

- ¹ Ekin İlkeli
- ¹ Ahmet Bollukçu
- ¹ Ufuk Çiloğlu
- ¹ Şebnem Alibeyoğlu
- ¹ Sabri Dağsalı

¹ Siyami Ersek Training and Research Hospital, Cardiovascular Surgery Clinic, Istanbul.

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Corresponding Address / Yazışma Adresi:

Ekin İlkeli

Siyami Ersek Training and Research Hospital, Cardiovascular Surgery Clinic, Istanbul, Turkey.

Phone: +0905056384372

Fax: +0902125137431

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EVALUATION OF MID-TERM CLINICAL AND ECHOCARDIOGRAPHIC OUTCOMES OF ALFIERI (EDGE-TO-EDGE) MITRAL VALVE REPAIR

Alfieri (Uç-uca) Mitral Kapak Tamirinin Orta Dönem Ekokardiografik ve Klinik Sonuçlarının Değerlendirilmesi

ABSTRACT

Aim: The present study aimed to evaluate mid-term clinical and echocardiographic outcomes of the Alfieri edge-to-edge repair performed on patients with moderate to severe mitral regurgitation (MR).

Methods: Thirty patients (mean age, 61.2±11.2 years; 18 males) with moderate to severe MR of different etiologies and a pulmonary artery pressure (PAP) of >40 mmHg who underwent a Alfieri repair between 2005 and 2011 were included. All patients were selected and followed by the same surgical team and cardiologist. The Alfieri edge-to-edge repair with ring annuloplasty was performed. The patients were postoperatively evaluated in terms of degree of MR, functional capacity according to the New York Heart Association (NYHA) classification, PAP, left atrial diameter (LAD), atrial fibrillation, ejection fraction (EF), risk of functional mitral stenosis, etiological factors, and mortality.

Results: Postoperative NYHA class, MR and LAD values of the study patients were significantly better as compared to the preoperative values (p<0.001). The rate of patients with increased mean PAP in the preoperative period significantly reduced in the postoperative period (70% vs. 30%, p<0.001). Functional mitral stenosis developed in only one patient. Mortality was found higher in the patients with ischemic MR with higher NYHA functional class than in those with degenerative or rheumatic MR.

Conclusion: Mid-term outcomes of the Alfieri edge-to-edge repair with ring annuloplasty, particularly in degenerative mitral valve pathologies, are promising. Regression in symptoms, improvements in functional capacity and examination findings, and decrease in the degree of MR, and the improvements in the echocardiographic findings including decrease in PAP and LAD values, and the absence of atrial fibrillation and thromboembolism are important clinical outcomes.

Key words: mitral regurgitation, mitral repair, Alfieri, valvular heart disease.

ÖZET

Amaç: Bu çalışmamızda alfieri prosedürü (edge-to-edge) uygulanmış orta –ileri mitral yetmezlikli hastalarda orta dönem klinik ve ekokardiografik sonuçları değerlendirildi.

Yöntem: 2005-2011 yılları arasında alfieri (edge-to-edge) tamir uygulanan ,farklı etyolojiye sahip orta ve ileri mitral yetmezliği olan ,pulmoner arter basıncı 40 mmhg ustunde bulunan 30 hasta (yaş ortalamaları 61,2±11,2 yıl olan 12 kadın, 18 erkek) çalışmaya dahil edildi.Tüm hastalar aynı cerrahi ekip ve kardiolog tarafından seçilmiş ve takip edilmiştir. Tüm hastalara alfieri (edge-to-edge) onarım yapılarak hepsinde ring implantasyonu eklendi.Hastalar postoperatif olarak ; mitral yetmezliğin derecesi,NYHA fonksiyonel kapasite,pulmoner arter basıncıları,sol atrıal boyut,atrıal fibrilasyon,ejeksiyon fraksiyonu,fonksiyonel mitral stenoz, riski,etyolojık değişkenler ile mortalite açısından karşılaştırıldı.

Bulgular: Çalışmaya dahil edilen hastaların NYHA, MY ve LAD postoperatif değerleri preoperatif değerlerinden istatistiksel anlamlı düşüktü .(p<0.001) Hastaların pre mPAP yüksekliği oranı %70, post mPAP oranı %30'du. PAP 'daki azalma istatistiksel olarak anlamlıydı (p<0,001). Bizim çalışmamızda sadece bir hastada fonksiyonel mitral stenoz gelişmiştir. İskemik mitral yetmezlikli fonksiyonel NYHA kapasitesi yüksek olan hastalarda mortalite, diğer etyolojilere(değeneratif,romatizmal) bağlı hastalara göre daha yüksek bulunmuştur.

Sonuç: Özellikle dejeneratif mitral kapak patolojilerinde; alfieri tipi edge-to-edge onarım ring anüloplasti ile uygulandığında orta dönem sonuçları yüzgüldürücüdür. Gerek hastalarda gözlemlediğimiz semptomlar, muayene ve fonksiyonel kapasitede düzelme ,mitral yetmezliğin derecesinde azalma, gerekse hastaların orta dönem eko bulguları itibarıyla PAP'ında düşme, LAD azalma, tromboemboli ve AF olmaması önemli birer sonuçtur.

Anahtar kelimeler: Mitral yetmezlik, mitral tamiri, alfieri, kalp kapak hastalığı.

INTRODUCTION

In cardiac surgery, mitral valve repair (MVR) has become a primarily preferred surgical technique over mitral valve replacement, as MVR is associated with lower morbidity and mortality rates (13), better-preserved left ventricle functions and quality of life (13), low rates of thromboembolism and stroke (10), resistance to endocarditis (10), and better long-term survival rate without reoperation (10).

According to the European statistics in 2001, however, the rate of MVR remained at 46.5% in patients undergoing mitral valve surgery (11). In the USA, the rate of MVR, which was 37.7% between the years 1999 and 2000, increased up to 69% between the years 2000 and 2007 (3,14).

In Turkey, despite the increase in the number of MVR performed in recent years, there is considerable uncertainty about MVR surgery due to the differences between patient populations undergoing mitral valve surgery in Turkey and those in Europe and in the North America.

Ischemic mitral regurgitation (MR) is an issue that has been particularly discussed in recent years in terms of both diagnostic and therapeutic approaches. Coexistence of ischemic MR and coronary artery disease (CAD) significantly influences patient survival. Severe MR should certainly be repaired together with coronary surgery. For this purpose, MVR should be the preferred surgical approach. The predominant opinion is that mitral valve should also be intervened in the presence of moderate MR in patients in whom cardiac surgery is planned.

The Alfieri edge-to-edge repair has begun to be used in the early 1990s as a simple and effective surgical procedure in the treatment of mitral regurgitation due to complex lesions. The basic principle of this technique is to simply repair a mitral regurgitation by suturing the free edge of the diseased leaflet, exactly at which the regurgitant jet flow is located, to the corresponding edge of the opposite leaflet. The main indication for this procedure is MR developed due to bileaflet prolapse (Barlow's syndrome), anterior leaflet prolapse, commissural prolapse, and functional mitral regurgitation (secondary to ischemic or idiopathic dilated cardiomyopathy).

Leaflet prolapse or flail, which is typically found in degenerative mitral valve disease, are the most common targets of the edge-toedge repair. These lesions can also be successfully repaired using the same technique even they appear due to endocarditis process.

The present study aimed to present mid-term clinical and echocardiographic outcomes of MVR option, Alfieri repair with ring annuloplasty, performed in patients with MR of various etiologies in our clinic between 2005 and 2011.





MATERIAL AND METHODS

Patient Selection and Follow-up: Thirty patients with moderate to severe MR who underwent the Alfieri edge-to-edge repair with annuloplasty ring implantation between 2005 and 2011 in our clinic were included in the study. Simultaneously, coronary artery bypass grafting (CABG) surgery was performed in 15 patients due to ischemic MR, and aortic valve replacement (AVR) was performed in one patient. Two patients were re-operated on due to CABG-related complications. All patients were selected and followed by the same surgical team and cardiologist.

Mitral valve patients who had moderate to severe MR, a functional capacity of the New York Heart Association (NYHA) class II or more, a pulmonary artery pressure (PAP) of >40 mmHg, degenerative/rheumatic valve with repair option, and accompanying CAD with low ejection fraction (EF<40%) and comorbidity.

Perioperative transesophageal echocardiography (TEE) was performed in the majority of patients. Functional capacity was evaluated by echocardiography, which was performed regularly in the early postoperative period, and on the postoperative 3rd and 6th month. Patients were postoperatively evaluated in terms of degree of MR, functional capacity according to the NYHA classification, PAP, left atrial size, atrial fibrillation, EF, risk of functional mitral stenosis, etiological variables, and mortality.

Surgical Technique: Median sternotomy was performed in all patients. Bicaval venous cannulation was done. Myocardial prevention was obtained by intermittent antegrade cold blood cardioplegia. The central parts of two leaflets were identified by subvalvular apparatus as a guide after left atriotomy subsequent to obtain sufficient exposu Median sternotomy was performed in all patients. Bicaval venous cannulation was done. Myocardial prevention was obtained by intermittent antegrade cold blood cardioplegia. The central parts of two leaflets were identified by subvalvular apparatus as a guide after left atriotomy subsequent to obtain sufficient exposure. Chordas connected to anterolateral and posteromedial papillary muscles were determined by a hook. Furthermore the middle anatomical points of anterior and posterior leaflets were determined. Consequently edge to edge reparation with 4/0 prolene suture was performed. Additionally a routine ring annuloplasty was done in all patients. Mitral valve space was evaluated by Hegar dilatator. Test control was done by injecting saline into the left ventricle. All patients were evaluated with peroperative transesophageal echocardiography.

Statistical analysis: Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL, USA) version 15.0 for Windows. Categorical variables were presented in frequency tables, and numerical variables were summarized using the descriptive statistics (mean, standard deviation, minimum and maximum). Between-group comparisons of categorical variables were analyzed by the Chi-square test using cross-tables. For non-normally distributed data, the Wilcoxon test was used for two dependent groups, whereas two independent groups were compared using the Mann-Whitney U test. A p value <0.05 was considered statistically significant.

RESULTS

Clinical, echocardiographic, and preoperative characteristics of the patients are presented in Table 1. Thirty patients [12 (40%) females, 18 (60%) males] with a mean age 61.2 ± 11.2 years were included in the study. Of the patients, 15 (50%) had ischemic MR, six (20%) had Barlow prolapse, and nine (30%) had rheumatic degenerative MR. Two (6.7%) patients had undergone reoperation (due to CABG-related complications).

In the present study, NYHA functional class, MR, and left atrial

diameter (LAD) values were significantly lower in the postoperative period than in the preoperative period (p<0.001). The rate of patients with increased mean PAP (mPAP) was 70% preoperatively, and this rate significantly decreased to 30% postoperatively (p<0.001, Figure 1).

The NYHA class was significantly higher in the patients in whom mortality was observed (p<0.001). Pre- and post-operative EF, NYHA functional class, MR, and LAD values of the patients are summarized in Table 2.

In the present study, functional mitral stenosis developed only in one patient.

The rate of mortality was found higher in the patients with ischemic MR with high NYHA functional class than in the patients with MR of other etiologies (degenerative and rheumatic). In these patients, the postoperative EF values were found to be low; however, it was not significant in the patients with ischemic MR because they had already poor left ventricular functions. (Table 3)

Mortality was observed in eight patients, of whom six had ischemic MR and two were in the degenerative-rheumatic group (Table 4).

DISCUSSION

Ischemic or degenerative MR leads to an ever-increasing morbidity and mortality due to aging of the population. Although exact rates for Turkish population are lacking, annually 7,800,000 subjects in the USA experience myocardial infarction with or without ST elevation; of these patients, 19% in average have the risk of ischemic MR of various degrees (from trace to advance stage). In such patients, surgical coronary revascularization alone fails to reduce ischemic MR (1,7), which points out that MVR should also be performed during surgical revascularization in patients with trace or mild MR (2,7). The rate of degenerative MR has been increasing in recent years due to aging of the population. Although the targeted treatment success levels were not achieved by MVR at the beginning in these patients, success rates have been gradually increasing with the advances in surgical techniques. Although there is a slight difference between patients with Barlow's disease and fibroelastic deficiency in terms of morbidity and mortality, MVR has become the preferred method over prosthetic valve implantation also in this patient group (4).

In the last 20 years, ring annuloplasty with artificial ring

 Table 1: Preoperative clinical characteristics of the study patients.

Characteristics	Patients (n=30)
Gender	
Male	18 (60)
Female	12 (40)
Age	61.2±11.2
Diabetes mellitus	7 (23)
Hypertension	18 (60)
CAD	15 (60)
COPD	6 (20)
Atrial fibrillation	4 (13)
Pulmonary hypertension	22 (73)
NYHA class>II	24 (80)
Mitral regurgitation	
Degenerative	9 (30)
Rheumatic	6 (20)
Ischemic	15 (50)
Reoperation (CABG)	2 (6)

CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, NYHA: New York Heart Association, CABG: coronary artery bypass grafting.

Data are presented as n (%) or mean±standart deviation, where appropriate.

implantation has become a routine procedure during surgical repair of both degenerative and ischemic MR. Based on current experiences, ring annuloplasty procedure significantly enhances success rate of valve repair (3,4,5,6,9). Rigid rings have been used for ring annuloplasty up to the recent years. However, the risk of redevelopment of regurgitation with the use of rigid rings has become a current issue mostly stressed on in the literature. Furthermore, it has been realized that the mitral valve annulus is not a stable configuration and contributes to the left ventricular workload in each ventricular systole with a reduction in its size. This contribution is eliminated using the rigid ring implantation.

The results of the present study support the general suboptimal outcomes of the Alfieri edge-to-edge repair technique. Combining an annuloplasty procedure with every Alfieri (edge-to-edge) repair has been a matter of debate for years. Based on the results of the present study, we can suggest combining annuloplasty with edge-to-edge technique, whenever required. Ring annuloplasty reduces the tension on the repair suture line, stabilizes the reconstruction, and enhances durability of the valves by increasing the coaptation area of the leaflets. Moreover, ring annuloplasty improves long-term outcomes of mitral repair by eliminating likelihood of a late annular dilatation (6).

In the presence of MR and a severely calcified annulus, the edgeto-edge technique is not recommended as an isolated procedure unless it is combined with the ring prosthesis (4, 6). During the follow-up period in the present study, except for two patients operated on due to ischemic MR, reoperation was not required in any of the patients.

Current clinical data have strongly suggested that surgical treatment of ischemic MR improves survival and reverses remodeling. This can be explained by the fact that, a moderate MR is an intensive and directly effective stimulator for remodeling, whereas slowly progressive MR of any etiology is a weak stimulator for remodeling (4,12) MR, which results from altered geometry and papillary muscle dysfunction after myocardial infarction, can initiate remodeling itself. MR leads to an increase in left ventricular load and in diastolic wall stress, which induces left ventricular dilatation and insufficiency. MR also increases end-systolic wall stress due to reduced contractility and increased end-systolic volume. Because of such a vicious cycle, MR leads to severer MR.

The lack of a significant difference between pre- and postoperative EF primarily resulted from the absence of severe EF loss in Barlow, degenerative and rheumatic MR, and from the fact that valvular insufficiency was the main problem in such patients. Thus, EF levels were found to be moderate or good, when these patients were individually evaluated. Evaluation of these patients in terms of NYHA functional class, MR, LAD and PAP values, significant improvements were determined in the postoperative period. The pre- and post-operative EF values showed no difference in the patients with ischemic MR because of co-morbid factors. It should be kept in mind that EF will be further reduced in such patients due to increased afterload after correction of MR (4).

Table 2: Pre- and post-operative values of the study patients.

	Pre-operative value	Post-operative value	Difference	р
EF	43.8±11.8	45.0±10.9	-1.2±8.2	0.579
NYHA class	2.9±0.7	1.5±0.5	1.4±0.6	< 0.001
MR	2.6±0.5	1.1±0.3	1.5±0.6	< 0.001
LAD	4.6±0.6	4.1±0.4	0.4±0.6	< 0.001

EF: ejection fraction, NYHA: New York Heart Association, MI: mitral regurgitation, LAD: left atrial diameter. Data are presented as mean±standart deviation.

Table 3: Mortality and survival rates according to EF, NYHA classification, PAP, MR, LAD.

	Alive	Deaths	р
EF	44.3±12.0	42.5±12.0	0.653
NYHA class	2.7±0.6	3.6±0.5	0.001
PAP	6 (66.7)	3 (33.3)	0.666
MR	2.6±0.5	2.5±0.5	0.507
LAD	4.7±0.6	4.3±0.5	0.334

EF: ejection fraction, NYHA: New York Heart Association, PAP: pulmonary artery pressure, MR: mitral regurgitation, LAD: left atrial diameter. Data are presented as n (%) or mean±standart deviation, where appropriate

In the present study, we determined the NYHA class to be 3-4 in the patients in whom mortality was observed, and a significant correlation was noted between mortality and NYHA functional class. We observed that the patients with NYHA class 3-4 preoperatively had the same NYHA class in the postoperative period. Thus, with regard to etiology, the majority of patients had ischemic MR, and there was no significant difference between pre- and post-operative NYHA classes of these patients. It can be suggested that mortality would be high and clinical improvement could not be achieved in ischemic MI patients with high NYHA functional class on preoperative clinical evaluation, and that the Alfieri procedure is more practical, easily applicable, and beneficial as it shortens cardio-pulmonary by-pass time in such patients. We concluded that there was no problem in mitral leaflet, and PAP and LAD values on echocardiography; however, loss of left ventricular function due to CAD and comorbid diseases [such as chronic renal failure (CRF), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM)] masked the benefits of the surgical procedure. We also determined that a more precise preoperative evaluation is required in such patients and that repair should be added if CABG would be performed; however, its effect on the survival rates of the patients is controversial.

Double orifice configuration of the mitral valve leads to certain doubts about the hemodynamics during ventricular filling. However, a computational model together with the clinical experiments has demonstrated that the double orifice configuration has no effect on mitral hemodynamics and that mitral hemodynamics depend only on total valve area and cardiac output (12). Indeed, in double orifice configuration, the velocity of the flow passing through each orifice is equal to the velocity of the flow passing through a single orifices. Additionally, the flow velocities passing through the two orifices are also equal to each other even the orifices have substantially different sizes. This indicates that Doppler sampling of any of these two orifices is adequate to assess mitral valve hemodynamics.

In the present study, the rate of patients with increased mPAP was 70% in the preoperative period and 30% in the postoperative period; the change was found to be statistically significant (mPAP>40). When the mean LAD values were evaluated, a significant reduction from a pre-operative value of 4.6 to a post-operative value of 4.1 was observed. This provided a significant clinical improvement in the postoperative period due to both symptomatic improvement and low atrial fibrillation rates.

Another issue that should be taken into consideration during such repair procedure is the potential development of systolic anterior motion (SAM) particularly with exercise. Low mitral gradients have been measured at rest in patients during short- and long-term follow-ups. Moreover, an exercise-echocardiography study clearly demonstrated that artificially created double orifice valves showed physiological behavior under stress conditions in response to good valvular reserve and increased cardiac output and without development of functional mitral stenosis. In our study, mitral stenosis developed only in one patient.

 Table 4: Characteristics of the patients who died and who were alive.

	Alive n=22	Deaths n=8	р
Gender			
Female	10 (83.3)	2 (16.7)	0.419
Male	12 (66.7)	6 (33.3)	
Age	60.0±12.1	64.6±8.1	0.324
Etiology			
Ischemic MR	9 (60.0)	6 (40.0)	
Barlow prolapse	6 (100.0)	0 (0.0)	0.198
Rheumatic	7 (77.8)	2 (22.2)	
Hypertension	11 (61.1)	7 (38.9)	0.099
Diabetes mellitus	4 (57.1)	3 (42.9)	0.345
Reoperation	0 (0.0)	2 (100.0)	0.064

Data are presented as n (%) or mean±standart deviation, where appropriate

In the present study, performing the Alfieri repair together with ring annuloplasty in mitral stenosis reduced the likelihood of SAM. On the other hand, this rate is considerably high in patients with MR who have not undergone ring annuloplasty (8,9).

Ischemic MR is a different entity from other MR conditions. It has been observed that while majority of the patients respond to medical therapy, patients with severe ischemic MR benefit from surgical therapy. Nevertheless, rates of operative morbidity and mortality are higher in ischemic MR as compared to that in MR of other etiologies. In the present study, preoperative risk factors (DM, COPD, CRF, high NYHA functional class) were shown to be the most common criteria affecting early- and late-term morbidity and mortality in the patients with ischemic MR. In the present study group, the patients who required intra-aortic balloon pump (IABP) and inotropic support in the postoperative period, and thus had longer intensive care stay, and the patients in whom mortality was observed were those who had low EF and underwent surgical procedure due to ischemic MR. Normally, mild MR is well-tolerated by the left ventricle. Since the mortality rate is high and the underlying mainspring is CAD, only coronary revascularization without intervention to mitral valve can be preferred for mild-to-moderate MR in patients with angina who have appropriate target arteries and reversible posterolateral ischemia on scintigraphy.

The reasons for mortality were low cardiac output syndrome and multiorgan failure in four patients who had preoperative left ventricular dysfunction, low EF, NYHA class 3-4 and comorbidity (CRF, COPD, left bundle branch block etc.). Of four patients with ischemic MI, mortality was observed due to chronic pulmonary hypertension in two patients and due to pulmonary infection and septic shock in two who underwent reoperation. Mitral valve surgery results in better outcomes particularly in patients with higher LAD. Thus, LAD and left atrial (LA) volume should be measured during routine echocardiographic evaluations and involved in clinical decision-making and in evaluation criteria. Early surgical intervention is recommended if there is an inconsistency between the severity of lesion and the symptoms (particularly in case of coexisting stenosis and insufficiency), and if there is a change in PAP and valve gradients with exercise, and if post-exercise PAP value is >60 mmHg.

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