

# MITRAL VALVE SURGERY IN PATIENTS WITH DEGENERATIVE MITRAL REGURGITATION AND LOW LEFT VENTRICULAR EJECTION FRACTION

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## ABSTRACT

**Objectives :** The objective of this study is to evaluate survival and changes in left ventricular dimensions and function following mitral valve surgery in patients with mitral regurgitation due to degenerative disease and low left ventricular ejection fraction (EF <40%).

**Methods :** Mitral valve surgery was performed in 51 patients (43 men and 8 women, mean age  $59 \pm 14$  years). All patients had myxomatous mitral valve disease. Patients with CAD were excluded. Thirty-seven patients (72%) had EF between 20-40% and 14 patients (28%) had EF <20%. Most patients (80%) were in NYHA

classes III and IV. All patients were on optimal medical therapy. Twenty-nine patients (57%) had mitral valve repair and 22 patients (43%) had mitral valve replacement with maintenance of the attachments between papillary muscles and mitral annulus. The mean  $\pm$  SD duration of follow-up was  $5.9 \pm 3.9$  years and was complete.

**Results :** There was one operative death (1.9%) and 20 (39%) late deaths, 10 (19.5%) were cardiac related. Five-year survival was  $82 \pm 5\%$ . & 95% of survivors were in NYHA classes II and I. Five-year freedom from reoperation was  $97 \pm 2\%$ . Five-year freedom from valve-related morbidity or mortality was  $95 \pm 3\%$ . All pa-

tients had echocardiographic assessment of LV function at  $3.4 \pm 2.6$  months (Mean  $\pm$  SD) postoperatively and the results are shown in the table below:

Variable	Preoperative (N)	Postoperative (N)	"p" value
Severity of Mitral regurgitation			
▪ 0	0	30	<0.0001
▪ 1	0	15	
▪ 2	0	3	
▪ 3	1	1	
▪ 4	50	0	
LV EF			
➤ 60%	0	9	<0.0001
➤ 40-60%	0	25	
➤ 20-40%	37	12	
➤ <20%	14	2	
Mean LV end-systolic diameter (mm)	44.7 $\pm$ 8.5	40.8 $\pm$ 9	0.02
Mean LV end-diastolic diameter (mm)	59.7 $\pm$ 7	54.4 $\pm$ 9.5	0.002
Mean Left Atrial Diameter (mm)	53.4 $\pm$ 9.1	47.4 $\pm$ 11.3	0.003

**Conclusion :** Mitral valve surgery improves left ventricular function and dimensions in patients with degenerative mitral regurgitation and LV dysfunction. It also offers symptomatic improvement and late survival benefit in this patient population.

## INTRODUCTION

Degenerative mitral valve disease is currently the most common cause of mitral regurgitation especially in North America and Europe. (1) Mitral regurgitation leads to chronic volume

overload of the left ventricle, progressively leading to left ventricular dysfunction. (2) Preoperative LV ejection fraction (EF) is a powerful predictor of postoperative heart failure and death. However, preoperative low left ventricular ejection fraction has been associated with an adverse clinical outcome in patients with mitral regurgitation, regardless of the type of surgery used for correction of chronic MR(3). Many reports have shown the effects of mitral valve repair or replacement for ischemic mi-

tral regurgitation and impaired left ventricular function. (4) However, to our knowledge, the studies about the effects of mitral valve surgery in patients with degenerative (myxomatous) mitral regurgitation and low ejection fraction very few.

The objective of this study is to evaluate the impact of mitral valve surgery "repair or replacement" on survival and changes in left ventricular dimensions and function in patients with severe mitral regurgitation due to degenerative disease and low left ventricular ejection fraction (EF < 40%).

## PATIENTS & METHODS

This study is a retrospective one involving patients who underwent mitral valve surgery (repair or replacement), due to degenerative mitral regurgitation and low LV ejection fraction. All patients had been operated upon at Cardiovascular Surgery Division, Toronto General Hospital, Toronto, Ontario, Canada during the period from 1995 to 2000.

## STUDY POPULATION

This study consists of 51 patients

with isolated severe or moderately severe mitral regurgitation and depressed LV function (EF <40%) without associated coronary artery disease as documented by Echocardiography and Coronary angiography studies.

### *Exclusion Criteria :*

Excluded from the study patients with :

1. Ischemic mitral regurgitation.
2. Rheumatic heart disease.
3. Predominant mitral stenosis.
4. Associated severe tricuspid regurgitation.

### *Patient's Evaluation:*

Patient's evaluation was performed through:

1. Review of patient's medical charts in Medical Records.
2. Outpatient clinical evaluation.
3. Telephone and fax communication with the patient's cardiologist office.

Patient's charts have been reviewed thoroughly regarding:

1. Clinical presentation, especially New York Heart Association (NYHA) functional class.
2. Patient's medications.
3. Pre- and postoperative Echocardi-

ography.

4. Operative notes for operative details: type of surgery (repair or replacement), technique of repair, type of prosthetic valve, X-clamp time, etc...
5. Operative mortality.
6. Follow-up Echocardiography.
7. Follow-up notes: survival and clinical status.

All patients had preoperative LV ejection fraction less than 40% as determined by echocardiography. The selection of LV ejection fraction less than 50% as the cut-off point between normal and depressed LV function was based on Veterans Administration Co-operative Study on Heart Valve Disease.

#### *Echocardiography :*

All patients were evaluated with transthoracic (TTE) and transesophageal (TEE) echocardiography within 3 months before surgery. Also, TEE was performed routinely intra-operatively specially in mitral valve repair cases at the conclusion of cardiopulmonary bypass.

#### *Transthoracic echocardiography*

(TTE) was repeated before patient's discharge from the hospital, within 3 months after surgery and then yearly after that. The results presented here are comparison between the preoperative and the last follow-up echocardiography.

Left ventricular (LV) systolic function was estimated from LV end-systolic diameter in mm (LVESD), LV end-diastolic diameter (LVEDD) and Ejection Fraction (EF %). EF was calculated using the modified Simpson method.

Mitral Regurgitation (MR) was evaluated semi-quantitatively by Color-Doppler imaging at TTE and TEE. The degree of mitral regurge was graded as follows:

Grade 1: Mild MR

Grade: Moderate MR

Grade 3: Moderately severe MR

Grade 4: Severe MR.

Finally, Echocardiography was utilized to estimate the size and diameter of left atrium (LA) in mm.

#### *Mitral Valve Surgery :*

Mitral valve repair was done in 29 patients (57%). Twenty-two patients

(43%) had mitral valve replacement with maintenance of the attachment between papillary muscles and mitral valve annulus.

The decision to repair or replace the mitral valve was dependent on:

- The anatomy of the mitral valve, fibrosis, degree of leaflet prolapse, annular dilation etc...
- Patient's age
- Cardiac rhythm whether sinus or AF, preoperative oral anticoagulation.
- Surgeon's experience.

This study is not a prospective randomized study and the aim is not to compare repair Vs replacement.

All patients were operated at the same center (Toronto General Hospital, CANADA) by the same group of surgeons.

#### *Follow-up :*

The mean follow-up period was  $5.9 \pm 3.9$  years (Range: 4.9- 11 years) and it was complete for all patients. Patient's follow-up was performed by evaluation at outpatient clinic yearly

and through communication with patient's cardiologist by phone or fax.

#### *Statistics :*

Statistical analysis was performed using the Statistical Package for the Social Science (SPSS) software, Version 16.

Numerical variables were expressed as mean  $\pm$  SD. Group comparisons were performed with standard student t-test or Chi-Square test as appropriate. The Kaplan-Meier method was used to estimate the cumulative probability of survival, clinical event-free survival. A p value of  $<0.05$  was considered as significant.

## RESULTS

The study included 51 patients, 43 male (84%) and 8 women (16%). The mean age of our patients was  $59 \pm 14$  years (range: 48 - 68 years). All patients had myxomatous mitral valve disease as an etiology for the mitral regurgitation. Half of the patients (51%) had preoperative sinus cardiac rhythm, 45% had atrial fibrillation and only 4% had permanent pace maker before surgery. The vast majority of

the patients (98%) were in NYHA class III and IV

Patient's demographics and pre-operative clinical characteristics are presented in Table (1) .

Clinically, the patient's functional class was improved significantly in the postoperative period compared to the preoperative status.

While 80% of the patients were in class III & IV in the preoperative period, 75% in the postoperative status became in class I & II which was statistically significant (p value = 0.001)

The vast majority of our patients (98%) had severe degree of mitral regurgitation, only one patient had moderately severe MR. Thirty seven patients (72%) had grade 3 LV function i.e. ejection fraction between 20 to 40%, while 14 (28%) patients had ejection fraction less than 20%. Both LV end-systolic and end-diastolic diameters were dilated in all patients. The mean LVESD was 44.7mm, while the mean LVEDD was 59.8mm. Also, left atrium was dilated in all patients, the mean diameter was 53.4 mm.

Twenty-nine patients (57%) had mitral valve repair and 22 patients (43%) had mitral valve replacement with maintenance of the attachments between papillary muscles and mitral valve annulus to preserve the LV function.

Different techniques have been used to repair the mitral valve: Chordal shortening or artificial chordae tendinea using 3/0 Gortex sutures, Triangular or quadrangular resection of the posterior leaflet, insertion of prosthetic ring to reduce the circumference of the mitral valve annulus. (Table 3).

Mitral valve replacement was performed utilizing prosthetic mechanical valves in 9 patients, and tissue bioprosthetic valves in 13 patients. In all cases, the continuity between the mitral valve annulus and papillary muscles was maintained by preservation of chordae tendinea & part of or the whole leaflet. The aim was to preserve ventricular function as much as we can. (Table 3).

The mean aortic x-clamp time in both groups was  $43 \pm 9$  minutes, and

the cardiopulmonary bypass time was  $71 \pm 6$  minutes.

In all cases of mitral valve repair, there was no significant degree of mitral regurgitation as confirmed by intraoperative TEE and postoperative TTE. While in the follow-up period, 3 patients developed moderate MR and 3 patients moderately severe MR which was an indication for reoperation.

### MORTALITY

There was one operative death (1.9%) and twenty (39%) late deaths, 10 of which (19.5%) were cardiac-

related. The other 10 patients (19.5%) died because of other non-cardiac causes. The operative mortality was due to severe pulmonary hypertension and the patient developed acute right sided heart failure and could not be weaned from heart-lung machine.

Five-year survival was  $82 \pm 5\%$ . Seventy-five (75%) of survivors were in NYHA class I & II.

Five-year freedom from reoperation was  $97 \pm 2\%$ . Five-year freedom from valve-related morbidity or mortality was  $95 \pm 3\%$ .

**Table (1): Patient's demographics and preoperative clinical characteristics**

<b>Total No. of patients:</b> 51 patients		
<b>Age</b>	Mean $\pm$ SD	59 $\pm$ 14 Years (Range: 48 – 68 years )
<b>Sex</b>	Male:	43 (84%)
	Female:	8 (16%)
<b>Underlying Mitral Valve Disease</b>		
	Degenerative:	51 (100%)
	Ischemic MR:	0
	Rheumatic MR:	0
<b>Cardiac Rhythm:</b>		
	Sinus:	26 (51%)
	Atrial Fibrillation:	23 (45%)
	Paced:	2 (4%)
<b>Preoperative NYHA Class:</b>		
	Class II:	12 (16%)
	Class III:	20 (41%)
	Class IV:	19 (37%)
Preoperative NYHA Class No. (%)		Postoperative NYHA Class No. (%)
NYHA Class I	0 (0%)	13 (26%)
II	10 (19.6%)	24 (48%)
III	16 (31.4%)	11 (22%)
IV	25 (49%)	2 (4%)
		p value = 0.001

**Table (2): Preoperative Echocardiographic Data & Measurements:**

Parameter	Number (%)
Degree of Mitral Regurgitation	
Moderately Severe	1
Severe	50
Ejection Fraction	
20 - 40%	37
< 20%	14
LV Measurements	
LVESD (mm)	44.7 (Range: )
Mean $\pm$ SD	59.8 (Range: )
LVEDD (mm)	
Mean $\pm$ SD	
LA Diameter (m)	53.4 (Range: )
Mean $\pm$ SD	

LVESD= Left ventricular end-systolic diameter, LVEDD= Left ventricular end-diastolic diameter, LA= Left atrial diameter



**Table (3):** Operative Data:

Techniques of Mitral valve repair **	15
Ring Annuloplasty	17
Chordal repair	29
Leaflet repair	
Type of Prosthetic valve	
Mechanical valve	9
Bioprosthetic valve	13
Cardiopulmonary Bypass Time (minutes)	71±6 minutes
Aortic x-clamp time (minutes)	43±9 minutes
Operative Mortality	1 (2%)

\*\* The average number of repair techniques / patient was 2.1

**Table (4) :** Comparison between Pre and Postoperative Echocardiographic Measurements:

Echocardiographic Parameter	Preoperative No.      %	Postoperative No.      %	P value
Degree of Mitral Regurgitation			
0	0 0	30	<0.0001
1	0 0	15	
2	0 0	3	
3	1    1.96	2	
4	50   98.04	0	
Ejection Fraction			
>60%	0 0	10 20	<0.0001
40-60%	0 0	25 50	
20-40%	37   72.5	13 26	
<20%	14   27.5	2   4	
LVESD	44.7±8 mm	41.2±7 mm	0.02
LVEDD	59.7±7 mm	53.2±6 mm	0.002
LAD	53.4±6	48±5	0.003

LVESD= Left ventricular end-systolic diameter, LVEDD= Left ventricular end-diastolic diameter, LA= Left atrial diameter

## DISCUSSION

Poor preoperative LV function has been associated with an adverse clinical outcome in patients with severe mitral regurgitation, while preoperative LV ejection fraction (EF%) may be a powerful predictor of postoperative heart failure & death, regardless the type of surgery used to correct mitral regurgitation.. This is generally attributed to the post-operative increase in LV afterload and abolition of the "pop-off" valve effect of the regurgitant leak, further decreasing the ejection fraction and cardiac output. (6)

The better clinical outcome after mitral valve surgery is directly related to the preservation of the subvalvular apparatus resulting in preservation of LV geometry. (7)

Patients with significant degree of LV systolic dysfunction (EF<40%) should undergo surgical correction of mitral regurgitation because a) surgical correction, compared to medical treatment, improves prognosis, and b) reduces the incidence of congestive heart failure. In this study, our aim was to study the effects of mitral

valve surgery on survival and LV function and dimensions in patients with poor LV function associated with severe mitral regurge due to only degenerative (myxomatous) mitral valve disease. Numerous reports studied the effects of surgery in ischemic MR, but very rare studies exist regarding degenerative mitral regurge. (8)

Since LV ejection fraction, in the presence of severe MR, is often supernormal, the slightest reduction in EF is synonymous to significant LV dysfunction. Heart failure is also an important postoperative complication and it is responsible for the majority of postoperative cardiac-related mortality and morbidity. (7, 8)

In our retrospective study, we were able to highlight the beneficial survival and recovery of postoperative LV function after mitral valve surgery in patients with preoperative low LV ejection fraction associated with degenerative MR.

Confirmed by Echocardiography, LV dimensions (LVESD and LVEDD) were significantly reduced during the study period and during the late fol-

low-up compared to the preoperative state. Also, the improvement in EF% was statistically highly significant in our study ( $<0.0001$ ). Preoperatively, 72.5% of patients had LV grade 3 i.e. EF between 20-40% and 27.5% were in grade 4 LV. Postoperatively, 70% of the patients had grade 1 & 2 LV i.e. EF between 50-60%. This was an expected finding since the cause of LV volume overload was eliminated. This improvement was evident in both mitral valve repair and replacement cases. This might be due to preservation of the continuity between the valve annulus and the papillary muscles in valve replacement cases. Although, our aim was not to compare the effect of valve repair Vs replacement, we found no difference between both types of surgery regarding the recovery of LV function.

Various reports (9, 10, 11, 12, 13, and 14) support that mitral valve replacement with preservation of papillary muscle-annulus continuity preserves LV geometry and shape. Without preserving this continuity, LV remodeling alters the shape of left ventricle towards a spherical geometry (decreased eccentricity index). In

a study performed by Kouris et al., (14) they concluded that mitral valve repair in patients with non-ischemic MR and preoperative LV dysfunction achieves better preservation of LV systolic indices than mitral valve replacement, probably due to preservation of the subvalvular apparatus and LV geometry.

Ren and colleagues (7) suggest that preservation of LVEF in mitral valve repair and in mitral valve replacement with chordal preservation is not caused by a decrease in end-systolic volume; the decrease in end-systolic volume is the result of a preserved EF (due to the maintenance of the functional components of the subvalvular apparatus), even though there is a decrease in end-diastolic volume. It is important to reserve the continuity between the leaflets and the subvalvular apparatus to maintain the function. Some surgeons even recommend preservation of the entire native valve if possible. This was recommended by Al-Saddique (15) in his study. He believes that in most patients with longstanding mitral valve regurgitation, thinned out papillary muscles and elongated chordae ten-

dinea that are not amenable to repair, valve replacement with the preservation of the entire native valve is possible and should be encouraged. This is especially valuable for those with depressed left ventricular function, who might otherwise suffer from left ventricular dysfunction in the long-term if the entire mitral valve apparatus were to be excised.

However, most surgeons prefer repair than replacement, if possible. Castedo et al, 2005 (4) in their study about mitral valve repair for chronic MR concluded that valve repair adequately corrects valvular maladaptation and facilitates functional recovery of patients with chronic MR. Since the subvalvular apparatus is preserved, postoperative systolic dysfunction is prevented and ventricular remodeling tends to revert. Hospital morbidity and mortality is low, complications inherent to the prostheses are avoided, and mid-term overall and reoperation-free survival is higher than 90%.

To evaluate the effect of mitral valve replacement on left ventricular function in mitral regurgitation, Huikuri (16) measured the a) end-systolic

stress/volume ratio, which is practically independent of changes in loading conditions, and b) the left ventricular contractile reserves upon isometric exercise, both before and one year after mitral valve replacement in 11 patients with mitral regurgitation. He found that ventricular function improves after mitral valve replacement in patients with mitral regurgitation, though the ejection fraction, which is affected by altered loading conditions, deteriorates. The left ventricular response to stress caused by isometric exercise is also improved after surgery.

Also, the improvement in LV function is explained by elimination of severe MR. This is very important, especially in patients who underwent valve repair. We routinely perform TEE intra-operative at the conclusion of CP bypass and we never accept residual mitral regurgitation more than mild degree in repair patients, otherwise, we go back on bypass, arrest the heart and perform additional maneuvers or replace the valve.

Nirupama et al (17) performed a retrospective study on 302 patients to

examine the outcome of mitral valve repair in relation to preoperative low left ventricular ejection fraction (LVEF). The study included two groups: Group I: patients with EF >35% and group II: patients with EF < 35%. Their conclusion was " Good symptomatic relief and acceptable overall survival can be obtained in patients in both groups after they have undergone mitral valve repair, 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 mitral valve repair electively before deterioration to end-stage heart disease would improve survival even in patients with low LVEF".

#### 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 mitral valve surgery. (18, 19) Therefore, mi-

tral valve surgery should be offered before deterioration in symptoms occurs in chronic cases. Furthermore, even in patients in preoperative NYHA class IV status, earlier surgery gives a better outcome. (20). 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 valve surgery 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 valve repair or replacement in chronic cases before the deterioration of functional status. (17-20)

NYHA functional class improved significantly in our patients during the follow-up period. Eighty percent of patients were in class III & IV preopera-

tively, but in the postoperative period, 75% were in class I & II. This could be explained by improvement in LV ejection fraction, reduction LVEDD, LVEDD, and also, by reduction of left atrial size.

This is generally attributed to the postoperative increase in LV afterload and abolition of the "pop-off" valve effect of the regurgitant leak, further decreasing the EF and cardiac output. The better clinical outcome after valve surgery is directly related to the preservation of the subvalvular apparatus resulting in preservation of LV geometry. Patients with a significant degree of LV systolic dysfunction ( $EF < 50\%$ ) should undergo surgical correction of MR because: (a) surgical correction, compared to medical treatment, improves prognosis and (b) reduces the incidence of congestive heart failure. (5, 8, 11, 12, 14, 15)

Atrial fibrillation was not a significant factor among our patients either in the preoperative or post-operative period. We could not demonstrate whether AF had any role in LV remodeling. However, there was a statistically significant difference in left

atrial size during the follow-up period. This might be an important factor in cardiac remodeling and towards improvement in the pump mechanism of the heart. It might have a role also in improving the patient's functional status. This finding meets that of Lim et al (21).

Five-year survival was  $82 \pm 5\%$ . Seventy-five (75%) of survivors were in NYHA class I & II. This survival benefit is a major outcome in our study because all of our patients were on full medications before surgery without significant clinical improvement and their survival would be affected by the ongoing heart failure in such group of patients.

Mitral valve surgery in this category of patients would change the natural history and improve the outcome especially towards survival.

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 as well as in cases of ischemic cardiomyopathy. (22) The study of

Gangemi et al (23) demonstrated improved survival and symptomatic status following mitral valve repair compared to cardiac transplantation or CABG alone. Some authors (22-26) advocate a combined approach of valve repair 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.

A study by Chen et al (22) has shown that mitral valve repair in the setting of ischemic MR and low LVEF appears to prolong survival and improve ventricular function. Their study also demonstrated that those with LVEF of < 20% did not fare worse than those with LVEF between 20% and 30%, as the decline in myocardial function has already occurred at such low levels of LVEF. They postulated that valve repair appears to prolong survival when offered before LVEF falls below 30% and heart failure symptoms occur.

In our study, Five-year freedom from reoperation was 97+/-2%. Five-

year freedom from valve-related morbidity or mortality was 95+/-3%. In all patients, there was no difference regarding the need for reoperation in valve repair or replacement cases. Two patients had progression of the degree of mitral regurgitation to more than moderate and they needed valve replacement during the follow-up period. Valve-related morbidity in the form of thrombo-embolism, anticoagulant-related hemorrhage, or endocarditis was 95+/-3%.

#### *Limitations of the Study*

Our goal was to find out whether mitral valve surgery can give good results in a group of patients with low LVEF due to degenerative mitral valve disease. It was not our objective to do a comparative analysis between mitral valve repair with mitral valve replacement.

This, along with the small sample size of the patients and the retrospective nature of the study, are the limitations of our series.

#### *Conclusion :*

Mitral valve surgery improves left ventricular function and dimensions in patients with degenerative mitral re-



gurgitation and LV dysfunction. It also offers symptomatic improvement and late survival benefit in this patient population.

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