Revascularization Versus Revascularization and Repair in moderate Chronic Ischemic Mitral Regurgitation

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Abstract: Objectives: The goal of this study is to determine whether the surgical management of moderate chronic ischemic mitral regurgitation is to revascularize only or to revascularize and adding mitral valve repair. **Background:** Ischaemic mitral regurgitation is a frequent complication of left ventricular global or regional pathological remodeling due to chronic coronary artery disease. There are numerous possible treatment modalities, but the management of patients with moderate chronic ischemic mitral regurgitation remains uncertain. **Methods:** Forty patients referred for coronary artery bypass grafting with moderate ischemic mitral regurgitation and an ejection fraction more than 30%, were randomized to receive coronary revascularization plus mitral valve repair (20 patients) or revascularization only (20 patients). Survivors were clinically and echocardiographically assessed at early post-operative and 3 months follow-up. **Results:** There was no significant difference between both groups as regards the preoperative and demographic data. The operative time, ventilation time and ICU stay were significantly higher in repair group. Use of cardiac supports, complications, in hospital mortality and ward stay were not statistically significant different. Postoperative and follow up echocardiographic data showed no statistical significant difference in left atrial dimension, left ventriculardimensions and function between both groups. Although, the grade of mitral regurgitation showed improvement in both groups, there was highly significant improvement in repair group more than revascularization only group. **Conclusion:** Adding mitral repair to coronary revascularization in patients with moderate ischemic MR may improve functional capacity, left ventricular reverse remodeling andmitral regurgitation severity without adding additional risk.

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1. Introduction:

Chronic ischemic mitral regurgitation (IMR) can be defined as follows: mitral regurgitation (MR) occurring more than 16 days after myocardial infarction (MI) with one or more LV segmental wall motion abnormalities; significant coronary artery (CAD) disease in a territory supplying the wall motion abnormalities and structurally normal mitral valve(MV) leaflets and chordae tendinae. The third criterion is important to exclude patients with organic MR and associated CAD**[1]**.

There is a vast inconsistency in the reported prevalence and severity of MR after MI and this is due to differences in diagnostic methods, MR severity classifications, amount ofleft ventricular (LV) dysfunction, treatment options, and time interval between MI and MR diagnosis**[2].**

Functional IMR occurs in up to 40% of patients after myocardial infarction. It is usually mild or moderate in severity but is associated with an increased incidence of heart failure and death**[3]**.

It is caused by LV remodeling and dilatation after myocardial infarction, which tethers and pulls the MV apart, resulting in MR; the MV is normal in structure but is incompetent as a result of a dilated and dysfunctional left ventricle**[4]**.

Chronic IMR can be reliably diagnosed with colour Doppler echocardiography. Two dimensional trans-thoracic echocardiography (TTE) and trans esophageal echocardiography (TEE) are the preferred diagnostic imaging tools. Echocardiography provides accurate information about LV dimensions and function, regional wall motion abnormalities, MR etiology, MR severity and mitral valve geometry, including annular dilatation and mitral valve tenting**[5]**.

A comprehensive intraoperative TEE examination in patients with IMR may have important implications for perioperative clinical decision making**[6].**

Being essentially a ventricular disease, caused by coronary stenosis, with effects on the papillary muscles, cords, and leaflet coaptation, ischemic mitral regurgitation lends itself to several therapeutic targets. Coronary artery revascularization is necessary to recruit any hibernating myocardium

and thus improve ventricular function. Revascularization can help limit future adverse remodeling that result from continuing ischemia or new infarction. Revascularization alone cannot, however, be relied on as sole therapy for ischemic mitral regurgitation, because the principal cause of the regurgitation leaflet tethering caused by regional infarction cannot usually be reversed by revascularization**[7].**

The ischemic MV can be repaired during coronary artery bypass graft(CABG) with the use of an annuloplasty ring, which achieves MV competency by restoring the size of the mitral annulus and increasing mitral leaflet coaptation**[8]**.

The restrictive (or downsized or undersized) annuloplasty is the currently recommended approach. Annuloplasty corrects circumferential annular dilation, whereas downsizing corrects the septolateral displacement and thus reduces the tethering distance**[9]**.

Observational studies have reported a reduction in the severity of MR with the addition of MV repair to CABG, but an improvement in functional capacity or survival has not been demonstrated[10].

2. Patients and methods:

Forty non selected, consecutive patients with moderate IMR on preoperative echocardiography had clinical and echocardiographic assessment before surgery, early after surgery and after 3 months follow up. All patients had coronary artery disease and grade 2+ or 3+ MR. All patients were prospectively randomized to either CABG in combination with MV repair (repair group, n_20) (group I), or CABG only (revascularization only group, n_20)(group II) with the decision of whether to perform MV repair being at the discretion of the surgeon.

Inclusion criteria include, Patients with moderate chronic IMR 8 cm2 < RJA > 4 cm2, (II / IV), (III / IV) with normal structure of all components of the mitral valve at the preoperative echocardiography.

Exclusion criteria include, patients with organic MV disease, including prolapse of mitral leaflets, ruptured chordae, and rupture of papillary muscles, mild (I / IV, R JA < 4 cm2) or severe (IV / IV, RJA > 8 cm2) mitral regurgitation, significant aortic valve disease, congenital heart diseases, redo or emergency surgery, ejection fraction less than 30% and impaired renal or liver functions.

Preoperative counseling:

In the preoperative visit prior to surgery, a brief explanation of the steps of the operation, the post-operative events and the intensive care stay.Also written patient consent was taken.

Patients in both groups were matched for demographic data including: age, sex, risk factors of ischemic heart disease, history of previous myocardial infarction.

Operative Technique

All patients had induction of anesthesia by fentanyl 5-10 µg/kg and sodium thiopental 4-5 mg/kg, endotracheal intubation was facilitated with use of non-depolarizing muscle relaxant pancuronium 0.08 mg/kg. Maintenance of anesthesia was given by using either sevoflurane or isoflurane 0.5-1% inhalational andsupplemental hypnotic dose of propofol 0.5-1 mg/ kg.

All surgical procedures were performed through midline sternotomy under normothermic cardiopulmonary bypass with intermittent ante grade warm-blood cardioplegia. All patients underwent full revascularization and prosthetic mitral annuloplasty was done only in repair group. All patients underwent conventional multivessel CABG with the use of internal mammary arteries (LIMA), and saphenous vein grafts (SVG).

Mitral valve exposure was done in repair group after completion of distal anastomoses. The exposure was routinely done through either left atriotomy incision, a vertical trans-septal approach along the right border of the foramen oval, leaving the left atrial roof untouched or biatrial trans septal incision. Direct visual inspection and assessment of the mitral valve leaflets, annulus, chordae tendineae, and papillary muscleswas done.

Ring size (Carpentier Edwards Physioring; Edwards Lifesciences, Irving, CA) was determined after careful measurement of the height of the anterior leaflet and standard measurement of the inter-trigonal distance and then downsizing by two sizes

Rings were inserted using 12 to 16 deep U-shaped simple horizontal sutures using ethibond 2-0. All the rings were size 28. However 1 patient received additional Alfieri Stitch as decided by the surgeon.

Left atriotomy was closed using running polypropylene 3/0 suture. Right atriotomy was closed using running polypropylene 4/0 suture.

All patients had intra-operative TEE assessment of LV and valve function. MV repair was considered successful if there was no residual MR and a leaflet coaptation length of at least 8 mm at the A2-P2 level.

Operative data including total pump time, aortic cross clamp time and number of distal anastomoses were collected.

Postoperative dataincludinguse of inotropic support, insertion ofintra-aortic balloon pump (IABP), time of mechanical ventilation, ICU stay, ward stay, postoperative echocardiography and in hospital morbidity and mortality were also collected.

Follow up data:

All the patients were followed up at our outpatient clinic after 3 months by assessment of NYHA functional class and echocardiography performed by the same cardiologists. Follow-up was 100% complete.

Statistical analysis:

The data collected were tabulated & analyzed by SPSS (statistical package for the social science software) statistical package version 20 on IBM compatible computer. Quantitative data were expressed as mean & standard deviation (X ± SD) and analyzed by applying student t test for comparison of two groups of normally distributed variables and two groups of not normally distributed variables by applying Mann-Whitney Test. Qualitative data were expressed as number and percentage (No & %) and analyzed by applying Chi-square test and for 2×2 table and one cell has expected number less than 5 Fisher's exact test was applied.

3. Results

Preoperative results:

The range of age was from 38 to 72 years (Group I) and from 44 to 65 year (Group II), there was no statistical difference in the mean age of both groups. There was also no statistical difference between the two groups regarding gender distribution **(table: 1).**

The distribution of risk factors for ischemic heart disease among both groups were checked for during history taking and summarized in **(table: 2)**, there was no statistical difference between the two groups.

The preoperative dyspnea classified by NYHA classification was not statistically different in both groups**(figure: 1).**

Preoperative echocardiographic data showed no statistical significant difference in preoperative left ventricular dimensions or function, but we had statistically significant higher left atrial dimension in repair group than revascularization only group**(table: 3).**

Operative data:

The operative time including total pump time and aortic cross clamp time was significantly higher in repair group (P value < 0.001) while the mean number of grafts per patient was statistically higher in revascularization only group (p value <0.05) **(table: 4).**

Immediate Postoperative Data:

All patients were transferred to the ICU where they were maintained on positive pressure ventilation, continuous monitoring of the vital signs.

The ventilation time and total ICU stay time were statistically higher in patients in the repair group **(table: 5).** However The total number of patients how needed postoperative cardiac support whether pharmacological or mechanical was 16 patients pharmacological (80%) and 4 patients mechanical (20%) in the repair group versus 11 patients pharmacological (55%) and 3 patients mechanical (15%) in the revascularization only group which is not significantly different (P value > 0.05) **(figure: 2).**

Although the mean time of ward stay in days was higher in the repair group, 7.33 ± 2.54 versus 6.18 ±2.64 in the revascularization only group, the difference was statistically insignificant (Pvalue = 0.16).

The postoperative complications in the form of reopening, postoperative atrial fibrillation, MI and nodal rhythm were insignificantly different between both groups (P value = 0.5).

As regard in hospital mortality, we had a total of 3 in hospital mortalities, 1 patient (5%) in repair group and 2 patients (5%) in revascularization only group; however the difference was statistically insignificant.

The postoperative echocardiographic data was collected from the surviving patients (19 out of 20 patients in group I and 18 out of 20 patients in group II), the data showed no statistical significant difference in left atrial dimension, left ventricular dimensions and function between both groups **(table: 6).** Although, the grade of mitral regurgitation showed improvement in both groups, there was highly significant improvement in repair group more than revascularization only group **(figure: 3).**

Follow up data:

Follow up data was collected from all surviving patients (18 out of 20 patients in group I and 18 out of 20 patients in group II).

Comparison of echocardiographic data between the two groups showed no statistical significant difference in all parameters **(table: 7)** except for the grade of mitral regurgitation which was significantly higher in revascularization only group **(figure: 4).**

Table (1): Sociodemographic characteristics of the studied groups of patients.

Sociodemographic characteristics	Studied groups				Test of significance	P value
	Group I(n=20)		Group II(n=20)			
Age (years): **Range** **Mean±SD**	**38.00 –72.00** **58.05 ±8.26**		**44.00 – 65.00** **57.14± 5.27**		**t=0.42**	**0.68** **NS**
Sex :	**No.**	**%**	**No.**	**%**		
Male **Female**	**15** **5**	**75.0** **25.0**	**12** **8**	**60.0** **40.0**	**X^2=1.02**	**0.31** **NS**

Table (2):Distribution of risk factors among studied groups.

Risk factors	Studied groups				Total studied patients (n=40)	
	Group I (n=20)		Group II (n=20)			
	NO.	%	NO.	%	NO.	%
Smoking	11	55.0	8	40.0	19	47.5
Hypertension	13	65.0	15	75.0	28	70.0
D.M.	10	50.0	9	45.0	19	47.5
Dyslipidaemia	14	70.0	13	65.0	27	67.5
Positive Family History	5	25.0	8	40.0	13	32.5

Table (3):Preoperative echocardiographic datafor both groups.

Preoperative echocardiography	Studied groups		t test	P value
	Group I (n=20)	Group II (n=20)		
ESD: Range Mean±SD	3.00 – 5.70 4.31±0.65	3.50 – 5.20 4.28 ± 0.45	0.19	0.84 NS
EDD: Range Mean±SD	4.70 – 6.70 5.76±0.62	4.00 – 6.40 5.60 ± 0.51	0.90	0.36 NS
EF: Range Mean±SD	35.00 – 77.00 47.00 % ±11.03	35.00 –76.00 % 48.75 % ± 9.72	0.53	0.59 NS
LA: Range Mean±SD	3.30 – 4.70 4.16 ± 0.38	3.20 – 4.60 3.88 ± 0.34	2.46	0.01 S

EDD = End Diastolic Diameter, ESD = End Systolic Diameter, EF = Ejection Fraction, LA = Left Atrium

Table (4): Intra-operative data for both groups.

Intra-operative data	Studied groups		t test	P value
	Group I (n=20)	Group II (n=20)		
Total pump time (min): Range Mean±SD	95.00 – 142.00 113.85 ±13.86	35.00 – 98.00 72.85 ± 18.92	7.81	< 0.001 HS
Ischemic time (min): Range Mean±SD	50.00 – 100.00 79.75 ±13.19	25.00 –71.00 48.40 ±13.70	7.41	< 0.001 HS
No of distal anastomoses: Range Mean±SD	2.00 – 4.00 2.70± 0.79	1.00 – 4.00 3.20 ± 0.68	2.15	0.03 S

Table (5): ICU data for both groups.

ICU Data	Studied groups		Mann-Whitney test (U)	P value
	Group I (n=20)	Group II (n=20)		
Ventilation (h): Range Mean±SD	 7.00 – 75.00 18.35 ± 8.35	 6.00 – 110.00 11.50 ± 10.34	2.30	0.02 S
ICU stay (h): Range Mean±SD	 42.00 – 110.00 67.60 ± 24.18	 30.00 –120.00 50.40 ± 25.27	3.50	< 0.001 HS

Table (6): Postoperative echocardiographic data of both groups.

Postoperative echocardiography	Studied groups		t test	P value
	Group I(n=19)	Group II(n=18)		
ESD: Range Mean±SD	 3.10 – 5.20 4.00±0.55	 3.30 – 5.60 4.10 ± 0.59	0.52	0.60 NS
EDD: Range Mean±SD	 4.70 – 6.80 5.48 ± 0.60	 4.90 – 6.80 5.53 ± 0.47	0.24	0.81 NS
EF: Range Mean±SD	 35.00 – 69.00 % 50.00 % ± 8.81	 28.00 – 68.00 % 48.88 % ± 8.96	0.37	0.71 NS
LA: Range Mean±SD	 3.30 –6.30 4.12 ± 0.63	 3.10 – 4.50 3.78 ± 0.34	1.99	0.06 NS

Table (7):Echocardiographic data of both groups at follow up.

follow up echocardiography	Studied groups		t test	P value
	Group I (n=18)	Group II (n=18)		
ESD: Range Mean±SD	 3.20 – 5.70 3.77 ±0.66	 3.00 –5.30 3.89± 0.61	0.57	0.57 NS
EDD: Range Mean±SD	 4.50 – 6.90 5.11± 0.65	 4.70 – 6.80 5.26 ± 0.52	0.76	0.44 NS
EF: Range Mean±SD	 30.00 – 70.00 % 54.66 % ± 10.43	 35.00 – 68.00 % 53.22 % ± 8.87	0.45	0.65 NS
LA: Range Mean±SD	 3.10 – 6.10 3.46 ± 0.69	 3.00 – 4.50 3.67 ± 0.40	1.12	0.27 NS

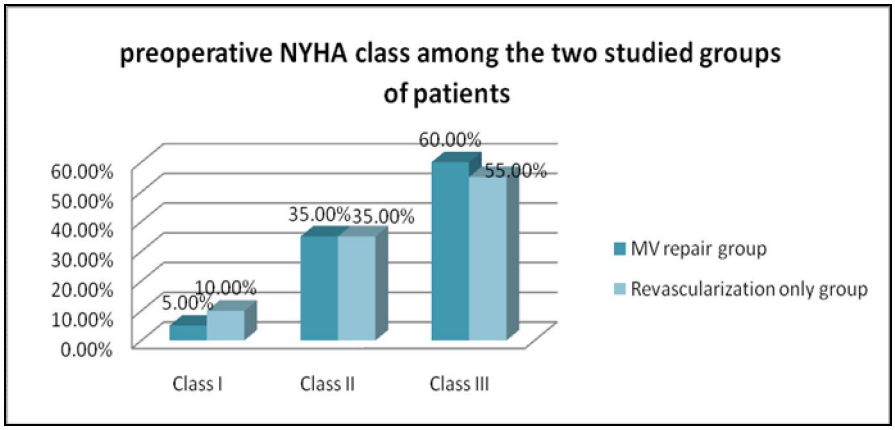

Figure (1):NYHA class among the two groups.

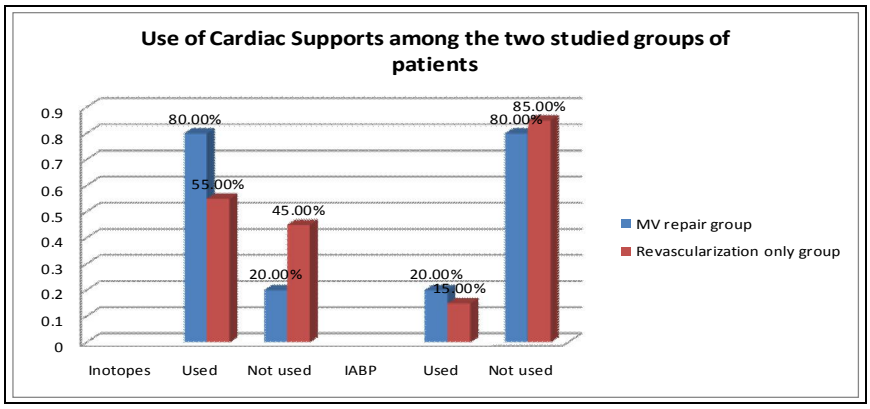

Figure (2): Use of cardiac supports.

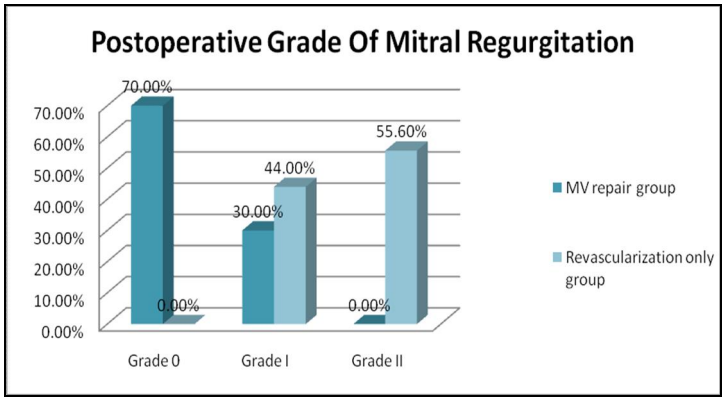

Figure (3):Postoperative grade of mitral regurgitation of both groups.

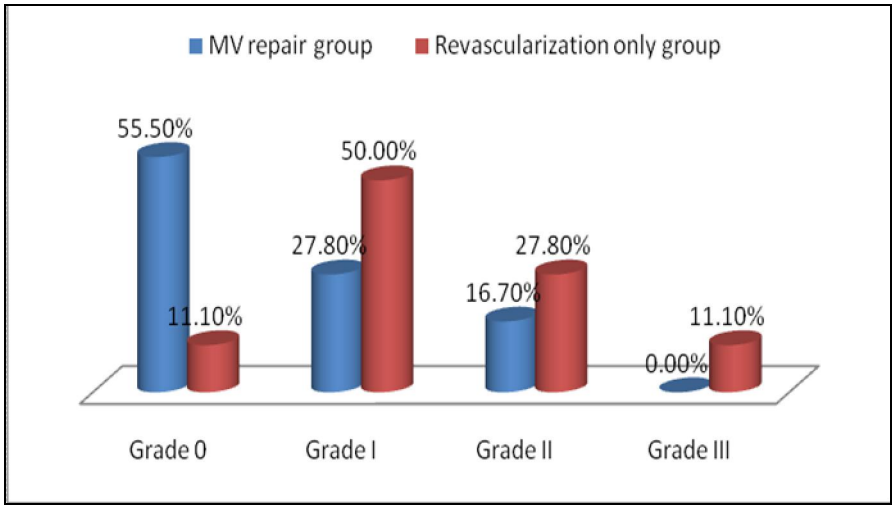

Figure (4): Grade of mitral regurgitation of both groups at follow up.

4. Discussion:

Most of IMR patients have the etiologic basis of previous MI.

The number of patients who had positive history of previous MI, was 17 patients in Group I (85%), and 14 patients in Group II (70%), with no statistical difference in between, only 31 (77.5%) of all patients.

This percentage of patients who had positive history of previous MI was comparable to other studies by **Chan et al.[11]** (72.6%), **Wong et al**. **[12] (**79.3%) and**Harris et al**. **[13]** (80%).

Analysis of the NYHA functional class of dyspnea.

In our study we had (5%), (35%) and (60%) of patients in Group I with mean of 2.55 ±0.60 and (10%), (35%) and (55%) of Group II with mean of 2.45 ±0.68 in grade I-II-III NYHA functional class of dyspnea respectively with no statistical significant difference in between.

This result was slightly different from other study by **Chan et al.** [11] as they have their patients in group I 1 (3%) 22 (65%), 11 (32%) in grade I-II-III NYHA versus 1 (3%), 25 (64%), 13 (33%) in group II.

Analysis of the preoperative echocardiographic data.

The mean for the EF was 47.00 % ±11.03 in Group I and 48.75 % ± 9.72 in group II with no statistical difference in between. And that was relatively higher than other studies by **Chan et al.**[11] (40.0±17.3 and40.3±16.1), **Goland et al** 168 (37% ± 11% and 39% ± 11%), **Harris et al** 165 (38% ± 13.8% and 38.7% ± 12.6), and **Wong et al**. [12](39 ± 13.6% and 42.2 ± 15.3%) in the repair group and revascularization only group respectively.

The preoperative mean grade of mitral regurgitation was 2.50 ±0.51 in group I versus 2.35 ±0.48 in group II, with no statistical significant difference in between. In repair group 10 (50%) patients were in grade II and 10 (50%) patients were in grade III versus 13 (65%) and 7 (35%) patients in CABG only group respectively. This was comparable with other studies by **Harris et al**. **[13]** and **Wong et al**. **[12]** where the mean grade of severity was 2.6±0.5, 2.1±0.3 and 2.0±0.9, 2.6±0.8 in repair group and CABG only group respectively. However, in both studies there was statistical significant difference between the two groups (P= 0.001 and 0.005 respectively), where the mean grade of severity was higher in repair group in the study by **Harris et al**. [13] and it lowers in the same group in **Wong et al**. [12]study.

Analysis of the operative data.

Analysis including total pump time and ischemic time revealed a significant difference between the two groups. This significant difference that was observed in favor of group I was due to the mitral valve procedure which adds this time.

As regard to the use of cardiac support, either pharmacological (Inotropic drugs) or mechanical (IABP) there was no statistically difference between the two groups. In group I, 16(80%) patients needed inotropic support, of those 4(20%) patients IABP was inserted, while in group II, 11(55%) patients received inotropic support and in only 3(15%) patients IABP was inserted.

Likewise, **Chan et al**.[11] reported use of IABP in 11 (33%), of patients in group I, and 11 (29%) group II with no statistical difference, (P value 0.57).

The survival rate was 95% in group I versus 90% in group II. **Chan et al.** [11] reported 30 days mortality in 1 (3%) patient in group I versus 1 (3%) patient in group II (P value 1.00).

When evaluating the efficacy of concomitant CABG plus MV repair compared with CABG alone in patients with moderate chronic IMR on the grade of MR we found the following:

Our early post-operative results showed high statistical difference between the two groups in the grade of reduction of grade of MR as follows: complete resolution of MR in 12(63%) patients in group I versus none in group II. Some reduction in the severity of MR to grade I was noticed in 6(31%) patients in group I versus 8(44%) patients and to grade II in 10 (55%) patients in group II. However, these immediate changes in grade of MR did not accompanied by similar changes in LA dimension, LV dimensions and function, and this was an expected finding as reverse remodeling if any to occur needs longer time interval.

At follow up time interval, the mean grade of MR showed statistical significant reduction in the mean grade of severity in comparison with base line grade in group I from 2.55 ±0.60 to 0.61 ± 0.77 versus only from 2.35 ±0.48 to 1.37 ± 0.88 in group II with statistical significant difference in between. In addition to reduction in grade of severity of MR at follow up the echocardiographic data showed accompanied reverse remodeling in LA and LV dimensions together with improvement in LV function in both groups.

These results were comparable to a study by **Chan et al.[11]** on 73 patients, 34 of them underwent concomitant mitral valve repair at time of CABG and 39 patients underwent CABG only, found significant improvement in MR grade and LV volumes in their CABG + MV repair patients, in comparison with their CABG only patients within 12 months follow up and these translated into an improvement in functional capacity and symptoms at 1 year.

These results were also comparable to another study from the Cleveland clinic foundation reported that moderate (2+) IMR does not resolve with CABG alone, and furthermore, is associated with reduced survival[**14].**

In the same fashion, **Goland et al**. **[15]** in their study on 83 patients who had moderate IMR, 28 patients underwent concomitant mitral valve

repair at time of CABG and 55 patients underwent CABG only, found significant improvement in MR grade in their CABG + MV repair patients, in comparison with their CABG only patients within 12 months follow up (P<0.0001).

Although, the mean NYHA functional class showed no statistical significant group difference (P=0.62), it was significantly improved over time interval of follow up in both groups included in our study, however, the improvement was higher in group I (1.33 ± 0.48) than in group II (1.43±0.72) without reaching statistical significance.

Conclusion:

The ischemic mitral valve can be repaired during CABG with the use of an annuloplasty ring, which achieves mitral valve competency by restoring the size of the mitral annulus and increasing mitral leaflet coaptation.

The benefits of mitral valve repair over and above that of CABG alone is that reduction in the severity of MR with the addition of MV repair to CABG. LV improvement in functional capacity, NYHA functional class and survival has been demonstrated in both procedures.

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