Comparison of Early and Delayed Scintigraphy with ^{99m}Tc-Apcitide and Correlation with Contrast-Enhanced Venography in Detection of Acute Deep Vein Thrombosis

Raymond Taillefer, Eric Thérasse, Sophie Turpin, Raymond Lambert, Pierre Robillard and Gilles Soulez

Departments of Nuclear Medicine and Radiology, Centre Hospitalier de l'Université de Montréal, Montréal, Canada

Preliminary studies with ^{99m}Tc-apcitide (^{99m}Tc-P280), a synthetic peptide that binds to glycoprotein IIb/IIIa receptors expressed on activated platelets, have shown promising results in the detection of acute deep vein thrombosis (ADVT). The purpose of this study was to compare the diagnostic value of early and delayed imaging with ^{99m}Tc-apcitide in patients with suspected ADVT, using contrast-enhanced venography as the gold standard. **Methods:** Thirty-nine patients (17 women, 22 men; mean age 59 y) with signs or symptoms suggestive of ADVT (within 10 d of onset) and scheduled for contrast-enhanced venography were prospectively studied. The patients were injected with approximately 740 MBq (20 mCi) ^{99m}Tc-apcitide within 36 h of contrast-enhanced venography. Both anterior and posterior planar images (8–10 min/view) of the lower extremities using a dual-head gamma camera were obtained at 10, 60 and 120 min after the injection of ^{99m}Tc-apcitide. The three sets of images initially were interpreted randomly and separately by three experienced observers unaware of the clinical history, the site of ADVT and results of contrast-enhanced venography. All images from the three sets for a given patient were then analyzed together during a second session. Conventional contrast-enhanced venography was performed on 31 patients before ^{99m}Tc-apcitide scintigraphy and in the remaining 8 patients after ^{99m}Tc-apcitide scintigraphy. ^{99m}Tc-apcitide findings were considered positive for ADVT when a focus of increased uptake was found to correspond to the location of a deep vein. Disagreements were resolved by consensus. **Results:** Twenty-two patients had ADVT observed on contrast-enhanced venography, whereas 17 had normal findings. Six cases of ADVT were infrapopliteal. One patient did not complete the third set of images with ^{99m}Tc-apcitide. The sensitivity of ^{99m}Tc-apcitide in detecting ADVT was 63.6% (14/22), 68.2% (15/22), 76.2% (16/21) and 86.4% (19/22) for images obtained at 10, 60 and 120 min and for the three sets analyzed together, respectively. The specificity was 82.4% (14/17), 76.5% (13/17), 88.2% (15/17) and 88.2% (15/17) for images obtained at 10, 60 and 120 min and for the three sets of images together, respectively. **Conclusion:** Although the set of ^{99m}Tc-apcitide images obtained 120 min after injection showed good overall diagnostic accuracy, the combination of at least two sets of images provided the highest accuracy in detecting ADVT.

Received Nov. 30, 1998; revision accepted Apr. 9, 1999.

For correspondence or reprints contact: Raymond Taillefer, MD, Department of Nuclear Medicine, Centre Hospitalier de l'Université de Montréal, Pavillon Hotel-Dieu, 3840 St-Urbain, Montréal H2W 1T8, Canada.

Key Words: acute deep venous thrombosis; glycoprotein IIb/IIIa receptor imaging; venography; ^{99m}Tc-apcitide; ^{99m}Tc-P280

J Nucl Med 1999; 40:2029–2035

Acute deep vein thrombosis (ADVT) and its more serious complication, pulmonary embolism, are common clinical conditions associated with significant morbidity and mortality. Because of the clear link between ADVT and pulmonary embolism, and also because of other sequelae such as postphlebitic syndrome, prompt diagnosis and appropriate treatment of this condition are important (*1–3*). Unfortunately, ADVT may be clinically silent: approximately 70% of patients presenting with confirmed pulmonary embolism have asymptomatic venous thrombosis (*4*). Conversely, ADVT may be associated with nonspecific signs and symptoms: approximately only 30%–40% of patients presenting with signs and symptoms of the disease can be confirmed to have ADVT (*5–6*). Although contrast-enhanced venography is considered the gold standard for diagnosis of ADVT (*7*), this test is not used routinely because it is lengthy and expensive, causes patient discomfort and evokes safety concerns. In addition, contrast-enhanced venography has some contraindications, produces some images that are uninterpretable and cannot reliably differentiate between recurrent ADVT and an old organized thrombus with postphlebitic syndrome (*8*).

The most common method for diagnosing ADVT is real-time sonography with compression, often in combination with Doppler sonography (*9*). This technique is considered accurate, sensitive and specific in patients with signs and symptoms of ADVT above the knee and with no history of thrombosis in the affected extremity (*10–12*). However, this technique also has limitations, including poor accuracy below the knee and low sensitivity in asymptomatic, high-risk patients (*13*). Therefore, an objective and noninvasive diagnostic procedure allowing the detection and localization of ADVT would be useful.

Recently, ^{99m}Tc-apcitide (also known as ^{99m}Tc-P280), a

synthetic glycoprotein (GP) IIb/IIIa receptor–binding peptide, has been investigated in humans for detection of ADVT (*14–16*). ^{99m}Tc-apcitide is capable of binding avidly and specifically to the GP IIb/IIIa receptors expressed on activated platelets involved in ADVT. The purpose of this study was to compare the diagnostic accuracy of early and delayed ^{99m}Tc-apcitide scintigraphy in patients with suspected ADVT of the lower extremities using contrast-enhanced venography as the gold standard.

MATERIAL AND METHODS

Study Design and Patient Population

This study was a prospective, single-center, single-dose, within-patient comparison of ^{99m}Tc-apcitide scintigraphy and contrast-enhanced venography in detecting ADVT of the lower extremities and was approved by the institutional review board. ^{99m}Tc-apcitide scintigraphy was conducted either before or after venography, and the two procedures were performed within a 36-h period. Patients were excluded if their symptoms began more than 10 d previously or if they were less than 18 y old, pregnant or lactating, of childbearing potential (unless the possibility of pregnancy had been ruled out by either β-human chorionic gonadotropin testing, an age greater than 60 y, a postmenopausal status for at least 1 y or surgical sterilization) or had received an investigational drug within 30 d before enrollment. Thirty-nine patients (17 women, 22 men; age range 25–84 y, mean age [±SD] 59.4 y ± 17.1 y) were enrolled over 8 mo, and all gave written informed consent. Their weight range was 46–102 kg (mean weight 76.6 ± 13.5 kg). Seven patients (17.9%) had a history of ADVT, and 5 patients (12.8%) had a history of pulmonary embolism.

^{99m}Tc-Apcitide Preparation and Administration

Nonradioactive kits for the preparation of ^{99m}Tc-apcitide (AcuTect) were supplied by Diatide Inc. (Londonderry, NH). Each 10-mL vial contained a sterile, nonpyrogenic, lyophilized formulation of 100 μg P280 peptide under nitrogen. The active binding region of apcitide or P280 is an analog of the arginyl-glycyl-aspartic acid sequence present in fibrinogen. The kit was reconstituted with sterile, nonpyrogenic, oxidant-free ^{99m}Tc-sodium pertechnetate obtained from commercial generators. The pH of the reconstituted product was approximately 6.5.

Before reconstitution for administration, each kit was allowed to warm to room temperature (15°C–30°C). With aseptic technique and adequate shielding, each kit was reconstituted with 1 mL ^{99m}Tc-sodium pertechnetate containing approximately 1110 MBq (30 mCi) ^{99m}Tc. The kits were then swirled to dissolve the contents and heated upright at 100°C for 15 min in a shielded boiling water bath. Before administration to the patient, the vials were allowed to cool to room temperature and the reconstituted vial contents were inspected for particulate matter or any discoloration and assayed for radiochemical purity of the ^{99m}Tc-apcitide. The reconstituted vials were stored at room temperature and administered within 6 h after radiolabeling.

^{99m}Tc-Apcitide Radiochemical Purity Determination

The reconstituted contents of the vials containing ^{99m}Tc-apcitide were tested for radiolabeling efficiency and the presence of other radiolabeled species by instant thin-layer chromatography (ITLC). Three different developing solvents—saturated sodium chloride solution (SAS), distilled water and methyl ethyl ketone (MEK)—were used to assess the percentage of colloids, pertechnetate, glucoheptonate and ^{99m}Tc-apcitide.

Three ITLC-SG strips (Pall Gelman Sciences, Fayetteville, NC) were used. One drop of approximately 10 μL ^{99m}Tc-apcitide was placed at the origin of each strip using a 21-gauge needle. Before the spots were dry, the first ITLC-SG strip was placed in the solvent chamber containing distilled water, the second strip was placed in the chamber containing SAS solution and the third strip was placed in the MEK developing solvent. The strips were placed upright in the respective developing solvent such that the spots were above the solvent line and the top of the strips leaned against the side of the developing chamber. Once the solvent front had moved to the top of the strips, the strips were removed from the developing chamber and allowed to dry. The strip from the distilled water was then cut at 0.25 R_f (25% of the distance from the origin to the solvent front), and the strips from the SAS solution and MEK solvent were cut at 0.75 R_f. Each strip was counted in an adequate dose calibrator. The count from the strip in water was the percentage of ^{99m}Tc nonmobile impurities or colloids (A), the count from the strip in SAS solution was the percentage of ^{99m}Tc-pertechnetate and ^{99m}Tc-glucoheptonate (B) and the count from the strip in MEK solvent was the percentage of ^{99m}Tc-pertechnetate (C). The percentage of ^{99m}Tc-glucoheptonate was found by subtracting C from B, and the percentage of ^{99m}Tc-apcitide was found by subtracting the sum of A and B from 100. The ^{99m}Tc-apcitide preparation was administered only when the radiochemical purity was more than 90%.

^{99m}Tc-Apcitide Scintigraphy

Satisfactory hydration was maintained at all times to reduce radiation exposure to nontargeted organs. Whenever possible, patients were asked to drink at least one glass of water before tracer administration and to void frequently after the injection. ^{99m}Tc-apcitide was injected intravenously (butterfly or running intravenous line). Each patient received a dose of approximately 740 MBq (20 mCi) and 70–100 μg of peptide.

^{99m}Tc-apcitide scintigraphy was performed using a large-field-of-view dual-head gamma camera (Isocam II; Park Meditech, Lachine, Canada) fitted with a low-energy, parallel-hole, high-resolution collimator. The energy photopeak was set at 140 keV ± 10%. Clothing was removed before imaging. The patients were positioned supine on the imaging table, and the lower extremities were symmetrically and comfortably positioned without any compression of the limbs to avoid motion during imaging. Planar studies were acquired in a 256 × 256 matrix. Three sets of planar images were obtained approximately 10, 60 and 120 min after the injection of tracer. Images of the calves, knees, thighs and pelvis were obtained in both anterior and posterior views (simultaneous anterior and posterior acquisition). The data acquisition time was 8–10 min per view, according to each patient's body habitus.

Contrast-Enhanced Venography

A vein of the dorsum of the foot was punctured with a 22-gauge Angiocath (Becton-Dickenson, Cockeysville, MD), and the needle tip was directed toward the toes whenever possible. Tourniquets were not routinely used. When the patient could tolerate no more than a shallow upright position, venography was performed on a long film changer and 60 mL of full strength iso-osmolar contrast

medium was injected with a power injector at a rate of 3 mL/sec. When the patient could tolerate a semiupright position, venography was performed on a tilt table, with 35.6 × 43.2 cm (14 × 17 in.) films and hand injection of 60 mL 60% contrast medium or 100 mL 43% contrast medium. A box was placed under the other extremity so that the leg being examined bore no weight. With both techniques, images were obtained with the leg in both internal and external rotation from the foot to the iliac vein.

Data Analysis

^{99m}Tc-Apcitide. ^{99m}Tc-apcitide images were displayed digitally for the masked reading and compiled randomly. Three observers experienced in nuclear medicine were asked to analyze the ^{99m}Tc-apcitide images without knowing the patients' age, sex, clinical history or contrast-enhanced venography results. During a first session, the observers separately and randomly analyzed each of the three sets of images of each patient. During a second session a few days later, the observers analyzed the three sets of images together to obtain, by consensus, a final diagnosis for each patient using all data available. Nine anatomic regions—right and left calves, right and left knees, right and left thighs, right and left iliac regions and inferior vena cava—were analyzed and scored for the presence of ADVT using four categories: positive, negative, indeterminate or not done. For positive findings, the observers were asked to qualify the extent of the vessels involved.

Each ^{99m}Tc-apcitide study was evaluated in the same manner from a computer screen with appropriate contrast adjustment. For the initial session, ADVT was considered to be present if asymmetrically increased deep venous uptake of ^{99m}Tc-apcitide was seen on both anterior and posterior images. For the second session, two criteria were added: evidence of the asymmetric increase on two or more imaging sets and persistence or enhancement of the asymmetric increase on delayed images (Figs. 1–4). These criteria were added because of information obtained from the different sets of images over time. The final diagnosis was reached by consensus.

Contrast-Enhanced Venography. As for ^{99m}Tc-apcitide images, contrast-enhanced venograms were compiled randomly and interpreted independently by experienced observers who were unaware of the patients' age, clinical history or ^{99m}Tc-apcitide findings. The final diagnosis was based on the consensus of either two or three observers. In cases of disagreement, the observers reinterpreted the venogram and reached a consensus.

Two regions of each leg were assessed: proximal (iliac, common femoral, superficial femoral, deep femoral and popliteal veins) and distal (calf and peroneal, posterior tibial and anterior tibial veins up to and including the trifurcation of the calf veins). Findings were considered positive for ADVT when an intraluminal filling defect was present. Such a defect was defined as an area of reduced or absent filling at least partially surrounded by contrast medium and constant on more than one image. The defect could also consist of a lack of filling in a vessel that was seen to be filling more proximally, with the cutoff point having the configuration of a thrombus. Negative findings were defined as visualization of all deep veins with no evidence of an intraluminal filling defect.

Statistical Analysis

The relationship between the findings of ^{99m}Tc-apcitide scintigraphy and contrast-enhanced venography was given in terms of sensitivity, specificity and accuracy (true-positives plus true-negatives divided by the sum of all cases). To compare the diagnostic performance of ^{99m}Tc-apcitide scintigraphy at various

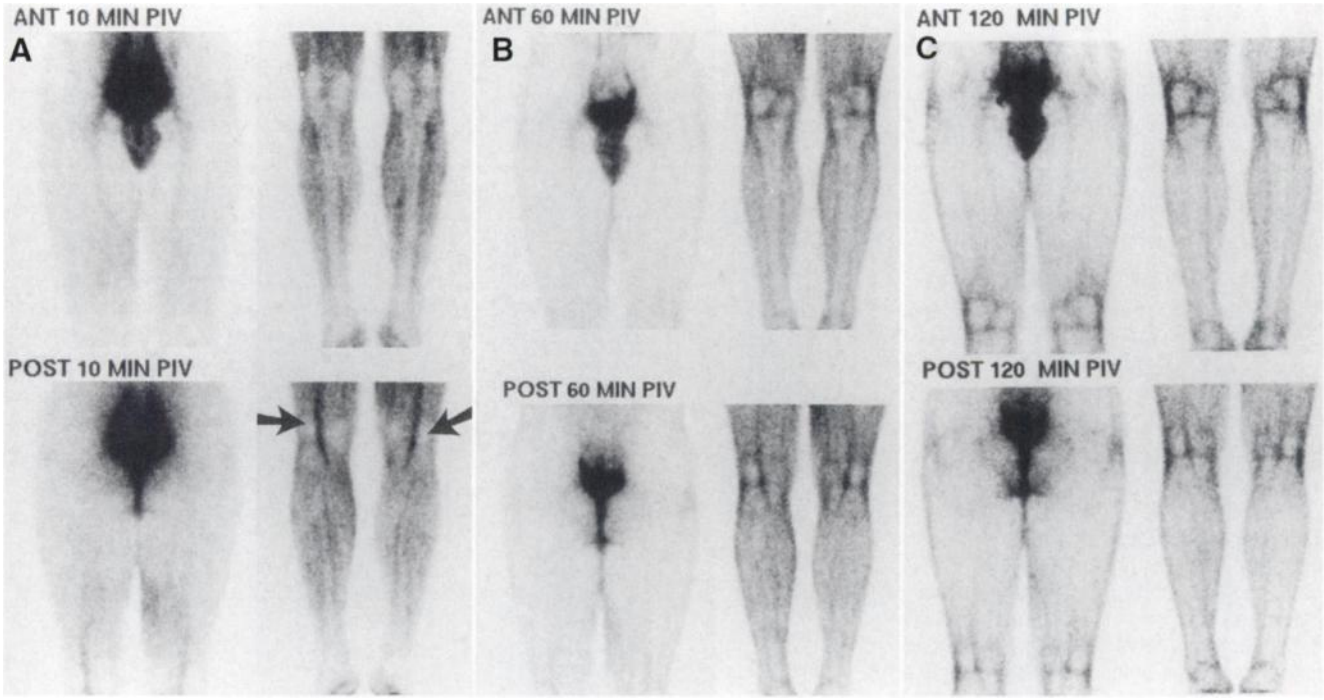

FIGURE 1. Scintigraphic images obtained 10 (A), 60 (B) and 120 min (C) after injection of 740 MBq (20 mCi) ^{99m}Tc-apcitide show normal findings. Anterior views (top row) and posterior views (bottom row) of pelvis, thighs, knees and calves show that symmetric blood-pool activity (arrows) seen on earliest images decreases over time. No persistent or increased vascular uptake is seen on 120-min images. ANT = anterior view; PIV = after tracer injection; POST = posterior view.

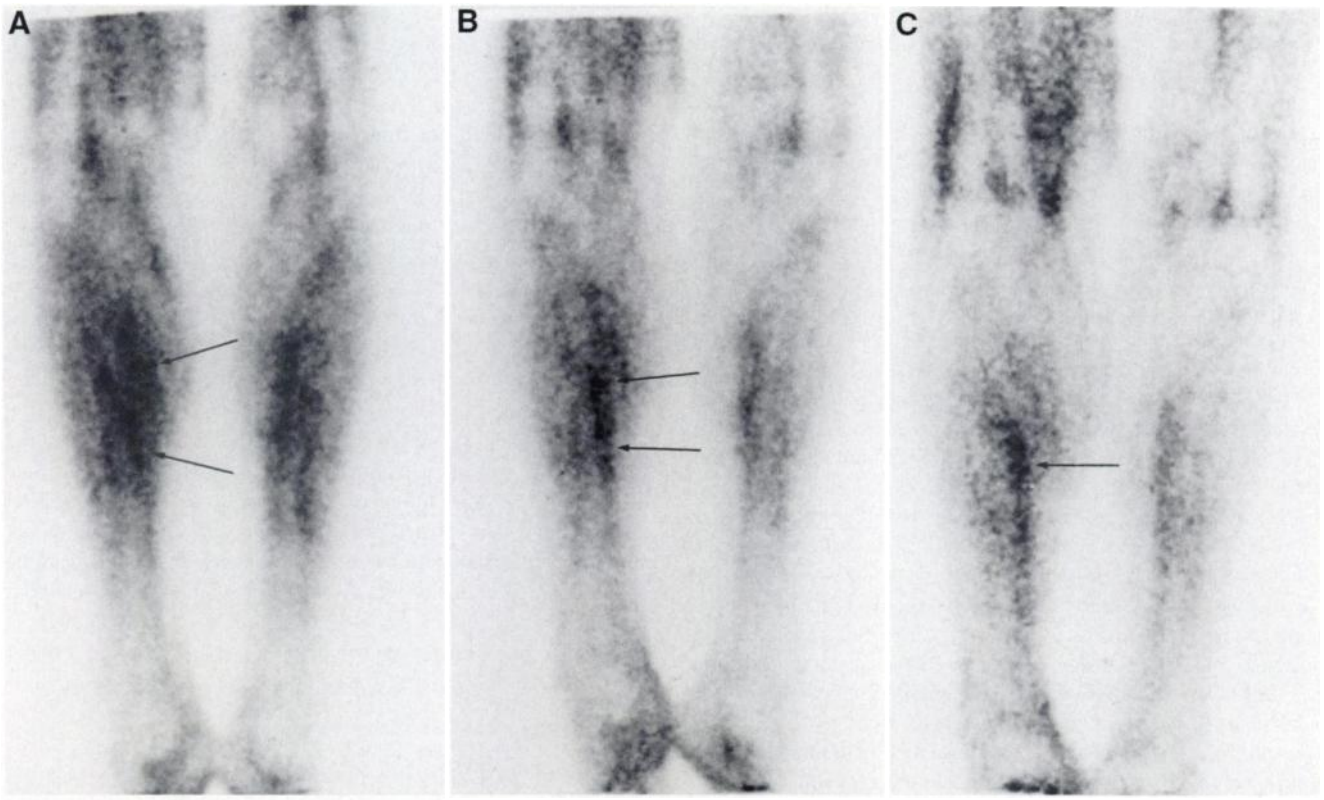

FIGURE 2. Scintigraphic images (posterior knee and calf views) obtained 10 (A), 60 (B) and 120 min (C) after injection of ^{99m}Tc-apcitide in patient with recent left knee surgery and acute thrombosis of posterior tibial and peroneal deep veins of left calf. Slight asymmetry of vascular uptake seen in left calf (arrows) on earliest image becomes more obvious on later images.

intervals, odds ratios for sensitivity and specificity (determined as sensitivity divided by 1 minus specificity) were calculated.

RESULTS

The distribution of days from the onset of symptoms to the time of the first imaging procedure (either contrast-enhanced venography or ^{99m}Tc-apcitide scintigraphy) was as follows: for 4 patients (10.4%), less than 1 d; for 16 patients (41.0%), 3 d or less; for 34 patients (87.2%), 5 d or less; and for 38 patients (97.4%), 7 d or less. The mean interval between onset of symptoms and first diagnostic study was 3.7 d. Clinical signs and symptoms were divided into five

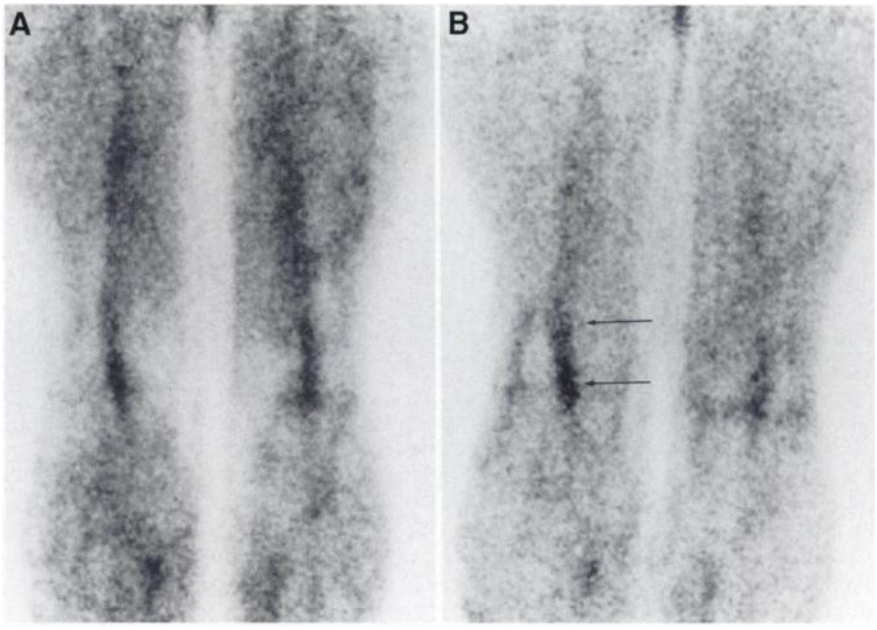

FIGURE 3. Scintigraphic images (posterior knee view) of patient with ADVT of left popliteal and distal superficial femoral veins. (A) Image obtained 10 min after injection of ^{99m}Tc-apcitide shows normal, symmetric uptake in popliteal veins. (B) Image obtained 120 min after injection of ^{99m}Tc-apcitide shows clearly abnormal uptake in left popliteal vein and ipsilateral distal superficial femoral vein (arrows), corresponding to site of ADVT.

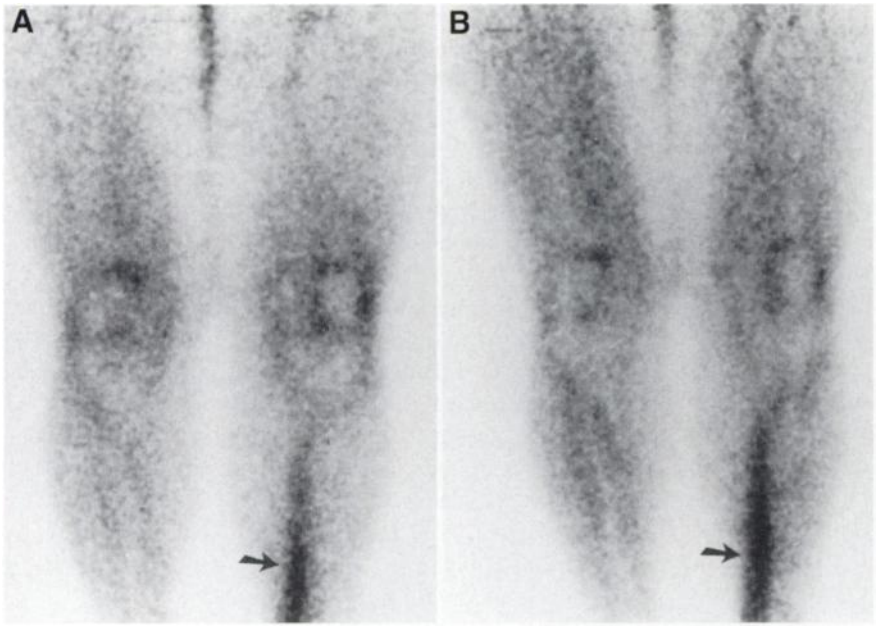

FIGURE 4. Scintigraphic images (posterior knee view) of patient with ADVT of posterior tibial and peroneal veins of right calf. Abnormally increased ^{99m}Tc-apcitide uptake (arrows) seen on image obtained 60 min after injection (A) is seen more clearly on image obtained 120 min after injection (B).

categories: pain, tenderness or Homans' sign; swelling; increased warmth; erythema; and a palpable cord. The dominant signs and symptoms were pain, tenderness or Homans' sign (36 patients [92.3%]) and swelling (33 patients [84.6%]). Increased warmth and erythema were observed in 24 patients (61.5%) and 11 patients (28.2%), respectively. A palpable cord was observed in only 1 patient. Abnormalities were most prevalent in the calf, with progressively fewer abnormalities observed in regions closer to the abdomen.

Thirty-one patients (79.5%) received at least one antiplatelet drug or anticoagulant: 30 patients (76.9%) took medications from the heparin group, and 11 patients (28.2%) took vitamin K antagonists including warfarin sodium. Seven patients (17.9%) received no thrombus medication. In patients taking heparin, the mean interval between the first administration of the drug and the first study was 2.8 ± 2.0 d.

^{99m}Tc-Apcitide Scintigraphy Data

The mean radiolabeling efficiency of ^{99m}Tc-apcitide was 96.2% ± 1.7% (range 91.4%–98.7%). The mean injected activity was 791.8 ± 33.3 MBq (21.4 ± 0.9 mCi) (range 728.9–865.8 MBq [19.7–23.4 mCi]) with an injected peptide dose of 90.0 μg. The injected ^{99m}Tc-apcitide volume was 0.7–1.0 mL.

Contrast-Enhanced Venography Data

Contrast-enhanced venography showed ADVT localized to the calf in 6 patients (27.3%), extending to the knee in 8 patients (36.4%) and extending to the thigh in 6 other patients (27.3%). ADVT was localized to the knee in 1 patient and to the thigh in another patient.

Interval Between ^{99m}Tc-Apcitide Scintigraphy and Venography

Thirty-six patients (92.3%) underwent ^{99m}Tc-apcitide scintigraphy and contrast-enhanced venography within a 36-h interval: 16 patients (41.0%) from 0 to 12 h and 34 patients (87.2%) from 0 to 24 h. The mean interval between ^{99m}Tc-apcitide scintigraphy and contrast-enhanced venography was 16.0 ± 13.6 h (range 1–40 h). Contrast-enhanced venography was performed before ^{99m}Tc-apcitide scintigraphy in 31 patients.

Comparison of ^{99m}Tc-Apcitide Scintigraphy and Venography

Table 1 summarizes the sensitivity, specificity and accuracy of ^{99m}Tc-apcitide scintigraphy performed at three

TABLE 1
Indices for Detection of Acute Deep Vein Thrombosis with ^{99m}Tc-Apcitide Scintigraphy

Time after tracer injection (min)	Sensitivity	Specificity	Accuracy	Odds ratio
10	63.6% (14/22)	82.4% (14/17)	71.8% (28/39)	3.6 (0.8–16.5)
60	68.2% (15/22)	76.5% (13/17)	71.8% (28/39)	2.9 (0.7–12.1)
120	76.2% (16/21)	88.2% (15/17)	81.6% (31/38)	6.5 (1.1–38.6)
Together*	86.4% (19/22)	88.2% (15/17)	87.2% (34/39)	7.3 (1.1–49.7)

*Three sets of images analyzed together.

different time points in the detection of ADVT using contrast-enhanced venography as the gold standard. A comparison of imaging performed at 10, 60 and 120 min after radiotracer injection shows that the 120-min images had the highest sensitivity, specificity and overall accuracy (76.2%, 88.2% and 81.6%, respectively). These numbers were higher when the three sets of images were read together: 86.4% sensitivity (19/22), 88.2% specificity (15/17) and 87.2% accuracy (34/39). The sensitivity of ^{99m}Tc-apcitide scintigraphy for detection of ADVT was 83.3% (5/6) for thrombi localized to the calf, 100% (8/8) for thrombi involving both the calf and the knee and 83.3% (5/6) for thrombi extending from the calf to the thigh. Scintigraphy revealed the thrombus in the patient in which it was localized to the thigh but did not reveal the thrombus in the patient in which it was localized to the knee.

Table 2 summarizes the ^{99m}Tc-apcitide studies with false-negative findings in patients with proven ADVT. In the analysis of the three sets of images together, the three studies with false-negative findings occurred in patients with calf and knee thrombosis and in patients with a thrombus more than 3 d old. Although the set of images obtained at 120 min showed the highest sensitivity, the combination of at least another set of images, either at 10 or 60 min, improved the overall accuracy. Of the patients with false-negative findings at 120 min, 1 (patient 5) had positive findings at 10 min only and 1 (patient 6) had positive findings at both 10 and 60 min.

DISCUSSION

Detection and localization of ADVT is critical for determining clinical treatment. Diagnosis of ADVT is based on clinical signs and symptoms in conjunction with anatomically based diagnostic imaging studies such as Doppler sonography and contrast-enhanced venography. Both procedures provide anatomic information on vascular obstruction, but neither is specific for the detection and localization of ADVT—false-positive findings are possible.

TABLE 2
^{99m}Tc-Apcitide Studies with False-Negative Findings in Patients with Proven Acute Deep Vein Thrombosis

Patient no.	Time after tracer injection (min)			Together*	Thrombus location	Thrombus age† (d)
	10	60	120			
1	−	−	+	+	Calf	3
2	−	−	−	−	Calf	3
3	−	+	+	+	Calf	5
4	−	−	−	−	Knee	4
5	+	−	−	+	Calf + knee	4
6	+	+	−	+	Calf	5
7	−	−	−	−	Calf + knee	9
8	−	+	+	+	Calf	6
9	−	−	+	+	Calf + knee	4
10	−	−	+	+	Calf + knee	4
Total	8	7	5	3		

*Three sets of images analyzed together.
†Days from symptom onset to first diagnostic study.
Acute deep vein thrombosis was proven by contrast-enhanced venography.
+ = findings positive for acute deep vein thrombosis; − = findings negative for acute deep vein thrombosis.

Unlike chronic venous thrombi, which have become organized, acute venous thrombi are involved in a dynamic process of continued thrombosis and thrombolysis in which platelets are being incorporated into, and exposed on the surface of, the thrombus. For this reason, radiolabeled platelets have been investigated for imaging thrombi in vivo (*17–20*). However, although radiolabeled platelets are incorporated into acute thrombi, the long blood-pool clearance time of platelets that are not bound to thrombi results in poor target-to-background ratios until long after administration of the radiolabeled platelets. A radionuclide imaging agent that binds to platelets being incorporated into an active thrombus but that, if not bound, clears rapidly from the blood would have great potential for ADVT detection.

Platelets express the cell surface GP IIb/IIIa receptors. Only when a platelet is activated do its GP IIb/IIIa receptors undergo the conformational change that makes them available for binding fibrinogen. Cross-linkage of activated platelets by the bivalent fibrinogen molecule to form a hemostatic plug is the primary event of thrombosis. An imaging agent, ideally radiolabeled with ^{99m}Tc and capable of binding avidly and specifically to the GP IIb/IIIa receptor on activated platelets, would provide images of active or acute venous thrombosis. The tripeptide sequence arginyl-glycyl-aspartic acid participates in the binding of fibrinogen to the GP IIb/IIIa receptor (21, 22). Small synthetic peptides or peptidomimetics that contain this sequence or a structure that mimics this sequence bind to the GP IIb/IIIa receptor and, at sufficiently high concentrations, inhibit platelet aggregation. The active binding region of apcitide is an analog of the arginyl-glycyl-aspartic acid sequence present in fibrinogen. Studies have shown that ^{99m}Tc-apcitide binds to thrombi by attaching to GP IIb/IIIa receptors on activated platelets (*23,24*).

The results of this study confirm that ^{99m}Tc-apcitide scintigraphy is highly accurate in detecting ADVT, even in patients receiving heparin therapy. This study also shows that the accuracy of ^{99m}Tc-apcitide scintigraphy can be increased when at least two sets of images are obtained at different times after tracer injection. Having two sets allows use of a larger number of interpretation criteria for the presence of ADVT: the asymmetry of increased ^{99m}Tc-apcitide uptake in the deep veins should be seen during two or more imaging sessions, and early asymmetric radiotracer uptake should persist or enhance on delayed images. Therefore, the use of at least two sets of ^{99m}Tc-apcitide images allows not only spatial criteria on the location of increased uptake but also temporal criteria on changes in uptake at different times. Ideally, the first set of images should be obtained early after ^{99m}Tc-apcitide administration. These early images serve as a reference for the location of deep

veins in the lower extremities. Comparison of delayed images with early images allows better evaluation of the evolution of the increased deep venous uptake and, therefore, better diagnosis of ADVT. In this study, although the ^{99m}Tc-apcitide images obtained at 120 min were the set with the best diagnostic accuracy, analysis of the three sets together resulted in even better accuracy. No statistically significant difference was seen between the results of analyzing the 10- and 60-min, 10- and 120-min and 60- and 120-min images in combination. Therefore, use of at least two sets of images—an initial set obtained early after the injection and a second set obtained 60–120 min later—produces the highest accuracy for ^{99m}Tc-apcitide scintigraphy in detection of ADVT.

CONCLUSION

^{99m}Tc-apcitide scintigraphy is highly accurate in the noninvasive detection of ADVT, especially thrombosis involving the deep veins of the calf. Although images obtained 2 h after tracer injection show the greatest overall accuracy in comparison with earlier images, combined analysis of image sets from at least two time points provides greater accuracy in the detection of ADVT.

REFERENCES

1. Anderson FA, Wheeler HB, Goldberg RT, et al. A population-based perspective of the hospital incidence and case facility rates of deep vein thrombosis and pulmonary embolism. *Ann Intern Med.* 1991;151:933–938.
2. Freiman DG. The structure of thrombi. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice.* Philadelphia, PA: JB Lippincott; 1987:1123–1135.
3. Salzman EW, Hirsh J. The epidemiology, pathogenesis, and natural history of venous thrombosis. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice.* 3rd ed. Philadelphia, PA: JB Lippincott; 1993:1275–1296.
4. Hull RD, Hirsh J, Carter CJ, et al. Pulmonary angiography, ventilation lung scanning, and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. *Ann Intern Med.* 1983;98:891–899.
5. Hull RD, Carter CJ, Jay RM, et al. The diagnosis of acute recurrent deep vein thrombosis: a diagnostic challenge. *Circulation.* 1983;67:901–906.
6. Lensing AWA, Prandoni P. Distribution of venous thrombi in symptomatic patients. *Thromb Haemost.* 1991;65:1730–1736.
7. Lensing AWA, Hirsh J, Buller HR. Diagnosis of venous thrombosis. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice.* Philadelphia, PA: JB Lippincott; 1987:1297–1302.
8. Hull RD, Hirsh J, Carter C, et al. Diagnostic efficacy of impedance plethysmography for clinically suspected DVT: a randomized trial. *Ann Intern Med.*1985;102: 21–28.
9. Cronan JJ. Venous thromboembolic disease: the role of ultrasound. *Radiology.* 1993;186:619–630.
10. Lensing AWA, Prandoni P, Brandjes D, et al. Detection of deep venous thrombosis by real-time B-mode ultrasonography. *N Engl J Med.* 1989;320:342–345.
11. Cronan JJ, Leen V. Recurrent deep venous thrombosis: limitations of ultrasound. *Radiology.* 1989;170:739–742
12. Rose SC, Zwiebel WJ, Nelson BD, et al. Symptomatic lower extremity deep venous thrombosis: accuracy, limitations, and role of color duplex flow imaging in diagnosis. *Radiology.* 1990;175:639–644.
13. Davidson BL, Elliott CG, Lensing AWA. Low accuracy of color Doppler ultrasound in the detection of proximal leg vein thrombosis in asymptomatic high-risk patients. *Ann Intern Med.* 1992;117:735–738.
14. Weiland FL, Carretta RF, Holder LE, et al. Tc-99m P280 detection of deep venous thrombosis (DVT) in patients with a prior history of DVT [abstract]. *J Nucl Med.* 1997;38(suppl):98P.
15. Taillefer R, Abdel-Nabi HH, Buxton-Thomas M, et al. Multicenter clinical trial comparing Tc-99m P280 to contrast venography for detection and localization of acute deep venous thrombosis [abstract]. *J Nucl Med.* 1997;38(suppl):98P.
16. Weiland FL, Carretta RF, Holder FE, et al. Safety and efficacy of Tc-99m P280 for the detection and localization of acute deep venous thrombosis [abstract]. *J Nucl Med.* 1997;38(suppl):98P.
17. Clark-Pearson DL, Coleman RE, Siegal R, et al. ^{111}In platelet imaging for the detection of deep venous thrombosis and pulmonary embolism in patients without symptoms after surgery. *Surgery.* 1985;98:98–104.
18. Ezekowitz MD, Pope CF, Sostman HD, et al. ^{111}In platelet scintigraphy in the diagnosis of acute venous thrombosis. *Circulation.* 1986;73:668–674.
19. Seabold JE, Conrad GR, Kimball DA, et al. Pitfalls in establishing the diagnosis of deep venous thrombosis by ^{111}In platelet scintigraphy. *J Nucl Med.* 1988;29:1169–1180.
20. Thakur ML, Welch MJ, Joyst JH, Coleman RE. ^{111}In labeled platelets: studies in preparation and evaluation of in vitro and in vivo functions. *Thromb Res.* 1976;9:345–357.
21. Marguerie GA, Plow EF, Edgington TS. Human platelets possess an inducible and saturable receptor specific for fibrinogen. *J Biol Chem.* 1979;254:5357–5363.
22. Plow EF, Piershbacher MD, Ruoslahti E, et al. The effect of Arg-Gly-Asp-containing peptides on fibrinogen and von Willebrand factor binding to platelets. *Proc Natl Acad Sci USA.* 1985;82:8057–8061.
23. Muto P, Lastoria S, Varrella P, et al. Detection of deep venous thrombosis with ^{99m}Tc-labeled synthetic peptide P280. *J Nucl Med.* 1995;36:1384–1391.
24. Lister-James J, Knight LC, Maurer AH, et al. Thrombus imaging with a technetium-99m-labeled, activated platelet receptor-binding peptide. *J Nucl Med.* 1996;37:775–781.