Mitral valve repair for ischemic moderate mitral regurgitation in patients undergoing coronary artery bypass grafting

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ABSTRACT

الأهداف: الأهداف: دراسة إمكانية إصلاح الصمام التاجي (MVR) في وقت تحويل الشريان التاجي لدى المرضى الذين يعانون من الارتجاع المتوسط للصمام الميترالي الناتج عن نقص التروية (MR) وإمكانية تحسن نتائج مرض الشريان التاجي بعد العملية الجراحية على المدى القصير والمتوسط الأجل.

الطريقة: خضع 90 مريض يعانون من الارتجاع المتوسط للصمام الميترالي MR لتحويل الشريان التاجي لأول مرة في مستشفى بورصة يكساس ايهتاس للتدريب والأبحاث، بورصة، تركيا وذلك خلال الفترة من 2013–2015. من بين 90 مريض، خضع 44 (48.9%) لتحويل مسار الشريان التاجي و MVR، بينما خضع 46 (51.1%) لتحويل مسار الشريان التاجي فقط. تم تقييم وظائف البطين وقدرات الجهد للمرضى في كلا المجموعتين بتخطيط صدى القلب وسريرياً في فترة ما قبل التنفيذ و في أول سنة بعد العملية الجراحية .

النتائج: تغير الحجم القلسي بعد العملية وفقاً للقيم ماقبل التنفيذ 19±24.76– مل/نبضة في مجموعة تحويل مسار الشريان التاجي و MVR و7.2±8.70– مل/نبضة في مجموعة تحويل مسار الشريان التاجي فقط p=0.001. وكان التغير في عرض الوريد النابض 0.2±3.40– ملم في مجموعة تحويل مسار الشريان التاجي و MVR و 0.7±1.45– ملم في مجموعة تحويل مسار الشريان التاجي فقط p=0.019. وكانت التغيرات في مؤشر حجم البطين الأيسر نهاية الانقباض 25.9±30.77– مل/متر مربع في مجموعة تحويل مسار الشريان التاجي و MVR و –15.6 ± 9.4 مل/متر مربع في مجموعة تحويل مسار الشريان التاجي (p=0.096). وكانت تغييرات الكسر القذفي في مجموعة تحويل مسار الشريان التاجي و MVR 1.51 ± 5.3 ٪ و في مجموعة تحويل مسار الشريان التاجي كانت 1.15 ± 4.3%، ولم يظهر فرق ذو دلالة إحصائية بين المجموعتين (p=0.604). وكانت قيم جمعية نيويورك للقلب قبل الجراحة في مجموعة تحويل مسار الشريان التاجي و MVR 2.18 ± 0.45 و 2.13 ± 0.54 في مجموعة تحويل مسار الشريان التاجي.

الخاتمة: الارتجاع المتوسط للصمام الميترالي MR في المرضى الخاضعين لتحويل الشريان التاجي CABG يؤثر على النتائج سلباً كما أنه ليس موثوق للتحسين بعد تحويل مسار الشريان التاجي CABG. ولذلك، ينبغي على المرضى الذين يعانون من الارتجاع المتوسط للصمام الميترالي الخضوع لإصلاح الصمام التاجي في وقت تحويل مسار الشريان التاجي.

Objectives: To investigate whether mitral valve repair (MVR) at the time of coronary artery bypass grafting (CABG) in patients with ischemic moderate mitral regurgitation (MR) and coronary artery disease could improve short- and mid-term postoperative outcomes.

Methods: Between March 2013 and December 2015, 90 patients with moderate ischemic MR underwent first-time CABG in Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey. Out of 90 patients, 44 (48.9%) underwent combined CABG+MVR. The remaining 46 (51.1%) underwent CABG alone. Ventricular functions and effort capacities of patients in both groups were evaluated echocardiographically and clinically in the preoperative period, and in the first postoperative year.

Results: Postoperative regurgitant volume changes according to preoperative values were -24.76±19 ml/beat in the combined CABG+MVR group, and -8.70±7.2 ml/beat in the CABG alone group (p=0.001). The change of vena contracta width was -3.40±0.2 mm in the combined CABG+MVR group whereas in the CABG alone -1.45±0.7 mm (p=0.019). The changes of left ventricular end-systolic volume index were -30.77±25.9 ml/m^2 in the combined CABG+MVR group and -15.6±9.4 ml/m^2 in the CABG alone group (p=0.096). Ejection fraction changes in the combined CABG+MVR group was +1.51±5.3% and in the CABG alone group was +1.15±4.3%.No statistically significant difference was found between both groups (p=0.604). Preoperative New York Heart Association class values in the combined CABG+MVR group was 2.18±0.45, and in the CABG alone group was 2.13±0.54.

Conclusions: Moderate MR in patients undergoing CABG affects the outcome adversely and it does not reliably improve after CABG alone. Therefore, patients with ischemic moderate MR should undergo simultaneous MVR at the time of CABG.

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Functional ischemic mitral regurgitation (MR) emerges in almost half of patients with myocardial infarction.[1] Such exposure may vary from mild MR to severe MR, which may lead to severe heart failure and death.[2] Diametrical and geometrical changes of the myocardium, depending on having myocardial infarction and coronary artery disease, and ischemia-affected chorda and papillary muscles make up the major cause of MR. When MR in patients undergoing coronary artery bypass grafting (CABG) is severe, surgical intervention of the mitral valve is mandatory. However, the role of intervening mitral valve of the patients with moderate MR who will undergo coronary bypass surgery, has been not agreed upon exactly due to the extra surgical process.[3] Some surgeons think that moderate MR also improves if they can correct the ischemia with CABG. Surgeons are more reluctant to perform mitral valve interventions, as they worry that mitral valve surgery together with coronary revascularization can increase the morbidity and mortality rate.[4,5] The aim of this study was to investigate whether MVR at the time of CABG in patients with ischemic moderate MR and coronary artery disease could improve short- and mid-term postoperative outcomes.

Methods. Ninety patients with moderate ischemic MR underwent first-time CABG in Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey, between March 2013 and December 2015. Out of the 90 patients, 44 (48.9%) underwent combined CABG + mitral valve repair (MVR). The remaining 46 (51.1%) underwent CABG alone (**Table 1**). During operation, the decision regarding MVR was at the surgeons' discretion. The Institutional Ethics Committee approved this retrospective study, and the patients written consent was received. In this study, exclusion criteria were as follows: serious left ventricular dysfunction (ejection fraction [EF] <25%), coexisting serious aortic valve disease, the existence of active endocarditis, history of any cardiac operation, experiencing emergencies such as pulmonary edema and cardiogenic shock, and serious organ dysfunction (renal failure, severe chronic obstructive pulmonary disease, liver failure). Ventricular functions and effort capacities of the patients in both groups were evaluated by echocardiographic study and clinical examination.

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Table 1 - Preoperative characteristics and demographic data of 90 patients with moderate ischemic mitral regurgitation undergoing CABG in Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey.

Demographic data	Combined CABG+MVR (n=44) n (%)	CABG alone (n=46) n (%)	*P*-value
Age (mean±SD)	61±3.2	63±2.7	0.8
Gender (female/male)	21/23	19/27	0.7
Body mass index (mean±SD)	28±5.0	29±3.1	0.7
COPD	6 (13.6)	8 (17.0)	0.3
Diabetes mellitus	26 (59.0)	27 (58.6)	0.7
Previous cerebrovascular accident	1 (2.2)	2 (4.3)	0.2
Peripheral artery disease	7 (15.9)	6 (13.0)	0.8
Atrial fibrillation	7 (15.9)	8 (17.3)	0.3
Tricuspid valve regurgitation (moderate to severe)	9 (20.4)	8 (17.3)	0.3
Single-vessel coronary disease	3 (6.8)	5 (10.8)	0.3
Two-vessel coronary disease	7 (15.9)	9 (19.5)	0.3
Triple-vessel coronary disease	15 (34.0)	14 (30.4)	0.7
Multi-vessel coronary disease	19 (43.1)	18 (39.1)	0.2

COPD - chronic obstructive pulmonary disease, CABG - coronary artery bypass grafting, MVR - mitral valve repair

Echocardiographic parameters and effort capacities of both patient groups were evaluated both preoperatively and postoperatively at months 3 and 6, and in year one, whereas the patients who were followed up longer were evaluated every year. They were followed up on average for 17 months. The first-year measurements of these values were used in the study. Regurgitant volume, vena contracta, left ventricular end systolic volume index (LVESVI), and EF measurements of the combined CABG+MVR and CABG alone groups were compared echocardiographically. Mitral regurgitation was evaluated through echocardiography according to the criteria of moderate MR stated in the American Heart Association (AHA) and American Society of Echocardiography (ASE) guidelines. Patients who had effective MR area of 0.20-0.39 cm^2, regurgitant volume of 30-59 ml/beat, regurgitant fraction of 30-49%, and vena contracta width of 0.30-0.69 cm in this evaluation were included in the study group. Preoperative and postoperative effort capacities of the patients were evaluated according to the New York Heart Association (NYHA) functional classification (**Table 2**). Patients of both groups had similar optimal medical treatments in the postoperative period. Aspirin, beta blocker, angiotensin converting enzyme inhibitors (ACE), and statin were administered to all patients who had no contraindications. Warfarin was given to combined

Table 2 - New York Heart Association (NYHA) classes range from I to IV, with higher classes indicating poorer condition.

NYHA class	Preoperative effort capacity		Postoperative effort capacity	
	Combined CABG+MVR n=44	CABG alone n=46	Combined CABG+MVR n=41	CABG alone n=41
Class I (%)	3 (6.8)	4 (8.7)	12 (29.3)	9 (22.0)
Class II (%)	30 (68.2)	32 (69.6)	26 (63.4)	25 (61.0)
Class III (%)	11 (25.0)	10 (21.7)	3 (7.3)	6 (14.6)
Class IV (%)	-	-	-	1 (2.4)
Mean NHYA class (mean±SD)	2.18±0.45	2.13±0.54	1.78±0.56*	1.97±0.68**

*p=0.002, **p=0.02

Table 3 - Operative and postoperative results of 90 patients with moderate ischemic mitral regurgitation undergoing CABG in Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey.

Results	Combined CABG+MVR (n=44) n (%)	CABG alone (n=46) n (%)	*P*-value
Coronary artery distal anastomosis	3.0	3.1	0.7
Tricuspid valve annuloplasty	9 (20.4)	8 (17.3)	0.3
Cross-clamp time (min) (mean±SD)	92 ± 17	58 ± 22	0.002
IABP use	3 (6.8)	2 (4.3)	0.2
Intubation time (hours) (mean±SD)	17 ± 9	14 ± 5	0.2
Hemodialysis need	3 (6.8)	3 (6.5)	0.8
30-day mortality	1 (2.2)	1 (2.1)	
Cerebrovascular accident	1 (2.2)	-	
Bleeding revision	1 (2.2)	-	
Trianguler resection	12 (27.2)	-	
Comissuroplasty	5 (11.3)	-	
Neocorda implantation	7 (15.9)	-	

Data are expressed as number (percentage). CABG - coronary artery bypass grafting, MVR - mitral valve repair, IABP - intra-aortic balloon pumping

CABG+MVR patients in the first 3 months and the international normalized ratio (INR) value of 2.0-3.0 was adjusted.

Surgical technique. Standard on-pump surgery was applied to all patients. All severe stenosed coronary vessels of the patients were revascularized using the left internal thoracic artery and saphenous vein graft. Initially, the mitral valve apparatus were examined in detail for valve repair after distal anastomoses were completed. Structural defects of the valve were eliminated using appropriate techniques. Leaflet repair techniques such as triangular resection, quadranguler resection, neochorda and commissurotomy were applied additionally for the structural defects in the valve apparatus (**Table 3**). Rigid mitral ring (SJMTM Rigid Saddle Ring, St-Jude Medical, St. Paul, MN, USA) was used for all patients with mitral repair. A smaller size of anterior mitral leaflet dimension was used to select the ring measurement. De Vega annuloplasty, or ring annuloplasty was performed with Teflon patch strips applied to tricuspid valves of all patients in both groups who had moderate and severe tricuspid regurgitation. Operative details are given in **Table 3**.

Statistical analysis. All the data was analyzed using the Statistical Package for Social Sciences version 12.0 (SPSS Inc., Chicago, IL, USA). Data are given as mean ± standard deviation. Numbers and percentages are presented for categorical data. Mann-Whitney test was applied to independent variables. Categorical comparisons were made using the x^2 test, or Fisher exact

test as appropriate. A probability value of ≤0.05 was considered statistically significant.

Results. Demographic characteristics of the patients are shown in **Table 1**. No significant differences between preoperative demographic characteristics of both groups were observed. In this study, the cause of the tricuspid regurgitation is not searched. Tricuspid valve annuloplasty was carried out in both groups in order to decrease the effect of tricuspid regurgitation to postoperative echocardiographic parameters (**Tables 1 & 3**). The ring sizes used in patients who had undergone MVR varied between 26 and 34. A 26 number ring was used in 2 patients (4.5%), 28 in 21 (47.7%), 30 in 18 (40.9%), 32 in 2 (4.5%), and 34 in one patient (2.2%). Nine patients in the combined CABG+MVR group and 8 patients in the CABG alone group underwent tricuspid valve annuloplasty. Any significant difference in the tricuspid valve intervention between both groups was not observed (p=0.3). The mean amounts of postoperative drainage in the CABG alone group was 700 cc and in the combined CABG+MVR group was 900 cc. The amount of postoperative blood loss and transfusion of blood products (platelets and fresh frozen plasma) were similar in both groups.

A patient of combined the CABG+MVR group was taken to re-operation for mediastinal bleeding. In the combined CABG+MVR group, operative mortality in the first 30 days was 2.2% with one case (multi-organ failure, which developed due to low cardiac output). In the CABG alone group, the operative mortality was 2.2% with one case of pulmonary infection, which developed as a result of extended intubation and sepsiss. One patient (2.2%) from the combined CABG+MVR group had hemiparesis. Two patients of each group with preoperative renal dysfunction were temporarily subjected to hemodialysis. Two died patients who were in the separate groups had hemodialysis during their extended organ failure period in the intensive care and during the sepsis period. Thus, a total of 6 patients (combined CABG+MVR of 6.8%, CABG alone of 6.5%) were subjected to hemodialysis (**Table 3**).

Although the mean hospitalization period of the patients in the combined CABG+MVR group was longer (8.2 days), it was not statistically significant. The difficulty of dosage for Warfarin treatment applied in the first 3 months necessitated the extended hospitalization period.

The mortality rate for 30 days was 2.2%, and included one case from each group. Within the follow-up period, one patient from the combined CABG+MVR group had exitus due to additional cardiac reasons. One patient had no follow-up due to living out of town. Thus, the number of cases in the combined CABG+MVR group, which was 44 initially decreased by 3 and became 41. In the CABG alone group, the number of cases was 46 in the beginning of the study. In addition to one patient who died in the first 30 days, one patient had exitus due to cardiac and extra cardiac reasons. Two patients of the same group could not be reached, so they did not attend for to follow-up. As a result, 41 patients were followed up in the CABG alone group. Eighty-two patients were followed up until the end of the first year.

There was no significant difference in preoperative variables between both study groups (**Table 1**). Complete revascularization was performed in both groups. The left internal thoracic artery on the left anterior descending coronary artery as arterial conduit was anastomosed in all patients. The saphenous vein grafts were used in other target coronary vessels. During postoperative evaluations, a statistically significant difference in parameters such as an number of bypass performed (p=0.7), intra-aortic balloon pump (IABP) need (p=0.2), intubation time and hospitalization period (p=0.2) between both groups was not found. The cross clamp period from the combined CABG+MVR group (92±17 min) was longer compared with the CABG group (58±22 min) in terms of statistical significance

Table 4 - Preoperative and postoperative one year in the combined CABG+MVR group versus the CABG alone group among 90 patients.

Variables	CABG+MVR (n=44)	CABG +MVR (n=41)		CABG alone (n=46)	CABG alone (n=41)		
	Preoperative	Postoperative one year	Mean change in values	Preoperative	Postoperative one year	Mean change in values	*P*-value
Regurgitan volume (ml/ beat)	34.16±6.52	9.4±3.7	-24.76±19	33.63±6.43	24.70±9.3	-8.70±7.2	0.001
Vena contracta (mm)	4.79±0.73	1.39±0.73	-3.40±0.2	4.93±0.77	3.48±1.07	-1.45±0.7	0.019
Ejection fraction (%)	46.09±7.2	47.6±14.3	+1.51±5.3	42.45±6.6	43.6±16.4	+1.15±4.3	0.604
LVESVI (ml/m^2)	75.86±7.8	45.09±14.7	-30.77±25.9	75.0±7.6	59.4±22.8	-15.6±9.4	0.096

Data are express as mean±standar deviation. LVESVI - left ventricular end systolic volume index, CABG - coronary artery bypass grafting, MVR - mitral valve repair

(**Table 3**). The regurgitant volume, vena contracta, left ventricular end systolic volume index, and ejection fraction of combined CABG+MVR and CABG alone groups are summarized in **Table 4**. Preoperative and postoperative change of the regurgitant volume, vena contracta, ejection fraction, and LVESVI was observed (**Table 4**). Preoperative and postoperative values and changes of echocardiographic parameters in which we evaluated the ventricular functions are also shown in **Table 4**. In both groups, a significant improvement was observed compared with the preoperative period, but the improvement in the combined CABG+MVR group was found to be better than that of the CABG alone group in terms of statistical significance. At the end of one year, echocardiographic evaluation showed a decrease in MR in all patients who had MVR. But it was observed that there was mild-moderate MR in 3 patients. But it was observed that MR levels of 3 patients continued to be mild-moderate. Although the change of regurgitant volume and LVESVI values of these patients decreased by 20%, we considered them as a relapse group, since their measurement values stayed within moderate MR limits. For 3 patients, it was calculated as 7.3%.

The effort capacity of both groups improved after the operation. In the evaluation of effort capacity made preoperatively, the NYHA functional classification was used. The patient number and changes of preoperative and postoperative NYHA classification are summarized in **Table 2**. When the mean values were examined, preoperative means of NHYA class in the combined CABG+MVR group was 2.18±0.45 and in the CABG alone group was 2.13±0.54. In the first postoperative year, the mean NHYA class of the combined CABG+MVR group was 1.78±0.56 (p=0.002) whereas the CABG alone group was 1.97±0.68 (p=0.02). Even though such changes showed significance in both groups, the change in the combined CABG+MVR was more significant.

Discussion. Various levels of MR accompany coronary artery disease in most patients who referred to cardiovascular surgery for coronary artery revascularization. In patients with severe MR, there is general agreement for mitral valve repair surgery at the time of CABG. However, the value of mitral valve surgery has still not been clarified in moderate MR. Although there are numerous studies on this subject asserting valve repair, many studies argue that valve repair is not advantageous.[4-9] According to the results of our study, MVR was applied on the mitral valves of patients with ischemia-related moderate MR, together with coronary revascularization to eliminate the mechanical problem causing MR although it was regarded as an extra process that extends the pumping period. This situation affected both the clinical results of the patients in the repair group and their echocardiographic evaluation parameters positively.

One of these parameters, LVESVI is accepted as an indicator of left ventricular remodeling and prognosis of ischemic myocardial disease as well.[10] In our study, a statistically significant change was seen in LVESVI, an important indicator of ventricular remodeling of the group who had MVR together with CABG, compared to the group undergoing CABG alone. Furthermore, it was observed in clinical evaluation that the change of effort capacities of the group with mitral annuloplasty was better than that of the other group. Despite the fact that a significant decrease in the regurgitant volume was observed in the combined CABG+MVR group, compared with the CABG alone group, the ejection fraction measured did not create a significant difference between both groups. We considered its reason depend on the regurgitant volume of left atrium is measured as the ejection fraction for calculation system during the ventricular contraction due to the ongoing MR in the CABG alone group. In our study, the cross clamp time of the group who had MVR together with CABG, one of the operative parameters was found to be longer than that of the group who were not subjected to valve intervention. This finding became the single significant value found in the group undergoing CABG alone.

The randomized Ischemic Mitral Evaluation (RIME) trial published by Chan et al,[9] evaluated the measurements of plasma B-type natriuretic peptide (BNP) for prognosis and severity of heart failure, and the use of peak oxygen consumption as an objective measure of the functional capacity. The RIME trial showed significant increase of LVESVI, a decrease of mitral regurgitant volume, a rise of peak oxygen volume, and a fall of BNP level in the combined CABG+MVR group compared with those undergoing CABG alone at one-year follow-up.[9] In the current study, we observed that the clinical results of MVR performed in addition to CABG were much better than those of the patients that underwent CABG alone in the first year. Our results are compatible with the results of RIME trial. Similar to our study, the RIME trial includes only one-year results and this requires the contribution of MVR to patient's survival, and its results to be revised further over a longer term. Another study[11] that supports our results reported on animal testing using on sheep. In this functional and molecular study, there were 2 groups

moderate MR. Only minor changes of left ventricular volume and left ventricular remodeling were observed in the group that still had MR, whereas an increase in the left ventricular volume and an improvement of the left ventricular remodeling were seen in the group that underwent MVR.[11] In contrast to our study, it was stated in a similar study of Smith et al[8] that MVR of 301 patients who underwent CABG and had moderate MR did not contribute to improvement of left ventricular remodeling positively. In the same study, it was specified that the results of one-year follow-up and clinical evaluations did not show any additional benefit of MVR. Furthermore, it was mentioned that the number of undesired events was higher in the group subjected to MVR.[8] Srivastava et al[12] analyzed 16 from 465 studies to find the answer to the question. "Should mitral repair, or mitral replacement be applied to patients with mild, or moderate ischemic MR and underwent CABG?" They concluded that moderate MR in patients undergoing CABG alone negatively affects the survival, and MR did not safely improve after CABG alone. It was stated that the ideas favoring the application of MVR at the same time in patients who underwent CABG and had moderate MR were dominant. Some surgeons recommended concomitant mitral valve surgery with CABG surgery in order to optimize the cardiac function and long-term prognosis of the patients. On the other hand, several surgeons recommended CABG alone as combined CABG+MVR are associated with higher morbidity and mortality.[13]

An important reason for this evaluation is the possibility of MR, which repeats, or creates residue after MVR, and concerns associated with it. Likewise, Dion et al[14] reported in their studies that residue MR of 15% remains after MVR. However, the most important reason for this may be suboptimal surgical techniques, insufficient downsizing of annuloplasty rings, and incomplete revascularization.[15] An important reason for ischemic MR is the posterior papillary muscle dysfunction. In our opinion, important reason of the residue MR can be that adequate emphasis is not placed on the posterior descending artery revascularization or the process is not performed. There are reports on a significant recurrent MR after full-rigid, or semi-rigid ring mitral valve annuloplasty, which usually emerges after 3 years.[15] In our study, recurrent MR occurred in 3 patients (7.3%) within the first follow-up period. The use of three-dimensional rigid annular ring in valve repair may be the reason of this recurrence. According to the 2014 ACC/AHA guidelines,[16] MVR may be considered in patients with chronic moderate secondary MR (stage B) undergoing other cardiac surgery (Class IIb, Level of Evidence: C).[16]

Study limitations. One limitation was the lack of assessment of viability of the myocardium. One could argue that the patients offered CABG alone had a significant burden of scar tissue and hence did not show improvement in echocardiographic parameters. Another limitation of the study is the possible impact of inter-observer variation in the interpretation of echocardiograms. The mean follow-up period for their study was one year, so the course of MR of both groups over a longer term.

In conclusions, what is not known moderate MR in patients undergoing CABG affects the outcome adversely and it does not reliably improve after CABG alone. An increase in the effort capacity, improvement of ventricular remodeling, and regression of MR are more significant in patients with combined CABG+MVR compared with those of CABG alone patients. Therefore, patients with ischemic MR should undergo simultaneous MVR at the time of CABG. This positive effect should be supported by longer-term randomized studies.

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