Twenty-Year Analysis of Autologous Support of the Pulmonary Autograft in the Ross Procedure

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Background. The Ross procedure is seldom offered to adults less than 60 years of age who require aortic valve replacement except in a few high-volume centers with documented expertise. Inserting the pulmonary autograft as an unsupported root replacement may lead to increasing reoperations on the aortic valve in the second decade.

Methods. Of 333 patients undergoing the Ross procedure between October 1992 and June 2012, the study group of 310 consecutive patients (mean age ± standard deviation, 39.3 ± 12.7 years (limits 16–63) had the aortic root size adjusted to match the pulmonary autograft, which was inserted as a root replacement, with the aorta closed up around it to provide autologous support.

Results. The mean follow-up time was 9.4 years; the actuarial survival was 97% at 16 years; and freedom from the composite of all reoperations on the aortic valve and late echocardiographic-detected aortic regurgitation greater than mild was 95% at 5 years, 94% at 10 years, and 93% at 15 years. Overall freedom from all reoperations on aortic and pulmonary valves was 97% at 5 years, 94% at 10 years, and 93% at 15 years. All results were better for the patients presenting with predominant aortic stenosis (98% freedom at 15 years) than for those with aortic regurgitation (p = 0.01).

Conclusions. Autologous support of the pulmonary autograft leads to excellent results in the groups presenting with aortic stenosis and mixed aortic stenosis/regurgitation and to good results for those presenting with pure aortic regurgitation. The Ross procedure, using one of the proven, durable techniques available, should be considered for more widespread adoption.


The Ross operation for treatment of aortic valve disease in younger patients has a lot of advantages when compared with other aortic valve replacement (AVR) options, particularly with regard to improved survival [1–3], hemodynamic performance similar to that in patients with a normal aortic valve [4, 5], and the lack of necessity to take oral anticoagulant drugs.

However, the Ross procedure (RP) is not often performed unless the patient is operated on in one of the few high-volume centers that have documented expertise with this operation. The main reason is a variability in the durability of the pulmonary autograft (PA) in the aortic position, and this in turn is also influenced by the technique of PA insertion. The known techniques that have led to good long-term outcomes include the subcoronary technique [6, 7] and root replacement methods [2, 3, 8]. With the root replacement method, however, it is very important that the PA root is trimmed distally to just above the commissures to achieve good aortic valve function in the long term. When this has not been done, late PA root dilatation early in the second decade of follow-up has been increasingly reported, leading to aortic regurgitation (AR) and reoperation [9–12].

Treatment of this series of patients used a variant of the inclusion cylinder (IC) technique whereby the aortic root size was adjusted to match the PA, which was inserted as a root replacement with the aorta closed up around it to provide autologous support [13, 14]. It is different from other previously described IC methods [15, 16].

Patients and Methods

Between October 1992 and June 2012, 333 consecutive patients underwent the RP as a surgical treatment for aortic valve disease. Of these, in 310 patients, a variant IC method was used to insert the PA, and these patients constituted the study patients. Of the 23 patients in whom this IC method was not used, a root replacement (unsupported) was used in 8 patients and a subcoronary technique in 2. In 13 patients, the PA was inserted inside a Valsalva Dacron graft. The ethics committee at the Royal Melbourne Hospital approved the study of these
patients, and each individual patient gave informed consent for participation in this study.

The demographics of the patients operated on can be seen in Table 1. Patients classified as having pure aortic stenosis (AS) had either severe aortic valve stenosis or symptomatic moderate to severe AS, with less than moderate regurgitation. Those with mixed AS/AR had at least moderate stenosis and regurgitation combined, and those presenting with pure AR had no additional significant AS. The technique used has been previously described [13]. All operations were performed by use of median sternotomy, cardiopulmonary bypass, and cardiac arrest with tepid blood cardioplegia delivered both antegrade and retrograde. The sequence of events after aortic cross-clamping was as previously described [13]. With respect to the aortic root procedure, the sequence of steps was as follows:

1. Transverse aortotomy with transection of the aorta 5 mm above the sinotubular junction (STJ).
2. Aortic valve excision and debridement of aortic annulus.
4. Vertical extension of aortotomy down into the non-coronary sinus, all the way to aortic annulus.
5. Reduction of aortic annulus by using partial circumference external Dacron ring and reduction of aortic sinus and STJ if required. By using wedge or quadrangular excision to achieve aortic annulus diameter of 24 to 26 mm in male patients and 22 to 24 mm in female patients, similar STJ diameter.
6. If the aortic annulus or STJ diameter exceeded 32 to 34 mm, indicating excessive mismatch between the aortic and pulmonary roots, the variant IC method described was inappropriate, and the PA was inserted either by root replacement or inside a Valsalva Dacron graft, or the RP was abandoned in favor of either a mechanical or another bioprosthetic valve.
7. Insertion of the PA root with interrupted (predominantly) or continuous 4-0 Prolene suture.
8. Coronary anastomosis to the PA as previously described [13].
9. Closure of vertical extension of aortotomy using 5-0 Prolene suture, thus enclosing the PA root inside the aortic root.
10. Anastomosis of the PA root distally to the ascending aorta, including part or all of the aortic root remnant in this suture line.

The aortic cross-clamp and cardiopulmonary bypass times, and adjunctive aortic root manipulation and concomitant other cardiac procedures, are listed in Table 2. Enlargement of the aortic annulus, if required, used the Manougian technique (2 patients). When the aortic sinuses or STJ required enlargement, this was performed by using autologous pericardial patch enlargement (21 patients). The diagram of the completed standard operation can be seen in Figure 1.

All patients have been followed up with clinical review by the surgeon and/or cardiologist yearly, and follow-up echocardiograms have been obtained before hospital discharge, 6 to 12 months after the operation, and every second year thereafter.

Table 1. Patient Demographics (n = 310)

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Mean ± SD</th>
<th>Limits</th>
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<tbody>
<tr>
<td>39.3 ± 12.7</td>
<td>16–63</td>
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<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
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<tr>
<td>216 (69.7%)</td>
<td>94 (30.3%)</td>
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| Aortic valve lesion | 141 (45.5%) | 68 (21.9%) | 101 (32.6%) |
| Bicuspid aortic valve | 285 (92.0%) |

| NYHA class | I | 58 (18.7%) | II | 193 (62.3%) | III | 57 (18.4%) | IV | 2 (0.6%) |

| Previous operation | 30 (9.7%) |
| Aortic valve repair | 13 (4.2%) | AVR | 9 (2.9%) |

| ASD/PFO = atrial septal defect/patent foramen ovale; CABG = coronary artery bypass graft; SD = standard deviation. | AR = aortic regurgitation; AS = aortic stenosis; AVR = aortic valve replacement; NYHA = New York Heart Association; SD = standard deviation. |

Table 2. Operative Data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD</th>
<th>Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic cross-clamp time (min)</td>
<td>172.9 ± 20.4</td>
<td>122–247</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>199 ± 22.4</td>
<td>139–290</td>
</tr>
</tbody>
</table>

| Adjunctive aortic root procedure | 168 (54.2) | 109 (35.2) | 23 (7.4) |

| Concomitant procedures | Ascending aorta replacement | 43 (13.9) | Tailoring aortoplasty | 65 (21.0) | Subaortic resection/myomectomy | 4 (1.3) | CAGB | 3 (1.0) | ASD/PFO | 4 (1.3) | Miscellaneous | 4 (1.3) |

AR = aortic regurgitation; AS = aortic stenosis; AVR = aortic valve replacement; NYHA = New York Heart Association; SD = standard deviation.
Echocardiographic parameters assessed include aortic and pulmonary valve function, left ventricular size and function, and aortic root size.

**Statistical Analysis**
Cumulative survival and freedom from events were analyzed by the Kaplan-Meier method. The log-rank test was used to compare survival between different groups. All statistical tests were two-sided, and tests with \( p \) values of 0.05 or lower were considered significant. All statistical analyses were done with the Statistical Package for Social Sciences software, version 20.0 (SPSS, Chicago, IL). GraphPad Prism 5.00 for Windows (GraphPad Software, La Jolla, CA) was used to obtain life tables and corresponding Kaplan-Meier survival curves.

**Results**

**Early and Late Mortality**
There were no in-hospital deaths, but there was one death within 30 days, from myocardial infarction, an early mortality of 0.3%. Late follow-up is 97%, complete with 9 patients lost to clinical follow-up. There have been 5 late deaths, all from noncardiovascular causes at 3, 4, 5, 10, and 12 years postoperatively (ie, no late cardiac deaths). As can be seen from Figure 2, late actuarial survival is 97% at 16 years. The mean follow-up time is 9.4 years and encompasses 2/915 patient-years.

**In-Hospital Complications**
For a group of adult patients less than 60 years of age, in-hospital complications were as expected. Please refer to Table 3 for a full list of these.

**LATE AORTIC VALVE FUNCTION. Reoperation for progressive AR.** Ten patients required reoperation and AVR. Nine of these were in the group presenting with pure AR before

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**Table 3. In-Hospital Complications**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVA</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>5 (1.6)</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Low CO needing inotropes</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Ventricular arrhythmias</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Atrial arrhythmias</td>
<td>31 (10.0)</td>
</tr>
<tr>
<td>Pericardial effusion/tamponade</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>Re-exploration for low cardiac output</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>HB/PPM</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Antibiotic/positive homograft culture</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Repair/graft septal perforated artery</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Reintubation</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>AMI</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Coronary artery kink</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Other</td>
<td>15 (4.8)</td>
</tr>
</tbody>
</table>

AMI = acute myocardial infarction; CO = cardiac output; CVA = cerebrovascular accident; HB/PPM = heart block/permanent pacemaker.
operation. Thus, freedom from redo AVR can be seen in Figure 3, 96%, at 15 years.

1. Late Doppler echocardiography detected AR. Only 2 patients, other than those who have already undergone redo AVR for progressive AR, have greater than mild AR detected during serial follow-up Doppler echocardiography.

2. Endocarditis affecting aortic valve. Two patients required operation for late endocarditis affecting the aortic valve. In 1 patient, this was a consequence of primary pulmonary valve endocarditis, where paravalvular infection also involved the neoaortic valve. In this patient, both aortic and pulmonary valves were replaced with Medtronic freestyle valves. In the other patient, infection involved a partial circumferential external Dacron ring around the aortic annulus. A surgical procedure was required, although the ring, which was surrounded by purulent material, was excised, and the normally functioning neoaortic PA valve was able to be left in situ. These operations were performed 2 and 9 years postoperatively, respectively. Both patients survived reoperation.

3. Composite of freedom from all reoperations on the aortic valve and greater than mild postoperative AR can be seen in Figure 4, 93% at 15 years. There is a significant ($p = 0.01$) difference in this outcome measure between those patients presenting with AS and AS/AR, compared with those presenting with AR (at 15 years, 98% for AS, 98% for AS/AR, and 82% for AR presentation), as can be seen in Figure 5.

LATE PULMONARY VALVE FUNCTION. Late assessment and management of pulmonary valve function has been as follows.

1. Doppler echocardiography: The mean ± standard deviation pulmonary valve gradient measured by Doppler echocardiography was $10 ± 5.3$ mm Hg (limits 2-44). The indication for redo pulmonary valve replacement (PVR) in these patients was mean pulmonary valve gradient exceeding $40$ mm Hg or the development of right ventricular (RV) hypertrophy, or enlargement, or symptoms associated with a lower gradient than that described. Only 1 patient met these criteria and underwent successful redo PVR 11 after operation. With regard to late pulmonary regurgitation (PR), only 12 patients (4%) had more than mild PR detected during follow-up (all moderate in degree), and none have required reoperation for this problem. The indication for redo PVR is the development of severe PR in association with significant enlargement, reduced RV systolic function, or both, or the development of symptoms.

2. Endocarditis of the pulmonary valve: Endocarditis affecting the pulmonary valve developed in 3 patients, 1 already mentioned who required redo AVR and redo PVR. The other 2 patients experienced endocarditis isolated to the pulmonary valve 3 and 7 years after operation, and both required redo PVR. Both survived reoperation.

3. Freedom from reoperation on both the aortic and the pulmonary valves during follow-up: Including all causes (ie, structural degeneration and endocarditis), a total of 15 patients have required reoperation on either valve (or in the case of 1 patient, both), as can be seen in Figure 6. Once again, the outcome is significantly better for AS and AS/AR presentations, as shown in Figure 7. The respective freedoms at 15 years are 98% for AS, 98% for AS/AR, and 82% for AR presentation ($p = 0.01$).

Comment

The variant IC method described has been used in 310 of 333 consecutive patients undergoing the RP during the past 20 years, most of whom presented with congenital bicuspid aortic valve disease. Early in the authors’ experience, during the initial 10 RPs performed, 4 patients underwent an unsupported root replacement (RR) method to insert the PA, and in 6 patients, an IC method
was used. In the patients undergoing RR, it was noted that after release of the aortic cross-clamp, the neoaortic root dilated significantly. Although no AR was associated with this enlargement, because of concern about further potential aortic root enlargement later, the RR method was abandoned. It was only used in another 4 patients subsequently in special circumstances dictated by unusual technical factors.

After that observation, the authors decided to use an IC method nearly exclusively. This method differs from previously described IC methods in two significant ways. First, as described by the senior author in 1995 [14], the coronary arteries are excised as buttons, brought inside the aortic root, and anastomosed to the PA root as shown in Figure 1. Second, the aortic root is adjusted in size, incorporating an external Dacron ring annuloplasty, mostly partial circumference only, and reduction in the aortic sinus diameter and STJ by the use of longitudinal excision of noncoronary sinus tissue, as described in the Methods section. In 1999, the senior author showed that these maneuvers were successful in maintaining normal aortic root size, in comparison with the 4 earlier patients in whom a RR method was used for PA implantation, in whom the aortic root significantly dilated [13].

It is highly likely that supporting the PA root with the patient’s own aorta in this manner, which has been adjusted to the correct size, is responsible for the very durable results reported in this study. By closing the patient’s aorta up around the PA, this autologous support does away with the need for prosthetic material to support the aortic sinuses and STJ. The only situation in which prosthetic support has been used more recently is when aortic dilatation is marked, and with such excessive mismatch of aorta to pulmonary artery size; if an RP is to be performed, the PA has been inserted inside a Valsalva Dacron graft. These patients are not included in the study group, as mentioned in the Methods section.

The method used has given outstanding results both in patients with AS and those with mixed AS/AR. In both these groups, the composite freedom from reoperation on the aortic valve and late AR greater than mild is 97% and 98%, respectively at 15 years after operation. Excluding 2 patients who have required aortic valve reoperation because of late endocarditis, this composite freedom would be 99%. Thus, there is no late tendency for increasing postoperative AR. For this procedure to be compared with mechanical AVR, one needs to take into account patients who have also had to undergo reoperation on the pulmonary valve. There have been four of these procedures, three of which were for endocarditis. Allowing for this, the 15-year freedom from reoperation on both aortic and pulmonary valves is 98% for both the AS group and the AS/AR group. This compares very favorably with the incidence of late redo AVR, after mechanical AVR, which varies from 91% to 97% [17–20].

The results obtained with this IC method have not been as good when applied to patients with pure AR,
with 79% composite freedom from reoperation on the aortic valve and postoperative AR greater than mild. In this group, progressive AR led to redo AVR in 9 patients, all within 6 years of operation, with no failures beyond that time frame. During the initial few years of the senior author’s experience (1992 to 1998 inclusive), all patients presenting with AR underwent the RP. Six of the 30 patients with AR operated on in that time, the majority of whom had marked aortic root enlargement, needed redo AVR. At the end of 1998, when it was appreciated that excessive aortic root dilatation was a significant risk factor for the development of postoperative AR, the RP was abandoned in this subset of patients presenting with excessively dilated aortic root. For the past 3 years, the authors again offered the RP to patients in this group, albeit with insertion of the PA inside a Valsalva Dacron graft, although these patients have not been analyzed as part of this study because the follow-up period is too short to allow a meaningful analysis. Other groups have also noted worse late results in patients presenting with AR [8, 12]. With regard this IC method in patients presenting with AR, if the aortic root is not excessively dilated (>32 to 34 mm at the aortic annulus, the STJ, or both), good results have been obtained.

If a reoperation is required for progressive AR in patients having this IC method, a mechanical AVR has been performed. Valve-sparing surgical procedures have not been possible in this situation, as has been reported after a failed RR method [9]. Fortunately, this is seldom required, particularly with AS or AS/AR. Also, of note in the group presenting with AR, if failure and redo AVR are necessary, this becomes apparent early, and all reoperations are performed within 6 years, with no late failures. Thus, if failure has not occurred early, stable aortic valve function has been observed even in the group presenting with AR. This is in stark contrast to failure after the RR method, when increasing failures occur during the second decade of follow-up [9, 10, 12], and an earlier failure phase, related to technical factors [11].

When reoperations after the RP are considered, the pulmonary allograft also needs mention. Four patients required redo PVR, and in 3, the indication was endocarditis. Admittedly 5% to 6% of patients do have mild to moderate tubular pulmonary stenosis of the conduit that develops 6 to 12 months after operation, and fortunately, these patients have stable Doppler echocardiography parameters across the pulmonary valve, up to 17 years postoperatively, in this series. No doubt with further follow-up into the second and third decades, some of these patients will come to reoperation, either by further open procedures, or via percutaneous methods.

The other options for patients in this age group (15 to 60 years) who require AVR are mechanical valve replacement and tissue AVR, both xenograft and aortic allograft. Not only do mechanical AVR recipients require oral anticoagulants such as warfarin indefinitely, but their long-term survival is worse than that of an age-matched and sex-matched population [21]. When one takes into account valve-related deaths and thromboembolic and bleeding complications, fewer than 50% of patients after mechanical AVR are free of valve-related complications 15 years after operation [17, 19]. In this series of 310 patients followed up over a 20-year period, there have been no late valve-related deaths.

With regard to bioprosthetic AVR, not many studies have analyzed survival rates in the younger patient group reported on here. However, those that have show reduced life expectancy in comparison with the general population [22, 23]. There is also the problem of poor durability in younger patients [22]. The modern trend toward bioprosthetic AVR insertion in patients under 60 years, with the plan to insert “valve-in-valve” transcatheter AVR, is as yet untested, but it is difficult to see how this will lead to comparable survival and subsequent reoperation rates, considering that a smaller
References