Thrombus volume is similar in patients with ruptured and intact abdominal aortic aneurysms

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Objective: **Most abdominal aortic aneurysms (AAAs) contain intraluminal thrombus (ILT), which has been demonstrated to contain proteolytic enzymes and proinflammatory cytokines implicated in AAA progression and rupture. In animal models, anticoagulants have been shown to limit AAA progression. Whether ILT plays a role in AAA rupture is unknown.**

The aim of this study was to compare the volume of ILT in patients with ruptured and intact AAAs.

Methods: **We matched by maximum axial diameter alone, on a 1:2 basis, 28 patients with ruptured AAAs and 56 patients with intact AAAs. Total infrarenal aortic volume and ILT volume were measured from computed tomography angiograms using a previously validated and reproducible semiautomated workstation protocol. Clinical risk factors were also recorded. The Mann-Whitney *U* test was used to compare ILT volumes between patients with ruptured and intact AAAs.**

Results: **Median (interquartile range [IQR]) maximum AAA diameter (84.0 [77.5-93.9] mm vs 82.6 [77.1-93.3] mm; $P = .769$) and median (IQR) total AAA volume (372.8 [277.4-486.1] cm^3 vs 358.4 [289.1-563.4] cm^3; $P = .977$) were similar in patients with ruptured and intact AAAs. Median (IQR) AAA ILT volume was similar in patients with ruptured (152.7 [84.8-252.4] cm^3) and intact (180.1 [89.9-254.8] cm^3; $P = .414$) AAAs.**

Conclusions: **This study suggests that ILT volume is not different in ruptured and intact AAAs. (J Vasc Surg 2014;59:315-20.)**

Aortic dilatation and weakening, known as an aortic aneurysm, is an important cause of death in older adults due to aortic rupture.[1-5] The prevalence of abdominal aortic aneurysms (AAAs) is ~2% to 5% in men and 1% in women aged >65 years, and in some countries, screening programs have been introduced to detect AAAs at an early stage.[1-3,5]

There is considerable current interest in identifying medications that effectively limit AAA progression and avoid later complications of AAA, particularly AAA rupture.[6] One suggested approach to the medical management of AAAs is that based on inhibiting thrombosis.[3,6] Intraluminal thrombus (ILT) is present in most AAAs, and ILT volume has been shown to correlate with AAA size.[7] ILT contains high concentrations of proteolytic enzymes and proinflammatory cytokines implicated in AAA rupture.[7-13]

Antiplatelet and antithrombotic strategies have both been found to inhibit AAA progression in an autoimmune model of AAAs in which decellularized guinea pig aortas were transplanted into rats.[14,15] One clinical study reported the association of aspirin prescription with reduced AAA progression in 148 patients with small AAAs.[16] In contrast to these data, ILT has also been suggested to physically protect against AAA rupture by decreasing aortic wall stress.[17-24]

ILT quantity would be expected to be different in ruptured and intact AAAs if it plays an important role in AAA rupture. Previous studies designed to compare ILT in intact and ruptured AAAs have provided conflicting results, perhaps due to difficulty comparing between AAAs of different sizes and absence of reproducible means to measure ILT quantity.[25-29] The aim of the current study was to compare AAA thrombus volume in intact and ruptured AAAs. Patients with ruptured and intact AAAs were matched for maximum AAA diameter, and infrarenal aortic thrombus volume was measured using a reproducible workstation protocol.[7,30,31] The hypothesis being tested was that thrombus volume would be greater in ruptured than in intact AAAs.

METHODS

This study was granted ethics approval by the Human Research Ethics Committees of the Royal Brisbane and Women's Hospital (RBWH) Health Service District and the Townsville Health Service District.

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Patients. Participants were identified through retrospective analyses of the databases maintained by the Departments of Vascular Surgery at the RBWH and The Townsville Hospital (TTH). These databases include patients who have undergone treatment since 2002. Both hospitals are tertiary referral centers for vascular surgery in their regions. The RBWH is one of the largest teaching hospitals in Australia, serving a population of ~1 million and undertaking ~100 AAA repairs annually. TTH is the largest hospital in North Queensland, serving a population of ~400,000 and performing ~30 AAA repairs annually.

The inclusion criteria in the cohort with a ruptured AAA were a diagnosis of a ruptured AAA by a consultant vascular physician and the availability of a computed tomography angiogram (CTA) obtained after rupture but before any surgical intervention. A ruptured AAA was defined as an AAA associated with clear evidence of blood within the retroperitoneum or peritoneum on the CTA and at operation. Patients with symptomatic but intact AAAs were not included.

Patients with intact AAAs were identified from those undergoing elective surgical repair at the two hospitals involved. For inclusion, these patients had to have undergone a CTA and been able to be matched to one of the patients with ruptured AAAs.

Matching was based on maximum axial AAA diameter because AAA diameter is an important determinant of both AAA rupture risk and ILT volume.[1,4,5,9,12,17-19,21,23,25-28,31-35] Matching by AAA diameter was performed by obtaining two patients with intact AAAs for every one with a ruptured AAA. Maximum AAA diameter was matched to within 1 mm.

CTA protocol. Multislice CTAs were performed under a set acquisition protocol as previously described at both centers.[31] Ultravist 300 contrast (100 mL; Bayer, Wayne, NJ) was delivered intravenously under a validated CTA protocol by an automatic injection driver system (MEDRAD, Warrendale, Pa).[7,30,31] A low-dose preliminary CT locater was set above the renal arteries, which triggered the CTA when the Hounsfield unit (HU) at the center of the aorta reached 130 after the delivery of the contrast agent.

Assessment of AAA morphology and ILT volume. Analysis was conducted using a Philips MxView Visualization Workstation at TTH by a single investigator (V.I.) using a previously validated protocol.[7,31] Analysis was restricted to images of the infrarenal abdominal aorta, commencing at the origin of the lowest renal artery (excluding accessory arteries) and concluding at the aortic bifurcation. Maximum axial AAA diameter was recorded from two-dimensional axial slices using the largest of eight diameter measurements taken using electronic callipers. Images were assessed using the CTA viewer function. The aorta was scouted to find the region of maximal diameter by taking many measurements. Axial diameters were measured on a horizontal axial slice as previously described.[31] The maximal diameter was recorded in millimeters (to the nearest 0.1 mm). ILT volume, total infrarenal aortic volume, and thrombus percentage were recorded using a previously validated technique, with an interobserver coefficient of variation of ~5%.[33,34] The intraobserver reproducibility was examined in the current study through assessment of the first 10 scans on two separate occasions. The mean coefficient of variation for thrombus and total aortic volume were <5%.

A volume of interest (VOI) was created around the infrarenal abdominal aorta for each slice, and the volumes were recorded using the "thrombus" and "total volume of aneurysm" HU settings. The settings in this study used HU parameters that have previously been validated to identify thrombus and contrast.[7,31] ILT (center HU, 0; window width HU, 140) and total aneurysm volume (center HU, 1000; window width HU, 4000) were measured in this way. AAA thrombus percentage was calculated as the ratio of AAA thrombus to total infrarenal aortic volume presented as a percentage.

Clinical risk factors. Age at the date of the patient's CTA and sex were recorded. Smoking was defined as ever or never smoked. The presence or absence of hypertension, ischemic heart disease, stroke, and chronic obstructive pulmonary disease was defined by history or current treatment for these conditions, taken from the patient's medical record or preoperative interview. Medications recorded were aspirin, other antiplatelet agents, and statins. These were recorded from the departments' AAA databases or from the preoperative notes found in the patients' records.

Statistical analysis and sample size calculation. A previous study of patients with large AAAs demonstrated that mean (± standard deviation) thrombus volume was 97.6 ± 50 cm^3.[36] Based on demonstrating a 40% difference in thrombus volume at a power of 85%, we estimated that we required 28 cases and 56 controls (based on a one

Table I. Demographic and clinical risk factors in patients with ruptured and intact abdominal aortic aneurysms (*AAAs*)

Clinical variable[a]	*Ruptured AAA (n = 28)*	*Intact AAA (n = 56)*	P
Age, years	74.0 (67.5-80.0)	71.5 (65.3-77.0)	.083
Male sex	21 (75)	54 (96)	.003
Smoking	22 (84)[b]	54 (96)	.056
Hypertension	21 (81)[b]	36 (64)	.131
Diabetes mellitus	4 (15)[b]	9 (35)	.937
Coronary heart disease	11 (42)[b]	29 (52)	.424
Stroke	0 (0)[b]	5 (9)	.116
COPD	4 (15)[b]	12 (21)	.520
Aspirin	13 (50)[b]	29 (52)	.880
Other antiplatelet medication	4 (15)[b]	16 (29)	.196
Statins	13 (50)[b]	38 (68)	.121

COPD, Chronic obstructive pulmonary disease.
[a]Nominal variables are presented as numbers (%) and were compared using Pearson χ^2 test. Continuous variables are presented as median (interquartile range) and were compared using the Mann-Whitney *U* test.
[b]n = 24 (data unavailable for two patients).