**ABSTRACT**

**Background:** This is a prospective randomized-controlled study aiming to determine whether the optimal surgical management of moderate ischemic mitral regurgitation is to revascularize the heart through performing coronary artery bypass grafting alone or together with repairing the mitral valve.

**Methods:** Between April 2014 and November 2014, 40 patients with ischemic heart disease associated with moderate ischemic mitral regurgitation at our University hospitals were divided into 2 matched groups. Group 1 received both coronary artery bypass grafting surgery together with mitral valve repair, while Group 2 underwent coronary artery bypass grafting surgery alone.

**Results:** No statistically significant difference was found between both study groups, in terms of operative data, except for cardiopulmonary bypass time and aortic cross-clamp time, which were significantly longer in Group 1 (\(P < .001\)). Only one case died in the study in Group 1 on the third postoperative day, due to severe low cardiac output syndrome. During the follow up, NYHA class improved in Group 1 from 2.6 to 1.35 (\(P < .004\)), but in Group 2 NYHA class improved from 2.5 to 1.72 (\(P = .07\)). The degree of MR improved in 19 patients (95%) in Group 1 compared with 15 (75%) patients in Group 2 (\(P < .0001\)).

**Conclusion:** Our study showed meaningful advantages of adding mitral-valve repair to CABG in patients with ischemic heart disease and moderate ischemic mitral regurgitation, regarding the degree of MR and functional NYHA class. On the other hand, there was no statistically significant difference between both groups in postoperative coarse and in-hospital mortality.

**INTRODUCTION**

Chronic ischemic mitral regurgitation (CIMR) can be defined as mitral regurgitation (MR) occurring as a sequel of myocardial infarction (MI) or chronic myocardial ischemia without evidence of structural pathology of the valve apparatus [Gorman 2003]. Valve incompetence in such a case is the result of papillary muscle (PM) displacement, leaflet tethering, and annular dilatation [Kumanohoso 2003].

Currently, there is a general agreement that moderate-to-severe and severe (grade 3+ to 4+) CIMR should be corrected at the time of coronary artery bypass grafting (CABG), whereas trace-to-mild (grade 1+) CIMR does not require any surgical treatment. On the other hand, the optimal management of moderate (grade 2+) CIMR is still controversial [Fattouch 2009]. This controversy is based in part on the lack of data from rigorous trials that could help to determine whether the potential benefits of concomitant mitral valve repair (MVR) during CABG surgery would outweigh the increased risks of the combined procedure or not [El Bardissi 2012; Lee 2011]. Proponents of CABG alone for the treatment of moderate ischemic mitral regurgitation (IMR) argue that revascularization may improve regional left ventricular (LV) function and reduce the left ventricular chamber size, thereby restoring the functional integrity of the sub-chordal mitral valve apparatus [Penicka 2009; Roshanali 2006].

Advocates for MVR in addition to CABG cite the adverse consequences of persistent ischemic mitral regurgitation and further argue that in patients with reduced LV function, mitral valve repair may prevent progressive adverse remodeling, improve cardiac function, and reduce the risk of heart failure [Flynn 2009; Bax 2004].

**PATIENTS AND METHODS**

This is a prospective randomized-controlled study done at the Department of Cardiothoracic Surgery of Cairo University between April 2014 and November 2014. The study was conducted on 40 patients with ischemic heart disease (IHD) undergoing CABG with moderate IMR. Patients were eligible for enrollment in this study if they were referred for off-pump CABG and had moderate IMR measured by echocardiography at rest. Patients with mild or severe IMR, MR not of ischemic origin, other valve diseases warranting intervention, associated left ventricular aneurysm or ischemic VSD, and previous open heart surgeries (redo cases) as well as off-pump cases were not included in our study. Patients were
Table 1. Preoperative patient’s characteristics

| Variables | Group 1 (CABG & MVR) (N = 20) | Group 2 (CABG) (N = 20) | P  | Significance |
|-----------|-------------------------------|-------------------------|----|-------------|
| Age (years) | 54.3 ± 4.9 | 53.9 ± 4.7 | 0.8 | NS          |
| Male sex | 11 (55%) | 12 (60%) | 0.9 | NS          |
| Female sex | 9 (45%) | 8 (40%) | 0.9 | NS          |
| Diabetes | 12 (60%) | 11 (55%) | 0.9 | NS          |
| Hypertension | 12 (60%) | 9 (45%) | 0.5 | NS          |
| Previous M.I. | 13 (65%) | 12 (60%) | 0.9 | NS          |
| Mean NYHA class | 2.6 | 2.55 | 0.9 | NS          |
| Two-vessel disease | 4 (20%) | 3 (15%) | 0.7 | NS          |
| Three-vessel disease | 14 (70%) | 15 (75%) | 0.7 | NS          |
| Four-vessel disease | 2 (10%) | 2 (10%) | 1.0 | NS          |
| LA | 4.2 ± 0.25 | 4 ± 0.4 | .07 | NS          |
| LVEF % | 0.49 ± 0.04 | 0.51 ± 0.05 | .17 | NS          |
| LVESD | 4.45 ± 0.35 | 4.4 ± 0.25 | .61 | NS          |
| LVEDD | 6.0 ± 0.45 | 5.9 ± 0.33 | .43 | NS          |

Data are presented as means ± standard deviation or number (percentage) as shown. CABG, Coronary artery bypass grafting; MVR, mitral valve repair; MI, myocardial infarction; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVEDD, left ventricular end-diastolic dimension; LA, left atrial dimension.

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Intra-operative time parameters as well as surgical procedures were noted. Similarly, postoperative data were recorded, including ICU course, postoperative complications, in-hospital mortality, echocardiographic outcomes (left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), and left ventricular ejection fraction (LVEF) as a measure of left ventricular remodeling as well as the degree of residual MR and regional wall motion abnormalities (RWMA), New York Heart Association (NYHA) functional class, and the Canadian Cardiovascular Society (CCS) class for heart failure and angina as a measure of clinical status of patients. Patients were followed up at our outpatient clinic both clinically and through echocardiography 3 months after surgery as well as at intervals of 6 months.

Statistical analysis: Data were collected, coded, translated to English to facilitate manipulation and then doubly entered into Microsoft Access, where data analysis was performed using SPSS software version 18 under Windows 7. Quantitative data were summarized using mean ± standard deviation, median, while categorical data were presented as frequency (count) and relative frequency (percentage). For comparison between quantitative parametric data student t-Test was used and for qualitative data Chi square as well as McNemar tests were implied. The level $P \leq .05$ was considered the cut-off value for significance.

Surgical technique: All surgical procedures were performed through a longitudinal median sternotomy during normothermic cardiopulmonary bypass (CPB) with intermittent ante-grade warm blood cardioplegia. All patients underwent conventional multivessel CABG surgery with the use of left internal mammary artery (LIMA) grafted to the left anterior descending (LAD) coronary artery and the great saphenous vein (GSV) was used to revascularize any other coronary artery. In patients randomized to CABG plus MVR, the mitral valve was inspected through left atriotomy to confirm the absence of any structural abnormalities. MVR was performed using a rigid incomplete annuloplasty ring.
(Carpentier–Edward). Ring sizing was based on the length of the anterior leaflet or inter-trigonal distance according to surgeon’s preference, and the ring was downsized by two sizes when possible to correct annular dilatation. Operative data are summarized in Table 2.

RESULTS

Operative data: No statistically significant difference was found between both study groups in terms of operative data, except for CPB time and aortic cross-clamp time which were significantly longer in Group 1 with a median of 91 minutes compared with 56.25 minutes and a median of 74.1 minutes compared with 42.6 minutes in Group 2, respectively. These differences are due to the additional time needed to place the annuloplasty ring ($P < .001$ in both time parameters). The right coronary artery (RCA) or its posterior descending branch (PDA) was grafted in 16 patients (80%) in Group 1 and 15 patients (75%) in Group 2. Smooth weaning off bypass was achieved in 12 patients (60%) of Group 1 and 8 patients (40%) in Group 2. The rest of the patients needed inotropic support to achieve weaning and only one patient in Group 1 needed an intra-aortic balloon pump (IABP) support as depicted in Table 2.

Postoperative data: All the patients were discharged to the cardiothoracic intensive care unit (ICU) mechanically ventilated. Postoperative intensive care unit management was standardized for all patients. Patients were discharged from the ICU when haemodynamically stable on no inotropic support, with no drains, and with satisfactory postoperative laboratory results and electrocardiogram (ECG). Table 2 shows the postoperative early results (Table 2). As can be seen from the table, all the differences were insignificant. There was only one case of postoperative bleeding due to sternal wires that needed re-exploration in Group 1 and another case was complicated by postoperative low cardiac output syndrome (LCOS) in the same group. Only one case died in the study in Group 1 on the third postoperative day due to severe LCOS not responding to maximal inotropic support and IABP application without evidence of peri-operative infarction.

Follow up data: Patients could be followed up for a mean period of $4 \pm 1.3$ years after discharge. Follow up was complete in 39 patients in both groups. Only one patient skipped follow up, due to loss of updated contact data. No mortality was detected in all patients followed up. During the follow up, NYHA class improved in Group 1 from 2.6 to 1.35 ($P < .004$), but in Group 2 NYHA class improved from 2.55 to 1.72 ($P = .07$). NYHA class II or greater was present in 8 (40%) patients in Group 1, which is statistically significant when compared with the preoperative data ($P = .004$), and in 14 (70%) patients in Group 2, which is statistically insignificant when compared with the preoperative data ($P = .07$).

The degree of MR improved in 19 patients (95%) in Group 1 compared with 15 (75%) patients in the Group 2 ($P < .0001$). In Group 1, the grade of mitral regurgitation dropped in 14 patients to absent and to grade 1+ in 5 patients, while in Group 2 the grade of mitral regurgitation dropped to grade 1+ in 15 patients, remained as grade 2+ in 4 patients, and progressed to grade 3+ in one patient. These differences were statistically significant between the 2 study groups ($P < .001$). These data suggest that CABG alone left 20% of

| Table 2. Intraoperative and postoperative patient’s data |
|----------------------------------------------------------|
| Variables                                                   | Group 1 (CABG & MVR) (N = 20) | Group 2 (CABG) (N = 20) |    | Significance |
|-------------------------------------------------------------|-------------------------------|----------------------------|----|--------------|
| Intraoperative data:                                        |                               |                            |    |              |
| Bypass time (min)                                           | $91 \pm 10.2$                | $56.25 \pm 8.7$            | $.001$ | HS          |
| Cross-clamp time (min)                                      | $74.1 \pm 7.9$               | $42.6 \pm 8.8$             | $.001$ | HS          |
| Number of grafts                                            | $2.9 \pm 0.55$               | $2.9 \pm 0.51$             | $.8$ | NS          |
| Inotropic support                                          | $8$ (40%)                    | $12$ (60%)                 | $.3$ | NS          |
| IABP support                                               | $1$                           | $0$                        | $.3$ | NS          |
| Early outcomes:                                             |                               |                            |    |              |
| Mechanical ventilation (hrs)                                | $6.2 \pm 1.2$                | $7.2 \pm 1.8$              | $.06$ | NS          |
| ICU stay (days)                                             | $2.8 \pm 0.52$               | $3.15 \pm 0.67$            | $.08$ | NS          |
| Hospital stay (days)                                        | $10.35 \pm 1.22$             | $10.15 \pm 1.18$           | $.6$ | NS          |
| LCOS                                                       | $1$ (5%)                     | $0$ (0%)                   | $.3$ | NS          |
| Re-exploration for bleeding                                 | $1$ (5%)                     | $0$ (0%)                   | $.3$ | NS          |
| In-hospital mortality                                       | $1$ (5%)                     | $0$ (0%)                   | $.3$ | NS          |

Data are presented as means ± standard deviation or number (percentage), as shown. CABG, Coronary artery bypass grafting; MVR, mitral valve repair; CPB, cardiopulmonary bypass; IABP, intra-aortic balloon pump; LCOS, low cardiac output syndrome; ICU, intensive care unit.
patients in moderate MR, and in only one patient, the grade of MR worsened, from moderate to severe.

Otherwise, there is no statistically significant difference with \( P > .05 \) between other preoperative and postoperative echo findings during follow up among patients in Group 1 and Group 2. Table 3 summarizes the follow up data (Table 3).

### DISCUSSION

There’s much evidence from several studies that CIMR is related to a worse prognosis and higher mortality rate in CABG patients. This not only is related to its presence, but also more importantly to the grade of MR. However, the evaluation of CIMR under resting conditions might underestimate the clinical effects of the lesion. Indeed, CIMR is a dynamic lesion, and its severity can vary over time [Grigioni 2001; Aklog 2001; Hickey 1988; Di Mauro 2006]. Clinical studies have many conflicts regarding the correction of moderate ischemic mitral regurgitation at the time of CABG surgery. This conflicting decision mainly is affected by the lack of prospective studies and by the comparison of outcome in dissimilar patient groups [Fattouch 2009].

Authors favoring a conservative approach believe that CABG alone can be sufficient to obtain a reduction in MR postoperatively and to improve clinical symptoms. These authors suggest that myocardial revascularization alone, restoring a good myocardial perfusion, leads to an enhancement of left ventricular segmental and global kinesia, a reduction in left ventricular dimensions, and finally a significant reduction in MR because of restored valvular function [Lee 2011; Penicka 2009]. We believe these findings are partially false because in many patients with scarred area of myocardium after infarction, CABG would not be effective alone in improving myocardial function. In addition left ventricular remodeling cannot be maintained and postoperative reverse remodeling is not predictable. Therefore, in our study we tracked the course of moderate ischemic mitral regurgitation after CABG surgery alone and after doing both CABG surgery and MVR on the immediate outcome and mid-term follow up of patients with IHD undergoing CABG.

The preoperative profile of both patient groups was similar with no statistically significant differences with regard to age, sex, and risk factors for IHD, clinical status, and preoperative investigations. There was, however, a certain point in the preoperative evaluation worth mentioning. It was found in both groups that 65% of the patients in Group I had a previous postero-inferior infarction and 60% of the patients in Group II had a previous postero-inferior infarction. This validates data by other authors stating that, although anterior infarctions are common to occur in IHD patients, the occurrence of IMR is more common after a postero-inferior MI [Kumanohoso 2003]. In their series on 102 patients with IMR, Calafiore and colleagues found that a posterior or inferior MI occurred in 61.3% of cases. This could be explained by the fact that the posterior papillary muscle is supplied by only one segmental artery and therefore when occluded, the papillary muscle invariably infarcts, producing tethering of the posterior mitral leaflet and thus causing mitral regurgitation [Calafiore 1989].

The postoperative course as well as the in-hospital mortality for both groups in our series showed no statistically significant difference. This is similar to the results obtained by Fattouch and colleagues [Fattouch 2009]. However in other series, the longer bypass time and more complicated surgery in the CABG and MVR group including the obligatory cardiectomy to perform mitral-valve repair were associated with more complicated postoperative course for the combined group [Tolis 2002; Kim 2005; Kang 2006; Ryden 2001; Duarte 1999].

This might not have been evident in our study, due to the relatively small study cohort. On the other hand, the efficacy of adding MVR to the CABG surgery was well demonstrated by the improvement of postoperative NYHA class and by the decrease of postoperative mitral regurgitation grade. There is discrepancy in the literature regarding these results. In their study, Fattouch and colleagues included 102 patients for CABG alone or CABG with mitral repair with

| Table 3. Clinical and echocardiographic follow-up data in all patients |
|------------------------------|---------------|---------------|-----------------|---------------|---------------|---------------|
|                            | CABG + MVR group (N = 20) | CABG group (N = 20) |                  |               |               |               |
|                             | Baseline | Follow-up | \( P \) | Significance | Baseline | Follow-up | \( P \) | Significance |
| LA                          | 4.2 ± 0.25 | 4.12 ± 0.24 | .31 | NS | 4.00 ± 0.29 | 4.01 ± 0.36 | .92 | NS |
| LVEF%                       | 0.49 ± 0.08 | 0.54 ± 0.1 | .09 | NS | 0.51 ± 0.06 | 0.55 ± 0.1 | .13 | NS |
| LVESD                       | 4.45 ± 0.46 | 4.21 ± 0.53 | .13 | NS | 4.4 ± 0.4 | 4.11 ± 0.6 | .08 | NS |
| LVEDD                       | 6.0 ± 0.47 | 5.81 ± 0.59 | .27 | NS | 5.9 ± 0.52 | 5.65 ± 0.44 | .11 | NS |
| Mean NYHA class             | 2.6 | 1.4 | .004 | HS | 2.55 | 1.75 | .07 | NS |
| Mean MR grade               | 2 | 0.26 | < .001 | HS | 2 | 1.3 | .07 | NS |

Data are presented as means ± standard deviation as shown. CABG, Coronary artery bypass grafting; MVR, mitral valve repair; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LA, left atrial dimension; NYHA, New York Heart Association functional class; MR, mitral regurgitation.
an average follow-up period of 32 months. They concluded that the left ventricular function, degree of mitral regurgitation, and NYHA functional class all improved with combined CABG and mitral valve repair as compared with CABG alone [Fattouch 2009]. A reduction in the degree of mitral regurgitation with CABG alone also previously has been reported by Wong et al., Kang et al., Ryden et al., and Mallidi et al [Kang 2006; Ryden 2001; Wong 2005; Mallidi 2004]. However, Kim and coworkers observed a similar improvement in NYHA class at 2-year follow-up in their revascularization alone (from 3.12 ± 1 to 1.12 ± 0.38) and revascularization with repair (from 3.22 ± 0.82 to 1.29 ± 0.63) groups [Kim 2005]. We believe that any differences in the outcome between our study and other previous studies may in part reflect differences in end points assessed, methods of classifying the severity of mitral regurgitation, the duration of mitral regurgitation from initial diagnosis to trial enrollment, and rates of subsequent myocardial infarction either due to progression of IHD or graft failure especially of the right coronary artery. For example, Campwala and colleagues found in their series that failure of the graft to the PDA territory is an independent predictor of postoperative IMR progression [Campwala 2006]. Also in the study of Lam et al., postoperative echocardiography was done in only 156 of their 467 patients at the discretion of the attending cardiologist. Therefore, it must be acknowledged that some of these echocardiograms may have been “clinically driven” by patient symptoms (heart failure) or physical examination (murmur); this would tend to cause over-representation of patients with more severe MR [Lam 2005]. Finally, the series by Aklog and co-authors defined moderate IMR as grade 2+, which is different than most series, including our own, which define it as 2+. Therefore, it can be argued that these investigators examined a cohort of patients with a more advanced grade of IMR preoperatively [Aklog 2001].

**CONCLUSION**

Our study showed meaningful advantages of adding mitral-valve repair to CABG in patients with IHD and moderate IMR, regarding the degree of MR and functional NYHA class. On the other hand, there was no statistically significant difference between both groups in postoperative coarse and in-hospital mortality.

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