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What Happens to Functional Mitral Regurgitation after Aortic Valve Replacement for Aortic Stenosis?

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ABSTRACT

Background: Patients with aortic stenosis (AS) treated with aortic valve replacement (AVR) may also present with associated functional mitral valve regurgitation (FMR). Whether to also address the mitral valve at the time of AVR remains unclear. This study was designed to determine the influence of MR on survival and its evolution over time.

Methods: We retrospectively reviewed 74 patients with FMR who underwent isolated AVR between 1999 and 2006 at our institution. Inclusion criteria were surgery for AVR with severe AS (mean age, 69 years; N = 47; 64% women) and FMR (grade I, 80%; grade II, 19%; grade III, 1%). Echocardiography follow-up data were obtained by mail questionnaires sent to the referring cardiologists of all survivors. All parameters were analyzed with the Kaplan-Meier method and the sign test.

Results: The operative mortality rate was 2%, and 9 patients (12%) died during follow-up. The mean (SD) follow-up time was 48 ± 33 months, and follow-up 96% complete. The follow-up demonstrated a decrease of FMR by 2 degrees in 3 patients (4%), and 1 degree in 14 patients (19%); regurgitation remained unchanged in the majority of patients (n = 47; 63%). FMR worsened in 10 patients overall (14%), and new-onset atrial fibrillation was found in 24 patients (33%); however, the statistical analysis failed to demonstrate an impact of worsening FMR on survival.

Conclusion: MR in patients with severe AS and FMR at the time of AVR does not appear to worsen significantly over time. Not dealing with the mitral valve at the time of AVR might be warranted for selected patients.

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INTRODUCTION

Valvular aortic stenosis (AS) is the most common acquired valvular heart disease in adults of industrialized countries [Tassan-Mangina 2003]. Aortic valve replacement (AVR) is the treatment of choice for patients with severe AS, and patients with AS in this setting often may also present with some degree of functional mitral regurgitation (FMR). According to the literature, the incidence of this disease constellation may be >60% in these patients [Moazami 2004; Vanden Eynden 2007; Caballero-Borrego 2008]. The mortality and morbidity for isolated AVR is low and acceptable. The presence of a second valve requiring an intervention increases the risk of the surgical procedure, and therefore this additional risk is integrated into the new EuroSCORE II risk stratification model. In addition to being surgically more challenging, whether MR improves, remains unchanged, or worsens over time has not been clearly documented in these patients to date [Tassan-Mangina 2003; Moazami 2004; Unger 2008; Waisbren 2008; Takeda 2010]. Consequently, the opinions about simultaneous surgical treatment of concomitant MR remain controversial. Because there are no established guidelines for the treatment of concomitant FMR, clear results from investigations on this issue are essential for developing ideal therapeutic strategies for these patients. The aim of the present study was to determine the influence of MR on survival and its evolution over time after AVR for AS.

PATIENTS AND METHODS

Overall, 1075 patients underwent isolated AVR at our institution between 1999 and 2006. Of this group, we analyzed 89 patients (8.3%) with concomitant untreated FMR of less than grade 4.

Inclusion criteria for the study were patients who had severe AS undergoing AVR and had associated FMR. MR was classified according to the following severity code: 0, none; 1, trivial; 2, mild; 3, moderate; 4, severe. An additional criterion for inclusion was a complete pre- and postoperative echocardiography workup for each patient. Patients with any surgical intervention on the mitral valve or AVR for a reason other than AS were excluded from the analysis; patients not discharged from the hospital were also excluded. A total of

74 patients remained. Approval by the local ethics committee and a waiver for signed consent were obtained.

Clinical and echocardiography data were collected from all patients before and after AVR. Our clinical database was the primary source for data collection. From this registry, we collected all pre- and postoperative data, such as patient demographics, preoperative risk factors, preoperative echocardiography data, operative data, intraoperative and postoperative complications, and 30-day mortality. Follow-up data were obtained by Dendrite Clinical Systems (Oxfordshire, UK) and completed with a mail questionnaire sent to referring cardiologists of all surviving patients. These questionnaires contained clinical and echocardiography data (see tables). If no death was documented, the patient was considered alive at the time of follow-up.

Echocardiography examinations were performed pre- and postoperatively. AS severity and valve area were reported, along with mean and peak pressure gradients across the aortic valve. The severity of MR was defined as follows: 0, none; 1, trivial; 2, mild; 3, moderate; and 4, severe. Only patients with FMR (Carpentier type 1) were included. The evolution of pre- and postoperative MR was deemed significant if it changed by at least 1 grade.

Left ventricular dimension and function were assessed by measuring the left ventricular muscle mass index (LVMMI), the left ventricular end-diastolic and end-systolic dimensions (LVEDD and LVESD), the thicknesses of the interventricular septum and the posterior wall, left ventricular hypertrophy or dilatation, and ejection fraction. The examinations were performed with 2-dimensional, M-mode, pulsed, continuous, and color Doppler transthoracic and transesophogeal echocardiography.

All surgical procedures were performed via median sternotomy in a standardized fashion.

Statistical Methods

Continuous variables are presented as the mean ± SD. Preoperative continuous values were compared with follow-up data with the Wilcoxon signed rank test. Nominal and ordinal data are presented as a number and a percentage. Preoperative nominal values were compared with follow-up results by means of the McNemar test. Preoperative ordinal values were compared with follow-up values with the sign test. Overall survival for the 2 groups was analyzed with the Kaplan-Meier method, and the results were compared with the log-rank test. Changes in MR between groups were compared with the chi-square test for trend. Correlations of continuous and ordinal data were analyzed by Spearman rank correlation analysis. P values <.05 were considered statistically significant. IBM SPSS Statistics software (version 19; SPSS, Chicago, IL, USA) was used for all analyses.

RESULTS

Patient Characteristics and Demographics

In the study, we included 74 patients with preoperative FMR and AVR caused by severe AS. The mean age was 68.7 years, and 27 (36%) of the patients were male. Table 1 summarizes all relevant patient demographic data.

Table 1. Preoperative Clinical Characteristics (N = 74)*

Patient Characteristic	
Age, y	68.7 ± 11.7
Female sex, n	47 (64%)
Hypertension, n	53 (72%)
Pulmonary artery hypertension, n	14 (19%)
Body mass index, kg/m^2	27.6 ± 5.0
Dyslipidemia, n	35 (47%)
Diabetes mellitus, n	8 (11%)
Smoking, n	22 (30%)
Congestive heart failure	20 (27%)
Atrial fibrillation	11 (15%)
Angina pectoris	37 (50%)
Dyspnea	61 (82%)
NYHA class (n = 62), n	
1	5 (8%)
2	22 (36%)
3	28 (45%)
4	7 (11%)

*Data are presented as the mean ± SD where indicated. NYHA indicates New York Heart Association.

Table 2. Preoperative Echocardiography Data (N = 74)*

Patient Characteristic	
Aortic valve	
Valve area, cm^2	0.7 ± 0.2
Mean pressure gradient, mm Hg	54.9 ± 13.8
Left atrial dilatation, n	40 (54%)
Mitral regurgitation grade, n	
1	59 (80%)
2	14 (19%)
3	1 (1%)
4	0%
Leaflet calcification, n	40 (54%)
Annulus calcification, n	30 (41%)
Tricuspid valve insufficiency (grades 1 and 2), n	39 (53%)
Left ventricular dilatation (LVEDD >4.0 cm), n	19 (26%)
Left ventricular ejection fraction, n	
>50%	50 (68%)
30%-50%	21 (28%)
<30%	3 (4%)
Left ventricle hypertrophy, n	63 (85%)
LVMMI, g/m^2	176.1 ± 64.6

*Data are presented as the mean ± SD where indicated. LVEDD indicates left ventricular end-diastolic diameter; LVMMI, left ventricular muscle mass index.

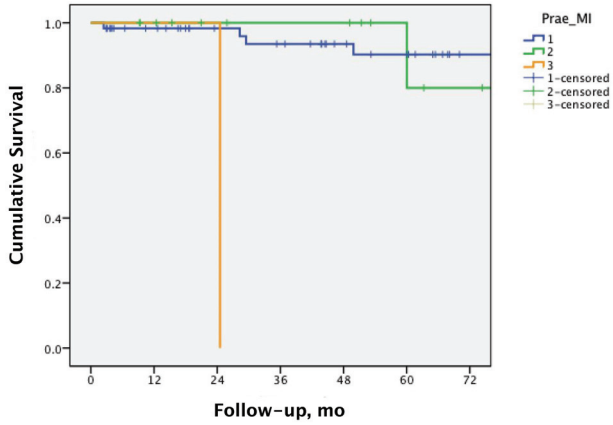

Figure 1. Kaplan-Meier survival functions. Prae_MI indicates preoperative mitral regurgitation grade.

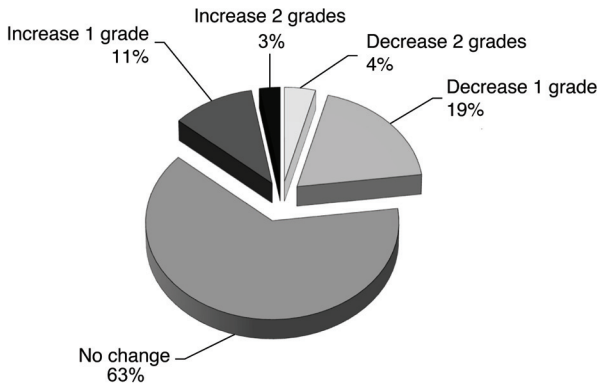

Figure 2. Evolution of mitral regurgitation (MR) over time. Evolution after aortic valve replacement.

Table 2 summarizes the preoperative echocardiography data. In addition to severe AS, preoperative echocardiography demonstrated a dilated left atrium in 40 patients (54%) and an enlarged left ventricle in 19 patients (26%). The left ventricular ejection fraction (LVEF) was normal in 50 patients (68%) and <30% in just 3 patients (4%). Functional tricuspid valve insufficiency (grade <4) not requiring surgical repair was present in 39 patients (53%). The distribution of preoperative FMR severity was as follows: 59 patients (80%) had grade 1 FMR, and 14 patients (19%) had grade 2. Only 1 patient (1%) had FMR of severity grade 3. All patients had type I dysfunction, and most of the mitral valves (70 patients, 95%) also presented with leaflet or annulus calcification.

Operative and Postoperative Data

The majority of the patients (72%) received a biological aortic valve prosthesis. The mean diameter of the implanted prosthesis was 23 ± 2 mm. The mean cardiopulmonary bypass time was 111 ± 25 minutes, and the mean aortic cross-clamp time was 67 ± 20 minutes. The mean overall length of hospital stay was 12 ± 5 days.

Mortality and Morbidity

The operative mortality was 2%, and 9 patients died during follow-up (12%). The statistical analysis showed no impact of preoperative FMR severity on survival (P = .45). Overall, 8 patients required pacemaker implantation after AVR (see Figure 1).

Long-term Follow-up

Clinical. All surviving patients were discharged to a specialized rehabilitation center and then home. The mean follow-up time was 47.7 ± 33.5 months, and follow-up was 96% complete. Unfortunately, changes in New York Heart Association classification could be followed up in only 29 patients; nearly all of these patients showed improvement. Anginal symptoms of AS were obviously decreased, as well as dyspnea. New onset of atrial fibrillation (AF) occurred in 24 patients (32.6%), and AF was still present at the most recent follow-up in 9 patients (12%).

Echocardiography. AVR decreased the mean pressure gradient across the aortic valve, from a preoperative mean of 54.9 ± 13.8 mm Hg to a postoperative value of 16.6 ± 8.4 mm Hg. LVEF and LVMMI values improved significantly. Postoperatively, 57 patients (77%) had an LVEF >50%, and 14 patients (19%) had an LVEF of 30% to 50%. The number of patients with an LVEF <30% remained unchanged. Compared with the preoperative data, in which 50 patients (68%) had an LVEF >50%, the LVEF improved in only a small number of patients (7 patients). Improvements in LVMMI were also observed, from 176.1 ± 64.6 g/m2 to 139.6 ± 37.0 g/m2. Tricuspid insufficiency (less than grade 3) increased during follow-up from 39 patients (53%) to 47 patients (63%) (Table 3).

After AVR, the distribution of MR severity was as follows: FMR grade 0, 9 patients (12%); FMR grade 1, 51 patients (69%); FMR grade 2, 11 patients (15%); FMR grade 3, 3 patients (4%). None of the patients had severe FMR (Table 3). Patient follow-up revealed a decrease in FMR by 2 grades in 3 patients (4%) and by 1 grade in 14 patients (19%), but FMR remain unchanged in the majority of patients (n = 47; 63%, not significantly different). MR severity increased by approximately 1 grade in 8 patients (11%) and by approximately 2 grades in 2 patients (3%) (Figure 2). The statistical analysis showed no significant FMR evolution after AVR (P = .4); just 17 of 74 cases demonstrated an improvement.

Influencing Factors

To assess a potential correlation between different influencing factors and the evolution of MR, we assessed the following variables: sex and such cardiovascular risk factors as hypertension, diabetes mellitus, adiposity, smoking, cardiac insufficiency, AF, LVEF, and left ventricle and atrial dilatation. We able to identify none of these factors as significantly correlated with the evolution of MR.

Table 3. Echocardiography Outcomes*

Patient Characteristic	Preoperative	Follow-up	Change	*P*
Diastolic pressure, mm Hg	54.9 ± 13.8	16.6 ± 8.4	38.5 ± 15.2	<.001
Left atrial dilatation, n	40 (54%)	38 (51%)	−2 (−3%)	.189
Mitral regurgitation grade (N = 74), n				.248
None	0	9 (12%)	+12%	
1	59 (80%)	51 (69%)	−8 (−11%)	
2	14 (19%)	11 (15%)	−3 (−4%)	
3	1 (1%)	3 (4%)	+2 (+3%)	
4	0	0	0	
Tricuspid regurgitation (grade <3), n	39 (53%)	47 (63%)		.127
Left ventricular ejection fraction, n				.170
>50%	50 (68%)	57 (77%)	+7 (+9%)	
30%-50%	21 (28%)	14 (19%)	−7 (−9%)	
<30%	3 (4%)	3 (4%)	0%	
Left ventricle hypertrophy, n	63 (85%)	39 (53%)	−24 (−32%)	.250
LVMMI, g/m^2	176.1 ± 64.6	139.6 ± 37.0	−42.1 ± 58	.001

*Data are presented as the mean ± SD where indicated. LVMMI indicates left ventricular muscle mass index.

DISCUSSION

We found that the patients in our series with severe AS and FMR at the time of surgery for AS had very good immediate outcomes. During the follow-up period, the clinical outcomes showed significantly improved symptoms for all patients. We also found that MR does not appear to change over time; that is, it does not get worse. In addition, we found no significantly increased tricuspid valve insufficiency over time; however, we did observe a slight increase in new-onset AF during follow-up. It appears that mitral valve repair, if feasible at the time of AVR, may be warranted only in selected patients with moderate MR or less.

Earlier studies have suggested a significant reduction in the degree of MR after AVR for AS. Unger et al [2008] reported an improvement in MR that was related to the severity of the preoperative MR. Similarly, Vanden Eynden et al [2007] found that MR improved. The most significant prognostic factor they evaluated was the etiology of MR, which showed that MR was more frequently improved in cases of ischemic and functional MR. This result has been confirmed in part by others [Joo 2011]. More-recent studies showed the effects of different influencing factors on the evolution of MR after AVR. Tassan-Mangina et al [2003] reported that the peak velocity of tricuspid regurgitation and the left ventricular mass are important preoperative predictors of MR regression and that mitral annular calcification predicts the long-term postoperative persistence of MR. Waisbren et al [2008], however, reported different influencing factors, such as preoperative congestive heart failure and small left atrium size. AF appeared to be a negative factor, because AF was accompanied by less of an improvement in MR. Caballero-Borrego et al [2008] reported that coronary lesions prior to surgery also affect MR improvement.

In contrast with the studies mentioned above, Moazami et al [2004] reported no consistent improvement in MR severity could be expected. Of the 107 patients included in their study, only 48 showed an improvement. Similarly, we found no significant improvement in MR after AVR for AS. Only 17 of 74 patients demonstrated an improvement. Although these patients experienced significant clinical improvement, MR was still present in 88% of the patients at follow-up. Therefore, we can draw the conclusion that MR does not improve after AVR alone. There was also no clear correlation to any predictive factors.

MR is known to increase perioperative mortality, as Caballero-Borrego et al [2008] have reported, and the best treatment for concomitant MR remains controversial. Given that we could not verify a significant improvement in untreated MR after AVR or an increase in tricuspid valve insufficiency, but only in AF, we conclude that concomitant mitral valve intervention may be warranted only in certain circumstances with low operative risk. A prospective, randomized trial with comparable patient cohorts would provide more evidence for the appropriate strategy in such cases.

Limitations

Our study presented limitations. The study was retrospective in nature, and there was no echocardiography core laboratory. Because of the strict inclusion criteria, the number of cases we have presented is small, and because we collected data from 1999 to 2006, the operations were performed over a long time period. We also limited our analysis to a small number of echocardiography parameters.

REFERENCES

Caballero-Borrego J, Gómez-Doblas JJ, Cabrera-Bueno F, et al. 2008. Incidence, associated factors and evolution of non-severe functional mitral regurgitation in patients with severe aortic stenosis undergoing aortic valve replacement. Eur J Cardiothorac Surg 34:62-6.

Joo HC, Chang BC, Cho SH, Youn YN, Yoo KJ, Lee S. 2011. Fate of functional mitral regurgitation and predictors of persistent mitral regurgitation after isolated aortic valve replacement. Ann Thorac Surg 92:82-7.

Moazami N, Diodato MD, Moon MR, et al. 2004. Does functional mitral regurgitation improve with isolated aortic valve replacement? J Card Surg 19:444-8.

Takeda K, Matsumiya G, Sakaguchi T, et al. 2010. Impact of untreated mild-to-moderate mitral regurgitation at the time of isolated aortic valve replacement on late adverse outcomes. Eur J Cardiothorac Surg 37:1033-8.

Tassan-Mangina S, Metz D, Nazeyllas P, et al. 2003. Factors determining early improvement in mitral regurgitation after aortic valve replacement for aortic valve stenosis: a transthoracic and transesophageal prospective study. Clin Cardiol 26:127-31.

Unger P, Plein D, Van Camp G, et al. 2008. Effects of valve replacement for aortic stenosis on mitral regurgitation. Am J Cardiol 102:1378-82.

Vanden Eynden F, Bouchard D, El-Hamamsy I, et al. 2007. Effect of aortic valve replacement for aortic stenosis on severity of mitral regurgitation. Ann Thorac Surg 83:1279-84.

Waisbren EC, Stevens LM, Avery EG, Picard MH, Vlahakes GJ, Agnihotri AK. 2008. Changes in mitral regurgitation after replacement of the stenotic aortic valve. Ann Thorac Surg 86:56-62.