Mural Thrombus and the Progression of Abdominal Aortic Aneurysms: A Large Population-based Prospective Cohort Study

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WHAT THIS PAPER ADDS

The role of the intraluminal thrombus (ILT) is still heavily debated with regard to whether it accelerates growth or is simply a passive bystander. This large prospective cohort study reveals unique information about patients with abdominal aortic aneurysms (AAA) and the possible interactions between the AAA and the ILT. There appears to be a weak, yet significant, correlation between the initial thrombus size and an increased growth rate, but whether the ILT is harmful, protective, or both remains unclear.

Objective: To investigate whether the relative size of intraluminal thrombus (ILT) in abdominal aortic aneurysms (AAAs) is associated with AAA growth.

Methods: This large observational study was based on a randomised population-based screening trial. Six hundred and fifteen AAAs were diagnosed in men aged 65—74 years. The relative cross-sectional area covered by the mural thrombus was estimated by a semiautomatic method using ultrasound equipment to measure the area of the ellipses, and adapting the inner ellipse (IA) to the luminal border of the thrombus and the outer ellipse to the area inside the media border (OA). The relative thrombus area was then calculated as ((OA—IA)/OU) $\times$ 100%. Four hundred and sixteen of the patients with AAA were eligible for analysis.

Results: The mean size of the AAA was 40.6 mm, and the mean observation time was 1.78 years. In the group with AAAs measuring 30—34 mm, 42% had ILT, with a mean relative size of 12% of the outer area. In the group with AAAs measuring >64 mm, the presence of ILT increased to 100%, with a mean relative size of 70% of the outer area. Univariate analysis showed relative ILT size, aortic diameter, smoking history, and diastolic blood pressure were significantly positively associated with growth rate, while the presence of diabetes mellitus was significantly negatively associated with growth rate. The relative ILT size remained significantly positively associated with the growth rate after a multivariate linear regression adjusting for potential confounders.

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

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INTRODUCTION

In virtually any aneurysm of clinically important size, intraluminal thrombus (ILT) can be found.[1,2] It is believed that the ILT is a natural phenomenon that is based on the deposition of blood components when an abdominal aortic aneurysm (AAA) grows to a certain size. Whether the presence of ILT has any influence on the natural history of the AAA continues to be a matter of debate. It may be that the ILT's structural elastic integrity buffers the mechanical stress on the AAA wall.[3] Alternatively, it has been thought that biologically active substances infiltrate through the aortic wall by centrifugal convection and centripetal filtration, destabilising the matrix-rich aortic media,[4,5] increasing the inflammatory response and therefore increasing the risk of progression and rupture. The complex biological interaction between the ILT and the aortic wall appears to be divided into layers. The biological activity in the blood—ILT zone encourages platelet aggregation.[5] Together with endothelial injury, the platelets become activated by the biomechanical circumstances occurring in the in-flow part of the AAA and are then deposited when released further down in the aneurysm.[6,7] Earlier experimental studies suggested that the presence of ILT is associated with a higher risk of accelerated growth and rupture.[1,4,8] The two latter complications are the major concerns among clinicians. A recent study looked at the association between the AAA thrombus volume and cardiovascular events and AAA

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growth.[9] Although a smaller study, the thrombus volume showed a significant association with both cardiovascular events and AAA growth.

One component of the creation and growth of ILT relies on platelets. Observational human-based studies suggest that these complex interactions take place in the ILT of an AAA,[5] and small human cohort studies suggest a potential benefit of antiplatelet treatment of medium-sized AAAs.[10] Nevertheless, the association between the role of ILT with the progression of AAA is poorly understood. Several diagnostic modalities have been used to try to describe the association, each with its own strengths and drawbacks. In this study, ultrasonography was chosen for its portability and therefore its ability to screen a large number of patients.

The aim of this study was to analyse whether ILT may be an independent risk factor for the ongoing enlargement in AAA diameter after adjusting for the other risk factors of AAA growth.

MATERIALS AND METHODS

In this prospective cohort study, data from the population-based Viborg Vascular (VIVA) trial were used.[11] More than 50,000 white men aged 65–74 years living in the Central Denmark Region were randomised 1:1 using the Civil Registration System registry either to receive an invitation to vascular screening or to participate in a control group (clinicaltrials.gov identifier: NCT00662480). The control group consisted of those not randomised for participation because there was no current population-based screening programme for AAA in Denmark during the study period. The participation rate in the VIVA study was 75% (18,628/25,065). From October 2008 until January 2011 trained project nurses diagnosed 615 patients with an AAA ($\geq$30 mm) by abdominal ultrasound examination (Logiq E, using a curved array probe 4C-RS with a 4-MHz setting; GE Healthcare, Fairfield, CT, USA). AAAs $<$50 mm in antero-posterior diameter were followed up annually by ultrasound; AAAs $>$50 mm and those that showed progression above 50 mm during the control visits were referred to a vascular surgery department in the Central Denmark Region for evaluation. Those growing rapidly were also followed up until they were $>$50 mm and then referred. At the baseline visit, informed consent was obtained from all those invited before their participation. Only those who were randomised to participate and agreed to join gave their written consent.

The study was approved by the local ethics committee and the data protection authorities, and was performed in accordance with the Declaration of Helsinki.

After diagnosing an AAA, an informative baseline consultation was offered for information, interview, weight, height, preventive actions (i.e., initiation of aspirin treatment, smoking cessation), examination of systemic blood pressure, ankle blood pressure measurement, first-degree relative with AAA, and an additional abdominal ultrasound scanning to secure high-quality videos and pictures of the AAA.

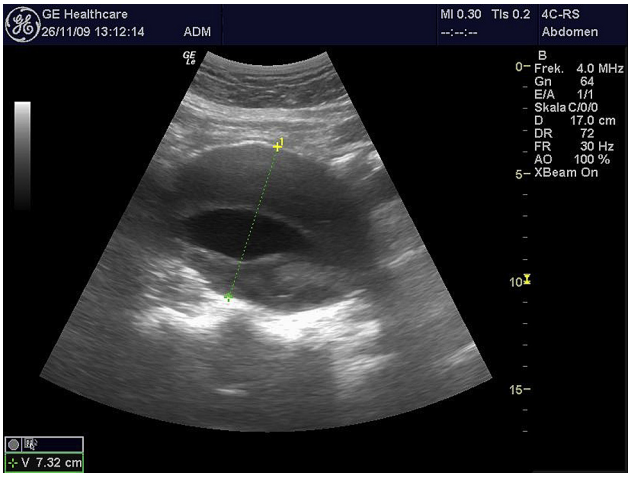

Figure 1. Large abdominal aortic aneurysm in longitudinal view showing anterior to posterior measurements.

AAAs were detected in 615 patients, 590 of whom had images that were sufficient for determining the relative maximal ILT area at the baseline. One hundred and seventeen of the AAAs were $\geq$50 mm in size and were therefore referred for a computed tomography angiography and surgical evaluation. The remaining 498 patients were offered annual follow-up visits. Of these, 416 had undergone a follow-up scan at the time of the data analysis and had sufficient images stored at baseline and at follow-up, as well as a complete baseline assessment.

AAA measurements

As in the VIVA screening study, the systolic longitudinal anterior to posterior maximal inner diameter was measured as shown in Fig. 1. The interobserver variability of these standardised measurements has been estimated to be as low as 0.86 mm.[12]

Systolic cross-sectional recordings were also performed with a semi-automated built-in program (Figs. 2 and 3). The systolic measurement was determined by a combination of

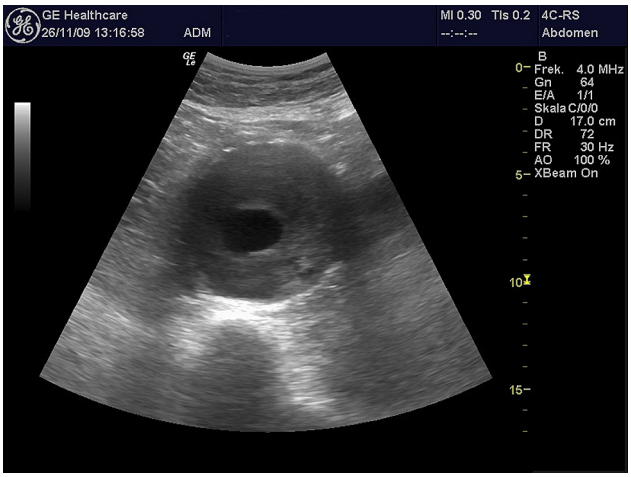

Figure 2. Same abdominal aortic aneurysm as in Fig. 1 in cross-sectional view, visualising the large intraluminal thrombus, the blood–intraluminal thrombus interface and the central lumen.