Predictors of the Long-Term Outcome After Combined Aortic and Mitral Valve Surgery

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Background—The influence of preoperative clinical, hemodynamic, and surgical procedures on long-term prognosis after combined aortic and mitral valve surgery is not well known.

Methods and Results—One hundred seventy patients (mean age, 50.5 years; 102 men and 68 women) who underwent surgery for chronic combined aortic and mitral valvular disease between 1975 and 1989 were followed up for an average of 10.6 years. Additional repair of tricuspid valve was performed in 29 patients (17%), and aortocoronary bypass graft surgery was performed in 7 patients (4.1%). The perioperative mortality rate was 4%, and 10- and 20-year survival rates were 61% and 33%. Only 12 of 94 deaths (11%) were non–cardiac related. At 10 and 20 years, 57% and 21% of patients were free of reoperation, respectively. The main predictors of late survival in univariate analysis were age at surgery ($P=0.0002$), preoperative left ventricular ejection fraction ($P=0.002$), cardiac index ($P=0.007$), tricuspid surgery ($P=0.03$), pulmonary vascular resistance ($P=0.03$), NYHA class ($P=0.04$), and additional aortocoronary bypass graft surgery ($P=0.04$). Duration of symptoms, gender, cause of valvular disease, and type of prosthesis were not predictive of postoperative outcome. In multivariate stepwise Cox analysis, ejection fraction ($P=0.0008$), age at surgery ($P=0.0011$), and tricuspid surgery ($P=0.007$) were independent predictors of late survival.

Conclusions—In combined aortic and mitral valve disease, preoperative myocardial function is the main predictor of long-term survival. Low operative mortality rates and good late outcome make valve replacement mandatory before deterioration of myocardial function occurs. Additional tricuspid valve disease requiring surgery significantly decreases the late survival rate. (Circulation. 1999;100[suppl II]:II-48–II-53.)

Key Words: surgery ■ valves ■ survival ■ prognosis ■ transplantation

Surgery for combined aortic and mitral valve disease was introduced in the early 1960s; until the mid-1970s, it was associated with a high operative mortality rate and unsatisfactory late results.1–3 Despite well documented improvement in surgical techniques with a marked decrease in operative mortality rates and a considerable increase in late postoperative survival rates in the 1980s and 1990s, some reluctance to refer a patient with combined aortic and mitral disease has persisted.1,6,7 This was the main reason for reassessment of preoperative clinical, hemodynamic, and surgical predictors for long-term survival after combined aortic and mitral valve surgery in patients operated on at our institution from the mid-1970s to the late 1980s.

Methods

All 170 patients who underwent combined aortic and mitral valve surgery and associated procedures at the Cardiology Division of Medical Policlinic at the University Hospital in Zurich between 1975 and 1989 were included in the study. All except 2 patients underwent right and left heart catheterization, and all except 2 had left ventricular (LV) angiography. All patients >40 years old and those with angina pectoris underwent coronary angiography. For the calculation of LV volume and ejection fraction (EF), only high-quality angiograms were considered. Hence, preoperative EF and volume were reported in only 159 of 170 patients (94%). NYHA class was determined according to symptoms and functional impairment at the time of preoperative evaluation and operation regardless of previous symptoms and history.

Patients

The main characteristics of the study patients are presented in Table 1. The age of the patients at the time of surgery ranged from 21 to 79 years (mean, 50.5 years). The cause of valvular disease was rheumatic in 41% of patients, and 18% had a history of bacterial endocarditis; in other patients, the origin of valvular disease was not specified and was assumed to be degenerative. None of the patients were operated while they had acute endocarditis, and in the majority of patients, endocarditis antedated surgery by several years. Previous surgery of the heart and great vessels had been performed in 35 patients (21%).

Clinical and Hemodynamic Data

Preoperative NYHA class was 2.9, whereas 24% of patients were in class II, 62% were in class III, and 14% were in class IV (Figure 1).
Heart failure was present or was previously found in 45% of patients. The mean duration of cardiac symptoms was 5.2 years; in 51% of patients, symptoms were present for 4 years, and in 12% of patients, symptoms were present for 12 years. The most important hemodynamic variables are shown in Table 1 and Figure 1. According to type and hemodynamic severity of aortic and mitral disease, patients were divided into different groups (Figure 2). The combination of aortic regurgitation and mitral regurgitation was the most common disease (50%).

Follow-Up
After surgery, all patients were seen at least once in our outpatient clinic, generally 6 months after surgery. Additional information was obtained through the use of standardized questionnaires that were mailed to patients and their physicians. Causes of death and cardiac complications were classified according to guidelines and were obtained from medical reports, death certificates, and telephone contact with physicians. The mean follow-up was 10.6 years (1802 patient-years); in surviving patients, it was 14.5 years, with the longest follow-up being 22.3 years. During the follow-up, 14 patients (8% of the entire group) were lost 1.7 to 15.6 years after the operation (mean follow-up, 7.2 years).

Statistical Analysis
Statistical evaluations and all calculations were performed with StatView 4.5 software (Abacus Concepts, Inc). Survival was calculated according to the Kaplan-Meier method. Univariate analysis was performed for all data presented in Table 1 separately for cardiac survival and reoperation-free survival. Multivariate analysis (Cox hazard regression) was applied in a stepwise manner for all significant parameters in univariate analysis in both groups of data.

Surgical Procedures
All 170 patients had combined aortic and mitral valve surgery. In 41 patients (24%), additional surgical procedures were performed: reconstruction of the tricuspid valve due to significant regurgitation \(\text{n}=29 (17\%)\), aortocoronary bypass graft surgery \(\text{n}=7 (4\%)\), and surgery of the ascending aorta \(\text{n}=7 (4\%)\). Replacement (n=280) and repair (n=60) of the aortic and mitral valves were both performed (Figure 3). Mechanical prostheses (mainly Björk-Shiley) were used in most patients; bioprostheses (mainly Carpentier-Edwards) were used after 1977 until the mid-1980s, more often in the aortic (32%) than in the mitral (18%) position (Table 2). Intraoperative myocardial protection also evolved during this period. During the first years of the study, ice-cold saline perfusion of the coronary arteries was used, combined with intermittent aortic cross-clamping, moderate total body hypothermia (26° to 28°C), and cold pericardial irrigation; after 1978, the use of cold potassium cardioplegia became the standard method.
Results

Survival

Ninety-four patients died and 14 were lost to follow-up (Table 3); the early mortality rate (<1 month) was 4%, and 10- and 20-year survival rates were 61% and 33%, respectively (Figure 4). The mortality rate remained stable during the entire follow-up period (5%/patient-year). Most patients (72%) died of cardiac causes; heart failure and sudden, unexpected death were the most frequent causes of cardiac death (Table 3). Noncardiac death occurred in 12 patients, with malignancies (n=5) and infections (n=4) being the most common causes. In 14 patients, the cause of death remained unknown; these cases were regarded as probably cardiac related. In calculations, they were grouped together with cardiac death. Due to the low number of non-cardiac-related deaths, survival curves for general and cardiac survival are very similar, especially during the first 10 years (Figure 4). The average NYHA class of long-term survivors was 2.1; 17% were in class I, 65% were in class II, 13% were in class III, and 6% were in class IV (Figure 1).

Reoperations

During the follow-up, 46 cardiac reoperations were performed in 37 patients, with an early mortality rate of 7%. Prosthesis replacement was performed in the aortic and mitral (n=12), aortic (n=9), mitral (n=10), and tricuspid (n=2) positions. In 4 patients, refixation of mitral prosthesis had to be performed; 4 heart transplantations became necessary 8, 10, 11, and 12 years after initial valve replacement due to intractable heart failure. Valvular reoperations were combined with surgery of the ascending aorta (n=5), aortocoronary bypass graft surgery (n=2), and tricuspid reconstruction (n=2). Bioprosthesis degeneration was the reason for reoperation in two thirds of the cases. Elective heart transplantation was performed in 3 patients at 8, 10, and 12 years after valve replacement, without early and late deaths; the only emergency transplantation performed due to early postoperative intractable myocardial failure after reoperation of aortic and mitral prosthesis and aortocoronary bypass graft surgery was not successful. Mean duration of function for bioprostheses was 10.2±0.3 years in aortic and 8.2±0.4 years in mitral position. Reoperation-free survival rates were 57% after 10 years and only 21% after 20 years (Figure 4).

Cardiac Complications

During the follow-up, 45 major complications other than reoperation (death included) were encountered; the most
common were stroke (n=16), endocarditis (n=11), embolism (other than cerebral) (n=7), myocardial infarction (n=6), and bleeding during anticoagulation (n=5). Due to diagnostic difficulties, we have not differentiated between embolic and hemorrhagic stroke as causes. The incidence of all thromboembolic and bleeding complications (stroke, embolism, and bleeding) was 1.6%/patient-year, whereas the incidence of lethal complications was 0.3%/patient-year. The incidence of bacterial endocarditis was 0.6%/patient-year, and that of lethal outcome was 0.1%/patient-year.

### Survival

The impact of different parameters on long-term survival after combined aortic and mitral surgery is presented in Table 4. Univariate analyses were performed separately for overall and cardiac survival and for operation-free survival. Age, duration of symptoms, pressure, and volume parameters were calculated as continuous variables; all other data were analyzed as dichotomous variables. Higher age at surgery, higher preoperative NYHA class, higher pulmonary artery resistance, lower cardiac index, lower LVEF, additional tricuspid surgery, and aortocoronary bypass graft surgery were significantly (P<0.05) related to poorer late survival rates (Table 4). When preoperative NYHA classes are analyzed separately, only NYHA class II was clearly related to better long-term outcome, with the differences in survival curves for NYHA classes III and IV being minimal during the entire follow-up period (Figure 5). Only a cohort of patients with the lowest EF (<40%) had clearly decreased survival rates. The survival rates for patients with moderately decreased EF (40% to 54%) and normal EF (>54%) were very similar (Figure 5). Neither cause of the valvular disease, duration of symptoms, nor previous heart failure was a predictor of late outcome. A certain trend for better late outcome was noted with lower preoperative right and left atrial and pulmonary artery pressures; only pulmonary vascular resistance was a significant survival predictor in univariate analysis.

The type of prosthesis (mechanical versus bioprosthesis) had no major impact on long-term outcome; a strong tendency for better long-term survival, falling short of statistical significance (P<0.08), was seen for 55 patients with mitral valve repair. Additional tricuspid regurgitation requiring surgery decreased the late survival rate (Figure 5). Despite bypass surgery, the outcome of patients with coronary artery disease was poor.

In multivariate stepwise regression analysis of the foregoing parameters, only age (P=0.0011, exponential coefficient [Exp(Coef)]1.034), LVEF [P=0.0008, Exp(Coef) 2.10], and

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<th>Parameter</th>
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<th>Operation-Free Survival</th>
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<tr>
<td>Sex</td>
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<tr>
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<tr>
<td>Aortocoronary bypass</td>
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</table>

### Figure 5

Cardiac survival for different NYHA classes, LVEF cohorts, and according to tricuspid valve repair (TCR). Survival rates at 10 years are indicated.
Influence of Surgery
The period between 1975 to 1989 is rather long, and surgical techniques and valvular prosthesis evolved considerably during this time. In the 1970s and early 1980s, some older mechanical prostheses and a higher number of bioprostheses were used. Two late deaths were due to acute dysfunction of Björk-Shiley prostheses in the mitral position, which was later a well recognized problem of convex-concave modification of this prosthesis. The durability of bioprostheses, especially in the mitral position, is limited, and two thirds of repeat operations in our patients were due to prosthesis degeneration. The type of prosthesis remained without major importance for long-term survival due to the low mortality rates for reoperation, confirming the results of randomized studies of aortic or mitral valve replacement with mechanical prostheses or bioprostheses. The reoperation for combined aorto-mitral replacement has a higher operative mortality rate than that for isolated valve replacement, so we abandoned the use of bioprostheses for combined aortic and mitral replacement during the late 1980s.

Repair of mitral valve was performed in one third of our patients. In isolated mitral regurgitation, valve repair is superior to valve replacement in cases with suitable valvular pathology. In our patients, we noted the trend for better long-term survival rates with mitral repair compared with replacement, but the difference did not reach the level of statistical significance.

Survival Predictors
Preoperative LVEF appeared to be the best single predictor of survival after combined aorto-mitral valve surgery. Information on preoperative myocardial function in combined valvular disease is rare. Significantly decreased late outcome was demonstrated only for patients with severely reduced EF (<40%). On reflection of the experience with valve replacement in isolated aortic or mitral regurgitation, the potential for recovery after successful double valve replacement is equally limited when preoperative systolic function is severely decreased. The presence of severe tricuspid regurgitation requiring surgery is the second important predictor of late outcome. Preoperative clinical status is of only limited predictive value for postoperative outcome. Lower late survival rates for patients in preoperative NYHA class III or IV could be demonstrated on univariate analysis, but neither duration nor severity of previous symptoms had any major impact on late survival.

Retrospectively, the indication for combined aortic and mitral surgery in our patients in the 1970s and 1980s appears to have been too conservative. Half of our patients had a reduced LVEF and cardiac index, three fourths of them were in NYHA class III or IV over a long period of time, and heart failure developed in the majority. In these patients, the potential for improvement of surgical outcome is indicated by earlier surgery, before severe decrease in myocardial function began.

Summary and Prospects for Future Development
With modern surgical perioperative treatment and durable prostheses that have excellent hemodynamic performance, late postoperative results in combined aortic and mitral valve disease depends crucially on preoperative LV function. Low operative mortality rates and good late results make valve

Discussion
The optimal timing of surgical treatment for combined aortic and mitral surgery is not well defined. The decreased operative mortality rates and improved late survival rates during the past decade require reassessment of indication for surgery in patients with combined valvular disease. This study summarizes the experience with combined aortic and mitral surgery during the late 1970s and 1980s, with an emphasis on preoperative clinical and hemodynamic data and the choice of surgical procedures as predictors of long-term survival.

Surgical Results
Our observations demonstrate that combined valvular surgery can be performed with a low operative mortality rate of <5% and good late results (10-year survival rate, 61%), whereas three fourths of long-term survivors had a fair quality of life (NYHA classes I and II). Similar results in comparable patient cohorts have been reported. Nevertheless, the early operative mortality rate is higher and the late survival rate is lower than those after isolated aortic or mitral valve replacement.

Heart failure and sudden, unexpected death are the major late causes of death. Heart failure can occur slowly and insidiously, many years after valve replacement, and heart transplantation might become necessary when myocardial failure is refractory to medical therapy. Thus, current late postoperative survival rates do not exactly correspond to “survival of the heart.” In particular, patients with preoperative severe chronic volume overload and reduced myocardial function might require heart transplantation late after valve replacement.

Tricuspid regurgitation requiring surgical repair worsened the prognosis. The prognostic importance of preoperatively increased pulmonary vascular resistance points to the importance of chronic pressure load on the right ventricle for postoperative outcome. Thus, it is not only genuine tricuspid valve disease but also the chronic overload of the right ventricle with dilation and myocardial failure that burdens the late postoperative outcome. Tricuspid repair should be performed when hemodynamic significant regurgitation is present, because such disease does not disappear after correction of the left-side valvular disease. In our relatively young patient group, the incidence of coronary artery disease was very low, but the long-term prognosis of these patients was less favorable despite aortocoronary bypass graft surgery.
replacement mandatory even in moderately symptomatic patients before LV function dysfunction ensues. Durable, modern mechanical substitutes such as bileaflet prostheses should be chosen for valve replacement, but when possible, mitral repair should be attempted. Close surveillance of patients after successful valvular surgery should be maintained, especially in patients with preoperatively decreased myocardial function. Consequent modern medical treatment of postoperative myocardial dysfunction should be provided. Elective heart transplantation should be considered when refractory LV dysfunction occurs. The implantation of an automatic defibrillator might become necessary when malignant arrhythmias arise.

References
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