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## Imaging techniques in aortic valve and root surgery

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## Chapter 6:

### Transthoracic echocardiography for selection of tubular graft size in David reimplantation technique

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## Abstract

**Background:** Selection of tubular graft size during David reimplantation technique for aortic root dilation is based on perioperative leaflet height measurements. The present study evaluated whether transthoracic echocardiography (TTE)-based algorithms may help in selecting the graft size preoperatively.

**Methods:** Thirty patients (52±11 years old, 73% men) who underwent David reimplantation technique were evaluated. The implanted graft size was based on the David's formula. Leaflet height (diameter =  $1.1 \cdot ((2 \cdot 2/3 \cdot \text{leaflet height}) + 2)$ ), leaflet length (diameter =  $((2 \cdot 2/3 \cdot \text{leaflet length}) + 2)$ ) and leaflet area (diameter =  $0.8 \cdot ((2 \cdot \sqrt{(\text{total leaflet area} / \pi)}) + 2)$ ) TTE-derived formulas were retrospectively developed. The percentage of under- or oversized implanted grafts was calculated and the association between the adequacy of graft sizing using TTE-derived formulas and the incidence of residual aortic regurgitation (AR) was evaluated retrospectively.

**Results:** The incidence of postoperative mild residual AR was 23%. The actually implanted graft diameter was oversized based on leaflet height in 15 (50%) patients, based on leaflet length in 13 (43%) patients and based on leaflet area TTE-derived formula in 11 (37%) patients. The incidence of mild AR was significantly lower in undersized grafts compared with oversized grafts based on leaflet length TTE-derived formula (6% vs. 46%,  $p=0.032$ ) and leaflet area TTE-derived formula (5% vs. 55%,  $p=0.009$ ).

**Conclusion:** In patients undergoing David reimplantation technique, grafts considered undersized according to the leaflet length or leaflet area TTE-derived formula were associated with less incidence of residual AR than patients with oversized grafts.

## Introduction

The David reimplantation technique is a feasible and effective surgical valve-sparing aortic root replacement for patients with aortic regurgitation (AR) due to dilation of the aortic root.<sup>1</sup> The incidence of recurrent significant AR (AR  $\geq$  grade 3) during follow-up ranges between 4 and 22%.<sup>2,3</sup> The presence of residual AR after the surgery has been associated with a 5-fold higher risk of recurrent AR during follow-up.<sup>2</sup> To prevent residual AR, adequate sizing of the tubular graft is pivotal.<sup>4</sup> Leaflet coaptation may be insufficient if the graft is too large (oversized), whereas leaflet prolapse and cusp abrasion may occur if the graft is too small (undersized). In current practice, the tubular graft size is based on intraoperative measurement of the average leaflet height using the David's formula (diameter =  $2 \cdot 2/3 \cdot h_{\text{leaflet}} + (2 \cdot A_{\text{O}_{\text{wall}}})$ ) where  $h_{\text{leaflet}}$  is the leaflet height measured with surgical callipers and  $A_{\text{O}_{\text{wall}}}$  is the thickness of the aortic wall.<sup>5</sup> We hypothesized that preoperative transthoracic echocardiography (TTE) may be helpful in determining the appropriate graft size in David reimplantation technique. Therefore the aims of the present study were first to develop TTE-derived formulas to calculate the recommended graft size and second to assess whether there was an association between graft sizing using the TTE-derived formulas and the presence of residual AR after surgery.

## Methods

### *Patients*

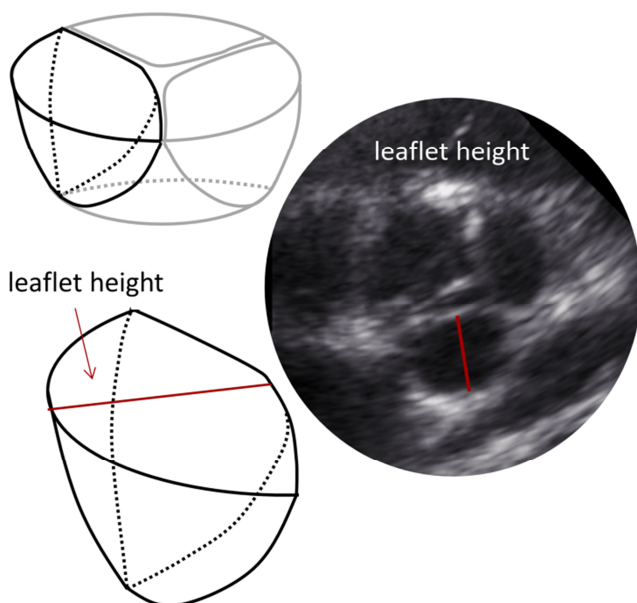
Thirty patients with aortic root pathology who underwent surgical valve-sparing aortic root replacement using the David reimplantation technique at the Leiden University Medical Center between 2001 and 2014 with sufficient echocardiographic data were included in the present study. Patients who underwent additional aortic leaflet repair were excluded. Patients who underwent concomitant mitral valve or tricuspid valve surgery were not excluded. Clinical and surgical data were collected at the departmental Cardiology Information System (EPD-Vision, Leiden University Medical Center, Leiden, Netherlands) and retrospectively analysed. AR grade and aortic valve geometry were assessed retrospectively with preoperative two-dimensional (2D) TTE. Three TTE-derived formulas were developed to select the graft size for the David reimplantation technique, based on leaflet height, leaflet length and leaflet area (see below). The implanted graft was sized using the David's formula based on surgically measured leaflet height.<sup>5</sup> Transesophageal echocardiography (TEE) was used to assess residual AR directly after the surgery. The percentage of under- or oversized implanted grafts was reported and the association between the adequacy of graft sizing using the TTE-derived formulas and the incidence of residual AR was evaluated. The institutional review board approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent.

### *Two-dimensional transthoracic echocardiography*

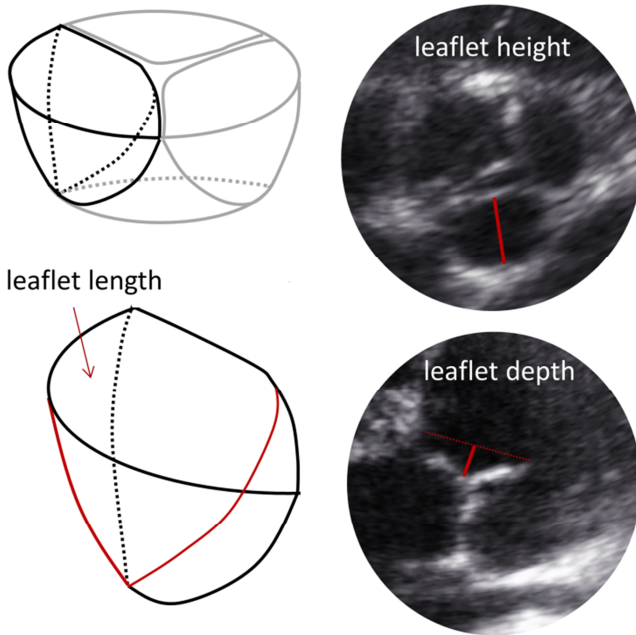
Preoperative TTE was performed at rest using commercially available ultrasound systems (System Five, Vivid 7 and E9, General Electric Healthcare, Vingmed, Horten, Norway) equipped with 3.5-MHz or M5S transducers. 2D and Doppler echocardiographic data were acquired at the parasternal and apical views according to current recommendations.<sup>6</sup> The echocardiographic data were digitally stored in cine-loop format and were retrospectively analysed using EchoPac (112.0.1, GE Medical Systems, Horten, Norway).

AR grade was assessed using colour, pulsed and continuous wave Doppler recordings and using a multiparametric approach that includes the measurement of the jet width relative to the LV outflow tract diameter, vena contracta and the pressure half time of the regurgitant flow (if feasible) according to current recommendations.<sup>7</sup> AR was graded as 0 (absent), 1 (mild), 2 (mild-moderate), 3 (moderate-severe) or 4 (severe). The AR jet was classified as central or eccentric.

Aortic valve geometry was measured during end-diastole (just before opening of the aortic valve) in the parasternal short-axis and long-axis view. The image was zoomed on the aortic valve. The leaflet height was measured in the parasternal short-axis view from the internal border of the aortic root to the free edge of the leaflet and was averaged per patient (Figure 1). The leaflet depth was measured in the parasternal long-axis view as the distance between the line from the leaflet insertion to the leaflet tip and the most convex point of the leaflet.

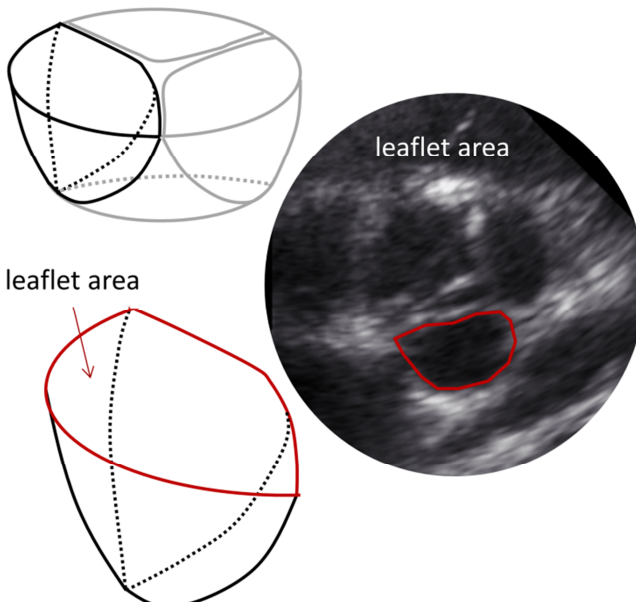


**Figure 1. Leaflet height on transthoracic echocardiography.** Leaflet height was measured during end diastole in parasternal short-axis view from the internal aortic root border to the free edge of the leaflet.



**Figure 2. Leaflet length on transthoracic echocardiography.** The leaflet length over the belly of the leaflet was subsequently calculated as the half perimeter of the ellipse described by the average leaflet height as major axis and twice the leaflet depth as minor axis. The leaflet height was measured in the parasternal short-axis view from the internal border of the aortic root to the free edge of the leaflet. The leaflet depth was measured in the parasternal long-axis view as the distance between the line from the leaflet insertion to the leaflet tip and the most convex point of the leaflet.

The leaflet length over the belly of the leaflet was subsequently calculated as the half perimeter of the ellipse described by the average leaflet height as major axis and twice the leaflet depth as minor axis (Figure 2). The leaflet area was measured in the parasternal short-axis view per leaflet and was then summed per patient to obtain the total leaflet area (Figure 3).



**Figure 3. Leaflet area on transthoracic echocardiography.** Leaflet area was measured during end diastole in parasternal short-axis view.

### *Surgery*

After median sternotomy, cardiopulmonary bypass was set through cannulation of the distal ascending aorta or proximal aortic arch. In patients with aortic dissection or dilation of the distal ascending aorta, cannulation via the sub-clavian or femoral arterial route was performed. The aorta was incised 2 cm above the ostium of the right coronary artery and resected until the aortoventricular junction (AVJ).

The height of all leaflets was measured using surgical callipers from the nadir of the leaflet insertion on the AVJ to the free margin of each leaflet and then averaged. The size of the graft at the level of the AVJ was determined using the David's formula:  $(\text{diameter} = (h_{\text{leaflet}} \cdot 2 \cdot 2/3) + (2 \cdot A_{\text{owall}}))$ , where  $h_{\text{leaflet}}$  was the average leaflet height measured with surgical calipers.<sup>5</sup> The thickness of the aortic wall ( $A_{\text{owall}}$ ) was estimated as 1 mm. David I procedure was performed in 6 patients (20%) as previously described.<sup>5</sup> A modified David V procedure was performed in 24 patients (80%), resizing the ventricular rim of the graft according to the calculated size of the AVJ following the David's formula.<sup>8</sup> In both David I and modified David V techniques, the coronary buttons were reimplanted into the respective neosinuses. Directly after the procedure, the presence of residual AR was assessed using TEE. Residual AR was graded as none, trace or mild based on the TEE report. There was no more than mild AR after the procedures. Furthermore, the coaptation length of the aortic valve was measured on TEE during diastole when the valve was closed.

### *Statistical analysis*

Analyses were performed using the SPSS software version 20 (SPSS, Chicago, IL, USA). Continuous variables were displayed as mean  $\pm$  standard deviation if normally distributed and as median and interquartile range if non-normally distributed. TTE-derived formulas based on leaflet height, leaflet length and leaflet area were retrospectively developed using linear regression analysis without including an intercept. Per patient, the recommended graft diameter was calculated for each TTE-derived formula and rounded to whole millimetres. Patients with an implanted graft smaller than or equal to that recommended by TTE-derived formulas (undersized) were compared with patients with an implanted graft larger than recommended by TTE-derived formulas (oversized) using the chi-square test. All statistical tests were two-sided. A  $p$ -value  $< 0.05$  was considered statistically significant.

## **Results**

### *Development of transthoracic echocardiography-derived formulas*

A total of 30 patients (mean age  $52 \pm 11$  years, 73% men) who underwent the David reimplantation technique because of aortic root pathology were evaluated. The clinical, echocardiographic and surgical characteristics are presented in Table 1.



**Table 1: Baseline clinical, echocardiographic and surgical characteristics.**

	All patients (n=30)
<i>Clinical characteristics:</i>	
Age (years)	52 ± 11
Male	22 (73%)
Body surface area (m <sup>2</sup> )	2.02 ± 0.16
Smoking	8 (27%)
Diabetes	0 (0%)
Hypertension	7 (23%)
Dyslipidaemia	5 (17%)
NYHA functional class	
I	17 (57%)
II	6 (20%)
III	7 (23%)
IV	0 (0%)
<i>Echocardiographic characteristics:</i>	
Aortic regurgitation	
Grade 0	5 (17%)
Grade 1	4 (13%)
Grade 2	12 (40%)
Grade 3	5 (17%)
Grade 4	4 (13%)
Aortic regurgitation jet direction	
No jet	5 (17%)
Central jet	15 (50%)
Eccentric jet	10 (33%)
Average leaflet height (cm)	1.9 ± 0.3
Total leaflet area (cm <sup>2</sup> )	10.9 ± 3.0
<i>Surgical characteristics:</i>	
Bicuspid aortic valve	3 (10%)
EuroSCORE II (%)	1.9 (1.2 – 2.6)
Reimplantation technique	
David I	6 (20%)
David V	24 (80%)
Graft diameter at level of AVJ (mm)	30 ± 3

Data are presented as number (percentage), as mean ± standard deviation or as median (interquartile range). AVJ = Aortoventricular Junction. EuroSCORE = European System for Cardiac Operative Risk Evaluation. NYHA = New York Heart Association.

The ratio between the surgically measured leaflet height and echocardiographic measured leaflet height was on average 1.1±0.2, indicating that TTE underestimated the leaflet height. This correction factor was taken into account when the TTE-derived formula based on leaflet height was developed similar to the David's formula. Linear regression analysis was performed to compare the calculated diameter based on TTE-measured leaflet height and the diameter based on surgically measured leaflet height (both: diameter =  $(2 \cdot 2/3 \cdot h_{\text{leaflet}}) + 2$ ) (Figure 4). The slope was 1.1 (95% confidence interval: 1.0-1.2; p<0.001) indicating that the diameter obtained by TTE-derived formula based on the leaflet height had to be multiplied by factor 1.1

to obtain the recommended diameter. Therefore the TTE-derived formula based on leaflet height was: diameter =  $1.1 \cdot ((2 \cdot 2/3 \cdot \text{height}) + 2)$ .

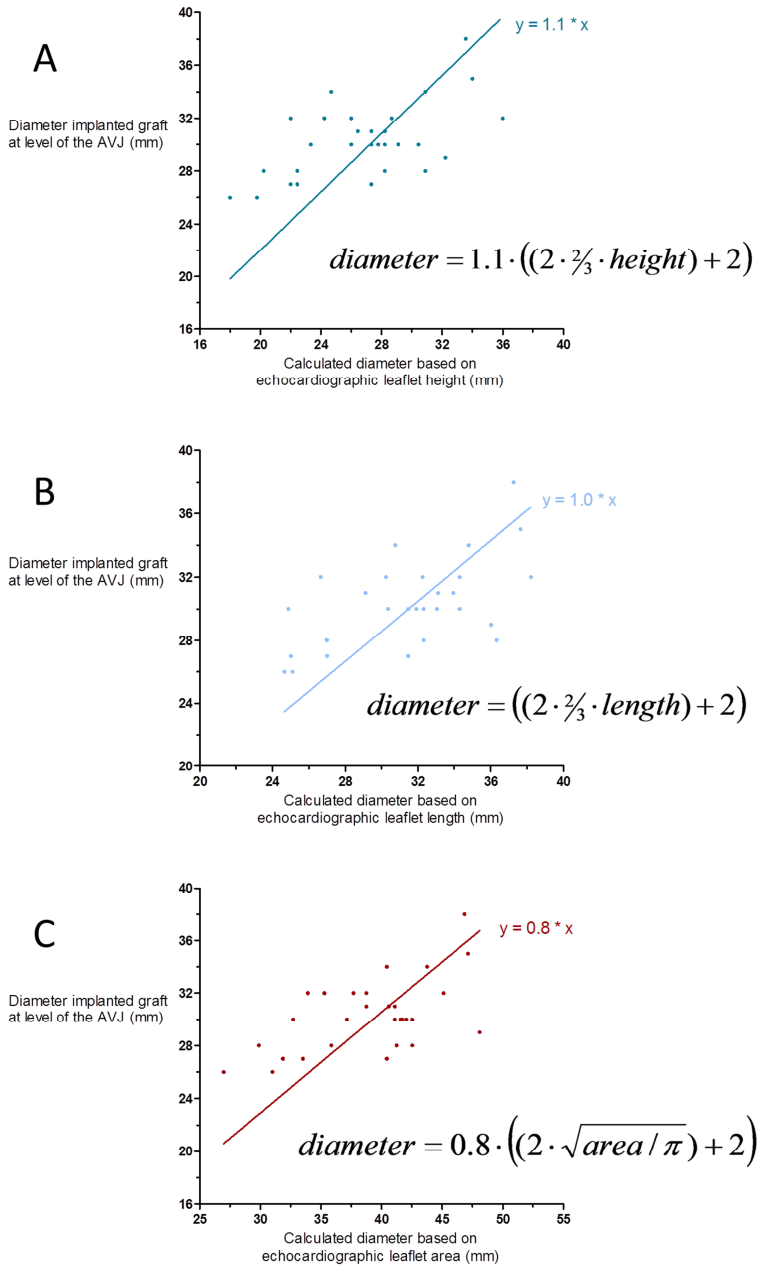
Secondly, the leaflet length TTE-derived formula was developed. Linear regression analysis was performed to compare the calculated diameter based on leaflet length and the diameter of the actually implanted graft (Figure 4). The slope was 1.0 (95% confidence interval: 0.9-1.0;  $p < 0.001$ ); therefore, no correction factor is needed resulting in the TTE-derived formula based on leaflet length: diameter =  $((2 \cdot 2/3 \cdot \text{length}) + 2)$ .

Lastly, the TTE-derived formula based on leaflet area was developed. As area equals  $\pi$  times the squared radius, the diameter was calculated as diameter =  $(2 \cdot \sqrt{(\text{total leaflet area} / \pi)}) + 2$ . Linear regression analysis was performed to obtain a correction factor for converting the diameter based on TTE measurements to a surgically applicable diameter (Figure 4). The slope was 0.8 (95% confidence interval: 0.7-0.8;  $p < 0.001$ ) indicating that the diameter obtained by TTE-derived formula based on leaflet area had to be multiplied by factor 0.8 for the recommended diameter. The TTE-derived formula based on leaflet area was: diameter =  $0.8 \cdot ((2 \cdot \sqrt{(\text{total leaflet area} / \pi)}) + 2)$ .

#### *Relation between oversizing and residual aortic regurgitation*

The implanted graft diameter was considered oversized based on leaflet height TTE-derived formula in 15 (50%) patients, based on leaflet length TTE-derived formula in 13 (43%) patients and based on leaflet area TTE-derived formula in 11 (37%) patients. For the overall population, mild residual AR, assessed with intraoperative TEE, was present in 7 (23%) patients whereas the remaining 23 (77%) patients did not have AR.

Chi-square test was performed to assess whether an oversized graft according to TTE-derived formulas was associated with higher rates of residual AR. The results are presented in Figure 5. Residual AR was present in 5 (33%) patients with oversized graft according to the leaflet height TTE-derived formula, and in 2 (13%) patients with an undersized graft ( $p = 0.388$ ). According to the leaflet length TTE-derived formula, residual AR was more often present in patients who received an oversized graft (6 (46%) patients) compared with patients who received an undersized graft (1 (6%) patients;  $p = 0.032$ ). In patients who received an oversized graft according to leaflet area TTE-derived formula, the prevalence of residual AR was 55%. In patients who received an undersized graft, there was only 1 (5%) patient with residual AR ( $p = 0.009$ ). The coaptation length of the aortic valve after surgery was at least 6 mm in all patients and on average  $7.6 \pm 1.3$  mm.

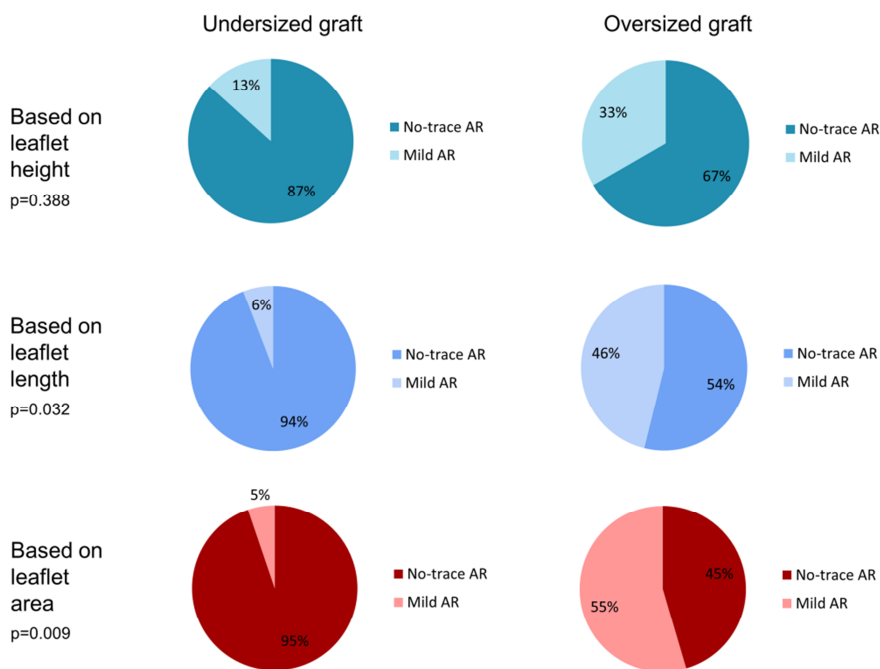


**Figure 4. Linear regression analysis for the development of TTE-derived formulas**

(A) Linear regression analysis in the development of the leaflet height-based TTE-derived formula. The correction factor of 1.1 should be applied in the general formula.

(B) Linear regression analysis in the development of the leaflet length-based TTE-derived formula. No correction factor is necessary in the general formula.

(C) Linear regression analysis in the development of the leaflet area-based TTE-derived formula. The correction factor of 0.8 should be applied in the general formula. AVJ: aortoventricular junction; TTE: transthoracic echocardiography



**Figure 5. Residual aortic regurgitation in patients with an undersized graft compared to patients with an oversized graft.**

AR: aortic regurgitation

## Discussion

The David aortic valve reimplantation technique has shown favourable mid- and long-term results in patients with aortic root or ascending aorta aneurysms.<sup>9-11</sup> Accurate sizing of the tubular Dacron graft where the valve is inserted into is pivotal to ensure durable repair. After the first description of the surgical technique by Drs David and Feindel, where the size of the tubular graft was selected upon perioperative measurement of the average leaflet height,<sup>5</sup> several modifications have been developed, including the creation of neosinuses of Valsalva by achieving an area of the Dacron fabric contained within two commissures larger than the anatomical area.<sup>12</sup> However, selection of the appropriate size of the tubular graft remains challenging and several investigational groups have proposed alternative methods for graft sizing. For example, Svensson et al. proposed the implantation of a 28- or 30-mm graft for men and 26- or 28-mm for women and the use of a Hegar's dilator of a size equivalent to the patient's expected normal LV outflow tract size.<sup>13</sup> The proximal end of the graft is sutured and crimped down to the Hegar's dilator size creating neosinuses of Valsalva where the graft is 7-9 mm larger than the LV outflow tract. After sewing the aortic valve in position, the anchoring

sutures at the level of the commissures are placed 4 mm apart narrowing the graft at the level of the neosinotubular junction. One of the advantages of this technique is its reproducibility.<sup>13</sup> Alternatively, de Kerchove et al. proposed a method to select the tubular graft size based on the hypothesis of preserved height of the aortic commissures in aortic root aneurysms.<sup>14,15</sup> Usually measured from the base of the interleaflet triangle to the top of the non-coronary/left-coronary commissure, the height corresponds to the size of the graft and theoretically to the size of the sinotubular junction in normally functioning aortic valves. Eventually, if the height does not correspond to the available labelled graft sizes, the next larger size is selected. This methodology tested in 27 consecutive patients undergoing aortic valve-sparing surgery using the reimplantation technique (59% bicuspid valve, 53% with severe preoperative AR) showed acute favourable results with no (54%) or mild AR (46%) at discharge TTE.<sup>14</sup>

However, all the aforementioned series based the sizing of the graft on surgical inspection and direct intraoperative measurements. Ex-vivo studies have demonstrated that the aortic valve leaflet length is influenced by the pressure on the aortic leaflets<sup>16</sup> and the distensibility of the leaflet tissue may challenge the accurate measurement of the aortic leaflets at the surgical field under cardioplegia.<sup>17</sup> Accordingly, echocardiography could overcome these limitations as measurements are performed in diastole under physiological pressures.

This hypothesis-generating study evaluated the prevalence of under- or oversized tubular graft using a TTE-derived formula and its association with residual mild AR after aortic valve-sparing surgery using the reimplantation technique. The incidence of mild AR was 23% and was significantly higher among patients who received an oversized tubular graft according to the leaflet length and leaflet area TTE-derived formula. The reported incidences of mild AR after aortic valve-sparing surgery using the reimplantation technique range between 24 and 46%.<sup>14,18,19</sup> Leaflet height was easily measured on TTE, however there was a factor 1.1 difference between the TTE-measured and surgically measured leaflet height; therefore a correction factor had to be applied into the leaflet height TTE-derived formula. In addition, there was no significant difference in residual AR in oversized and undersized grafts based on the TTE leaflet height formula. In addition, using the leaflet length formula, oversizing was associated significantly with more residual AR. The leaflet area was easily measured and also resulted in a significant association between oversizing based on the leaflet area formula and more residual AR.

Awaiting prospective evaluation of the performance of these proposed TTE-derived formulas, the present results suggest that the graft size should not be larger than calculated by the leaflet length and leaflet area formula. The leaflet area is easier to measure on TTE in comparison with leaflet length. In our series, the leaflet area TTE-based formula performed best in demonstrating residual AR in relation to oversizing, hence this formula seems to be the

most promising when using TTE in determining the appropriate graft size. Eventually, additional manoeuvres to tailor the size of the graft at the levels of the aortoventricular and sinotubular junctions would be required to achieve good leaflet coaptation while avoiding prolapse or direct contact between cusp and graft that may lead to erosion or retraction of the aortic cusps.<sup>4,20</sup>

### *Study limitations*

The present study was limited by the relatively small number of patients with a heterogeneous cohort including aortic valve reimplantation using the David I technique as well as the David V modified technique. The formulas were retrospectively developed and evaluated. Therefore it remains unknown whether the clinical course of the patients would be different if a graft size based on echocardiography would have been implanted. Nevertheless, the TTE-derived formulas may be helpful to assist the surgeon in decision-making and to prevent oversizing. The present study is a first step in the use of echocardiography to standardize the selection of the graft size in David reimplantation technique. Firstly, retrospective validation of the formulas in a larger cohort and secondly, prospective application of the formulas is needed before introduction into routine clinical practice. In addition, the use of a 2D imaging technique may be limited by the use of off-axis images that may underestimate the leaflet size. The aortic root size probably influences the measurements of the leaflet size on echocardiography since the leaflet height was taken from the internal border of the aortic root to the free edge of the leaflet. The small number of patients hampered subanalysis of performance of the formulas in small and large aortic roots. This topic might be of interest in further clinical research. 3D echocardiography may refine the geometric assessment of the aortic valve and root and should be used in future studies. Automated software for 3D reconstruction of the aortic root might provide more accurate measurements of the leaflet height and area.<sup>21</sup>

The present study shows that undersizing based on the leaflet length and leaflet area TTE-derived formula is better in preventing residual AR compared with oversizing; however, prolapse or direct contact between the leaflet and the graft should be avoided. Therefore, the effect of using a smaller graft on aortic valve degeneration during follow-up should be closely monitored.

### **Conclusion**

In patients undergoing David reimplantation technique, grafts considered undersized according to leaflet length and leaflet area TTE-derived formulas are associated with less AR than patients with oversized grafts. This study provides a proof-of-concept on the use of echocardiography to standardize the selection of the appropriate graft size in David

reimplantation technique. However, future studies are needed to validate the formulas and make them applicable in routine clinical practice.

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