Abdominal Aortic Aneurysms with High Thrombus Signal Intensity on Magnetic Resonance Imaging are Associated with High Growth Rate

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WHAT THIS PAPER ADDS
A layer of intraluminal thrombus is commonly observed in abdominal aortic aneurysms (AAA). AAA thrombus may play a significant role in AAA progression and rupture. Whereas prior studies mainly focused on the presence and size of thrombus, the results from the present study show that AAA growth rate is associated with thrombus consistency. AAA with unorganized loose thrombus, characterized by high thrombus signal intensity on T1-weighted MRI, exhibit higher growth rates. MR thrombus characterization is therefore a promising technique for the clinician to differentiate fast growing aneurysms from slow growing aneurysms.

Objectives: A layer of intraluminal thrombus is commonly observed in abdominal aortic aneurysms (AAAs). The purpose of this study was to investigate whether AAAs with high thrombus signal intensity (SI) at T1-weighted (T1w) magnetic resonance imaging (MRI) exhibit a faster aneurysm growth rate.

Methods: This was a prospective follow-up study. Patients with a small AAA underwent MRI examinations at 6 month intervals. Aneurysm thrombus and psoas muscle SI at the point of maximal diameter on T1w images were measured and expressed as a ratio (thrombus SI/muscle SI). Based on these measurements, patients were categorized into three groups: AAA with relative thrombus SI above (group A) and below (group B) the mean relative thrombus SI of 1.20. Patients with AAA without thrombus constituted group C. Eight patients were scanned twice within 2 weeks to investigate scan—rescan reproducibility. Aneurysm growth rates were expressed as the change in maximal cross sectional area (cm²).

Results: A total of 35 patients (m/f: 26/9; age 72±7 years; AAA maximal diameter 4.9±0.5 cm) were included. Mean aneurysm growth rate for patients in group A (n = 11, 1.87 cm²/0.5 year) was two-fold higher than group B (n = 17, 0.78 cm²/0.5 year, p = .005) and eight-fold higher than group C (n = 7, 0.23 cm²/0.5 years, p = .004) at 6 months’ follow-up. At 12 months’ follow-up, the mean aneurysm growth rate remained significantly higher in group A (n = 7, 3.03 cm²/year) than groups B (n = 10, 1.63 cm²/year, p = .03) and C (n = 7, 0.73 cm²/year, p = .004). The reproducibility for thrombus SI measurements was found to be high with a coefficient of variation of 6.2%. Aneurysm maximal cross-sectional area at baseline was not significantly different for the three groups.

Conclusions: Abdominal aortic aneurysms with high thrombus SI on T1w MR images are associated with higher aneurysm growth rates.

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INTRODUCTION
Abdominal aortic aneurysm (AAA) is a dilatation of the abdominal aorta with maximal diameter more than 3 cm or 1.5 times larger than the normal aorta.¹ AAA rupture is a lethal event in over 80% of the cases and is the 13th most common cause of death in Western countries.² To prevent rupture and future adverse events, patients with AAA larger than 5.5 cm in diameter are currently treated by

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endovascular or open repair. However, some AAAs expand more quickly and may rupture before reaching 5.5 cm in diameter. In addition, AAAs with the same maximal diameter can exhibit differential growth rates. Many studies have therefore been carried out to understand the underlying mechanisms that drive aneurysm growth. Biomechanically, AAA progression and rupture occurs when the circulatory stress that acts on the vessel wall exceeds aortic wall strength. It is now widely recognized that infiltration of inflammatory leukocytes, neovascularization, and activation of proteolytic enzymes in the AAA vessel wall are involved in the degradation of the extracellular matrix resulting in wall weakening. From this perspective, the presence of intraluminal thrombus can play a significant role in the evolution of AAA because it has been shown that thrombus can alter the wall stress and the inflammatory composition of the vessel wall. A recent study found that thrombus compressibility during the cardiac cycle can vary significantly among patients, irrespective of thrombus volume and pulse pressure. The mechanical protective effect of the thrombus, most likely depending on its consistency, can therefore vary among patients and modulate AAA growth. However, a clear link between thrombus consistency and AAA growth needs to be determined. The aim of the present study was to investigate the relationship between the presence of thrombus, thrombus consistency, and aneurysm growth rate. To this end, patients with small AAAs underwent a dedicated T1-weighted (T1w) magnetic resonance imaging (MRI) technique to characterize thrombus signal intensity (SI) and consistency.

**MATERIALS AND METHODS**

Patients from the outpatient Vascular Surgery Clinic with an AAA were invited to participate in this prospective study. Patients presenting between October 2010 and November 2012 were included. Patients with contraindications for MRI and/or severely impaired renal function (estimated glomerular filtration rate [eGFR] ≤ 30 mL/min/1.73 m²) were excluded. Sex, age, comorbidities, smoking status, anti-coagulation, and statin use were recorded. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or treatment with antihypertensive medication. Diabetes mellitus was defined as reported use of medication for diabetes. Additionally, symptoms of abdominal or back pain were recorded. The local medical ethics committee approved the study including the substudy on scan—rescan reproducibility and all patients provided written informed consent prior to inclusion.

**MRI protocol**

Patients were imaged on a 1.5-Tesla whole-body MRI system (Intera, release 11.1.4.6, Philips Healthcare, Best, The Netherlands) using a standard four-channel surface body receiver coil. The AAA thrombus imaging protocol consisted of the following two sequences: (a) a non-contrast enhanced three-dimensional (3D) T1w turbo field echo (TFE), also referred to as magnetization prepared rapid acquisition gradient echo (MPRAGE) scan, with the following parameters: repetition time/inversion time/echo time (TE) = 15.0/730/1.5 ms, flip angle = 15°, 38 shots, field of view (FOV) = 400 × 400 mm, matrix size = 268 × 364, number of signal averages (NSA) = 1, slice thickness = 5 mm, slice orientation = axial, number of slices = between 15 and 20 (the first and last slice covered the proximal aneurysm neck and distal aortic bifurcation, respectively); and (b) a contrast-enhanced 3D T1w TFE with identical parameters as the first sequence except for the slice thickness of 1.5 mm. There were between 40 and 60 slices (the first and last slice covered the proximal aneurysm neck and distal aortic bifurcation, respectively). Scan duration was typically 3:00 and 6:30 minutes for the pre- and post-contrast T1w sequences, respectively. The chosen inversion time of 730 ms was based on previously published literature about carotid atherosclerotic plaque hemorrhage. Compensation for cardiac and respiratory motion was not applied during acquisition. Between the two acquisitions, 0.1 mmol/kg body weight of gadobutrol (Gadovist 1.0 mmol/mL Bayer, Berlin, Germany) was injected at 0.5 mL/second using a power-injector (Medrad Spectris, Indianola, PA, USA).

All patients were asked to undergo a second (6-month follow-up) and third (12-month follow-up) MRI examination using the same imaging protocol. The distance to the aortic bifurcation and fiducial landmarks on the vertebral column (e.g. vertebral discs and spinal processes) as well as the origins of the renal arteries were used as orientation points for co-registration of the images at baseline, 6-, and 12-month follow-up. The first eight patients, who gave permission for another MRI scan within 2 weeks, were included to investigate scan—rescan reproducibility. The scan—rescan reproducibility for thrombus and muscle SI as well as maximal surface area on the slice covering the maximal diameter was investigated.

**Thrombus and muscle signal intensity**

One contour surrounding the thrombus and another contour surrounding the left paravertebral psoas muscle were drawn at the level of maximal diameter of the AAA to measure thrombus and muscle SI, respectively. With respect to the size of contours, the entire cross-sectional thrombus and psoas muscle at the level of the maximum AAA diameter were covered by the contours. No distinct area(s) within the thrombus and muscle were selected. Please note that thrombus and muscle SI can vary slightly within the drawn contours. Aneurysm thrombus SI and psoas muscle SI at the maximal diameter on T1w images were measured and expressed as a ratio (thrombus SI/muscle SI). This ratio is referred to as the relative SI. Based on the relative SI, patients were categorized into three groups: AAA with relative thrombus SI above (group A) and below (group B) the mean relative thrombus SI of 1.20, and patients with no thrombus (group C). Patient categorization to group A or B...
was based on the thrombus SI/muscle SI ratio in the first MRI scan irrespective of the second and third MRI scan.

AAA growth rate

A contour was drawn around the outer AAA vessel wall on the contrast-enhanced T1w MR images at the level of the maximal diameter to compute the maximal cross-sectional area. Possible recall bias between the different sessions for the reader was minimized by analyzing the blinded images with an interval of 8 weeks and randomization of the order of the images. Aneurysm growth rate was expressed as the change in maximal cross-sectional area (cm²) at 6 and 12 months.

Histology

One patient from the follow-up underwent open repair and pre-operative MRI. Thrombus samples from this patient were collected to validate MRI findings. The maximal diameter was localized and marked by the surgeon before opening the aneurysm sac and sampling of the mural thrombus. Hematoxylin and eosin (H&E) staining of paraffin-embedded sections was performed to investigate AAA thrombus structure and presence of erythrocytes. MRI findings and histological staining of the thrombus were compared.

**Data analysis**

All values are shown as mean ± SD. Differences in thrombus SI, muscle SI, and AAA growth rates between the groups were investigated by the Mann—Whitney U test. The chi-square test was used to compare patients’ demographic characteristics and comorbidities between the groups. Scan—rescan reproducibility for thrombus and muscle SI were assessed with the intraclass correlation coefficient (ICC, one-way random, single measures) and the coefficient of variation (CV). The CV was calculated by dividing the overall mean within-subject standard deviation by the mean measurement value for all subjects. All statistical tests were performed with the statistical software package SPSS 20.0 (SPSS Inc., Chicago, IL); p < .05 was considered significant.

**RESULTS**

During the study period, 35 asymptomatic patients (M/F 26/9; age 72 ± 7 years; AAA maximal diameter 4.9 ± 0.5 cm) underwent at least two MR examinations with a time interval of 194 ± 25 days and were therefore included for growth rate analysis. All acquisitions were successfully acquired and the images were free of any significant motion artifacts. There was no thrombus in seven patients. The mean relative thrombus SI at baseline was 1.20 (range 0.80–2.21) in AAA with thrombus. The relative

![Figure 1](image1.png)

Figure 1. (A) Pre-contrast T1-weighted (T1w) magnetic resonance (MR) image at the level of the maximal diameter (4.9 cm) from one patient categorized in group A. The thrombus signal intensity was significantly higher than muscle signal intensity. The relative thrombus signal intensity at this level was 1.94. (B) Co-registered contrast-enhanced anatomical T1w MR images clearly depicting the aneurysm lumen, intraluminal thrombus (ILT) and vessel wall at the same level as in (A). (C) Pre-contrast T1w MR image at the level of the maximal diameter at 6 months follow up. (D) Pre-contrast T1w MR image at the level of the maximal diameter at the 12-month follow-up.

![Figure 2](image2.png)

Figure 2. (A) Pre-contrast T1-weighted (T1w) magnetic resonance (MR) image at the level of the maximal diameter (4.6 cm) from one patient categorized in group B. The thrombus signal intensity was similar to muscle signal intensity. The relative thrombus signal intensity at this level was 0.99. (B) Co-registered contrast-enhanced anatomical T1w MR images clearly depicting the aneurysm lumen, intraluminal thrombus (ILT) and vessel wall at the same level as in (A). (C) Pre-contrast T1w MR image at the level of the maximal diameter at 6 months follow up. (D) Pre-contrast T1w MR image at the level of the maximal diameter at 12 months follow up.
thrombus SI was higher than 1.20 in 11 patients (group A). Seventeen patients had a relative thrombus SI lower than 1.20 and therefore were categorized in group B. MR images from one representative patient categorized in group A and one representative patient categorized in group B are shown in Figs. 1 and 2, respectively.

A total of 24/35 (68%) patients underwent a third MRI scan with a mean follow-up time of 389 ± 40 days. Between the 6- and 12-month follow-up, two patients underwent endovascular repair of the aneurysm (1 in group A and 1 in group B) and one patient was lost to follow-up (group B). The other eight patients refused a third MRI scan because of other health issues (1 in group A and 1 in group B).

The given -values are comparisons between groups A and B. Group A versus Group C for 

### Table 1. Patient demographic characteristics and comorbidities.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Group A (n = 11)</th>
<th>Group B (n = 17)</th>
<th>Group C (n = 7)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, year</td>
<td>76 ± 7</td>
<td>69 ± 7</td>
<td>73 ± 7</td>
<td>.03</td>
</tr>
<tr>
<td>Male/Female</td>
<td>9/2</td>
<td>11/6</td>
<td>6/1</td>
<td>.33</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>3 (27)</td>
<td>6 (35)</td>
<td>1 (14)</td>
<td>.66</td>
</tr>
<tr>
<td>In the past</td>
<td>7 (64)</td>
<td>10 (59)</td>
<td>6 (85)</td>
<td>.80</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>1 (9)</td>
<td>4 (24)</td>
<td>1 (14)</td>
<td>.33</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>7 (64)</td>
<td>14 (82)</td>
<td>6 (85)</td>
<td>.26</td>
</tr>
<tr>
<td>Peripheral arterial disease (%)</td>
<td>1 (9)</td>
<td>1 (6)</td>
<td>3 (42)</td>
<td>.75</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>1 (9)</td>
<td>4 (24)</td>
<td>0 (0)</td>
<td>.33</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>5 (45)</td>
<td>6 (35)</td>
<td>4 (57)</td>
<td>.59</td>
</tr>
<tr>
<td>Anti-coagulation use (%)</td>
<td>9 (82)</td>
<td>16 (94)</td>
<td>7 (100)</td>
<td>.30</td>
</tr>
<tr>
<td>Statin use (%)</td>
<td>9 (82)</td>
<td>12 (71)</td>
<td>6 (85)</td>
<td>.50</td>
</tr>
</tbody>
</table>

The given p-values are comparisons between groups A and B. Group A versus Group C for 

### Table 2. AAA signal intensity (SI) and maximal cross sectional area measurements at baseline, 6, and 12 months follow-up.

<table>
<thead>
<tr>
<th>Baseline measurements</th>
<th>Group A (n = 11)</th>
<th>Group B (n = 17)</th>
<th>Group C (n = 7)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus SI</td>
<td>257 ± 85</td>
<td>147 ± 32</td>
<td>n.a.</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Muscle SI</td>
<td>158 ± 31</td>
<td>157 ± 24</td>
<td>139 ± 30</td>
<td>0.85</td>
</tr>
<tr>
<td>Relative SI</td>
<td>1.62 ± 0.35</td>
<td>0.94 ± 0.12</td>
<td>n.a.</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Maximal diameter (cm)</td>
<td>5.1 ± 0.5</td>
<td>4.8 ± 0.5</td>
<td>4.6 ± 0.4</td>
<td>0.26</td>
</tr>
<tr>
<td>Maximal cross sectional area (cm²)</td>
<td>20.5 ± 4.6</td>
<td>18.7 ± 3.9</td>
<td>17.4 ± 2.3</td>
<td>0.40</td>
</tr>
</tbody>
</table>

6 months follow-up (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 11)</th>
<th>Group B (n = 17)</th>
<th>Group C (n = 7)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus SI</td>
<td>247 ± 56</td>
<td>152 ± 44</td>
<td>n.a.</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Muscle SI</td>
<td>144 ± 27</td>
<td>152 ± 30</td>
<td>141 ± 25</td>
<td>0.75</td>
</tr>
<tr>
<td>Relative SI</td>
<td>1.75 ± 0.43</td>
<td>1.00 ± 0.21</td>
<td>n.a.</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Follow-up time (days)</td>
<td>199 ± 38</td>
<td>196 ± 19</td>
<td>182 ± 11</td>
<td>0.40</td>
</tr>
<tr>
<td>Maximal cross sectional area (cm²)</td>
<td>22.3 ± 4.4</td>
<td>19.5 ± 4.2</td>
<td>17.6 ± 2.4^a</td>
<td>0.11</td>
</tr>
<tr>
<td>12 months follow-up (mean ± SD)</td>
<td>(n = 7)</td>
<td>(n = 10)</td>
<td>(n = 7)</td>
<td></td>
</tr>
<tr>
<td>Thrombus SI</td>
<td>232 ± 59</td>
<td>133 ± 88</td>
<td>n.a.</td>
<td>0.07</td>
</tr>
<tr>
<td>Muscle SI</td>
<td>149 ± 20</td>
<td>149 ± 26</td>
<td>130 ± 27</td>
<td>1.00</td>
</tr>
<tr>
<td>Relative SI</td>
<td>1.56 ± 0.30</td>
<td>1.09 ± 0.49</td>
<td>n.a.</td>
<td>0.04</td>
</tr>
<tr>
<td>Follow-up time (days)</td>
<td>396 ± 50</td>
<td>393 ± 44</td>
<td>376 ± 23</td>
<td>1.00</td>
</tr>
<tr>
<td>Maximal cross sectional area (cm²)</td>
<td>24.2 ± 3.2</td>
<td>20.5 ± 4.4</td>
<td>18.1 ± 2.5^a</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Note. The given p-values are comparisons between group A and B. Group A versus Group C for p < .05. Group B versus Group C for p < .05.

### Signal intensity measurements

Thrombus, muscle, and relative SI as well as maximal AAA cross-sectional area measurements at baseline, 6-, and 12-month follow-up are listed in Table 2. At baseline, the median relative thrombus SI was significantly higher for group A 1.40 (range 1.24–2.21) than for group B 0.89 (range 0.80–1.15) (p < .001). The relative thrombus SI for group A remained significantly higher than group B at the 6 (1.75 ± 0.43 vs. 1.00 ± 0.21, respectively; p < .001) and 12 (1.56 ± 0.30 vs. 1.09 ± 0.49, respectively; p < .04) months follow-up. The mean relative SI slightly increased at 6- and 12-month follow-up for patients in group B, but this was not statistically significant. The muscle SI for group A was comparable with groups B and C at baseline, 6- and 12-month follow-up (p > .1). There was a poor correlation between AAA maximal cross-sectional area and relative thrombus SI at baseline (Pearson r = 0.20; p = 0.3) (Fig. 3). The scan–rescan reproducibility for thrombus, muscle and relative SI obtained from eight (7 men, age 70 ± 7 years) patients are listed in Table 3. The time interval between the first and second scan for these patient was 7.6 ± 2.2 days. High scan–rescan reproducibility was found for thrombus (ICC = 0.98; CV = 6.2%) and relative thrombus SI (ICC = 0.95; CV = 7.9%) measurements. The scan–rescan reproducibility for maximal cross-sectional area measurements was excellent (ICC = 0.99;
CV = 1.4%). The within-subject difference was not dependent on the mean cross-sectional area measurements.

**AAA growth rate**

There were no statistically significant differences between groups A, B, and C with respect to baseline maximal diameter (5.1 ± 4.6, 4.8 ± 0.5, and 4.6 ± 0.4, respectively) and maximal cross-sectional area (20.5 ± 4.6, 18.7 ± 3.9, and 17.4 ± 2.3, respectively). The mean follow-up time at 6 and 12 months’ follow-up was not significant different between group A (199 ± 38 and 396 ± 50 days, respectively), group B (195 ± 18 and 393 ± 43 days, respectively), and group C (182 ± 11 and 376 ± 23 days, respectively) (all p > 0.2). A poor correlation between baseline AAA maximal cross-sectional area and growth rate after 6 months follow-up was found (r = 0.11; p = 0.5) (Fig. 3). Fig. 4 shows the aneurysm growth rates for the three groups at 6 and 12 months’ follow-up. At 6 months’ follow-up, patients categorized in group A (1.87 ± 1.07 cm²) had a two-fold higher overall aneurysm growth rate than patients in group B (0.78 ± 0.81 cm²) (p = 0.005) and an eight-fold higher overall aneurysm growth rate than group C (0.23 ± 0.75 cm²) (p = 0.004). At 12 months’ follow-up, the growth rate for group A (3.03 ± 1.16 cm²) remained significantly higher than group B (1.63 ± 1.22 cm²) (p = 0.03) and group C (0.72 ± 0.99 cm²) (p = 0.004). The growth rate between groups B and C was not significantly different at 6 (p = 0.08) and 12 (p = 0.32) months’ follow-up. A subgroup analysis showed no significant differences in AAA growth rate between male and female patients after 6 (0.54 ± 0.62 vs. 0.55 ± 0.59 cm², respectively; p = .7) and 12 (0.56 ± 0.64 vs. 0.79 ± 0.26, respectively; p = .5) months of follow-up. It should be noted that the majority (67%) of the females had low relative thrombus SI and were therefore categorized in group B, the group with low AAA growth rate. There was also no statistically significant difference in AAA growth rate between diabetics and non-diabetics after 6 months of follow-up (0.46 ± 0.75 vs. 0.56 ± 0.58 cm², respectively; p = .3). The number of diabetic patients at the 12-month follow-up was too small to compare the two groups.

**Table 3.** Scan-rescan reproducibility for thrombus, muscle and relative thrombus signal intensity (SI) as well as maximal cross sectional area measurements (n = 8).

<table>
<thead>
<tr>
<th></th>
<th>Scan 1</th>
<th>Scan 2</th>
<th>ICC</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus SI</td>
<td>181.7</td>
<td>190.2</td>
<td>0.98</td>
<td>6.2</td>
</tr>
<tr>
<td>Muscle SI</td>
<td>151.0</td>
<td>165.2</td>
<td>0.67</td>
<td>10.1</td>
</tr>
<tr>
<td>Relative SI</td>
<td>1.21 (0.58)</td>
<td>1.16 (0.50)</td>
<td>0.95</td>
<td>7.9</td>
</tr>
<tr>
<td>Cross sectional area (cm²)</td>
<td>20.3 (4.6)</td>
<td>20.2 (4.73)</td>
<td>0.99</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Note: ICC = intraclass correlation coefficient; CV = coefficient of variation. SI values are presented as mean (SD). All ICCs were statistically significant (p < .05).

**Figure 3.** (A) Correlation between abdominal aortic aneurysm (AAA) maximal cross sectional area and relative thrombus signal intensity (SI) (Pearson r = .20; p = .3). (B) Correlation between AAA maximal cross sectional area and growth rate at the 6-month follow-up for all patients (r = .11; p = .5).

**Figure 4.** Mean aneurysm growth rate was significantly higher for patients in group A (n = 11, 1.87 ± 1.07 cm²/0.5 years) compared with groups B (n = 17, 0.78 ± 0.81 cm²/0.5 year) (p = .005) and C (n = 7, 0.23 ± 0.75 cm²/0.5 years) (p = .004) after 6 months’ follow-up. At 12 months’ follow-up, the aneurysm growth rate for group A (n = 7, 3.03 ± 1.16 cm²/year) remained significantly higher than the groups B (n = 10, 1.63 ± 1.22 cm²/year) (p = .03) and C (n = 7, 0.72 ± 0.99 cm²/year) (p = .004). Aneurysm expansion rate was not significantly different between groups B and C at 6 (p = .08) and 12 (p = .32) months’ follow-up.
Histology

Thrombus structure was examined by histological analysis of thrombus sampled during open repair of the aneurysm in one patient in group A. MRI was performed 3 days before surgery. The MR images, vessel wall, and thrombus samples as well as H&E sections are shown in Fig. 5. Macroscopically, the luminal thrombus corresponding to low thrombus SI on MRI was firm and organized. The abluminal thrombus corresponding to high thrombus SI on MRI was dark, loose, and hemorrhagic. Histological examination showed that high thrombus SI corresponded to non-structured thrombus with abundant free erythrocytes. The area with low thrombus SI corresponded to thrombus that showed a complex network of fibrin fibers without erythrocytes.

DISCUSSION

The primary finding of the present study is that the presence of high SI thrombus in AAA on T1w MRI is associated with a higher aneurysm growth rate. A high thrombus SI on T1w MR images has been shown to reflect unorganized loose thrombus. Although a causative relationship between thrombus consistency and AAA growth must be investigated, the results indicate that AAAs with different thrombus SI behave differently with respect to aneurysm growth. This may explain why expansion of AAAs 4.0–4.9 cm was found to be unpredictable.16

There are several possible explanations for the fact that AAAs with high thrombus SI exhibit higher growth rates. As mentioned, thrombus compressibility can vary significantly among patients irrespective of the thrombus volume and pulse pressure.14 Thrombus with low SI may reduce the wall stress that acts on the vessel wall significantly better than thrombus with high SI. Since high wall stress has been related to both higher expression of AAA inflammatory biomarkers and a faster growth rate,17 this is a potential explanation for the observed differences in aneurysm growth rate. Secondly, several authors have suggested that proteolytic enzymes produced by entrapped inflammatory leukocytes in the luminal part of the thrombus can leak into the AAA vessel wall thereby causing more AAA vessel wall inflammation and weakening.18,19 It is possible that the thrombus inflammatory burden and/or enzyme leaking through the thrombus is more effective in AAA with high thrombus SI than AAA with low thrombus SI. Taken together, future MRI studies with thrombus characterization, analysis of wall stress and vessel wall inflammation will provide valuable information that can further improve understanding of the behavior of AAA with different kinds of thrombus consistency.

High SI of AAA thrombus on T1w MR images is thought to be caused by the presence of methemoglobin, which is a breakdown product of hemoglobin in erythrocytes. Methemoglobin has the property of shortening the T1 relaxation time which increases the SI on T1w MR images. Chu et al.20 found that T1w MRI mainly detects recent instead of old hemorrhages within atherosclerotic plaques. Therefore, the diffuse high AAA thrombus SI on T1w MR images observed in patients categorized in group A is most likely caused by continuous remodeling of hemorrhagic thrombus and not by discrete large hemorrhages. This line of thought is supported by Castrucci et al.,15 who showed that diffuse high thrombus SI in AAA indeed reflects unorganized hemorrhagic thrombus which was validated with macroscopic inspection of the thrombus during surgery. In the present study, histological staining of thrombus tissue confirmed that areas with low and high thrombus SI corresponded respectively with structured firm thrombus and non-structured loose thrombus with abundant erythrocytes.

An average maximal cross-sectional area growth rate of 1.8 cm²/year for all patients was found in this study, which is in concordance with a former study reporting an average AAA growth rate of 1.9 cm²/year.21 In group A, an average increase in maximal cross-sectional area of 3.03 cm²/year, which equals a maximal diameter growth rate of 7–8 mm/year, can be considered clinically significant because a mean growth rate of 4–5 mm/year has been reported for AAAs with a maximal diameter between 4.0 and 4.9 cm.22

Recent ultrasonographic (US) and computer tomographic (CT) studies have attempted to link thrombus consistency with AAA rupture. A retrospective study showed that inhomogeneous thrombus echogenicity, suggesting unorganized thrombus, on US occurs in 20 of 29 (69%) patients with ruptured AAA.23 In other retrospective studies it was found that the hyperattenuation crescent sign, which indicates hemorrhage within AAA thrombus,10 on contrast-enhanced CT images can indicate impending rupture.25,26 MRI is an interesting alternative to US and CT because of its superior soft-tissue contrast and because it gives the possibility of low-risk serial imaging for surveillance of small AAA as well as surgical planning of large AAA.27–30 As aneurysm growth rate is associated with easily observable thrombus characteristics on routine MRI, simple T1w MRI assessment of AAA thrombus SI is a promising technique for the clinician to differentiate fast-growing aneurysms from slow-growing aneurysms which could potentially lead to individualized follow-up schedules for patients. Since more rapidly expanding AAAs are associated with a higher risk of clinical adverse events, patients with high AAA thrombus SI on T1w MRI should be investigated more frequently and may benefit from a more aggressive medical treatment aimed at lowering AAA vessel wall inflammation as well as other cardiovascular risk factors.31–33 However, larger studies are still needed to corroborate results from this exploratory study and to investigate the clinical advantages including the cost-effectiveness of MRI over the currently recommended techniques.

The present study has several limitations. First, because of the relative short follow-up time, insights into the evolution of AAA thrombus cannot be provided in the long term. However, longer follow-up time would not be possible for all patients because some reached the diameter for intervention and some refused further participation. Secondly, the number of included patients was too small to perform multivariate analysis of different risk factors for AAA growth. However, exploratory analysis showed no
Figure 5. Magnetic resonance (MR) images, vessel wall, and histological sections from one patient (group A). (A) Longitudinal midline survey MR image shows abdominal aortic aneurysm (AAA) with maximal diameter of 5.7 cm. The white arrow indicates maximal diameter. The rectangle indicates the area of wall sampling during surgery. (B) Transverse pre-contrast T1-weighted (T1w) MR image at the level of the maximal diameter. White asterisk indicates abluminal thrombus with very high signal intensity. The white triangle indicates luminal thrombus with low signal intensity. The broken line indicates the lumen boundary. L = lumen; T = thrombus; m = psoas muscle. (C) Sample of anterior aortic vessel wall (W) and adjacent thrombus corresponding with the white rectangle in (A). There is a dark thrombus layer adjacent to the vessel wall suggesting hemorrhage (white asterisk). Before dissecting the aneurysm sac, the maximal diameter was localized and marked with a stitch by the surgeon (white arrow). (D) Hematoxylin and eosin stain (H&E) (×1.25) of the vessel wall and adjacent thrombus at the point of maximal diameter. (E) H&E stain (×40) shows non-structured thrombus with abundant erythrocytes (black arrows). (F) Sample of thrombus with intact lumen in transversal plane at the point of maximal diameter. White triangle indicates thrombus area with low signal intensity. (G) H&E stain (×40) shows structured thrombus with a complex network of fibrin fibers and sporadically entrapped leucocytes (black arrow). There were no erythrocytes in this area of the thrombus.
significant differences between groups A and B with regard to patient characteristics including gender, current smoking, non-diabetic, hypertension and aneurysm size, which are presently considered risk factors for rapid AAA growth. A significant higher mean age for patients in group A was found than group B. Therefore, it cannot be ruled out that age has an affect on differences in AAA growth rate between the two groups. Furthermore, most of the patients included in this study were on anti-coagulation therapy. Although this may have altered AAA thrombus composition compared with patients not on anti-coagulation, the fraction of patients on anti-coagulation medication was similar in both groups and is unlikely to have been the cause of the observed differences in thrombus SI. Additionally, there were no patients in which anti-coagulation was started or stopped after the first MRI examination. However, the role of anti-coagulation in the process of thrombus formation and progression in patients with AAA remains unclear and merits further study. Thirdly, an analysis of local growth of distinct area(s) within AAAs with only high and low thrombus SI could have provided additional information on the relationship between thrombus and the adjacent AAA vessel wall. However, such analysis was only possible in two patients because thrombus SI was diffusely high or low in the other patients. Finally, histological validation could only be performed in one patient, and it cannot be ruled out that changes occurred in the erythrocyte content of the thrombus as a result of tissue processing for histological analysis. Despite this limitation, correlation of MRI with histology provided valuable insights into the anatomical composition of the thrombus substrates.

In conclusion, this exploratory study shows that AAA with high thrombus SI are associated with more rapid aneurysm growth than AAA with low thrombus SI. Larger studies with a longer follow-up are needed to evaluate whether it can improve the follow-up schedule and treatment plans of individual patients.

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CONFLICT OF INTEREST
None.

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abdominal aortic aneurysms.


