Valvular Heart Disease

Combined Mitral and Tricuspid Valve Repair in Rheumatic Valve Disease

Fewer Reoperations With Prosthetic Ring Annuloplasty

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Background—We examined predictors of early and very long-term outcome after combined mitral and tricuspid valve repair for rheumatic disease.

Methods and Results—Between 1974 and 2002, 153 consecutive patients (mean age, 46.0±13.2 years) underwent combined mitral and tricuspid valve repair for rheumatic disease. Mitral disease was predominantly stenosis (82.3%); 100% of patients had organic tricuspid valve disease, predominantly with regurgitation (53.6%) or some degree of tricuspid stenosis (46.4%). Mitral repair included commissurotomy in 132 patients (86.3%) associated with a flexible annuloplasty in 108. Tricuspid valve repair included flexible annuloplasty in 68 patients (44.4%) and suture annuloplasty in 20 patients (13.1%) combined with tricuspid commissurotomy in 62 patients (42.5%). Thirty-day mortality was 5.9%. Late mortality was 60.1%. The median follow-up was 15.8 years (interquartile range, 6 to 19 years). Follow-up was 97.9% complete. Age >65 years was the only predictor of late mortality. Kaplan-Meier survival probability was 74.4% at 10 years and 57.0% at 15 years. Sixty-three patients required valve reoperation (mitral valve, 59; tricuspid valve, 38). Predictors of valve reoperations were either mitral or tricuspid commissurotomy without associated prosthetic ring annuloplasty. At 20 years, Kaplan-Meier freedom from reoperation was 48.5±5.1%.

Conclusions—Combined mitral and tricuspid valve repair in rheumatic disease showed satisfactory early results. Long-term results were poor because of high mortality and a high number of valve-related reoperations. The use of prosthetic ring annuloplasty was significantly associated with a reduced incidence of both mitral and tricuspid valve reoperations. (Circulation. 2010;121:1934-1940.)

Key Words: mitral valve ■ mortality ■ rheumatic heart disease ■ surgery ■ tricuspid valve

S tudies of the long-term outcome after valve repair in patients with rheumatic heart disease are old,1,2 because rheumatic heart disease is anecdotal in developed countries and existing experience dates back several decades. In addition, evidence shows that in rheumatic valvular disease, valve repair when feasible is associated with better early and long-term results3–5 compared with prosthetic valve replacement. This is true for both the mitral valve and the tricuspid valve but is much more doubtful for repair of the aortic valve.6

Clinical Perspective on p 1940

There is little information about the outcome of patients with mitral or mitroaortic valve disease of rheumatic origin associated with tricuspid valve dysfunction. Different studies have analyzed the results of surgical treatment for functional tricuspid valve insufficiency,7 but data from patients with organic tricuspid valve disease have been exceptionally reported.8–10

Therefore, this retrospective, single-center study was conducted to assess the very long-term outcome and predictors of clinical results in patients with rheumatic valvular disease of the mitral and tricuspid valves undergoing combined surgical repair of both valves. The durability and predictors of dysfunction for the valve repair techniques were analyzed.

Methods

Study Subjects

From 1974 to 2002, a total of 5040 consecutive patients underwent surgical correction at our institution for valve disease of rheumatic origin. Of these patients, 153 with organic tricuspid valve disease requiring mitral and tricuspid valve repair at the same time were selected for the present study. None of the patients had previously...
underwent valve surgery with extracorporeal circulation. A previous close mitral commissurotomy was performed in 16 patients (10.4%). This retrospective study was approved by the Ethics Committee of the hospital.

There were 132 women and 21 men with a mean age of 46.0 ± 13.2 years (range, 14 to 81 years). Operations were performed on 53 patients between 1974 and 1977, on 53 patients between 1978 and 1982, and on 47 patients between 1983 and 2002. Preoperative characteristics of the patients are shown in Table 1.

All patients were investigated preoperatively by means of echocardiography of different modes according to the year of the study. Hemodynamic studies were performed in 120 patients (78.3%) to complete echocardiographic studies or coronary angiographic studies when indicated. After completion of preoperative studies, mitral and tricuspid valve disease of rheumatic origin with significant lesions in both valves was diagnosed in all patients. Predominant tricuspid insufficiency was present in 31 patients (20.3%) and predominant tricuspid stenosis in 82 patients (53.6%). Mixed tricuspid lesions (stenosis and insufficiency) were present in 40 patients (26.1%). All patients had organic rheumatic tricuspid valve disease. This diagnosis was established by visual inspection of dilatation of the ring and involvement of the leaflet or the subvalvular apparatus at the time of operation. Given that all patients underwent tricuspid valve repair procedures, histopathological studies could not be performed. Fifty-nine patients were found to have an associated aortic valve disease, with double-valve disease in 27 and predominant aortic insufficiency in 32.

### Surgical Procedure

All patients signed an informed consent form preoperatively. Operations were performed through median sternotomies with cardiopulmonary bypass. Myocardial protection was achieved with crystalloid cardioplegia in patients operated on until 1993 and with antegrade or retrograde blood cardioplegia after that. The median duration of myocardial ischemia was 49 minutes (range, 15 to 157 minutes); cardiopulmonary bypass, 89 minutes (range, 17 to 193 minutes); and postclamping time, 41 minutes (range, 10 to 130 minutes). Postclamping time was defined as the interval between the release of the aortic clamp and the end of cardiopulmonary bypass. An intraventricular counterpulsation balloon was implanted in 4 patients.

### Follow-Up

The follow-up data for this study were procured in a 4-month period (October 2008 to January 2009). The patients were followed up through visits in our outpatient clinic (n = 71), direct contact at home (n = 42), or direct contact with their cardiologists (n = 25). When follow-up was not possible, information on vital status (alive or death) was obtained through the Social Security database (n = 6). Of a possible maximum follow-up of 2279 years, 2248 years were obtained. Follow-up was 97.9% complete (141 of 144), with a median follow up of 15.8 years (interquartile range, 6 to 19 years). The follow-up was incomplete for 3 patients who were lost after 9.4, 16.6, and 18.5 years of follow-up. At follow-up, patients were seen by a cardiac surgeon and a cardiologist in the outpatient clinics of the hospital or by the cardiologist in charge when patients lived far away from the hospital. Annual echocardiographic studies were not performed during the first half of the study.

### Statistical Methods

Values for continuous variables are expressed as mean ± SD. Percentages are used for categorical variables. Categorical variables were compared by use of the χ² test or the Fisher exact test when necessary. Variables associated with early mortality were not ana-
lyzed because the number of 30-days events was too small to conduct a detailed statistical analysis. Survival curves for overall mortality, reoperation, and valve-related complications were obtained by the Kaplan-Meier method. Cox proportional-hazards regression was used to study the influence of covariates on late mortality and reoperation. The start point for analysis of late mortality was 30 days after surgery. Results are expressed as hazard ratios. In the model for late mortality, patients alive at the end of follow-up were considered censored. In the model for reoperation, patients who did not undergo reoperation and were alive at the end of the follow-up were considered censored, whereas those not reoperated but who died during the follow-up were considered a competing risk. Multivariable models were performed with the forward selection procedure with a value of $P=0.25$ to remove variables. Year of operation was divided into tertiles and was forced to remain in models for mortality. Variables included in the multivariable analysis were those with values of $P<0.30$ in the univariate analysis. Variables analyzed in the univariate analysis were age; sex; body surface area; date of operation; previous valve surgery and type of operation; New York Heart Association functional class; heart rhythm; presence of congestive heart failure; ejection fraction; pulmonary artery pressure; pulmonary capillary systolic pressure; cardiac index; aortic, mitral, and/or tricuspid valve gradient; left ventricular end-diastolic pressure; right ventricular systolic pressure; total pulmonary vascular resistance; pulmonary alveolar resistance; valve and type of lesions; type of valve repair; ischemic, cardiopulmonary, and postclamping times; use of intraaortic balloon; and postoperative complications. Multivariable analysis was performed with the Stata Intercooled computer program, release 6 (State Corp, College Station, Tex). Statistical significance was set at $P<0.05$.

**Results**

**Thirty-Day Mortality**
Thirty-day mortality was 5.9% (9 patients). Causes of death were cardiac in 100% of cases associated with respiratory insufficiency in 2 and bleeding in 1.

**Late Mortality**
There were 92 late deaths among 144 perioperative survivors (late mortality, 60.1%). Causes of death were cardiac in 63 patients, 30-day mortality at the first and successive valve-related reoperations in 20, and noncardiac in 9. The Kaplan-Meier survival probabilities were 69.0±3.7% at 10 years, 57.0±3.9% at 15 years, and 28.8±4.9% at 20 years (Figure 1). In the univariate analysis, late mortality was higher in the presence versus absence of severe postoperative complications (Kaplan-Meier estimates at 10 years, 64.2±9.7% and 79.7±4.3%, respectively; $P<0.001$). Year of operation was also unrelated to late mortality. Kaplan-Meier probability of survival at 10 years was 70.1±7.0% for 1974 to 1977, 81.3±5.6% for 1978 to 1982, and 71.2±7.1% for 1983 to 2002. The mean postclamping time was longer in patients who died than in survivors (46.6±31.9 versus 35.5±27.5 minutes; $P<0.001$).

In the multivariable analysis, age >65 years (hazard ratio, 6.03) was the only predictive factor for late death after adjustment by year of operation and concomitant aortic valve surgery. Body mass index <20 kg/m² (hazard ratio, 1.64) or >25 kg/m² (hazard ratio, 1.71) was also included in the model, but statistical significance was not reached (Table 3).

**Reoperations**
Of the 144 patients who survived the operation, 63 (41.2%) required reoperation because of valve dysfunction. Indications for surgery included progression of rheumatic valve disease in 44 patients, structural deterioration of aortic and/or mitral bioprosthesis in 7, perioperative dehiscence of an aortic prosthesis in 2, early failure of mitral valve repair in 9, and aortic prosthetic valve endocarditis in 1. Overall, reoperation was required because of isolated mitral dysfunction in 15; isolated tricuspid dysfunction in 1; isolated aortic dysfunction in 1; mitral and aortic dysfunction in 8; mitral and tricuspid dysfunction in 19; aortic and tricuspid dysfunction in 1; and mitral, aortic, and tricuspid dysfunction in 17.

Mitral valve disease at reoperation (n=59) included predominant mitral restenosis in 33 patients and mixed lesions associated with progression of rheumatic valve disease in 17, as well as regurgitation resulting from early failure of mitral valve repair in 9. Tricuspid valve lesions included predominant insufficiency in 21 patients and mixed lesions in 15 patients caused by the progression of rheumatic disease and early insufficiency resulting from failure of tricuspid valve repair in 2.

Reoperations included mitral valve replacement in 56 patients and a second mitral valve repair in 3. All patients with previous aortic valve operations underwent prosthetic valve replacement. Twenty-four patients underwent tricuspid valve replacement, 14 of whom had a second mitral valve repair. Reoperations were performed with homograft prostheses in 30 patients and 29 with bioprostheses. Five patients required replacement of a second homograft prosthesis and 2 of a second bioprosthesis.

**Table 3. Predictors of Mortality in the Multivariable Analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;65</td>
<td>6.03 (2.45–14.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index &lt;20 kg/m²</td>
<td>1.64 (0.88–3.07)</td>
<td>0.12</td>
</tr>
<tr>
<td>Body mass index &gt;25 kg/m²</td>
<td>1.71 (0.99–2.97)</td>
<td>0.06</td>
</tr>
<tr>
<td>Year of operation, 1978–1982</td>
<td>0.64 (0.37–1.11)</td>
<td>0.11</td>
</tr>
<tr>
<td>Year of operation, 1982 and later</td>
<td>0.79 (0.43–1.46)</td>
<td>0.45</td>
</tr>
<tr>
<td>Concomitant aortic valve surgery</td>
<td>1.24 (0.64–2.38)</td>
<td>0.52</td>
</tr>
<tr>
<td>Reoperation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No mitral prosthetic ring annuloplasty</td>
<td>5.69 (2.94–11.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No tricuspid prosthetic ring annuloplasty</td>
<td>2.10 (1.21–4.80)</td>
<td>0.03</td>
</tr>
<tr>
<td>Concomitant aortic valve surgery</td>
<td>2.13 (0.95–4.76)</td>
<td>0.07</td>
</tr>
</tbody>
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valve replacement (mechanical prosthesis, 15; bioprosthesis, 9), and the remaining 14 had a second tricuspid valve repair: Duran flexible annuloplasty ring in 8, suture annuloplasty in 5, and commissurotomy in 1.

There were 14 deaths among 63 patients undergoing first reoperation (30-day mortality, 22.2%). Death resulted from cardiac causes in 8 patients, neurological causes in 2, renal failure in 1, respiratory insufficiency in 2, and bleeding in 1. The Kaplan-Meier curve values for freedom from reoperation were $74.1\pm3.0\%$ at 10 years, $63.4\pm3.8\%$ at 15 years, and $48.5\pm5.1\%$ at 20 years (Figure 2).

In the univariate analysis, need of reoperation was significantly higher among patients undergoing mitral commissurotomy without flexible annuloplasty than among patients undergoing mitral commissurotomy with flexible annuloplasty, as well as in patients treated with tricuspid commissurotomy without annuloplasty compared with those treated with tricuspid commissurotomy in association with annuloplasty with a flexible ring. The use of mitral or tricuspid commissurotomy together with flexible annuloplasty was associated with statistically significant differences in the Kaplan-Meier curve for freedom from reoperation compared with mitral or tricuspid commissurotomy without annuloplasty (Figures 3 and 4, respectively). For mitral commissurotomy with flexible annuloplasty, the Kaplan-Meier estimate for freedom from valve-related reoperation was $90.2\pm4.0\%$ at 10 years. The corresponding number for mitral commissurotomy without flexible annuloplasty was $57.3\pm8.9\%$ at 10 years (Figure 3). For tricuspid commissurotomy with flexible ring annuloplasty, the Kaplan-Meier estimate for freedom from valve-related reoperation was $86.6\pm4.4\%$ at 10 years. The corresponding number for patients with tricuspid commissurotomy without flexible ring annuloplasty was $75.5\pm5.5\%$ at 10 years (Figure 4).

During the follow-up, 1 patient had infective endocarditis and was treated surgically. Thromboembolic episodes were recorded in 26 patients (central without sequelae in 12, central with sequelae in 10, and peripheral in 4). Major bleeding episodes related to anticoagulation were recorded in 34 patients. The Kaplan-Meier estimates for freedom from valve-related complications were $52.1\pm4.0\%$ at 10 years and $23.7\pm4.5\%$ at 20 years. At the follow-up closing date, 39 survivors (75.0%) were in New York Heart Association functional class I or II, 11 (21.2%) were in class III, and 2 (3.8%) were in class IV.

**Discussion**

Although rheumatic heart disease has almost disappeared in industrialized countries, this disease remains a major public health problem in the third world where it is the leading cause of illness and death of cardiac origin. Among socially and economically disadvantaged populations with overcrowded living conditions in developing countries, the incidence of
rheumatic fever ranges from 100 to 200 per 100,000 school-age children,\textsuperscript{15} essentially a productive age group, contributing significantly to the maintenance of poverty in these countries. Despite this high prevalence, few studies of valve surgery for rheumatic heart disease have been reported, most of them being published in the 1970s and 1980s.\textsuperscript{1–3} When rheumatic fever became rare in wealthy countries, it disappeared from the scientific literature. In Spain, a large population of patients with rheumatic valve disease have undergone diagnosis and treatment during the past 30 years\textsuperscript{5,16,17} not only because eradication of rheumatic fever occurred later there than in other developed countries but also because there has been a resurgence of the disease as a result of the influx of immigrants from countries where rheumatic fever is prevalent.

It is now well known that surgical valve repair is considered the gold standard in heart valve surgery. However, in patients with rheumatic valve disease, durability of valve repair is compromised by the active and progressive characteristics of the disease process. In this respect, there is a paucity of studies in the literature on the very long-term results and valve repair durability for rheumatic heart disease. The population selected for the present study includes all patients consecutively diagnosed with tricuspid and mitral valve disease or tricuspid, mitral, and aortic valve disease of rheumatic origin, but in contrast to most series previously reported, all patients had organic rheumatic tricuspid valve disease. Organic tricuspid valve lesions involve the commissural area, leaflets, and/or subvalvular apparatus. In these circumstances, valve repair is technically difficult, and the short- and long-term results of reparative procedures are unknown. All patients in the present series underwent combined mitral and tricuspid valve repair with initial satisfactory results. The 30-day mortality rate of 5.9\% can be considered a good surgical outcome in a series of patients with polyvalvular disease diagnosed and treated over a 30-year period. This number compares favorably with in-hospital death rates between 8\% and 28\% reported in other studies.\textsuperscript{1,3}

In the present series of patients with rheumatic disease of the mitral and the tricuspid valves, the use of a prosthetic ring after open mitral commissurotomy for treating rheumatic mitral lesions was a protective factor in the long-term outcome. To the best of our knowledge, this observation has not previously been reported. Mitral ring annuloplasty has been recommended by different authors not only to correct dilatation of the native ring but also to increase coaptation of the leaflets or as a final technique to support other reparative procedures.\textsuperscript{18,19} In a previous study by our group, mitral repair without implantation of a prosthetic ring was a risk factor for reoperation.\textsuperscript{20} In a recent study of 3057 patients undergoing primary isolated posterior leaflet repair for degenerative mitral disease either with or without prosthetic annuloplasty, valve repair without a prosthetic annuloplasty was associated with accelerated return of mitral regurgitation.\textsuperscript{21} Some authors also consider that a prosthetic ring is necessary in tricuspid valve repair because of functional or rheumatic disease.\textsuperscript{7} The present experience suggests that prosthetic annuloplasty in both the mitral and tricuspid positions may reduce the need for reoperation resulting from valvular dysfunction. This is a major and clinically relevant finding of the study, although it should be considered with caution given the relatively small number of patients included in this retrospective long-term study and the long study period (>30 years). On the other hand, performing a prospective randomized study is not feasible because rheumatic fever and rheumatic disease are eradicated in developed countries. Open mitral commissurotomy is a surgical technique with consistently proven efficacy.\textsuperscript{8,10} The implantation of a prosthetic ring is indicated in patients with concomitant mitral regurgitation grade 3 or greater or when a residual regurgitation is observed after commissurotomy. In case of confirmation that prosthetic ring annuloplasty associated with open mitral commissurotomy substantially improves the long-term outcome, percutaneous mitral valvuloplasty may be a suboptimal treatment. Song et al\textsuperscript{22} have shown that in the presence of significant tricuspid regurgitation associated with mitral stenosis, tricuspid valve repair combined with mitral valve surgery was related to better clinical outcomes than percutaneous mitral valvuloplasty alone.

This group of patients was selected according to the cause of valvular lesions: rheumatic disease of the native valve, the combination of mitral and tricuspid disease, and the mitral and tricuspid disease with organic lesions of the leaflets and the subvalvular apparatus. Tricuspid commissural fusion, retraction, fibrosis and/or calcification of the leaflets, and fusion and thickening of the subvalvular apparatus documented at surgery confirmed that tricuspid valve lesions were of rheumatic origin rather than secondary to mitral valve disease. In fact, open commissurotomy of the tricuspid valve was performed in 42.5\% of patients. A final objective of the study was to assess whether the use of a prosthetic ring improved the prognosis in terms of survival and less need for reoperation. This retrospective and very long-term outcome study demonstrates that the use of a prosthetic ring annuloplasty, in both the mitral and tricuspid positions, improved the results significantly, reducing the need of reoperation as a result of valvular dysfunction.

Patients treated with combined mitral and tricuspid valve repair performed better than those undergoing prosthetic valve replacement of the mitral valve. A historical comparison with a subset of 149 patients with double mitral and tricuspid rheumatic valve disease undergoing mitral valve replacement (mechanical, 98; bioprosthesis, 51) and tricuspid repair in the same time period illustrates this point.\textsuperscript{1,3} There were no differences in the 30-day mortality rate, but at 15 years, the probability of survival and freedom from valve dysfunction-related reoperation were less favorable. Besides these data based on our experience, other studies of rheumatic heart disease have shown that patients with mitral valve repair (or open mitral commissurotomy) survived longer than those undergoing mitral valve replacement with any type of prosthesis.\textsuperscript{23–25} With regard to valve-related reoperation, it is well known that it depends on the type of valve substitute used. In young patients such as those in the present study, implantation of a bioprosthesis was associated with a high incidence of late reoperation; in contrast, the use of a mechanical prosthesis significantly decreased the need of...
reoperation even if a comparison is made with repair surgery of the mitral valve of rheumatic origin.23,24

One of the most significant findings of this experience is, on the one hand, the relatively satisfactory immediate result with 30-day mortality of 5.9% for a group of patients with polyvalvular disease and organic involvement of the tricuspid valve. If the long study period and the fact that most patients were operated on many years ago and had polyvalvular disease are considered, this 30-day mortality rate is relatively acceptable. However, the long-term results obtained over this 30-year experience are poor. A relatively young group of patients (mean age, 46 years) showed a mortality rate of 60% at follow-up. This high late mortality rate can be attributed to rheumatic disease itself. A total of 63 patients (41.2%) required valve-related reoperations. Reoperation was associated with a very high mortality (22.2%). This finding has rarely been documented in the literature. A previous study by our group showed that reoperations after tricuspid valve repair were associated with a high mortality.16

The high mortality rate for reoperation, which is consistent with data reported in previous studies,13,16,26,27 is explained by different reasons, including the fact that annual echocardiographic studies were not performed during the first half of the study, the patients’ clinical profile (polyvalvular disease, previous valve surgery in all cases), the fact that indications for reoperation were not established early or were not established at all, and the long-standing condition of rheumatic heart valve disease. The rest of the mortality is mostly of cardiac origin. Because this is a young group of patients, mortality resulting from causes other than cardiac is low, and most patients died at follow-up as a result of terminal heart failure or complications in successive reoperations. This fact shows that rheumatic disease is incurable and that surgery is only palliative, like the majority of procedures in heart surgery. However, it can be concluded that organic lesions of the tricuspid valve of rheumatic origin can be repaired successfully, with results probably better than those from prosthetic valve replacement according to our experience28 and that of other authors.1–4 In contrast, very long-term results are disappointing because of the progression of rheumatic heart disease. It is likely that the prosthetic ring may prevent the recurrence of a regurgitation lesion such as that which occurs in reoperative surgery of degenerative or ischemic lesions of the mitral valve. However, the impact of prosthetic ring annuloplasty in preventing the appearance of restenosis or mixed lesions related to the course of rheumatic heart disease is unclear.

Conclusions

Combined mitral and tricuspid valve repair in rheumatic disease showed satisfactory early results. Long-term results were poor as a result of high mortality and a high number of valve-related reoperations. The use of prosthetic ring annuloplasty was significantly associated with a reduced incidence of both mitral and tricuspid valve reoperations. However, there is not enough evidence to support the use of prosthetic ring annuloplasty for all rheumatic mitral or tricuspid valves.

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Disclosures

None.

References

This study with very long-term results shows, probably for the first time, that in patients undergoing either mitral or tricuspid valve repair when both lesions have a rheumatic origin, the results obtained are more favorable with the use of a prosthetic ring annuloplasty. Implantation of a prosthetic ring in the mitral or tricuspid position was associated with significantly fewer valve dysfunction–related reoperations and a longer reoperation-free survival. As a result of this finding, mitral valve repair using percutaneous balloon dilatation of the valve might be a suboptimal technique. On the other hand, the historical comparison of patients with double rheumatic valve disease (mitral and tricuspid) treated with prosthetic mitral valve replacement confirms, even at very long-term follow-up, that mitral repair offers a better alternative with longer survival and fewer valve dysfunction reoperations. The present study is the largest experience of surgical treatment of rheumatic mitral/tricuspid valve disease with the longest follow-up. Although rheumatic disease is eradicated in the developed world, rheumatic fever is still the first cause of heart valve disease in 5 million people around the world.
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