Studying the expansion of small abdominal aortic aneurysms: is there a role for peak wall stress?

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Aim. The aim of this paper was to study the characteristics of three distending small abdominal aortic aneurysms (AAAs), with an increase in maximal diameter from 5 to 5.5 cm or above.

Methods. Peak Wall Stress (PWS) in the presence and absence of intraluminal thrombus (ILT) was evaluated in 3 cases of small AAAs (5 cm), at initial presentation and after their expansion, at maximum diameters ±2.5 cm using finite element analysis. Furthermore, AAA sac volume (Vsac), the percentage volume of ILT (ILT%) and the percentage change of Vsac (AV%) and ILT (ILT%) were estimated and the location of PWS was recorded.

Results. Two AAA expanded from 5 cm to 5.5 cm in a period of 6 months after initial presentation, with increase of sac volume by 20% and 30%, respectively. The third AAA expanded to a diameter of 6.5 cm after a follow-up period of 13 months, with a subsequent increase in sac volume of 78%. The expansion of AAA max diameter did not correlate with differences in peak wall stress (PWS) values at the initial presentation, ranging from 20.5 to 21.3 N/cm².

Conclusion. PWS values cannot solely serve as a predictive tool for small AAA expansion. Small AAA expansion seems to be a multifactorial process, not solely described by PWS values but rather by a combination of mechanical, hemodynamic and biological factors.

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Aneurysm is defined as a local dilatation of more than 1.5 times the expected normal arterial diameter. In clinical practice, a definition for Abdominal Aortic Aneurysm (AAA) as a transverse diameter of greater than 3 cm can be used.

The natural history of an untreated abdominal aortic aneurysm (AAA) is one of progressive, exponential expansion. The two, large prospective studies, UK SAT, ADAM, reported expansion rates between 2.6 and 3.3 mm/year for small AAAs. Vega de Céniga et al. associated AAA growth rate with the diameter of AAAs. In their study, AAAs between 4.0 to 4.9 cm showed an increase in diameter of 4.7±5.9 mm/year, whereas the smaller AAAs (3.0 to 3.9 cm diameter) only increased by 2.1±3.2 mm/year, a difference reported to be statistically significant. Furthermore, Lederle et al. reported that the median enlargement for AAAs 4.0-5.5 cm is about 3 mm per year and 50% greater for AAAs >5.5 cm.

There is considerable individual variability in enlargement rates and a variety of diseases and conditions appear to influence these rates. In UK SAT no association was found between age, gender and growth rate. Among the other potential factors, including hypertension, total or HDL plasma cholesterol concentration, peripheral arterial disease, and diabetes, only the last two influenced AAA growth, whereas cigarette smoking was associated with an increased growth rate.

The rate of growth of small AAAs has been recently associated with the amount of AAA intraluminal thrombus (ILT) and the peak wall stress (PWS). Speelman et al. showed that low AAA wall stress is associated with low aneurysm growth rate. Growth rate in the low stress group was significantly lower than that of the medium stress, despite the fact that this difference was non-significant between low and high stress.
groups. Moreover, the existence of ILT accelerated small AAA growth rate, reducing, on the other hand the magnitude of PWS.

The purpose of our study was to investigate if any of these recently proposed parameters have altered in time in three small AAAs which showed a significant increase in diameter during follow-up, setting the indication for surgery, with the use of finite element analysis (FEA).

**Materials and methods**

Three small AAAs with an initial diameter of 5.0 cm were followed up with ultrasound every 6 months and with CT imaging when an increase in max-diameter was detected. All patients underwent elective surgery. FEA was used to compute PWS in presence of ILT using methodology previously described in detail. We assumed a 2 mm thick hyperelastic AAA wall material model and a 120 mmHg systolic uniform wall loading. The AAA wall was assumed to be homogenous, incompressible and isotropic material. The thrombus was modeled as an isotropic, elastic, homogenous and incompressible material. All patients gave their full informed consent.

All patients were male, had a history of smoking and were normotensive (120 mmHg), under medication. Case 2 presented a sudden increase in diameter only after the second follow-up. Geometry volume of the wall sac and the lumen were calculated with Amira 4 (Visage Imaging Inc, Andover, MA, USA), having excluded the aortic neck and common iliac arteries of the AAA model. The difference between the volume of the whole AAA sac and the volume of the patent lumen is referred to as the thrombus volume (ILT) and can be further expressed as percentage (%) of the sac volume.

**Results**

Wall stress distributions in each AAA model, at initial presentation and after expansion, are displayed in Figure 1. PWS and its distribution, the percentage volume of ILT (ILT%), the initial AAA sac volume and their percentage change (ΔILT% and ΔV%) are depicted in Table I.

Case 2 had a smaller percentage of ILT (28%) and a larger sac volume (167 mL) at its initial presentation compared with the other 2 cases (ILT%: 69% and 76%; sac volumes: 100mL and 160mL, respectively; Table I). Cases 1 and 3 presented with a maximum diameter growth rate of 5mm after 6-months; Case 2 had a growth rate of 15 mm per 13-months. Sac volume expansion (ΔV%) was also greater in Case 2; 78% versus 30% and 20% in the other two cases (Table I). At initial presentation there was no particular variance in the PWS values between the 3 AAAs, being 21, 20.5 and 21.3 Nt/cm², respectively. A marked alteration in the PWS location in the AAA sac, comparing the sites before and after expansion was not marked (Table I).
<table>
<thead>
<tr>
<th>Case #</th>
<th>Follow up (months)</th>
<th>Diameter (cm)</th>
<th>PWS</th>
<th>PWS location</th>
<th>V_sac (ml)</th>
<th>ILT (%)</th>
<th>ILT distribution</th>
<th>After Expansion</th>
<th>Diameter (cm)</th>
<th>PWS</th>
<th>ΔILT (%)</th>
<th>ΔV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>5</td>
<td>21</td>
<td>Anteriorly</td>
<td>100</td>
<td>69%</td>
<td>Posterior and right lateral</td>
<td>5.5</td>
<td>23.5</td>
<td>3%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>5</td>
<td>20.5</td>
<td>Posteriorly</td>
<td>167</td>
<td>28%</td>
<td>Anterior</td>
<td>6.5</td>
<td>32.3</td>
<td>40%</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>5</td>
<td>21.3</td>
<td>Right laterally, neck-sac conjunction</td>
<td>160</td>
<td>76%</td>
<td>Anterior, left lateral</td>
<td>5.5</td>
<td>21.2</td>
<td>20%</td>
<td>20%</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

Expansion of small AAAs has been suggested to correlate with the amount of aneurysm intraluminal thrombus. Speelman et al. have compared two groups of small AAAs of identical diameter range, that were followed up with CT, and observed that those with larger amounts of ILT had a higher diameter growth rate, despite the statistically significant lower PWS values in the presence of ILT. Moreover, the same authors concluded that low PWS values were associated with lower AAA growth rates than in AAA groups with medium or higher stress values. However there was an insignificant difference in growth rate of AAAs between medium and higher PWS values group. Interestingly, the presence of ILT had not been incorporated in the FEA models of the aforementioned study. So, our effort focuses on the study of PWS and simultaneous ILT changes in 3 small expanding AAA models.

Our study included three small AAAs of the same initial diameter with similar levels of PWS at initial presentation. Cases 1 and 3 had equal maximum diameter and PWS and comparable ILT percentage volume. The PWS values for these cases were comparable after the expansion, more confined with the diameter of the AAA rather than the ILT percentage, the increase of which was not identical (3% vs. 20%) between these cases. This brings up the issue of PWS and ILT location, since though case 3 had an increase of the ILT% of 20%, PWS elevation was nearly the same compared to case 1, where there was an elevation of PWS of only 3%. In case 3, PWS was located in the neck-sac conjunction, where it seems to be least influenced by the ILT. This could explain the fact that PWS value remained quite unaltered after the expansion of AAA. The location of PWS at these sites unaffected by amount of ILT such as at the inflection sites of the AAA sac (near the neck) could actually negatively affect the predictive role of ILT regarding growth rate or even the determination of sites prone to rupture. Different degrees of PWS reduction are caused among equal ILT relative volumes, relating proportionally to the value of shear modulus. Truijers et al. reported that ILT compressibility inside the AAA sac during the cardiac cycle varies from patient to patient. The large variety in this compressibility, ranging from 0.4% to 43.6%, implies that the compensatory volume effect of thrombus during the cardiac cycle is not observed in all patients, thus acting as a biomechanical buffer (reducing PWS) in some patients but having little effect in others. Since the ILT compressibility is irrespective of AAA, pulse pressure and ILT volume, it seems that its buffering properties are regulated by intrinsic elements rather than its amount. So, the hypothesis “greater amount of ILT leads to more profound PWS reduction” is an oversimplification. In case 2 the ILT was located anterior and PWS posterior. Though the ILT% elevated by 40% the PWS was also vastly elevated (from 20.5 to 32.3 N/cm²), not significantly affected by the increase of the posteriorly located ILT.

Moreover, under the sight of the importance of thrombus distribution, it’s obvious that two AAAs of the same diameter; blood pressure levels and amount of ILT, do not necessarily share the same reduction in PWS. Though Helderman et al. showed that locations of high wall stress shift during aneurysm formation, its model excluded the presence of ILT, which can affect both the
value and location of PWS, if the amount ILT is not negligible.

Recently, Speelman et al. studied the growth rate of small AAAs with regard to wall stress and circulating biomarkers (matrix metalloproteinase-9, tissue inhibitor of matrix metalloproteinase-1, C-reactive protein and alpha 1-antitrypsin). Their results suggested no clear correlation between stress values and biomarkers. The study showed also that AAA growth rate was also positively related to MMP-9 plasma concentration. Furthermore, growth rate of the low stress group was significantly lower than that of the medium stress, despite the fact that this difference was not large between low and high stress groups. The average MMP-9 and CRP concentrations increased with increasing degrees of relative wall stress, though the absolute and relative wall stress did not correlate with any of the biomarkers. Since these factors attribute to the weakening of AAA wall strength, and ILT has also been implicated in their production, one could argue that the sudden increase in diameter (rendering it amenable to operative therapy) could be attributed to the possible influence of ILT on wall weakening, since the PWS at the initial presentation was equal to cases 1 and 3. Moreover, it has been suggested that AAA wall mechanics may contribute more significantly to peak wall stress than pressure or stress variations within the system.

Many other parameters can also efficiently affect small AAA expansion, such as the calcification of the AAA wall more than 50% of the initial maximal AAA circumference and local geometric parameters, the latter contributing by two thirds to the AAA expansion rate, compared to the traditional risk factors, such as gender, peripheral arterial disease, peripheral arterial disease or use of nitrates, affecting, lesser, by almost one third. Of note, geometric parameters such as the neck angulation (>25°) result in localisation of PWS near the neck-wall binding site, where less, if any, thrombus exists, like in case 3. Of note, Pappu et al. suggested that the tortuosity index of the lumen of small AAAs, could serve as a predictive criterion for the distention of small AAAs, a finding that renders further evaluation.

Hemodynamic factors may also influence the distension of AAA, especially in the early stages, where the amount of intraluminal thrombus could be negligible. Increased flow turbulence, depending on AAA geometry, results in increased stress values. The kinetic energy generated by turbulence increases wall and fluid shear stress distally. The increased fluid shear stress can result in further dilation and hence further turbulence, while the wall shear stress may be a mechanism for aneurysmal growth. This pattern provides an additional explanation theory of small AAA distension, potentially applied in cases where neither differences in PWS nor biomarkers values conjugate satisfactory with the different growth rates.

It can be hypothesised that small AAA expansion is a multifactorial process, not solely described by PWS values but rather by a combination of mechanical, hemodynamic and biological factors. The degenerative effects of ILT on wall integrity can be addressed as a causative agent of AAA expansion along with the stress values. Larger studies are needed in order to delineate the possible role of PWS in expansion, with regard to its location, especially when it is not located at sites of greatest inflection, such as at the sac-neck junction. Numerical models for AAA expansion prediction should also incorporate well addressed epidemiological risk factors.

Conclusions

In conclusion, PWS values alone cannot not serve as a strong predictive tool for expansion in the 3 small AAAs of our study. The existence of ILT on wall mechanics may prove to play a more important role on the expansion of small AAAs, compared with the stress values.

References


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