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Three-dimensional transoesophageal echocardiography of the aortic valve and root: changes in aortic root dilation and aortic regurgitation

Madelien V. Regeer[1], Vasileios Kamperidis[1], Michel I.M. Versteegh[2], Martin J. Schalij[1], Nina Ajmone Marsan[1], Jeroen J. Bax[1], and Victoria Delgado[1]*

[1]Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands; and [2]Department of Cardio-Thoracic Surgery of the Heart Lung Center Leiden, Leiden University Medical Center, Leiden, The Netherlands

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Aims It has been hypothesized that in response to dilation of the aortic root, the aortic valve cusps may remodel to prevent aortic regurgitation (AR). The aim of the present study was to evaluate the association between aortic cusp dimensions and aortic root geometry.

Methods and results Three-dimensional transoesophageal echocardiography was performed in 40 patients with aortic root dilation (mean age 57 ± 12 years, 75% men, 35% bicuspid aortic valve) and 20 controls with a normal aortic root (mean age 61 ± 13 years, 65% men). Aortic valve geometry was measured, and the ratio between closed cusp area and sinotubular junction (STJ) area as a measure of the aortic cusp remodelling relative to the aortic root dilation was assessed. Patients with aortic root dilation with tricuspid aortic valve ($n = 26$) showed significant increase in aortic cusp size. However, the closed cusp area to STJ area ratio was smaller in dilated aortic roots [0.88 (95% confidence interval: 0.78–0.98)] compared with normal aortic roots [1.22 (95% confidence interval: 1.02–1.41); $P = 0.002$]. In addition, in patients with central AR, there was insufficient cusp tissue, as suggested by a closed cusp area to STJ area ratio of 0.75 (95% confidence interval: 0.67–0.82), compared with relative excess of cusp tissue in eccentric AR with a ratio of 1.14 (95% confidence interval: 1.01–1.27; $P < 0.001$).

Conclusion Aortic root dilation was associated with significant increase in aortic valve cusp size. However, this increase seemed insufficient to match aortic root size, particularly in central AR, whereas in eccentric AR, there was relative abundance of cusp tissue resulting in relative cusp prolapse.

Keywords aortic cusp remodelling • 3DTEE • aortic root dilation

Introduction

Aortic root dilation involving particularly the aortic annulus can lead to aortic regurgitation (AR) due to malcoaptation of aortic valve cusps.[1] Idiopathic aortic root dilation is the leading cause of valvular insufficiency in ~10–30% of patients with AR.[2,3] However, not all patients with aortic root dilation exhibit AR. It could be hypothesized that in patients with aortic root dilation, the aortic valve cusps may be exposed to increased wall stress that triggers their remodelling and growth to compensate and preserve valvular competence. Indeed, computational models have shown that the aortic valve can adapt in response to aortic root dilation.[4] However, in clinical practice, these models are time consuming and require high computational costs. In patients who underwent clinically indicated three-dimensional transoesophageal echocardiography (3DTEE), we evaluated whether the aortic valve cusps show remodelling to compensate for the aortic root dilation. The aims of the present study were (i) to assess whether patients with aortic root

* Corresponding author. Tel: +31 71 526 2020; Fax: +31 71 526 6809. E-mail: v.delgado@lumc.nl

dilation show remodelling of the aortic valve cusps to prevent AR and (ii) to investigate whether this remodelling is different in patients with central and eccentric regurgitant jets.

Methods

Patients

A total of 40 patients with aortic root dilation [defined as maximum diameter of the sinus of Valsalva (SOV) of ≥40 mm in men and ≥36 mm in women or maximum diameter of the sinotubular junction (STJ) ≥36 mm in men and ≥32 mm in women[5,6]], who underwent clinically indicated 3DTEE, were included. Patients with tricuspid aortic valve were divided into two subgroups according to the presence of AR and according to the presence of a central or eccentric AR jet. Patients with more than mild aortic stenosis were excluded. In addition, a control group of 20 patients who underwent clinically indicated 3DTEE (i.e. evaluation of the mechanism of mitral regurgitation, suspected endocarditis, and evaluation of cerebrovascular accident or in the context of left atrial appendage closure) and who had normal dimensions of the aortic root and normal functioning tricuspid aortic valve was included.

Clinical characteristics were prospectively collected in the Departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center, Leiden, The Netherlands) and retrospectively analysed. 3DTEE data of the aortic valve and root geometry were analysed offline and compared between patients with aortic dilation and controls. In addition, aortic valve and root geometry were compared between patients with central and eccentric AR. 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

Transthoracic echocardiography was performed using commercially available ultrasound system (Vivid E9, General Electric Healthcare, Vingmed, Horten, Norway) equipped with M5S transducer. Two-dimensional and Doppler data were acquired in the parasternal and apical views according to current recommendations.[7,8] AR grade was assessed using a multiparametric approach including the measurement of the jet width relative to the left ventricular outflow tract width and the vena contracta in parasternal long-axis and apical views. AR was graded as 0 (no), 1 (mild), 2 (mild–moderate), 3 (moderate–severe), or 4 (severe).[7] Left ventricular end-diastolic and end-systolic volumes were measured, and left ventricular ejection fraction was calculated in the apical two- and four-chamber views according to the Simpson's biplane method.[8]

3DTEE data acquisition and analysis

3DTEE was performed using commercially available ultrasound system (Vivid E9, General Electric Healthcare) equipped with a fully integrated 2D/3D matrix transducer (GE 6VT-D, General Electric Healthcare). Mid-oesophageal images of the aortic valve and aortic root were obtained in the short axis at 30°–45° and in the long axis at 120°–130°. To acquire 3DTEE images, the aortic root was imaged from the aorto-ventricular junction (AVJ) to the STJ in two orthogonal planes. Thereafter, single-beat and multi-beat 3DTEE data of the aortic valve and root were acquired to optimize spatial and temporal resolution. Attention was paid to avoid stitching artefacts in the multi-beat data acquisition. The echocardiographic data were digitally stored in cine-loop format, and data were retrospectively analysed using commercially available software (EchoPac 112.0.1, GE Medical Systems, Horten, Norway).

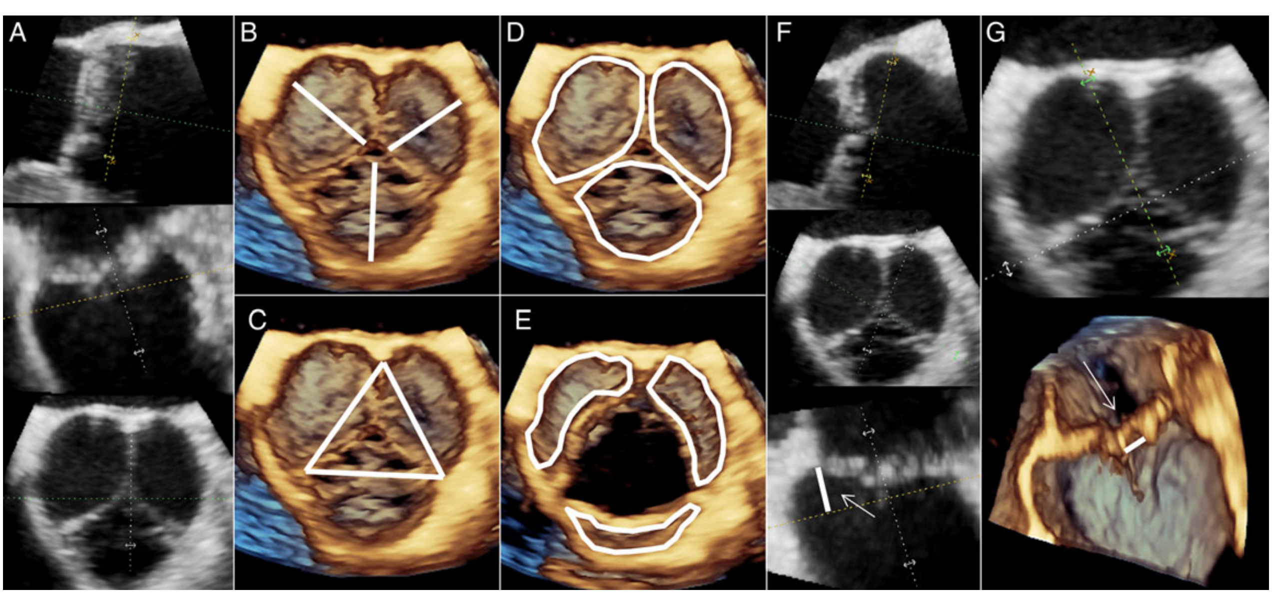

Figure 1 Measurements of aortic valve geometry in 3D TEE images. (*A*) Flexi-slice method was used to obtain a true short axis of the aortic valve at the level of cusp coaptation. (*B*) Cusp height was measured during end-systole from the internal border of the aortic root till the free edge of the cusp. (*C*) Intercommissural distance was measured during end-systole between the commissures. (*D*) Closed cusp area was measured during end-systole for all cusps. (*E*) Open cusp area was measured during mid-systole for all cusps. (*F*) Cusp depth was measured during end-systole per cusp in the cross-sectional image of the middle of the cusp between the deepest point of the belly of the cusp and the cross-sectional plane. (*G*) Central coaptation deficit was measured during end-systole at the central coaptation point between each pair of coapting cusps.

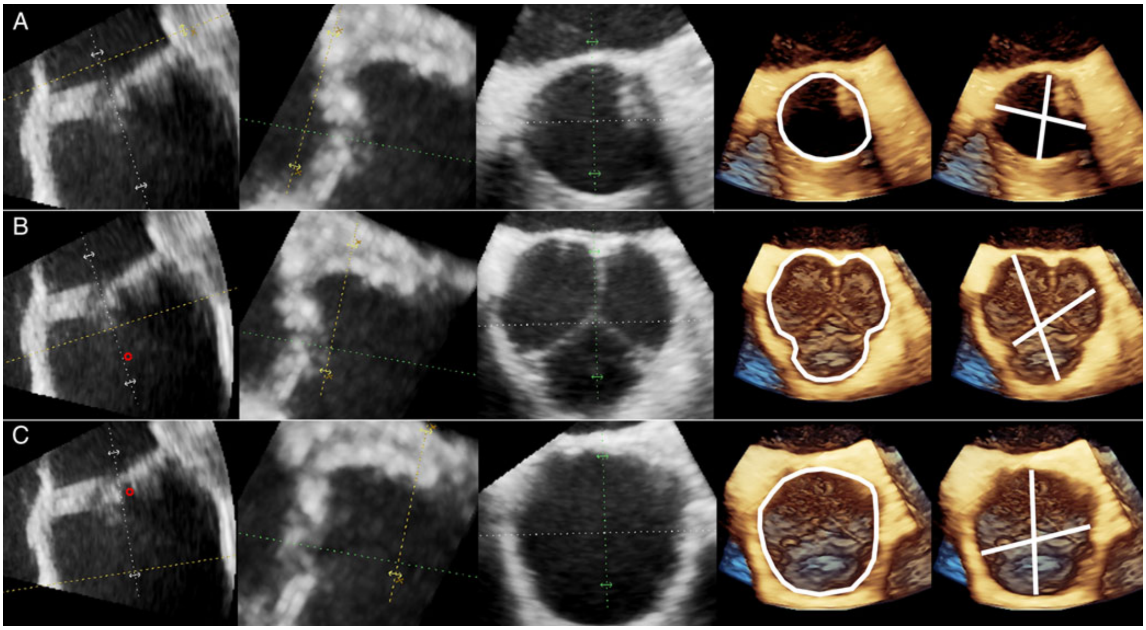

Figure 2 Measurements of aortic root geometry in 3D TEE images. Flexi-slice method was used to obtain a true short axis of the aortoventricular junction (*A*), sinus of Valsalva (*B*), and sinotubular junction (*C*). Aortic root area, minimum, and maximum diameter were measured during end-systole in 3DTEE images.

Table 1 Echocardiographic characteristics of patients with normal vs. dilated aortic root with tricuspid or bicuspid aortic valve

	Normal aortic root (*n* = 20)	Dilated aortic root with TAV (*n* = 26)	Dilated aortic root with BAV (*n* = 14)	*P*-value
Age (years)	61 ± 13	59 ± 13	55 ± 11	0.436
Male gender	13 (65%)	21 (81%)	9 (64%)	0.392
Body surface area (m^2)	1.95 ± 0.17	2.04 ± 0.15	1.92 ± 0.22	0.093
Left ventricular end-diastolic volume (mL)	123 ± 24	151 ± 50	158 ± 69	0.080
Left ventricular end-systolic volume (mL)	49 ± 18	64 ± 26	72 ± 44	0.070
Left ventricular ejection fraction (%)	60 ± 10	58 ± 6	57 ± 10	0.364
Cusp height	15.7 (13.8–16.3)	18.2 (16.3–20.2)	19.5 (18.1–22.1)	<0.001
Intercommissural distance	19.3 (17.8–20.6)	25.8 (22.3–28.3)	24.5 (21.8–27.5)	<0.001
Total closed cusp area (cm^2)	6.7 (6.0–7.7)	10.1 (8.5–12.5)	10.0 (7.7–11.4)	<0.001
Total open cusp area (cm^2)	2.5 (2.1–3.4)	5.6 (3.8–6.9)	3.9 (2.6–6.0)	<0.001
Central coaptation deficit	0 (0–0)	2.5 (1.3–4.0)	2.0 (0.8–3.8)	<0.001
Cusp depth	9.0 (7.1–9.3)	10.3 (9.3–12.3)	10.3 (7.4–12.6)	0.003
AVJ area (cm^2)	4.2 (3.7–4.4)	5.2 (4.6–6.2)	5.8 (3.7–6.4)	0.002
AVJ minimum diameter	20 (19–21)	24 (22–26)	24 (21–25)	0.001
AVJ maximum diameter	26 (25–27)	29 (26–31)	29 (25–31)	0.044
AVJ eccentricity index	0.76 (0.71–0.83)	0.80 (0.74–0.89)	0.82 (0.77–0.90)	0.127
SOV area (cm^2)	7.4 (6.7–8.3)	12.1 (10.4–14.8)	11.2 (9.8–14.6)	<0.001
SOV minimum diameter	27 (25–29)	36 (33–38)	33 (29–37)	<0.001
SOV maximum diameter	34 (31–36)	42 (40–47)	42 (39–45)	<0.001
SOV eccentricity index	0.80 (0.76–0.83)	0.83 (0.79–0.87)	0.80 (0.73–0.84)	0.291
STJ area (cm^2)	5.3 (4.9–6.3)	11.4 (8.3–14.4)	9.3 (8.0–13.0)	<0.001
STJ minimum diameter	25 (25–26)	35 (32–40)	34 (29–38)	<0.001
STJ maximum diameter	27 (26–30)	40 (36–44)	38 (33–43)	<0.001
STJ eccentricity index	0.93 (0.85–0.96)	0.91 (0.86–0.95)	0.89 (0.87–0.93)	0.796

Data are presented as number (percentage), mean ± standard deviation, or median (inter-quartile range). Dimensions are displayed in millimetre unless otherwise specified.
AVJ, aortoventricular junction; BAV, bicuspid aortic valve; SOV, sinus of Valsalva; STJ, sinotubular junction; TAV, tricuspid aortic valve.

For 3DTEE data analysis, three orthogonal multiplanar reformation planes were reconstructed and aligned in the centreline of the aortic root to obtain the true short axis of the aortic valve at the level of cusp coaptation. *Figure 1* shows the different aortic valve geometric measurements. An end-systolic 3DTEE frame with the aortic valve closed was used to measure the cusp height, intercommissural distance, and closed cusp area. The cusp height was measured from the internal border of the aortic root till the free edge of the cusp for each cusp separately and averaged. The intercommissural distance was measured between each commissure and also averaged. In patients with a bicuspid aortic valve, the intercommissural distance was defined as the distance between the two non-fused commissures. The cusp area was measured per each cusp and then summed to obtain the total closed cusp area. A mid-systolic 3DTEE frame was used to measure each cusp area and then summed to obtain the open cusp area. Two additional measurements were performed during end-systole: the cusp depth was measured per cusp in the cross-sectional image of the middle of the cusp between the deepest point of the belly of the cusp and the cross-sectional plane and thereafter averaged, whereas the central coaptation deficit was measured at the central coaptation point between each pair of coapting cusps and averaged. When there was full coaptation of the cusps in the centre, the coaptation deficit was defined as 0 mm.

In addition, the aortic root measurements were performed in the true short axis of the aortic root at three levels as displayed in *Figure 2*. The area, minimum, and maximum diameter of the AVJ, SOV, and STJ were measured during an end-systolic frame on the 3DTEE image. The eccentricity index was calculated per each level of the aortic root dividing the minimum diameter by the maximum diameter at each particular level.

Statistical analysis

All data analyses were performed using the SPSS software (Version 20.0. IBM Corp., Armonk, NY, USA). Continuous variables were reported as mean $\pm$ standard deviation and compared with the Student's *t*-test when normally distributed. Median and inter-quartile range were reported for non-normally distributed variables and were compared with the Mann–Whitney *U*-test. Categorical variables were reported as counts and percentages and compared using the χ^2 test. Differences between controls, patients with dilated aortic root and bicuspid aortic valve, and patients with dilated aortic root and tricuspid aortic valve were reported. Further analyses were performed in subjects with tricuspid aortic valve (patients with aortic root dilation vs. controls), to make sure the morphology of the aortic valve was not responsible for the differences between patients with aortic root dilation and controls. Linear regression analysis without including an intercept was used to assess the ratio between the aortic root area at the level of the STJ and the closed cusp area. Subanalysis was performed between aortic dilation patients with tricuspid aortic valve with and without AR and between aortic dilation patients with tricuspid aortic valve with central AR and eccentric AR. The intra-observer and inter-observer variabilities were evaluated in 10 individuals randomly selected. The mean difference and 95% confidence interval between two measurements for all aortic valve and aortic root measurements were calculated. A *P*-value $<$0.05 was considered statistically significant.

Results

Table 1 outlines the echocardiographic characteristics of patients with aortic root dilation (mean age 57 $\pm$ 12 years, 75% men) divided by aortic valve morphology and controls (mean age 61 $\pm$ 13 years, 65% men). There were no differences in age, gender, and body surface area. Per definition, controls showed normal anatomy and dimensions of aortic valve and aortic root. Left ventricular volumes were significantly larger, and left ventricular ejection fraction was slightly lower in patients with aortic root dilation compared with controls.

Aortic valve and root geometry in aortic root dilation

Table 1 shows the aortic valve and root geometric measurements in patients with aortic root dilation compared with controls. Per definition, all aortic root measurements were larger in patients with aortic root dilation in comparison to controls. In patients with dilated aortic roots, the AVJ was slightly more rounded [eccentricity index: 0.80 (inter-quartile range: 0.75–0.89)] compared with normal oval-shaped aortic roots [eccentricity index: 0.76 (inter-quartile range: 0.71–0.83); $P = 0.052$]. There was no difference in eccentricity index of the SOV and STJ between controls and patients with dilated aortic root. Patients with aortic root dilation showed enlarged aortic cusps as displayed by a larger cusp height, closed cusp area, and open cusp area. In patients with normal dimensions of the aortic root, there was no central coaptation deficit, compared with a median central coaptation deficit of 4.0 mm (inter-quartile range: 2.0–6.4 mm; $P < 0.001$) in patients with dilated aortic root. Furthermore, the cusp depth was larger in patients with dilated aortic root compared with controls. *Table 1* shows the aortic valve geometric measurements for patients with dilated root and tricuspid aortic valve and for patients with dilated root and bicuspid aortic valve.

In controls, the closed cusp area was on average 1.22 times the STJ area (95% confidence interval: 1.02–1.41), whereas in patients with dilated aortic root with tricuspid aortic valve, the closed cusp

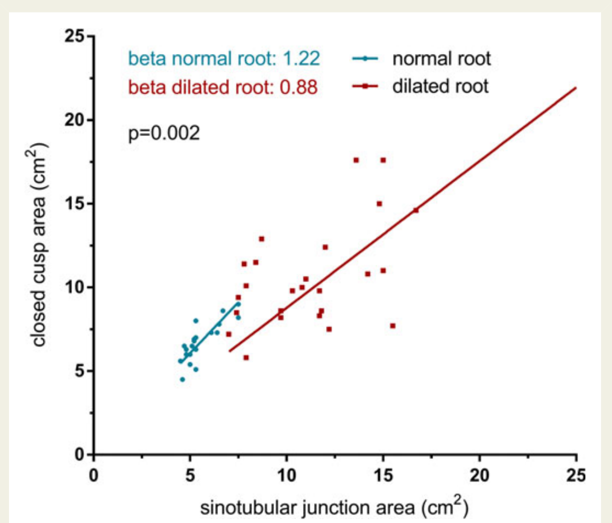

Figure 3 Ratio between closed cusp area and sinotubular junction area in patients with normal vs. dilated aortic root with tricuspid aortic valve. Linear regression analysis through origin was performed to assess the ratio between closed cusp area and sinotubular junction area, which was 0.88 in dilated aortic roots and 1.22 in normal controls.

area was only 0.88 times the STJ area (95% confidence interval: 0.78–0.98; $P = 0.002$). This indicates that, although aortic root dilation was associated with cusp enlargement and increase in closed cusp area, this enlargement was not sufficient compared with normal aortic roots, resulting in more frequent AR (*Figure 3*).

Aortic valve and root geometry in patients with aortic root dilation and with or without AR

Among the 26 patients with aortic root dilation and tricuspid aortic valve, 15 patients showed AR grade ≥2 (mean age 60 ± 12 years, 87% men) and the remaining 11 patients showed AR grade <2 (mean age 56 ± 14 years, 73% men; *Table 2*). Patients with AR had significant larger left ventricular volumes and slightly lower left ventricular ejection fraction compared with patients without AR. In terms of aortic dimensions, both groups of patients were comparable. However, there was a difference in the central coaptation deficit, which was only 1.7 mm (inter-quartile range: 0.7–2.7 mm) in patients with AR grade <2, compared with 3.3 mm (inter-quartile range: 2.0–5.0 mm; $P = 0.010$) in patients with AR grade ≥2. The ratio between closed cusp area and STJ area was 0.91 (95% confidence interval: 0.73–1.10) in patients without AR and 0.86 (95% confidence interval: 0.74–0.98; $P = 0.660$) in patients with AR.

Aortic valve and root geometry in aortic root dilation patients with central and eccentric AR jet

There were 15 patients with aortic root dilation with tricuspid aortic valve with AR grade ≥2 who were divided into two subgroups: patients with central AR jet ($n = 8$, mean age 64 ± 13 years, 75% men) were compared with patients with eccentric AR jet ($n = 7$, mean age 56 ± 12 years, 100% men). There were no differences in left ventricular volumes and function between these subgroups. *Table 3* shows the aortic valve and root geometric measurements in patients with aortic root dilation with central AR jet and patients with eccentric AR jet. Patients with central AR jet were comparable to those with eccentric AR jet regarding aortic cusp size. Furthermore, there were no significant differences in cusp depth and central coaptation deficit. Patients with central AR jet had slightly larger STJ area compared with patients with eccentric AR jet. Furthermore, the morphology of the aortic root was different between patients with central and eccentric AR jet with more oval AVJ in central

Table 2 Echocardiographic characteristics of patients with dilated aortic root with tricuspid aortic valve with and without aortic regurgitation

	AR grade <2 (n = 11)	AR grade ≥2 (n = 15)	P-value
Age (years)	56 ± 14	60 ± 12	0.482
Male gender	8 (73%)	13 (87%)	0.698
Body surface area (m^2)	2.02 ± 0.17	2.05 ± 0.14	0.610
Left ventricular end-diastolic volume (mL)	125 ± 34	170 ± 52	0.019
Left ventricular end-systolic volume (mL)	48 ± 15	76 ± 26	0.004
Left ventricular ejection fraction (%)	61 ± 5	55 ± 5	0.004
Cusp height (mm)	17.3 (16.0–20.0)	18.3 (16.7–20.7)	0.467
Intercommissural distance (mm)	24.7 (20.0–28.0)	26.3 (23.0–28.3)	0.125
Total closed cusp area (cm^2)	10.0 (7.7–11.5)	10.5 (8.6–14.6)	0.406
Total open cusp area (cm^2)	4.3 (3.6–6.6)	5.7 (4.1–7.9)	0.392
Central coaptation deficit (mm)	1.7 (0.7–2.7)	3.3 (2.0–5.0)	0.010
Cusp depth (mm)	10.7 (9.7–12.3)	10.3 (9.3–12.3)	0.695
AVJ area (cm^2)	5.6 (4.8–5.8)	4.7 (4.5–6.3)	0.897
AVJ minimum diameter (mm)	24 (21–26)	23 (22–26)	0.793
AVJ maximum diameter (mm)	29 (28–30)	29 (25–31)	0.979
AVJ eccentricity index	0.77 (0.72–0.80)	0.84 (0.75–0.89)	0.287
SOV area (cm^2)	11.5 (9.1–13.4)	12.6 (10.5–16.4)	0.377
SOV minimum diameter (mm)	34 (32–38)	37 (33–42)	0.152
SOV maximum diameter (mm)	41 (38–47)	42 (40–53)	0.251
SOV eccentricity index	0.83 (0.81–0.87)	0.80 (0.78–0.89)	0.795
STJ area (cm^2)	9.7 (7.9–12.2)	11.8 (9.7–15.0)	0.232
STJ minimum diameter (mm)	33 (32–38)	38 (32–41)	0.322
STJ maximum diameter (mm)	36 (33–41)	43 (37–45)	0.138
STJ eccentricity index	0.92 (0.90–0.97)	0.90 (0.85–0.95)	0.311

Data are presented as number (percentage), mean ± standard deviation, or median (inter-quartile range).
AR, aortic regurgitation; AVJ, aortoventricular junction; SOV, sinus of Valsalva; STJ, sinotubular junction.

Table 3 Echocardiographic characteristics of patients with dilated aortic root and tricuspid aortic valve with central vs. eccentric aortic regurgitation

	Central AR (n = 8)	Eccentric AR (n = 7)	P-value
Age (years)	64 ± 13	56 ± 12	0.284
Male gender	6 (75%)	7 (100%)	0.509
Body surface area (m^2)	2.10 ± 0.16	1.99 ± 0.09	0.123
Left ventricular end-diastolic volume (mL)	160 ± 58	182 ± 47	0.444
Left ventricular end-systolic volume (mL)	73 ± 30	80 ± 22	0.637
Left ventricular ejection fraction (%)	54 ± 4	56 ± 5	0.533
Cusp height (mm)	18.5 (16.5–20.4)	18.0 (16.7–22.3)	0.908
Intercommissural distance (mm)	26.3 (25.2–28.3)	26.3 (22.3–31.0)	0.601
Total closed cusp area (cm^2)	10.7 (8.9–13.7)	9.4 (8.5–17.6)	0.862
Total open cusp area (cm^2)	5.7 (3.6–7.6)	5.7 (4.1–8.7)	0.728
Central coaptation deficit (mm)	3.7 (2.4–5.8)	2.7 (1.3–4.0)	0.201
Cusp depth (mm)	10.3 (8.1–11.9)	9.7 (9.3–14.0)	0.907
AVJ area (cm^2)	4.7 (3.5–6.0)	5.8 (4.6–7.2)	0.245
AVJ minimum diameter (mm)	22 (19–24)	26 (23–29)	0.016
AVJ maximum diameter (mm)	28 (26–31)	30 (25–32)	0.642
AVJ eccentricity index	0.75 (0.70–0.83)	0.89 (0.84–0.96)	0.005
SOV area (cm^2)	12.9 (10.7–15.7)	11.1 (10.0–20.2)	0.602
SOV minimum diameter (mm)	37 (35–41)	34 (32–42)	0.384
SOV maximum diameter (mm)	44 (40–51)	42 (40–54)	0.770
SOV eccentricity index	0.87 (0.80–0.90)	0.80 (0.76–0.85)	0.083
STJ area (cm^2)	13.0 (11.7–16.3)	9.7 (7.4–13.6)	0.093
STJ minimum diameter (mm)	40 (35–41)	32 (29–40)	0.093
STJ maximum diameter (mm)	44 (40–47)	34 (31–45)	0.131
STJ eccentricity index	0.91 (0.85–0.95)	0.89 (0.84–0.87)	0.908

Data are presented as number (percentage), mean ± standard deviation, or median (inter-quartile range).
AR, aortic regurgitation; AVJ, aortoventricular junction; SOV, sinus of Valsalva; STJ, sinotubular junction.

AR jet compared with eccentric AR jet (eccentricity index 0.75 vs. 0.89; $P = 0.005$).

The ratio between the closed cusp area and the STJ area was different between groups (*Figure 4*). Patients with central AR jet had a closed cusp area of 0.75 times the STJ area (95% confidence interval: 0.67–0.82), indicating that there was not enough cusp tissue in relation to the STJ area to cover the aortic orifice. In patients with an eccentric AR jet, the closed cusp area was 1.14 times the STJ area (95% confidence interval: 1.01–1.27), indicating that there was excess cusp tissue in relation to the STJ area to cover the aortic orifice area resulting in a relative prolapse.

Intra-observer and inter-observer variabilities

The variability in measurements within an observer and between observers was evaluated in 10 subjects. The mean and 95% confidence interval of the difference between two measurements were displayed in *Table 4*.

Discussion

The present study hypothesized that in patients with aortic root dilation, remodelling of the aortic valve cusps occurs with enlargement of the cusp surface. Patients with aortic root dilation showed significant enlargement of the aortic valve cusps. However, this remodelling might be insufficient to match the aortic root area, resulting in AR. Various types, of AR seem to result from different remodelling processes. Central AR was associated with cusp tissue deficiency, whereas eccentric AR was associated with relative abundance of cusp tissue resulting in relative prolapse.

The aortic valve and root form a complex structure in which the valvular function is largely dependent on the aortic root dimensions and morphology. In a normal aortic root, the dimensions depend on body size and gender and increase during a life time.[5,6] Computational models have shown that an increase in AVJ diameter was associated with a decrease in coaptation height and coaptation area.[9] Furthermore, in patients with STJ dilation, an increase in the ratio between STJ and AVJ was associated with a decrease in the coaptation height resulting in an incomplete closure of the aortic valve.[10] In addition, in models with aortic root dilation, the aortic cusps are pulled apart resulting in increased stress (defined as force per area) and increased strain (defined as percentage extension of cusp tissue) on the aortic cusps.[4] This may lead to aortic cusp remodelling to bear the higher stress posed on the cusps. Studies on valvular biomechanical properties showed increased cellular stiffness of valvular interstitial cells in left-sided heart valves (aortic

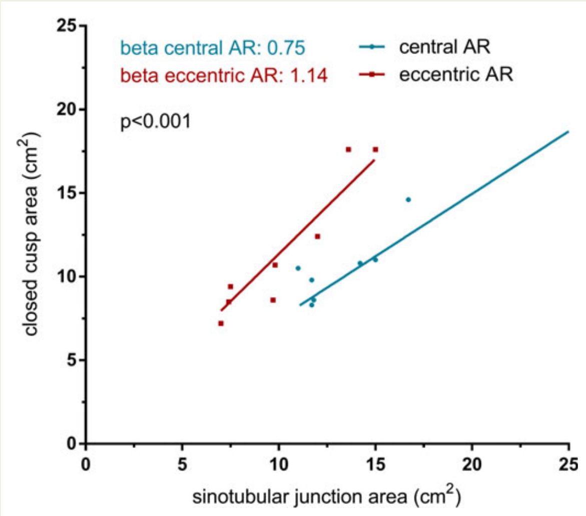

Figure 4 Ratio between closed cusp area and sinotubular junction area in patients with tricuspid aortic valve with dilated aortic root and central vs. eccentric aortic regurgitation. Linear regression analysis through origin was performed to assess the ratio between closed cusp area and sinotubular junction area, which was 0.75 in patients with central aortic regurgitation and 1.14 in patients with eccentric aortic regurgitation. AR, aortic regurgitation.

valve and mitral valve) as opposed to right-sided heart valves.[11] This suggests that valvular interstitial cells respond to increased cusp stress by altering cellular stiffness.[12] Aortic valvular interstitial cells are phenotypically plastic and can transdifferentiate into myofibroblasts during cusp remodelling.[13] However, exact changes in aortic cusp biomechanics on a microscopic level in aortic root dilation have not been described.

Recent studies using advanced non-invasive imaging of the aortic valve suggest the presence of differences in aortic cusp size between dilated and normal aortic roots.[14,15] Measurements of the aortic valve and root geometry with 3DTEE and computed tomography have shown good correlations.[14] Using computed tomography, Kim *et al.*[15] showed significant changes in aortic cusp sizes in patients with aortic root dilation compared with normal aortic roots. Patients with aortic root dilation had significantly larger aortic cusps compared with patients with normal aortic roots. Furthermore, the ratio between the closed cusp area and aortic root area was reduced in patients with aortic root dilation without AR and even more reduced in patients with AR. In this particular subgroup of patients, AR results from a central coaptation defect due to larger aortic root area.[15] Of note, patients with eccentric AR due to aortic valve prolapse were excluded. To understand whether remodelling of the aortic cusps also occurs in eccentric AR due to prolapse, Sato *et al.*[16] demonstrated that the prolapsing cusp was elongated and expanded in comparison with the other cusps on surgical inspection. The present study shows that in aortic root dilation patients with eccentric AR, there was a relative abundance of cusp tissue which may result in relative prolapse. However, the underlying mechanism and whether it is indeed an inappropriate adaptation of the cusps to the increased stress due to aortic root dilation remain unclear.

Table 4 Intra-observer and inter-observer variabilities

	Intra-observer variability	Inter-observer variability
Cusp height (mm)	0.7 (−1.3 to 2.7)	−0.6 (−2.2 to 1.1)
Intercommissural distance (mm)	0.7 (−2.9 to 4.3)	−0.5 (−3.6 to 2.6)
Total closed cusp area (cm^2)	0.8 (−1.1 to 2.7)	0.4 (−1.0 to 1.7)
Total open cusp area (cm^2)	−0.1 (−3.2 to 3.0)	−0.3 (−1.5 to 0.9)
Cusp depth (mm)	0.0 (−4.0 to 4.1)	−2.1 (−5.2 to 1.0)
AVJ area (cm^2)	0.0 (−1.4 to 1.4)	0.0 (−0.9 to 0.9)
AVJ diameter (mm)	0.0 (−6.8 to 6.8)	0.3 (−5.7 to 6.2)
SOV area (cm^2)	0.0 (−1.4 to 1.4)	0.0 (−1.3 to 1.3)
SOV diameter (mm)	0.0 (−5.0 to 5.0)	0.3 (−3.8 to 4.4)
STJ area (cm^2)	0.5 (−1.3 to 2.3)	0.3 (−0.8 to 1.5)
STJ diameter (mm)	0.3 (−4.2 to 4.7)	0.6 (−2.7 to 3.8)

Data are presented as mean difference between measurements (95% confidence interval).
AVJ, aortoventricular junction; SOV, sinus of Valsalva; STJ, sinotubular junction.

Clinical implications

The present study provides insight into aortic cusp adaptation in patients with aortic root dilation. This might impact on the timing and type of aortic valve reconstructive surgery. Insufficient coaptation of aortic valve cusps in aortic root dilation may result in AR. Current guidelines recommend aortic valve and root surgery in patients with significant aortic root dilation, symptomatic AR, or asymptomatic AR with left ventricular dilation or dysfunction.[17] However, long-lasting increased stress on the cusps may result in thickening of the cusps with implications for reparability of the aortic valve. Furthermore, the mechanism of AR is important for the selection of the appropriate technique to reconstruct the aortic valve and root complex. In central AR, purely caused by aortic root dilation, valve-sparing root replacement techniques (remodelling or reimplantation technique) may be sufficient to reduce the aortic root diameter to match the aortic valve cusp size.[1] However, in eccentric AR, cusp reconstruction with central cusp plication, triangular resection, or cusp resuspension may be needed.[1] In addition to the AR mechanism, the ratio between closed cusp area and STJ area might help in determining which aortic valve reconstructive technique is most appropriate. Further research should elucidate how this ratio can be implemented into clinical practice.

Study limitations

The present study was limited by a small sample size. 3DTEE was performed in all patients and controls with the same vendor. The measurements were performed manually by the same investigator. In future research, automated measurements may be of incremental value for which dedicated software is needed. In addition, although the planes were oriented to obtain the true short axis and long axis of the aortic valve and root, the measurements were performed in one plane. Therefore, the cusp length over the belly of the cusp could not be determined. In addition, the present software was not able to measure curved lengths such as the free edge cusp length. In the present study, histological samples were not available. Therefore, it cannot be proved that actual cusp remodelling occurred. To obtain more insight into the effects of aortic root dilation on the aortic valve cusps, further research including histological samples of aortic valve cusps in dilated aortic root is needed.

Conclusion

The present study showed an increase in aortic cusp size in patients with aortic root dilation in comparison to patients with normal aortic roots. However, the enlargement seemed insufficient to match the aortic root area as indicated by a decrease in closed cusp area to STJ area ratio in patients with a dilated aortic root. Furthermore, in patients with tricuspid aortic valve and central AR, the cusp area in relation to the aortic root area was small, whereas in patients with tricuspid aortic valve and eccentric AR, there was relative abundance of cusp tissue resulting in relative cusp prolapse. This provides further insight into aortic valve cusp remodelling in patients with aortic root dilation. Additionally, the ratio between closed cusp area and STJ area may be helpful in the future to determine the timing and type of aortic valve reconstructive surgical technique.

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