Midterm Outcomes of Rheumatic Mitral Repair Versus Replacement

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SUMMARY

Mitral repair is feasible for patients with degenerative or ischemic heart disease, however, the appropriateness of repair for rheumatic heart disease remains controversial. We compared our outcomes for primary isolated mitral repair versus replacement in an elderly population. From November 1997 to July 2005, mitral repair (group I) was performed in 33 patients while 59 underwent replacement (group II). Survival and risk factors were evaluated by Kaplan-Meier and Cox regression analysis. Mean age at operation for groups I and II was 49.7 ± 13.2 versus 58.1 ± 11.2 (P = 0.002). No statistically significant differences with regards to demographic parameters were observed except for there being fewer percutaneous transvenous mitral commissurotomy procedures and a lower severity of pulmonary hypertension in group I. Patients with a greater Wilkins score and more valvular calcification underwent replacement more often (P < 0.001). In-hospital mortality, ICU/hospital stay, and postoperative congestive heart failure functional class did not differ significantly. Major adverse cardiac events occurred in 13 and 19 patients, respectively (P = 0.50). There were 4 versus 6 late deaths (P = 0.74). Only two from group I underwent subsequent mitral reoperation. Kaplan-Meier overall survival and event-free survival at 5 years for groups I and II were 0.81 ± 0.08 versus 0.81 ± 0.06 (P = 0.90) and 0.52 ± 0.10 versus 0.51 ± 0.10 (P = 0.21), respectively. Old age, renal insufficiency, LVEF < 40%, and a history of stroke were poor predictors of patient survival. Compared with replacement, mitral repair for rheumatic heart disease was associated with a lower surgical mortality, higher repeat-surgery rate, and good survival. Rheumatic mitral valves should be repaired in select patients with appropriate valvular pathology. (Int Heart J 2008; 49: 565-576)

Key words: Rheumatic heart disease, Congestive heart failure, Pulmonary hypertension, Mitral valve surgery, Maze procedure, Atrial fibrillation

RHEUMATIC heart disease (RHD) has become rare in the Western world, but remains a common health problem in developing countries and especially amongst a number of poor, mainly indigenous populations internationally. It has

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been well-recognized that mitral repair is the procedure of choice for patients with degenerative regurgitation, a procedure which has long been associated with low surgical mortality and morbidity rates, and a lower likelihood of repeat surgery and/or thromboembolic events than is the case for replacement. Moreover, mitral repair is associated with better blood flow dynamics across the mitral valve, good preservation of left ventricular function, and improved late survival for sufferers of heart disease of an ischemic origin. However, few direct comparisons have been made between replacement in the mitral position and mitral valve repair among RHD patients. Such studies might prove particularly informative in view of the demonstrated inferior durability of mitral reconstruction in rheumatic patients. Most of the previously published studies pertaining to rheumatic mitral repair appear to have focused upon younger patients and patients featuring mixed etiologies, and/or were related to the relative influence of recurrent episodes of rheumatic inflammation. The purpose of this investigation was to compare mitral repair with replacement for a study sample of homogenous older RHD patients, and to investigate those variables that had an impact on surgical mortality, the level and significance of postoperative complications, and midterm survival for mitral valve disease patients being treated at our institution.

METHODS

Our study consisted of 92 consecutive RHD patients who had undergone primary isolated mitral +/- tricuspid valve surgery at Chang Gung Memorial Hospital, Linkou, Taiwan during the period from November 1997 to July 2005. Mitral repair (group I) using the Carpentier technique was performed in 33 patients, while 59 patients (group II) underwent replacement (mechanical/tissue valve: 41/18). A diagnosis of RHD was made by the surgeons and consulting cardiologists on the basis of previous clinical presentations and findings at the time of cardiac catheterization and echocardiography. The decision for mitral repair or replacement was made based upon the preferences of the surgeons and individual mitral valvular pathology seen on operative mitral analysis, factors which could not be analysed herein given the acknowledged confines of this retrospective study. In order to simply clarify the necessary conditions for mitral surgery, patients who underwent concomitant aortic valve surgery, or aortic aneurysm or coronary-artery bypass surgery were excluded from the study. A variety of surgical techniques used for the repair of mitral valves have already been described in the relevant literature. At the time of completion of the surgical procedures, mitral competence was evaluated by cold saline bulb syringe injection. In addition, perioperative transesophageal echocardiography was undertaken in all patients for the purposes of the assessment of the effectiveness of valve repair or replacement,
subsequent to weaning from cardiopulmonary bypass support. In some selected patients with chronic permanent atrial fibrillation (Af), a microwave or cryo-ablation maze procedure was performed to correct the atrial arrhythmia.

The majority of the surviving patients underwent a monthly follow-up postoperatively for 3 months and then a 3-month follow-up until April 2007. Echocardiography was performed annually or as needed thereafter. Anticoagulants were prescribed for patients having mechanical valve replacement, the presence of persistent or permanent atrial fibrillation, a past history of thromboembolism, or an advanced congestive heart failure (CHF) functional class. Major adverse cardiac events (MACE) were defined as readmission to hospital for any disease(s) of cardiac origin such as heart failure, anticoagulant-induced hemorrhagic or thromboembolic episodes to the brain or vital organs, or infective endocarditis or recurrent mitral valve disease that necessitated compulsory repeat-surgery.

Statistical analysis was performed with the Statistical Package for Social Sciences statistical software (SPSS for Windows, version 13.0, SPSS Inc., Chicago, IL, USA). Categorical patient variables were compared using the $\chi^2$ test or Fisher’s exact test where appropriate, and the results were reported as a proportion (percentage) of a group. The mean ± standard deviation of continuous variables was compared using the Student $t$-test for normally distributed variables and the Wilcoxon rank sum test was used for variables that featured a nonparametric distribution.

Midterm survival and freedom from MACE postsurgery were compared using the Kaplan-Meier method. The association of potential risk factors with survival was assessed by univariate analysis, and factors which featured a $P$ value of less than or equal to 0.3 were included in a stepwise logistical regression-analysis model. A number of variables were selected for univariate and multivariate analyses, including age > 65 years, gender, obesity (body mass index; BMI > 27), comorbid diseases (hypertension, diabetes mellitus, peripheral vascular disease, atrial fibrillation, cerebrovascular disease, chronic renal insufficiency), New York Heart Association (NYHA) functional class, a LVEF < 40%, type of mitral valve procedure undertaken, type of cardioplegia delivery, and cardiopulmonary bypass time and aortic cross-clamp time.

**Results**

**Hospital outcomes:** The preoperative and surgical characteristics of the patients are summarized in Table I and Table II. Mean age at the time of surgery for group I versus group II was 49.7 ± 13.2 versus 58.1 ± 11.2 years ($P = 0.002$), and there were 12 (36.4%) and 20 (33.9%) male patients in groups I and II, respectively ($P$
For group I and II patients, 5 of 33 (15.2%) versus 3 of 59 (5.1%) were categorized as belonging to NYHA functional class II, 22 (66.7%) versus 25 (42.4%) to class III, and 6 (18.2%) versus 5 (8.5%) were accorded class-IV status ($P = 0.09$), while 31 (93.9%) versus 57 (96.6%) patients suffered from atrial fibrillation. A significantly smaller proportion of group I patients (18.2% versus 42.4%) had received percutaneous mitral commissurotomy (PTMC) prior to their mitral surgery. The underlying mitral valve pathologies were stenosis for 14.1% of the study population, regurgitation for 15.2%, and both stenosis and regurgitation for 70.7%. Reparative procedures included annuloplasty with a mitral ring ($n = 33, 100\%$), commissurotomy ($n = 12, 36.3\%$), chordal resection ($n = 6, 18.2\%$), decalcification ($n = 3, 9.1\%$), chordal transfer ($n = 1, 3\%$), and posterior leaflet annuloplasty with pericardial patching ($n = 7, 21.2\%$). Not all mitral leaflets were preserved in the replacement group. Tricuspid valve repair was carried out for 15 (45.6%) versus 36 (61.0%) in group I and II, respectively ($P = 0.19$). In addition, 13 patients from group I and 5 from group II received a modified maze procedure (39.4% versus 8.5%, $P = 0.01$) subsequent to mitral surgery after the introduction of microwave or cryo-ablation equipment into our institution.

Surgery-related mortality for all 92 study patients was 5, with only one from group I ($P = 0.65$). The causes of death included low cardiac output in 4 patients

<table>
<thead>
<tr>
<th>Table I. Preoperative Characteristics of RHD Patients Undergoing Mitral Surgery</th>
<th>Group I MV repair ($n = 33$)</th>
<th>Group II MV replacement ($n = 59$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.7 ± 13.2</td>
<td>58.1 ± 11.2</td>
<td>0.002</td>
</tr>
<tr>
<td>Female gender (%)</td>
<td>63.7</td>
<td>66.1</td>
<td>0.82</td>
</tr>
<tr>
<td>BMI &lt; 20 (kg/m²)</td>
<td>2.1</td>
<td>13.6</td>
<td>0.74</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>12.1</td>
<td>25.4</td>
<td>0.18</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>12.1</td>
<td>6.8</td>
<td>0.45</td>
</tr>
<tr>
<td>Peripheral vascular disease (%)</td>
<td>3.1</td>
<td>5.1</td>
<td>0.99</td>
</tr>
<tr>
<td>Chronic renal insufficiency (%)</td>
<td>9.1</td>
<td>8.5</td>
<td>0.99</td>
</tr>
<tr>
<td>Preoperative stroke (%)</td>
<td>15.6</td>
<td>23.7</td>
<td>0.45</td>
</tr>
<tr>
<td>Chronic lung disease (%)</td>
<td>12.1</td>
<td>28.8</td>
<td>0.08</td>
</tr>
<tr>
<td>Peptic ulcer disease (%)</td>
<td>9.1</td>
<td>11.7</td>
<td>0.99</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>6.0</td>
<td>13.6</td>
<td>0.32</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>57.8 ± 10.1</td>
<td>61.2 ± 12.4</td>
<td>0.19</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>61.4 ± 12.8</td>
<td>58.4 ± 13.0</td>
<td>0.31</td>
</tr>
<tr>
<td>Pulmonary hypertension (%)</td>
<td>21.2</td>
<td>52.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>93.9</td>
<td>96.6</td>
<td>0.62</td>
</tr>
<tr>
<td>PTMC (%)</td>
<td>18.2</td>
<td>42.4</td>
<td>0.02</td>
</tr>
<tr>
<td>NYHA class: III-IV (%)</td>
<td>84.8</td>
<td>94.9</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Values are the mean ± SD. BMI indicates body mass index; LVEF, left ventricular ejection fraction; LA, left atrium; PTMC, percutaneous transvenous mitral commissurotomy; and NYHA, New York Heart Association. ($n = 92$)
and septic shock in one. There were 10 postoperative events in group I and 19 in group II ($P = 1.0$). We observed no statistically significant difference between the groups with respect to the prevalence of early events, although group I patients had a slightly shorter ICU stay and a shorter overall hospital stay compared with the group II patients.

**Midterm outcomes:**

*Overall survival.* Group I and II patients were followed-up for 2.8 ± 2.1 and 3.1 ± 1.8 years ($P = 0.47$) subsequent to surgery, respectively, and overall, follow-up was completed in 81.5% of the patients. The overall 5-year survival rate for group I and II patients was 0.81 ± 0.08 versus 0.81 ± 0.06. ($P = 0.90$, Figure 1), respectively, and there were 4 and 6 late deaths ($P = 0.74$). Three of these 10 deaths were of a cardiac origin, 5 were due to a cerebrovascular accident, and the remaining 2 were due to sepsis from delayed mediastinitis and ischemic bowel syndrome at the 13th and 43rd month postoperatively, respectively. By Cox regression analysis of multiple variables, the predictors of poor survival for all patients following rheumatic mitral valve surgery were age > 65 years, renal insufficiency, LVEF < 40%, and a history of stroke (Table III).

*Postoperative functional class.* At the latest follow-up, 36 were classified as belonging to NYHA functional class I, 45 to class II, and 6 to classes III and IV.
LVEF increased from 57.8 ± 10.1% prior to surgery to 64.1 ± 9.4% after surgery for group I patients \((P = 0.01)\), and from 61.2 ± 12.4% to 61.7 ± 11.6% for group II patients \((P = 0.78)\).

**Repeat surgery for mitral valve disease.** At the latest echocardiography, 3 patients had mitral regurgitation at a level above moderate (> 3), while mild mitral stenosis was noted in 5 patients and more than moderate in 2 patients, all of whom were from the repair group. Mitral valvular area increased significantly from 1.23 ± 2.79 cm² prior to surgery to 3.17 ± 5.16 cm² postoperatively \((P = 0.015)\). Two patients who suffered from severe postoperative mitral regurgitation successfully underwent repeat mitral replacement with a mechanical valve 2.4
and 26.4 months subsequent to initial surgery, respectively. Three patients required tricuspid replacement due to recurrent tricuspid regurgitation. We did not note any cases of late endocarditis. Freedom from repeat mitral surgery 5 years after the initial surgery was 0.91 ± 0.06 for group I and 100% for group II ($P = 0.046$, Figure 2).

**Figure 2.** Freedom from repeat mitral surgery for RHD patients undergoing mitral repair versus replacement ($P = 0.046$).

**Figure 3.** Overall MACE-free survival for RHD patients undergoing mitral repair versus replacement ($P = 0.21$).
Thromboembolic and hemorrhagic complications. At the latest follow-up, only 38.9% of patients undergoing a maze procedure had a normal sinus rhythm. Eight patients (one from group I and 7 from group II) experienced thromboembolic events during their follow-up period, while 6 patients (one from group I and 5 from group II) experienced hemorrhagic complications. Freedom from any thromboembolic event at 5 years was 0.92 ± 0.07 for group I and 0.87 ± 0.06 for group II patients (P = 0.45). Freedom from any hemorrhagic event at 5 years was 0.94 ± 0.05 for group I individuals and 0.79 ± 0.08 for group II patients (P = 0.26). The overall MACE-free survival rate, including all valve-related complications at 5 years was 0.52 ± 0.10 for group I and 0.51 ± 0.10 for group II patients (P = 0.21, Figure 3).

DISCUSSION

RHD is the most common form of cardiac disease that affects people of low socioeconomic status. Treatment of patients with rheumatic mitral disease should optimally be based upon the integration of a number of parameters including subjective as well as objective parameters such as functional capacity, drug compliance, patient age, level of pulmonary hypertension, overall cardiac function, and associated valvular abnormalities. Since the pioneering work of Carpentier in the 1970s, mitral reconstruction has been considered to be an established and valid alternative to mitral replacement. In fact, mitral repair has proved to be superior to mitral replacement in terms of hospital mortality and postoperative quality of life1-3) and it has been assumed for some time now that every effort must be directed toward mitral conservation regardless of the underlying pathology. Although there exists some literature-based evidence suggesting that mitral repair following rheumatic mitral disease is technically more difficult and less stable than is the case for certain degenerative lesions of the mitral valve,5-12) most of these reports tend to describe the results for adolescents and mixed populations with different etiologies, including patients featuring degenerative disease or those whose treatment for mitral valve disease was combined with coronary-artery bypass or aortic valve surgery. Here, we compared mitral repair with valve replacement for a homogenous group of rheumatic patients from a middle-aged population.

In our study, no statistically significant difference was apparent with regards to demographic parameters between the two groups, with the exceptions of the younger age, fewer PTMC procedures, and lower severity of pulmonary hypertension in the repair group. Patients featuring a greater mitral Wilkins score and more valvular calcification underwent mitral replacement (P < 0.001). All of these differences implied that the repair group had better mitral valvular pathol-
ogy favourable to the repair procedure, but also inherent selection bias from our retrospective study design. Our patients from the replacement group were significantly older than those from the repair group, a result which appeared to be consistent with the results reported by Duran, et al that mitral repair is age-dependent and inversely related. Further, the lower Wilkins score for mitral valve abnormality associated with fewer PTMC and a greater number of maze procedures for the repair group than was the case for the replacement group, reflects a more aggressive attitude toward mitral conservation for these younger patients from the repair group. The overall in-hospital mortality rate of our study was 5.4% (3.0% for the repair group and 6.8% for the replacement group, \( P = 0.65 \)). These data are consistent with previously published results and the intergroup difference as regards in-hospital mortality may be partially explained by patients from the repair group being younger than those from the replacement group. In spite of this significant intergroup age difference, the 5-year actuarial survival rate for both groups was 81%, which was somewhat lower than that of the previous reports of Antunes and Duran. The difference between our results and those of the above authors probably reflects the significantly older age of our patients, and that our patients were more likely to have chronic geriatric illnesses than was the case for the subjects in these two previous studies. In addition, most of our patients had a significantly greater number of episodes of atrial fibrillation and previous history of stroke compared to the groups in other studies. Multiple variable Cox analysis in our study suggested that survival subsequent to RHD mitral surgery was dependent upon age, the presence of prior stroke, renal function impairment, and preoperative cardiac performance status. Having said this, however, Cox regression analysis did not identify mitral repair as a predictor of better cardiac survival of rheumatic mitral patients as compared to those individuals from other studies who had degenerative valve pathology, partially suggesting the important impact of an underlying disease entity upon patient survival.

It is well known that acute rheumatic mitral disease is characterized by mitral annular dilatation, chordal elongation, mitral valve prolapse, and predominant mitral regurgitation for individuals of a young age. As time passes and inflammation or scarring occurs during the chronic phase, mitral stenosis becomes more predominant for older RHD patients, as we observed in our study and has been reported in another study which revealed that the number of pure mitral regurgitation cases declined with increasing age. This ongoing activity and complicated valvular pathology may make mitral repair more difficult and have a less favorable outcome postoperatively, as in our results with significantly greater residual or recurrent mitral stenosis occurring in our repair group than was the case for the replacement group. In addition, freedom from the need for repeat mitral surgery at 5 years postsurgery was 0.91 for the repair group, a
result which was quite consistent with the results of several other studies,\textsuperscript{5,7,10} but significantly greater than the corresponding figure for the mitral replacement group. Yet LVEF increased in both groups but was significantly higher after mitral repair. Nevertheless, in combination with an outcome featuring a better LVEF and a trend toward shorter hospitalization plus fewer anticoagulant-induced complications such as thromboembolic or hemorrhagic events as compared to valve replacement patients, the benefits of mitral repair should not be overlooked.

Although the surgical results of the maze procedure for cases of atrial fibrillation concomitant with mitral diseases have been shown to be excellent,\textsuperscript{19,20} the results for maze treatment of atrial fibrillation associated with rheumatic mitral disease have been reported to be somewhat less effective.\textsuperscript{21-23} Such an outcome appears to be quite consistent with the results of our study group, for which the conversion rate to normal sinus rhythm was 38.9\% at the latest follow-up, a figure which was far lower than the results reported by others.\textsuperscript{19-21} The higher atrial fibrillation recurrence rate for such rheumatic patients was assumed to derive from the occurrence of chronic pressure and/or volume overloading to the atrial wall or degeneration or inflammation of the atrial tissue, resulting in enlargement of the left atrium. Most previous studies described some risk factors for late failure of sinus rhythm restoration such as the presence of an enlarged left atrium, fine fibrillation wave size, and longer duration of Af in cases of atrial fibrillation concomitant with mitral surgery.\textsuperscript{20,22,24} On the basis of such results, in 1998, Fukada and associates\textsuperscript{21} even went to the extent of suggesting that the indications for the maze procedure for Af associated with rheumatic mitral disease might need to be reconsidered.

The thromboembolic and hemorrhagic event-free rates at 5 years postoperatively in our study are consistent with those in the literature for replacement or repair series.\textsuperscript{5,7,9,25,26} Although the results were slightly better in our repair versus replacement group, which contrasts with the significant superiority of the repair groups in other studies. However, in our series almost 95\% of the patient population had atrial fibrillation and they were more likely to have suffered a stroke preoperatively. In addition to the lower sinus restoration after the maze procedure in both groups, the majority were anticoagulated with warfarin postoperatively. We believe that the rate of thromboembolic or hemorrhagic events after mitral surgery depends more on the patient population differences such as age, presence of atrial fibrillation and past history of stroke, compliance with anticoagulants, and the meticulous recording of any neurological deficits.

There are several important limitations of our study. First, it was a retrospective design, the sample size was relatively small, and the follow-up period was rather short in comparison with the risk evaluation. The small number of partici-
pants and the short follow-up period made accurate assessment of the relative need for late repeat surgery for patients difficult because fewer patients were followed-up beyond 6 years following surgery, and it may be that prosthetic tissue valve degeneration appears subsequent to such a period of time. Second, our study had an 81.5% follow-up rate, which may limit the statistical significance of the results. We found that those who were lost to follow-up were mainly aborigines of Taiwan Island and/or those of a lower socioeconomic status. They had to pay an extra fee not covered by public health insurance if they came to this tertiary referral center. They were lost to follow-up sooner after discharge. Third, the maze procedure for treating Af was performed predominantly in the mitral repair group, an outcome which reflected a more aggressive attitude toward valve conservation, but made analysis difficult. Finally, patients from both groups were not matched equally in terms of most of the relevant demographic parameters, a situation which may warrant propensity adjustment in a larger-scale patient population.

In our experience, a variety of surgical repair techniques can be successfully used in patients afflicted with rheumatic mitral valve disease. The midterm results for the mitral repair group appeared to be satisfactory and are superior to the corresponding results for mitral replacement, particularly with regards to cardiac performance and thrombo-hemorrhagic events. We recommend that mitral repair be performed whenever possible for these RHD patients.

**REFERENCES**