Effect of Aortic Valve Replacement, for Aortic Stenosis, on Concomitant Mitral Valve Regurgitation

Mitral Kapak Regürjitasyonunda Aort Stenozu İçin Aortik Kapak Replasmanının Etkisi

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ABSTRACT Objective: Mild-to-moderate mitral regurgitation (MR) often coexists with severe aortic stenosis and has been reported to be presented in up to 2/3 patients requiring aortic valve replacement (AVR). MR in patients with aortic stenosis is often functional in nature although organic mitral disease may coexist. Increased afterload and left ventricular remodeling have been implicated to explain the functional MR in patients with aortic valve stenosis. Furthermore, remodeling observed after AVR may impact the outcome of MR postoperatively. However, the clinical outcome of persistent MR after AVR is uninvestigated. On the other hand, concomitant replacement of the aortic and mitral valves is associated with an increased morbidity and mortality compared to an isolated AVR. This study aims to assess the change in MR severity following AVR for severe AS and to determine the factors associated with the MR improvement. **Material and Methods:** The clinical and surgical characteristics were compared in a cohort of 149 consecutive patients who underwent isolated AVR in Aleppo University Hospital for cardiac surgery. **Results:** Non-severe functional mitral valve regurgitation was detected prior to surgery in 25.5% of the patients. These patients were older (p = 0.007), more often had ventricular dysfunction (p = 0.02) and pulmonary hypertension (p = 0.04), and had been admitted more frequently for heart failure (0.008), with fewer of them conserving sinus rhythm (p = 0.003). In addition, the pre-surgery existence of MR was associated with greater morbidity and mortality (5.2% vs. 3.7%; p = 0.025). The MR disappeared or improved prior to hospital discharge in 56.2% and 15.6%, respectively. Independent factors predicting this improvement were the presence of coronary lesions (OR 3.74, p = 0.03), and the absence of diabetes (OR 0.28, p = 0.005) as well as pulmonary hypertension (OR 0.34, p = 0.01). **Conclusion:** In this study, MR decreased or disappeared in a high percentage of patients after AVR surgery. Independent factors predicting this improvement included the presence of prior coronary lesions, although the improvement is influenced by the diabetic status of the patient, as well as pulmonary hypertension.

Key Words: Cardiac valve annuloplasty; cardiomegaly; cardiac resynchronization therapy; vascular stiffness; venous valves; thoracic surgery

ÖZET Amaç: Hafiften ılımlıya mitral regürjitasyonda (MR) genellikle şiddetli aort stenozu (AS) birlikte bulunur ve başvuran hastaların 2/3'ünden fazlasında aort kapağı replasmanı (AVR) gerektiği bildirilmiştir. Aort stenozlu MR olguları sıklıkla işlevsel yapıda olmalarına rağmen, organik mitral kapak hastalığı eş zamanlı bulunabilir. Aortik kapak stenozlu fonksiyonel MR hastalarında artmış ard yük ve sol ventrikülün yeniden şekillenmesi söz konusudur. Hatta, AVR sonrası gözlenen bu yeniden şekillenme, postop MR sürecini etkileyebilir. Bununla birlikte AVR sonrası inatçı MR'ın klinik seyri, sonlanımı incelenmemiştir. Diğer taraftan, aortik ve mitral kapakların eş zamanlı replasmanının yol açacağı morbidite ve mortalite, izole AVR'ye göre daha yüksek olmaktadır. Bu çalışmada amacımız, şiddetli AS nedeniyle AVR sonrası MR şiddetindeki değişiklikleri araştırmak ve MR düzelmesiyle ilişkili faktörleri belirlemektir. **Gereç ve Yöntemler:** Aleppo Üniversitesi Hastanesi Kardiyak Cerrahi bölümünde izole AVR yapılan ardışık 149 hasta populasyonunda elde edilen klinik ve cerrahi özellikler karşılaştırılmıştır. **Bulgular:** Hastaların %25,5'inde cerrahiden önce, şiddetli olmayan fonksiyonel mitral kapak geri kaçışı saptanmıştır. Bu hastalar daha yaşlı (p=0,007), ventriküler fonksiyonları daha kötü (p=0,02) ve pulmoner yönden daha hipertansif (p=0,04) idiler, üstelik kalp yetmezliği bunlarda daha sık (0,008) idi, birkaçında sinüs ritmi mevcuttu (p=0,003). Ek olarak, operasyon öncesi MR varlığı daha fazla morbidite ve mortalite ile ilişkili idi (%3,7'ye karşı %5,2, p=0,025). Hastaların %56,2'sinde MR kayboldu, %15,6'sında ise taburcu öncesi düzelme oldu. Bu düzelmenin öngördürücü bağımsız faktörleri koroner lezyonların varlığı (OR 3,74, p=0,03), diyabet yokluğu (OR 0,28, p=0,005) ve pulmoner hipertansiyon yokluğu (OR 0,34, p=0,01) idi. **Sonuç:** Bu çalışmada, AVR cerrahisi sonrası hastaların çoğunda MR azalmış ya da kaybolmuştur. Bunun öngördürücü bağımsız faktörleri, pulmoner hipertansiyonda olduğu gibi, hastanın diyabetik durumunu etkileyen eski koroner lezyonların varlığıdır.

Anahtar Kelimeler: Kardiyak kapak annuloplasti; kardiyomegali; kardiyak resenkronizasyon tedavisi; damar sertliği; venöz kapaklar; göğüs cerrahisi

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Aortic valve replacement (AVR) for aortic stenosis (AS) is the most frequently performed heart valve surgery, and functional mitral regurgitation (MR) is a common finding in aortic stenosis, with an incidence as high as 60%.[1-3] It isn't often corrected because it is believed to be reduced after AVR.[4] Although improvements in degree of MR have been reported after isolated AVR.[5,6] The ability to predict persistent MR after AVR is considered important, but relatively few studies have analyzed the clinical impact of functional MR. Furthermore, the majority of performed studies have been of small scale and have not examined functional outcomes or sought to identify predictors of persistent MR.

This study aims to assess the change in MR severity following aortic valve replacement for severe AS and to determine the factors associated with the MR improvement.

MATERIAL AND METHODS

STUDY POPULATION

This retrospective study involved a cohort of patients who underwent surgical aortic valve replacement for severe AS in Aleppo University Heart Hospital from January 2005 to June 2012. Patients were excluded if the aortic valve replacement was: (a) performed for predominant aortic regurgitation; (b) accompanied with intervention on any other heart valve; (d) accompanied with structural mitral valve disease; or (e) performed of AS secondary to hypertrophic obstructive cardiomyopathy.

Collected data was included demographic, epidemiologic, clinical, electrocardiographic and echocardiographic characteristics of the patients, as well as coronary arteriography results (we defined significant or important coronary lesion when the lumen is narrowed more than 70%), and the type and size of the prosthesis, morbidity and mortality during the perioperative period (defined as the time from hospital admission immediately prior to surgery up to the time of discharge), and the need for reoperation.

DOPPLER ECHOCARDIOGRAM

Echocardiographic examination was performed prior to surgery and before hospital discharge using Philips (sonos 7500 - HD 11 - HD invisor). The standard examination included M-mode, two-dimensional (2D), spectral and color Doppler, obtaining the usual planes including the long and short parasternal axis, and apical 3, 4 and 5 chamber planes. One appropriately trained observer (O. O.) reviewed all echocardiograms. These results were verified by two expert echocardiographers (B. A., A. S.) to confirm accuracy. In the present study functional MR was defined as MR from failure of coaptation of the mitral valve leaflets without coexisting structural changes of the valve itself. MR severity was graded as none, trace, mild, moderate, or severe according to the American Society of Echocardiography recommendations.[11]

STATISTICAL ANALYSIS

The continuous variables were expressed as mean ± standard deviation and the qualitative variables as percentages. The χ^2-test was used for qualitative variables and Student's *t*-test for continuous variables. Values were considered to be statistically significant if the $p < 0.05$. A stepwise logistic regression multivariate analysis was done, expressing the results as OR with confidence interval.

RESULTS

STUDY POPULATION

This study included 149 patients who underwent isolated aortic valve replacement and meet the inclusion criteria with mean age was 58.3 ± 18.2 years (57.7% men), prevalence of cardiovascular risk factors was as following: 58.3% for hypertension, 26.38% for active or ex-smokers, 28.5% for diabetes mellitus and 35.4% for dyslipidemia. For the symptoms, dyspnea was found in 63.19% of the patients, angina in 55.6%, effort syncope in 15.97%, and heart failure in 52.8% of patients.

Echocardiography findings of the study population were summarized in Table 1. Preoperative MR was found in 25.5% of patients.

TABLE 1: Echocardiography findings in the study population.

Maximum gradient (mmHg)	76.8±26.3
Mean gradient (mmHg)	52.6±17.4
Aortic valve area (cm^2)	0.56±0.22
Aortic regurgitation (%)	65.2
Mitral regurgitation (%)	26.3
Mitral annular calcium (%)	23.6
Left atrial dilatation (%)	20.6
Tricuspid regurgitation (%)	15.9
Left ventricular hypertrophy (%)	86.11
Ejection fraction (%)	56.3±16.7
Systolic pulmonary artery pressure (mmHg)	44.5±22.4

Prior to surgery, 85.4% of the patients were in sinus rhythm. Coronary arteriography was performed in 80% of the patients, with 20 % of these having important coronary lesions.

PREVALENCE OF MITRAL REGURGITATION AND ASSOCIATED FACTORS

Out of 149 patients who underwent aortic valve replacement due to AS, 38 (25.5%) had non-severe MR prior to surgery, and accompanying MR was more often in older patients. Comparison results between patients, with intermediate MR prior to surgery (group 1) and others, who had no MR (group 2), showed that patients of group (1) had a greater incidence of left ventricular dysfunction, mitral annular calcium, tricuspid regurgitation and aortic regurgitation, as well as a greater prevalence and severity of pulmonary hypertension, a larger left atrium, and more commonly had dyspnea and heart failure Table 2. However, patients with severe AS and accompanying functional MR were less often in sinus rhythm.

SURGICAL RESULTS

A biological prosthesis was implanted in 8 patients (5.55%), more often in the patients with accom-

TABLE 2: Univariate analysis of the preoperative presence of mitral regurgitation (MR).

	p-Value	No MR (n = 106)	MR (n = 38)
Age (years)	62.3±13.3	58.2±9.4	0.007
Sex (female)	18 (47.3%)	43 (40.5%)	0.1
Hypertension	22 (57.9 %)	62 (58.4%)	0.9
Smokers	9 (23.6%)	29 (27.3%)	0.6
Dyslipidaemia	8 (18.4%)	43 (23.5%)	0.03
Diabetes mellitus	10 (26.3%)	31 (29.2%)	0.7
Dyspnoea	29 (76.3%)	62 (58.4%)	0.05
Angina	15 (39.4%)	65 (61.3%)	0.02
Syncope	2 (5.2%)	21 (19.6%)	0.03
Admission for heart failure	27 (65.7%)	49 (46.2%)	0.008
Sinus rhythm	27 (71.05%)	96 (90.5%)	0.003
Coronary disease	9 (23.6%)	27 (25.4%)	0.8
Aortic regurgitation	30 (78.9 %)	64 (60.3%)	0.003
Tricuspid regurgitation	15 (39.4%)	8 (7.5%)	0.000
Mitral annular calcium	15 (39.4%)	19 (17.9%)	0.007
Left atrial dilatation	16 (42.1%)	14 (13.2%)	0.000
Ejection fraction (%)	55.0±12	62±11	0.000
Left ventricular hypertrophy	33 (86.8%)	91 (85.8%)	0.8
Pulmonary hypertension	9 (23.6%)	11 (10.3%)	0.04
Systolic pulmonary artery pressure (mmHg)	54±17.3	35±22	0.004

Univariate analysis of the preoperative presence of mitral regurgitation.

TABLE 3: Univariate analysis of complications according to the presence or absence of mitral regurgitation (MR) prior to surgery.

	MR (38)	No MR(106)	p-Value
Low output	11 (28.9%)	24 (22.6%)	0.048
Kidney failure	4 (10.5%)	6 (5.66%)	0.028
Perioperative MI	1 (2.6%)	3 (2.8%)	0.2
Neurological complications	3 (7.8%)	4 (3.7%)	0.069
Respiratory complications	4 (10.5%)	10 (9.4%)	0.1
Infectious endocarditis	1 (2.6%)	2 (1.8%)	0.3
Superficial infection	5 (13.3%)	11 (10.3%)	0.2
Postoperative block	2 (5.2%)	6 (5.6%)	0.2
Reoperation due to bleeding	1 (2.6%)	3 (2.8%)	0.2
Death	2 (5.2%)	4 (3.7%)	0.025

MI: Myocard infarctus.

panying MR. Significant coronary lesions were presented in 20.0% and a concomitant Aorto-coronary bypass was performed in 80.0% of them. Postoperative mortality was 6.9% of the study population. Preoperative MR was associated with Renal failure (10.5% vs 5.66%; $p = 0.028$) and low output (28.9% vs 22.6%; $p = 0.048$) during the immediate postoperative period, as well as greater perioperative mortality (5.2% vs 3.7%%; $p = 0.025$) (Table 3).

EVOLUTION OF THE MITRAL REGURGITATION IN SURVIVORS AFTER SURGERY

Of the 38 patients with preoperative MR, improvement was noted in 27 of whom 21 had no MR on the pre-discharge echocardiogram following aortic valve replacement (Figure 1). The degree of mitral regurgitation in the postoperative recording worsened in tow patients. In comparison between patients who experienced an improvement in MR and the others (Table 4), the improvement in MR was associated with angina (48.1% vs 10%; $p = 0.03$) and the presence of coronary lesions prior to surgery (33.3% vs 0.0%; $p = 0.03$), while no improvement in MR after aortic valve replacement was associated with diabetes mellitus (14.8% vs 60%; $p = 0.005$) and pulmonary hypertension (11.1% vs 50%; $p = 0.01$). Multivariate analysis also showed that the presence of coronary lesions was an independent marker for MR improvement after surgery (OR 3.74; 95% CI 0.3–8.2; $p = 0.03$), and that diabetes mellitus (OR 0.28; 95% CI 0.1–0.43; $p = 0.005$) and pulmonary hypertension (OR 0.34; 95% CI 0.07–0.98; $p = 0.01$) were independent markers for lack of MR improvement after surgery (Table 5).

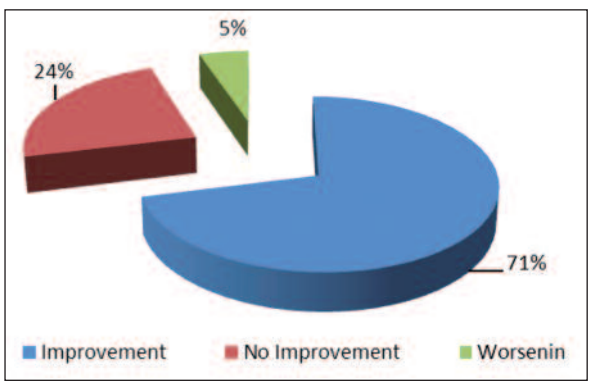

FIGURE 1: Evolution of the mitral regurgitation in survivors after surgery.

DISCUSSION

We found that 25.5% of our patients with severe AS had intermediate degrees of MR with no clear organic substrate. This was possible due to the pressure overload that characterizes this entity and the resulting anatomic and geometric modification of the left ventricle.[6]

Mitral regurgitation in our population is more common among those patients with left ventricular dysfunction and, although this left ventricular dysfunction is associated with a greater presence of coronary lesions,[7] and the association between coronary lesions and aortic stenosis with ventricular dysfunction is known,[8] this does not occur with the MR these patients presented, that suggesting an additional mechanism apart from that of the ischemic MR itself.

The patients in our series with non-severe MR were older, a factor that also favored the presence of greater accompanying valve disease, had a greater amount of mitral calcium and a greater left atrial dilation, with the resulting lower preservation of sinus rhythm. These factors explain the more unfavorable haemodynamic status that, in turn, could account for the greater presence of pulmonary lesions in the patients with MR, and a greater incidence of admissions due to heart failure.[9-13]

TABLE 4: Univariate analysis of the presence or absence of improvement of mitral regurgitation (MR) after aortic surgery.

	P-Value	No improvement MR (n=10)	Improvement MR (n=27)
Age (years)	63±12	66.5±9	0.6
Sex (female)	12 (44.4%)	5(50%)	0.7
Hypertension	16 (59.2%)	6 (60%)	0.6
Smokers	6 (22.3%)	3 (30%)	0.6
Dyslipidaemia	6 (22.2%)	2 (20%)	0.8
Diabetes mellitus	4 (14.8%)	6 (60%)	0.005
Dyspnoea	20 (74.0%)	8 (80%)	0.7
Angina	13 (48.1%)	1 (10%)	0.03
Admission for heart failure	19 (70.3%)	8 (80%)	0.5
Sinus rhythm	20 (74.0%)	6 (60%)	0.4
Coronary disease	8 (29.6%)	1 (10%)	0.04
Aortic regurgitation	22 (81.4%)	7(70%)	0.4
Tricuspid regurgitation	10 (37.0%)	4(40%)	0.8
Mitral annular calcium	11 (40.0%)	4 (40%)	0.9
Left atrial dilatation	11 (40.0%)	5 (50%)	0.6
Ejection fraction (%)	53±13.2	57.8±14.6	0.3
Left ventricular hypertrophy	24 (88.8%)	8 (80%)	0.4
Pulmonary hypertension	3 (11.1%)	5 (50%)	0.01
Systolic pulmonary artery pressure (mmHg)	50.8±15.	45±13.4	0.02
Size of prosthesis	21.1±1.8	21.2±1.6	0.7
Coronary revascularization	5 (18.5%)	1 (10%)	0.25

The presence of intermediate degrees of MR seemed in our series, unlike the series of Absil et al,[4] to increase perioperative mortality during surgery for aortic valve replacement, this may be explained mostly by the fact that our patients were older, and had greater left ventricular dysfunction as well as greater associated valve disease, which would partly agree with the results of Barreiro, et al.[14] Where the presence of moderate MR was an independent factor predicting long-term survival, although Barreiro study included various etiologies (with myxomatous involvement and calcified or ischemic degeneration in 70% of the patients).

The immediate postoperative evolution in patients who had intermediate degrees of MR was excellent, as has been seen in other studies, [4,6] with a high percentage of improvement (71.05%). Our study found that, improvement of MR was not associated with the mitral calcification or atrial dilation reported elsewhere,[5] though this may be due to the low prevalence of mitral calcification (29.8%) in comparison with other studies.[15] Our study agree with Emily et al,[16] study as we found that: conservative, tailored approach to concomitant mitral surgery in patient presenting for correction of aortic stenosis who demonstrate functional mitral regurgitation.[16] Moreover, the association between a greater presence of coronary disease and improvement in the MR could be related to the coronary revascularization, which would reduce the restrictive component of the MR, thus favoring its improvement after surgery. The role of diabetes mellitus in

TABLE 5: Multivariate analysis of the factors associated with improvement of mitral regurgitation after surgery.

	OR	95% CI	p-Value
Smoking	0.49	0.35—1.97	0.6
Diabetes mellitus	0.28	0.10—0.43	0.005
Angina	1.88	1.62—5.7	0.03
Admission for heart failure	0.89	0.5—1.09	0.5
Coronary disease	3.74	1.3—8.2	0.03
Tricuspid regurgitation	1.09	0.46—1.96	0.8
Pulmonary hypertension	0.34	0.07—0.98	0.01

the lack of improvement of the MR after surgery may be explained by two mechanisms; first, the indirect association between diabetes mellitus and coronary atherosclerosis, which in both its acute symptomatic form and its silent form does little or nothing to favour ventricular remodeling. However, in our series this first possibility would not appear to be especially relevant in the lack of short-term improvement in non-severe MR, but rather the opposite, as explained above for coronary disease. Second, the role of diabetic cardiomyopathy should be considered. A recent review by Boudina et al.,[17] discussed the relation between diabetes mellitus and the development of heart failure, and the role played in this latter by myocardial fibrosis or diabetic microangiopathy suggesting that, in this case, patients with diabetes mellitus, even in the absence of important coronary atherosclerosis, may have a less favorable ventricular geometry as a direct consequence of the diabetes on the ventricle, thus hindering improvement of the MR after surgery.[17] The results of our study could be relevant in older patients with severe aortic stenosis and functional non-severe mitral regurgitation with high perioperative risk and poor prognosis who could be candidates to trans catheter aortic valve implantation as a new therapeutic option.

LIMITATIONS

The study was retrospective and its results do not enable an identification of patients who would most benefit from combined replacement or concomitant mitral repair.

CONCLUSION

In this study, mitral regurgitation decreased or disappeared in a high percentage of patients after Aortic valve replacement surgery. Independent factors predicting this improvement included the presence of prior coronary lesions, although the improvement is influenced by the diabetic status of the patient, as well as pulmonary hypertension.

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