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◆ CLINICAL INVESTIGATION ◆

In-Vivo Imaging of Changes in Abdominal Aortic Aneurysm Thrombus Volume During the Cardiac Cycle

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Purpose: To evaluate in-vivo thrombus compressibility in abdominal aortic aneurysms (AAAs) to hopefully shed light on the biomechanical importance of intraluminal thrombus. **Methods:** Dynamic electrocardiographically-gated computed tomographic angiography was performed in 17 AAA patients (15 men; mean age 73 years, range 69–76): 11 scheduled for surgical repair and 6 under routine surveillance. The volumes of intraluminal thrombus, the lumen, and the total aneurysm were quantified for each phase of the cardiac cycle. Thrombus compressibility was defined as the percent change in thrombus volume between diastole and peak systole. Continuous data are presented as medians and interquartile ranges (IQR).

Results: A substantial interpatient variability was observed in thrombus compressibility, ranging from 0.4% to 43.6% (0.2 to 13.5 mL, respectively). Both thrombus and lumen volumes varied substantially during the cardiac cycle. As lumen volume increased (5.2%, IQR 2.8%–8.8%), thrombus volume decreased (3.0%, IQR 1.0%–4.6%). Total aneurysm volume remained relatively constant (1.3%, IQR 0.4–1.9%). Changes in lumen volume were inversely correlated with changes in thrombus volume ($r = -0.73$; $p = 0.001$).

Conclusion: In-vivo thrombus compressibility varied from patient to patient, and this variation was irrespective of aneurysm size, pulse pressure, and thrombus volume. This suggests that thrombus might act as a biomechanical buffer in some, while it has virtually no effect in others. Whether differences in thrombus compressibility alter the risk of rupture will be the focus of future research.

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Key words: abdominal aortic aneurysm, biomechanics, computed tomography, dynamic CTA, thrombus compressibility, rupture risk

Elective aneurysm repair aims to prevent aneurysm rupture and is considered when the

See commentary page 320

risk of rupture exceeds the risks of repair.¹ In general, an abdominal aortic aneurysm (AAA)

larger than 5.5 cm is repaired, whereas small AAAs (<5.5 cm) are kept under surveillance. This commonly used 5.5-cm threshold for intervention was confirmed in 2 large clinical trials that showed a low annual rupture risk (0.6%–1%) in small AAAs.^{2–4} However, as 60%

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of all patients in the observation groups underwent elective repair for rapid expansion or symptoms, it is questionable whether these data accurately reflect the natural history of AAA.⁵ The simple observation that even small aneurysms rupture questions the validity of maximum diameter as the single criterion for surgical intervention.^{1,6,7}

To differentiate rupture-prone from “stable” aneurysms, several investigators have focused on the biomechanical properties of associated intraluminal thrombus and suggested that thrombus could act as a potential mechanical buffer or cushion.^{8–10} Results from these studies were, however, based upon 2-dimensional testing of relatively well organized thrombus and little is known about the biomechanical role of thrombus in vivo. We used dynamic electrocardiographically (ECG)-gated computed tomographic angiography (CTA) and volumetric analysis to quantify changes in thrombus volume (compressibility) during the cardiac cycle.

METHODS

Patient Characteristics and Data Acquisition

Under a protocol approved by the local ethics committee and with written patient consent, dynamic CTA was performed in 17 consecutive AAA patients (15 men; mean age 73 years, range 69–76) scheduled for diagnostic CTA imaging. Patient medical history and use of medication were prospectively collected and are summarized in the Table. All patients were scanned using a 64-slice CT scanner (Somatom Sensation; Siemens, Erlangen, Germany) and simultaneous ECG registration. Data acquisition started after reaching a predefined contrast enhancement threshold (bolus triggering), seconds after intravenous contrast administration (Xenetix 350; Guerbet, Paris, France). Radiation dose and scanning parameters were similar to conventional CTA and included a tube voltage of 120 kV/120 mAs and a pitch of 0.34. Reconstruction of the raw data resulted in 1-mm slice thickness with 0.75-mm overlap.

Blood pressure was recorded before and directly after CT data acquisition using a standard cuff. Systemic pulse pressure was

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TABLE
Patient Demographics

Age, y	73 (69–76)
Men	15 (88%)
Hypertension*	13 (77%)
Hypercholesterolemia†	12 (71%)
Diabetes mellitus	1 (6%)
CAD	5 (29%)
COPD	3 (18%)
Stroke	5 (29%)
PAOD	5 (29%)
Smoking, current	12 (71%)
Anticoagulant therapy‡	15 (88%)
Lipid-lowering therapy	11 (65%)
Antihypertensive therapy	10 (59%)

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Continuous data are presented as means (range); categorical data are given as counts (percentages). CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, PAOD: peripheral artery occlusive disease.

* Use of antihypertensive medication or recorded systolic blood pressure >140 mmHg.

† Use of lipid lowering therapy (e.g., statin) or LDL cholesterol >240 mg/dL.

‡ Aspirin or warfarin derivatives.

calculated by subtracting diastolic from systolic blood pressure.

Image Postprocessing

Based upon the simultaneously acquired CTA and ECG information, 10 datasets per patient were created to represent a different phase of the cardiac cycle (one tenth of the R-R interval) and covered the entire abdominal aortic volume (from distal renal to iliac bifurcation). Based upon these reconstructions, 170 3-dimensional (3D) aneurysm models were created (Fig. 1), representing 10 complete 3D aneurysm models per patient, one for each segment of the R-R interval.

Volumetric Analysis

Thrombus, lumen, and total aneurysm volumes were quantified from the distal renal artery to the iliac bifurcation. The models with maximal and minimal lumen volumes were considered to represent peak systole and minimum diastole. Thrombus compressibility was defined as the difference in thrombus volume between peak systole and minimum diastole and is expressed as the relative or

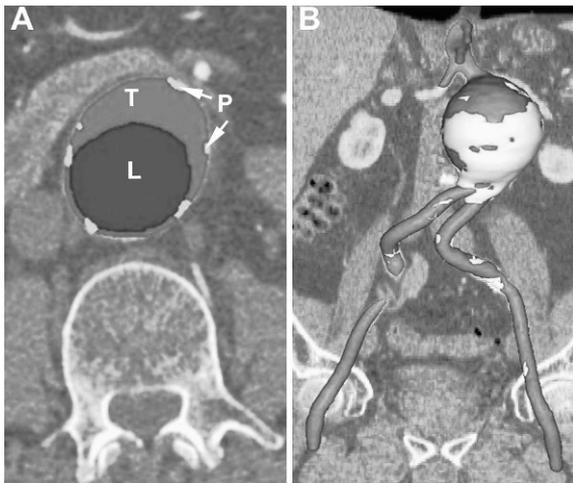


Figure 1 ♦ Image postprocessing. (A) Segmentation identifies the aneurysm’s lumen (L), thrombus (T), and calcified plaque (P). (B) Based upon the segmentation, a 3D aneurysm model was created to calculate thrombus, lumen, and total aneurysm volumes.

percent change in thrombus volume. Image postprocessing and volumetric analysis were performed using validated proprietary software (M2S, Inc. West Lebanon, NH, USA).

Statistical Analysis

Continuous data are reported as median with interquartile range (IQR); $p < 0.05$ was considered significant. Changes in intraluminal thrombus, lumen, and total aneurysm volumes were analyzed using the Wilcoxon signed rank test for paired nonparametric data. The Spearman correlation coefficient was calculated to assess any correlation between changes in thrombus, lumen, and total aneurysm volumes. Any relationships between changes in thrombus volume and aneurysm size, pulse pressure, and total intraluminal thrombus volume were analyzed by means of a Spearman correlation test. Statistical analysis was performed using SPSS (version 14.0; SPSS Inc., Chicago, IL, USA).

RESULTS

Median aneurysm size was 54 mm (IQR 45–55). Thrombus was present in all AAAs; median thrombus volume was 50.1 mL (IQR 35.7–112.0). A substantial interpatient vari-

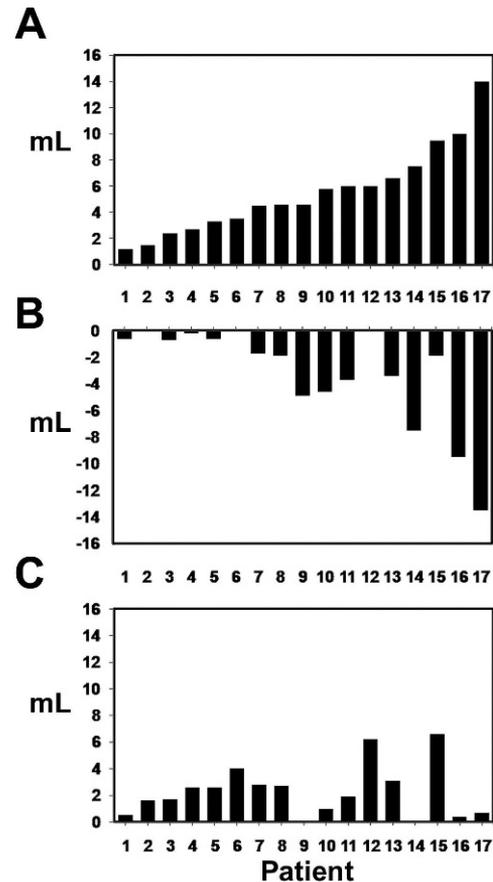


Figure 2 ♦ Changes in lumen (A), thrombus (B), and total AAA (C) volumes during the cardiac cycle in the 17 individual aneurysm patients.

ability was observed in thrombus compressibility ranging from 0.4% to 43.6% (0.2 to 13.5 mL, respectively). Both thrombus and lumen volumes (Fig. 2) changed considerably during the cardiac cycle ($p < 0.001$). As lumen volume increased (5.2%, IQR 2.8%–8.8%), thrombus volume decreased (3.0%, IQR 1.0%–4.6%). Total aneurysm volume remained relatively constant (1.3%, IQR 0.4%–1.9%). Changes in lumen volume were inversely correlated with changes in thrombus volume ($r = -0.73$; $p = 0.001$; Fig. 3) but not to changes in total aneurysm volume ($r = 0.01$; $p = 0.97$). Thrombus volume was positively correlated with aneurysm size ($r = 0.74$; $p = 0.001$), while thrombus compressibility was not correlated with aneurysm size ($r = 0.07$; $p = 0.8$), total thrombus volume ($r = 0.21$; $p = 0.4$), or pulse pressure ($r = 0.1$; $p = 0.7$).

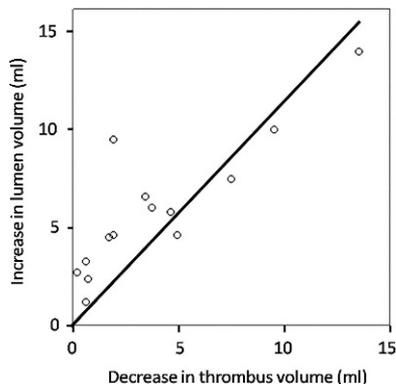


Figure 3 ♦ Correlation between changes in thrombus and lumen volume during the cardiac cycle.

DISCUSSION

During the cardiac cycle, changes in thrombus volume are inversely correlated to changes in lumen volume. As lumen volume increases, thrombus volume decreases. This compensatory volume effect of thrombus was, however, not observed in all patients, which strongly suggests that thrombus could act as a biomechanical buffer in some, while it has little to no effect in others. The observed differences in thrombus compressibility are not correlated with aneurysm size. This is of particular interest as it shows that ECG-gated CTA has the potential to quantify differences in thrombus compressibility for equally sized AAA. Future studies will have to focus on the possible effect of differences in thrombus compressibility on aneurysm rupture risk. The effect of thrombus on rupture risk is controversial. Previous imaging studies showed increased thrombus volume in expanding and ruptured AAA.^{11,12} This, however, could simply result from the fact that large aneurysms have an increased risk of rupture and also contain more thrombus.^{13–15} A later study confirmed this theory, showing no difference in thrombus volume between diameter-matched intact and ruptured AAAs.¹⁶ Results from the present study support these findings, as large AAAs contained more thrombus. Interestingly, thrombus compressibility was not related to thrombus volume or pulse pressure and therefore most likely results from intrinsic biomechanical properties of thrombus.

The development of intraluminal thrombus is a complex and dynamic process. Near the

luminal surface, fibrin is deposited by penetrating platelets, resulting in a dense luminal layer. At the abluminal surface, thrombus contains fewer viable cells and shows increased fibrin degradation.¹⁷ This remodeling process results in different biomechanical properties for different thrombi and even for different layers within the same thrombus.⁹ The net effect of this rather heterogeneous material on pressure transmission and aneurysm rupture risk has been studied extensively. Based upon in-vitro studies, it was postulated that aneurysm wall stress and thus rupture risk is reduced in the presence of thrombus.^{10,18–20} Although this is an important finding, it results from in-vitro testing of excised, well-structured thrombus. Because of the limitations related to in-vitro biomechanical testing, extrapolating experimental data to in-vivo thrombus dynamics might be inappropriate. The present study using dynamic ECG-gated CTA describes the distinct in-vivo response of different thrombi in 3 dimensions.

Previous studies using dynamic CTA and magnetic resonance angiography have shown 2D changes in AAA geometry during the cardiac cycle and addressed the possible impact of dynamic imaging on patient selection for endovascular aneurysm repair.^{21–23} The current study focused on the potential of dynamic CTA to quantify 3D changes in thrombus volume (compressibility) and the possible impact on aneurysm biomechanics. This required a novel approach using dynamic CTA and advanced 3D volumetric analysis.

As with any measurement, the accuracy of 3D volumetric analysis depends on many factors, including pixel spacing, slice spacing, and size of the volume being measured. The smaller the volume, the more uncertainty there is in the measurement. However, the software used in this study is widely recognized as an accurate tool for measuring AAA volumes: using standard CT scanning parameters (2-mm slice spacing, 0.74-mm pixel spacing) results in accurate (to <2%) volume measurements for blood vessels.

Limitations

A possible limitation of the current study is that the data do not provide information on the

biomechanical properties of the aneurysm wall. If we assume a completely rigid aneurysm wall lined with an extremely compliant thrombus, it requires little force to compress the thrombus. The remaining force will still be exerted to the rigid aneurysm wall, leaving total aneurysm volume unchanged. However, even in this rather hypothetical situation, thrombus deforms and thus absorbs energy. In addition, our results are in line with a previous 8-patient dynamic ultrasound imaging study that suggested that thrombus acts as a biomechanical buffer.²⁴ However, we observed larger variations in thrombus compressibility (ranging from 0.1% to 43.6%) and therefore assumed that thrombus could act as a biomechanical buffer in some patients and not in others.

Conclusion

In-vivo thrombus compressibility varies considerably from patient to patient, and this variation is irrespective of aneurysm size, pulse pressure, and thrombus volume. This suggests that intraluminal thrombus might act as a biomechanical buffer in some, while it has virtually no effect in others. Whether differences in thrombus compressibility alter the risk of rupture will be the focus of future research.

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