Age-related increase in wall stress of the human abdominal aorta: An in vivo study

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Background: The regulation of wall stress in the abdominal aorta (AA) of humans might be of specific interest, because the AA is the most common site for aneurysm formation in which wall stress seems to be an important pathophysiological factor. We studied the age-related changes in wall stress of the AA in healthy subjects, with the common carotid artery (CCA) as a comparison.

Methods: A total of 111 healthy subjects were examined with B-mode ultrasonography to determine the lumen diameter and intima-media thickness (IMT) in the AA and the CCA.

Results: Aortic IMT was affected by age in men and by both age and lumen diameter in women. Carotid IMT was affected by age and pulse pressure in both men and women. Wall stress was higher in the AA than in the CCA (P < .001), and men had higher wall stress than women in both the AA (P < .001) and the CCA (P < .05). Furthermore, wall stress was constant during life in the CCA of men and women and in the AA of women. In the male aorta, however, wall stress increased with age (P < 0.01).

Conclusions: Arterial diameters increase with age, and a compensatory thickening of the arterial wall prevents the circumferential wall stress from increasing. However, this compensatory response is insufficient in the male AA and results in an increase in stress with age. These findings might explain the propensity for aneurysms to develop in the AA of men. (J Vasc Surg 2005;42:926-31.)

The abdominal aorta (AA) in humans is of interest from both a physiological and pathophysiological perspective because of the predilection for pathologic dilation and aneurysm formation. The possibility of an imbalance between wall stress and wall strength—an underlying factor responsible for pathologic dilation—has been emphasized by the relationship between blood pressure and increasing aneurysm diameter, as well as that between aneurysm diameter and the risk of rupture.1,3 Furthermore, a direct relationship between wall stress and the risk of aneurysmal rupture has been proposed.4-6 Remodeling of the arterial wall is an important physiological response to changes in wall stress, and mechanical stimuli seem to play a major role.7 The AA dilates approximately 25% to 30% between the ages of 25 and 70 years in healthy subjects and dilates to a larger extent than other studied elastic arteries.8 Furthermore, the wall stress in the aorta seems to be greater than that found in other arteries.9 To understand the factors that contribute to aortic pathology, it is important to explore the regulation of wall stress and the remodeling of the healthy aortic wall. We hypothesized that the regulation of wall stress in the aging process of the AA in humans might differ from that of other central elastic arteries that are not prone to pathologic dilation and aneurysm formation.

MATERIALS AND METHODS

A total of 111 healthy Caucasian subjects, 52 men and 59 women, participated in the study. All were nonsmokers without hereditary factors regarding aneurysmal disease. They had no history of cardiopulmonary, cerebrovascular, or peripheral vascular disease. The ankle-brachial index was 1 or greater in all subjects. The women received no hormone-replacement therapy. No subject took any prescribed drugs. The 111 subjects were examined twice consecutively by an experienced ultrasonographer regarding intima-media thickness (IMT), lumen diameter (LD), and blood pressure.

The AA was examined at the midpoint between the renal arteries and the aortic bifurcation. The right common carotid artery (CCA) was examined 1 to 2 cm proximal to the bifurcation. All examinations were performed after at least 15 minutes’ rest with the subjects in a supine position. At the beginning of the investigation, the noninvasive pressure was measured with a cuff in the upper arm bilaterally. Because no significant difference in pressure was found between the arms, the right arm was used because of the location of the ultrasound equipment in the investigation room. The brachial cuff pressure has been shown to generate a slight overestimation of the aortic diastolic pressure (DBP), but without sex- or age-related differences.10

For measuring the IMT and the LD, we used a Philips P700 ultrasound device (Philips Ultrasound, Santa Ana,
Calif) with a 7.5-MHz linear transducer for scanning the CCA. For aortic imaging, either a 5-MHz or a 3.5-MHz transducer was used. A longitudinal perpendicular image of the vessel was insonated and recorded on a video monitor, two images of good quality were frozen in diastole, according to the prevailing standard of IMT measurements, and the IMT of the far wall and the LD were measured manually by tracing a cursor along the echo edges on a section of 10 mm with the aid of the digitizer.\(^9,11,12\) This provides approximately 100 boundary points from which the mean value of IMT and LD is automatically calculated (VAP version 2.0; Department of Applied Electronics, Chalmers University of Technology, Gothenburg, Sweden). The accuracy of the technique was studied by Pignoli et al,\(^12\) who showed a good correlation between ultrasonographic and histologic measurement of the aortic wall. The variability in our laboratory has recently been described.\(^9\) The aortic interobserver and intraobserver variability was 6% to 8% regarding IMT and 2% to 3% regarding LD. Stress is the force per unit of cross-sectional area. In the artery, stresses are present along the circumferential, radial, and longitudinal axes. Because arteries elongate little during the cardiac cycle and because the compression of the vessel wall is small, we focused on the circumferential wall stress (calculated according to the law of Laplace\(^13,14\):)

\[
\text{Wall stress} = \frac{\text{DBP} \times \text{LD}}{2 \times \text{IMT}}
\]

DBP (dynes/cm\(^2\)) was used because IMT measurements were performed in diastole. Informed consent was obtained from each patient, and the ethics committee in Lund, Sweden, approved the study.

For calculating the relationship between age and the different parameters (IMT, wall stress, LD, and DBP), we used linear regression and the Pearson correlation coefficient (Figs 1-3).
between wall stress and age in the female AA (Fig 1, circles). In the CCA, there was no correlation between wall stress and age. When this increase was adjusted for body-surface area, however, the sex difference disappeared. Male aortic LD was not correlated with blood pressure (SBP, DBP, MAP, or PP) or IMT: only with age and body-surface area. The female aortic LD showed a correlation with IMT, as well as with age and body-surface area.

In adults, the CCA diameter increased from 5.9 to 7.1 mm (19%) in men and from 5.6 to 6.3 mm (12%) in women. Men had larger diameters (P < .001) and a more pronounced diameter increase with age (P < .05). There was no correlation between LD and IMT, body-surface area, and blood pressure (SBP, DBP, MAP, or PP), but there was a correlation with age. Men and women were analyzed separately. Because there was no correlation between body-surface area and LD, we did not correct the age-related diameter increase for body-surface area in the CCA.

**RESULTS**

Systolic blood pressure (SBP), DBP, pulse pressure (PP), mean arterial blood pressure (MAP), and age were not significantly different between men and women (Table I). In 12 subjects, it was not possible to evaluate IMT in the AA because of bowel gas, plaque formation at the site of interest, obesity, or other problems in visualizing the vessel. Also, in 3 of those 12 subjects, it was not possible to visualize the IMT of the CCA because of plaque formation at the site of interest. Thus, in 48 men and 51 women, the IMT of the AA was visualized, and in 50 men and 58 women, the IMT of the CCA was visualized.

Figure 1 shows the changes in diameter with age in the AA (Fig 1, A) and the CCA (Fig 1, B). LD increased with increasing age in both the AA and CCA in both men and women (P < .001). The diameter was larger in men than in women in both the AA and the CCA (both P < .001). The dilatation was larger in men than in women in both the AA and the CCA (both P < .01). In adults, the AA diameter increased between the ages of 25 and 70 years increased from 13.3 to 17.3 mm (30%) in men and from 11.4 to 14.3 mm (25%) in women. When this increase was adjusted for body-surface area, however, the sex difference disappeared. Male aortic LD was not correlated with blood pressure (SBP, DBP, MAP, or PP) or IMT: only with age and body-surface area. The female aortic LD showed a correlation with IMT, as well as with age and body-surface area.

In adults, the CCA diameter increased from 5.9 to 7.1 mm (19%) in men and from 5.6 to 6.3 mm (12%) in women. Men had larger diameters (P < .001) and a more pronounced diameter increase with age (P < .05). There was no correlation between LD and IMT, body-surface area, and blood pressure (SBP, DBP, MAP, or PP), but there was a correlation with age. Men and women were analyzed separately. Because there was no correlation between body-surface area and LD, we did not correct the age-related diameter increase for body-surface area in the CCA.

**Fig 3.** The relationship between circumferential wall stress and age in the abdominal aorta (AA) (A) and the common carotid artery (CCA) (B). The wall stress increased with age in the male AA (r = 0.40; filled circles). There was, however, no correlation between wall stress and age in the female AA (r = 0.06; open circles). In the CCA, there was no correlation between wall stress and age (men, r = −0.06; women, r = −0.20). NS, Not significant.

In the male AA, there was no correlation between IMT and body-surface area, LD, or blood pressure, but there was a correlation with age, which accounted for 60% of the increase in IMT. In the female AA, LD accounted for 43% and age for 9% of the increase in IMT, but no correlation with blood pressure or body-surface area was found.

In the male CCA, age accounted for 47% and PP for 10% of the increase in IMT, but no correlation with LD or body-surface area was found. In the female CCA, age accounted for 47% and PP for 7% of the increase in IMT, but no correlation with LD or body-surface area was found.

**Figure 3** shows the changes in wall stress with age in the AA (Fig 3, A) and the CCA (Fig 3, B). Wall stress was larger in the AA than in the CCA in both sexes (P < .001). Furthermore, men had higher wall stress in both the AA and the CCA (P < .001 and P < .05, respectively; Table I). Despite this fact, female aortic wall stress was significantly higher than male CCA wall stress (9.0 ± 1.8 vs 5.7 ± 1.3 × 10^6 dyn/cm²; P < .001). Aortic wall stress in men increased between the ages of 25 and 70 years by 14% (r = 0.40; r² = 0.16; P = .005). No such increase was found in the female AA. In the CCA, no age-related change in wall stress was found in men or women.
In both men and women, there was a similar age-related increase in DBP (P < .001). Above the age of 50 to 60 years, however, the increase in DBP diminished, and a slight reduction was seen. There was no sex difference in the age-related changes in DBP. MAP increased similarly in both sexes with age (P < .001). PP increased in women with age (P < .001). The same tendency was found in men but did not reach statistical significance (r = .26; P = .067). SBP increased in both sexes with age (P < .001). The increase in SBP was larger in women (P < .05).

**DISCUSSION**

To calculate circumferential wall stress, we measured IMT as a surrogate measurement of arterial wall thickness and used the law of Laplace to calculate wall stress.9 A B-mode ultrasound technique was used as described by Pignoli et al.12 Because of the increase in diameter and pressure in the CCA, an increase in wall stress with age might have been expected, but instead wall stress was unchanged as a result of a compensatory increase in IMT (Figs 1-3).7,15-17 Thus, arterial wall stress seems to be restored and stabilized on a predetermined level according to the law of Laplace and may be an important determinant for vessel wall remodeling during aging in humans (Fig 3, B). Metalloproteinases (MMPs) seem to play an important role in the remodeling process with the ability to degrade extracellular matrix, and it has been shown in experiments that increased pressure activates MMP-2 and MMP-9.18,19 Furthermore, there are indications that MMPs are directly correlated with IMT in animal models.20,21

Despite increasing wall thickness in the AA in men, wall stress still increased with age (Fig 3A). An analysis of the underlying factors responsible for the increase in wall thickness showed that only age affected wall thickness in the male AA, whereas in the female AA, as well as in the CCA of both men and women, arterial diameter and blood pressure affected the increase in wall thickness, thus keeping wall stress unchanged with age. Therefore, the male aorta seems to have a defect in wall stress autoregulation.

To our knowledge, there are no earlier studies regarding the age-related changes in the circumferential wall stress of the human AA. Bader14 studied the circumferential wall stress in the thoracic aorta in vitro and found that the aortic wall stress decreased with age. There are, however, several differences between his study and ours. The adventitia was included in his calculation of wall stress. The thoracic instead of the infrarenal AA was studied, and this might be important because there is a higher frequency of aneurysmal dilatation in the AA.22,23 Furthermore, his study was performed in vitro, without recognition of the fact that blood pressure increases with age. Also, no separation of sex was performed, and this seems to be of fundamental importance (Fig 3, A).

The high wall stress found in the AA and the tendency for the stress to increase with age in men points to the fact that the aorta is a vulnerable artery (Fig 3, A). A smaller number of lamellar elastic units have been found in the human AA than in any other mammalian aorta with vascularized media; this means that the estimated mean tension per lamella in the human aorta is higher. Furthermore, the inner part of the aortic wall lacks vasa vasorum. Thus, the nutrition of the wall might deteriorate with increasing thickness.24 In the AA in humans, in contrast to other mammals, the main load-bearing media may increase in thickness to a lesser extent than the intima during

### Table I. Baseline clinical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 50)</th>
<th>Women (n = 58)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>45.9 ± 21.8</td>
<td>48.3 ± 21.7</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76 ± 14</td>
<td>63 ± 10</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>177 ± 10</td>
<td>165 ± 8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 ± 3.1</td>
<td>22.9 ± 3.0</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.92 ± 0.22</td>
<td>1.69 ± 0.15</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>130 ± 16</td>
<td>128 ± 21</td>
<td>NS</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>77 ± 9</td>
<td>75 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>94 ± 10</td>
<td>92 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>PP (mm Hg)</td>
<td>53 ± 14</td>
<td>54 ± 16</td>
<td>NS</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>60 ± 9</td>
<td>62 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Carotid LD (mm)</td>
<td>6.47 ± 0.84</td>
<td>5.93 ± 0.62</td>
<td>&lt;.001</td>
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<td>Carotid IMT (mm)</td>
<td>0.60 ± 0.16</td>
<td>0.58 ± 0.14</td>
<td>NS</td>
</tr>
<tr>
<td>Carotid wall stress (dynes/cm²)</td>
<td>5.7 ± 1.3 × 10⁵</td>
<td>5.2 ± 1.0 × 10⁵</td>
<td>&lt;.05</td>
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<tr>
<td>Aortic LD (mm)</td>
<td>14.91 ± 2.76</td>
<td>12.88 ± 2.32</td>
<td>&lt;.001</td>
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<tr>
<td>Aortic IMT (mm)</td>
<td>0.73 ± 0.15</td>
<td>0.73 ± 0.16</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic wall stress (dynes/cm²)</td>
<td>10.7 ± 2.2 × 10⁵</td>
<td>9.0 ± 1.8 × 10⁵</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

NS, Not significant; BMI, body mass index; BSA, body-surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial blood pressure; PP, pulse pressure; HR, heart rate; LD, lumen diameter; IMT, intima-media thickness.
aging.25-27 This indicates greater wall stress within the aortic media than calculated in our study, although the intima might bear a greater load with age and thickening.28,29 Because MMPs in the arterial wall are activated by wall stress, it may be hypothesized that a more proteolytic profile is found in the AA compared with other arteries and possibly forms a background to the preponderance for aneurysm formation in the AA.18,19,22,23

The fact that our study provides only cross-sectional data regarding the age-related changes in the arterial parameters must be considered as a limitation, and our data should be confirmed in a longitudinal study. We used the DBP in the calculation of circumferential wall stress because the IMT measurements were performed in diastole, according to the prevailing standard. A weakness with the study was that we did not measure local pressure in the AA but instead used auscultatory brachial pressure. This means a slight overestimation of the aortic DBP, but without sex- or age-related differences.10 It is evident that the major part of the total wall thickness is included in the IMT measurements.30,31 Furthermore, the relationship between adventitial thickness and IMT is unaffected by sex and age.32 Accordingly, IMT has recently been used as a surrogate measurement for arterial wall thickness in the calculation of wall stress.28,33,34 It may be argued that the exclusion of the adventitial layer of the wall gives erroneous results because it contributes to the strength of the wall. The wall stress, however, is not affected by histologic characteristics, but by wall thickness only, in contrast to wall strength, which is defined by the constituents of the wall.

In conclusion, arterial diameters increase with age. A compensatory thickening of the arterial wall prevents the circumferential wall stress from increasing. However, this compensatory response is insufficient in the male AA, in which the stress increases with age. This might form a background to the preponderance of dilating disease in the AA in men.

REFERENCES


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