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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.

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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.

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Abbreviations and Acronyms

AR = aortic regurgitation
AS = aortic stenosis
AV = aortic valve
CABG = coronary artery bypass grafting
Fc = functional class
LVEF = left ventricular ejection fraction

METHODS

Study patients. Between 1975 and 1992, a total of 574 patients underwent mitral valve surgery in our cardiothoracic surgery division. One-hundred and sixty were excluded from the study because of nonrheumatic valvular disease, presence of severe aortic valve disease at the time of operation, performance of a double aortic and mitral valve replacement in the same session, congenital heart disease other than congenital bicuspid aortic valve or bacterial endocarditis (due to aortic valve deformation). Rheumatic valve disease was present in 414 patients. Two-hundred patients were excluded because of inadequate follow-up procedures. Eighty-three patients died during the first postoperative year (64 died on the day of the operation and 19 died during the following year). The remaining 131 patients with rheumatic heart disease who were followed periodically by Doppler-echocardiography in our valvular clinic formed the study group. Each patient was evaluated by a preoperative cardiac catheterization and by postoperative transthoracic Doppler-echocardiography examinations (for at least one year after the surgery). Clinical data obtained from the hospital records included age, gender, heart rhythm, New York Heart Association functional class and presence of concomitant medical problems (coronary heart disease, diabetes, hypertension, hyperlipidemia and chronic renal failure).

Cardiac catheterization measurements. All 131 patients had undergone cardiac catheterization by standard femoral percutaneous or brachial cut-down techniques. Before the injection of contrast material, left ventricular end-diastolic pressure and transvalvular gradient were obtained by the left ventricular aortic root pull-back method.

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 Fick method, and the aortic valve area was calculated by the Hakki formula (6). Aortic regurgitation (AR) grade was estimated by injecting contrast material into the aortic root. Regurgitation was qualitatively assessed on a scale +1 to +4 (7) using the right anterior oblique view. Coronary artery disease was defined as ≥70% obstruction of the luminal diameter of at least one epicardial artery by visual assessment.

Echocardiographic analysis. Echocardiographic studies were performed in a standard manner and included the parasternal long- and short-axis views and the two-, four- and five-chamber and apical long-axis views. Mean and peak transthoracic gradients were calculated with the modified Bernoulli equation (8) using continuous-wave Doppler recordings. The aortic valve area was computed with the continuity equation (9) using standard methods when systolic function of the left ventricle was decreased. In the presence of normal left ventricle systolic function (estimated qualitatively and by measurement of fractional shortening above 30%) the mean gradient was used to define the severity of AS (mild ≤25 mm Hg, moderate 25–50 mm Hg, severe ≥50 mm Hg). In cases of systolic left ventricular dysfunction, an AV area of ≥1.5 cm^2 or more was considered mild AS; 1.1 to 1.5 cm^2, moderate and 1.0 cm^2 or less, severe (10). Aortic regurgitation grade was estimated 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).

Table 1. Demographic and Clinical Characteristics of the Patients

Characteristics	Number (%)
Gender	
Male	44 (34)
Female	87 (66)
Age (yr) at Mitral Valve Surgery	
Mean ± SD	45 ± 15
Range	12–77
Age (yr) at End of Follow-up	
Mean ± SD	61 ± 13
Range	35–89
Type of Surgery	
Mitral valve replacement	101
Single disk (Caster-Hall, Bjork-Shiley, Sorin)	32
Double disk (St. Jude, Carbomedics)	20
Starr-Edwards	19
Xenograft (Hancock)	25
Unknown	5
Commissurotomy	30
Duration of Follow-up (yr)	
Mean ± SD	13 ± 7
Range	1–33
Number of Patients During Follow-up	
≤2 years	12
≤5 years	26
≤10 years	61
Coronary Heart Disease*	10 (7)
Hypertension†	12 (8)
Hyperlipidemia‡	2 (1)

*≥70% obstruction of lumen (≥50% in left main coronary artery); †Diastolic pressure >90 mm Hg and systolic pressure >160 (in patients >65 yr); ‡Fasting serum cholesterol >200 mg/dL.

Table 2. Aortic Valve Disease at the Time of Mitral Valve Surgery and at Follow-up

Entry			Follow-up
No AVD	72		35
AVD*	59 (45%)		96 (73%)
Pure AS	1		6
Mild	1		6
Pure AR	52		63
Mild	52		5
Moderate	0		4
AS/AR†	6		27
Mild	6	AS:	
		Mild	18
		Moderate	7
		Severe	2
		AR:	
		Mild	24
		Moderate	2
		Severe	1

*All patients with aortic valve disease (either AS or AR). †All patients with AS and AR (at the same time).
AR = aortic regurgitation; AS = aortic stenosis; AVD = aortic valve disease.

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.

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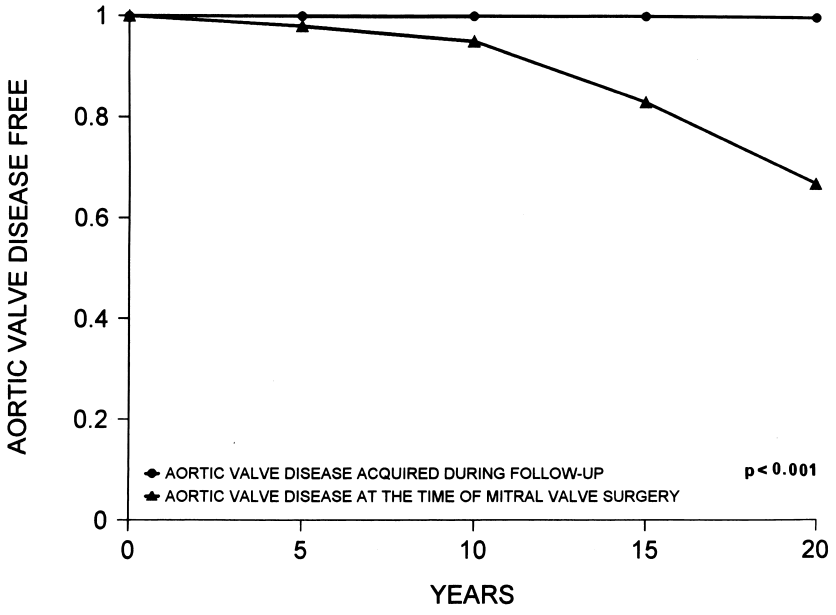

Figure 1. Life table (Kaplan-Meier) analysis comparing aortic valve disease progression (to moderate or severe) between patients with an aortic valve disease at the time of mitral valve surgery and patients who acquired aortic valve disease during the follow-up period.

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.

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

Years of Follow-Up	Group 1 (*)	Group 2 (*)
5 (yr)	0.98 ± 0.01 (49)	1.0 ± 0 (71)
10 (yr)	0.95 ± 0.02 (34)	1.0 ± 0 (57)
15 (yr)	0.83 ± 0.06 (19)	1.0 ± 0 (39)
20 (yr)	0.67 ± 0.1 (4)	1.0 ± 0 (19)

*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.

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 cm^2 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

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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REFERENCES

1. Roberts WC, Virmani R. Aschoff bodies at necropsy in valvular heart disease. Circulation 1978;57:803–15.
2. Clausen BJ. Rheumatic heart disease: an analysis of 796 cases. Am Heart J 1940;20:454–74.
3. Wilson MG, Lubschez R. Longevity in rheumatic fever. JAMA 1948;138:794–8.
4. Bland EF, Jones TD. Rheumatic fever and rheumatic heart disease: a twenty year report on 1,000 patients followed since childhood. Circulation 1951;4:836–43.
5. Kirklin JW, Barratt-Boyes BG. Combined aortic and mitral valve disease with or without tricuspid valve disease. In: Kirklin JW, ed. Cardiac Surgery. 2nd ed. New York: Churchill-Livingstone, 1993: 573–88.
6. Hakki AH, Iskandrian AS, Bemis E, et al. A simplified valve formula for the calculation of stenotic cardiac valve area. Circulation 1981;63: 1050–5.
7. Baim DS, Grossman W. In: Pine JW, Jr., ed. Cardiac Catheterization, Angiography, and Intervention. 5th ed. Baltimore (MD): Williams & Wilkins, 1996:750–3.
8. Yeager M, Yock PG, Popp RL. Comparison of Doppler-derived pressure gradient to that determined at cardiac catheterization in adults with aortic valve stenosis: implication for management. Am J Cardiol 1986;57:644–8.
9. Perakis AC, Montarello JK, Rosenthal E, et al. In vitro measurement of stenotic human aortic valve orifice area in a pulsatile flow model. Validation of the continuity equation. Eur Heart J 1990;11:492–9.
10. Rahimtoola SH. Aortic valve stenosis. In: Braunwald E, ed. Atlas of Heart Disease. Volume 11. St. Louis (MO): C.V. Mosby, 1977: 6.01–2.
11. Grayburn PA, Handshoe R, Smith MD, Harrison MR, Demaria AN. Quantitative assessment of the hemodynamic consequences of aortic regurgitation by means of continuous wave Doppler recordings. J Am Coll Cardiol 1987;10:135–41.
12. Bouchard A, Yock P, Schiller NB, et al. Value of color Doppler estimation of regurgitation volume in patients with chronic aortic insufficiency. Am Heart J 1989;117:1099.
13. Reynolds T, Abate J, Tenney A, Warner MG. The JH/LVOH method in the quantification of aortic regurgitation: how the cardiac

sonographer may avoid an important potential pitfall. J Am Soc Echocardiogr 1991;4:105–8.
14. BMDP Statistical Software. Chief editor: Dixon WJ. University of California Press, 1990.
15. Wagner S, Selzer A. Patterns of progression of aortic stenosis: a longitudinal hemodynamic study. Circulation 1982;65:709–12.
16. Selzer A. Changing aspects of natural history of valvular aortic stenosis. N Engl J Med 1987;317:91–8.
17. Kennedy KD, Nishimura RA, Holmes DR Jr, Bailey KR. Natural history of moderate aortic stenosis. J Am Coll Cardiol 1991;17:313–9.
18. Brener SJ, Duffy CI, Thomas JD, Stewart WJ. Progression of aortic stenosis in 394 patients: relation to changes in myocardial and mitral valve dysfunction. J Am Coll Cardiol 1995;25:3305–10.
19. Faggiano P, Ghizzoni G, Sorgagto A, et al. Rate of progression of valvular aortic stenosis in adults. Am J Cardiol 1992;70:229–33.
20. Bogart DB, Murphy BL, Wong BY, Pugh DM, Dunn MI. Progression of aortic stenosis. Chest 1979;76:391–6.
21. Ng AS, Holmes DR Jr, Smith HC, et al. Hemodynamic progression of adult valvular aortic stenosis. Cathet Cardiovasc Diagn 1986;12: 1445–550.
22. Davies SW, Gershlick AH, Baloon R. Progression of valvular aortic stenosis: a long-term retrospective study. Eur Heart J 1991;12:10–4.
23. Thoreau WA, Siu SC, Thoreau DH, Vandervort DM, Thomas JD, Weyman AE. The rate and pattern of change in valve area in aortic stenosis: long-term Doppler follow-up (abstr). J Am Coll Cardiol 1992;19:331A.
24. Akins CW. Long term results with the Medtronic-Hall valvular prosthesis. Ann Thorac Surg 1996;61:806–13.
25. Davies SW. Progression of aortic stenosis. Role of age and concomitant coronary artery disease (letter). Chest 1994;107:1902.
26. Faggiano P, Aurigemma GP, Rusconi C, Gaasch WH. Progression of valvular aortic stenosis in adults: literature review and clinical implication. Am Heart J 1996;132:408–17.
27. Padial LR, Oliver A, Vivaldi M, et al. Doppler echocardiographic assessment of progression of aortic regurgitation. Am J Cardiol 1997;80:306–14.
28. Collins JJ Jr, Aranki SF. Management of mild aortic stenosis during coronary artery bypass graft surgery. J Cardiac Surg 1994;9 Suppl 2:145–7.
29. Antunes MJ. Coronary artery bypass surgery and minor aortic stenosis. To replace or not replace? An alternative: to repair. J Heart Valve Dis 1994;3:235.
30. Mindich BP, Guarino T, Goldman ME. Aortic valvuloplasty for acquired aortic stenosis. Circulation 1986;74 Suppl 3(pt 2):I130–5.
31. Shapira N, Lemole GM, Fernandez J, et al. Aortic valve repair for aortic stenosis in adults. Ann Thorac Surg 1990;50:110–20.