Ascending aorta dilatation rates in patients with tricuspid and bicuspid aortic stenosis: the COFRASA/GENERAC study

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Background
Ascending aorta (AA) dilatation is common in aortic valve stenosis (AS) but data regarding AA progression, its determinants and impact of valve anatomy [bicuspid (BAV), or tricuspid (TAV)] are scarce.

Methods and Results
Asymptomatic AS patients enrolled in a prospective cohort (COFRASA/GENERAC) with at least 2 years of follow-up were considered in the present analysis. A transthoracic echocardiography (TTE) and a computed tomography (CT) scan were performed at inclusion and yearly thereafter. We enrolled 195 patients [mean gradient 22 ± 11 mmHg, 42 BAV patients (22%)]. Mean aorta diameters assessed using TTE were 35 ± 4 and 36 ± 5 mm at the sinuses of Valsalva and tubular level, respectively. Ascending aorta diameter was >40 mm in 29% of patients (24% in TAV vs. 52% in BAV, \(P < 0.01\)). Determinants of AA diameters were age, sex, BSA, and BAV, but not AS severity. After a mean follow-up of 3.8 ± 1.5 years, AA enlargement rate assessed using TTE was \(+0.18 ± 0.34 \text{mm/yr}\) and \(+0.36 ± 0.54 \text{mm/yr}\) at the Valsalva and tubular level, respectively. Determinants of the progression of AA size were smaller AA diameter (\(P < 0.01\)) but not baseline AS severity or valve anatomy (all \(P > 0.05\)). Only four patients presented an AA progression >2 mm/year. Correlations between TTE and CT scan were excellent (all \(r > 0.74\)) and similar results were obtained using CT. During follow-up, two BAV patients underwent a combined AA surgery; no surgery was primarily performed for AA aneurysm and no dissection was observed.

Conclusion
In this prospective cohort of AS patients determinants of AA diameters were age, sex, BSA, and valve anatomy but not AS severity. AA progression rates were low and not influenced by AS severity or valve anatomy.

Keywords
aortic stenosis • ascending aorta • echocardiography • computed tomography

Introduction
Aortic valve stenosis (AS) is the most common valvular heart disease in Western countries. Aortic valve stenosis affects 2–7% of the population aged over 70 years, and its prevalence is going to dramatically increase with the ageing of the population. Ascending aorta (AA) enlargement is a common feature in AS patients, especially in those with bicuspid aortic valve (BAV). According to the current guidelines, a combined AA surgery at the same time than the valve surgery is recommended at significantly lower threshold (45 mm) than for isolated ascending aorta aneurysm (55 mm). The rational for this strategy is that AA will progress over years and that a preventive combined surgery will prevent the need for a second intervention. However a combined AA replacement is associated with an
increase surgical morbidity and mortality\(^1\) and the natural history of
the AA progression in patients with AS, by far the most common in-
dication for valve replacement is poorly known. These gaps are even
further crucial to address as transcatheter aortic valve replacement
(TAVR) has profoundly change the clinical management of AS pa-
tients and indications will extend in the near future to intermediate-
risk and possibly low-risk patients.\(^5\) Thus, the aims of this study were
to evaluate the determinants of AA size and of its enlargement in pa-
tients with AS and more specifically to assess the impact of AS sever-
ity and valve anatomy.

**Methods**

**Study design**

Patients with degenerative AS enrolled between November 2006 and
February 2015 in the COFRASA/GENERAC cohort (clinicalTrial.gov
number NCT00338676 and NCT00647088) which aimed to evaluate
the determinants of AS occurrence and progression and with at least
2 years of follow-up constituted our study population. Inclusion criteria
were pure, at least mild (defined by a mean pressure gradient (MPG)
\(\geq 10\) mm Hg and aortic valve structural changes (thickening/calcification)]
asymptomatic AS (patients had to be free of dyspnoea, angina and chest
pain). Exclusion criteria were AS due to rheumatic disease or radiother-
apy, more than mild coexisting aortic regurgitation (defined by a vena contracta width \(\geq 3\) mm or a regurgitant volume \(\geq 30\) mL), associated valvular disease or severe renal insufficiency
(creatinine clearance \(\leq 30\) mL/min). All patients underwent, the same day,
a clinical evaluation, a transthoracic echocardiography (TTE) and a multi-
slice computed tomography (MSCT) at inclusion and yearly thereafter
blinded of each other. Our regional ethic committee approved the study
and all patients gave a written informed consent.

**Echocardiography**

All echocardiographies were performed at baseline and on yearly basis
by one single trained echographer (D.M.-Z). The AA was measured at
the sinuses of Valsalva and at the tubular level, according to the
American Society of Echocardiography and the European Association of
Cardiovascular Imaging recommendations,\(^6,7\) i.e. in end-diastole (onset of
the QRS) from the leading edge of the anterior aortic wall to the leading
deck of the posterior aortic wall, on the parasternal long-axis view, per-
pendicular to the long axis of the aorta (Figure 1). We subsequently
indexed the AA size to the body surface area (BSA). AS severity was as-
sessed by MPG, aortic peak velocity (PV), and aortic valve area (AVA) cal-
culated by continuity equation, secondarily indexed to the BSA (AVAi).\(^8\)
Mild AS was defined as a MPG \(<20\) mm Hg, moderate AS as a MPG be-
tween 20 and 40 mm Hg, and severe AS as a MPG \(\geq 40\) mm Hg. Aortic
valvular anatomy (bicuspid or trileaflet) was determined using TTE at in-
clusion in a parasternal short axis view.

**MSCT measurements**

Multi-slice computed tomography was performed at baseline and yearly
thereafter the same day than TTE using a Philips scanner (MX 8000 IDT
16, Philips Medical Systems, Andover, MA, USA) or a General Electric
scanner (Light speed VCTTM, General Electric Company, Fairfield,
Connecticut, USA). All MSCT were electrocardiogram-gated without
contrast enhancement or any B-blockers use. Ascending aorta size was
measured by one single experienced radiologist (N.P.) blinded from TTE
measurements. According to the European Association of Cardiovascular
Imaging recommendations,\(^6\) AA was measured from inner edge to inner
diameter. At the level of the sinuses of Valsalva, four diameters were meas-
ured, three from a short axis view: diameter from the left coronary cusp
(LLC) to the right coronary cusp (RCC) (Valsalva 1), diameter from the
left coronary cusp (LLC) to the non-coronary cusp (NCC) (Valsalva 2),
and diameter from the right coronary cusp (RCC) to the non-coronary
cusp (NCC) (Valsalva 3). The fourth diameter of the sinuses was meas-
ured in a 3-chambers view (Valsalva 4). The tubular ascending aorta was
measured on a plane strictly perpendicular to the main axis of the aorta, at
the larger AA level. MSCT measurements are illustrated in Figure 2.

**Statistical analysis**

Categorical variables were expressed as number of patients (per cent)
and analysed with the \(\chi^2\) test or Fisher exact test. Continuous variables

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**Figure 1** Parasternal long-axis view illustrating measurement of the ascending aorta at the sinuses of Valsalva and tubular level at end-diastole (leading edge–to–leading-edge method) using transthoracic echocardiography.
were expressed as mean ± standard deviation or median and 25–75th percentile for non-normally distributed variables and analysed using the Student’s t-test or the Mann–Whitney–Wilcoxon test as appropriate. Correlation between TTE and MSCT measurements was calculated using Pearson correlation coefficient. Aortic aneurysm was defined as an aorta diameter ≥ 40 mm (at the sinuses or at the tubular level). Yearly AA enlargement rate (in mm/year) was calculated as: final AA diameter—baseline AA diameter/follow-up duration. Enlargement rate was calculated at the level of the sinuses of Valsalva and at the level of the tubular aorta for both TTE and MSCT. Based on previous studies and on the upper tertile of tubular progression rate in our study population, rapid progression was defined as AA enlargement rate ≥ 0.50 mm/year. Linear regressions in univariate analysis and in multivariate analysis after adjustment for age, gender, valve anatomy (bicuspid or trileaflet aortic valve) and baseline AS severity were performed to assess the determinants of AA size and enlargement. A P-value <0.05 was considered statistically significant. All the statistical analyses used JMP 9 software.

Results

Baseline characteristics
Among the 374 asymptomatic AS patients enrolled between November 2006 and February 2015, 58 patients did not yet reach the 2 years visit, 62 were operated on within 2 years and 59 refused to remain in the study or were lost of follow-up. Thus, 195 patients with at least 2 years of follow-up constituted our study population. Most patients were men (n = 147, 75%) and mean age was 72 ± 9 years. Mean MPG was 22 ± 11 mmHg; 99 patients (51%) had mild AS, 82 (42%) moderate, and 14 patients (7%) severe AS. Aortic valve was tricuspid in 153 patients (78%) and bicuspid in 42 (22%). Most patients had normal systolic function and mean LVEF was 64 ± 4%. Characteristics of the population are presented in Table 1 (left part).
Table 1  Baseline characteristics of the population and progression overall, according to the size of the ascending aorta above or below 40 mm (at the Valsalva and/or tubular level) and according to the progression rate of the ascending aorta

<table>
<thead>
<tr>
<th>AA</th>
<th>Overall (N = 195)</th>
<th>AA size &lt;40 mm (N = 138)</th>
<th>AA size ≥40 mm (N = 57)</th>
<th>P-value</th>
<th>AA progression rate &lt;0.5 mm/ year (n = 130)</th>
<th>AA progression rate ≥0.5 mm/ year (n = 65)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72 ± 9</td>
<td>72 ± 9</td>
<td>72 ± 9</td>
<td>0.82</td>
<td>72 ± 10</td>
<td>74 ± 8</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>147 (75%)</td>
<td>98 (71%)</td>
<td>49 (86%)</td>
<td>0.03</td>
<td>98 (75%)</td>
<td>49 (75%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28 ± 5</td>
<td>28 ± 5</td>
<td>28 ± 5</td>
<td>0.97</td>
<td>28 ± 5</td>
<td>28 ± 6</td>
<td>0.89</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.9 ± 0.2</td>
<td>1.9 ± 0.2</td>
<td>2.0 ± 0.2</td>
<td>0.04</td>
<td>1.9 ± 0.2</td>
<td>1.9 ± 0.2</td>
<td>0.81</td>
</tr>
<tr>
<td>Treated hypertension</td>
<td>128 (66%)</td>
<td>87 (63%)</td>
<td>41 (72%)</td>
<td>0.23</td>
<td>85 (65%)</td>
<td>43 (66%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Smoking</td>
<td>93 (48%)</td>
<td>64 (46%)</td>
<td>29 (51%)</td>
<td>0.57</td>
<td>63 (48%)</td>
<td>30 (46%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Aortic severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean pressure gradient (mmHg)</td>
<td>22 ± 11</td>
<td>22 ± 12</td>
<td>23 ± 11</td>
<td>0.19</td>
<td>22 ± 11</td>
<td>24 ± 13</td>
<td>0.06</td>
</tr>
<tr>
<td>Peak velocity (cm/s)</td>
<td>297 ± 65</td>
<td>294 ± 66</td>
<td>305 ± 64</td>
<td>0.21</td>
<td>293 ± 61</td>
<td>305 ± 73</td>
<td>0.14</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.75 ± 0.20</td>
<td>0.74 ± 0.17</td>
<td>0.80 ± 0.23</td>
<td>0.22</td>
<td>0.77 ± 0.19</td>
<td>0.73 ± 0.20</td>
<td>0.20</td>
</tr>
<tr>
<td>Mild aortic stenosis</td>
<td>99 (51%)</td>
<td>72 (52%)</td>
<td>27 (47%)</td>
<td>0.77</td>
<td>72 (55%)</td>
<td>27 (42%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Moderate aortic stenosis</td>
<td>82 (42%)</td>
<td>57 (41%)</td>
<td>25 (44%)</td>
<td>0.77</td>
<td>50 (38%)</td>
<td>32 (49%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Severe aortic stenosis</td>
<td>14 (7%)</td>
<td>9 (7%)</td>
<td>5 (9%)</td>
<td>0.77</td>
<td>8 (6%)</td>
<td>6 (9%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>42 (22%)</td>
<td>20 (15%)</td>
<td>22 (39%)</td>
<td>&lt;0.01</td>
<td>30 (23%)</td>
<td>12 (19%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Left ventricle ejection fraction (%)</td>
<td>64 ± 4</td>
<td>64 ± 5</td>
<td>64 ± 3</td>
<td>0.45</td>
<td>64 ± 5</td>
<td>64 ± 4</td>
<td>0.49</td>
</tr>
<tr>
<td>Ascending aorta—echocardiography (mm)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Valsalva</td>
<td>35.3 ± 3.9</td>
<td>33.8 ± 3.1</td>
<td>30.8 ± 3.2</td>
<td>&lt;0.01</td>
<td>35.7 ± 4.0</td>
<td>34.5 ± 3.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Tubular aorta</td>
<td>36.2 ± 4.5</td>
<td>34.1 ± 3.0</td>
<td>41.1 ± 3.7</td>
<td>&lt;0.01</td>
<td>36.6 ± 4.5</td>
<td>35.4 ± 4.5</td>
<td>0.07</td>
</tr>
<tr>
<td>Ascending aorta—computed tomography (mm)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Valsalva 1</td>
<td>36.0 ± 4.2</td>
<td>34.7 ± 3.5</td>
<td>39.1 ± 4.1</td>
<td>&lt;0.01</td>
<td>36.0 ± 4.2</td>
<td>35.8 ± 4.2</td>
<td>0.81</td>
</tr>
<tr>
<td>Valsalva 2</td>
<td>35.8 ± 4.0</td>
<td>34.3 ± 3.3</td>
<td>39.3 ± 3.4</td>
<td>&lt;0.01</td>
<td>35.9 ± 4.1</td>
<td>35.4 ± 3.8</td>
<td>0.50</td>
</tr>
<tr>
<td>Valsalva 3</td>
<td>34.9 ± 4.1</td>
<td>33.5 ± 3.3</td>
<td>38.5 ± 3.7</td>
<td>&lt;0.01</td>
<td>35.0 ± 4.2</td>
<td>34.6 ± 3.8</td>
<td>0.49</td>
</tr>
<tr>
<td>Valsalva 4</td>
<td>34.1 ± 3.8</td>
<td>32.8 ± 3.1</td>
<td>37.3 ± 3.4</td>
<td>&lt;0.01</td>
<td>34.2 ± 3.8</td>
<td>33.8 ± 3.6</td>
<td>0.60</td>
</tr>
<tr>
<td>Tubular aorta</td>
<td>37.7 ± 4.3</td>
<td>35.8 ± 2.9</td>
<td>42.2 ± 4.0</td>
<td>&lt;0.01</td>
<td>37.5 ± 4.1</td>
<td>37.8 ± 4.7</td>
<td>0.84</td>
</tr>
<tr>
<td>Aortic stenosis progression</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean pressure gradient progression (mmHg/year)</td>
<td>+3.1 ± 3.0</td>
<td>+3.1 ± 2.9</td>
<td>+3.0 ± 3.2</td>
<td>0.70</td>
<td>+2.6 ± 2.8</td>
<td>+4.0 ± 3.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peak velocity progression (cm/s/year)</td>
<td>+15.6 ± 13.8</td>
<td>+16.2 ± 14.4</td>
<td>+14.2 ± 12.3</td>
<td>0.53</td>
<td>+13 ± 13</td>
<td>+20 ± 14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AVA progression (cm²/year)</td>
<td>-0.08 ± 0.07</td>
<td>-0.08 ± 0.06</td>
<td>-0.09 ± 0.08</td>
<td>0.31</td>
<td>-0.08 ± 0.07</td>
<td>-0.09 ± 0.07</td>
<td>0.11</td>
</tr>
<tr>
<td>Ascending aorta progression—echocardiography (mm/year)</td>
<td></td>
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<tr>
<td>Valsalva</td>
<td>+0.18 ± 0.34</td>
<td>+0.18 ± 0.32</td>
<td>+0.20 ± 0.40</td>
<td>0.86</td>
<td>+0.07 ± 0.13</td>
<td>+0.42 ± 0.48</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tubular aorta</td>
<td>+0.36 ± 0.54</td>
<td>+0.39 ± 0.56</td>
<td>+0.27 ± 0.46</td>
<td>0.14</td>
<td>+0.10 ± 0.15</td>
<td>+0.88 ± 0.65</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ascending aorta progression—computed tomography (mm/year)</td>
<td></td>
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</tr>
<tr>
<td>Valsalva 1</td>
<td>+0.30 ± 0.50</td>
<td>+0.26 ± 0.44</td>
<td>+0.40 ± 0.61</td>
<td>0.18</td>
<td>+0.32 ± 0.52</td>
<td>+0.26 ± 0.46</td>
<td>0.39</td>
</tr>
<tr>
<td>Valsalva 2</td>
<td>+0.26 ± 0.48</td>
<td>+0.27 ± 0.47</td>
<td>+0.23 ± 0.51</td>
<td>0.18</td>
<td>+0.24 ± 0.45</td>
<td>+0.31 ± 0.54</td>
<td>0.40</td>
</tr>
<tr>
<td>Valsalva 3</td>
<td>+0.20 ± 0.38</td>
<td>+0.23 ± 0.42</td>
<td>+0.14 ± 0.22</td>
<td>0.26</td>
<td>+0.17 ± 0.32</td>
<td>+0.07 ± 0.47</td>
<td>0.55</td>
</tr>
<tr>
<td>Valsalva 4</td>
<td>+0.17 ± 0.28</td>
<td>+0.16 ± 0.27</td>
<td>+0.19 ± 0.30</td>
<td>0.84</td>
<td>+0.18 ± 0.28</td>
<td>+0.14 ± 0.27</td>
<td>0.18</td>
</tr>
<tr>
<td>Tubular aorta</td>
<td>+0.16 ± 0.21</td>
<td>+0.17 ± 0.22</td>
<td>+0.13 ± 0.19</td>
<td>0.19</td>
<td>+0.14 ± 0.19</td>
<td>+0.21 ± 0.25</td>
<td>0.07</td>
</tr>
</tbody>
</table>

AA, ascending aorta; AVA, aortic valve area.
Determinants of ascending aorta size

Mean AA size measured by TTE was 35.3 ± 3.9 mm (18.6 ± 2.2 mm/m²) at the sinuses of Valsalva and 36.2 ± 4.5 mm (19.1 ± 3.1 mm/m²) at the tubular level (Table 1 and Figure 3). Fifty-seven patients (29%) presented an AA diameter ≥40 mm at the Valsalva or at the tubular level (definition for aneurysm). As shown in Table 1, patients with AA aneurysms tend to be more frequently male, with larger BSA but there was no other difference in terms of clinical characteristics or AS severity. Importantly, the rate of patients with BAV was significantly higher in patients with AA ≥40 mm (39% vs. 15%, P < 0.01). In multivariate analysis, independent determinants of indexed AA size were age and valve anatomy (all P < 0.01) and with PV yearly progression rate (Valsalva’s enlargement rate increased with PV progression rate, P = 0.01), whereas AA enlargement rate at the tubular level was only associated with tubular diameter at baseline (smaller tubular diameter had higher AA enlargement rate, P < 0.01). Using MSCT, the only determinant of AA enlargement rate was also the AA diameters measured at baseline.

Clinical outcome

Forty-three patients underwent an aortic valve replacement (AVR) for severe AS. Four of them presented AA diameters ≥45 mm. Two patients underwent a TAVI due to fragile condition, and the two others—with BAV—underwent a combined aortic valve replacement and AA surgery for AA aneurysm with supra-coronary tube implantation. No aortic dissection was reported, and no surgery for AA aneurysm as primary indication was performed.

Table 2 Ascending aorta measurements using MSCT and correlation coefficient with TTE

<table>
<thead>
<tr>
<th>Correlation coefficient (TTE/MSCT)</th>
<th>P-value</th>
<th>Difference (MSCT-TTE) (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsalva 1</td>
<td>0.74</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Valsalva 2</td>
<td>0.77</td>
<td>0.03</td>
</tr>
<tr>
<td>Valsalva 3</td>
<td>0.81</td>
<td>0.02</td>
</tr>
<tr>
<td>Valsalva 4</td>
<td>0.83</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tubular aorta</td>
<td>0.89</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

TTE, transthoracic echocardiography; MSCT, multi-slice computed tomography.

Determinants of the progression of ascending aorta size

After a mean follow-up of 3.8 ± 1.5 years [median 3.4 years (2.5–5.0)], the AA enlargement rate assessed using TTE was +0.18 ± 0.34 mm/year at the level of sinuses of Valsalvas and approximately twice, +0.36 ± 0.54 mm/year, at the tubular level (Figure 5). Sixty-six patients (34%) had no progression at both the sinuses of Valsalva and the tubular level, and sixty-five patients (37%) were considered as rapid progressors (progression rate ≥0.5 mm/year at either the Valsalva or tubular level). Rapid progressors were characterized by smaller aorta at baseline and a higher AS progression rate according to their PV and MPG progression rates (Table 1, right part). Among patients with initially non-dilated aorta at baseline, only 24 patients (13%) developed AA aneurysm >40 mm during follow-up. The threshold of 2 mm/year for rapid AA enlargement rate proposed in ESC guidelines was never reached at the sinuses of Valsalva and was reached in only 4 patients (2%) at the tubular level. These four patients had tricuspid aortic valve (TAV) and all but one had a small aorta at baseline (mean diameter was 34 mm at sinuses level and 31 mm at the tubular level); the other patient had 42 mm and 39 mm at the sinuses of Valsalva and at the tubular level, respectively.

Age, gender, BSA, valve anatomy (Figure 6), and AS severity were not associated with AA enlargement rate in univariate analysis. In multivariate analysis, AA enlargement rate at the Valsalva level was associated with baseline diameters (smaller Valsalva diameters presented higher AA enlargement rate, P < 0.01) and with PV yearly progression rate (Valsalva’s enlargement rate increased with PV progression rate, P = 0.01), whereas AA enlargement rate at the tubular level was only associated with tubular diameter at baseline (smaller tubular diameter had higher AA enlargement rate, P < 0.01).
Discussion

In this large prospective cohort of patients with AS, AA size was independently determined by age, gender, BSA, and BAV, but not by AS severity. The mean AA enlargement rate was overall low, twice at the tubular level than at the sinuses of Valsalva, and was determined neither by AS severity nor by valve anatomy.

Ascending aorta size and determinants in aortic stenosis

Ascending aorta diameters measured in the present study were similar to those previously described in AS patients, and AA aneurysm was observed in one-quarter of AS patients, which is higher than its prevalence in normal subjects. Most importantly, even if AA dilatation was common in AS, AA size was not related to AS severity, which is consistent with the results described by Crawford and Roldan. Ascending aorta size was determined by aortic valve anatomy, with larger diameters among BAV patients. A large number of studies have previously analysed BAV-associated aortopathy, characterized by fibrillar reduction, elastin fragmentation, and increased collagen within aortic wall. Clinically, BAV patients present more frequently with AA dilatation, leading to a higher risk of life-threatening complications such as AA dissection or rupture, that hopefully remained rare thanks to early detection and treatment of these patients. For Hahn et al., aortic wall disease associated to BAV was more related to genetic anomalies than to hemodynamic valve dysfunction, as AA size was similar in BAV patients regardless of the aortic valve function (normal, regurgitation, or stenosis). Some studies suggested that AA size is related to the type of BAV, but this is still debated, and our limited population of BAV did not allowed us to draw any conclusion relative to this particular point. Finally, AA diameters were also independently associated with age, gender, and BSA, which are well-known determinants of AA size in normal subjects. One explanation for the larger diameters among older patients is that, with ageing, increased collagen production within aortic wall results in increasing AA stiffness. It is also important to mention that even if male patients presented larger absolute AA diameters, when indexed to the BSA, female sex that was associated with larger AA size.

Rate of ascending aorta enlargement and determinants

We found that the AA enlargement rate was overall low, using both TTE or MSCT, and similar to the AA enlargement rate (0.16 mm/
This AA enlargement observed in normal population seems to be an adaptive response to the aortic stiffness augmentation aiming at limiting the pulsed pressure increase. Moreover, we observed that AA enlargement rate in AS was twice higher at the tubular level than at the sinuses of Valsalva level. This phenotype of predominant tubular progression was primarily described in BAV population in opposition to patients with Marfan syndrome.

In the present study, AA enlargement rate was not determined by AS severity at baseline. Detaint et al. also found no impact of AS severity on AA enlargement rate, although they studied only a small number of AS patients, all with BAV. However, Yasuda et al. observed that the AA enlargement rate was slower after AVR for AS, suggesting a possible hemodynamic impact of AS on AA enlargement rate. Moreover in our population, we found that AA enlargement rate was associated with AS yearly progression rate: patients with faster PV or MPG increase had higher AA enlargement rate, according to TTE measurements. Yet, we were not able to confirm these results when we used AVA progression rate, or MSCT diameters. Thus, these results need to be confirmed in further studies.

We found that the AA enlargement rate was not determined by aortic valve anatomy. These results could be seen alongside those of La Canna et al. who studied consecutive transoesophageal echocardiographies in BAV and TAV patients presenting AA aneurysm and normally functioning aortic valve during a mean follow-up of 3 years. The rate of AA aneurysms progression was similar regardless of the valve anatomy. Moreover, studying 325 patients with AA aneurysm and AS followed up to 15 years after isolated AVR, Girdauskas et al. found that the proportion of proximal aortic redo surgery was similar in BAV and TAV patients (only 3% and 5%, respectively).

Finally, the main determinant of AA enlargement rate was the AA size at baseline. Patients with smaller AA diameters had higher AA enlargement rate. This finding was previously reported. We are not sure whether this reflects a true phenomenon. One hypothesis is that minimal error measurements may have a greater impact in this population.

Clinical implications
The aim of this study was not to validate the actual proposed threshold of 45 mm for combined surgery at the time of AVR. However, given the relatively low AA progression rates observed in our AS patients, combined surgery indications should be discussed in heart team, in order to individualize this decision. It seems even more crucial given the frailty of some AS elderly patients, and the increasing number of percutaneous aortic valve replacements. Moreover, the upper limit of 2 mm/year of AA enlargement rate suggested in the European guidelines for BAV and Marfan patients was almost never reached in our population, suggesting that this threshold may be not appropriate in AS patients, regardless of valve anatomy.

Study limitations
This study has several limitations. First, this is a single-centre study, with mostly old-male patients. However, very few studies aimed at evaluating prospectively AA size and enlargement rate in AS with both BAV and TAV patients. Moreover, we prospectively included a relatively large population of 195 patients, with a wide range of AS severity. Second, a limited number of patients with severe AS were enrolled. The low number of patients with severe AS is explained by the fact that only patients with at least 2 years of follow-up were considered for the present study. Therefore, conclusions related to this subgroup of patients should be confirmed in larger sample. Finally, MSCT measurements were not performed with contrast enhancement. However, a major strength of this study is the use of two independent imaging modalities. Both TTE and MSCT were performed by one single trained specialist and showed similar
results with excellent correlation and small variability. In addition, each measurement was performed blindly one of each other.

**Conclusion**

In this prospective study, AA size was associated with age, gender, BSA and BAV, but not with AS severity. Overall AA enlargement rates remained lower, large at the tubular than at the Valsalva level, and were not determined by AS severity or valve anatomy. Given the overall low progression of AA diameters, even for BAV patients, our results suggest individualizing the decision to perform a combined AA surgery above 45 mm at the time of AS surgery especially in elderly patients.

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**References**


