Bleeding into the intraluminal thrombus in abdominal aortic aneurysms is associated with rupture

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Objective: **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.)**

Rupture of abdominal aortic aneurysms (AAA) is an important cause of death constituting approximately 1% to 2% of the mortality in males over the age of 65 in the United States.[1] Both the incidence of AAA[2] and rupture[3] have increased during later years. Numerous factors, mostly related to proteolytic enzymes, have been shown to be of importance for growth of AAA and thereby secondarily related to the risk of rupture. For overview see Choke et al, 2005.[4] In spite of this, the only widely accepted predictor of rupture today is aneurysm size.

Most aneurysms of a size associated with rupture contain an intraluminal thrombus (ILT).[5] The growth rate of AAA is related to thrombus growth[6] and the growth of the ILT is associated with an increased risk of rupture.[7,8] The aneurysm wall underlying the thrombus is thinner[9,10] and also shows signs of a higher degree of proteolysis and infiltration of inflammatory cells compared with wall segments exposed to flowing blood.[11] These findings indicate a decreased tensile strength of the wall underlying the thrombus. In order for rupture to occur through this wall segment, bleeding into the thrombus has to occur. In fact such observations have been made demonstrating a "crescent sign" caused by contrast entering the ILT.[12,13]

The purpose of the present study was to investigate signs of bleeding into the thrombus and to locate the site of rupture in patients undergoing computed tomography (CT) examinations with modern multislice technique. The localization of the rupture was recorded anatomically, and also, if it was located in areas free of thrombus or in the wall under or immediately adjacent to the thrombus. Comparisons were made between nonruptured and ruptured aneurysms regarding signs of bleeding in the thrombus.

METHODS

Patients. We searched computerized medical records to identify patients with ruptured AAA who had been admitted to two hospitals in Stockholm during a 36-month period. The inclusion criterion was that the patient had undergone multislice CT where the scans indicated ruptured AAA, by showing signs of retroperitoneal bleeding. Patients with suprarenal and inflammatory aneurysms were excluded. Of note, even patients who were not operated were included in the study. A total of 42 patients (34 men, 8 women, mean age 75.5 years) with ruptured AAA were identified. As controls, we analyzed CT scans of 36 patients (31 men, 5 women, mean age 75.8 years) with comparable

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Competition of interest: none.

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0741-5214/$34.00

doi:10.1016/j.jvs.2008.06.063

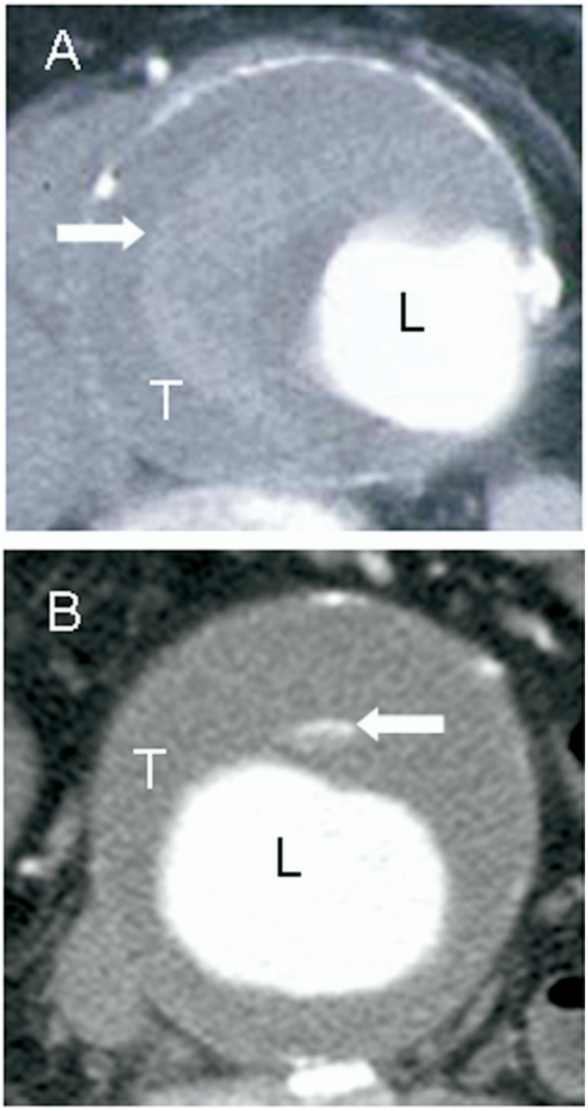

Fig 1. CT scans showing the crescent sign (*white arrow*) in a ruptured AAA (**A**) and a localized area of high attenuation (*white arrow*) in an intact AAA (**B**). *L*, Lumen; *T*, intraluminal thrombus.

age and AAA diameters, who had been diagnosed with intact AAA and operated at the same hospitals during the same time period. One patient in the control group was symptomatic, and the rest were operated on solely on the basis of AAA diameter larger than 5.5 cm.

Computerized tomography. Two radiologists reviewed all CT scans. The slice thickness in the CT examinations were 0.6 mm in 3 patients, 1.0 mm in 7, 1.25 mm in 40, 2.0 mm in 1, 2.5 mm in 15, 3.0 mm in 2, 5.0 mm in 6, and 7.5 mm in 4 patients. Thrombus was considered to be present if there was at least a 0.5 cm thick thrombus at any level of the aneurysm. A crescent sign was considered to be present when a curvilinear zone of higher attenuation was present within the thrombus (Fig 1, *A*). This zone could be seen not only in axial projections but could also be followed in coronal and sagittal image reconstructions and represents dissections in the thrombus. In cases where there was a limited small zone of higher attenuation without a typical curvilinear shape, we classified this as a localized area of hyperattenuation (Fig 1, *B*). These areas were defined as small areas of hyperattenuation, which is less than those caused by calcification. They may be in continuity with the lumen and represent fissures in the intraluminal thrombus. To quantify the level of attenuation in the thrombus, we used the CT software and measured the mean attenuation in Hounsfield units of the thrombus surface in an axial image at the level of the largest diameter in all aneurysms with a thrombus. We related the attenuation of the thrombus to that in the contrast-filled lumen (blood) to evaluate presence of bleeding in the thrombus and expressed it as a ratio. We were able to measure this ratio in 36/42 cases of rupture and in 35/36 intact aneurysms. Six of the patients in the ruptured group had undergone CT examination without contrast enhancement in the arterial phase and were excluded from attenuation data. One AAA in the intact group did not have an intraluminal thrombus and was also excluded from the attenuation data (Table). Two radiologists independently reviewed all the scans. The rupture site was identified in patients where a clear leakage of contrast from the aortic lumen through the aortic wall or discontinuation in the aortic wall with the presence of an adjacent periaortic hematoma could be seen. This was possible since we could perform reconstructions from very thin slices in most patients.

Table. Contrast enhancement, presence of ILT and ability to locate rupture site in abdominal CT scans

	Rupture (n = 42)	*Control (n = 36)*
Contrast enhancement in arterial phase	36	35
Presence of thrombus	42	35
Able to localize rupture site	29	NA

A majority of the patients in the two groups had received intravenous contrast in the arterial phase of the CT scan. Only one patient in the control group did not have a thrombus and in 29/42 patients could we localize the site of rupture.

Statistical analysis. Age, aneurysm diameter, and attenuation according to Hounsfield units were compared between ruptured and intact AAA using the Mann Whitney test. The Fisher exact test was used to determine whether there were any significant differences in the number of patients with a crescent sign or an area of hyperattenuation in the thrombus between the different groups. *P* values less than .05 were considered to be significant. Statistical analyses were performed using the GraphPad Prism software for Windows, version 4.03 (GraphPad Software Inc, La Jolla, Calif).

RESULTS

Presence and signs of bleeding into the thrombus. Mean aneurysm diameter was 8.1 cm (range 5.2-13.5) in

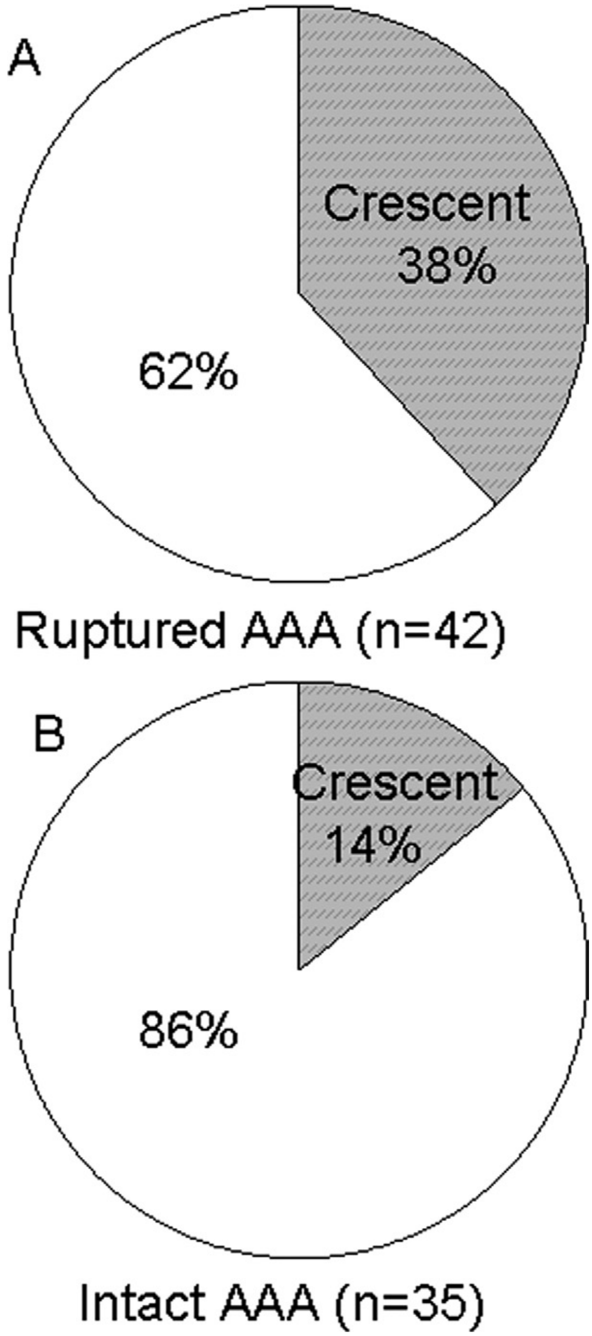

Fig 2. Percentage of patients with ruptured AAA (**A**) and intact AAA (**B**) with a crescent sign.

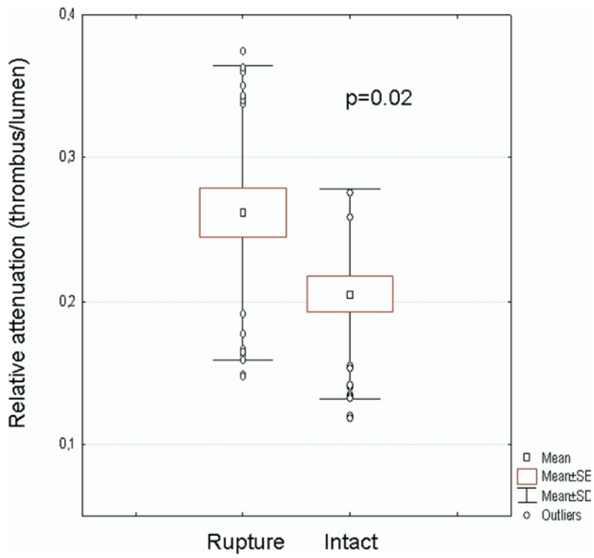

Fig 3. Relative attenuation in the ILT compared with the lumen in ruptured and intact AAA.

the group with ruptures and 7.4 cm (range 5.5-12.7) in the intact group ($P = .13$). Thrombus was present in all aneurysms except one in the intact group (Table). A crescent sign was seen significantly more often in the ruptured group (16/42, 38.1%) than in the intact group (5/35, 14.3%, $P = .02$, Fig 2). In both groups, there was a tendency for the aneurysms that had a crescent sign to be larger than the aneurysms that lacked the sign but the difference was not statistically significant (7.5 cm vs 8.4 cm, $P = .09$). Only localized areas of hyperattenuation that did not have a typical curvilinear shape in patients that lacked a crescent sign were seen in 12/26 (46.2%) in the ruptured group compared with 8/30 (26.7%) the intact group ($P = .17$). To quantify the presence of blood in the thrombus, we measured attenuation in Hounsfield units and found that the relative level was significantly higher in ruptured compared with intact AAAs ($P = .02$, Fig 3).

Rupture localization. Multislice CT with thin slices enabled us to detect the site of rupture in 29/42 patients (Table). Ruptures occurred in the wall underlying the thrombus in 15/29 (52%) patients, and in 4/29 (14%), it occurred at the edge of the thrombus (Fig 4, *A* and *B*). In 10/29 (34%), patients it occurred through the aneurysm wall distant from the thrombus (Fig 4, *C*). Even though ruptures occurred through the thrombus free wall, the thrombus in these AAA had significantly higher levels of attenuation compared with intact aneurysms ($P = .03$). There was no difference in thrombus attenuation between cases with rupture through the thrombus covered and thrombus free wall ($P = .95$). In patients with a crescent sign, ruptures occurred in 5/16 cases through the thrombus-covered wall, in 3/16 through the thrombus-free wall, and 3/16 at the edge of the thrombus. In 5/16 patients with a crescent sign, we could not detect the rupture site.

We also observed the localization of the rupture and determined its localization based on four sectors: anterior (315° to 45°), left (45° to 135°) or right lateral (225° to 315°), or posterior (135° to 225°). The rupture localization was in the anterior sector in 7/29 cases, in the posterior sector in 2/29, on the left side in 13/29, and on the right side in 7/29 (Fig 5).

Fig 4. CT scans showing the rupture site through a thrombus covered aortic wall (**A**), through a thrombus-free wall (**B**), and at the edge of the thrombus (**C**). *L,* Lumen; *T,* intraluminal thrombus.

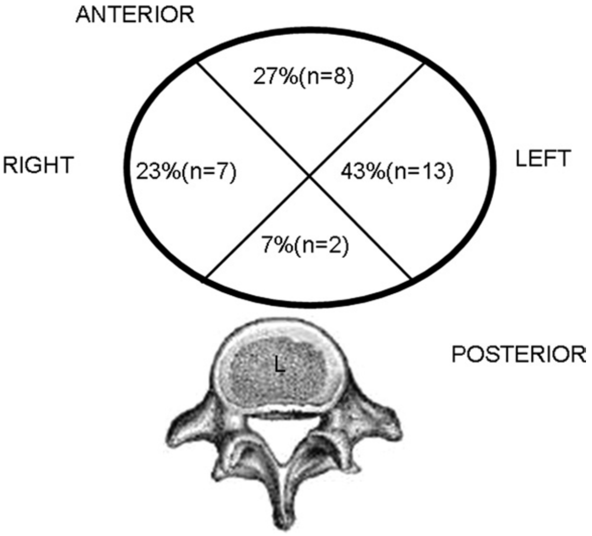

Fig 5. Observed rupture locations on the aortic wall. Few occurred in the posterior sector where the aorta is supported by the lumbar vertebrae (*L*).

DISCUSSION

The present study demonstrates an association between bleeding into the ILT and rupture of abdominal aortic aneurysms. The bleeding was evaluated by presence of a crescent sign and local accumulation of contrast or differences in attenuation measured by Hounsfield units in the thrombus comparing patients with and without rupture.

The crescent sign most likely represents dissection of blood into the thrombus.[12] Since the dissection in the thrombus directly communicates with the lumen, this sign is best appreciated with contrast agent in the arterial phase in scans. Initially, the crescent sign was described in noncontrast enhanced CT scans and was described as having attenuation greater than the adjacent psoas muscle. However, with the latest generation multidetector tomographs, we are able to perform scans rapidly with the contrast in the arterial phase and at this time the contrast has not reached the psoas muscle. We therefore chose to relate the attenuation in the thrombus with the attenuation in the lumen.

This study supports previous reports of the finding of crescent sign in cases of rupture and reinforces the suggestion that this sign should be an indication for urgent surgery in patients without obvious signs of rupture.[13-16] The presence of localized bleedings identified as small local areas of hyperattenuation, however, did not differ significantly between ruptured and nonruptured cases. We can therefore not recommend that this particular sign should be an indication for urgent surgery. Further work with larger patient groups including symptomatic AAA patients will have to be done before a cut-off value can be determined, above which relative attenuation in Hounsfield units could be indicative of an impending rupture.

Crescent signs were also seen but less commonly in cases with intact aneurysms. One patient, however, with an aneurysm judged to be intact had a prominent crescent sign. He had a painful aneurysm and was classified as having an impending rupture irrespective of the bleeding in the thrombus, which was not reported by the radiologist. We could not record symptoms in the remaining few patients with crescent signs in the ILT of intact AAA. Since they were operated shortly after the CT examination, we are unable to evaluate if the crescent sign in these patients was a sign of an impending rupture.

There were an equal number of ruptures localized in the thrombus covered wall and in wall segments free from thrombus. It should be noted, however, that many of those occurring in the thrombus free wall were localized at the edge of the thrombus. In an autopsy study of patients with ruptured AAA, it was found that the majority of ruptures occurred through the wall covered by thrombus.[17]

The thrombus is metabolically active, containing cells that contribute to proteolytic activity.[18] Both matrix metalloproteases (MMP) 2 and 9, as well as fibrinolytic activity have been identified in the ILT.[19] The fibrinolytic activity is of importance since plasmin is an activator of MMPs. The thrombus, thus, contains activity, which could contribute to degradation of the aneurysm wall. The wall underlying the thrombus is thinner and shows more signs of proteolytic degradation compared with wall segments without thrombus.[9-11] If blood enters the thrombus, it will reach a wall segment that has been shown to be weaker than segments devoid of thrombus. This mechanism could explain ruptures through the thrombus covered wall but cannot explain ruptures localized to the thrombus-free wall.

The attenuation of the thrombus measured by Hounsfield units in patients where ruptures occurred through the thrombus-free wall was the same as for ruptures occurring through the thrombus covered wall or at the edge of the thrombus. Furthermore, crescent signs were seen also in cases with rupture through the thrombus free wall. The findings may indicate that bleeding in the thrombus is of general importance for the risk of rupture.

Reports about the role of the ILT for pressure transmission to the underlying wall differ. It has been suggested that the ILT protects the underlying wall from pressure induced wall stress both in experimental,[20] and clinical studies,[21,22] but other studies have failed to detect such an effect.[23] Even if the ILT should diminish stress on the underlying wall, this does not apply if bleeding occurs into the thrombus. Prerequisites for bleeding into the thrombus exist since it is vulnerable against fatigue and fails at load levels far below its ultimate strength under pulsatile loading.[24]

One limitation of this study is that no definite causal relationship between bleeding into the thrombus and rupture can be demonstrated. In cases where the rupture occurs through the thrombus covered wall, it is tempting to speculate that it represents blood eventually reaching the underlying wall segment. On the other hand, the crescent sign may arise due to the aneurysm wall expanding faster than the thrombus, leading to the creation of fissures in the ILT. However, previous reports showing a clear correlation between thrombus volume and aneurysm diameter[5] and the recent study by Gasser and coworkers[24] supports the converse, ie, that changes in the thrombus affects the aneurysm wall.

If the crescent sign predicts rupture, it can be argued that it arises when the aneurysm rapidly expands in size. In support of this, we found that aneurysms with a crescent sign were larger than aneurysms that lacked a crescent sign but the difference was not statistically significant. This may be due to the small number of patients and larger studies with repeated CT measurements will have to be done to understand how the crescent sign arises.

It is generally thought that most ruptures occur in the posterior part of the aneurysm and more often to the left mostly based on the fact that the hematoma is localized posteriorly. The present study demonstrates that the site of rupture is most often seen in the left lateral part of the AAA represented by the sector 45° to 135°and only seldom is seen in the posterior sector 135° to 225° where the aneurysm is close to the lumbar vertebrae. Our study can of course not determine the site of rupture in patients who die from aneurysm rupture without reaching hospital.

It is often argued that patients with clear signs of rupture should be sent to the operating room without undue delay caused by further investigations. In the era of endovascular repair of ruptured aneurysms, this attitude has been modified. The concept of hypotensive hemostasis has gained increased popularity and made it possible to perform CT investigations on patients with ruptured aneurysms.[25] The speed with which a CT examination with modern equipment is made and the location of the equipment in close proximity to the operating room further minimizes the delay induced by the investigation. Furthermore, CT examination can also exclude the presence of an aneurysm with or without rupture as well as indicating other differential diagnoses, thus, avoiding unnecessary operations. A CT examination can also be advantageous, not only for a possible endovascular procedure, but also for open surgery. Location of the rupture and a hematoma close to the aneurysm neck may help the surgeon to decide to perform a supra-coeliac infradiaphragmatic approach for a temporary clamping.

In summary, rupture of AAA is associated with bleeding into the ILT and the crescent sign is significantly more frequently observed in ruptured than in intact aneurysms of the same size.

AUTHOR CONTRIBUTIONS

Conception and design: JR, JS
Analysis and interpretation: JR, JS, FL, MB, JD, GJ
Data collection: JR, JD, FL
Writing the article: JR, JS, FL, GJ
Critical revision of the article: JS, FL, MB, JD, GJ
Final approval of the article: JR, JS, FL, MB, JD, GJ
Statistical analysis: JR, FL, JS
Obtained funding: JR, JS
Overall responsibility: JR

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Submitted Apr 2, 2008; accepted Jun 30, 2008.