The Aortic Root: Natural History After Root-Sparing Ascending Replacement in Nonsyndromic Aneurysmal Patients

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Background. **Leaving native aortic tissue in situ in root-sparing ascending aortic replacement raises concern regarding potential later need for root reoperation or for the potential occurrence of localized dissections or rupture in the residual root. The purpose of this study was to evaluate the natural growth of the aortic root after root-sparing aortic replacement.**

Methods. **In all, 102 consecutive patients (mean age 61.8 ± 12.5 years; 60% male) who had undergone root-sparing aortic replacement had sufficient retrievable information regarding their aortic root diameter at postoperative baseline and follow-up imaging by computed tomography or echocardiography. The annual growth rate was evaluated and also compared according to the influence of valve morphology and concomitant aortic valve replacement. Furthermore, the years of natural history that would require for root enlargement to meet a 50 mm threshold of the root diameter were calculated.**

Results. **The estimated growth rate of the aortic root after root-sparing aortic replacement is between 0.27 and 0.51 mm per year (mean 0.41 mm, varying according to the underlying diameter) and therefore fivefold less than other aortic regions. Accordingly, a root aneurysm indicating reoperation would not be expected for 29.1 years on average. Only patients with a diameter of 45 mm or more are at risk for reoperation, and not until at least after 10.4 years have passed. Neither the valve morphology ($p = 0.62$) nor concomitant aortic valve replacement ($p = 0.86$) influenced rate of root dilation.**

Conclusions. **In nonsyndromic patients, the aortic root is the slowest growing portion of the thoracic aorta. Leaving the native root, as in root-sparing ascending aortic replacement, is a safe approach regarding secondary root intervention for aortic root diameters of 45 mm or less.**

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The incidence of thoracic aortic aneurysms has been determined to be approximately 6 to 15 cases per 100,000 patient-years [1–3]. Approximately 60% of the aneurysms involve proximally the aortic root or ascending portion, 10% the aortic arch, 40% the descending, and 10% the thoracoabdominal region (some patients have dilations at more than one level) [4]. Aortic dissection and rupture are the most devastating natural complications of aortic aneurysm, and data from our group revealed aneurysm size to be an important predictor in the course of these events [5]. Whereas the international guidelines follow a more conservative approach (recommending replacement at 55 mm in case of the proximal aortic regions [6–8]), most specialized centers tend to intervene on the proximal aorta at somewhat smaller sizes.

It still remains controversial at which size a proactive replacement of a specific portion of the aorta is indicated and how extensive the resection should be, especially in case of the aortic root [9]. Sparing a nondilated or slightly dilated root during an ascending replacement simplifies the surgical technique, but concern exists when leaving the native root in situ with regard to further, future dilation. The concerns surround possible dissection and rupture in the residual root segment or potential need for reoperation for progressive dilation.

Despite these concerns, the specific growth dynamic of the root is not well reported for nonsyndromic (for example, non–Marfan syndrome) patients in the literature. The aim of this study was to quantify the natural

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growth of the residual nonaneurysmal aortic root portion after root-sparing ascending aortic replacement. We also aimed to estimate the interval until a reoperation after a root-sparing approach might be necessary. Furthermore, we tried to determine the influence of concomitant aortic valve replacement (AVR) and of different valve morphologies on the dilation progress.

Patients and Methods

Study Design

To determine the natural growth rate of the aortic root, we analyzed postoperative inner root diameters in patients who received root-sparing/supracoronary ascending replacements, and determined rates according to initial root size. Further subanalyses were performed to evaluate a possible stabilizing effect of a concomitant AVR on the growth rate of the root and any potential impact of the natural aortic valve morphology.

The study was approved by the Human Investigation Committee of the Yale University School of Medicine. All patients gave written informed consent for participation in the study.

Inclusion Criteria

All consecutive patients undergoing a root-sparing/supracoronary ascending aortic replacement at the Yale Aortic Institute between 2004 and 2011 were retrospectively reviewed in this study. Patients with two or more retrievable images or evaluable transparent measurements were included. Postoperative imaging assessments were done according to Institute policy regarding follow-up consultations and images. Patients after 2011 were excluded both to prevent measurement errors from short follow-up (due to an expected slow growth rate) and to ensure identifying secondary aortic root dilation. Within this time frame, a total of 366 aneurysm patients underwent elective ascending aortic replacement by a root-sparing technique and were reviewed according to the inclusion criteria. Contemporaneously, a root replacement was performed in 239 aneurysm patients [10].

Exclusion Criteria

According to the aim of the study, the following exclusion criteria were defined: root remodeling/replacement operation (any type), syndromic genetic disorders (Marfan syndrome, Ehlers-Danlos, and others), aortic dissections, intramural hematomas, and redo cardiac operations.

Data Collection and Analysis

This study was performed retrospectively. To determine growth rates, baseline computed tomography (CT) or echocardiography imaging was reviewed for all patients after surgery and compared with subsequent available imaging studies. Aortic root variables were measured by two cardiac surgeons independently (J.A.E. and S.P.) and evaluated from imaging reports (if those reported separately sizes for the annulus, sinus of Valsalva, sinotubular junction, and ascending aorta) from Department of Radiology or Department of Cardiology at Yale–New Haven Hospital. For quality control, repetitive blinded and randomly assigned reviews were performed in 100 imaging studies (31.8%). If an interobserver discrepancy greater than 5% was detected (between measurements of the two surgeons, or between the surgeons' measurements and the radiology reports), for each such patient a collaborative decision was reached between the surgeons and the radiologists regarding the size of the aorta to include in the study (12.4%; 14 of 113 identified patients) [11]. Owing to the known and identified interobserver differences in evaluating the aortic root sizes by either of theses modalities and to enhance transparency of the taken measures, reports from outside institutions were excluded. The impact of imaging modality—echocardiography (12.4%; 14 of 113) or CT (87.6%; 99 of 113)—was tested and was highly insignificant ($p = 0.54$). Therefore, the modality had virtually no effect on the other estimated coefficients of the growth model in the present study.

The measurements were taken at the maximum inner diameter of the sinus of Valsalva and compared with later measurements by the same modality in the same planes (because of the known differences between ultrasonographic and radiographic evaluation) [12]. With regard to the surgical procedure—ascending aortic replacement with or without AVR—measurements at the annulus and sinotubular junction were renounced owing to proximity of the anastomosis site.

We also calculated the number of years needed to reach 50 mm and 55 mm intervention thresholds. However, according to our institutional policy, indication for operative repair of aortic root aneurysm (in an asymptomatic patient) is a diameter greater than 45 mm, or an annual dilation of 5 mm or more (very rare), except in higher risk patients or if contraindications exist.

Statistical Analyses

As described previously by our group, we analyzed the growth rate of the aortic root by performing a multivariate regression analysis to estimate the growth pattern [13, 14]. Further details are reported in the Appendix.

Results

Patient Population and Follow-Up

Between 2004 and 2011, 113 patients underwent elective ascending aortic replacement by a root-sparing technique and fulfilled the inclusion and exclusion criteria. Among these, 9 patients were excluded owing to incomplete follow-up data by collaborative decision round and another 2 patients were determined to be outliers with observed aortic measurements greater than two standard deviations from the mean by our statistical experts. Therefore, the final cohort in this study consisted of 102 patients. However, as a number of patients had more than one imaging studies, 199 observations (change in aortic size between two images) were available for statistical

analysis. Mean time between Image_{T-1} and Image_T was 19.55 ± 16.52 months (range, 0 months to 8.75 years), and between first postoperative and most recent image, 41.62 ± 26.08 months (range, 2 months to 9.17 years). Patient demographics, characteristics, and comorbidities are depicted in Table 1.

Surgical Data

The proximal ascending aorta was replaced in all patients by a root-sparing technique; 66 of those (63.7%) received a concomitant AVR. In the distal ascending portion, 74 patients (72.5%) underwent extension into the arch under deep hypothermic circulatory arrest. Among those, the hemiarch was replaced in 60 (58.8% of all patients) and the total arch in 14 (13.7% of all patents). An elephant trunk stage-1 procedure was performed in 11 patients (10.8% of all patients). Sixteen patients (16%) underwent concomitant coronary artery bypass graft surgery.

Aortic Root Diameter and Growth Rate

The mean postoperative baseline diameter was 37.4 ± 3.76 mm (range, 27 to 48 mm), evaluated 5.63 ± 1.29 months postoperatively on average. Owing to inclusion of longitudinal observations, mean sizes at Image_T and Image_{T-1} were 38.79 ± 3.55 mm (range, 28 to 48 mm) and 38.20 ± 3.51 mm (range, 27 to 47 mm), respectively. In multivariate regression analysis, the coefficient on *TIME* was positive (0.000652) and highly significant ($p < 0.0001$). That indicates that the aortic root does grow over time. Mean growth rate is estimated at 0.41 mm per year (95% confidence interval: 0.35 to 0.46 mm per year). According to initial root size, the growth rate increases with larger diameter (Table 2, Fig 1). The time interval until 50 mm would be reached would be 29.1 years on average (Fig 2).

Table 1. Preoperative Patient Data

Measures	Study Group (n = 102)
Demographics	
Age, years	61.8 ± 12.5
Male	61 (59.8)
Characteristics	
Weight, kg	85.1 ± 19.1
Height, cm	172.0 ± 10.5
Body mass index, kg/m^2	28.6 ± 5.2
Root, initial diameter, mm	37.4 ± 3.8
Aortic valve pathology	
Stenosis	35 (34.3)
Insufficiency	36 (35.2)
Ratio	0.97:1
Bicuspid morphology	47 (46)
Comorbidities	
Coronary artery disease	23 (22.5)
Arterial hypertension	86 (84.3)
Dyslipidemia	50 (49.0)
Diabetes mellitus	7 (6.9)
Chronic renal failure	3 (2.9)
History of stroke	4 (3.9)
History of smoking	26 (25.5)

Values are mean ± standard deviation or n (%).

Effect of Contemporaneous AVR and Valve Morphology on Root

The dilation of the root is estimated respectively at 0.40 mm per year on average with concomitant AVR and at 0.42 mm per year on average without AVR. The coefficient on the interaction term *AVR*TIME* in multivariate regression analysis is small (−0.0000230) and insignificant ($p = 0.86$). These findings indicate that growth in the aortic root is unaffected by concomitant AVR after the root-sparing operation.

The distribution by native aortic valve morphology showed dilation of 0.42 mm per year for bicuspid valves and of 0.40 mm per year for tricuspid valves on average. The coefficient on the interaction term *BAV*TIME* is also small (0.0000593) and insignificant ($p = 0.62$). Data are summarized in Table 3.

Follow-Up

The mean clinical follow-up period was 72.0 ± 30.9 months (median 71.9; range, 13.9 to 143.8). One-year, 5-year, and 10-year survival estimation was 100%, 94.4% ± 2.5%, and 85.3% ± 5.3%, respectively. In total, 4 patients (3.9%) required aortic or aortic valve reoperation during follow-up. One of those each underwent AVR (because of endocarditis), arch replacement with elephant trunk stage-1 procedure, open descending aortic replacement, and abdominal aortic replacement. No patient required replacement of the primarily untouched root or had dissection of the proximal aorta. Freedom from aortic/aortic valve reoperation was 100%, 96.6% ± 1.9%, and 93.9% ± 3.2% at 1, 5, and 10 years, respectively; and freedom from aortic root events (aortic root replacement, aneurysm, or dissection of the untouched root) was 100% each at 1, 5, and 10 years.

Comment

Growth Behavior of Aortic Root and Other Portions

The aortic root, defined anatomically by the scaffold of the valve leaflets (aortic annulus) inferiorly and by the sinotubular junction superiorly, grows on average 0.41 mm per year after root-sparing aortic replacement. Other portions of the aorta show a considerably higher growth rate. In a recent study from our group, we evaluated the growth rates from our institutional database at the Aortic Institute at Yale–New Haven and found a growth rate of 2.0 mm per year in the ascending and arch portion, 2.26 mm per year in the descending aorta, and 2.3 mm per year in the thoracoabdominal sector (data are displayed in Fig 1) [15]. The dilation over time in these portions also increases with larger diameter. Given these preliminary data, the results of the present study indicate that the aortic root dilates at a rate almost fivefold less than all other parts of the aorta at the same size.

Table 2. Estimated Average Annual Growth Rates of Aortic Root by Initial Size

	Annual Growth Rate (mm per year)				
Initial Aortic Size	Total Cohort (n = 102)	No AVR (n = 36)	AVR (n = 66)	BV Morphology (n = 47)	TV Morphology (n = 55)
25 mm	0.27	0.27	0.26	0.28	0.26
30 mm	0.32	0.33	0.31	0.33	0.31
35 mm	0.37	0.38	0.35	0.39	0.36
40 mm	0.43	0.43	0.42	0.44	0.41
45 mm	0.48	0.49	0.48	0.50	0.47
50 mm	0.51	0.54	0.53	0.55	0.52
Mean, 37.3 mm	0.41	0.42	0.40	0.42	0.40

AVR = aortic valve replacement; BV = bicuspid valve; TV = tricuspid valve.

Although the macroscopic morphology of the aorta suggests a continuous and homogeneous network of tissue, the aorta is actually composed of distinct microscopic structures. The regional heterogeneity begins during embryogenesis [16, 17] and impacts the elasticity determining aortic media. The aortic media tunic, impaired by the remodeling process in aneurysms, consists of elastin, collagen, and vascular smooth muscle cells. These smooth muscle cells, derived from different embryologic origins, are suspected to affect the activity of matrix metalloproteinase [5], for example, differently in different aortic regions [18]. The vascular smooth muscle cells forming the tunics of the aortic root, originate from the secondary heart field—a derivate of the lateral plate mesoderm. The cells of the ascending aorta and aortic arch originate from the neural crest, and the descending portion is built by paraxial mesoderm (so-called “somatic mesoderm”) [16–18]. These embryologic differences likely effect not only the development of aneurysms, but also the long-term adult behavior. Furthermore, the “seams” between the different originating regions are hypothesized to be the vulnerable locations of the aorta and predisposing areas of aortic dissection [16].

Clinical Implications

Guidelines, published as a consensus paper of multiple associations, recommend replacing the aortic root in nonsyndromic patients at 55 mm or at a dilation of 5 mm or more per year [6–8]. Given the growth rate in the present study, the aortic root, found with an initial diameter of 37.4 mm (in patients aged 62 years on average), would not meet the 50 mm threshold for more than an immense 29 years. Only patients with a diameter of 45 mm and above are found to be at any substantial risk of a contemporary growth up to critical root dilation (at approximately 10 years after initial surgery). Our institutional policy regarding root replacement—in consent with many high-volume and specialized academic centers—anticipates intervention at lower thresholds than guidelines state, and recommends surgery at 45 mm.

These findings attest strongly to the safety of root-sparing aortic replacement in case of nonaneurysmal roots. The root-sparing technique, used in all patients of

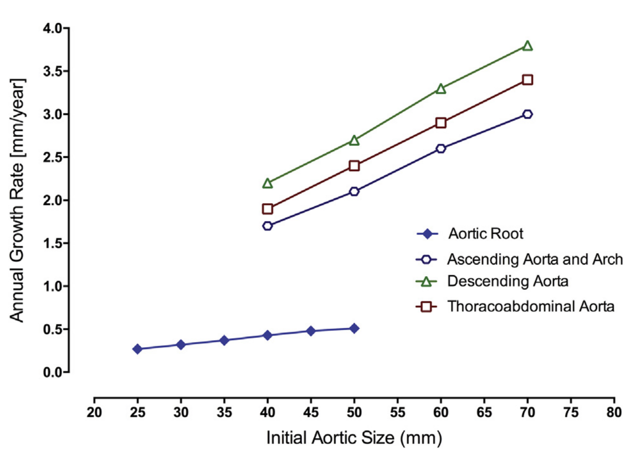

Fig 1. Annual growth rates according to different portions of the aorta: aortic root (bright blue line); ascending aorta and arch (dark blue line); descending aorta (green line); and thoracoabdominal aorta (brown line). (Data on the ascending aorta and arch, descending aorta, and thoracoabdominal aorta were evaluated and taken from a recent publication of our group [15]).

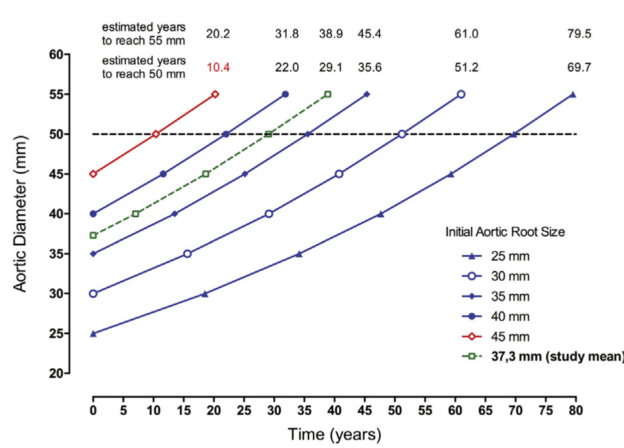

Fig 2. Aortic diameter according to initial aortic root size and growth rate: 25 mm (triangles); 30 mm (open circles); 35 mm (solid diamonds); 40 mm (solid circles); and 45 mm (open diamonds). Study mean was 37 mm (open squares). Horizontal dashed line represents the 50 mm diameter threshold.

Table 3. Results of Regression Models

Eq.	Variable	Adj. R^2	F	Coefficient Mean	Coefficient 95% CI	T Statistic	*p* Value
4.1	TIME	0.38	122.77	0.00065	0.00053–0.00077	11.08	<0.0001
4.2	TIME	0.38	61.10	0.00067	0.00046–0.00088	6.28	<0.0001
	AVR			−0.000023	…	0.18	0.857
4.3	TIME	0.38	61.27	0.00063	0.00048–0.00078	8.21	<0.0001
	BICUSPID			0.000059	−0.00018–0.00030	0.49	0.622

Interaction terms between growth rate, time (TIME), and both aortic valve replacement (AVR) and bicuspid valve morphology (BICUSPID). The equation numbers refer to the numbering in the Methods section.

Adj. = adjusted; CI = confidence interval; Eq. = equation.

the present cohort, replaces the ascending aorta superior to the level of the aortic valve suspension (sinotubular junction), and consequently, the coronary arteries (alternative terms: supracoronary or supracommissural), and leaves the native root tissue in situ. Sparing the root is the technically more simple approach compared with root replacement procedures (composite replacements, valve-sparing, remodeling, and so forth) because of lack of coronary artery reimplantation, and results in excellent clinical outcomes [9, 19–22]. Leaving the root behind in ascending aortic replacements, both De Paulis and colleagues [23] and Park and associates [24] noted that neither a progressive dilation of nonreplaced sinuses nor an incidence of root reoperations is evident in aneurysm patients, in contrast to aortic dissection. Their findings support the thrust of the current paper.

Dilation of the native root over time, however, is just one component of the complex decision whether to address the aortic root. Pathology and phenotype of the aortic aneurysm, underlying aortic valve pathology and its functional correlates, and the operative risk of primary aortic root replacement or of a potential reoperation at the aortic root need to be taken into account and individually weighed. In a separate upcoming publication, we report long-term outcomes of more than 600 aortic root replacements done contemporaneously with the patients reported in this study; our results, like those at other experienced centers, confirm the low risk of aortic replacement at high-volume institutions [10]. Therefore, the root-sparing procedures in our current report were accumulated because we believed they were appropriate for the patients and their anatomy—not out of any concern that full aortic root replacement was too dangerous.

A concomitant replacement of the aortic valve showed no significant impact on the growth rate of the aortic root. Any hypothesized effect of a proximal affixation by the prosthetic scaffold, either positively as root stabilization or negatively as decreased stretching capability, could not be confirmed.

Impacting Factors

The morphology of the aortic valve, which shares the neural crest as embryonic heritage with the ascending aorta [25], appeared not to affect the growth rate in the present study. Della Corte and colleagues [26] reported in bicuspid (but nonoperative) patients a growth rate of 0.3 mm per year, comparable to the 0.42 mm per year in our study. They also found a correlation between root phenotype of the aorta and valve morphotype with right-left fusion. In total, 41% in their cohort had an increase of the root diameter over time.

The most important impact on root dilation is exerted by the Marfan syndrome. Based on a mutation in the *FBN1* gene encoding *fibrillin-1* [27], Marfan patients had progressive dilation of the root (approximately 60% to 84% of all patients [28]) with the risk of dissection, rupture, and valve regurgitation. The growth rate in this connective tissue disorder was estimated to be approximately 1.5 mm per year by Lazarevic and colleagues [29] in 2006, and therefore was 3.5-fold higher than in the present nonsyndomic cohort. Although Meijboom and colleagues [30] calculated only a rate of 0.42 mm per year for males and 0.38 mm per year for females, 1 in 7 men and 1 in 9 women showed a fast growing root of more than 1.5 mm per year, resulting in a significant increase of aortic dissection in those patients (both studies examined nonsurgical patients). Therefore, an aortic replacement in root-sparing technique is not recommended for patients with syndromic diseases.

Study Limitations

The study is retrospectively based on a relatively small number of patients with an imaging interval between first and most recent image of approximately 3.5 years, which potentially raises concerns about selection bias and generalizability. Advanced analysis focusing on the influence of age, sex, valve pathology, and comorbidities were denied statistically owing to small subgroup sizes.

Thin slices (5 to 10 mm), orthonormal projection, and electrocardiography-gated imaging were preferred, but not available in all cases (especially for patients operated on in the earlier years of this study). We made every effort to evaluate the size in a plane perpendicular to the blood flow (avoiding obliquity); we made full use of all images available, including axial, coronal, and sagittal. Furthermore, follow-up scans were measured in the very same projection and modality used for the baseline measurements; therefore, technical issues should not significantly influence the change in size.

As noted, 9 patients were excluded because of incomplete follow-up, which was defined as inadequate quality of the images (for example, distorted projection, lack of contrast [CT], solely axial images [CT], or no available reconstruction [CT]), incomparable projection between S_B and S_L, or, if raw images were not available, lack of precise aortic root measurement. Two patients were classified as outliers by measurements greater than two standard deviations from the mean, and excluded based on the recommendation of our collaborative statistician. Even if they would be included into the study, however, the results are little affected.

Conclusions

The aortic root grows significantly more slowly than the remaining portions of the aorta. Neither a concomitant AVR nor the valve morphology appears to impact its growth rate. Seen in conjunction with clinical results, the replacement of the aorta by a root-sparing technique is an appropriate and safe approach, even in the long run, for patients with a root diameter less than 45 mm. Decision making with regard to aortic root procedures requires a multidimensional view, however; knowing the efficacy of a root-sparing approach is one important step in this process.

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References

1. Bickerstaff LK, Pairolero PC, Hollier LH, et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982;92:1103–8.
2. Clouse WD, Hallett JW, Schaff HV, Gayari MM, Ilstrup DM, Melton LJ. Improved prognosis of thoracic aortic aneurysms: a population-based study. JAMA 1998;280:1926–9.
3. Olsson C, Thelin S, Stahle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation 2006;114:2611–8.
4. Isselbacher EM. Thoracic and abdominal aortic aneurysms. Circulation 2005;111:816–28.
5. Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002;73:17–27.
6. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 Guidelines for the diagnosis and management of patients with thoracic aortic disease. J Am Coll Cardiol 2010;55:e27–129.
7. Erbel R, Aboyans V, Boileau C, et al. 2014 ESC guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. Eur Heart J 2014;35:2873–926.
8. Hiratzka LF, Creager MA, Isselbacher EM, et al. Surgery for aortic dilatation in patients with bicuspid aortic valves: a statement of clarification from the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol 2016;67:724–31.
9. Rinewalt D, McCarthy PM, Malaisrie SC, et al. Effect of aortic aneurysm replacement on outcomes after bicuspid aortic valve surgery: validation of contemporary guidelines. J Thorac Cardiovasc Surg 2014;148:2060–9.
10. Mok S, Ma WG, Mansour A, et al. Twenty-five year outcome of composite graft aortic root replacement: near "curative" impact on aortic root disease. Paper presented at: Annual Meeting of the Society of Thoracic Surgeons; January 23-27, 2016; Phoenix, AZ.
11. Elefteriades JA, Farkas EA. Thoracic aortic aneurysm: clinically pertinent controversies and uncertainties. J Am Coll Cardiol 2010;55:841–57.
12. Berger JA, Elefteriades JA. Toward uniformity in reporting of thoracic aortic diameter. Int J Angiol 2012;21:243–4.
13. Rizzo JA, Coady MA, Elefteriades JA. Procedures for estimating growth rates in thoracic aortic aneurysms. J Clin Epidemiol 1998;51:747–54.
14. Coady MA, Rizzo JA, Goldstein LJ, Elefteriades JA. Natural history, pathogenesis, and etiology of thoracic aortic aneurysms and dissections. Cardiol Clin 1999;17:615–35,vii.
15. Elefteriades JA, Ziganshin BA, Rizzo JA, et al. Indications and imaging for aortic surgery: size and other matters. J Thorac Cardiovasc Surg 2015;149(Suppl):10–3.
16. Waldo KL, Hutson MR, Ward CC, et al. Secondary heart field contributes myocardium and smooth muscle to the arterial pole of the developing heart. Dev Biol 2005;281:78–90.
17. Ruddy JM, Jones JA, Ikonomidis JS. Pathophysiology of thoracic aortic aneurysm (TAA): is it not one uniform aorta? Role of embryologic origin. Prog Cardiovasc Dis 2013;56:68–73.
18. Cheung C, Bernardo AS, Trotter MWB, Pedersen RA, Sinha S. Generation of human vascular smooth muscle subtypes provides insight into embryological origin-dependent disease susceptibility. Nat Biotechnol 2012;30:165–73.
19. Reece TB, Singh RR, Stiles BM, et al. Replacement of the proximal aorta adds no further risk to aortic valve procedures. Ann Thorac Surg 2007;84:473–8.
20. Sioris T, David TE, Ivanov J, Armstrong S, Feindel CM. Clinical outcomes after separate and composite replacement of the aortic valve and ascending aorta. J Thorac Cardiovasc Surg 2004;128:260–5.
21. Castrovinci S, Tian DH, Murana G, et al. Aortic root replacement with biological valved conduits. Ann Thorac Surg 2015;100:337–53.
22. Peterss S, Charilaou P, Dumfarth J, et al. Aortic valve disease with ascending aortic aneurysm: impact of concomitant root-sparing (supracoronary) aortic replacement in non-syndromic patients. J Thorac Cardiovasc Surg 2016 May 28 [E-Pub ahead of print].
23. De Paulis R, Cetrano E, Moscarelli M, et al. Effects of ascending aorta replacement on aortic root dilatation. Eur J Cardiothorac Surg 2005;27:86–9.
24. Park CB, Greason KL, Suri RM, Michelena HI, Schaff HV, Sundt TM. Fate of nonreplaced sinuses of Valsalva in bicuspid aortic valve disease. J Thorac Cardiovasc Surg 2011;142:278–84.
25. Fernandez B, Duran AC, Fernandez-Gallego T, et al. Bicuspid aortic valves with different spatial orientations of the leaflets are distinct etiological entities. J Am Coll Cardiol 2009;54:2312–8.
26. Della Corte A, Bancone C, Buonocore M, et al. Pattern of ascending aortic dimensions predicts the growth rate of the aorta in patients with bicuspid aortic valve. J Am Coll Cardiol Img 2013;6:1301–10.
27. Milewicz DM, Dietz HC, Miller DC. Treatment of aortic disease in patients with Marfan syndrome. Circulation 2005;111:e150–7.
28. Aburawi EH, O'Sullivan J. Relation of aortic root dilatation and age in Marfan's syndrome. Eur Heart J 2007;28:376–9.
29. Lazarevic AM, Nakatani S, Okita Y, et al. Determinants of rapid progression of aortic root dilatation and complications in Marfan syndrome. Int J Cardiol 2006;106:177–82.
30. Meijboom LJ, Timmermans J, Zwinderman AH, Engelfriet PM, Mulder BJ. Aortic root growth in men and women with the Marfan's syndrome. Am J Cardiol 2005;96:1441–4.