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Original Article

The effect of the revascularization strategies on the severity of ischemic moderate mitral regurgitation

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Abstract. Although it is known that revascularization is useful for the treatment of patients with ischemic mitral regurgitation (MR), the effects of revascularization on MR have not been well examined. In this study, we aimed to show the effect of revascularization strategies on patients with moderate ischemic MR, quantitatively and prospectively.

Forty-seven patients with moderate MR (2 to 3 +) who were offered revascularization due to the diagnosis of coronary artery disease were enrolled in the study. Patients were divided into three groups according to their treatment strategies. Patients who underwent percutaneous coronary intervention (PCI) were defined as group 1 (n=18), patients who underwent surgical revascularization (CABG) as group 2 (n=17) and patients who received only medical treatment as group 3 (n=12). Transthoracic echocardiography (TTE) was performed for all patients at the beginning of the study, and after three months. MR grading was performed using semi-quantitative (I-IV) and quantitative (EOA, RV, and RF) methods.

Initial MR grading parameters of the three groups were similar. When the initial and the third month MR parameters of patients were compared, there was a significant decrease in group 1 in effective orifice area (EOA) (p=0.002), regurgitant volume (RV) (p=0.005), regurgitant fraction (RF) (p=0.002) and semi-quantitative MR (p=0.002). There was also a significant decrease in group 2 in EOA (p=0.002), RV (p=0.001), RF (p=0.001) and semi-quantitative MR (p=0.005) grades after 3 months. However, mitral regurgitation severity was not changed with medical treatment in group 3. . There was no difference between groups when residual MR grades at the third month were compared with each other (p>0.05).

Our study showed that percutaneous or surgical revascularization strategies significantly improved MR parameters, on the other hand no improvement was obtained with medical treatment. In spite of the improvement in the severity of MR, there were still significant residual MR after revascularization strategies without valvular intervention. For this reason it can be suggested that revascularization strategies without valvular intervention is effective but not sufficient for the treatment of patients with ischemic MR.

Key words: Ischemic mitral regurgitation, PISA, revascularization

1. Introduction

Ischemic mitral regurgitation (MR) is a common encountered problem in patients with coronary artery disease and it can be an important cause of mortality (1, 2, 3). However the treatment of ischemic MR remains controversial. The general approach is that in addition to revascularization, mitral valve repair should be performed in cases with severe MR and just revascularization will be satisfactory for mild MR. However, the treatment is still unknown for patients with moderate MR.

Recent studies conducted in moderate MR patients have shown that revascularization alone was associated with severe residual MR (3, 4, 5). On the other hand, some studies qualitatively examined the severity of residual MR and the benefits of revascularization. In this study, changes in MR parameters after percutaneous or surgical revascularization in patients with moderate ischemic MR were examined prospectively and quantitatively.

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2. Materials and methods

2. 1. Patient selection

Sixty-seven patients (40 male, 27 female) with moderate MR (2 to 3+) who were offered percutaneous or surgical revascularization due to the diagnosis of coronary artery disease were enrolled in the study. Exclusion criteria were defined as previously known mitral valve disease, mild (1+) or severe (4+) MR, history of percutaneous or surgical revascularization, structural abnormality in the mitral valve apparatus, technical insufficiency of echocardiography, absence of suggested revascularization, acute coronary syndrome after revascularization, accelerated angina or restenosis.

Researchers repeated transthoracic echocardiography (TTE) on all patients at the beginning of the study. Patients were then divided into three groups according to their treatment strategies. Patients who underwent percutaneous coronary intervention (PCI) were defined as group 1, patients who underwent surgical revascularization (coronary artery bypass graft surgery - CABG) as group 2, and patients who denied the offer of revascularization and received medical treatment alone as group 3 (MEDICAL). All patients were contacted by phone three months after TTE and the TTE was repeated (at the third month).

2. 2. Echocardiographic studies

All patients who were enrolled in the study underwent TTE. In our study, the "GE Vivid 7 Cardiovascular Ultrasound System" device and the 1.7 MHz phased array cardiac transducer were used. M-Mode measurements were performed with respect to recommendations of the American Society of Echocardiography (6, 7). Left ventricular ejection fraction (LVEF) was measured using M-mode or two-dimensional (2-D) measurements based on area-length formula (8). The benefit setting for colored Doppler measurements just under the level where artifacts disappear, the Nyquist limit is set at the most appropriate level for each patient where the PISA circle border can clearly be determined. This value was 41±4 cm/s (30–52 cm/s) in our study.

TTE was performed totally two times in all patients at the beginning and at the third month of the study. MR was evaluated both semi-quantitatively and quantitatively. Color flow mapping method was used as a semi-quantitative method and PISA method was used in order to determine quantitative MR parameters such as EOA, RV and RF.

2. 3. Functional evaluation

Functional capacities of patients were assessed according to the New York Heart Association (NYHA) classification at the beginning and at the third month.

2. 4. Statistical analysis

Quantitative variables were given as mean ± standard deviation and qualitative variables were given as percent (%). The data for both groups were tested using normal distribution and variance analysis before the analysis. Group data were compared using Student's t-test and Wilcoxon Signed test. Chi-square test was used for proportional data, whereas the Student's t-test, Mann-Whitney U test, and post hoc Tukey test were used for quantitative data, for inter-group comparison. $P<0.05$ which was obtained during analyses was accepted as statistically significant. All statistical analyses were performed using SPSS 13.0 software.

3. Results

All patients were contacted by phone at the third month. During this period 12 patients were excluded from the study because of death, 1 patient because of mitral valve replacement, 2 patients because of accelerated angina, and 5 patients because they were not accept for TTE at the third month. TTE was performed again on 47 patients at the end of the third month.

Of those who completed the study, PCI was performed on 18 patients (group 1), CABG on 17 patients (group 2), and medical treatment was given to 12 patients (group 3). There was a difference between the groups for the gender and distribution of coronary artery lesions, when comparison of initial clinical characteristics of patients was performed. As there were more males in group 1, whereas there were more left anterior descending artery (LAD) and left circumflex artery (LCx) disease in group 2 and 3 compared to group 1 ($p<0,05$). Groups were similar with respect to other clinical and echocardiographic characteristics (Table 1).

When the initial and the third month MR parameters of patients were compared, there was a significant decrease in group 1 in effective orifice area (EOA) ($p=0.002$), regurgitant volume (RV) ($p=0.005$), regurgitant fraction (RF) ($p=0.002$) and semi-quantitative MR ($p=0.002$). There was also a similar significant decrease in group 2 in EOA ($p=0.002$), RV ($p=0.001$), RF ($p=0.001$) and semi-quantitative MR ($p=0.005$) grades, however MR parameters at the third month were found to be similar to the initial values in group 3 (Table 2). On the other hand the

Table 1. Clinical, angiographic, and echocardiographic features of patients

	Group 1 (n=18)	Group 2 (n=17)	Group 3 (n=12)	p
AGE (year)	66±7	64±9	69±6	>0.05
GENDER				
Male (%)	18 (100)	11 (64.7)	3 (25)	<0.05*
Female (%)	0 (0)	6 (35.3)	9 (75)	
BMI	28±2	29±6	29±6	>0.05
HT	9 (50)	10 (58.8)	9 (75)	>0.05
DM	3 (16.7)	5 (29.4)	7 (58.3)	>0.05
SMOKING	11 (61.1)	7 (41.2)	2 (16.7)	>0.05
CLINICAL DIAGNOSIS				
SAP	3 (17)	2 (12)	3 (25)	>0.05
UAP/NSTEMI	7 (39)	6 (35)	4 (33)	
STEMI	8 (44)	9 (53)	5 (42)	
CORONARY STENOSIS				
LMCA	0 (0)	1 (5.9)	1 (8.3)	>0.05
LAD	9 (50)	16 (94.1)	10 (83.3)	<0.05*
LCx	10 (55.6)	15 (88.2)	11 (99.7)	<0.05*
RCA	14 (77.8)	16 (94.1)	12 (100)	>0.05
BETA-BLOCKER	16 (88.9)	17 (100)	11 (91.7)	>0.05
ACE-I/ARB	17 (94.4)	16 (94.1)	11(91.7)	>0.05
NYHA				
II	12 (67)	11 (65)	5 (42)	>0.05
III	6 (33)	6 (35)	6 (50)	
IV	0 (0)	0 (0)	1 (8)	
LVEDD (mm)	57±6	57±4	57±4	>0.05
LVESD (mm)	41±5	43±4	42±5	>0.05
LVEF (%)	47±8	44±7	46±5	>0.05
LVEDV (ml)	121±29	134±23	128±22	>0.05
LVESV (ml)	65±26	71±19	71±19	>0.05
MR (I-IV)	2.2±0.4	2.4±0.5	2.4±0.6	>0.05
EOA (mm^2)	16±3	18±7	18±5	>0.05
RV (ml)	26±6	27±10	30±9	>0.05
RF (%)	27±8	26±8	31±13	>0.05

BMI: Body mass index, SAP: stable angina pectoris, UAP: unstable angina pectoris, NSTEMI: No ST-segment elevation MI, STEMI: ST-segment elevation MI, LMCA: left main coronary artery, LAD: left anterior descending artery, LCx: left circumflex artery, RCA: right coronary artery, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, LVEF: left ventricular ejection fraction, LVEDV: left ventricular end-diastolic volume , LVESV: left ventricular end-systolic volume, MR: mitral regurgitation, EOA: effective orifice area, RV: regurgitant volume, RF: regurgitant fraction *p<0.05.

PCI group showed improvement in EOA (5±5 mm^2), RV (9.7±12 ml) and RF (10±12%), while patients in CABG group showed improvement in EOA (5±5 mm^2), RV (11±8 ml) and RF (11±6%). There was a significant improvement in left ventricular ejection fraction (LVEF) in group 1 and 2, when left ventricular systolic functions were assessed (p<0.05), while there was also an improvement tendency in left ventricular end-diastolic and systolic diameter. The initial and the third month TTE findings were similar for all parameters in group 3.

There was no difference between group 1 and group 2 with respect to improvement, when MR parameters were compared (Table 3). On the other hand, when the initial and the third month functional status of patients were compared according to the NYHA classification, there was a significant improvement in group 1 (p=0.003) and group 2 (p=0.025), however no improvement was observed in group 3 (p=0.564). According to these data, there was a functional improvement in patients of group 1 and 2 after revascularization. Also when the relationship between residual MR and NYHA classification was examined, initial NYHA decreased from 2.4±0.5 to 1.6±0.7 in patients with mild residual MR (0 to 1+) and from 2.4±0.5 to 2.2±0.5 in patients with moderate residual MR (2 to 3 +) (p=0.011).

When residual MR of patients at the third month was assessed according to color flow mapping method;, there were 9 patients (50%) in

Table 2. Results of groups at the beginning and at the third month

	TTE (at the beginning)	TTE (3rd month)	p
Group 1 (n=18)			
EOA (mm^2)	16±3	11±5	0.002*
RV (ml)	26±6	17±12	0.005*
RF (%)	27±8	16±10	0.002*
MR (I-IV)	2.2±0.4	1.6±0.6	0.002*
Group 2 (n=17)			
EOA (mm^2)	18±7	13±7	0.002*
RV (ml)	27±10	16±10	0.001*
RF (%)	26±8	14±1	0.001*
MR (I-IV)	2.4±0.5	1.7±0.9	0.005*
Group 3 (n=12)			
EOA (mm^2)	18±5	16±6	0.102
RV (ml)	30±9	25±12	0.193
RF (%)	31±13	24±12	0.071
MR (I-IV)	2.4±0.6	2.2±0.8	0.480

group 1, 9 patients (52.9%) in group 2, and 9 patients (75%) in group 3 with mild (2 to 3+) degree of residual MR (p>0.05) (Table 4). There was no patient with severe MR (4+) at the third month.

The relationship between the initial and the third month MR parameters with other parameters was examined. According to this examination there was a positive correlation between EOA and left ventricular end-diastolic volume (LVEDV) (r=0.421 p=0.003) and left ventricular end-systolic volume (LVESV) (r=0.423 p=0.003) (Figure 1) and a negative correlation between initial left ventricular end-diastolic diameter (LVEDD) (r=-0.311 p=0.033) and RV. There was no correlation between EOA and left ventricular ejection fraction (LVEF) (r=0.24 p>0.05).

Table 3. Comparison of in-group variations of MR parameters between group 1 and group 2

	Group 1 (n=18)		Group 2 (n=17)		p
	At the beginning	3rd month	At the beginning	3rd month	
EOA (mm^2)	16±3	11±5	18±7	13±7	>0.05
RV (ml)	26±6	17±12	27±10	16±10	>0.05
RF (%)	27±8	16±10	26±8	14±1	>0.05
MR (I-IV)	2.2±0.4	1.6±0.6	2.4±0.5	1.7±0.9	>0.05

EOA: effective orifice area, RV: regurgitant volume, RF: regurgitant fraction, MR (I-IV): semi-quantitative mitral regurgitation grades.

Table 4. Residual MR grades at the third month

RESIDUAL MR	Group 1 (n=18)	Group 2 (n=17)	Group 3 (n=12)	p
MILD (0-1 +)	9 (50)	8 (47)	3 (25)	>0.05
MODERATE (2-3 +)	9 (50)	9 (53)	9 (75)	

4. Discussion

Ischemic mitral regurgitation (MR) is a common encountered problem in patients with coronary artery disease and residual MR can be an important cause of mortality despite treatment in these patients (3). Unfortunately, recent studies have been unable to come up with an optimal approach to the treatment of ischemic MR. Revascularization alone remains the common approach in the treatment of ischemic MR due to the technical difficulties and insufficient results obtained with mitral valve repair and other methods.

It was shown that early thrombolysis in inferior myocardial infarction reduced localized left ventricle (LV) remodeling and MR (10, 11) however benefit from late coronary revascularization is still controversial. Studies conducted by Balu et al. (11) in 1982 and Christenson et al. (12) reported a significant improvement in MR and left ventricular systolic functions after CABG alone, however no homogeneous MR grade of the patients were observed in these two studies. On the other hand, the opinion that residual MR is an important problem in the treatment of moderate ischemic MR with revascularization alone is becoming increasingly acceptable. The study conducted by Aklog et al. (4) in patients with moderate ischemic MR (3+) reported that 40% of patients continued to have at least moderate MR (3 to 4+) and only 8% of the patients had mild residual MR (<2+) after CABG alone. In another study Harris et al. (5) reported that residual MR grade was 36% in this group of patients. Campwala et al. (3), in their study reported the residual MR grade as 47% after CABG alone. In our study there was a significant improvement in MR parameters of patients who underwent both PCI and CABG. There was no improvement in patients who received medical treatment. However in our study it was found that 50% of patients who underwent PCI, 53% of patients who underwent CABG and 75% of patients who received medical treatment had moderate residual MR ($\geq$ 2+) and residual MR grades were similar between the groups. Although this case supported that revascularization had positive effect on ischemic MR, it is still deemed insufficient.

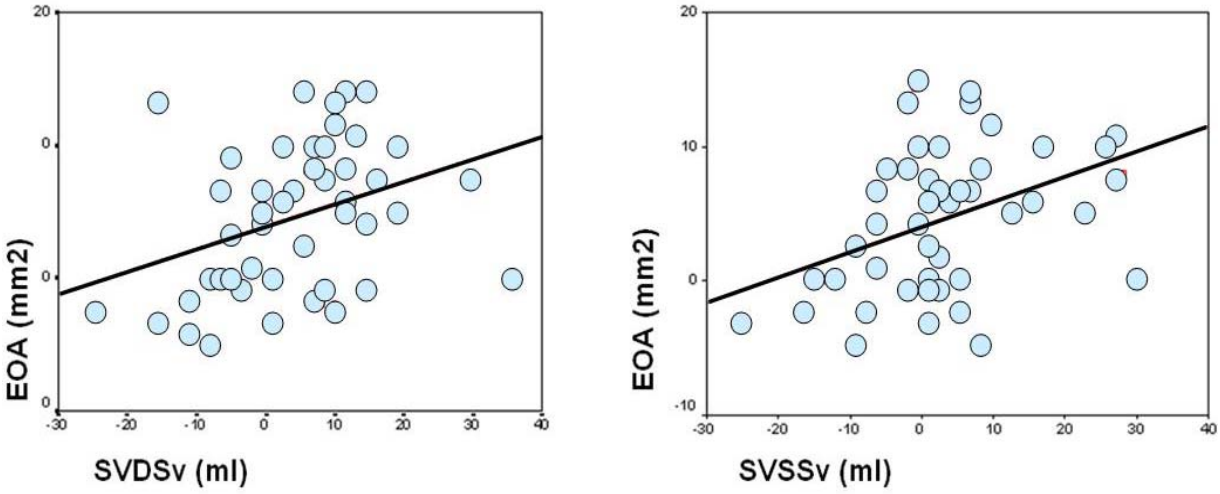

Fig 1. Relationship between effective orifice area (EOA) with left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV).

The effects of residual MR on the surveillance in patients with ischemic MR after coronary revascularization also remains controversial, however many studies have reported that residual MR negatively affected functional status. In our study, it was demonstrated that there was a significant improvement at the third month in the functional status of patients who underwent PCI and CABG. NYHA grades were similar in the medical treatment group at the beginning and at the third month. There was also a significant correlation between improvement in NYHA and MR. On the other hand, initial NYHA of patients with mild residual MR decreased from 2.4±0.5 to 1.6±0.7, and from 2.4±0.5 to 2.2±0.5 in patient with moderate residual MR (p=0.011). As a result, our data supports the fact that moderate residual MR affects the functional status of patients with ischemic MR negatively whether or not they undergo revascularization.

In our study, there was an improvement of 5±5 mm^2 in EOA of patients of both PCI and CABG groups when compared to the beginning. An important feature of great importance is the fact that standard deviation was high for the decrease in EOA. This indicates that the alteration of parameters of patients with MR is not homogeneous after revascularization, MR parameters of some patients never improve or get worse and some patients almost get better. Hence, it can be suggested that the expected benefit from revascularization alone could be different for

every patient. The recently conducted limited number of studies have demonstrated that determinant for residual MR were myocardial activity, appropriate revascularization, excess atherosclerotic load and use of beta blockers (3, 13). In our study a significant correlation was found between MR parameters and LV volumes. As a result it could be predicted that there will be a decrease in MR of patients with anticipated improvement in left ventricular geometry and functions due to revascularization. Revascularization may also has an evident great advantage over medical treatment in the long term due to its positive effects on remodeling.

Both PCI and CABG were preferred method of coronary revascularization in our study. It was observed that prevalence of coronary arteriosclerosis and LAD involvement was an important criterion for determining the mode of treatment. There were also significantly less female patients in the PCI group and it could be related to female patients with more comorbidity, however at the end of the study similar benefits were provided with both two methods for MR parameters. Few studies examining the effects of PCI and CABG on ischemic MR did not show superiority of these two methods over each other in the surveillance (14). However no study has ever examined the effect of PCI and CABG on ischemic MR both prospectively and quantitatively. Thus, we tried to show quantitatively the benefits of revascularization in the treatment of moderate ischemic MR. In our study, percutaneous intervention was similarly effective as a surgical revascularization in MR parameters. Due to the increased perioperative risk in this group of patient, PCI as a less invasive method could be preferred in patients with moderate MR who are planned to undergo revascularization alone.

5. Conclusion

In our study short term outcomes of PCI, CABG and medical treatment in the treatment of ischemic MR were examined prospectively and quantitatively. These data demonstrated that whereas percutaneous or surgical revascularization strategies significantly improved MR parameters, no difference was obtained in the medical treatment group. In our study, benefits obtained inpatients who would undergo revascularization were exhibited quantitatively. In light of these data, the extend to which revascularization alone will be sufficient and the grade of residual MR after the procedure can be estimated. Thus, assessment of alternative treatment strategies would be suitable in cases where revascularization alone is considered inadequate.

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