THE ROLE OF INTRALUMINAL THROMBUS IN AAA EXPANSION AND RUPTURE

Hemodynamics and biomechanics in aortic aneurismal disease
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AAA Intraluminal Thrombus
INTRODUCTION

THE FACT:
There is general consensus that ILT plays an important role in AAAs evolution not being an innocent bystander.

SIMULTANEOUSLY:
❖ Computational analysis has indicated a buffering effect postulating a protective role of ILT.
❖ On the contrary - mechanical studies show that ILT leads to wall weakening

SO: Where do we stand?

Effect of intraluminal thrombus on wall stress in patient-specific models of abdominal aortic aneurysm.

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Author information

Abstract

PURPOSE: The role of intraluminal thrombus (ILT) on abdominal aortic aneurysm rupture is still not clear. Rupture of an aneurysm occurs when the wall stress exceeds the wall strength at any location on the wall. The purpose of this study was to address the hypothesis that the presence of ILT alters the wall stress distribution or wall stress magnitude in AAA.

METHODS: Patient-specific 3D AAA geometries were reconstructed from computed tomographic images. Two geometric features, ILT surface ratio (ILT surface area divided by the total AAA surface area) and ILT volume ratio (ILT volume divided by the total AAA volume), were calculated for each AAA. Two models were created for each patient: one with ILT and one without ILT. Systolic pressure measured at the time of computed tomographic imaging was applied to the internal surface of each model. A nonlinear large deformation algorithm was used to compute wall stress distribution with the finite element method. The Wilcoxon matched pairs test was used to compare the peak wall stress between the two models of each patient.

RESULTS: Four patients were studied with ILT surface ratios that ranged from 0.29 to 0.72 and ILT volume ratios that ranged from 0.12 to 0.66. The peak wall stress was reduced (range, 6% to 36% reduction; P = .067) for all models with ILT included (range, 28 to 37 N/cm²) as compared with models with no ILT (range, 30 to 44 N/cm²). Visual inspection also revealed a marked effect of ILT on the wall stress distribution.

CONCLUSION: The presence of ILT alters the wall stress distribution and reduces the peak wall stress in AAA. For this reason, ILT should be included in all patient-specific models of AAA for evaluation of AAA wall stresses.

Table III. Peak wall stress for each patient with and without ILT and peak ILT stress for models with ILT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Peak stress without ILT (N/cm²)</th>
<th>Peak stress with ILT (N/cm²)</th>
<th>Decrease of peak stress</th>
<th>ILT peak stress (N/cm²)</th>
<th>Peak ILT stress to peak wall stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>34</td>
<td>6%</td>
<td>11</td>
<td>32%</td>
</tr>
<tr>
<td>2</td>
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<td>36%</td>
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<td>26%</td>
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<tr>
<td>3</td>
<td>40</td>
<td>37</td>
<td>6%</td>
<td>3</td>
<td>8%</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>28</td>
<td>38%</td>
<td>8</td>
<td>29%</td>
</tr>
</tbody>
</table>

*P = .067 with Wilcoxon paired test compared with AAA without ILT.
The influence of intraluminal thrombus on abdominal aortic aneurysm wall stress.

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Abstract
AIM: The aim of this study was to examine the effect of intraluminal thrombus (ILT) on the peak wall stress (PWS) in abdominal aorta aneurysm models (AAA).

METHODS: Anatomically correct patient specific AAA models were created by 3D reconstruction of in vivo acquired computed tomography images from 19 male patients. Patients were divided in two groups according to aneurysm peak transverse diameter, 5-7 cm (10 patients, "intermediate" group) and >7 cm (9 patients, "large" group), respectively. PWS was evaluated in the presence and absence of ILT. The percentage of PWS reduction (Delta PWS %) was estimated as a percentage of PWS value in the absence of ILT. Finite element analysis was used to numerically compute the wall stress distribution assuming a 2-mm thick hyperelastic AAA wall material model and a 120 mmHg systolic uniform wall loading. The thrombus was modeled as an isotropic, elastic, homogenous and incompressible material. The volume of ILT was estimated as a percentage of the AAA sac volume.

RESULTS: The ILT volume was 49.9%+/-10.6% in the "large" group and 58.6%+/-13.2% in the "intermediate" group (t-test P=0.14). The "large" AAAs have higher PWS values than the "intermediate" group, both in the presence of ILT (36.9+/−5.8 vs. 23.5+/−6.2 Nt/cm(2), P=0.0001) as well as in the absence of ILT (52.6+/−15.4 vs. 35.0+/−10.5 Nt/cm(2), P=0.01). The presence of ILT resulted in a decrease of PWS (Delta PWS) in all cases. There was no statistical difference between the two groups in the mean PWS reduction, in the presence of ILT (26.9+/−12.5 Nt/cm(2) in the "large" group and 31.0+/−11.7 Nt/cm2 in the "intermediate" group, t-test P=0.48). However, a strong correlation between the ILT relative volume (ILT%) and the degree of PWS reduction was found only in the "intermediate" AAA group (Pearson correlation 0.86, P<0.001), whereas no correlation was observed in the "large" AAA group (Pearson correlation 0.05, P=0.9).

CONCLUSIONS: The presence of ILT reduced the PWS in all cases. In the "intermediate" AAAs our results showed a linear correlation between ILT relative volume and cents PWS. However, in "large" aneurysms no such correlation was found. This indicates that the degree of ILT influence on the reduction of PWS in "large" AAAs may be related to other factors such as the geometric configurations of the AAA.
ILT and Peak Wall Stress

- PWS reduction correlated well with AAA ILT (relative volume) for AAA 5-7cm
- Not that well for AAA > 7cm
- Possible implication of other factors involved such as AAA and ILT Geometry

Georagakarakos E et al. Int Angiol 2009; 28: 325-33
ILT and Peak Wall Stress

Stress field in the AAA models with asymmetric ILT.

- PWS was always located in the side where ILT thickness is minimum.
Low Time-Average Wall Shear Stress (TAWSS) values were found in all AAAs in comparison to the healthy aorta.

TAWSS values were lower in aneurysms with ILT.

Thrombus deposition was observed to negatively correlate with TAWSS values.

The odds of a location (patch) to develop thrombus increased 9-fold with each 0.1 Pa TAWSS decrease.

Conclusion: WSS distribution may emerge as a tool to identify regions of AAA thrombus deposition.
ILT is formed at areas with flow recirculation

• Recirculation was observed in the sac.
• The recirculating flow in AAAs may explain the generation of intraluminal thrombi.
• The asymmetry and complexity of flow in asymmetric AAAs may explain the asymmetric thrombi distribution.

ILT Growth and Flow Velocity

- Color contour of magnitude of time-averaged velocity plotted at particular longitudinal cross sections.
- Regions of low time-averaged velocity coincided with the regions of ILT accumulation.
ILT Accumulation Process

Spatial distribution of ILT thickness

- All ILTs began as a localized buildup at the region of maximum diameter.

- From this region, ILTs spread to the surrounding areas at the same time as an increase in ILT thickness was observed on areas previously covered by ILT.

- This process occurred gradually as the aneurysm expanded.
A positive linear correlation between ILT accumulation rate and AAA expansion rate was found.

In other words, ILT accumulates at the same rate as the aneurysm expands.

while the AAA cross-section area increased, the lumen cross-section area remained nearly constant

Effect of Intraluminal Thrombus Asymmetrical Deposition on Abdominal Aortic Aneurysm Growth Rate

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Abstract

Purpose: To determine the relationship between asymmetrical intraluminal thrombus (ILT) deposition in abdominal aortic aneurysm (AAA) and growth rate and to explore its biomechanical perspective. Methods: Thirty-four patients with AAA underwent at least 2 computed tomography scans during surveillance. The volumes of the AAA (V_{AAA}) and thrombus (V_{ILT}) and the maximum thrombus thickness (ILT_{thick}) were computed. Thrombus distribution was evaluated by introducing the asymmetrical thrombus deposition index (ATDI), with positive and negative values (−1<ATDI<1) associated with anterior and posterior ILT deposition, respectively. Finite element analysis was applied to estimate wall stress. Aneurysms were divided into high and low growth rate groups based on the cohort’s median growth rate, and the above-mentioned parameters were compared between groups. Results: Most AAAs had asymmetrical anterior thrombus deposition. The high and low growth rate groups did not present significant differences in maximum diameter, V_{AAA}, V_{ILT}, or maximum ILT_{thick}. However, the high growth rate group had significantly higher ATDI (p=0.02). The ATDI<0 group (posterior ILT distribution) presented a significantly lower median growth rate compared to that of ATDI≥0 group (anterior or symmetrical ILT deposition; p=0.029). The specificity of an ATDI<0 criterion for identifying AAAs with a growth rate below the cohort median was 89%. The ATDI<0 group had a significantly lower posterior maximum wall stress compared with that of the ATDI≥0 group (p=0.03). Overall peak wall stress did not differ between groups. Conclusion: Posterior thrombus deposition in AAAs is associated with significantly lower growth rate and lower posterior maximum wall stress compared with that of AAAs with anterior thrombus deposition and could potentially indicate a lower rupture risk.
To obtain a measure of the degree of asymmetrical ILT distribution, the asymmetrical thrombus deposition index (ATDI) was defined:

\[ \text{ATDI} = \left( \text{AL}_{\text{post}} - \text{AL}_{\text{ant}} \right) / \text{AL}, \]

- \( \text{AL} \): lumen area
- \( \text{AL}_{\text{post}} \): areas of the posterior regions
- \( \text{AL}_{\text{ant}} \): areas anterior lumen regions

**ATDI is**
- positive when the lumen geometrical center lies on the posterior section of the sac (ie, dominant anterior ILT distribution)
- negative when it lies on the anterior section (ie, dominant posterior ILT distribution).

- In the absence of ILT or if ILT deposition is antero-posteriorly balanced in the maximum diameter cross section, then ATDI becomes zero.
- ATDI is 1 or -1 when ILT is deposited only posteriorly or anteriorly in the cross section, respectively (\(-1<\text{ATDI}<1\)).

*Metaxa E et al. J Endovasc Ther 2015; 22(3): 406-12*
ATDI and Wall Stress Distribution

- PWS: no difference
  mean: 19.8 vs 20.5 N/cm²
  \( p=0.69 \)

- +ATDI → PWS
  posterior surface
  \( \rightarrow \upaarrow \) PMWS

- -ATDI → PWS
  anterior surface

Asymmetrical Thrombus Deposition Index (ATDI)

Significantly lower for Low GR group vs High GR group
Mean -0.032 vs 0.336 (p=0.035)

ATDI < 0 → Lower median growth rate: 2.1 mm/y
ATDI > 0 → Higher median growth rate: 3.4 mm/y (p=0.029)

References:
Asymmetrical Deposition of ILT

- High specificity (89%)
- Moderate sensitivity (47%)

### Posterior ILT deposition (- ATDI)
- As a possible low rupture risk marker
  - Increase the time intervals between CT scans
  - Decrease follow up costs
  - Potentially reduce unnecessary interventions

**Conclusion:**
- Posterior thrombus deposition in AAAs is associated with significantly lower growth rate and lower posterior maximum wall stress compared with that of AAAs with anterior thrombus deposition and could potentially indicate a lower rupture risk.

ILT in Ruptured & Intact AAAs

**Ruptured AAAs:** ILT relative area 37.5% —> presented mostly an anterior ILT deposition

**Non-Ruptured:** ILT relative area 73.5% (P = 0.004) —> a more symmetrical pattern

**CONCLUSIONS:**
In similar sized AAAs, ILT is reduced in ruptured compared to nonruptured cases
The ILT cushioning effect...

✓ Inzoli 1993
✓ Vorp 1996
✓ Wang 2002
✓ Georgakarakos 2009
✓ Molacek 2011
✓ Kontopodis 2013
ILT and Wall Strength

The ILT degenerative effect...

✓ Vorp 2001
✓ Kazi 2003
✓ Vande Geest 2006
✓ Tong 2011
✓ Khan 2012
✓ Koole 2013
Influence on AAA Wall Structure

- The thrombus covered wall was found to be
  - thinner
  - contained fewer cells,
  - structural orientation was disrupted
  - contain significantly less elastin,
  - disorganized elastic lamellae
  - broken elastin bands

A significantly increased positive staining for SMC-actin was found in samples *without* thrombus.

Significantly increased number of CD3-positive T cells and CD20-positive B cells in the wall covered *with* thrombus.

ILT has been shown to relate with aortic wall degeneration, reduced wall strength and decreased O2 delivery to aortic tissue.
Association of intraluminal thrombus in abdominal aortic aneurysm with local hypoxia and wall weakening

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Edwin M. Nemoto, PhD,d Satoshi Ogawa, MD,e and Marshall W. Webster, MD,a Pittsburgh, Pa, and
Kanazawa, Japan

Purpose: Our previous computer models suggested that intraluminal thrombus (ILT) within an abdominal aortic aneurysm (AAA) attenuates oxygen diffusion to the AAA wall, possibly causing localized hypoxia and contributing to wall weakening. The purpose of this work was to investigate this possibility.

Methods: In one arm of this study, patients with AAA were placed in one of two groups: (1) those with an ILT of 4-mm or greater thickness on the anterior surface or (2) those with little (\(< 4\) mm) or no ILT at this site. During surgical resection but before aortic cross-clamping, a needle-type polarographic partial pressure of oxygen (Po2) electrode was inserted into the wall of the exposed AAA, and the Po2 was measured. The probe was advanced, and measurements were made midway through the thrombus and in the lumen. Mural and mid-ILT Po2 measurements were normalized by the intraluminal Po2 measurement to account for patient variability. In the second arm of this study, two AAA wall specimens were obtained from two different sites of the same aneurysm at the time of surgical resection: group I specimens had thick adherent ILT, and group II specimens had thinner or no adherent ILT. Nonaneurysmal tissue was also obtained from the infrarenal aorta of organ donors. Specimens were subjected to histologic, immunohistochemical, and tensile strength analyses to provide data on degree of inflammation (% area inflammatory cells), neovascularization (number of capillaries per high-power field), and tensile strength (peak attainable load). Additional specimens were subjected to Western blotting and immunohistochemistry for qualitative evaluation of expression of the cellular hypoxia marker oxygen-regulated protein.

Results: The Po2 measured within the AAA wall in group I \((n = 4)\) and group II \((n = 7)\) patients was 18% ± 9% luminal value versus 60% ± 6% (mean ± SEM; \(P < .01\)). The normalized Po2 within the ILT of group I patients was 39% ± 10% \((P = .08 WITH the respect to the group I wall value). Group I tissue specimens showed greater inflammation \((P < .05)\) compared with both group II specimens and nonaneurysmal tissue: 2.9% ± 0.6% area \((n = 7)\) versus 1.7% ± 0.3% area \((n = 7)\) versus 0.2% ± 0.1% area \((n = 3)\), respectively. We found similar differences for neovascularization (number of vessels/high-power field), but only group I versus control was significantly different \((P < .05)\): 16.9 ± 1.6 \((n = 7)\) vs 13.0 ± 2.3 \((n = 7)\) vs 8.7 ± 2.0 \((n = 3)\), respectively. Both Western blotting and immunohistochemistry results suggest that oxygen-regulated protein is more abundantly expressed in group I versus group II specimens. Tensile strength of group I specimens was significantly less \((P < .05)\) than that for group II specimens: 138 ± 19 N/cm² \((n = 7)\) versus 216 ± 34 N/cm² \((n = 7)\), respectively.

Conclusion: Our results suggest that localized hypoxia occurs in regions of thicker ILT in AAA. This may lead to increased, localized mural neovascularization and inflammation, as well as regional wall weakening. We conclude that ILT may play an important role in the pathology and natural history of AAA. (J Vasc Surg 2001;34:291-9.)
ILT & AAA Wall Hypoxia

- Thick ILT significantly lowered PO$_2$ in the AAA wall (18±9% vs 60±6%)

- marked PO$_2$ gradient through the AAA with ILT was present
  - PO2 highest in the lumen and lowest in the AAA wall

ILT & AAA Wall Hypoxia

Wall Neovascularization

AAA with thick ILT had a significantly greater number of capillaries as compared with nonaneurysmal controls.

**Wall Inflammation**

**AAA with thick ILT** had a significantly greater percentage area of inflammatory cells.

*Vorp DA et al. J Vasc Surg 2001; 34:291-9*
ILT & AAA Wall Hypoxia

Wall Tensile Strength

AAA with thick ILT were significantly weaker as compared with nonaneurysmal controls.

✓ Hypoxia is present in regions of AAA wall adjacent to thick ILT.
✓ This may lead to increased localized inflammation and possibly neovascularization at these sites and appears to result in localized wall weakening.
✓ ILT may play an important role in the pathology and natural history of AAA.

These findings may help to explain

- Higher risk for AAA growth in **males**
- Higher risk of ruptures of smaller sized AAAs in **females**

*Figure 7. Mass fractions of elastin and collagen within the thrombus-covered adventitia for male and female patients. A significant difference is noted for the dry weight percentage of collagen between male and female.*

*Tong J et al. Eur J Vasc Endovasc Surg 2011; 42:207-219*
The **crescent sign** most likely represents dissection and the presence of blood into the thrombus.

This study demonstrated:
- Rupture of AAA is associated with bleeding into the ILT.
- Crescent sign is significantly more frequently observed in ruptured than in intact abdominal aortic aneurysms of the same size.

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Objectives: The aim of this study was to determine signs of bleeding in the intraluminal thrombus and the site of rupture using multislice computed tomography (CT) imaging in patients with abdominal aortic aneurysms (AAA).

Methods: We analyzed CT images of 42 patients with ruptured infrarenal AAA in two hospitals in Stockholm, Sweden during a 3-year period. A “crescent sign” or localized areas with higher attenuation in the thrombus were interpreted as signs of bleeding in the thrombus. A localized area of hyperattenuation did not have the typical crescent shape and was distinguished from calcifications in the thrombus. We measured the attenuation in Hounsfield units in the intraluminal thrombus using CT software to quantify the presence of blood in the thrombus. As controls, we analyzed 36 patients with intact AAA and a comparable aneurysm diameter and age.

Results: The crescent sign was more frequent in the ruptured group (38% vs 14%, P = .02), but there was no significant difference in the presence of localized areas of hyperattenuation in the two groups. The attenuation in the thrombus was significantly higher in patients with rupture than in those with intact aneurysms (P = .02). The site of rupture could be localized in 29/42 patients. Ruptures occurred both through the thrombus-covered and the thrombus-free wall. In 45% of the patients, the rupture site was localized in the left lateral wall, in 24% in the anterior wall, in 24% in the right lateral wall, but only in 7% in the posterior wall.

Conclusion: The site of rupture could be identified in a majority of cases of AAA with routine multislice CT. This study demonstrates an association between the presence of blood in the thrombus as suggested by higher attenuation levels and a crescent sign and AAA rupture. If these findings also predict AAA rupture, remains to be established. (J Vasc Surg 2008;48:1108-13.)
In conclusion, the present study demonstrates that not all cracks in the ILT are dangerous, but those reaching the aneurysm wall or constituting large volume portions of the ILT clearly increase AAA rupture risk.

Results: Univariate analysis showed relative ILT size, aortic diameter, smoking history, and diastolic blood pressure were significantly positively associated with growth rate.

Conclusion: These findings suggest that ILT may play a part in the progression of AAAs.
Conclusion

ILT reduces stresses

Causes degeneration and reduces strength of aortic wall

Intra luminal Thrombus (ILT)

Is related to increased growth rate and rupture risk
While the ILT influence on AAA evolution is complex and currently a field of extensive research and debate...

Its negative effect seems to be apparent...
Thank You