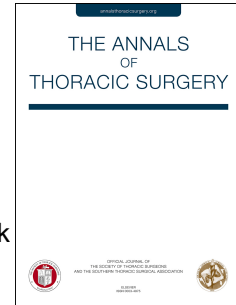


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Rajdeep Bilkhu, MRCS, Maite Tome, PhD, FRCP, Anna Marciniak, PhD, FRCP, Mark Edsell, FRCA, Marjan Jahangiri, FRCS(CTh)



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# Does the aortic annulus dilate following aortic root remodelling?

Rajdeep Bilkhu MRCS<sup>1</sup>, Maite Tome PhD, FRCP<sup>2</sup>, Anna Marciniak PhD, FRCP<sup>2</sup>, Mark Edsell FRCA<sup>3</sup>,

Marjan Jahangiri FRCS(CTh)<sup>1</sup>

Departments of Cardiothoracic Surgery<sup>1</sup>, Cardiology<sup>2</sup> and Cardiac Anaesthesia<sup>3</sup>

St. George's Hospital, London

**Running Head:** Annular dilatation and root remodelling

**Address for correspondence:**

Marjan Jahangiri  
Department of Cardiac Surgery,  
St. George's Hospital,  
Blackshaw Road,  
London SW17 0QT, United Kingdom  
Email: [marjan.jahangiri@stgeorges.nhs.uk](mailto:marjan.jahangiri@stgeorges.nhs.uk)

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**Background.** The two main techniques of valve sparing aortic root replacement (VSRR) are remodelling and reimplantation. There is concern that the aortic annulus, which is not stabilized in remodelling technique, may dilate over time and cause aortic regurgitation (AR). Our aim was to assess whether the aortic annulus dilates following VSRR with remodelling technique without aortic annuloplasty.

**Methods.** Data on patients undergoing elective or urgent VSRR remodelling technique between 2005 and 2018 were collected. Patients undergoing arch and emergency surgery for acute type A aortic dissection were excluded. Pre-operative aortic annulus diameter was measured by transthoracic echocardiography (TTE) and this was compared to annulus diameter measured from the most recently available TTE. The requirement for re-intervention during follow up was recorded.

**Results.** Between 2005 and 2018, 98 patients underwent VSRR. Sixty-six (67.3%) had Marfan or Loeys Dietz syndrome. Median age was 60 (18-68) and 71 (72.4%) were male. Median cross clamp and cardiopulmonary bypass times were 122 (104-164) and 138 (121-198) minutes respectively. Median ICU and hospital stay were 1 and 6 days respectively. No patients suffered perioperative stroke. There was no in-hospital mortality. At median follow up of 7.1 years (5-129 months), mean post-operative annular diameter was 25.7mm, from 24.2mm pre operatively,  $p=0.403$ . One patient required aortic valve replacement during follow up. Freedom from moderate or severe AR was 97%.

**Conclusions.** There was no significant aortic annular dilatation in selected patients undergoing remodelling VSRR. Our data does not support routine use of annuloplasty in patients with annular diameter  $\leq 25$ mm.

The mainstay of treatment for patients with aortic root pathology has been replacement of the aortic root and valve with a composite valved graft [1].

Given the largely prophylactic nature of surgery in patients with aortic root dilatation, and the young age at which these patients undergo surgery, there has been an increasing focus on aortic valve sparing techniques (valve sparing aortic root replacement, VSRR). This allows preservation of the native valve leaflets and has the major advantage of avoiding anticoagulation in a patient who may otherwise have received a mechanical composite graft. In addition, VSRR has been associated with reduced mortality and valve related complications, compared to aortic root replacement with either a biological or mechanical composite graft [2]. VSRR is also recognised to be an appropriate alternative to composite valved graft conduit root replacement (Bentall) and has been demonstrated to show excellent post operative haemodynamics, with low incidence of perioperative mortality and morbidity [3].

There are two methods of VSRR which have been performed for more than 20 years. These are the remodelling technique [4] described by Yacoub and colleagues and the reimplantation [5] technique described by David and colleagues. A number of modifications to both these techniques have been made since their introduction. The remodelling technique is a more physiological root repair with the formation of neo-aortic sinuses. The reimplantation technique however involves reimplanting the aortic valve into a straight tubed graft, as originally described. By nature of the technique, the aortic annulus is stabilised in the reimplantation procedure. The originally described remodelling technique does not specifically address the aortic annulus and there is therefore concern that the aortic annulus may dilate over time, particularly in patients with Marfan syndrome [6,7]. Some have advocated the use of an annuloplasty ring or suture at the time of root remodelling to avoid possible dilatation of the aortic annulus [8,9]. Despite this, there is conflicting evidence suggesting that the annulus does not dilate over time [10].

Our aim was therefore to assess the outcomes of VSRR in patients undergoing the remodelling technique, as originally described, without the use of annuloplasty ring or suture.

## **Patients and Methods**

Between 2005 and 2018, demographic, clinical and operative data for all patients undergoing VSRR was prospectively collected. Local ethical approval was obtained. The primary outcome was diameter of the aortic annulus at follow up. Secondary outcomes were incidence of AR and reintervention during follow up.

### *Indications for Surgery*

The indications for surgery were root aneurysm with normal or near normal valve function and diameter  $\geq 5.5$ cm in symptomatic or asymptomatic individuals without connective tissue disease. Patients with aortic root diameter  $\geq 4.5$ cm and who were symptomatic or asymptomatic with connective tissue disease, without risk factors were offered surgery. In patients with aortic root diameter of  $\geq 4.5$  cm and if there was a family history of dissection or growth  $> 0.3$  cm/year, then they were also offered surgery.

### *Operative Technique*

Our standardised method of root remodelling is as follows. Following median sternotomy, cardiopulmonary bypass is established at 35°C. If the dilatation of the ascending aorta extends to its distal section, then to maximize excision after cross-clamping, peripheral cannulation is used, otherwise central aortic cannulation is performed. A left ventricular vent is inserted via the right superior pulmonary vein. Myocardial protection is achieved using antegrade cold blood-based cardioplegic solution with topical cooling.

The diseased aorta is excised and coronary ostia mobilised as buttons, leaving a 3–5 mm rim of tissue above the aortic annulus and around the coronary buttons. A prosthetic graft larger (3 mm added to the annular size) than the measured annulus size is selected. This avoids inducing aortic stenosis or cusp prolapse. If annulus size is 25mm or above, then we consider annuloplasty, providing there is no more than moderate AR. Teflon-butressed 4/0 polypropylene stay sutures are placed on each of the commissures and traction applied upwards until optimum coaptation of the valve cusps is achieved. The graft is cut at three points to match the commissures of the aortic valve and shaped to match the aortic sinuses of Valsalva in depth and width, which is measured using a ruler and marked on the graft (Fig. 1A and 1C). The three commissures are sutured to the corresponding apices of the cuts on the graft, using 4/0 polypropylene. Care is taken to ensure symmetry (Fig 1). The graft is then lowered into position and the sutures tied, with the knots on the outside. Continuous 4/0 polypropylene is used to suture the graft to the small rim of remaining aortic tissue. The coronary buttons are reimplanted with continuous 5/0 polypropylene and the distal aortic anastomosis is completed with continuous 4/0 polypropylene.

Pre operative aortic annulus diameter was measured by transthoracic echocardiography. All patients underwent echocardiography prior to discharge and were followed up at 8 weeks, 6 months and then annually with echocardiography and CT or MRI. Annulus diameter, measured from the most recently available transthoracic echocardiogram, was compared to the pre operative diameter. The annulus was measured in the long axis view at the hinge point of the aortic valve leaflets in mid-systole. The first author (RB) measured all the annular sizes being blind to the reported measurement of the echocardiographers. If there was a discrepancy, measurements were redone by the cardiologist specialising in imaging (AM). The requirement for any re-intervention during follow up was recorded.

### *Statistical Analysis*

Continuous variables are expressed as mean  $\pm$  SD and percentage for categorical variables. Median is provided for continuous variables not following normal distribution. Student's t-test was used as appropriate to assess the difference between aortic annular dimensions, pre and post operatively, with values of  $p < 0.05$  considered statistically significant. Analyses were performed using SPSS® (Statistical Package for Social Sciences, USA) version 24.

### **Results**

Between 2005 and 2018, 98 patients underwent remodelling VSRR at our institution. Sixty six (67.3%) had connective tissue disease of which 61 (92.4%) had Marfan Syndrome and 5 (7.6%) had Loeys-Dietz syndrome. Two patients (2%) had bicuspid aortic valve. One patient (1%) during the study period was pregnant at the time of surgery. Clinical characteristics are shown in Table 1 and operative details in Table 2.

During the period of the current study, 453 patients underwent complete aortic root and ascending aorta replacement (Bentall procedure). This cohort excludes aortic dissection and VSRR. 340 patients (75%) had predominantly aortic stenosis and 86 patients (19%) had AR of moderate and severe degrees. The hospital mortality in this group was 1.2%. Survival at a median follow-up of 5.6 years was 93.5%. We have reported this cohort previously [11].

### *Preoperative AR*

Of 98 patients, 45 (45.9%) had no pre operative AR. Forty-nine (50%) and 4 (4.1%) had mild and moderate AR respectively.

#### *Graft Sizing and Cusp Repair*

Median aortic graft size was 28mm (range 20-30mm). A straight vascular graft was used in each case. Cusp repair was performed in 2 patients, where the edges of the non coronary cusp required reduction. In 2 patients, suspension/lifting of the non/right coronary commissure was performed.

#### *Follow up and Annular Dimension*

The median aortic annulus diameter measured on transthoracic echocardiogram prior to surgery was  $24.2 \pm 7.1$ mm. At a median follow up of 7.1 years (5-129 months), mean aortic annulus diameter was  $25.7 \pm 5$ mm,  $p=0.403$ .

#### *Early Mortality and Complications*

Operative mortality and complications are shown in Table 2. There were no in-hospital deaths and no incidence of stroke, re-sternotomy for bleeding, hemofiltration, peripheral vascular injury or laparotomy. One patient required coronary artery bypass graft surgery. In this patient, it was not possible to perform a coronary angiogram prior to surgery due to access problems and she had a CT angiogram instead which showed grossly normal coronary arteries. However, an hour following cessation of cardiopulmonary bypass she developed ECG changes in the lateral leads and coronary artery bypass grafts were performed. She did well and was discharged 12 days later. A later angiogram revealed ostial narrowing of the circumflex vessel.

Median intensive care unit (ICU) and hospital stay were 1 and 6 days respectively.

#### *Outcomes Following Hospital Discharge and Reintervention*

Follow-up was complete in 94% of the patients. At a median follow up of 7.1 years (5-129 months), freedom from moderate or severe aortic regurgitation was 97%. One patient required reoperation and underwent aortic valve replacement for cusp prolapse. One patient developed moderate AR. This was a patient with Marfan syndrome who was noted to have valve deterioration during pregnancy, but this was not related to annular dilatation.

**Comment**

We have demonstrated that in patients undergoing VSRR using the remodelling technique that the aortic annulus does not dilate over time in patients with annular diameter of 25mm or less. In addition, we have demonstrated that surgery can be performed with minimal complications and very low mortality, with a low incidence of AR during follow up.

The occurrence or recurrence of AR in patients undergoing root remodelling has been attributed to aortic annular dilatation, particularly in those with Marfan syndrome [7,12]. David and colleagues identified that in their smaller cohort of 22 Marfan patients undergoing root remodelling, half were noted to have dilatation of the annulus over a mean follow up of  $49 \pm 38$  months [12]. However, Yacoub and colleagues in their 10 year follow up of the technique they originally described suggested that the aortic annulus is generally spared in both aneurysm and dissection [6]. Our data is consistent with this and demonstrates that the aortic annulus does not dilate with time, even in patients with Marfan syndrome.

In recent years, the addition of the annuloplasty ring or suture to the remodelling technique has been advocated [8,13,14]. Lansac and colleagues have demonstrated excellent early and long term outcomes following VSRR. In a series of 177 patients from the AVIATOR (Aortic Valve repair InternATIOnal Registry) registry, annular dimension greater than 25mm prompted stabilization of the annulus with an annuloplasty ring. This requires further dissection of the aortic root to the level of the subvalvular plane to allow placement of the ring, which may prolong ischaemic time. In addition, in their early experience, they used a self-made ring of Dacron from the vascular graft to create an annular ring, which arguably has the disadvantage of being non expansile. However, they have now changed to using an expansile custom made ring. The theoretical benefit of the addition of the ring is therefore to reduce annular size and thereby reduce long term failure, of which uncorrected annular dilatation at time of surgery has been shown to be a risk factor.



Failure of the remodelling technique, or valve sparing procedures, we feel is likely to be related largely to leaflet geometry as well as the pre-operative annular dimension. This has been explored by Kuniyama and colleagues, who have demonstrated in their large series of 430 patients, that the long term durability of VSRR is not related solely to the technique or repair but to the configuration of the leaflets and also the preoperative annular dimension [15]. In a review by David, they suggest that remodelling be considered in those with a normal annular dimension and this is similar to the conclusion by Lansac and colleagues that an annular dimension of  $>25\text{mm}$  is predictive of late failure of valve sparing operations [7,13]. As a result, our routine practice is to consider VSRR without annuloplasty in those with pre operative aortic annulus of  $\leq 25\text{mm}$ . In patients with annular dimension of  $>25\text{mm}$ , we would consider annuloplasty providing there is no significant AR.

In relation to leaflet geometry, Schäfers and colleagues have suggested that cusp prolapse can be induced by root repair, particularly in the remodelling technique and they attribute part of their success in remodelling technique to the measurement of leaflet effective height, which should be 9-10mm as measured by a specially designed caliper [16]. We did not employ this technique in our series, however we would perform cusp plication if there was evidence of cusp prolapse at the time of surgery.

Furthermore, with regard to annular stabilization, Schäfers and colleagues studied a large number of patients undergoing the remodelling technique, up to two years. More than half of the 798 patients studied underwent no annular stabilization [10]. They measured the pre and post operative annular diameter and concluded that the aortic annulus rarely dilates over time and that even without annuloplasty, the aortic annular dimension is reduced following remodelling. They suggest that by achieving valve competence, then the annulus is unlikely to dilate. Our results are consistent with their findings in that the annulus does not dilate following surgery at a median follow-up of 7.1 years.

In David reimplantation technique the aortic annulus is stabilized. However, reimplantation, as originally described, was based on the aortic valve being reimplanted into a straight vascular graft. One of the theoretical benefits of the remodelling technique is the creation of neo-aortic sinuses. In an experimental study by Fries and colleagues, they demonstrated using an in vivo model that leaflet motion was much smoother in a model of the remodelling technique compared to reimplantation [17]. This was also demonstrated by DePaulis and colleagues [18]. Maintaining leaflet motion may improve valve durability and

thereby provide longevity of repair, which we feel is an important advantage of the remodelling technique, particularly given the younger cohort of patients who undergo this procedure.

In addition to valve leaflet durability, it has been demonstrated that the remodelling technique also maintains and preserves normal geometry as well as dynamic function of the root. In a small study by Yacoub and colleagues, they demonstrated using multimodality imaging techniques, including CT scanning, cardiac MRI and computational fluid dynamics that the remodelling technique reduced postoperative annular dimension without the use of annuloplasty ring or suture and that the elliptical shape of the aortic annulus was maintained and changed during the cardiac cycle and that there was preserved reservoir function of the aorta as well as a normalised pattern of flow in the aortic root, ascending aorta and distal aorta [19]. Whilst they did not relate these to clinical outcomes, these findings may clearly have an impact on long term function of the aortic root and therefore may have an impact on clinical outcomes and quality of life.

Our study is limited by the number of patients and only midterm follow-up. There was no dilatation of the annulus seen at median follow-up of seven and maximum of eleven years. It may be that, in particular, patients with connective tissue disease, that there may be dilatation at longer follow-up. The current series is a select population of patients who are referred early in the course of their disease. Furthermore, the occurrence of BAV and more than moderate AR was low. These contribute to the good outcomes reported.

### *Conclusion*

We have demonstrated that the aortic annulus does not dilate over time in patients undergoing VSRR with the remodelling technique with a preoperative annular dimension of 25mm or less. There is a low incidence of AR during follow up and surgery can be performed with minimal complications and mortality. Our data does not support the routine use of annuloplasty in patients with annular diameter  $\leq 25$ mm.

**Figure legends**

Fig 1. Steps of measuring the depth of each sinus (A); fashioning the prosthetic graft (B-E) and fixing the commissures (F, G).

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*Table 1 Demographics*

Demographic	No. (range or %)
N	98
Age: median (range)	60 (18-68)
Male	71 (72.4%)
Connective tissue disease	64 (65.3%)
Marfan Syndrome	59 (92.2%)
Loeys-Dietz Syndrome	5 (7.8%)
Bicuspid aortic valve	2 (2%)
Logistic Euroscore $\pm$ SD	3 $\pm$ 2
LV function <45%	8 (8.2%)
Median ascending aorta diameter (mm)	39 (28-50)
Preoperative mild AR	49 (50%)
Preoperative moderate AR	4 (4.1%)
No preoperative AR	45 (45.9%)

SD = standard deviation; LV = left ventricular; AR = aortic regurgitation

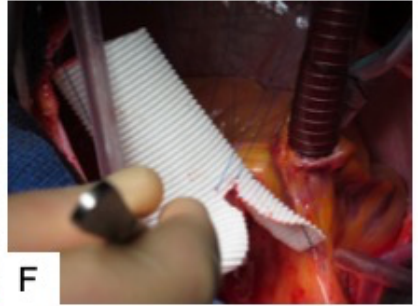
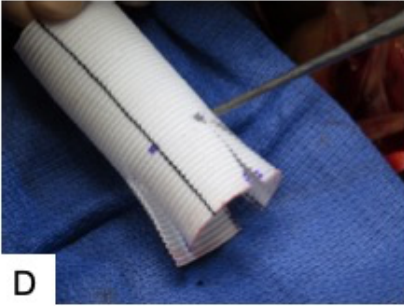
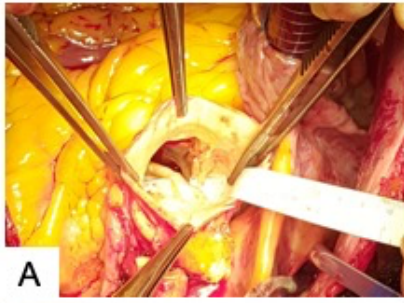
*Table 2 Operative Details*

Outcome	Number (range or %)
<i>Operative</i>	
Cross clamp time (mins)	122 (104-164)
Cardiopulmonary bypass time (mins)	138 (121-198)
Conversion to aortic root replacement	1 (1.0%)
<i>Post-operative</i>	
Total hospital mortality	0
Stroke	0
Re-sternotomy for bleeding	0
Hemofiltration	0
Peripheral vascular injury	0
Laparotomy	0
Median intensive care unit stay (days)	1 (1-3)
Median hospital stay (days)	6 (5-7)

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