Imaging Arterial Thrombosis: Comparison of Technetium-99m-Labeled Monoclonal Antifibrin Antibodies and Indium-111-Platelets

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Imaging with the ^{99m}Tc-T2G1s monoclonal antifibrin antibody fragment (Fab') has demonstrated promise in the noninvasive detection of venous thrombi in humans. The purpose of this study was to determine whether chronic arterial thrombi can also be detected by antifibrin antibody imaging. **Methods:** Eighteen subjects with chronic arterial thrombi were studied with planar and tomographic imaging at 0 to 24 hr postinjection of ^{99m}Tc-labeled T2G1s monoclonal antifibrin antibody fragment. Imaging with ^{111}In-labeled platelets was also performed. Images were visually graded by two observers as 0, 1, 2 or 3 (no, faint, moderate or marked) uptake, and quantitative analysis of tomographic images was done in 13 subjects. **Results:** On visual analysis of planar images, 44% (8 of 18) of antifibrin patient studies were 1.0 or more and 66% (10 of 18) were judged negative compared with 94% (15 of 16) of platelet patient studies judged 1.0 or more and 6% (1 of 16) judged as negative ($p < 0.01$). Visual analysis of tomographic images was similar, with 61% (11 of 18) of antifibrin studies graded 1.0 or more compared with 100% (17 of 17) of platelet studies ($p < 0.01$). The tomographic target-to-background ratio was higher with platelets than with antifibrin antibody (2.5 ± 1.4 versus 1.8 ± 1.0, $p < 0.05$). **Conclusion:** In the large-vessel chronic arterial thrombi studied, the results of ^{99m}Tc-labeled monoclonal T2G1s antifibrin Fab' imaging were positive in only one-half of the patients studied, significantly less than the findings with platelet imaging, which were positive in all subjects. The higher rate of positive images with labeled platelets than with labeled antifibrin antibodies may be largely due to thrombus age, with continued platelet deposition but little active fibrin deposition.

Key Words: thrombosis imaging; platelet imaging; monoclonal antibodies

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Intra-arterial platelet-fibrin thrombus formation is the final common pathway that leads to most complications of atherosclerosis, including acute myocardial infarction, unstable angina, stroke and sudden death. In addition, intra-arterial thrombosis is a major cause of the complications associated with intravascular prosthetic materials, such as arterial bypass grafts and heart valves. Given the importance of arterial thrombus formation, noninvasive, rapid and accurate in vivo methods capable of thrombus detection would be of great clinical value. Thrombosis imaging with radionuclide techniques involves the injection of a tracer that accumulates preferentially in the areas of thrombosis.

To date, most arterial thrombosis imaging in humans has utilized ^{111}In-labeled platelets. Platelet imaging is noninvasive and semiquantitative, allows serial studies and can detect large vessel thrombosis. In addition, findings on platelet imaging may be able to stratify patients into low-risk or high-risk groups for subsequent arterial thromboembolic events (*1,2*). However, platelet imaging suffers from several limitations (*3*). The technique is too complex and time consuming for routine use because imaging at 48 to 72 hr is typically required. In addition, platelet imaging cannot detect small thrombi of enormous clinical importance, such as coronary artery thrombi. This limitation is partly due to the relatively high circulating background blood pool activity that occurs with the injection of radiolabeled platelets. Thus, newer techniques of thrombosis imaging are clearly needed.

One new approach is the use of antifibrin antibodies labeled with ^{111}In or ^{99m}Tc. Antifibrin antibodies bind specifically to fibrin but not to circulating fibrinogen, which should enhance image contrast by lowering the background activity. In addition, the relatively rapid blood clearance of antibody fragments might also enhance thrombus-to-background ratios (*4*). The lower energy and higher injected dose of ^{99m}Tc might also improve imaging of thrombi compared with the use of ^{111}In. Both animal and, more recently, human studies suggest that labeled antifibrin antibodies offer great promise for the diagnosis of venous thrombi (*5–13*). In animal models of venous thrombosis, thrombus-to-blood ratios are relatively high, ranging from 2:1 to as high as 24:1 (*9,14–16*). In recently reported human

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studies, labeled antifibrin antibodies appeared promising for the early diagnosis of deep venous thrombosis in humans, with sensitivities of 81% to 97% and specificities of 84% to 100% compared with contrast venography (*5,8,10–12*). Moreover, sensitivity appears to remain high in patients who are receiving heparin therapy.

To date, there are no published data regarding the ability of labeled antifibrin antibodies to detect arterial thrombi in humans. Compared with venous thrombi, which are composed predominantly of fibrin and red blood cells, arterial thrombi, at least acute arterial thrombi, contain more platelets with lesser amounts of fibrin and red blood cells (*17*). Thus, labeled antifibrin antibody might be less sensitive for the detection of arterial thrombi. Nevertheless, in a dog model, the authors recently reported that all acute arterial thrombi were visually detected within 2 hr of ^{99m}Tc-labeled antibody injection (*18*). The mean ex vivo thrombus-to-blood ratio was 4.2:1. By quantitative analysis of planar images, the mean thrombus-to-normal artery ratio was 2.3:1 at 2 hr after injection. An isotype-matched control monoclonal antibody had no selective thrombus uptake. These results clearly demonstrated the feasibility of the noninvasive detection of arterial thrombi with labeled antifibrin antibody.

The first purpose of this study was to determine the ability of ^{99m}Tc-labeled antifibrin antibody fragment imaging to detect large vessel chronic arterial thrombi in humans in disorders in which thrombi are known to be present (abdominal aortic aneurysm thrombi, left ventricular thrombi and prosthetic arterial grafts, which have a lining of platelets and fibrin) (*3,19–22*). The second purpose of the study was to compare antifibrin antibody findings to more conventional thrombosis imaging using ^{111}In-labeled platelets.

METHODS

Subjects

Eighteen men aged 44 to 84 yr (mean = 67 ± 10 yr) were chosen for this study because they had conditions in which chronic large-vessel arterial thrombosis occurs. Two subjects had left ventricular thrombi documented by two-dimensional echocardiography performed immediately before thrombosis imaging. In both subjects, the myocardial infarction that caused the thrombus was remote, 2 mo in one patient and 11 yr in the other patient. The specificity of two-dimensional echocardiography for left ventricular thrombi in the authors' laboratory is 95% (*23*). Three subjects had abdominal aortic aneurysms with associated thrombi documented by ultrasound; in all subjects, the aneurysm and thrombus had been present for more than 1 yr. Thirteen subjects had arterial grafts, which are uniformly associated with ongoing thrombosis for indefinite periods after implantation (*3,22*). The grafts had been in place for 3 mo to 15 yr. Of the subjects with arterial grafts, six had polytetrafluoroethylene above-the-knee femoropopliteal grafts, and seven had Dacron aortic bifurcation grafts (n = 5) or isolated Dacron aortic grafts (n = 2). Thus, only chronic (longer than 2 mo) arterial thrombi were studied.

The subjects were studied over a 5-day period. On Day 1, ^{111}In-labeled platelets were injected with imaging, as described subsequently, to 48 to 72 hr after the injection. On Day 4, ^{99m}Tc-labeled antifibrin antibody Fab' was injected with imaging on Days 4 and 5. This protocol was approved by the Human Subjects Committee of the University of Washington, and all subjects gave informed consent. The radiation dose was 0.3 rem whole-body for the ^{99m}Tc-labeled antifibrin antibody and 0.2 rem whole-body for the ^{111}In-labeled platelets.

Antifibrin Labeling and Imaging

The Fab' fragment of the T2G1s antifibrin antibody was used. Antifibrin antibody labeling was performed with a packaged labeling kit (Centocor, Malvern, PA) by the addition of 30 to 40 mCi of ^{99m}Tc to a lyophilized mixture of D-glucaric acid (the ligand used to chelate the reduced ^{99m}Tc), stannous chloride, concentrated hydrochloric acid buffered with sodium bicarbonate to a final pH of 7.0 and 0.5 mg of the antibody Fab' (*18*). After incubation of the mixture for 15 min at room temperature, the labeling efficiency was determined with thin-layer chromatography. If the initial labeling efficiency was less than 90%, which occurred in seven of 18 instances, the incubation was continued for another 10 min, and the labeling efficiency was again measured. The 15-min labeling efficiency was 88% ± 7%, and the final labeling efficiency was 91% ± 1%. The mean injected dose of ^{99m}Tc-labeled antifibrin antibody was 19.2 ± 2.9 mCi. No subject exhibited an adverse clinical reaction to the administration of the antifibrin antibody.

Serial antifibrin antibody imaging of the region of suspected thrombosis was performed with planar and/or tomographic methods at 0 to 10 min postinjection in all subjects, at approximately 2 hr in all subjects and again at 4 to 24 hr after antibody injection in 15 of the 18 subjects. Planar imaging (5 to 10 min/view) was done with a large-field-of-view gamma camera and a general all-purpose parallel-hole collimator. Planar imaging of the target area was done in the anterior view in all patients; patients with left ventricular thrombi also had left lateral images. SPECT imaging of the target region was performed as previously described (*24,25*) at the same intervals with a GE 400ACT (Milwaukee, WI) interfaced to a Siemens Microdelta (Burlingame, CA) imaging computer. A 20% energy window was used, and data were collected over the anterior 180° in all subjects, except those with left ventricular thrombi, who had data collected over the 180° centered on the cardiac long-axis (left posterior oblique to right anterior oblique). Data were collected for 10 to 25 sec at each of 64 stops separated by 2.81 angular degrees. Reconstruction was performed in the transaxial projection in 0.6-cm increments with filtered backprojection techniques and correction for uniformity and center of rotation with no attenuation correction, as previously reported (*24,25*). Adjacent 0.6-cm thick tomographic slices were then summed into 1.2-cm slices prior to visual and quantitative analysis. The subjects were asked to void prior to abdominal imaging to avoid obscuring abdominal images caused by bladder activity.

Platelet Labeling and Imaging

Platelet imaging was done on 17 of the 18 subjects. Autologous platelets were labeled with ^{111}In using a modification of Thakur et al.'s (*26*) original technique, as previously described from the authors' laboratory (*21,27*). The mean injected dose was 322 ± 15 μCi. Serial platelet imaging was performed with both planar and tomographic techniques, as previously described (*24*). Tomographic images were acquired and reconstructed as described for ^{99m}Tc, except that a medium-energy collimator was used, both major photopeaks (173 and 247 keV) of ^{111}In were collected, and the acquisition time per stop was increased to 32 sec in all cases because of the lower injected dose of ^{111}In. Platelet imaging was

TABLE 1
Mean Visual Analysis Scores for Planar and Tomographic Images

	^{99m}Tc-labeled antifibrin antibody				^{111}In-labeled platelets		
	0–10 min	2 hr	24 hr	Maximum	2–24 hr	48–72 hr	Maximum
Planar	0.9 ± 1.1	0.7 ± 0.8	0.5 ± 0.8	0.9 ± 1.1	0.9 ± 1.0	2.3 ± 0.6	2.3 ± 0.8
Tomographic	0.9 ± 0.9	1.1 ± 0.9	1.0 ± 1.2	1.2 ± 1.0	1.3 ± 1.0	2.1 ± 0.9	2.4 ± 0.6

done early (2 to 24 hr) postinjection in all patients and again at 48 to 72 hr in all but one of the patients.

Visual Image Analysis

Images were analyzed by both visual and quantitative methods. For visual analysis, each image at each imaging time was read independently by two experienced observers. The images were interpreted on the following scale: 0 = no detectable uptake compared with adjacent or contralateral vascular structures; 1 = faint uptake, slightly greater than adjacent or contralateral vascular activity; 2 = moderate uptake; and 3 = marked uptake, much greater than adjacent or contralateral vessels. In cases of disagreement, the mean value of the two readers was used. The studies were also graded as uninterpretable if uptake in adjacent organs (spleen, liver, kidneys or bladder) overlapped or obscured the region being studied, which commonly occurred on the 24-hr antifibrin abdominal images. All of the immediate (0 to 10 min) planar and tomographic antifibrin studies were judged to be interpretable, but at 2 hr after injection, three planar and four tomographic images were judged uninterpretable. At 24 hr, six planar and eight tomographic images were judged uninterpretable. Only one planar platelet image (at 24 hr) and one tomographic image (at 48 hr) were judged uninterpretable because of overlapping activities or low counts. Images that were judged as uninterpretable were not used for the calculation of the mean visual analysis scores reported in the text or tables. For each subject studied, the maximal image score achieved at any imaging time with both planar and tomographic methods was also noted.

Quantitative Image Analysis

To compare antifibrin and platelet imaging findings further, quantitative analysis of the tomographic images was performed on the images of 13 subjects. Five subjects did not have quantitative analysis for the following reasons: one subject had only antifibrin imaging, one subject's digital images were lost due to a computer problem, one subject with bilateral femoropopliteal grafts had no suitable background control area available and two subjects with left ventricular thrombi could not have accurate target regions drawn on the antifibrin images because they were visually negative.

For quantitative analysis, target-to-background ratios were determined as follows. Computer-generated circular regions of interest (ROIs) were applied to transaxial 1.2-cm thick tomographic slices of both the antifibrin and the platelet studies of each patient according to previously described methods (*24,25*). The ROIs were identically sized and positioned for both the antifibrin and platelet images. For abdominal aortic aneurysms, the circular region was applied to three to four slices to obtain target counts and from three to four slices of normal aorta above or below the aneurysm to obtain background counts. Patients with isolated Dacron aortic tube grafts had a similar analysis, with the background also being a region of adjacent aorta. In patients with femoropopliteal grafts, circular ROIs were applied to all slices that encompassed the graft, and a background region was obtained from an identical region placed around vascular activity on the contralateral leg. In patients with aortic bifurcation grafts, no comparably sized normal background vascular region was available on the tomographic images; therefore, the background region was taken from a nonvascular area adjacent to the graft that avoided the bladder, kidneys, liver and spleen. Tomographic slices in which there was clear interference from activity in the kidneys, liver, spleen or bladder were not analyzed. For each subject, the target-to-background ratio was calculated at each imaging time; in addition, the maximal achieved target-to-background ratio was noted.

Statistical Analysis

All data are reported as the mean ± s.d. Differences in the percentage of positive studies between antifibrin and platelet imaging were compared by chi-square analysis with continuity correction. Differences between the quantitative target-to-background ratios with antifibrin and platelet imaging were compared with the Wilcoxon signed-rank test. Differences in the visual analysis ratios between the three patient groups (abdominal aortic aneurysms, left ventricular thrombi and prosthetic arterial grafts) were compared by analysis of variance.

RESULTS

Visual Analysis in Antifibrin Studies

The mean visual analysis scores for both planar and tomographic antifibrin images are presented in Table 1. The mean visual analysis score for antifibrin images was 0.9 ± 1.1 within 5 min after injection, and it tended to decline over time. By tomographic imaging, the maximal visual score achieved was similar to that achieved with planar imaging (1.1 ± 1.0 tomographic versus 0.9 ± 1.1 planar, p = not significant).

The percentage of patients with maximal visual analysis scores above two different cutoff points for both planar and tomographic imaging was calculated. A visual score of 1 corresponded to faint uptake; a visual analysis score of 2 corresponded to moderate uptake. Among all subjects, 44% had a maximal score on planar imaging of 1.0 or more, and 61% of patients had maximal tomographic scores 1.0 or more. The percentage of patients with antifibrin studies graded as 2.0 or more was only 28% by planar techniques and 39% by tomographic imaging.

Comparison of Visual Analyses in Antifibrin and Platelet Imaging Studies

The visual analysis scores for the platelet imaging studies are presented in Table 1. There was no significant difference in the visual analysis score between the initial

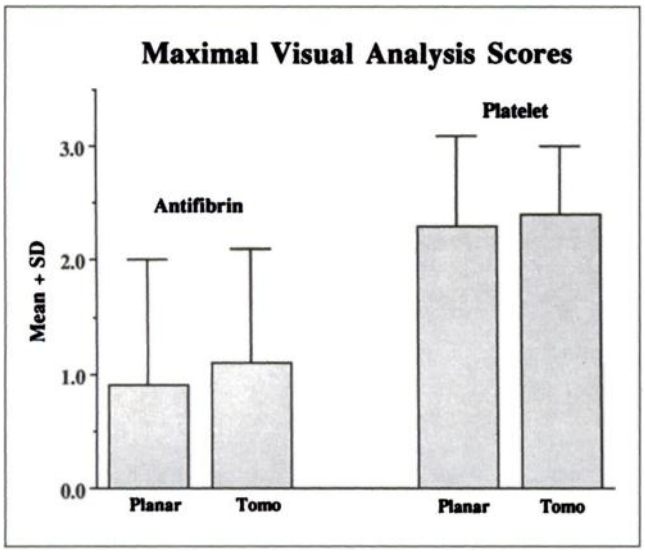

FIGURE 1. The maximal visual analysis scores for antifibrin and platelet studies are displayed. By both planar and tomographic analyses, platelet imaging was superior (both $p < 0.05$).

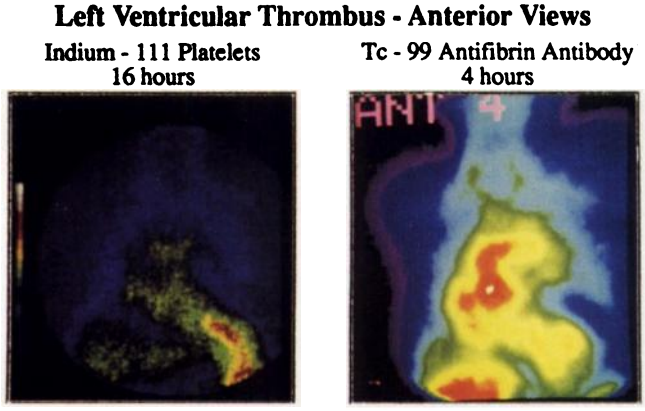

FIGURE 3. Left ventricular thrombus. This patient had a very large left ventricular thrombus, which measured approximately 9.0 cm across by two-dimensional echocardiography. Platelet imaging showed a large area of definite uptake onto an apical left ventricular thrombus, visually graded as 3. In contrast, antifibrin imaging at all times was negative (visual grade = 0). The location of greatest antifibrin activity was the overlap of the atria and outflow tract vessels, but no increased uptake was present in the area of the thrombus at the cardiac apex.

planar or tomographic platelet images obtained at 2 hr postinjection compared with either the 0- to 10-min postinjection antifibrin images or the 2-hr antifibrin images. However, the maximal visual analysis score achieved with labeled platelets, which was on the 48- to 72-hr images in 15 of the 17 subjects, was approximately twofold higher than the comparable maximal score by both planar antifibrin imaging (2.2 ± 0.8 versus 0.9 ± 1.1, $p < 0.01$) and tomographic antifibrin imaging (2.4 ± 0.6 versus 1.2 ± 1.0, $p < 0.01$, Fig. 1). Examples of antifibrin and platelet images are presented in Figures 2 to 4.

Using a cutoff point of 2.0, the percentage of positive studies was greater with labeled platelets with either planar imaging (28% antifibrin versus 88% platelet, $p < 0.01$) or tomographic imaging (39% antifibrin versus 88% platelet, $p < 0.01$, Fig. 5).

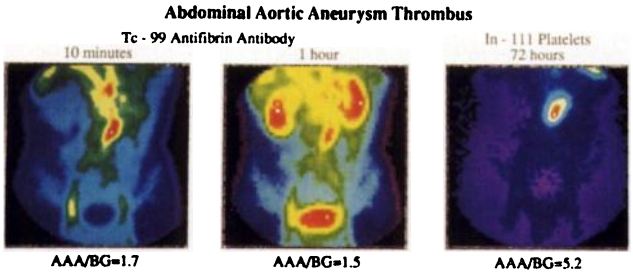

FIGURE 2. Abdominal aortic aneurysm thrombus. On the early (10 min) antifibrin image, uptake was clearly present. On the 1-hr image, antifibrin antibody uptake was still detectable, but increased activity in the kidneys and bladder had begun to obscure aortic thrombus activity. Both antifibrin images were visually graded as 1.5. Platelet imaging at 72 hr showed intense uptake, visually graded as 3.0. The tomographically determined abdominal aortic aneurysm (AAA) to background (BG) ratio for platelet imaging was 5.2 compared to only 1.5–1.7 for antifibrin imaging.

There were no significant differences in antifibrin or platelet imaging visual analysis scores between the three patient groups (left ventricular thrombi, aortic aneurysm thrombi and prosthetic grafts), but the numbers in each group were small.

Quantitative Analysis of Tomographic Images

The mean target-to-background ratios determined from tomographic images are presented in Table 2. The maximal target-to-background ratio with labeled platelets was significantly higher than with antifibrin antibody (2.5 ± 1.4 versus 1.8 ± 1.0, $p = 0.03$, Fig. 6).

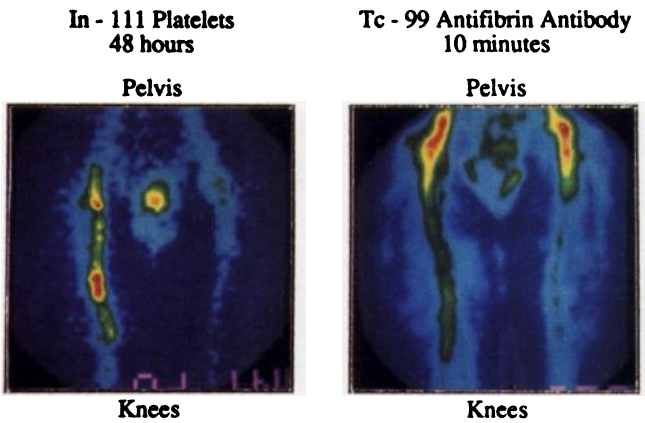

FIGURE 4. Polytetrafluoroethylene femoropopliteal graft. Intense platelet uptake was present in several sections of the graft (visual grade = 2). In contrast, antifibrin uptake in the grafted leg was more diffuse and even (visual grade = 2). The tomographic graft to blood pool ratio was 1.21 by platelet imaging and 1.17 by anti-fibrin imaging.

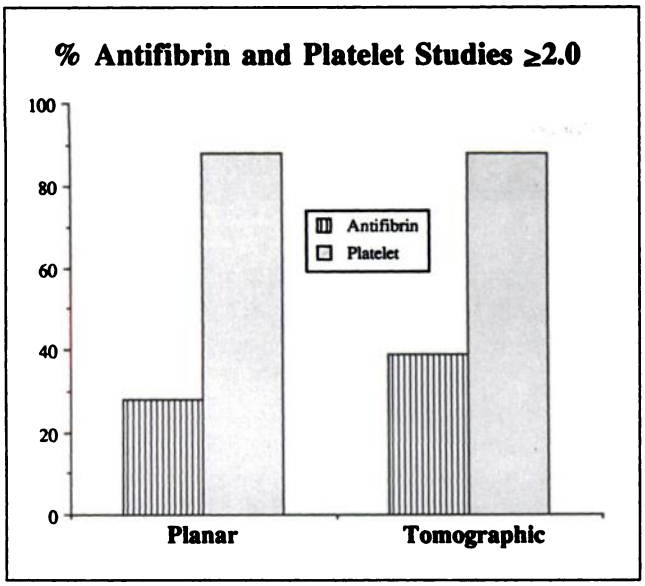

FIGURE 5. The percentage of patient studies graded visually as ≥2.0 (moderate or greater uptake) was higher for both planar and tomographic platelet imaging compared to antifibrin imaging (both $p < 0.01$).

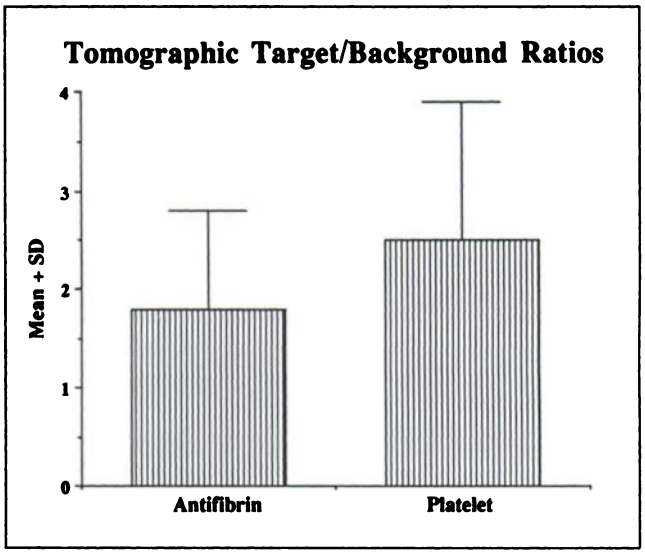

FIGURE 6. The maximal target-to-background ratio determined from tomographic images in 13 subjects was higher for labeled platelets than for labeled antifibrin antibody ($p = 0.03$).

DISCUSSION

Antifibrin antibody imaging has shown considerable promise in both animal models and in human studies of venous thrombosis. The antibody used in this study, T2G1s, recognizes an epitope that is only exposed after fibrinogen is cleaved to fibrin. Thus, the labeled antibody does not bind to circulating fibrinogen present throughout the blood pool but only to fibrin present in areas of thrombosis. The use of an antibody fragment (Fab') rather than whole antibodies has been a further potential advance because fragments are cleared more rapidly than the whole antibody, which is desirable to optimize early thrombus-to-blood ratios. Fragments may penetrate into thrombi better because of their small size, and fragments also may have a lesser likelihood of causing human antimouse antibody reactions compared with the whole antibody (*4,28*).

In animal models of venous thrombosis, thrombus-to-blood ratios of 4:1 to as high as 24:1 have been obtained with a variety of antifibrin antibodies, including the one used in this study. The images are typically positive within 2 hr after injection (*9,14–16,28,29*). Human studies with ^{111}In-labeled antifibrin antibodies have also demonstrated the ability to image deep venous thrombosis, with sensitivities ranging from 81% to 100% and specificities ranging from 84% to 100% in relatively small studies (*5,8,10–12*). Moreover, the presence of heparin did not appear to adversely affect the ability to detect thrombi (*5,12,13*).

Venous thrombi are relatively rich in fibrin; in contrast, arterial thrombi are relatively rich in platelets (*17,30*). Thus, the imaging results from venous studies may not be applicable to arterial thrombi. Nevertheless, in two animal models of thrombosis imaging that used antifibrin antibodies, the results have been encouraging. Liau et al. (*31*) detected 11 of 13 iliac artery thrombi by external imaging of an ^{131}I-labeled antifibrin antibody 3E6. With the same antibody fragment as utilized in the current study (T2G1s Fab') in an acute occlusive arterial model, the authors found a thrombus-to-blood ratio of 4.2:1 in 23 arterial thrombi (*18*). External imaging, which was done in 10 thrombi, was visually positive in all cases within 2 hr of antibody injection. Therefore, the existing data in both animals and humans suggest that antifibrin antibody imaging of arterial thrombi is feasible.

As an initial test of antifibrin imaging of chronic arterial thrombi in humans, the authors selected patients with conditions in which thrombi had been demonstrated by ultrasound (left ventricular thrombi and abdominal aortic aneurysm thrombi) or patients with prosthetic arterial grafts, which are uniformly associated with platelet-fibrin thrombus (*3*). The presence of thrombus in these patients was further confirmed by tomographic platelet imaging, which was positive in all subjects with a visual analysis score of 1

TABLE 2
Quantitative Analysis of Tomographic Images: Mean Target-to-Background Ratios

^{99m}Tc antifibrin antibody				^{111}In-platelets		
0–10 min	2 hr	24 hr	Maximum	2–24 hr	48–72 hr	Maximum
1.8 ± 1.0	1.6 ± 0.7	1.1 ± 0.1	1.8 ± 1.0	1.9 ± 0.9	2.3 ± 1.4	2.5 ± 1.4

or more. Such a score indicates mild or greater uptake. Thus, the negative results in many subjects by antifibrin imaging cannot be ascribed to the absence of thrombus or the presence of a hematologically inactive thrombus because platelet imaging findings were positive in all the study subjects.

Imaging of ^{99m}Tc-labeled monoclonal antifibrin antibody Fab' detected only 39% to 61% of thrombi, depending on the cutoff point for defining a positive study result. In nearly all instances, the antifibrin images appeared most positive at early imaging times (0 to 2 hr after isotope injection). Tomographic imaging of ^{111}In-labeled platelets, in contrast, detected 88% to 100% of the same thrombi, although platelet imaging usually required imaging to 48 to 72 hr after labeled platelet injection. Delayed imaging to 48 to 72 hr with ^{99m}Tc-labeled antifibrin antibody is not possible because of the much shorter half-life of technetium compared with that of indium (6 hr versus 68 hr) and the shorter in vivo half-life of the antibody fragment (less than 2 hr) compared with that of platelets (approximately 3 to 4 days in patients with vascular disease). The maximal visual analysis score was twice as high for platelet imaging compared with that in antifibrin imaging. The quantitative target-to-background ratios obtained by analysis of the tomographic images further confirmed the superiority of platelet imaging for thrombus detection in these types of thrombi.

The relatively low rate of positive images with antifibrin imaging may be explained by several factors. The first factor is thrombus composition and the presence of continued blood flow. In all three of the groups studied, the surface of the thrombus remained exposed to flowing blood, which allows accumulation of increasing numbers of labeled platelets but relatively less fibrin (*17*). In the authors' animal model of total arterial occlusion (*18*), the thrombus consisted largely of red blood cells and smaller, but probably equal, amounts of fibrin and platelets. A preponderance of platelets in the human arterial thrombi studied would explain, in part, these findings. Second, thrombus age likely influences the findings. Animal studies that evaluated antifibrin arterial imaging only studied recently formed thrombi. The human thrombi examined in the current study had been present for months to years and presumably had a relatively high platelet composition. Although 1- to 5-day-old venous thrombi have had acceptable thrombus-to-blood ratios in animal models (*14,15,29*) in one study of T2G1s, the thrombus-to-blood ratio decreased from 9.4 to 4.5 between 3-hr-old and 3-day-old thrombi (*14*). Thrombi greater than 5 days old have not been examined in animal models. In two human studies of deep venous thrombosis, the ability to detect older thrombi appeared significantly less than in patients with a recent onset of symptoms, probably because of the lesser exposed fibrin deposits in the older thrombi (*11,12*). Fibrin incorporated into thrombi is broken down over time, and the antibody fragment does not bind to the fibrin breakdown products. In addition, platelet imaging studies in animals and in humans have demonstrated that chronic thrombi are less likely to be positive, presumably as a result of lesser activity or lesser mass (*32–34*). Thus, the advanced age of the thrombi studied may have contributed to the negative results in some patients.

The relatively consistently positive images obtained with ^{111}In-labeled platelets were anticipated based on the authors' prior studies and those of others. Nearly all patients with vascular grafts have visually positive platelet study results, as do most patients with abdominal aortic aneurysm thrombi and approximately one-half to two-thirds of patients with left ventricular thrombi (*2,3,21,22,35*). Thus, even chronic arterial thrombi usually have demonstrable platelet uptake.

This study had several limitations. Relatively small numbers of subjects were studied, particularly in the groups with left ventricular thrombi or abdominal aortic aneurysm thrombi, and the conclusions in regard to each type of thrombus individually are limited. Nevertheless, there were no significant differences in findings between the three groups in the visual analysis scores. The authors studied only chronic arterial thrombi; thus, no conclusions can be drawn in regard to the ability of antifibrin imaging to detect acute arterial thrombi. Simultaneous imaging of labeled platelets and antifibrin antibody was not done because of the overlapping energies of ^{99m}Tc and ^{111}In; however, in these chronic thrombi, little if any change in thrombus activity would be anticipated over the 1-wk period of study. The authors previously documented that ^{111}In-labeled platelet uptake is stable over time in patients with left ventricular thrombi or prosthetic arterial grafts (*22,36*). They did not perform blood pool subtraction, which has been suggested as a possible method to improve thrombus detection by labeled platelets; however, an animal study documented that blood pool subtraction did not improve the quantitation of platelet uptake (*37*). Moreover, it has been the authors' impression that such methods can create false-positive results because of artifacts.

In summary, ^{99m}Tc-labeled T2G1s antifibrin antibody Fab' visually identified large vessel arterial thrombosis in only one-half of the patients studied, which was significantly less than ^{111}In-labeled platelet imaging results. The lower rate of image positivity in these subjects with arterial thrombosis compared with that in previously studied patients with deep venous thrombosis is probably due largely to differences in thrombus composition or activity. Positive images, when present, tended to occur early after antifibrin antibody injection, unlike the case of labeled platelets, which require several days. This is the first study of which the authors are aware that demonstrates the feasibility of imaging at least some arterial thrombi in humans with monoclonal antibody techniques. Further developments in thrombosis tracers, including monoclonal antibodies against activated platelets (*38*) or other portions of the fibrin molecule (*14*), and the development of other tracers that localize in arterial thrombi may provide improved arterial thrombus detection in humans.

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