Ascending aortic geometry and its relationship to the biomechanical properties of aortic tissue

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ABSTRACT

Objective: The objective of this study was to evaluate the relationship between ascending aortic geometry and biomechanical properties.

Methods: Preoperative computed tomography scans from ascending aortic aneurysm patients were analyzed using a center line technique (n = 68). Aortic length was measured from annulus to innominate artery, and maximal diameter from this segment was recorded. Biaxial tensile testing of excised tissue was performed to derive biomechanical parameters energy loss (efficiency in performing the Windkessel function) and modulus of elasticity (stiffness). Delamination testing (simulation of dissection) was performed to derive delamination strength (strength between tissue layers).

Results: Aortic diameter weakly correlated with energy loss ($r^2 = 0.10; P < .01$), but not with modulus of elasticity ($P = .13$) or delamination strength ($P = .36$). Aortic length was not associated with energy loss ($P = .87$), modulus of elasticity ($P = .13$) or delamination strength ($P = .90$). Using current diameter guidelines, aortas $>55$ mm (n = 33) demonstrated higher energy loss than those $<55$ mm (n = 35; $P = .05$), but no difference in modulus of elasticity ($P = .25$) or delamination strength ($P = .89$). A length cutoff of 110 mm was proposed as an indication for repair. Aortas $>110$ mm (n = 37) did not exhibit a difference in energy loss ($P = .40$), modulus of elasticity ($P = .69$), or delamination strength ($P = .68$) compared with aortas $<110$ mm (n = 31). Aortas above diameter and length thresholds (n = 21) showed no difference in energy loss ($P = .35$), modulus of elasticity ($P = .55$), or delamination strength ($P = .61$) compared with smaller aortas (n = 47).

Conclusions: Aortic geometry poorly reflects the mechanical properties of aortic tissue. Weak association between energy loss and diameter supports intervention at larger diameters. Further research into markers that better capture aortic biomechanics is needed. (JTCVS Open 2022;1:1-13)

CENTRAL MESSAGE

The geometry of the ascending aorta is not a reliable marker of material properties in aneurysmal aortic tissue. Additional research is needed before length-based thresholds can be considered.

PERSPECTIVE

Current diameter guidelines fail to identify most type A dissection patients, promoting the exploration of aortic length as a new marker for dissection risk stratification. However, compared with material properties of aneurysmal tissue, use of aortic length was inferior to diameter in distinguishing at risk aneurysms. Additional research is needed before length thresholds can be considered.

See Commentary on page XXX.
Patients with ascending thoracic aortic aneurysms (TAAs) are at increased risk of dissection or rupture. To prevent these events, current guidelines recommend elective repair of most ascending TAAs at diameters ≥55 mm.1-4 However, although enlarged aortas are undoubtedly at risk for dissection, data from the International Registry of Aortic Dissection and others report that this threshold fails to identify most patients who present with acute type A aortic dissection (ATAD).5,6 As such, alternate markers that capture dissection risk in aneurysms with smaller diameters are urgently needed.

Recently, aortic length has become a marker of interest for prediction of ATAD. The use of aortic length was first introduced as part of the Tübingen Aortic Pathoanatomy (TAIPAN) project, in which the lengths of the ascending aorta in 150 patients who had aortic dissection were observed to be significantly longer than in healthy aortic control participants.7 Our group confirmed that after adjusting for demographic covariates and the conformational changes associated with the dissection event, the dissected aortas were longer than normal aortas and aneurysms that had not dissected.8 Furthermore, the Yale group identified a hinge point rise in the probability of adverse aortic events for ascending aortas longer than 11.5 cm, prompting the authors to suggest an 11-cm length cutoff for offering elective repair.9 However, our group found only 45% of patients treated for ATAD presented with lengths >11 cm at the time of dissection.10 It therefore remains unclear whether aortic elongation can reliably predict the risk of aortic dissection.

Examination of aortic biomechanics might help clarify the usefulness of aortic length. Aortic biomechanics provides information on the material properties of aortic tissue and its susceptibility to dissection. Several biomechanical parameters have been previously described and include: 1) energy loss, a measure of the efficiency in which the aorta performs the necessary Windkessel function,10,11 2) modulus of elasticity, a measure of tissue stiffness,12-15 and 3) delamination strength, a measure of the adhesion strength between layers of tissue.11,16,17 Patients with aneurysmal ascending aortas exhibit increased energy loss11 and modulus of elasticity,14 as well as decreased delamination strength11,17 compared with healthy aortic control participants.

In this study we examined the relationship between aortic geometry of the ascending aorta (ie, aortic diameter and length), and the mechanical properties of aneurysmal aortic tissue. We hypothesized that increased aortic length, and not just aortic diameter, is associated with increased risk of mechanical failure in the aorta, as defined by increased energy loss and modulus of elasticity, and decreased delamination strength. Current and proposed geometric-based thresholds were also evaluated to determine whether they successfully segregate patients into high and low risk groups with respect to their biomechanical features.

**METHODS**

**Study Population**

This study was approved by the Research Ethics Board of the University Health Network (16-6285, July 27, 2017). All participants provided written informed consent. Ascending aortic samples from 112 patients who underwent elective aortic surgery were collected between March 2017 and August 2019. Patients without available preoperative computed tomography scans (n = 38) and patients without aortic biomechanics data (n = 6) were excluded, leaving a final cohort of 68 patients. All patient records were reviewed and relevant clinical data were collected.

All aneurysms were subdivided into a small or large aneurysm group using 3 definitions. First, a diameter threshold of 55 mm (>55 mm: n = 33, ≤55 mm: n = 35). Second, a length threshold of 110 mm (>110 mm: n = 37, ≤110 mm: n = 31). Third, a combined diameter and length threshold of 55 mm and length threshold of 110 mm (>55 mm and 110 mm: n = 24, ≤55 mm and 110 mm: n = 22).

**Sample Preparation**

Aneurysmal ascending aortic tissues from patients who underwent elective aortic surgery at Toronto General Hospital were collected from the operating room and immediately placed on ice. The tissues were then stored at 4 °C in Ringer lactate solution and tested within 24 hours of collection. Aortic samples were received in the form of a complete ring, with orientation marked by the surgeon (Figure 1, A). A custom-made 14 mm × 14 mm cutter was used to collect square samples from the outer and inner curvature for biaxial tensile tests. Up to 3 square samples were cut along the longitudinal (long) axis of the outer curvature, and 1 square sample was cut from the inner curvature. Adjacent to biaxial squares, a 6 mm × 30 mm rectangular piece was cut for delamination testing (Figure 1, B).

**Mechanical Testing**

**Biaxial tensile testing.** Aortic thickness for biaxial tensile testing was measured using a high magnification (12×) zoom lens (Navitar) before mechanical testing. Biaxial testing was performed as previously described.11 Briefly, each biaxial square sample was mounted onto a Biotester (CellScale) using tungsten rakes for displacement-controlled biaxial tensile testing in 37 °C Ringer lactate solution (Figure 1, C). Samples were

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**Abbreviations and Acronyms**

ATAD = acute type A aortic dissection
circ = circumferential
IQR = interquartile range
long = longitudinal
TAA = thoracic aortic aneurysm

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subjected to 10 preconditioning stretch cycles followed by 3 analyzed cycles under 25% equibiaxial strain. From the generated stress–strain curve, energy loss and the tangent modulus of elasticity at 10% strain were calculated in the long and circumferential (circ) directions of loading.

Energy loss is a measure of the efficiency with which the aorta performs the Windkessel function. Higher values of energy means a higher proportion of energy absorbed by the aorta during loading is dissipated and less of it is returned to the circulation. Modulus of elasticity measures tissue stiffness, with higher values indicating greater stiffness. Less healthy tissue would therefore have higher levels of energy loss and modulus of elasticity.

**Delamination testing.** Delamination tests were performed on the rectangular tissue samples as previously described. 11 Tissue width was confirmed using the built-in Biotester camera and measured using ImageJ version 1.52p (National Institutes of Health). An initial incision was made in the media and the medial layer was manually peeled from the proximal to distal end of the aorta tissue section until 14 mm of unpeeled length remained. The samples were then mounted onto the Biotester for uniaxially peeling at a constant rate of 0.01 mm/s in 37 °C Ringer lactate solution (Figure 1, D). Force measurements were recorded, and delamination strength was found by dividing average force by sample width. Aortic tissue that is resistant to dissection has a higher delamination strength than aortas that are prone to dissection.

**Aortic Dimension Measurements**

All image analysis for this study was performed using Aquarius iNtuition (TeraRecon, Inc). In the coronal view, digital markers were placed from the bottom of aortic annulus to proximal innominate artery to define proximal and distal boundaries of the ascending aorta (A). A center line is then generated between defined boundary points, and ascending aortic length and maximum aortic diameter within this region is measured (B).
annulus to the most distal end of the visible aorta, ensuring accurate coverage up to the aortic arch (Figure 2, A). A semiautomatic center line was generated through the entire length of the aorta, with manual inspection for appropriate symmetry around the center line. For aortic length measurements, manually placed markers at the annulus and proximal limit of the origin of the innominate artery were used to define the ascending aorta (Figure 2, B, Video 1). The maximal diameter measurements for this segment were then generated from built-in volume analysis tools, with manual inspections and adjustments to aortic boundaries made as needed.

Statistical Analysis

All continuous variables are presented as median and interquartile range (IQR). All categorical variables are presented as percentages. To compare between 2 continuous variables, Mann-Whitney tests were used. To compare between 2 categorical variables (eg, sex across groups), χ² tests were used. Linear regression models were used to quantify the association of aortic biomechanics with aortic diameter and length, separately, evaluated using coefficient of determination. To compare aortic biomechanics between defined aortic subgroups, unpaired Mann-Whitney tests were used. All analyses were completed using Prism 5 (GraphPad).

RESULTS

The average age of this 68-patient cohort was 64.50 years (IQR, 53.50-74.00 years) and 32% were female. Demographic data for the defined small and large diameter and length aneurysm groups are presented in Table 1. Patients with large lengthwise aneurysms (>110 mm) were taller than smaller lengthwise aneurysms (<110 mm; 1.75 m [IQR, 1.69-1.80 m] vs 1.70 m [1.54-1.78 m]; P = .056) and patients with large diametwise aneurysms (>55 mm) presented with fewer cases of aortic stenosis than smaller diameter aneurysms (<55 mm; n = 12 vs n = 40; P = .01). Otherwise, no other differences in patient demographic characteristics were observed between small and large aneurysms using either the diameter or length cutoffs (Table 1). In comparisons of aortic size in terms of diameter and length, larger aneurysms (diameter >55 mm and length >110 mm) presented with more cases of aortic insufficiency than smaller aneurysms (diameter <55 mm and length <110 mm; n = 54 vs n = 23; P = .04) and fewer cases of aortic stenosis (n = 8 vs n = 41; P = .01). No other differences in baseline characteristics between larger and smaller aneurysms when considering diameter and length were observed (Table E1).

Table 1. Patient demographic characteristics for study population divided according to diameter and length thresholds

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<th>Lengthwise aneurysms</th>
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<td>&lt; 55 mm (n = 35)</td>
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All continuous variables are presented as median and interquartile range. All categorical variables are presented as percentages. To compare between 2 continuous variables, Mann-Whitney tests were used. To compare between 2 categorical variables, χ² tests were used. Italic indicates P > .05. BAV, Bicuspid aortic valve; CTD, connective tissue disorder; AI, aortic insufficiency; AS, aortic stenosis.
\( r^2 = 0.04 \ [P = .13] \); long: \( r^2 = 0.02 \ [P = .22] \); Figure 3, E) or delamination strength (\( r^2 = 0.01 \ [P = .36] \); Figure 3, F) was observed. In the inner curvature, there was no correlation between aortic diameter and any of the 3 mechanical parameters (Figure 3, A, B, and C).

**Ascending aortic length.** Ascending aortic length (110.5 mm [IQR, 103.0-119.0 mm]) was compared against the same 3 biomechanical parameters: energy loss, modulus of elasticity, and delamination strength to evaluate association between aortic elongation and the biomechanics of the aorta. No correlations were observed in the outer curvature between elongation of the aorta and energy loss (circ: \( r^2 = 0.01 \ [P = .51] \); long: \( r^2 = 0.00 \ [P = .87] \)), modulus of elasticity (circ: \( r^2 = 0.01 \ [P = .36] \); long: \( r^2 = 0.04 \ [P = .13] \)), or delamination strength (\( r^2 = 0.00 \ [P = .90] \); Figure 4, D, E, and F). Similarly, energy loss (circ: \( r^2 = 0.00 \ [P > .90] \); long: \( r^2 = 0.02 \ [P = .40] \)); Figure 4, A), modulus of elasticity (circ: \( r^2 = 0.01 \ [P = .37] \); long: \( r^2 = 0.02 \ [P = .53] \); Figure 4, B), and delamination strength (\( r^2 = 0.00 \ [P = .70] \)) in the inner curvature were not correlated with lengths of the ascending aorta (Figure 4, A-C).

**Geometric-Based Thresholds of the Ascending Aorta Diameter threshold.** Aortic biomechanics between small (<55 mm in diameter; 48.60 mm [IQR, 45.60-53.30 mm]) and large (>55 mm in diameter; 58.60 mm [IQR, 57.05-61.05 mm]) diameterwise aneurysms were compared. In the outer curvature, larger diameter aneurysms exhibited greater energy loss in the circumferential axis but not the long axis (circ: \( P = .05 \); long: \( P = .16 \); Figure 5, A). No differences were observed in modulus of elasticity (circ: \( P = .25 \), long: \( P = .32 \)) or delamination strength (\( P = .89 \); Figure 5, B and C). In the inner curvature, no differences between small and large diameter aneurysms were detected for energy loss (circ: \( P = .68 \); long: \( P = .52 \); Figure 5, D) or delamination strength (\( P = .37 \); Figure 5, C). Smaller diameter aneurysms exhibited marginally increased modulus of elasticity in the circ axis (\( P = .06 \)) compared with larger diameter aneurysms (Figure 5, E).

**FIGURE 3.** Ascending aortic diameter and its association with the mechanical properties of aortic tissue. Energy loss in the outer curvature (OC) was the only mechanical property associated with ascending aortic diameter (A). No relationship between modulus of elasticity and aortic diameter (B) or delamination strength and aortic diameter (C) in the OC was observed. Similarly, no relationship between energy loss and aortic diameter (D); modulus of elasticity and aortic diameter (E), or delamination strength and aortic diameter (F) in the inner curvature (IC) was observed. Circ, Circumferential; long, longitudinal.
No difference in modulus of elasticity in the long axis was observed ($P = .10$).

**Length threshold.** Small (<110 mm in length; 103.0 mm [IQR, 95.90-108.0 mm]) and large (>110 mm in length; 119.0 mm [IQR, 113.0-123.0 mm]) lengthwise aneurysms were compared using aortic biomechanics to evaluate the newly proposed aortic length guidelines in dissection risk stratification. In the outer curvature, no differences in energy loss (circ: $P = .63$; long: $P = .40$), modulus of elasticity (circ: $P = .73$; long: $P = .69$), or delamination strength ($P = .68$) were detected between small and larger length aneurysms (Figure 6, A-C). Similarly, no differences were observed in the inner curvature for energy loss (circ: $P = .99$; long: $P = .92$), modulus of elasticity (circ: $P = .71$; long: $P = .77$), or delamination strength ($P = .22$) between aortic subgroups (Figure 6, D-F).

**Combined diameter and length threshold.** A combined diameter and length threshold was used to divide aneurysmal patients into small (diameter <55 mm and length <110 mm) and large (diameter >55 mm and length >110 mm) aneurysms for comparison with aortic biomechanics. In the outer curvature, there was no difference in energy loss (circ: $P = .35$; long: $P = .65$), modulus of elasticity (circ: $P = .55$; long: $P = .41$), or delamination strength ($P = .61$) between small and large aneurysms (Figure E2, A-C). Similarly, in the inner curvature, no difference in energy loss (circ: $P = .93$; long: $P = .61$), modulus of elasticity (circ: $P = .23$; long: $P = .34$), or delamination strength ($P = .30$) was observed (Figure E2, D-F).

**DISCUSSION**

In this study of systematic comparisons between aortic geometry and the biomechanics of the ascending aorta, we found aortic geometry poorly predicted material properties of aneurysmal aortic tissue. Although increasing aortic diameter weakly correlated with increasing energy loss in aneurysmal tissue, we observed no difference in delamination strength between small and large aneurysms using a diameter threshold. Furthermore, we found no differences in material properties of longer aortic aneurysms compared with shorter-length aneurysms. Finally, when we compared...
small and large aortic aneurysms defined using a combined aortic diameter and length criteria, we found no differences in their aortic biomechanics. Therefore, our study provides further evidence that aortic diameter alone is insufficient for dissection risk prediction, and that from a biomechanics perspective, the use of aortic length might not provide any additive value. We suggest that more study in this area is needed (Figure 7).

Previous studies have shown longer aortas in dissected populations compared with healthy aortic control participants. However, the observed lengthening might not be related to any changes in material properties that would render the longer aorta at greater risk of dissection. An alternative explanation is the notable relationship between aortic geometry and other factors common within the dissected aneurysm cohort, in particular, the presence of hypertension. Dotter and colleagues compared length from the sinus of Valsalva to the left subclavian artery in 26 hypertensive patients and 86 aortic controls and reported the presence of hypertension significantly added to the lengthening process of the ascending aorta. Craiem and colleagues, after correcting aortic length for the effects of age, reported unfolding due to the presence of hypertension was equivalent to approximately 5 years of aortic aging. In our previous study on aortic length, the group that suffered aortic dissection exhibited the highest rates of hypertension (73%), followed by nondissected aneurysms (54%). We must therefore consider that longer aortas might in fact reflect the important but common and nonspecific risk factor of hypertension, rather than the more specific correlation with the susceptibility to dissect in terms of the material properties of the aortic tissue. The consequences of recommending elective surgery to replace longer aortas requires closer examination.

This current study adds significantly to the scant literature on the association between aortic geometry and the biomechanics of the aorta. Iliopoulos and colleagues previously evaluated ascending aortic diameter and its relation to failure stress, a measure of tissue strength, and reported there was no evidence to support a relationship between increasing aortic diameter and decreasing tissue strength. In line with this study, we have also shown no decrease in delamination strength with increasing aortic diameter, and furthermore, our group has also evaluated the relationship of aortic lengthening with the biomechanics of the aorta, in which we found no difference in tissue strength between varying aortic lengths.

In previous studies, our group has found a weak association between increasing aortic diameter and decreased tissue strength within the ascending aorta. Although this relationship was not reproduced within this study population, our group did discover a weak association between aortic diameter and energy loss within aneurysmal aortic tissue, which was consistent with our previous findings.

FIGURE 5. Biomechanical comparison of large and small diameter-based aneurysms. Larger diameterwise aneurysms exhibited higher energy loss compared with smaller diameterwise aneurysms in the outer curvature (OC; A). No difference in modulus of elasticity (B) or delamination strength (C) was observed between large and small diameterwise aneurysms in the OC. Similarly, no difference in energy loss (D), modulus of elasticity (E), or delamination strength (F) was observed between large and small diameter-wise aneurysms in the inner curvature (IC). EL, Energy loss; circ, circumferential; long, longitudinal; E, Modulus of elasticity.
There is therefore evidence to support larger diameter aneurysms can be associated with unfavorable material properties (ie, higher energy loss) and thus, should be resected at current diameter thresholds. However, because most dissection patients present at diameters less than the 55-mm threshold,5,6 diameter alone is not a reliable predictor for changes in material properties for smaller diameter aneurysms. This mismatch between aortic geometry and material properties can be explained when considering the underlying microstructural changes seen in aneurysms of the ascending aorta. Mennander and colleagues21 captured medial degeneration between diameter-matched bicuspid aortic valve and tricuspid aortic valve patients, including medial fibrosis, elastic fiber loss/fragmentation, and mucoid extracellular matrix accumulation, and discovered only minimal medial degeneration within larger diameter bicuspid aortic valve aortas compared with tricuspid aortic valves. Chaudry and colleagues22 also analyzed this association between aortic size and medial degeneration in 100 resected thoracic aortas without separation for valve morphology and reported an overall weak association between increasing aortic diameter and increasing degree of medial degeneration in univariate analysis, with 20% of aortas <55 mm in diameter also presenting with medial degeneration similar to larger aortic aneurysms. Because changes in aortic wall material properties are a functional result of medial degeneration, the poor association between aortic size and material properties in this study is therefore explained by the equally poor association between size and degree of medial degeneration.

**Study Limitation**

Our study is limited by the fact that delamination strength is a surrogate for aortic dissection. The *ex vivo* experimental protocol is necessarily controlled and reproducible. In contrast, a patient’s aorta tears at various angles and directions, and under various loading conditions. Nonetheless, delamination strength was previously shown to be higher in transplant donor patients with normal aortas compared with patients who had aortic dissection, and patients with aortic aneurysms showing delamination strengths between these 2 controls.

We also acknowledge that the differences in patient demographic characteristics and comorbidities between comparison groups (ie, sex, height, and aortic valve function) can influence the material properties of the aorta as well as aortic geometry. In fact, our group and others have previously shown differences in material properties and geometry of the aorta when patient populations are divided on the basis of sex and aortic valve morphology.11,23,24 Furthermore, although in previous work our group did not show a change in aortic length following increasing patient height,8 the aortic cross-sectional area to height ratio is well published within the literature and is still accepted by our

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**FIGURE 6.** Biomechanical comparison of large and small length-based aneurysms. No difference in energy loss (A), modulus of elasticity (B), or delamination strength (C) was observed between longer and shorter length aneurysms in the outer curvature (OC). Similarly, no difference in energy loss (D), modulus of elasticity (E), or delamination strength (F) was observed in the inner curvature (IC). EL, Energy loss; circ, circumferential; long, longitudinal; E, Modulus of elasticity.
group. Future studies, with larger sample populations, will incorporate adjustments for confounding factors.25-27

CONCLUSIONS
The geometry of the ascending aorta is not a reliable marker of material properties in aneurysmal aortic tissue. Current diameter-based thresholds and newly proposed length-based thresholds cannot confidently discriminate aneurysms with high susceptibility to dissect. Additional research is needed before length-based thresholds can be considered to evaluate TAA patients for elective repair.

Webcast You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/2194.

Conflict of Interest Statement
The authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

**Key Words:** ascending aorta, aneurysm, dissection, aortic biomechanics
FIGURE E1. Ascending aortic length indexed to patient height and its association with the mechanical properties of aortic tissue. No relationship between energy loss and aortic length (A), modulus of elasticity and aortic length (B), or delamination strength and aortic length (C) was observed in the outer curvature (OC). Similarly, no relationship between energy loss and length (D), modulus of elasticity and length (E), or delamination strength and aortic length (F) was observed in the inner curvature (IC). Circ, Circumferential; long, longitudinal.
FIGURE E2. Biomechanical comparison of large and small geometric-based aneurysms, on the basis of a combined diameter and length threshold. No difference in energy loss (A), modulus of elasticity (B), or delamination strength (C) was observed between overall small and large geometric aneurysms in the outer curvature (OC). Similarly, no difference in energy loss (D), modulus of elasticity (E), or delamination strength (F) was observed in the inner curvature (IC). Circ, Circumferential; Long, longitudinal.
### TABLE E1. Patient demographic characteristics for study population divided by a combined diameter and length threshold

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<th>Small aneurysms &lt;55 mm diameter and &lt;110 mm length (n = 22)</th>
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All continuous variables are presented as median and interquartile range. All categorical variables are presented as percentages. To compare between 2 continuous variables, Mann–Whitney tests were used. To compare between 2 categorical variables, $\chi^2$ tests were used. Italic indicates $P > .05$. BAV, Bicuspid aortic valve; CTD, connective tissue disorder; AI, aortic insufficiency; AS, aortic stenosis.