Autograft Regurgitation and Aortic Root Dimensions After the Ross Procedure
The German Ross Registry Experience

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Background—Autograft regurgitation and root dilatation after the Ross procedure is of major concern. We reviewed data from the German Ross Registry to document the development of autograft regurgitation and root dilatation with time and also to compare 2 different techniques of autograft implantation.

Methods and Results—Between 1990 and 2006 1014 patients (786 men, 228 women; mean age 41.2±15.3 years) underwent the Ross procedure using 2 different implantation techniques (subcoronary, n =521; root replacement, n =493). Clinical and serial echocardiographic follow up was performed preoperatively and thereafter annually (mean follow up 4.41±3.11 years, median 3.93 years, range 0 to 16.04 years; 5012 patient-years). For statistical analysis of serial echocardiograms, a hierarchical multilevel modeling technique was applied. Eight early and 28 late deaths were observed. Pulmonary autograft reoperations were required in 35 patients. Initial autograft regurgitation grade was 0.49 (root replacement 0.73, subcoronary 0.38) with an annual increase of grade 0.034 (root replacement 0.0259, subcoronary 0.0231). Annulus and sinus dimensions did not exhibit an essential increase over time in both techniques, whereas sinotubular junction diameter increased essentially by 0.5 mm per year in patients with root replacement. Patients with the subcoronary implantation technique showed nearly unchanged dimensions. Bicuspid aortic valve morphology did not have any consistent impact on root dimensions with time irrespective of the performed surgical technique.

Conclusions—The present Ross series from the German Ross Registry showed favorable clinical and hemodynamic results. Development of autograft regurgitation for both techniques was small and the annual progression thereof is currently not substantial. Use of the subcoronary technique and aortic root interventions with stabilizing measures in root replacement patients seem to prevent autograft regurgitation and dilatation of the aortic root within the timeframe studied. (Circulation. 2007;116[suppl I]:I-251–I-258.)

Key Words: aortic regurgitation ■ aortic root dimensions ■ implantation technique ■ Ross procedure

The Ross procedure has the advantages of a viable autologous transplant and has gained increasing acceptance as an attractive alternative for aortic valve replacement.1 The procedure can be performed with low operative mortality, and it is associated with superior hemodynamic characteristics and a low incidence of infection and thromboembolism.1–3 There is growing concern, however, regarding autograft failure and surgical revisions. Progressive dilatation of the autograft with or without regurgitation of the autograft valve is a common cause of reoperation.4–6 This concern has led many to reconsider the indication for the Ross operation in the adult population for whom other surgical options are available.

Using the database of the German Ross Registry, we assessed the function of the pulmonary autograft and examined the association between autograft regurgitation and root dilatation after the Ross procedure.
Patients and Methods

Study Population and Operative Data

Data from the German Ross Registry database were analyzed. The registry includes patient data from 8 departments of cardiac surgery in Germany since February 1991. The follow-up data from each center were taken into the database and subsequently a common systematic, prospective registry was started in January 2002. Within the last 5 years, 1.9% to 2.7% of all aortic valve replacement procedures in Germany were performed as autograft procedures. In some specialized centers, this proportion is up to 11%. The responsible surgeon at each center determined the surgical technique. A total of 1014 patients were included in the database; of these, 521 patients were treated with the subcoronary autograft inclusion technique (SC) and 493 patients underwent autograft implantation as a full root replacement (RR). Patients’ characteristics and operative data are listed in Tables 1 and 2. Details of the operative techniques have been described elsewhere.7–9 Informed consent was obtained from all patients; the study was approved by the local ethics committee. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the article as written.

Clinical Follow Up

In the present study, all hospital survivors were enrolled in this ongoing follow-up assessment by means of physical examination in conjunction with echocardiographic evaluation. Follow-up investigations were scheduled at discharge and on a yearly basis thereafter. As a result of the different regional provenance of the patients and to support adherence to the program, complete clinical and echocardiographic examinations (documented on videotapes) from the referring cardiologists were also accepted.

Echocardiographic Data Acquisition and Measurements

Autograft dimensions were measured as described by Roman et al10 at 4 different levels: (1) annulus at the level of the autograft leaflet hinges, (2) sinus of Valsalva at the largest anteroposterior diameter, (3) supraaortic ridge level (sinotubular junction) at the distal rim of the sinuses of Valsalva, and (4) the proximal ascending aorta 2 cm above the sinotubular junction. Aortic regurgitation was assessed by multiple techniques with the parasternal long-axis and apical 5-chamber view. Pulsed wave Doppler and color flow Doppler imaging were used for mapping the left ventricular outflow tract, including determination of the ratio of jet height to left ventricular outflow tract height. Continuous Doppler imaging was applied to measure the deceleration slope and pressure half-time of the autograft regurgitation jet. Aortic regurgitation was graded with the use of standard criteria in a majority of the examinations.11 Because it is a multicenter study, the final decision of autograft regurgitation (AR) grading was left to the decision of the responsible echocardiographer’s preference and experience, and regurgitation severity was reported on a scale of grade 0 to 4. Trace (trivial) aortic insufficiency defined as a very tiny regurgitation jet in early diastole near the detection limit was included in the analysis as grade 0.5. Mean

| TABLE 1. Patient Demographics and Preoperative Characteristics (n=1014) |
|----------------|-----------------|-----------------|
|              | Total Group     | SC (n=521)      | RR (n=493)      |
| Mean age, years (SD, range) | 41.2±15.3       | 42.6±14.9       | 39.7±15.5*      |
| <20 years    | 127 (12.5)      | 51 (9.8)        | 76 (15.4)*      |
| 20–40        | 294 (29.0)      | 154 (29.6)      | 140 (28.4)      |
| 41–60        | 533 (52.6)      | 273 (52.4)      | 260 (52.7)      |
| >60          | 60 (5.9)        | 43 (8.3)        | 17 (3.5)*       |
| Gender       |                 |                 |                 |
| Male         | 786 (77.5)      | 404 (77.5)      | 382 (77.4)      |
| Female       | 228 (22.4)      | 117 (22.4)      | 111 (22.5)      |
| Left ventricular ejection fraction |                 |                 |                 |
| >50%         | 781 (77.0)      | 441 (84.6)      | 340 (69.0)      |
| 26–49%       | 106 (10.5)      | 54 (10.3)       | 52 (10.5)       |
| <25%         | 4 (0.40)        | 2 (0.4)         | 2 (0.40)        |
| Unknown      | 123 (12.1)      | 24 (4.6)        | 99 (20.0)*      |
| Predominant aortic hemodynamics and morphology |                 |                 |                 |
| Stenosis     | 178 (17.6)      | 73 (14.7)       | 105 (23.1)*     |
| Regurgitation| 281 (27.7)      | 145 (29.1)      | 136 (29.9)      |
| Mixed lesion | 494 (48.7)      | 280 (56.2)      | 214 (47.0)*     |
| Other        | 61 (6.0)        | 23 (4.4)        | 38 (7.7)*       |
| Tricuspid    | 293 (28.9)      | 135 (25.9)      | 158 (32.0)*     |
| Bicuspid     | 607 (59.9)      | 341 (65.4)      | 266 (54.0)*     |
| Unicuspid    | 39 (3.8)        | 16 (3.1)        | 23 (4.7)        |
| Other        | 27 (2.7)        | 14 (2.7)        | 13 (2.6)        |
| Unknown      | 48 (4.7)        | 15 (2.9)        | 33 (6.7)*       |
| Previous aortic valve intervention† | 98 (9.5)        | 23 (4.3)        | 75 (15.1)*      |

Values are presented as mean±SD (range) or n (%). *P<0.05. †In 17 patients, repeated aortic valve interventions were performed.
progression of these measurements. The following covariables were used: age, gender, arterial hypertension (medically treated), bicuspid valve disease, preoperative valvular hemodynamics (regurgitation, stenosis, combined lesion), surgical technique (RR versus SC implantation), autograft reoperation, previous aortic valve interventions, interventions at the annular level, and replacement of the ascending aorta. For the small subgroup of 30 patients with root inclusion technique, separate estimation of the initial AR grade and the annual increase thereof was performed. The authors had full access to the data and take responsibility for its integrity.

### Results

**Survival**

Data were collected from 1014 patients who underwent a Ross procedure between February 1990 and July 2006. Eight patients died during or shortly after the operation (0.78% hospital mortality, cardiac cause in all). These early deaths were not autograft-related. Heart failure occurred in 4, an embolic event in one, lethal arrhythmias in 2, and a myocardial infarction in one patient. Follow up was obtained for all patients until at least discharge. Long-term follow up was complete until at least July 2006. Key parameters (vital status, major adverse cardiac events) were obtained in 96%. Mean follow-up duration was 4.41 years (median 3.93, SD 3.11, range 0 to 16.04 years); mean follow up RR 4.13±3.03 years, SC 4.66±3.17 years, \( P=0.027 \) with a total follow up of 5012 patient-years (RR: 2250, SC: 2762 patient-years).

During follow up, 28 patients died (14 SC, 14 RR). Cause of late death was noncardiac in 13 patients (malignancies 8, cerebral and esophageal bleeding 2, multiorgan failure after noncardiac surgery one, pulmonary embolism after noncardiac surgery one, metabolic disorder one), cardiac in 15 patients (sudden death 9, myocardial infarction 2, aortic dissection one, heart failure one, endocarditis 2). In 3 patients, the cause of death was valve-related (multivalvular heart disease, autograft and homograft endocarditis). Cumulative overall survival was 98.7% at 1 year (95% CI 97.9% to 99.5%), 96.4% at 5 years (95% CI 95.0% to 97.8%), and 93.2% at 8 years (95% CI 90.3% to 96.1%). Probability of survival was not significantly different between both surgical techniques (log-rank Mantel-Cox \( P=0.91 \)).

**Reoperations on the Autograft**

During follow up, 35 patients required a reoperation on the autograft (11 cases with autograft reconstruction, 24 with replacement; mean time to reoperation 3.92±3.71 years, range 0.01 to 13.13 years), and 28 patients required a reoperation on the pulmonary homograft (mean time to reoperation 3.64±2.75, range 0.36 to 9.40 years). Four of 28 patients needed a reoperation of both the autograft and the homograft simultaneously (mean time to reoperation 4.90±5.85, range 0.24 to 13.13 years), and in 3 patients, repeated homograft reoperations were performed. The indication for autograft reoperation was structural valve failure in all patients with pure regurgitation in 29 (11 SC, 18 RR). Acute infective endocarditis with a variable degree of aortic regurgitation was present in 6 (3 SC, 3 RR). Seven of 14 SC redo patients showed cusp prolapse (one patient with acute endocarditis) and 4 of 14 patients cusp perforation (2 patients with acute endocarditis). Reasons for redo in RR patients were root dilatation in 8 of 21, cusp perforation in 5 of 21 (2 patient with acute endocarditis), technical problems in 3 of 21, subvalvular aneurysms in 2 of 21, and cusp prolapse in 3 of 21 (one patient with acute endocarditis). Freedom from

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### TABLE 2. Operative Data of 521 SC and 493 RR

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Total (n=1014)</th>
<th>SC (n=521)</th>
<th>RR (n=493)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bypass time, (mean, SD), min</td>
<td>185±42</td>
<td>206±35</td>
<td>163±37*</td>
</tr>
<tr>
<td>(range)</td>
<td>81–433</td>
<td>81–433</td>
<td>95–356</td>
</tr>
<tr>
<td>Cross clamp time, (mean, SD), min</td>
<td>148±35</td>
<td>166±33</td>
<td>129±25*</td>
</tr>
<tr>
<td>(range)</td>
<td>38–293</td>
<td>65–293</td>
<td>38–258</td>
</tr>
<tr>
<td>Circulatory arrest</td>
<td>23 (2.2)</td>
<td>20 (3.8)</td>
<td>3 (0.6)</td>
</tr>
</tbody>
</table>

Additional procedures:

- None: 605 (59.6) 314 (60.2) 291 (59.0)
- Ascending aorta reconstruction: 143 (14.1) 77 (14.7) 66 (13.3)*
- Ascending aorta replacement: 155 (15.2) 59 (11.3) 96 (19.4)*
- Other†: 251 (24.8) 201 (19.8) 50 (4.9)*
- Aortic annulus intervention: 533 (52.5) 156 (30.2) 377 (76.4)*

Clinical course <30 days:

- In-hospital death: 8 (0.7) 5 (0.9) 3 (0.6)
- Reoperation coronary embolism: 1 (0.09) 1 (0.1) 0 (0)
- Reoperation bleeding: 59 (5.8) 35 (6.7) 24 (4.8)
- Reoperation autograft: 3 (0.2) 2 (0.3) 1 (0.2)
- Reoperation homograft: 0 (0) 0 (0) 0 (0)
- Cerebral thromboembolism: 12 (1.8) 9 (1.7) 3 (0.6)
- Transient ischemic attack (<30 days): 6 (0.6) 6 (1.1) 1 (0.2)
- Completed stroke (<30 days): 5 (0.4) 3 (0.5) 2 (0.4)
- Permanent pacemaker: 7 (0.6) 4 (0.7) 3 (0.6)

Values are presented as mean±SD (range) or n (%).

*P<0.05.

†Right ventricular outflow tract intervention, bypass grafting, mitral valve reconstruction, tricuspid valve reconstruction, Morrow-Bigelow operation, Maze procedure, and ventricular septal defect closure.

The authors had full access to the data and take responsibility for its integrity.
reoperation on the autograft was 99.1% at 1 year (95% CI 98.5% to 99.7%), 96.1% at 5 years (95% CI 94.5% to 97.7%), and 93.9% at 8 years (95% CI 91.6% to 96.3%). The probability of freedom on autograft reoperation was not significantly different between both surgical techniques (log-rank Mantel-Cox \( P = 0.47 \)). Of the 28 patients who required reintervention on the allograft, all showed structural valve failure with stenosis in 18, pure regurgitation in 3, a combined lesion in 2, and acute infective endocarditis in 5 patients.

Freedom from allograft reintervention was 99.5% at 1 year (95% CI 99.1% to 99.9%), 97.3% at 5 years (95.9% to 98.7%), and 96.1% at 8 years (94.1% to 98.1%). All patients survived Ross-related reoperations.

### Autograft Regurgitation With Time

#### Model Fitting Analysis

Completeness of echocardiographic follow up with qualitatively good and complete examinations suitable for the present substudy with serial echocardiographic assessment was 82% (total number of measurements 3034, mean 4.59, median 5, range 2 to 14). The first echocardiographic measurements were performed at a mean of 0.802 years postoperation (median 0.0194, range 1 week to 8.58 years). After 5 years 756 and after 8 years 231 measurements were obtained and included in the model. Both a linear and quadratic model proved to be suitable for hierarchical multilevel modeling (Figure 1). A linear model was chosen to model AR over time:

\[
AR \text{ grade } (t) = (\text{initial grade of AR } \pm \text{SE}) + (\text{annual increase of AR grade } \pm \text{SE}) \times \text{times (yr)}
\]

#### Autograft Regurgitation With Time in the Total Study Group

Based on 3034 measurements, the mean initial AR grade is estimated as 0.49 with an average increase of AR grade 0.034 per year. There is significant evidence that AR increases with time, but the amount of this increase is not very substantial (Figure 2):

\[
f(t) = (0.49 \pm 0.02) + (0.034 \pm 0.004) \times t; P < 0.0001.
\]

For patients with reoperation on the autograft during follow up \( n = 35 \), there is significant evidence of a higher mean initial AR grade \( 0.83 \pm 0.08 \) versus \( 0.49 \pm 0.02; P < 0.0001 \) and higher annual increase of AR \( 0.345 \pm 0.022 \) versus \( 0.021 \pm 0.004; P < 0.0001 \), Figure 3) compared with Ross patients without autograft reoperation. Ascending aorta replacement \( 0.58 \pm 0.04 \) versus \( 0.47 \pm 0.02; P = 0.018 \), annulus interventions \( 0.64 \pm 0.02 \) versus \( 0.37 \pm 0.02; P < 0.0001 \), the presence of a nonbicuspid valve \( 0.56 \pm 0.03 \) versus \( 0.45 \pm 0.02; P = 0.0006 \), decreasing age \( -0.0025 \pm 0.0011 \) per extra year, related to the mean age of 45 years, \( P = 0.023 \), and surgical technique \( RR 0.73 \pm 0.03 \) versus \( SC 0.38 \pm 0.02; P < 0.0001 \) were associated with differences in mean initial AR. Gender, hemodynamic classification, age, previous aortic valve interventions, and year of surgery did not affect the initial AR grade. None of the listed covariables (with the exception of autograft reoperation) had an influence on the annual increase of AR grades. Additionally, the evolution of AR progression with time is not associated with the initial AR grade.

![Figure 1. Multilevel linear and quadratic modeling. Estimation of AR grade in the total study group. Comparison of linear (solid line) and quadratic models (dotted line).](http://circ.ahajournals.org/)

![Figure 2. Estimation of AR grade with time for the surgical subgroups RR and SC in comparison with the total study group (ALL).](http://circ.ahajournals.org/)

![Figure 3. Estimation of aortic regurgitation grade with time for patients with autograft reoperation and those who did not require reoperation on the autograft. The surgical subgroups RR and SC were displayed according to whether reoperation was performed (redo) or not (no redo).](http://circ.ahajournals.org/)
Autograft Regurgitation With Time: Root Replacement versus Subcoronary Implantation

In SC, the estimated initial AR grade is 0.38 (±0.02) and AR increases with time, but the amount of this annual increase is not substantial (0.023 AR grades/year). In RR, a higher initial AR grade was observed, but there is only a marginal significant increase of AR with time, also not very substantial (0.026±0.009 AR grades/year, Figure 2). The root-preserving operation techniques (SC and root inclusion technique) did not show any evidence that the initial AR grade and the annual increase thereof differ significantly between both techniques (P=0.56). RR and SC revealed higher rates of annual increase in AR grade in the subgroup of patients with the necessity of autograft reoperation during follow up (P<0.0001, Figure 3). Within the RR group, neither the initial AR grade nor the annual increase was affected by the presence of a bicuspid valve; in the SC group, a bicuspid valve was associated with a lower initial value of AR (P=0.015) and a slightly elevated rate of annual increase (P=0.013).

Annulus interventions led to a significant higher initial AR grade in both surgical groups (SC 0.48±0.03 versus RR 0.79±0.04, P<0.001); the annual increase thereof was attenuated in the RR group by the intervention (P=0.081, Figure 4). Compared with the RR group, in the SC group, there is marginal evidence that age affects the initial AR grade (decreasing AR with increasing age, P=0.037) and annual increase (increasing annual AR grade with increasing age, P=0.046), but the extent is very small. Previous aortic valve interventions, hemodynamic classification, ascending aorta replacement, gender, and arterial hypertension did not affect both the initial AR grade and the annual increase in both groups.

Diameters of the Aortic Root

The best fitting regression model to study diameter changes with time was a linear model with the term

\[\text{Diameter} (t) = (\text{initial diameter} \pm \text{SE}) + (\text{annual increase of diameter} \pm \text{SE}) \times \text{time (yr)}.\]

The diameters (in millimeters) tend to increase with time:

**Figure 4.** Estimation of AR grade with time for patients with annulus interventions. The surgical subgroups RR and SC were displayed according to whether annulus intervention was performed (RR-Y, SC-Y) or not (RR-N, SC-N).

**Figure 5.** Estimation of sinotubular junction (STJ) diameter with time for patients with RR and SC.

\[\text{Annulus} f(t) = (22.5 \pm 0.2) + (0.14 \pm 0.030) \times \text{time}\]

\[\text{Sinus} f(t) = (31.4 \pm 0.2) + (0.43 \pm 0.036) \times \text{time}\]

\[\text{Sinotubular junction} f(t) = (27.4 \pm 0.2) + (0.20 \pm 0.046) \times \text{time}\]

Ascending aorta \(f(t) = (33.4 \pm 0.3) + (0.41 \pm 0.056) \times \text{time}\)

For example, if the initial annular diameter is 22.5 mm, the estimated annual increase is 0.14 mm/year (P<0.0001). Thus, after 10 years, the estimated increase in diameter is 1.4 mm at the annular, 4.3 mm at the sinus, 2.0 mm at the sinotubular junction, and 4.1 mm at the level of the ascending aorta.

**Surgical Technique and Aortic Root Diameters**

Patients with RR had a significant greater annular diameter at time zero compared with SC patients (24.4±0.3 mm versus 21.5±0.2 mm, P<0.0001). In both groups, these diameters tend to increase with time, but with little evidence of a difference of the annual increase (P=0.32). Sinus diameters differed also at the time of the initial evaluation with a higher mean value in the RR group (RR versus SC 35.2±0.4 mm versus 29.1±0.2 mm, P<0.0001); an increase with time was apparent in both surgical subgroups (annual increase of diameter RR 0.427±0.075 mm/year versus SC 0.322±0.037 mm/year; P=0.26). In RR, there is significant evidence of a higher initial diameter of the sinotubular junction and of a higher mean increase in diameter per year (Figure 5). Thus, after 10 years, the diameter of the sinotubular junction was estimated to increase in RR by 5.1 mm and in SC by 0.3 mm. The surgical technique (RR versus SC) had no effect on either initial (34.7 versus 33.3 mm, P=0.33) or progression (0.39 versus 0.40 mm/year, P=0.96) of the ascending aorta diameter.

**Additional Procedures and Aortic Root Diameters**

Replacement of the ascending aorta did not affect the progression of sinus and sinotubular junction diameters in both surgical techniques. There is strong evidence that the initial
annulus diameter is higher in RR patients with ascending aorta replacement; the diameter over time is unchanged. Annu1
Interventions were associated with a higher initial annulus diameter in RR (RR 23.9±0.4 mm versus SC 22.1±0.3 mm; P<0.0001) and a more pronounced annual increase of the annulus diameter in RR patients (RR 0.329±0.009 mm versus SC −0.02±0.068 mm; P=0.0016). This translates to an increase of the annulus diameter after 10 years in the RR group from 23.8 mm to 27.1 mm, whereas in the SC group, the diameter remains unchanged over time. Annu1 interventions had no effect on the annual progression rates of the sinus and sinotubular junction diameters over time in both surgical groups.

Other Covariables and Aortic Root Diameters
Female gender was associated with smaller initial diameters at all levels of the aortic root when compared with male patients (annulus: male versus female 20.4 versus 23.1 mm, sinus 28.6 versus 32.2 mm, sinotubular junction 24.8 versus 28.0 mm, ascending aorta 31.6 versus 33.8 mm; P<0.001 at all levels); the annual increase did not differ between the sexes. The hemodynamic subgroup with aortic regurgitation had greater initial diameters at the level of annulus, sinus, and sinotubular junction, but the annual increase did not differ between the hemodynamic subsets. Patients who required a reoperation on the autograft during follow up did not have higher initial diameters or greater annual increase of the diameters at the annular, sinus, and sinotubular junction level compared with those without redo procedures on the autograft. There was only a trend of a greater annual increase in ascending aorta diameters in patients who underwent an autograft reoperation compared with those who did not (1.41 mm/year versus 0.4 mm/year, P=0.088). The presence of a bicuspid valve, arterial hypertension, and previous aortic valve interventions was not associated with progression of annulus, sinus, sinotubular junction, and ascending aorta diameters.

Discussion
The German experience with the Ross procedure using different surgical techniques provides some evidence that this alternative in aortic valve replacement is safe with an excellent long-term survival and favorable results in the midterm. Although the overall survival is indeed comparable to the general population and substantially superior to that of other valve substitutes, the need for reoperation remains the principal limitation of the procedure. Autograft failure necessitating reoperation has been observed in both the RR and SC techniques and was reported with increasing numbers. Relatively low reoperation rates have been reported in the first 5 years postoperatively in many studies, but a substantial number of studies indicate that patients continue to develop autograft regurgitation in the midterm and eventually require reoperation. There is growing evidence that remodeling of the full root autograft is a morphological prerequisite for a progressive deterioration in valvular hemodynamics. However, the exact magnitude of this phenomenon and its clinical impact is still a topic of controversy and some surgeons perform additional procedures to stabilize the root.

To address the issue of AR and to analyze precipitating risk factors, we performed a substudy of AR over time. Traditionally, the Kaplan-Meier method was often used to assess serial echocardiographic measurements. For several reasons, this method is inappropriate for analysis. Takkenberg et al introduced hierarchical multilevel linear modeling as an alternative statistical method to overcome these shortcomings. Curve fitting analysis revealed that both a linear and quadratic model proved to be suitable for a hierarchical multilevel modeling. There is significant evidence that changes of AR grade with time are not strictly linear but that the differences are small within the timeframe studied. Compared with the quadratic model, the linear approach is suitable except beyond 7 years when it predicts much higher values and in the first couple of years when the rate of increase in AR grade is smaller than for the quadratic model. Having only a linear term in time makes the model easier to interpret. In long-term studies, however, with a considerable number of patients followed for more than 10 years, the impact of the quadratic effect may be considerable. For these reasons, the linear model was chosen and comparability with a previous reported study is given.

According to the findings of Takkenberg and associates, the present prospective echocardiographic evaluation of autografts revealed an increase of AR over time, which was small but persistent. The progression in the total study cohort of the annual rate of AR increase was not directly comparable because the measures of AR grade were different between the 2 studies (grade I–IV versus AR jet length and diameter). Patients who required autograft reoperations had greater initial AR and a higher annual increase of AR grade compared with the group who did not undergo reoperation. Other covariables studied had an effect only on the initial AR grade; none of these factors had a substantial effect on the progression rate over time. The evidence that is lacking of a higher progression in patients with potential risk factors is in accordance with the previous study, and the higher initial AR grade in this study may be explained by the surgical technique; in the present study, SC (n=457, lower initial AR grade) and RR (n=385, higher initial AR grade) patients showed balanced numbers, whereas in the previous study, RR was present in 84 of 90 patients.

RR and SC showed substantial differences in the initial grade of AR early after operation with higher values in RR. There is no difference in the annual increase of AR grade between both surgical subgroups. However, this increase in both groups is not substantial and the clinical importance of this finding is unclear, because additional factors may play an important role in the long-term. In both groups, patients who required autograft reoperation showed higher initial AR and significantly higher rates of annual increase of AR grade. Surprisingly, patients who required reoperation on the autograft valve did not show higher initial diameters at all levels of the aortic root or greater annual progression irrespective of the surgical technique. This observation, which is in contrast to Takkenberg et al, suggests that additional factors may play an important role, and comparability of different Ross series reported in the literature is limited attributable to several reasons: the mean follow-up period in the present study is
short, the number of autograft reoperations within this time-frame is low (3.5%), and a high number of additional root stabilizing procedures were performed.

Patients at risk (annulus dilatation, ascending ectasia) were consistently treated with classic and innovative techniques for the autograft to avoid both early and progressive autograft dilatation. Whether these reinforcement techniques used in both surgical groups will result in sustained stable valve characteristics can only be determined in the long-term. Within this context, it is important to note that the use of surgical strategies to support the tissue (enlargement, reduction, tailoring, reinforcement) differs remarkably between the Ross series reported in the literature and therefore easy prima-vista comparison of the results is not feasible in this complex issue. In the present study group, the diameters at the annulus, sinus, sinotubular junction, and ascending aorta level tend to increase with time. Compared with the results reported by Takkenberg and associates, both diameters and their increase with time are remarkably smaller. The annual increase of root diameters in RR and SC differed only at the sinotubular junction level with a pronounced dilatation in the RR group, whereas in SC, the diameter was unchanged with time. This confirms the observations of Takkenberg et al but, with the limitations mentioned previously, in the present series, we can only speculate if this will result in a progressive autograft dysfunction caused by sinotubular ridge dilatation with splaying of the valve leaflets. For both surgical techniques, a dilatation of the tubular part of the ascending aorta has been observed. This phenomenon can contribute to the remodeling of the aortic root in RR patients (with a pronounced sinotubular junction dilatation), a mechanism that could be also of importance in SC patients in the long-term.

Replacement of the ascending aorta and annular interventions may contribute to a low annual progression rate of the diameters at different levels of the aortic root. In patients with ascending aorta replacement, no differences of the initial diameters and the progression rates of the sinotubular junction and the aortic sinus could be observed in both surgical groups. The annular diameter was initially greater if the ascending aorta was replaced in both groups; in the RR subgroup, an annual decrease of the diameter was apparent. This complex evolution can be explained by the high number of additional annular interventions and the mode of autograft insertion (inversion with continuous suturing). Indeed, annular interventions led to a reduction of the initial annulus diameter in the RR group. The procedure was performed in patients with marked dilated annulus to achieve a reverse remodeling by surgical means. Although stabilized, a gradual increase of the annular diameter over time was observed. In contrary, annular interventions led in the SC group to a slight increase of the initial diameter; in the long-term, no further dilatation occurs. This contradiction at the first glance must be interpreted with several factors in mind evolving since the beginning of the 1990s. A large inhomogeneous patient series with different root pathologies was treated at different departments by surgeons with individual philosophies and convictions. In addition, changes of surgical procedures with time attributable to personal and institutional experiences led to seemingly divergent results difficult to assess by simple mathematical assumptions. This complex issue will be addressed by a further study, including all variables, their combinations, and interactions.

Clinical Implications
In conclusion, the autograft procedure results in a good overall survival and a low number of reinterventions on the autograft irrespective of the surgical technique. A small increase in AR and aortic root dimensions with time is detectable. The progression rate is sustained but clinically insignificant in the midterm. The RR technique showed higher initial AR grades and aortic root diameters, but the annual progression rate is similar in both surgical groups. The high number of additional stabilizing and reinforcement procedures (annulus, sinotubular junction, ascending aorta) proved to be effective especially in full root replacement. Because a small but sustained AR progression over time does not differ between the surgical subgroups, a potential threat of more reoperations is possible in the long-term in both the SC and RR patients. The Takkenberg approach in analyzing valvular dynamics over time with multilevel modeling is an attractive statistical tool that overcomes shortcomings of conventional techniques.

Study Limitations
The current study presents several limitations. The mean follow-up time (4.41±3.11 years) is limited and the number of major cardiac events (eg, autograft reoperation) is small. It could be expected that the occurrence of autograft failure will increase with time. The conclusions drawn in this study must take this into account, although the present results are comparable with a previous study with a mean follow up of 7.1±2.9 years. Furthermore, a bias of the use of echocardiographic evaluations from different centers using different methods cannot be excluded and may influence the results. In addition, a small surgical subgroup with the use of the root inclusion technique was included in the SC group. Subanalysis of key items (eg, AR grade) did not reveal any difference between the SC and the root inclusion group. Finally, a main limitation of the study is the evolution of the surgical approach within the last 15 years. Additional interventions were introduced and applied in different root pathologies and personal/institutional experience changed over time. Therefore, further studies are necessary to evaluate multivariable effects on clinical important subsets (eg, the role of bicuspid valve disease and ascending replacement, the impact of different surgical reinforcement techniques combined with additional interventions in various disease states on autograft function and morphology).

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None.
References


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