The Natural History of Aortic Valve Disease After Mitral Valve Surgery

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OBJECTIVES
The present study evaluates the long-term course of aortic valve disease and the need for aortic valve surgery in patients with rheumatic mitral valve disease who underwent mitral valve surgery.

BACKGROUND
Little is known about the natural history of aortic valve disease in patients undergoing mitral valve surgery for rheumatic mitral valve disease. In addition there is no firm policy regarding the appropriate treatment of mild aortic valve disease while replacing the mitral valve.

METHODS
One-hundred thirty-one patients (44 male, 87 female; mean age 61 ± 13 yr, range 35 to 89) were followed after mitral valve surgery for a mean period of 13 ± 7 years. All patients had rheumatic heart disease. Aortic valve function was assessed preoperatively by cardiac catheterization and during follow-up by transthoracic echocardiography.

RESULTS
At the time of mitral valve surgery, 59 patients (45%) had mild aortic valve disease: 7 (5%) aortic stenosis (AS), 58 (44%) aortic regurgitation (AR). At the end of follow-up, 96 patients (73%) had aortic valve disease: 33 AS (mild or moderate except in two cases) and 90 AR (mild or moderate except in one case). Among patients without aortic valve disease at the time of the mitral valve surgery, only three patients developed significant aortic valve disease after 25 years of follow-up procedures. Disease progression was noted in three of the seven patients with AS (2 to severe) and in six of the fifty eight with AR (1 to severe). Fifty two (90%) with mild AR remained stable after a mean follow-up period of 16 years. In only three patients (2%) the aortic valve disease progressed significantly after 9, 17 and 22 years. In only six patients of the entire cohort (5%), aortic valve replacement was needed after a mean period of 21 years (range 15 to 33). In four of them the primary indication for the second surgery was dysfunction of the prosthetic mitral valve.

CONCLUSIONS
Our findings indicate that, among patients with rheumatic heart disease, a considerable number of patients have mild aortic valve disease at the time of mitral valve surgery. Yet most do not progress to severe disease, and aortic valve replacement is rarely needed after a long follow-up period. Thus, prophylactic valve replacement is not indicated in these cases. (J Am Coll Cardiol 1999;33:2003–8) © 1999 by the American College of Cardiology

A considerable proportion of patients who require mitral valve replacement present with a coexisting pathology of the aortic valve (AV). Rheumatic fever remains the leading cause for combined disease (1). Early series found that one-third of rheumatic hearts exhibited involvement of both mitral and AV. The rate increased to 99% when the follow-up period was extended to 20 years (2–4). The treatment of choice in cases in which one of the valves is less than moderately affected is questionable. Because combined aortic and mitral valve replacement is usually associated with higher risk and poorer long-term survival than replacement of either of the two valves alone (5), a higher threshold for double valve replacement is required. In the absence of a strict paradigm, the decision to replace more than one valve is often made by the surgeon during operation.

To help the clinician establish a uniform policy for the management of multivalvular involvement, we reviewed our experience with patients with rheumatic heart disease who underwent mitral valve replacement or commissurotomy and were followed for an average of 13 ± 7 years. The aim of the present study was to evaluate the course of AV disease after mitral valve surgery, including the need for further AV surgery.

See page 2009

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Aortic stenosis (AS) was considered mild when the peak gradient was 25 mm Hg or less, moderate when the peak gradient was between 25 to 50 mm Hg and severe for a peak gradient above 50 mm Hg. This scale was used only with normal left ventricular function (left ventricular ejection fraction [LVEF] equal or above 50%). In patients with decreased LVEF, cardiac output was measured with the modified Bernoulli equation (8) using continuous-wave Doppler recordings. The aortic valve area was computed by integrating the continuous wave Doppler signal (11) and the color flow mapping, as previously described (12,13). Imaging was performed using commercially available ultrasound systems (SONOS 500, 1000 and 2000, Hewlett Packard, Andover, Massachusetts) and interpreted by a cardiologist skilled in echocardiography.

Statistical analysis. Descriptive baseline characteristics were summarized by frequencies and percentages or by mean values and standard deviation. Univariate and multivariate analyses were used to identify predictors of deterioration of AV disease. Life table analysis based on Kaplan-Meier was done, using the BMDP statistical software (University of California Press) (14).

RESULTS

Average follow-up period for the 131 patients was 13 ± 7 years (range 1 to 33 yr, median 13) (Table 1).

All the patients had rheumatic heart disease. Sixty-three patients had mitral stenosis, 60 had combined mitral stenosis and regurgitation and 8 had mitral regurgitation. Mitral valve replacement was performed in 101, commissurotomy in 30 (Table 1). Forty-five patients of the cohort had mitral commissurotomy performed a decade before the beginning of the follow-up procedures. These patients had either normal AV or mild disease at the time of the first mitral valve surgery (based on preoperative cardiac angiography). None of them had progressed according to the angiography before the second mitral valve surgery. Thus, the follow-up period was extended accordingly.

At the time of mitral valve surgery, 59 patients (45%) had AV disease, 7 had AS and 58 had AR. Six patients had combined disease. Seventy-two patients (55%) had no evidence of AV disease (Table 2).
At the end of the follow-up period, 96 patients (73%) had AV disease (either pure stenosis, pure regurgitation or both), 33 of them had AS, 90 AR. Most had mild disease (Table 2). Twenty-seven had both AS and AR (only a single case of mild AS with severe AR and two cases of severe AS with mild AR). Thirty-five patients (27%) had no evidence of AV disease (Table 2).

According to the clinical evaluation at the end of the follow-up period, 37 patients had functional class (Fc) III and 3 had Fc IV. Yet only two patients with severe AS and a single patient with moderate AR had Fc III. The rest of the patients with advanced Fc were symptomatic due to deterioration of the mitral valve or because of diastolic dysfunction.

Of the patients with AS at the time of mitral valve surgery, only one progressed from mild to moderate disease and two progressed from mild to severe AS over a mean follow-up period of 16 ± 7 years (range 2 to 33 yr, median 18).

Of those with AR, 52 with mild disease (90%) remained stable, five (9%) progressed from mild to moderate and one (2%) from mild to severe over a mean follow-up period of 15 ± 8 years (range 1 to 33 yr, median 16).

Of the 72 patients without AV disease at the time of mitral valve surgery, 36 acquired AV disease during the follow-up period. Of the 26 cases of AS, 20 were mild and 6 were moderate. Of the 32 cases of AR, 31 were mild, 1 was moderate.

In only two patients (1.5%) with combined AV disease at the time of mitral valve surgery did the AS progress significantly (from mild to severe) after 17 and 22 years. Later on these patients had AV replacement.

The comparison between patients who already had AV disease at the beginning and patients who acquired AV disease during the follow-up period is presented in a life table (Kaplan-Meier) analysis (Fig. 1). A significant difference (p < 0.001) was found between the two groups, i.e., among patients with AV disease at the time of mitral valve surgery; moderate or severe AV disease developed sooner and in higher proportion than in patients who acquired AV disease during the follow-up period (Fig. 1, Table 3).

After a mean of 21 years of follow-up procedures (range 15 to 33 yr), six patients of the entire cohort (5%) required surgery for moderate to severe AV disease. Two patients had severe AS, three had moderate AS and one had severe AR. All were graded as NYHA functional class III–IV. In four of them, a major consideration for surgery was also the presence of severe prosthetic mitral valve dysfunction. These patients had a double valve replacement.
None of the clinical factors studied (age, gender, NYHA functional class, coronary heart disease, diabetes, hypertension, hyperlipidemia and chronic renal failure) identified the patients who would eventually need AV replacement.

**DISCUSSION**

The present study is the first to show that patients with rheumatic heart disease and mild AV disease at the time of mitral valve surgery rarely develop hemodynamically significant AV disease and seldom require AV surgery after a long follow-up period.

A considerable proportion of patients with valvular disease have multivalvular involvement. Follow-up studies on patients with rheumatic heart disease have demonstrated combined aortic and mitral valve disease in up to 99% over a period exceeding 20 years (2–4).

The high rate of multivalvular involvement in patients who undergo mitral valve surgery has raised the question of the need for prophylactic AV replacement at the same time; this decision is especially difficult when the AV disease is moderate or less. The alternative is to carefully follow these patients with the consideration that some may require a later operation to replace the AV. Although this option may potentially increase patient mortality and morbidity, it avoids the short- and long-term risks of an unnecessary dual valve replacement when the AV disease is stable.

To solve this controversy, the clinician must consider the pattern of progression of AV disease which varies by its etiology. Aortic stenosis may progress more rapidly in patients with degenerative disease than those with rheumatic or congenital disease (15–17). Reports on the long-term evolution of AS based on cardiac catheterization and Doppler studies have demonstrated an annual increment of 0.1 to 0.14 cm² in AV narrowing (15,18–20,21,22) and an annual increase of 8.3 mm Hg in the peak gradient (18). Brener et al. (18) found that disease progression was faster in the patients who had the mildest stenosis at presentation, progressive left ventricular hypertrophy or concomitant mitral regurgitation that worsened over time. The progression rate may also be related to the presence of a coexisting coronary disease or progressive leaflet calcification (23).

The linearity or nonlinearity of AS progression is multifactorial and may also influence the management policy. Thoreau et al. showed a linear pattern of progression when the AV area is large and a slower progression rate when the severity of stenosis increased (24). Although this finding was confirmed by others (25,26), larger studies are needed to establish its clinical relevance.

Data on the rate of progression of chronic AR are also limited. Recently, Padial et al. (27) studied 127 patients with variable degrees of chronic AR. After 59 ± 21 months

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**Table 3. Cumulative Proportion of Significant Aortic Valve Disease-Free Patients**

<table>
<thead>
<tr>
<th>Years of Follow-Up</th>
<th>Group 1 (*)</th>
<th>Group 2 (*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (yr)</td>
<td>0.98 ± 0.01 (49)</td>
<td>1.0 ± 0 (71)</td>
</tr>
<tr>
<td>10 (yr)</td>
<td>0.95 ± 0.02 (34)</td>
<td>1.0 ± 0 (57)</td>
</tr>
<tr>
<td>15 (yr)</td>
<td>0.83 ± 0.06 (19)</td>
<td>1.0 ± 0 (39)</td>
</tr>
<tr>
<td>20 (yr)</td>
<td>0.67 ± 0.1 (4)</td>
<td>1.0 ± 0 (19)</td>
</tr>
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*Number of patients at risk of developing moderate or severe aortic valve disease.
Group 1: Patients with aortic valve disease at the time of mitral valve surgery. Group 2: Patients with aortic valve disease acquired during follow-up.

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**Figure 1.** Life table (Kaplan-Meier) analysis comparing aortic valve disease progression (to moderate or severe) between patients with an aortic valve disease at the time of mitral valve surgery and patients who acquired aortic valve disease during the follow-up period.
of follow-up procedure, the regurgitation increased in 30%; of these 25% had previously mild disease and 44% had previously moderate disease. These findings show that chronic AR is a progressive disease after several decades.

Unlike the natural history of isolated AV disease or that associated with coronary heart disease, the natural history and the progression pattern of AV disease in patients undergoing mitral valve surgery are unknown. It may be that the repair or replacement of the mitral valve may change the flow characteristics near the AV as a result of the changes in blood jet direction from the prosthetic valve or the formation of a subaortic obstruction by a cage and ball in the mitral position. Thus, a different course of AV disease in the presence of mitral valve surgery might be expected.

In the present study, we showed that AS and AR have a slow rate of progression after mitral valve surgery, similar to that in patients with rheumatic AV disease without mitral valve surgery. Furthermore, AV replacement in the few cases in which it was needed was performed at least 21 years after the original mitral valve surgery. This exceeds the mean interval reported in patients with asymptomatic mild AS who underwent coronary artery bypass grafting (CABG) and were referred later for AV replacement (23). It is probably the different etiology of the AS (rheumatic among most of our patients and senile in the CABG group) that is responsible for this discrepancy.

A similar controversy exists concerning the management of asymptomatic mild valvular disease when coronary artery operation is indicated. Collins et al. (28) reported a 23.5% operative mortality for reoperative AV replacement after CABG compared with 7.6% for reoperative AV replacement without CABG and 6.6% for primary AV replacement with CABG. Because the risk of reoperation is high, several investigators have advocated valve repair (if possible) at the time of myocardial revascularization (29,30) by either incision of the fused commissures or removal of the lumps of calcium (usually discrete in senile disease) from the aortic surface of the valve. This alleviates the AS and delays the need for valve replacement without increasing the operative risk during CABG (31).

Be that as it may, we clearly showed that, despite the considerable number of patients with AV disease at the time of mitral valve surgery, in only 2% of those with mild disease was there significant progression after a mean follow-up period of 16 years. Thus, when the severity of the AV disease is less than moderate at the time of mitral valve surgery, prophylactic valve replacement is probably not justified.

**Study limitations.** Our study is limited by the lack of a comparative control group of patients with mild AV disease in whom prophylactic AV replacement or repair was performed at the time of mitral valve surgery and a similar group in whom AV replacement was performed selectively after the follow-up period.

Because the follow-up period took time, the changes in echocardiographic methods and improvement in equipment must be considered. Nevertheless, we believe that our finding was not severely biased because the echocardiographic findings were supported by the clinical follow-up findings.

**Conclusions.** Patients without AV disease or with mild AV disease at the time of mitral valve surgery rarely develop hemodynamically significant AV disease over a long follow-up period.

The minor progression in the AV disease over a long period of time and the increased perioperative and long-term mortality and morbidity of a dual valve replacement do not justify the performance of prophylactic AV replacement. This is true for both AS and AR. Because all of the patients in our study had rheumatic disease, this statement should be generalized only to this subgroup of cardiac patients. Our study does not provide an answer concerning patients with moderate AV disease at the time of mitral valve surgery.

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