Ross procedure in rheumatic aortic valve disease

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Abstract

Objective: To assess the results of aortic valve replacement with the pulmonary autograft in patients with rheumatic heart disease. Methods: From October 1993 through September 2003, 81 rheumatic patients with aortic valve disease, mean age 29.5 ± 11.9 years (11–56 years) underwent, the Ross procedure with root replacement technique. Forty patients were 30 years of age or below (young rheumatics). Associated procedures included mitral valve repair (n = 19), open mitral commissurotomy (n = 15), tricuspid valve repair (n = 2), and homograft mitral valve replacement (n = 2). Results: Early mortality was 7.4% (six patients). Mean follow-up was 92.3 ± 40.9 months (7–132 months, median 109 months). Sixty of the 73 patients whose follow-up was available (82%) had no significant aortic regurgitation. Re-operation was required in seven (8.4%) patients for autograft dysfunction with failed mitral valve repair (n = 3), autograft dysfunction alone (n = 2) and failed mitral valve repair alone (n = 2). No re-operations were required for the pulmonary homograft. There were six (7.5%) late deaths. Actuarial survival and re-operation-free survival at 109 months were 84.5\% and 52.9\%, respectively. Freedom from significant aortic stenosis or regurgitation was 78.4 ± 5.2\% and event-free survival was 64.6 ± 5.8\%. When compared to rheumatics above 30 years of age, the relative risk of autograft dysfunction was high in the young rheumatics. Conclusion: The Ross procedure is not suitable for young patients with rheumatic heart disease. However, it provides acceptable mid-term results in carefully selected older (>30 years) patients with isolated rheumatic aortic valve disease.

Keywords: Ross operation; Rheumatic heart disease; Aortic valve replacement; Autograft

1. Introduction

Aortic valve replacement (AVR) with a prosthetic valve is the most commonly performed operation for patients with rheumatic aortic valve disease. The pulmonary autograft, which was first used by Ross in 1967 [1] for AVR, has the advantages of good hemodynamics, ability to remodel, growth potential, and good long-term results in carefully selected patients [2–8]. We reported our early experience in young patients with rheumatic heart disease (RHD) in 1999 [9]. In this study, we present detailed results obtained in 81 consecutive rheumatic patients.

2. Patients and methods

Between October 1993 and September 2003, 81 patients with rheumatic heart disease underwent AVR with the
Clinical diagnosis

NYHA

I (%) 3 (7) 4 (10)
II (%) 6 (15) 12 (29)
III (%) 26 (65) 21 (51)
IV (%) 5 (13) 10 (24)

Symptoms

Dyspnoea (%) 30 (75) 29 (71)
Palpitations (%) 18 (45) 12 (29)
Chest pain (%) 9 (23) 6 (15)
CHF (%) 13 (33) 10 (24)

Associated procedures

MV repair 15 4
OMC 12 3
Tricuspid valve repair 2 —
HMVR 2 —

Early death 5 1
Bleeding 1 1
Arrhythmias 2 —
Low output 2 —

Follow-up (mean) (months) 7–132 (100 ± 3.5) 8–132 (84.1 ± 42.4)

Table 2
Operative data, post-operative results, and follow-up of patients undergoing the Ross procedure

Characteristics | <30 years | >30 years |
--- | --- | ---
Associated procedures | MV repair | 15 | 4 |
 | OMC | 12 | 3 |
 | Tricuspid valve repair | 2 | — |
 | HMVR | 2 | — |
 | Early death | 5 | 1 |
 | Bleeding | 1 | 1 |
 | Arrhythmias | 2 | — |
 | Low output | 2 | — |
 | Follow-up (mean) (months) | 7–132 (100 ± 3.5) | 8–132 (84.1 ± 42.4) |
 | Aortic regurgitation | 15 | — |
 | Mitral regurgitation | 4 | 1 |
 | Infective endocarditis | 1 | — |

MV: mitral valve, OMC: open mitral Commissurotomy, HMVR: homograft mitral valve replacement.

Aortic regurgitation (AR) was assessed on a scale of +1 to +4 according to published criteria [11]. AR of grade +1 was considered mild. Peak gradients less than 25 mmHg across the aortic valve were considered as mild aortic stenosis (AS) and those ≥50 mmHg were considered as significant AS.

No anticoagulants or anti-platelet drugs were prescribed. Long-acting benzathine penicillin 3 weekly was prescribed to all patients below 45 years of age. All patients received itraconazole for 6 weeks following surgery as prophylaxis against fungal endocarditis.

2.1. Statistical analysis

This was performed with SPSS for windows 10.0 software package (SPSS Inc., Chicago, IL, USA). Mean, median, and standard deviation have been calculated for continuous variables. Freedom from valve-related events and actuarial estimates were calculated using the Kaplan—Meier analysis. The estimates were compared with the Mantel—Cox (log-rank) test. A valve-related event was defined as any episode of thromboembolism, hemorrhage, congestive heart failure, infective endocarditis, structural deterioration, or significant gradients as per published criteria [12]. Linearized rates for these events are reported. Cox's proportional hazard model was used to analyze factors associated with a higher early and late mortality and the development of autograft dysfunction.

3. Results

3.1. Hospital mortality

All patients survived the operation. There were six (7.4%) early deaths due to bleeding (n = 2), malignant ventricular arrhythmias (n = 2), and persistent low cardiac output (n = 2).

3.2. Early re-operation

Two patients underwent re-operation for excessive mediastinal bleeding. In one patient, the bleeding was from the raw surface of the posterior wall of the right ventricular outflow tract. In the other patient, the source of bleeding was unrelated to the suture lines.

3.3. Early autograft function

Intra-operative TEE revealed satisfactory autograft function with trivial or no aortic regurgitation in all the patients. Three patients below 30 years of age had mild mitral regurgitation (MR).

3.4. Follow-up

All survivors were seen in the outpatient clinic at 6-monthly intervals and they underwent clinical examination and echocardiography. Between July 2004 and December...
2004, the records of 73 of the 75 survivors (97.3%) were obtained, and their last follow-up during this period was taken for statistical analysis. Overall mean follow-up was 92.3 ± 40.9 months for both groups (7—132 months, median 109 months) and total 561.5 years. In patients below 30 years, the follow-up was 7—132 months (mean 100 ± 3.5 months), whereas in patients above 30 years, it was 8—132 months (mean 84.1 ± 42.4 months). However, the results are reported at an overall median follow-up of 109 months. Among survivors, 15 (20%) were followed up for 10 or more years, 62 (82.7%) for 7 or more years, 67 (89.3%) for more than 5 years, 70 (9.3%) for more than 3 years, and 73 (100%) for more than 6 months.

There were no thromboembolic complications in the survivors. Three patients had significant hemolysis (0.5 events per 100 patient-years). In the first two patients, it was associated with excessive mediastinal bleeding, disseminated intravascular coagulation and early death. In the third patient, it was associated with mild mitral regurgitation which subsided gradually.

One 18-year-old patient developed bacterial endocarditis 9 months following initial operation and died.

3.5. Recurrent rheumatic fever

Two young rheumatics, aged 11 and 13 years (patient no. 3 of Table 3), who had undergone the Ross procedure and mitral valve repair, developed acute rheumatic activity and CHF requiring hospitalization after 8 and 12 months, respectively. In these patients, there was no polyarthritis, but the erythrocyte sedimentation rate (ESR) and antistreptolysin titer (ASLO) had risen significantly. Both these patients developed severe AR and moderate-to-severe MR. The first patient had not complied with post-operative penicillin prophylaxis, whereas the second patient was regularly taking it. Both patients were adequately decongested and advised re-operation; the first patient, however, died 6 months later and the second one underwent re-operation.

Patient nos. 1 and 4 of Table 3 had recurrent history of fever and joint pains starting 12 and 24 months, respectively, following initial operation, but there was no laboratory evidence supporting rheumatic activity. Both these patients had stopped regular penicillin prophylaxis. At re-operation, however, the autograft showed features of rheumatic valvulitis. Besides this, two other patients aged 14 and 17 years (Patient no. 2 of Table 3) and on regular penicillin prophylaxis had a similar history without laboratory evidence of rheumatic activity.

There was no clinical or laboratory evidence of recurrent rheumatic activity in the remaining patients.

3.6. Late autograft function

Out of the 73 survivors, whose follow-up was available, 60 (82%) had no significant AR. Fifteen patients had significant aortic regurgitation (2.67 events per 100 patient-years) which was moderate in 11 patients and severe in another four patients. These patients developed significant AR 57.6 ± 36.2 months after the operation; six of these patients had evidence of recurrent attacks of rheumatic fever and developed significant AR within 2 years of operation. The occurrence of rheumatic process in these patients is detailed above. In other nine patients, there was no clinical or laboratory evidence of recurrent rheumatic activity.

On multivariate analysis, the probability of development of AR was higher in young (<30 years) rheumatics (hazard ratio 62.5, 95% CI = 0.94—100, p = 0.053). All four patients with severe AR underwent re-operation; two of these required double valve replacement for failure of associated mitral valve repair. In all these patients, prosthetic valves were implanted. Out of the 11 patients with moderate AR, one underwent double valve replacement with a prosthetic valve 48 months after the initial operation for failed mitral repair in addition to the AR; two patients died of CHF 24 and 5 months, respectively, after the initial operation; one of bacterial pneumonia 2 months after operation and the remaining seven patients with moderate AR continue to be in NYHA class I and are being closely followed-up. At the median follow-up of 109 months, freedom from autograft dysfunction was 78.4 ± 5.2% (95% CI, 68—88.8) for the entire group; in young rheumatics, it was 65 ± 7.8% (95% CI, 49.4—80.6) as compared to 98.5 ± 1% (95% CI, 96.5—100) in older rheumatics group (log-rank = 13.83, p = 0.0002) (Fig. 1).

3.7. Fate of right ventricular outflow tract

Two patients had pulmonary homograft dysfunction (0.3 events per 100 patient-years). One patient has a gradient of 48 mmHg or more across the right ventricular outflow tract at 7 years of follow-up. The other patient has moderate pulmonary regurgitation. However, these patients are asymptomatic and are being followed up.

Table 3

Re-operations following the Ross procedure

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age/sex</th>
<th>Interval</th>
<th>Cause of re-operation</th>
<th>Operation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24/M</td>
<td>108</td>
<td>RHD, AR, dilated autograft</td>
<td>AVR</td>
<td>Survived</td>
</tr>
<tr>
<td>2</td>
<td>17/M</td>
<td>48</td>
<td>AR, MR</td>
<td>DVR</td>
<td>Survived</td>
</tr>
<tr>
<td>3</td>
<td>13/M</td>
<td>12</td>
<td>AR, MR, TR</td>
<td>DVR + TV repair</td>
<td>Survived</td>
</tr>
<tr>
<td>4</td>
<td>20/M</td>
<td>48</td>
<td>AR, MR, dilated autograft</td>
<td>DVR</td>
<td>Survived</td>
</tr>
<tr>
<td>5</td>
<td>21/M</td>
<td>56</td>
<td>AR</td>
<td>AVR</td>
<td>Survived</td>
</tr>
<tr>
<td>6</td>
<td>15/F</td>
<td>26</td>
<td>MR</td>
<td>HMVR</td>
<td>Died*</td>
</tr>
<tr>
<td>7</td>
<td>36/F</td>
<td>31</td>
<td>MR</td>
<td>MVR</td>
<td>Survived</td>
</tr>
</tbody>
</table>


* Patient no. 6 died due to congestive heart failure 3 months following re-operation.
3.8. Late re-operation (Table 3)

Late re-operation was required in seven patients (1.2 events per 100 patient-years) after a mean period of 47.5 ± 38.9 months (range 12—108 months, median 48 months). Two patients underwent re-operation for failed mitral valve repair with normal pulmonary autograft function. The first of these two patients underwent mitral valve replacement with a mitral homograft 26 months after the initial operation. However, she died 3 months later due to persistent congestive cardiac failure. The other patient underwent prosthetic mitral valve replacement 31 months after initial operation. Three patients required prosthetic double valve replacement for autograft failure with failure of associated mitral valve repair 12 and 48 months (two patients) following initial operation. Two patients with severe aortic regurgitation underwent aortic valve replacement with a mechanical prosthesis 56 and 108 months after initial operation. At re-operation, mechanical valves were implanted because of patients’ choice.

At re-operation, patient nos. 1 and 4 of Table 3 were found to have significant autograft dilatation due to recurrent attacks of rheumatic activity. In the other patient, the geometry of the aortic sinuses was maintained, but the autograft cusps showed thickening, retraction, and failure of co-apertureation without any prolapse or commissural fusion. On histological examination, there was valve thickening, fibrosis, and active chronic inflammation with small vessel and intimal proliferation as detailed in our prior publication [9].

At the median follow-up of 109 months, freedom from re-operation was 90.5 ± 3.7% (95% CI, 83.1—98.21) for the entire group; in young rheumatics, it was 83 ± 6.3% (95% CI, 70.4—95.6) as compared to 96.9 ± 3.1% (95% CI, 90.7—100) in older rheumatics (log-rank = 13.83, p = 0.0002) (Fig. 1).

3.9. Late deaths and survival

There were six late deaths (1 event per 100 patient-years). These were due to mitral homograft failure (n = 2), persistent CHF due to autograft failure (n = 2), bacterial pneumonia (n = 1), and bacterial endocarditis (n = 1). One patient who underwent mitral valve replacement with a homograft died 6 months later due to the mitral homograft failure. Another patient had a mitral homograft replacement following failed mitral valve repair and died 2 months later due to mitral homograft failure. Two patients with autograft failure died of persistent congestive heart failure 24 and 5 months, respectively, after the operation. The patients with bacterial pneumonia and infective endocarditis died 2 and 9 months, respectively, after initial surgery.

At 109 months, the actuarial survival was 84.5 ± 4.1% (95% CI, 76.3—92.7) for the entire group; in young rheumatics, it was 84.9 ± 5.7% (95% CI, 73.5—96.3) compared to 84.5 ± 5.8% (95% CI, 72.9—96.1) in older rheumatics (log-rank = 0.05, p = 0.82) (Fig. 3).
Event-free survival at 109 months was $64.6 \pm 5.8\%$ (95% CI, 53.1–76.2) for the entire group; in young rheumatics it was $51.6 \pm 8\%$ (95% CI, 43.6–59.6) compared to $81.9 \pm 6.2\%$ (95% CI, 69.5–94.3) in older rheumatics (log-rank = 5.21, $p = 0.022$) (Fig. 4).

There were no specific predictors of early or late death on multivariate analysis.

4. Discussion

The pulmonary valve has been shown to be a near ideal substitute for the disease aortic valve [2–8]. Realizing this, we were very enthusiastic in its use for AVR in patients of all aortic valve pathologies. In our early experience, most of the patients had RHD and were 30 years of age or below. Thirty-four of these patients had associated mitral valve disease amenable to repair. In these patients, we thought that the pulmonary autograft would be a good option once the mitral repair was satisfactory as it would offer to these young patients good hemodynamics, freedom from anticoagulation and thromboembolism, growth potential and ability to remodel, and relative resistance to infection as compared to prosthetic heart valves [3–7]. However, we were disappointed with the results. More than one-third of the young rheumatics (15 out of 36 followed up) developed significant autograft dysfunction within 5 years of surgery, six of them developed significant AR within 2 years and a majority of them required re-operation for autograft dysfunction or failed mitral valve repair.

The reason for involvement of the pulmonary autograft in rheumatic disease process has been widely debated [9,13–16]. Why it occurs in patients with recurrent rheumatic activity is unknown. Cessation of penicillin prophylaxis may not be the only reason for this as it has been shown that higher infection rates in overcrowded areas may render penicillin prophylaxis ineffective [17,18]. The lack of a definite history of carditis or recurrent joint pains does not entirely rule out disease recrudescence as a positive history is not always forthcoming [17]. In fact, only 6 of the 15 patients with significant AR in our study had some clinical or laboratory evidence of rheumatic fever, and only three of these patients had stopped penicillin prophylaxis but all patients undergoing re-operation demonstrated features of rheumatic valvulitis in the autograft.

Even despite recurrent rheumatic fever, involvement of the pulmonary valve in the rheumatic disease process is rare [19], and we have observed only two patients with quadrivalvular rheumatic heart disease in the last 20 years in whom there was clear evidence of pulmonary valve involvement [20]. The pulmonary autograft cusps looked perfectly normal at the first operation although at the microscopic level, their involvement in the rheumatic process cannot be ruled out entirely. But surprisingly, at re-operation, the intra-operative TEE findings were indistinguishable from those due to rheumatic aortic valve disease and at operation the cusps were thickened and retracted, and their histological examination showed changes typical of rheumatic valvulitis. We do not know why a valve which is relatively free from chronic rheumatic valvulitis should develop these changes when it is transplanted into the aortic position. The pulmonary autograft is now an aortic valve, and mechanical forces in the aortic position may make it susceptible to rheumatic involvement as this [9], but this is debatable.

We did not observe these findings in older rheumatics and those without associated mitral valve disease. The reasons are not clear, but this is probably related to the natural history of the disease in which the attacks of rheumatic fever become infrequent with advancing age. The results in older rheumatics have been far more satisfactory, and this has encouraged us to continue to perform this procedure in rheumatics older than 30 years of age without mitral valve disease.

5. Conclusion

The pulmonary autograft is not an ideal valve substitute in young rheumatics and carries a high failure rate. However, it provides satisfactory results in carefully selected older patients with isolated rheumatic aortic valve disease.

References

Appendix A. Conference discussion

Dr R. Lorusso (Brescia, Italy): Could you have the chance to evaluate histologically the explanted valve, I mean, the pulmonary valve you explanted, especially in the very young patients? And do you think that your results could be due to a very active rheumatic disease which involved also the pulmonary valve?

Dr Kumar: Yes, we did histological examination and we found characteristic features of rheumatic valvulitis in the autograft in the explanted valves. I have not shown the histopathological slides because of time, but that is our observation.

Dr Z. Al-Halees (Riyadh, Saudi Arabia): We also have a large population of rheumatic patients that underwent the Ross procedure and so far we have accumulated more than 400 patients who underwent the Ross procedure, more than 60% of them have rheumatic etiology. We basically came to almost the same conclusions. We looked at the failures in the rheumatics in particular, and the two strong predictors of failure were the presence of pure aortic valve regurgitation and dilated aortic roots.

In our analysis, we actually found that patients who have roots that are more than 27–28 mm are at much higher risk than those with smaller roots. And this was the case irrespective of the age of the patient. Since that time we have limited our Ross procedure in the rheumatics with aortic valve regurgitation to smaller roots. That seemed to have improved the results.

Another strong predictor of failure was the presence of concomitant severe rheumatic mitral valve regurgitation. So if you exclude those patients from the Ross, the ones with dilated aortic roots and those with concomitant rheumatic mitral valve regurgitation, I believe the outcome is going to be a little bit better than what you reported.

Dr Kumar: As a rule, we do not do Ross procedures for patients who have an aortic annulus diameter of more than 30 mm, or if they have a discrepancy in the aortic and pulmonary diameters of more than 5 mm. So we have not done this operation in patients with large aortic roots. And in India, we find that these patients who come with rheumatic aortic valve disease have relatively smaller roots.

And I agree with you, the second point which you raised about mitral valve disease, it’s unfortunate our enthusiasm to give these patients a much better life without anticoagulants actually backfired. And we do not any longer do Ross procedures for patients with associated mitral valve disease.

Dr Al-Halees: My question is, in our experience, we found that patients with predominant aortic stenosis, even if they’re rheumatic, they still behave well. Is that your experience as well?

Dr Kumar: Yes.

Dr Y. Yalcinbas (Istanbul, Turkey): Can you comment on the high incidence of endocarditis in your series. Was it related to the homograft or the autograft?

Dr Kumar: This problem of endocarditis was in the beginning of our experience and that was probably due to the homograft valve. And subsequently, we changed the air conditioning in our operating theaters and we got rid of this problem even in the homograft aortic valve replacement patients as well as in the Ross procedure.

Dr T. Chotivatanapong (Nonthaburi, Thailand): May I ask you about the post-operative blood pressure control in relation to the degree of aortic regurgitation post-operatively, since there is same relationship between these.

Dr Kumar: None of these patients had hypertension. They were all normotensive and we did not have any problem with hypertension in this group of patients.

Dr E. Akl (Cairo, Egypt): What’s your valve of choice for young patients below the age of 20 with repairable mitral valve or just isolated aortic regurgitation?

Dr Kumar: We have recently published our results with the aortic valve repair and mitral valve repair as well. Yesterday I presented our results with the mitral valve repair.

Our first choice of operation for these patients is an attempt at repair. We will repair the mitral valve and even attempt repair of the aortic valve. If it is not possible, and if only mitral valve can be repaired, we still use a mechanical valve for the aortic valve if it requires replacement.