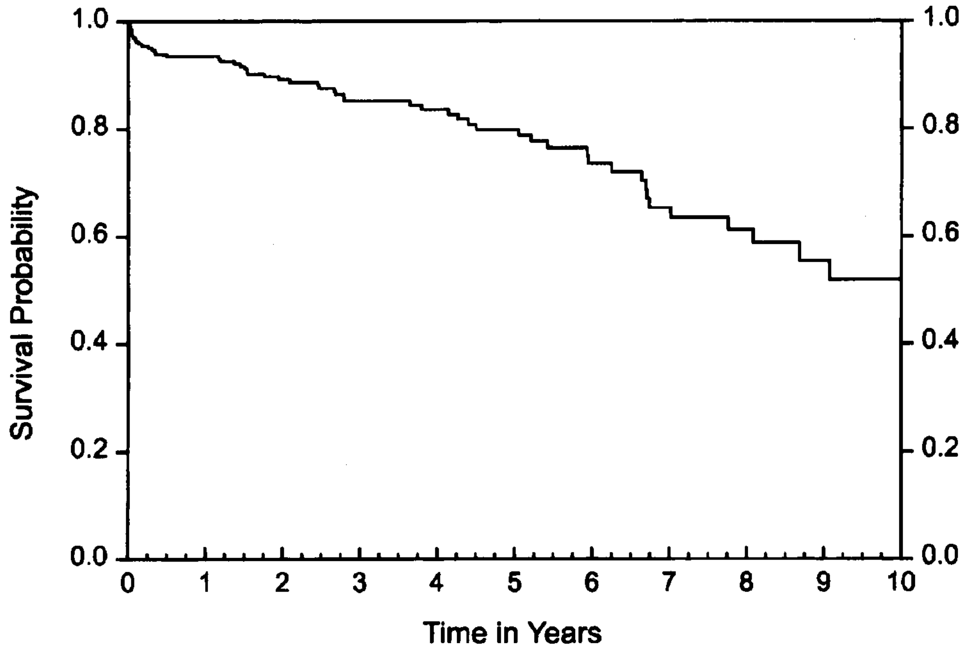

FIGURE 1. Kaplan-Meier overall survival estimates after MVP for the entire cohort (338 patients).

The preoperative NYHA class IV was the most important independent predictor of early and late mortality in our study. Compared to patients in group I, those in group II were more ill and had a significantly higher association with IHD, emergency surgery, and the use of AP alone as the type of repair. The conjoint effect of comorbidities, preoperative NYHA class IV status, and IHD was to decrease overall survival in both groups, but particularly in group II. Thus, end-stage heart disease, and especially end-stage IHD, had a drastically adverse effect in conjunction with low LVEF. On the other hand, low LVEF was not a significant risk factor *per se* on multivariate analysis.

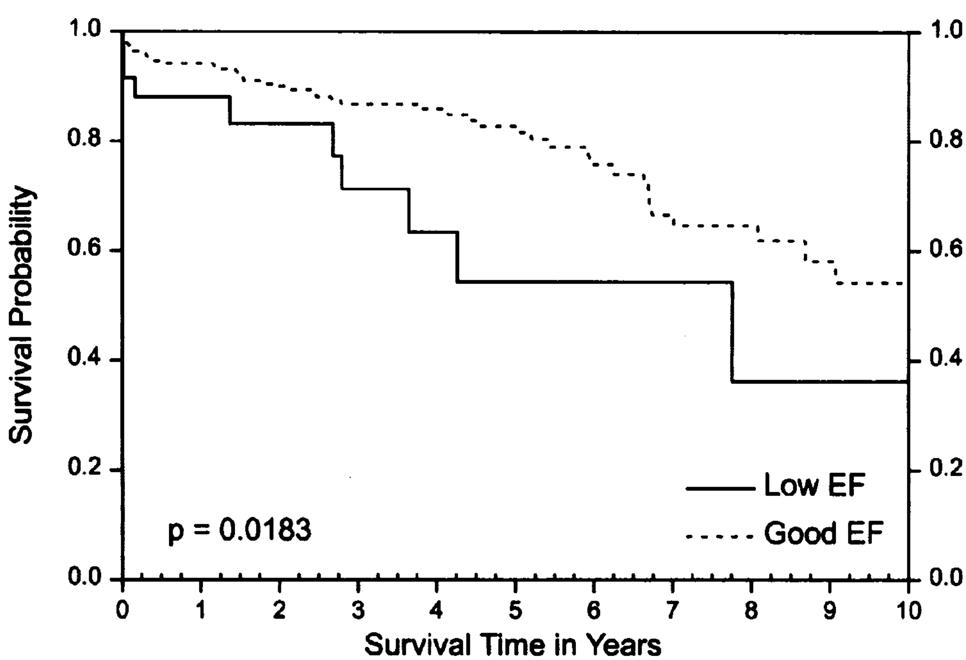

FIGURE 2. Kaplan-Meier overall survival estimates after MVP for patients in group I (302 patients) and group II (36 patients).

Table 5—*Overall Survival (Early + Late) After Mitral Valvuloplasty**

Variables	Kaplan-Meier Estimation of 5-yr Survival Rate, %	p Value†
Entire cohort	79	
Group I	82	< 0.02
Group II	54	
Preoperative NYHA non-class IV status	84	< 0.001
Preoperative NYHA class IV status	63	
No IHD	91	< 0.001
IHD	60	
Age < 65 yr	80	NS
Age > 65 yr	78	
Leaflet repair ± AP	95	
Leaflet + chordal repair ± AP	92	< 0.003
Chordal repair ± AP	81	
Annuloplasty alone	62	

*NS = not significant. Table 2 for abbreviations not used in the text.
†For 5 to 10-year survival rate.

Table 7—*Kaplan-Meier Estimation of Overall (Early + Late) Survival After MVP in Relation to Preoperative NYHA Class**

Variables	Patients, No.	5-yr Survival Rate, %	p Value†
NYHA non-class IV status + group I	248 (73)	85	
NYHA non-class IV status + group I	25 (7)	71	< 0.0001
NYHA class IV status + group I	54 (16)	69	
NYHA class IV status + group II	11 (3)	24	
No IHD + NYHA non-class IV status	177 (52)	93	
No IHD + NYHA class IV status	33 (10)	81	< 0.0001
IHD + NYHA non-class IV status	96 (28)	67	
IHD + NYHA class IV status	32 (9)	44	

*Values in parentheses are %.
†For 5 to 10-year survival rate.

The survival benefits of mitral valve surgery over medical treatment have been shown in the presence of mitral regurgitation and poor LV function in chronic, severe, nonischemic cases[12] as well as in cases of ischemic cardiomyopathy.[13] The study of Gangemi et al[13] demonstrated improved survival and symptomatic status following MVP compared to cardiac transplantation or CABG alone. Bolling[14] has advocated a combined approach of MVP and optimal medical management of heart failure in patients with end-stage cardiomyopathy with an LVEF of < 25% and refractory mitral regurgitation as a way to improve survival and avoid or postpone cardiac transplantation. In our series, the overall 5-year survival rates in group II patients who had previously received a CABG or had a prior MI were significantly low at 0% and 37%, respectively. If group II patients with a chronic course had been referred for the mitral valve surgery earlier, before the deterioration

Table 6—*Kaplan-Meier Estimation of Overall (Early + Late) Survival After Mitral Valvuloplasty In Relation to IHD and LVEF**

Variables	Patients, No.	5-yr Survival Rate, %	p Value†
No IHD + group I	108 (32)	91	
No IHD + group II	12 (4)	92	< 0.0001
IHD + group I	104 (31)	64	
IHD + group II	24 (7)	43	
No prior MI + group I	262 (78)	84	
No prior MI + group II	20 (6)	81	< 0.0001
Prior MI + group I	40 (12)	67	
Prior MI + group II	16 (5)	37	
No prior CABG + group I	289 (86)	84	
No prior CABG + group II	30 (9)	78	< 0.0001
Prior CABG + group I	13 (4)	32	
Prior CABG + group II	6 (2)	0	
No concomitant CABG + group I	237 (70)	85	
Concomitant CABG + group I	65 (19)	50	< 0.007
No concomitant CABG + group II	22 (7)	71	
Concomitant CABG + group II	14 (4)	63	

*Values in parentheses are %.
†For 5 to 10-year survival rate.

Table 8—*Overall Survival (Early + Late) in Relation to Technique of MVP*

Variables	Kaplan-Meier Estimation of 5-year Survival Rate, %	p Value*
Other repair	86	< 0.0009
AP alone	62	
Group I + other repair	87	
Group I + AP alone	65	< 0.003
Group II + other repair	65	
Group II + AP alone	48	
Other repair + preoperative NYHA non-class IV status	89	
Other repair + preoperative NYHA non-class IV status	74	< 0.0001
AP alone + preoperative NYHA non-class IV status	69	
AP alone + preoperative NYHA non-class IV status	46	
No IHD + other repair	94	
No IHD + AP alone	79	< 0.0001
IHD + other repair	69	
IHD + AP alone	43	

*For 5 to 10-year survival rate.

Table 9—*Overall Mortality (Early + Late): Multivariate Analysis (Cox Regression)**

Variables	RR (95% CL)	p Value
Factors associated with increased mortality		
IHD	4.5 (2.5, 8.0)	< 0.00001
Preoperative NYHA class IV status	2.6 (1.5, 4.4)	< 0.002
Emergency operation	5.0 (1.7, 14.8)	< 0.02
Preoperative non-sinus rhythm	1.9 (1.1, 3.4)	< 0.03
Factors associated with less mortality		
Leaflet repair only ± AP	0.2 (0.06, 0.55)	0.0003

*RR = relative risk. See Tables 2 and 4 for abbreviations not used in the text.

in their NYHA class functional status or IHD, a better late survival rate might have been achieved in some cases, as occurred in group I. A study by Chen et al[15] et al has shown that MVP in the setting of ischemic cardiomyopathy and low LVEF appears to prolong survival and improve ventricular function. Their study also demonstrated that those with an LVEF of ≤ 20% did not fare worse than those with an LVEF between 20% and 30%, as the decline in myocardial function has already occurred at such low levels of LVEF. They postulated that MVP appears to prolong survival when offered before LVEF falls below 30% and heart failure symptoms occur.

Other investigators[4] have noted that advanced age and preoperative AF reduce survival. Almost half of the patients in our series were > 65 years old, yet the age did not affect either early or late mortality significantly in our series. However, preoperative non-sinus rhythm contributed significantly to overall mortality.

Importance of Preoperative NYHA Status

Although NYHA functional status is subjective, it is a highly important prognostic indicator of immediate as well as long-term survival after MVP.[1,3–5,12–15] Therefore, MVP should be offered before a deterioration in symptoms occurs in chronic cases. Furthermore, even in patients in preoperative NYHA class IV status, earlier surgery gives a better outcome.[9,15,16] This was also reflected in the fact that performance of an emergency operation was an independent predictor of operative mortality; but in those patients who survived the operation, it did not affect the long-term mortality. If a patient presenting emergently in a precarious state cannot be stabilized by administering maximal medical therapy and IABP, and ends up undergoing an emergency MVP for correction of mitral insufficiency, the risk of operative mortality is extremely high, especially in the setting of NYHA class IV status. On the other hand, a better overall survival rate can be achieved even in patients with low LVEF by electively offering MVP in chronic cases before the deterioration of functional status.

Table 10—*Late Mortality (for Operative Survivors): Multivariate Analysis (Cox Regression)**

Variables	RR (95% CL)	p Value
Factors associated with increased mortality		
IHD	4.8 (2.4, 9.7)	< 0.00001
Preoperative NYHA class IV status	2.4 (1.3, 4.3)	< 0.007
Preoperative non-sinus rhythm	2.4 (1.3, 4.5)	< 0.007
Factors associated with less mortality		
Abnormal leaflet		
Nonischemic valve pathology	0.4 (0.2, 0.8)	< 0.03
Ischemic valve pathology	0.3 (0.1, 0.9)	< 0.04
Leaflet repair only ± AP	0.4 (0.1, 1.0)	< 0.03

*See Tables 2, 4, and 9 for abbreviations not used in the text.

Repair Techniques for MVP

The abnormalities of various components of the mitral valve were corrected using a variety of well-established techniques.[7,8,16–21] As in other series,[3–5,17,22,23] the posterior leaflet repair was the most common leaflet repair performed in our series. However, we also employed anterior leaflet repair in some cases. MVP involving only leaflet repair and AP gave the best overall survival on multivariate analysis, compared to MVP involving AP alone. This is because the mitral insufficiency resulting from abnormal leaflets or chordae, without a gross dilatation of the mitral valve annulus is more amenable to a satisfactory repair and is more often of nonischemic origin. IHD lowered the overall survival in all patients with any type of MVP,[2,3,5,6,11] but particularly more so in those with dilated ischemic cardiomyopathy with normal leaflets and chordae, and a dilated annulus requiring AP alone without leaflet/chordal repair for correction of mitral insufficiency. Nevertheless, in contrast to mitral valve replacement, MVP in patients with a compromised LV can give acceptable morbidity and mortality, and an improved LV function in the long term,[2,3,5,6,10,11,20,23–26] as the LV remodels to a smaller, more ellipsoid ventricle.

Limitations of the Study

Our goal was to find out whether MVP can give good results in a group of patients with low LVEF, with or without IHD. It was not our objective to do a comparative analysis with mitral valve replacement, cardiac transplantation, or medical treatment alone. As the patient populations differ significantly, such a comparison is problematic. Mitral valve regurgitation due to ischemia is known to be a greater risk than nonischemic mitral regurgitation associated with coexistent IHD. Nevertheless, due to the small sample size, we analyzed these two subsets together as mitral regurgitation with IHD. We did not compare acute vs chronic mitral valve regurgitation. This, along with the small sample size of group II and the retrospective nature of the study, are the limitations of our series.

Conclusions

There are several well-known advantages of MVP,[1–26] such as excellent durability and freedom from reoperation, freedom from thromboembolism and anticoagulant-related complications, freedom from endocarditis, and good symptomatic relief. Our study confirmed that acceptable results can be obtained even in patients with low LVEF values. A total of 78% of patients from both groups I and II were in NYHA class I/II postoperatively, with absent or mild mitral insufficiency in 96%. In the absence of serious comorbidities, a good overall survival rate and improved functional status can be obtained in group II as well as in group I. The risks of MVP in group II patients with prior CABG or end-stage coronary artery disease are very high. IHD and advanced functional status of the patient undergoing MVP seemed to play a more important role than low LVEF. When mitral insufficiency is secondary to severe ventricular dilatation from ischemic cardiomyopathy, and especially when the patients present long after the prior CABG, this appears to be an end-stage population in whom surgery should be considered as a salvage effort only and as an option along with maximal medical therapy or cardiac transplantation. In chronic cases, survival in group I as well as group II patients can be improved by offering MVP electively before a patient becomes moribund with end-stage disease and an irreversible decline in myocardial function sets in. Therefore, in nonemergency cases, surgery should not be delayed until the appearance of severe symptoms, and an early referral for MVP should be encouraged despite the presence of a low LVEF.

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