

# Serial Echocardiographic Assessment of Neo-Aortic Regurgitation and Root Dimensions after the Modified Ross Procedure

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**Background and aim of the study:** Concern exists regarding progressive root dilatation after the modified Ross procedure. The present prospective echocardiographic study aimed to provide further insight into neo-aortic regurgitation (nAR) and neo-aortic root dimensions over time in adult Rotterdam Ross root patients, and to study potential risk factors for nAR and dilatation.

**Methods:** All Rotterdam Ross patients aged  $\geq 16$  years at surgery were subjected to a prospective biennial standardized echocardiographic protocol. Analysis over time of nAR according to the jet length and jet diameter method, autograft annulus and sinotubular junction (STJ) diameters was carried out using a multilevel linear model in 90 patients who had two or more echocardiographic measurements (mean 5; range 2-9; total 458) up to 14 years (mean 7 years) after surgery.

**Results:** The mean ( $\pm$  SE) initial postoperative jet length nAR was grade  $0.9 \pm 0.09$ , and the annual increase  $0.1 \pm 0.02$  ( $p < 0.001$ ). Initial annulus and STJ diameters were  $25 \pm 0.5$  mm and  $36 \pm 0.6$  mm, while annual increases were  $0.4 \pm 0.07$  mm and  $0.5 \pm 0.09$  mm, respectively ( $p < 0.001$ ). Patients who eventually underwent an autograft reoperation ( $n = 10$ ) had significantly greater initial nAR and greater progression

of nAR, and a greater initial annulus diameter. The annual annulus and STJ diameter increase was greater in patients who underwent autograft reoperation. Compared to freestanding root replacement, patients with inclusion cylinder aortic root replacement had smaller initial annulus and STJ diameters that did not increase over time. Female gender was associated with a greater initial jet length and jet diameter nAR and a greater increase over time in jet diameter nAR. Preoperative aortic regurgitation or combined aortic stenosis and regurgitation were associated with greater initial annulus and STJ diameters. Neither bicuspid valve disease, patient age, preoperative ascending aorta aneurysm, prior aortic valve surgery nor hypertension had an effect on initial or progression of nAR, annulus, and STJ diameter.

**Conclusion:** The annual increase in nAR and root dimensions is small, but persistent, after autograft aortic root replacement in adults, and further reoperations should be anticipated. Use of the inclusion cylinder root replacement technique seems to prevent neo-aortic dilatation.

The Ross procedure (1) is the only surgical option that offers patients who require aortic valve replacement, a living valve substitute with regenerative capacities and an excellent hemodynamic profile.

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Although the durability of the Ross procedure appears thus far superior to the other available biological valve prostheses, there is growing concern regarding the longevity of the autograft valve, and in particular the progressive dilatation of the neo-aortic root after autograft aortic root replacement (2-4). Suggested risk factors for increased dilatation rates include bicuspid valve disease (4), younger patient age, preoperative aortic aneurysm, and aortic root replacement without support of the annulus and sinotubular junction (STJ) (2).

Serial echocardiography is a well-established and non-invasive means of monitoring autograft valve function and neo-aortic root dimensions over time.

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The statistical analysis of serial echocardiographic data is often performed by means of the Kaplan-Meier method. However, whilst this method considers the duration of follow up as a continuous variable, echocardiography data are usually available within a certain time frame and often incomplete in one or more time frames. In addition, the Kaplan-Meier method considers valve dysfunction to be an irreversible endpoint, while the severity of aortic regurgitation (AR) is often variable over time. Multilevel modeling techniques offer an alternative statistical method that adequately deals with these issues, and in addition allows multivariable risk factor analysis. In the present study a multilevel linear model was used to study autograft valve function and neo-aortic root dimensions over time, including potential risk factors for neo-aortic regurgitation (nAR) and root dilatation, in adult patients who underwent autograft aortic root replacement and who formed part of this ongoing, prospective cohort study (5).

## Clinical material and methods

### Patients

Between November 1988 and February 2003, a total of 94 patients aged  $\geq 16$  years underwent autograft aortic root replacement at the Erasmus University Medical Center Rotterdam. All hospital survivors (n = 91) were enrolled in the present ongoing, prospective follow up study (5). Institutional Review Board approval was obtained to conduct this prospective follow up study for which a need for patients to provide their informed consent was waived. The prospective echocardiographic database was frozen on September 27th 2004, and echocardiographic data on all autograft patients aged  $\geq 16$  years at the time of the Ross procedure were extracted. In total, 90 patients underwent two or more standardized echocardiographic measurements, and these patients comprised the study population. Patient and operative characteristics are listed in Table I.

### Operative technique

Autograft root replacement with a homograft or autograft was performed as a freestanding root with reimplantation of the coronary arteries in 84 patients; six patients had an inlay cylinder aortic root replacement. The autograft root was placed in the left ventricular outflow tract (LVOT) and annulus with a short rim of right ventricular muscle, which was kept to a minimum. Either a straight rim of muscle was left intact below the autograft valve or scalloping was performed to reduce the muscle rim to a minimum of approximately 3-4 mm. Either continuous (n = 67) or interrupted sutures (n = 23) were then used to insert the autograft in the aortic position, depending on the

Table I: Patient and operative characteristics (n = 90).

Parameter	Autograft root (n = 90)
Age (years)*	31 $\pm$ 9 (16-52)
Gender ratio (M:F)	59:31
Serum creatinine level (mg/dl)*	75 $\pm$ 15 (38-121)
Hypertension	3 (3)
Originally bicuspid valve	57 (63)
Hemodynamic diagnosis	
Aortic stenosis	28 (31)
Aortic regurgitation	33 (37)
Aortic stenosis and regurgitation	29 (32)
Aortic valve at start of autograft	
Bicuspid	51 (56)
Tricuspid	28 (31)
Prosthesis	6 (7)
Homograft	5 (6)
NYHA class	
I	30 (33)
II	41 (46)
III	18 (20)
IV	1 (1)
Preoperative sinus rhythm	90 (100)
Prior aortic valve operation	24 (27)
Urgent operation (<24 h)	0 (0)
LV function (n = 88)	
Good	74 (83)
Impaired	8 (9)
Moderate	5 (6)
Bad	1 (1)
Perfusion time (min)*	209 $\pm$ 49 (114-354)
Cross-clamp time (min)*	149 $\pm$ 29 (90-238)
Circulatory arrest (n = 1) (min)	11
Concomitant procedures	
None	78 (87)
CABG	2 (2)
Mitral valve operation	1 (1)
Extended root	2 (2)
Other	7 (8)

\*Values are mean  $\pm$  SD (range).

Values in parentheses are percentages.

CABG: Coronary artery bypass grafting;

LV: Left ventricular.

surgeon's preference. Initially in this series the autograft was placed on the annulus, but in more recent years particular attention was paid to placing the autograft inside the annulus. In two patients the proximal suture line was supported by an autologous pericardial strip. Surgical procedures were performed with the patient on cardiopulmonary bypass, with moderate hypothermia. Crystalloid cardioplegia and topical cooling were used for myocardial protection.

### Echocardiography

Since 1987, at the authors' institution, serial stan-

Standardized echocardiography has been carried out on all patients aged  $\geq 16$  years who received human tissue valves. Postoperative echocardiographic examinations were scheduled at six months, at one year, and biennially thereafter. The severity of aortic regurgitation was estimated by the jet length method on a scale of 0 to 4. As the severity of regurgitation may be overestimated using this method (6,7), this parameter has since January 1993 also been estimated by measuring the ratio of the maximal regurgitant jet diameter to the systolic LVOT diameter directly under the aortic valve in the parasternal long-axis view (jet diameter ratio) (5,6).

Initially, the echocardiographic examinations were performed using different equipment, but since January 1993 all examinations have been performed by two experienced technicians using a Vingmed ultrasound system (CFM 750; Vingmed, Trondheim, Norway) fitted with a 3.25 MHz transducer in order to limit inter-machine and inter-observer variability (5). Color Doppler examinations were started at low gain and increased until white noise appeared in the left ventricular cavity. The flow velocity was set at 0.7-1.0 m/s, depending on the depth. The threshold of the flow velocity was set at 0.25 m/s. Diameters were measured on-line on the video screen from frozen images by planimetry, using a trackball. The mean values of measurements from two cardiac cycles were noted. The mean duration of echocardiographic follow up was  $7.1 \pm 2.9$  years (median 7.0 years; range: 0.94 to 13.9 years); total follow up was 639 patient-years (pt-yr).

### Statistical analysis

Continuous variables were displayed as mean  $\pm$  SD, and categorical variables as proportions. Statistical analysis of clinical variables and initial fitting of the optimal echocardiographic regression model was performed with SPSS 11.0 for Windows (SPSS, Chicago, IL, USA). The echocardiographic data were analyzed by using a multi-level hierarchical linear model (HLM; MLWin 1.0, Centre for Multilevel Modeling, London, UK) (8). This model provided a linear regression line with an intercept and slope for individual patients. The intercept represented the initial nAR or neo-aortic diameter immediately after surgery, the slope being the annual progression of these measures. Co-variables were examined by complete case analysis and included patient age, gender, hypertension (diastolic pressure  $>95$  mmHg or medically treated), originally bicuspid valve disease, preoperative hemodynamic diagnosis (aortic stenosis (AS), AR and combined AS and AR), prior aortic valve surgery, preoperative ascending aortic aneurysm, surgical technique free-standing root versus inclusion cylinder root, and autograft reoperation.

## Results

### Jet length nAR

Ninety patients underwent two or more postoperative echocardiographic examinations over time (median 5; range: 2 to 9; total 458 measurements). Of these 90 patients, 10 underwent a redo aortic valve replacement during the follow up period, all for progressive dilatation and nAR. The median time to autograft reoperation in these 10 patients was 7.0 years (mean  $7.5 \pm 2.8$  years; range: 3.1 to 11.8 years). Using SPSS, the best fitting regression model for these echocardiography data was tested, and both a linear and a logistic model proved to be a good model to study AR over time in this dataset. The linear model was chosen. Using the software package MLwiN, the following formula was generated to model nAR over time:

$$\text{nAR (t)} = \text{Initial AR} + \text{Progression AR} \times \text{time (yr)}$$

For all 90 patients, the formula for jet length nAR was:

$$\text{nAR (t)} = (0.9 \pm 0.09) + (0.10 \pm 0.02) \times \text{time (yr)}$$

This translates to an initial nAR of grade 0.9 and an annual increase of 0.1 grade ( $p < 0.001$ ). Thus, after 10 years, the jet length nAR was estimated to rise by 1+ grade. Patients who underwent reoperation on the autograft during the follow up period ( $n = 10$ ) had a significantly greater initial nAR ( $1.24 \pm 0.34$  versus  $0.87 \pm 0.09$ ;  $p = 0.04$ ) and greater annual increase of nAR ( $0.29 \pm 0.08/\text{yr}$  versus  $0.08 \pm 0.02/\text{yr}$ ;  $p < 0.001$ ) compared to those who did not undergo reoperation ( $n = 80$ ) (Fig. 1). In addition, female gender was associated with a greater initial nAR in females ( $1.21 \pm 0.18$ ) compared to males ( $0.77 \pm 0.09$ ), though gender had no influence on the annual increase of nAR. Bicuspid valve disease, patient age, hypertension, preoperative

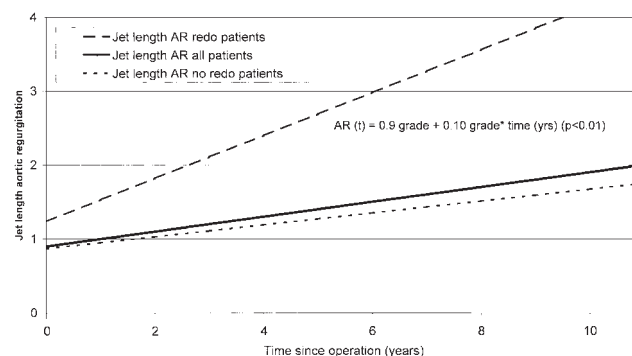


Figure 1: Multilevel linear model estimates of jet length aortic regurgitation (AR) over time for all patients, and for those who did and did not undergo reoperation on the autograft.

hemodynamic diagnosis, prior aortic valve surgery, surgical technique freestanding root versus inclusion cylinder root, and preoperative aneurysm of the ascending aorta had no effect on either initial nAR, or on its progression.

### Jet diameter nAR

Seventy-two patients underwent two or more echocardiographic measurements using the jet diameter method (mean 4; range: 2 to 7; total 287 measurements). Of these 72 patients, eight underwent a redo AVR during the follow up period. The following formula was generated to model jet diameter nAR over time:

$$\text{Jet diameter nAR}(t) = \text{Initial jet diameter} + \text{Progression jet diameter} \times \text{time (yr)}$$

For all 72 patients, the formula for jet diameter nAR was:

$$\text{Jet diameter nAR}(t) = (0.14 \pm 0.01) + (0.005 \pm 0.003) \times \text{time (yr)}$$

This translates to an initial jet diameter nAR of grade 0.14 and a borderline significant annual increase of 0.005 ( $p = 0.08$ ). Thus, after 10 years, the jet diameter nAR was estimated to rise by 0.19. Patients who underwent reoperation on the autograft during follow up ( $n = 8$ ) had a significantly greater initial jet diameter nAR ( $0.20 \pm 0.08$  versus  $0.13 \pm 0.01$ ;  $p < 0.01$ ) and a greater annual increase of jet diameter nAR ( $0.016 \pm 0.018/\text{yr}$  versus  $0.004 \pm 0.003/\text{yr}$ ;  $p < 0.01$ ) compared to those who did not undergo reoperation ( $n = 64$ ) (Fig. 2). In addition, female gender compared to male gender was associated with both a greater initial jet diameter nAR ( $0.16 \pm 0.02$  versus  $0.13 \pm 0.02$ ;  $p = 0.02$ ) and a greater increase over time in jet diameter nAR ( $0.008 \pm 0.004/\text{yr}$  versus  $0.002 \pm 0.003/\text{yr}$ ;  $p < 0.01$ ). Bicuspid

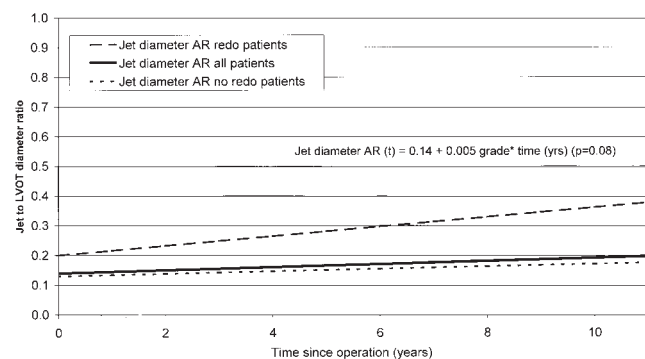


Figure 2: Multilevel linear model estimates of jet to left ventricular outflow tract (LVOT) diameter ratio aortic regurgitation (AR) over time for all patients, and for those who did and did not undergo reoperation on the autograft.

valve disease, patient age, hypertension, preoperative hemodynamic diagnosis, prior aortic valve surgery, surgical technique freestanding root versus inclusion cylinder root, and preoperative aneurysm of the ascending aorta had no effect on either initial or progression of jet diameter nAR.

### Aortic annulus and STJ diameter

Eighty-three patients had two or more echocardiographic measurements with measurements of the aortic annulus diameter and the STJ diameter (median 5; range: 2 to 8; total 389 measurements). Of these 83 patients, eight underwent a redo AVR during the follow up period. Using SPSS, the best fitting regression model for these echocardiography data was tested, and a linear model proved to be the best model to study aortic annulus and STJ diameters over time in this dataset. Using the software package MLwiN, the following formula was generated to model aortic annulus and STJ diameter over time:

$$\text{Diameter (t)} = \text{Initial diameter} + \text{Increase diameter} \times \text{time (yr)}$$

For all 83 patients, the formula for annulus diameter was:

$$\text{Annulus diameter (t)} = (25.2 \pm 0.51 \text{ mm}) + (0.40 \pm 0.07 \text{ mm}) \times \text{time (yr)}$$

This translates to an initial annulus diameter of 25.2 mm and a significant annual increase of 0.4 mm ( $p < 0.01$ ). Thus, after 10 years, the annulus diameter was estimated to increase to 29.2 mm. Patients who had reoperation on the autograft during follow up ( $n = 8$ ) had a significantly greater initial annulus diameter ( $27.6 \pm 1.9$  mm versus  $24.8 \pm 0.5$  mm;  $p < 0.01$ ) and a significantly greater annual increase of annulus diameter ( $0.7 \pm 0.36$  mm/yr versus  $0.4 \pm 0.07$  mm/yr;  $p < 0.01$ )

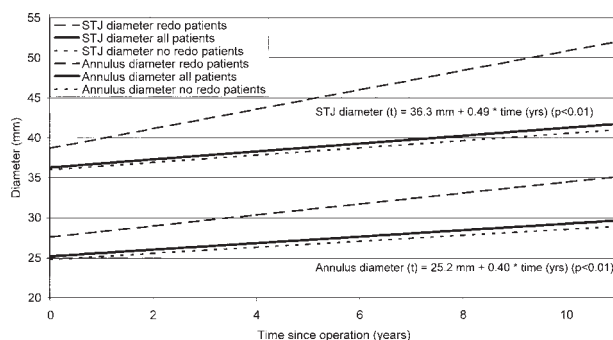


Figure 3: Multilevel linear model estimates of aortic annulus diameter and sinotubular junction (STJ) diameter over time for all patients, and for those who did and did not undergo reoperation on the autograft.

compared to those who did not undergo reoperation (n = 75) (Fig. 3). Compared to patients who had a free-standing root replacement, patients with inclusion cylinder aortic root replacement had a smaller initial annulus diameter ( $22.0 \pm 0.9$  mm versus  $25.5 \pm 0.5$  mm;  $p < 0.01$ ) that did not change over time ( $-0.1 \pm 0.1$  mm/yr versus  $0.4 \pm 0.07$  mm/yr;  $p < 0.01$ ). In addition, female gender was associated with a smaller initial annulus diameter ( $21.6 \pm 0.7$  mm in females versus  $27.1 \pm 0.7$  mm in males;  $p = 0.02$ ), but annual increase in annulus diameter did not differ between the sexes. Finally, patients who had preoperative AS had a smaller initial annulus diameter compared to those with preoperative AR or combined AS and AR ( $22.6 \pm 1.0$  mm versus  $26.6 \pm 1.0$  mm and  $25.8 \pm 1.1$ , respectively;  $p < 0.01$ ), but annual increase in annulus diameter did not differ between the hemodynamic diagnoses. Bicuspid valve disease, patient age, hypertension, prior aortic valve surgery and preoperative aneurysm of the ascending aorta had no effect on either initial or progression of annulus diameter.

For all 83 patients the formula for STJ diameter was:

$$\text{STJ diameter (t)} = (36.3 \pm 0.61 \text{ mm}) + (0.49 \pm 0.09 \text{ mm}) \times \text{time (yr)}$$

This translates to an initial STJ diameter of 36.3 mm and a significant annual increase of 0.5 mm ( $p < 0.01$ ). Thus, after 10 years, the STJ diameter was estimated to increase to 41.3 mm. The initial STJ diameter of patients who had a reoperation on the autograft during follow up (n = 8) showed a trend towards a greater diameter compared to those who did not undergo reoperation (n = 75) ( $38.0 \pm 1.8$  mm versus  $36.0 \pm 0.6$  mm;  $p = 0.10$ ). There was a significantly greater annual increase in STJ diameter ( $1.2 \pm 0.5$  mm/yr versus  $0.5 \pm 0.1$  mm/yr;  $p = 0.04$ ) in patients who underwent an autograft reoperation compared to those who did not undergo reoperation (Fig. 3). Compared to patients who had a freestanding root replacement, those with inclusion cylinder aortic root replacement had a smaller initial STJ diameter ( $32.1 \pm 1.6$  mm versus  $36.7 \pm 0.6$  mm;  $p < 0.01$ ) that did not change over time ( $-0.2 \pm 0.2$  mm/yr versus  $0.5 \pm 0.1$  mm/yr;  $p < 0.01$ ). In addition, female gender was associated with a smaller initial STJ diameter ( $32.9 \pm 0.8$  mm in females versus  $38.2 \pm 0.7$  mm in males;  $p < 0.01$ ), and a smaller annual increase in STJ diameter ( $0.33 \pm 0.13$  mm/yr in females versus  $0.58 \pm 0.13$  mm/yr in males;  $p < 0.01$ ). Finally, patients who had preoperative aortic stenosis had a smaller initial STJ diameter compared to those with preoperative AR or combined AS and AR ( $33.9 \pm 1.3$  mm versus  $37.1 \pm 1.3$  mm and  $37.6 \pm 1.3$ , respectively;  $p < 0.01$ ), but the annual increase in STJ diameter did not differ between the hemodynamic diagnoses. Bicuspid valve disease,

patient age, hypertension, prior aortic valve surgery and preoperative aneurysm of the ascending aorta had no effect on either initial or progression of STJ diameter.

## Discussion

The Ross procedure is currently a topic of controversy among cardiologists and cardiac surgeons. Although the survival of patients who undergo this procedure is remarkably good survival comparable to the general population, and is superior to that with other valve substitutes, an increasing number of reoperations for autograft failure have been reported (2-4,9). The mode of autograft failure is, in the majority of cases, slowly progressive dilatation of the neo-aortic root with subsequent AR (10). The present prospective standardized echocardiographic study shows that, in adult patients who underwent autograft aortic root replacement at the authors' center, the increase in nAR and root dimensions was small, but persistent, over the years, and therefore more reoperations should be anticipated. The present observations were in accord with the echocardiographic findings of three other groups that studied dilatation and regurgitation after autograft aortic root replacement (2-4).

The 10 patients who underwent reoperation for autograft dilatation and failure had greater initial nAR and faster progression of regurgitation over time compared to the 80 who did not undergo reoperation during the study period. The initial annulus diameter of these 10 patients was also significantly greater than that of patients who did not undergo autograft reoperation, as was the annual increase in annulus and STJ diameter. Thus, patients who underwent an autograft reoperation began with a less-than-perfect functioning valve substitute after their Ross procedure compared to patients who did not undergo such reoperation. Nevertheless, in patients who did not undergo a reoperation a somewhat slower but significant increase over time in both autograft regurgitation and dilatation of the neo-aortic annulus was observed. These observations suggest that, with time, more patients can be expected to return for a reoperation for autograft dilatation and regurgitation.

Several factors are reported to be associated with increased dilatation and failure rates of autograft roots. These include younger patient age, bicuspid valve disease, and preoperative ascending aorta aneurysm (2-4). The present study showed that none of these factors is associated with increased initial or progression of echocardiographic AR or neo-aortic root dilatation, and this was in accord with clinical observations (11). In addition, hypertension and prior aortic valve surgery did not affect the echocardiographic function and

dimensions of the neo-aortic root over time. Although only six of the present patients underwent aortic root replacement with the inclusion cylinder technique, it was associated with smaller initial annulus and STJ diameters that did not increase over time compared to the 84 patients who had a freestanding root replacement. This suggests that the use of this surgical technique may prevent neo-aortic root dilatation. Whether the root inclusion cylinder technique will prevent autograft failure yet remains unclear, as initial jet length and jet diameter AR and progression of AR over time did not differ compared to patients who underwent freestanding aortic root replacement. As expected, the initial annulus and STJ diameters were smaller in female patients than in males. Surprisingly, initial jet length and jet diameter AR and progression of jet diameter AR were significantly greater in females than in males, and contrasted with the observed smaller increase of STJ diameters in females than in males. This confirmed the observations of Luciani et al. (2), who found female gender to be associated with an increased risk of echocardiographic autograft dysfunction, but not with autograft dilatation. Thus far, female patients in the present authors' experience do not have higher autograft reoperation rates than males, though time will tell whether these echocardiographic observations will also translate to higher reoperation rates in females. Finally, patients with preoperative AR or combined AS and AR had greater initial neo-aortic root dimensions than patients with preoperative AS. As mentioned above, a greater initial annulus diameter was one of the factors associated with an increased risk of reoperation. Therefore, patients with preoperative AR or combined AS and AR may return sooner for a reoperation than would patients with preoperative AS. However, the observation that initial AR and progression of AR and neo-aortic root dilatation were comparable between the hemodynamic diagnoses suggests that the overall effect of hemodynamic diagnosis on echocardiographic and clinical outcome is most likely small.

Initially, Ross used a subcoronary implantation technique for the pulmonary autograft (12). The operation was subsequently modified to a free-standing pulmonary root auto-transplantation in order to preserve the geometry of the leaflets. It now appears that, following the modified Ross operation with a freestanding root replacement, a greater initial annulus and greater initial STJ diameter are predictive of late reoperation. Classic or innovative support techniques for the pulmonary autograft valve seem therefore warranted in an attempt to avoid early and continuing neo-aortic dilatation to prevent AR due to dilatation. Several authors have suggested that reinforcement or reduction of the neo-aortic annulus and STJ using

either pericardium, Dacron graft or Teflon felt may prevent dilatation and subsequent failure of the autograft (2-4,9). A relatively low insertion of the proximal suture line is another means of attempting to prevent pulmonary autograft annulus dilatation (13). The present authors were unable to study the effect of specific annulus reinforcement techniques on echocardiographic autograft function and dimensions over time, as the vast majority of patients underwent a freestanding autograft aortic root replacement without the use of any special techniques to reinforce the annulus. However, in recent years more specific attention was paid at their center to placing the autograft inside the aortic annulus compared to initial experiences.

A limitation of the above-mentioned reinforcement techniques is that they do not solve the problem of the continuing STJ dilatation. Other techniques that employ wrapping of the root with autologous pericardium have been proposed to reduce autograft dilatation (14,15). These techniques might potentially prevent both annular and STJ dilatation, but data relating to late follow up are still lacking (14,15). In the small cohort of the present series where an inclusion cylinder technique was used, no initial or late annulus and STJ dilatation was observed. However, this technique was applied only if the native aortic root had normal dimensions. A final means of preventing root dilatation is to use the subcoronary implantation technique that has regained popularity in recent years, closing the circle that Ross started almost four decades ago. This technique, in experienced hands, yields excellent intermediate results [16].

The statistical analysis of serial echocardiographic data is complicated by several factors: echocardiographic information is obtained at different time points and at different time intervals; echocardiography appointments may be missed; valve function is often variable over time; there is inter- and intra-observer variability; and the use of different types of echocardiographic equipment may also affect the measurements. The Kaplan-Meier method is often used to assess serial echocardiographic data, but it considers time of follow up as a continuous variable, whilst echocardiography data are usually available within a certain time frame and often incomplete in one or more time frames. In addition, the Kaplan-Meier method considers valve dysfunction as an irreversible end-point, while severity of valve dysfunction is often variable over time. Multilevel modeling techniques offer an alternative statistical method that adequately deals with these issues, and in addition allows multivariable risk factor analysis of initial valve function and dimensions and the course of these parameters over time. Thus, the present authors recommend the use of this statistical technique over the Kaplan-

Meier method for the analysis of serial echocardiographic data.

*In conclusion*, adult autograft aortic root replacement results in a small but persistent increase in nAR and neo-aortic dimensions over time. Given the fact that this increase is present both in patients who underwent autograft reoperation and those who did not, more reoperations should be anticipated. Surgeons who perform the autograft procedure should consider support and/or reduction of the annulus and STJ and, if technically possible, combine this with wrapping of the neo-aortic root.

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### References

1. Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. *Lancet* 1967;2:956-958
2. Luciani GB, Casali G, Favaro A, et al. Fate of the aortic root late after Ross operation. *Circulation* 2003;108(Suppl.1):II61-II67
3. Kouchoukos NT, Masetti P, Nickerson NJ, Castner CF, Shannon WD, Davila-Roman VG. The Ross procedure: Long-term clinical and echocardiographic follow-up. *Ann Thorac Surg* 2004;78:773-781; discussion 773-781
4. David TE, Omran A, Ivanov J, et al. Dilation of the pulmonary autograft after the Ross procedure. *J Thorac Cardiovasc Surg* 2000;119:210-220
5. Willems TP, Takkenberg JJ, Steyerberg EW, et al. Human tissue valves in aortic position: Determinants of reoperation and valve regurgitation. *Circulation* 2001;103:1515-1521
6. Perry GJ, Helmcke F, Nanda NC, Byard C, Soto B. Evaluation of aortic insufficiency by Doppler color flow mapping. *J Am Coll Cardiol* 1987;9:952-959
7. Switzer DF, Yoganathan AP, Nanda NC, Woo YR, Ridgway AJ. Calibration of color Doppler flow mapping during extreme hemodynamic conditions in vitro: A foundation for a reliable quantitative grading system for aortic incompetence. *Circulation* 1987;75:837-846
8. Bryk AS, Raudenbush SW. Hierarchical linear models: Applications and data analysis methods. Sage Publications, Newbury Park, 1992
9. Takkenberg JJ, Dossche KM, Hazekamp MG, et al. Report of the Dutch experience with the Ross procedure in 343 patients. *Eur J Cardiothorac Surg* 2002;22:70-77
10. Hokken RB, Takkenberg JJ, van Herwerden LA, Roelandt JR, Bogers AJ. Excessive pulmonary autograft dilatation causes important aortic regurgita-

tion. *Heart* 2003;89:933-934

11. Bogers AJ, Kappetein AP, Roos-Hesselink JW, Takkenberg JJ. Is a bicuspid aortic valve a risk factor for adverse outcome after an autograft procedure? *Ann Thorac Surg* 2004;77:1998-2003
12. Chambers JC, Somerville J, Stone S, Ross DN. Pulmonary autograft procedure for aortic valve disease: Long-term results of the pioneer series. *Circulation* 1997;96:2206-2214
13. Ross DN. Pulmonary autografts: The unresolved issues. *J Heart Valve Dis* 1997;6:330-332
14. Simon-Kupilik N, Bialy J, Moidl R, et al. Dilatation of the autograft root after the Ross operation. *Eur J Cardiothorac Surg* 2002;21:470-473
15. Pacifico AD, Kirklin JK, McGiffin DC, Matter GJ, Nanda NC, Diethelm AG. The Ross operation: Early echocardiographic comparison of different operative techniques. *J Heart Valve Dis* 1994;3:365-370
16. Sievers H, Dahmen G, Graf B, Stierle U, Ziegler A, Schmidtke C. Midterm results of the Ross procedure preserving the patient's aortic root. *Circulation* 2003;108(Suppl.1):II55-II60

### Meeting discussion

**DR. HANS-H. SIEVERS** (Luebeck, Germany): In a previous presentation, the increase in aortic regurgitation had a nonlinear function. Can you explain why in your model there is a linear relationship over time with an increase in aortic insufficiency? Are there sufficient patients to justify this linearity?

**DR. JOHANNA J. M. TAKKENBERG** (Rotterdam, Netherlands): We looked at several models, and the linear model had the best fit. Of course very soon after the operation there may be an early increased phase of dilatation and thereafter a steady phase. You should remember that these echocardiography measurements were started at six months after surgery, so the initial steep increase may have been passed by that time.

**DR. JOHN W. BROWN** (Indianapolis, Indiana, USA): Did you attempt to control the annulus in the sinotubular junction as a routine in this patient population?

**DR. TAKKENBERG**: No. We do not use any reinforcement techniques for the proximal suture line. Recently, we have paid more attention towards placing the autograft inside the aortic annulus. We may not have done that in earlier years, but it is difficult to retrieve after such a long time.

**DR. BROWN**: Was it a philosophical decision not to try to reinforce, even though much information published over the past 10 years says that it is helpful? Do you have a reason for not reinforcing the annulus in the sinotubular junction, particularly in this primarily

adult patient population?

**DR. TAKKENBERG:** That is the surgeon's decision, but I can't imagine that after seeing these results you would consider reinforcement, not only of the proximal suture line but also of the distal suture line.

**DR. BROWN:** I found the aneurysmal dilatation of the ascending aorta interesting. Many of these patients presented with a 36-45 mm ascending aorta, which may be post-stenotic dilatation. We have routinely replaced those ascending aortas with a prosthetic graft, thinking that even further dilatation would flare into the sinotubular junction, even if we had tried to limit it. The stretch phenomena has caused some of our patients to develop late regurgitation that they didn't have initially. It doesn't sound as though that was a risk factor in your patient population.

**DR. TAKKENBERG:** No, it was not a risk factor, but I know that if the ascending aorta is very dilated, the surgeon will carry out some tailoring to make it fit better to the autografts.

**DR. PAUL H. SCHOOF** (Leiden, Netherlands): We have similar worrisome findings in adult patients, and in fact we stopped the Ross operation in adults - we now only use it in children. Has your policy or your strategy changed in Rotterdam?

**DR. TAKKENBERG:** Yes, the number of Ross operations performed at our center has fallen dramatically. In the mid-1990s there were many Ross operations, but today we only use it in children.