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Factors Determining Early Improvement in Mitral Regurgitation after Aortic Valve Replacement for Aortic Valve Stenosis: A Transthoracic and Transesophageal Prospective Study

SOPHIE TASSAN-MANGINA, M.D., DAMIEN METZ, M.D., PIERRE NAZEYROLLAS, M.D., FRÉDÉRIC TOROSSIAN, M.D.,* CAMELIA POP, M.D., BERTRAND JAMET, M.D., BERNARD BAEHREL, M.D.,* JACQUES ELAERTS, M.D.

Departments of Cardiology and *Cardiac Surgery, University Hospital, Reims, France

Summary

Background: Mitral regurgitation (MR) is frequently associated with aortic stenosis. Previous reports have shown that coexisting mitral insufficiency can potentially regress after aortic valve replacement.

Hypothesis: This study sought to assess the frequency and severity of MR before and after aortic valve replacement for aortic stenosis and to define the determinants of its postoperative evolution.

Methods: For this purpose, 30 adult patients referred for aortic valve surgery underwent pre- and postoperative transthoracic and transesophageal echocardiography and color Doppler examination.

Results: Mean preoperative left ventricular ejection fraction was 57 ± 16% and remained unchanged postoperatively. Preoperative MR was usually mild to moderate and correlated with aortic stenosis severity and left ventricular systolic dysfunction. The color Doppler mitral regurgitant jet area significantly decreased during the postoperative period ($p = 0.016$) as left ventricular loading conditions returned to normal, suggesting an early decrease of the functional part of MR. On the other hand, the mitral regurgitant jet width at the origin remained unchanged. Statistical analysis found pulmonary artery pressure ($p = 0.02$) and indexed left ventricular mass ($p = 0.009$) to be preoperative predictive factors of postoperative MR improvement. Predictive factors of postoperative MR severity were left atrial diameter ($p = 0.02$), pulmonary artery pressure ($p = 0.003$), and the presence of mitral calcifications ($p = 0.004$).

Conclusion: In our cohort of patients with normal left ventricular ejection fraction, the majority of moderate MR, associated with severe aortic stenosis, regresses early after aortic valve replacement. Mitral calcifications and/or left atrial dilation seem to be predictive factors of fixed MR.

Key words: mitral regurgitation, aortic stenosis, aortic valve replacement, transthoracic echocardiography, transesophageal echocardiography

Introduction

Valvular aortic stenosis is the most common acquired valvular heart disease in adults of industrialized countries. When the aortic valve area is < 0.75 cm^2 or when symptoms appear, aortic valve replacement may be necessary. Mitral regurgitation (MR) is frequently associated with aortic stenosis.[1] When MR is moderate to severe, heart failure symptoms may increase. A concomitant mitral valve repair or replacement could then be performed resulting in a higher operative risk. Nevertheless, in a few studies the authors suggest that coexisting MR could improve after aortic surgery[2–4] whereas others do not agree.[5]

This study aimed to evaluate prospectively the frequency and degree of MR in patients with severe aortic stenosis using transthoracic (TTE) and transesophageal (TEE) echocardiography and its evolution after aortic valve replacement. Moreover, we tried to assess the relationships between MR, aortic stenosis, left ventricular (LV) function and mitral apparatus, before and after aortic valve replacement.

Methods

Patients

Thirty adults (18 men and 12 women, mean age 68 ± 8 years, range 48–86) referred to undergo aortic valve replacement for severe aortic stenosis were prospectively included in the study. Patients with severe aortic regurgitation, unstable hemodynamic state, arrhythmia, and contraindication to sur-

Address for reprints:

Sophie Tassan-Mangina, M.D.
CHU Robert Debré
Avenue du général Koenig
51092 Reims Cedex, France
e-mail: stassan@chu-reims.fr

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gery or TEE were excluded. We also excluded patients who had to undergo mitral valve or mitral annulus surgery. Twenty-four patients received mechanical prostheses and 6 received bioprostheses.

Echocardiography

The echographic study was performed using two-dimensional (2-D), M-mode, pulsed, continuous, and color Doppler TTE and TEE examination before and after aortic valve replacement. A Hewlett-Packard Sonos 1500 echograph (Philips Medical Systems/Agilent Technologies, Andover, Mass., USA) with a transthoracic 2.5 MHz transducer, a 2 MHz Pedoff probe, and a multiplan 5MHz transesophageal probe was used. All data were averaged over three measurements.

Preoperatively, the severity of aortic stenosis was quantified by measuring peak and mean pressure gradients across the aortic valve using continuous wave Doppler. The aortic valve area was assessed using the continuity equation.[6] Aortic regurgitation, if present, was evaluated with a color semiquantitative classification previously described.[7] Left ventricular end-diastolic and end-systolic dimensions, end-diastolic thickness of the interventricular septum, and posterior LV wall were assessed with M-mode parasternal echocardiography. The Penn formula was used to calculate LV mass that was indexed to the body surface area.[8] Echographic LV volumes and ejection fraction were determined by Simpson's rule formula.[9] The peak velocity of tricuspid regurgitation was also measured. Presence and severity of MR were assessed using color Doppler flow imaging. We measured the size of the larger mosaic regurgitant jet, obtained after studying transthoracic parasternal, apical, and four- and two-chamber views.[10] Mitral regurgitation was considered mild, moderate, or severe when the regurgitant jet area was < 4 cm^2, 4 to 8 cm^2, or > 8 cm^2, respectively. The left atrium surface was also noted using the same approach. The diameter of the mitral annulus and the length of the mitral anterior valve leaflet were recorded from the four-chamber view.

During the transesophageal study, the maximal area[11] and the maximal width at its origin[12] of the mitral regurgitant jet were also measured. The anatomy of the mitral apparatus and presence of mitral annular calcium were specified.

Postoperatively, the same transthoracic and transesophageal parameter measurements were performed 19 ± 10 days after aortic valve replacement, using the same methods.

Coronary Angiography

Coronary angiography was performed preoperatively. An associated coronary artery disease was defined as the presence of an occlusion or a narrowing > 50% of the luminal diameter of the major coronary arteries. Nine patients had coronary artery disease, three of whom underwent coronary artery bypass graft during the same surgery. The six other patients had no revascularization because of distal diffuse coronary lesions.

Statistical Analysis

All results are expressed as mean value ± 1 standard deviation. P- values are two tailed, with a significant level set to 0.05. Comparisons between pre- and postoperative data were performed using a paired *t*-test. Relationships were assessed using linear regression analysis when both variables were continuous; otherwise, Fisher's *t*-test was used.

Results

Aortic stenosis occurred on bicuspid valves in 4 cases and was degenerative in 26. A mild to moderate aortic regurgitation was associated in 21 patients preoperatively. The pre- and postoperative demographic characteristics of the group are listed in Table I.

TABLE I Pre- and postoperative descriptive data of the patients studied

	Preoperative value	Postoperative value	p Value
Aortic valve area	0.58 ± 0.15 cm^2		—
Aortic permeability index		0.46 ± 0.14	—
Peak pressure gradient across the aortic valve	82 ± 18 mmHg	29 ± 15 mmHg	< 0.0001
Mean pressure gradient across the aortic valve	55 ± 14 mmHg	18 ± 10 mmHg	< 0.0001
LV end-diastolic diameter	52 ± 7 mm	49 ± 6 mm	0.015
LV end-systolic diameter	35 ± 9 mm	34 ± 9 mm	NS
IVS end-diastolic thickness	13.1 ± 2.6 mm	12.9 ± 2.2 mm	NS
PLVW end-diastolic thickness	13.5 ± 2.2 mm	12.9 ± 2 mm	0.0025
LV mass	172 ± 60 g/m^2	147 ± 41 g/m^2	0.0057
LV ejection fraction (TTE) (%)	57 ± 16	60 ± 16	NS
Surface of left atrium	19 ± 5 cm^2	19 ± 5 cm^2	NS
Diameter of the mitral annulus	33 ± 5 mm	31 ± 5 mm	0.023
Length of the mitral anterior valve leaflet	22.5 ± 3.5 mm	22.5 ± 3 mm	NS

Abbreviations: IVS = interventricular septum, LV = left ventricular, NS = nonsignificant, PLVW = posterior left ventricular wall, SD = standard deviation, TTE = transthoracic echocardiography.

Preoperative Data

All patients had MR according to TTE or TEE examination. Using TTE, MR was absent in 3 patients (10%), mild in 21 (70%), moderate in 5 (16.6%) and severe in 1 (3.3%). The group of patients with mild MR included four patients (13%) with a regurgitant jet area < 1 cm^2, which could be considered as nonpathological. Using TEE, MR was absent in 4 patients (13%), the mitral regurgitant jet area was < 1.5 cm^2 in 12 patients (40%), between 1.5 and 4 cm^2 in 12 (40%), between 4 and 7 cm^2 in 1 (3%), and > 7 cm^2 in 1 (3%). Mitral annular calcium was present in 12 patients (40%) and was always associated with nontrivial MR. Intrinsic abnormality of the mitral apparatus was rare (dystrophic in two cases). No MR jet impinged on the left atrial wall.

Postoperative Data

Postoperatively, LV ejection fraction remained unchanged, including in patients with a coronary artery disease, whether or not they had had a coronary artery bypass. We found postoperative MR during TTE in 26 patients (87%) and in 28 (96%) during TEE. Using TTE, MR was mild in 22 patients (73%) and moderate in 4 (13%). The regurgitant jet area was < 1 cm^2 in nine patients (30%). Using TEE, the mitral regurgitant jet area was < 1.5 cm^2 in 17 patients (57%) and ranged from 1.5 to 4 cm^2 in 11 patients (37%). Evolution of MR for each patient is summarized in Figure 1.

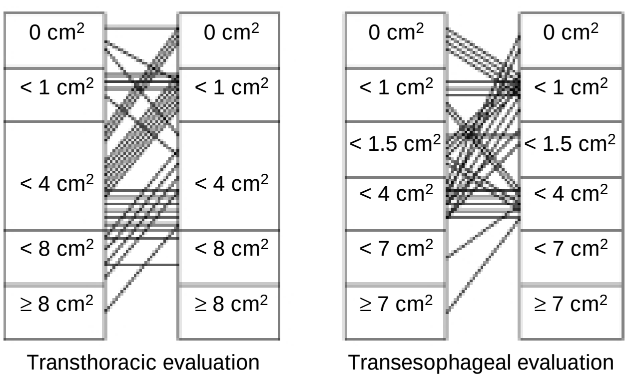

FIG. 1 Severity of mitral regurgitation: color Doppler area of the regurgitant jet before and after aortic valve replacement. Each line represents one patient.

Using either TTE or TEE measurements, the grades of MR for each patient were equal or differed only by one level. There was a significant correlation between the two ways of measurement ($r = 0.73$, $p < 0.0001$ regarding the maximal regurgitant jet areas obtained by TTE and TEE). There was also a significant correlation between the maximal regurgitant jet area and its width at the origin ($r = 0.72$, $p < 0.0001$ by using TEE).

Mitral regurgitation significantly improved after aortic surgery when considering the transthoracic measurements of the maximal mitral regurgitant jet area ($p = 0.016$). The transesophageal color Doppler MR area also regressed, but without reaching the significant threshold ($p = 0.20$). These decreases were mainly noted for MR whose preoperative mitral regurgitant jet area was > 1.5 cm^2 (Fig. 1). A few patients had a greater MR postoperatively; most of them had nonpathological MR preoperatively. In these cases, postoperative MR remained mild and was not associated with new mitral or ventricular abnormalities. There was no significant change in the width at the origin of the mitral regurgitant jet ($p = 0.45$).

Determinant Factors of Postoperative Mitral Regurgitation

The degree of improvement in MR jet area after aortic valve replacement correlated with the preoperative peak velocity of tricuspid regurgitation ($p = 0.02$; $r = 0.44$) and the preoperative indexed left ventricular mass ($p = 0.009$; $r = 0.53$).

The severity of postoperative MR was associated with the peak velocity of tricuspid regurgitation and the area of the left atrium (Table II). It also correlated with the preoperative presence of mitral annular calcifications ($p = 0.04$). The relationship between the grade of MR and the presence of coronary artery disease was nearly significant ($p = 0.06$). We found no significant correlation between the severity of MR and LV dimension or systolic function, nor the size of the mitral annulus.

Discussion

As previously described,[1] MR is frequently associated in patients with aortic stenosis using both TTE or TEE examination. The prevalence of coexisting mitral insufficiency was of 61% in the study of Tunick *et al.*[3] and 59% in that of Brener *et al.*[1] In this study, the prevalence is higher (100%) because of the combined use of TTE and TEE, since MR was absent in 10% of our patients using only TTE and in 13% using only

TABLE II Relationship between the postoperative severity of mitral regurgitation, left atrial area, and peak velocity of tricuspid regurgitation

	Color Doppler surface of MR (TTE)	Color Doppler surface of MR (TEE)	Width at the origin of the mitral regurgitant jet (TEE)
Peak velocity of tricuspid regurgitation	r = 0.73 p < 0.0001	r = 0.74 p < 0.0001	r = 0.54 p = 0.003
Left atrial area (transthoracic apical four-chamber view)	r = 0.40 p = 0.02	p = 0.23	r = 0.42 p = 0.02

Abbreviations: MR = mitral regurgitation, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography.

TEE. However, the inclusion of patients with nonsignificant MR could also explain this high prevalence. If we exclude MR with a surface area < 1 cm^2, the frequency of MR reaches 57% by TTE and 70% by TEE. Most of the MR are mild to moderate in our study, few are severe. Severe mitral insufficiencies associated with an inversion of the systolic pulmonary venous flow, for which surgical treatment was mandatory, were excluded; however, this occurred only once during the inclusion period.

After aortic valve replacement, LV volumes and mass, parietal thickness, and the diameter of the mitral annulus significantly decreased. Left ventricular remodeling results from changes in loading conditions (reduction of pressure gradients between aorta and left ventricle).[13] Left ventricular ejection fraction remained unchanged, probably because the preoperative values were normal in our patients.

The postoperative decrease of the MR jet area in our study is in agreement with most other reports.[2–4] The preoperative predictors for postoperative improvement in MR were peak velocity of tricuspid regurgitation and indexed LV mass. These results are in accordance with those obtained by Brasch *et al.* in a similar study.[14] They highlight the functional part of the preoperative severity of MR, as the increased LV mass was a consequence of the pressure overload that regressed postoperatively.

We previously described that preoperative MR importance appeared to be related to the severity of preoperative aortic stenosis and LV function impairment.[15] Postoperatively, the aortic valve area and the parameters that were related to preoperative systolic pressure overload (i.e., aortic pressure gradients, LV volumes) were no longer related to MR. Indeed, after aortic valve replacement, driving pressure across the mitral valve regressed as LV afterload decreased. Postoperative MR correlated with the left atrium area and the peak velocity of tricuspid insufficiency. Considering its low grade, MR alone could not induce left atrium dilation nor increase in tricuspid regurgitation velocity that we observed. These changes could be the result of the diastolic impairment induced by LV hypertrophy. Indeed, the left atrial area was associated with LV parietal thickness ($p = 0.006$ and $p = 0.14$, respectively, for the interventricular septum thickness pre- and postoperatively; $p = 0.016$ for the postoperative thickness of the posterior LV wall). On the other hand, the peak velocity of tricuspid insufficiency correlates with the end-diastolic volume of the left ventricle ($p = 0.032$), which depends on the quality of LV diastolic function and on the left atrial area ($p = 0.019$). A part of functional MR, a consequence of LV diastolic impairment, probably persists postoperatively in our study. Its improvement may occur later than at the time of our postoperative examination.

Postoperative MR severity appears to be associated with the presence of preoperative mitral annular calcifications, which is independent of the driving force reduction between left ventricle and atrium. Therefore, the presence of preoperative mitral structural abnormalities is important to notice because, in this case, there is a higher risk of lack of improvement in MR after surgery. Consequently, TEE is a useful tool that can contribute to the adequate study of the mitral apparatus anatomy.

The width at the origin of the regurgitant jet measured during TEE is less dependent on loading conditions[12] and remained stable despite aortic valve replacement. This also suggests a functional feature of the preoperative mitral insufficiency. Measurement of the MR jet width should be considered to determine MR severity before aortic valve replacement. Moreover, the MR grade obtained with this method is probably close to the grade that could be measured postoperatively

The study of Brasch *et al.* indicated that additional mitral surgery should be performed for every patient with severe MR associated with aortic stenosis, because postoperative MR improvement was noticed in only 52% of patients.[14] However, the magnitude of MR improvement seems greater with higher degrees of preoperative MR, and postoperative MR aggravation is rare. Because of the preoperative functional role of MR, it could be reasonable to consider concomitant mitral valve surgery only in patients whose MR severity is confirmed using an echocardiographic method that is less dependent on loading conditions than the measurement of color Doppler mitral jet area, such as the width at the origin of the regurgitant jet, or the study of the proximal isovelocity surface area. Moreover, this mitral surgery could be indicated by the preoperative presence of mitral anatomic abnormalities, as mitral annular calcifications.

Limitations

Our study has limits. Because MR was usually mild, we assessed its severity by preferentially using the maximal area of the mitral regurgitant jet, which is a semiquantitative tool. Nevertheless, we emphasized the benefit of the use of TEE, and particularly the measurement of the width at the origin of the regurgitant jet, to evaluate high-grade MR. The use of the proximal isovelocity surface area, which depends less on loading conditions, could also be of interest in this setting. Also, later postoperative echocardiography would better appreciate LV remodeling and its impact on the MR evolution.

Conclusion

Mitral regurgitation is frequently associated with severe aortic stenosis. It is usually mild to moderate and without hemodynamic consequence. Color Doppler MR regurgitant jet area postoperatively decreases while its width at the origin remains unchanged, suggesting an early decrease of the functional part of MR after aortic valve replacement. Moreover, the preoperative predictors of MR regression are LV mass and peak velocity of tricuspid regurgitation. Postoperative MR severity is related to LV diastolic dysfunction that may regress later and whose predominant consequences are an increase in tricuspid insufficiency velocity and left atrial dilation. The presence of mitral annular calcifications also predicts the long-term persistence of MR postoperatively. However, further studies including patients with aortic stenosis and more severe MR are needed to confirm these findings, allowing selection of patients whose preoperative MR may not require specific surgery.

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