Pitfalls in Establishing the Diagnosis of Deep Venous Thrombophlebitis by Indium-111 Platelet Scintigraphy

James E. Seabold, Gary R. Conrad, Debra A. Kimball, James A. Ponto, and John A. Bricker

Division of Nuclear Medicine, Department of Radiology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa

Forty-seven ^{111}In-platelet scintigraphs (In-PS) were analyzed retrospectively to identify sources of diagnostic error and to optimize the diagnostic criteria for active deep venous thrombophlebitis (DVT). The results of In-PS were compared with contrast venography, additional diagnostic studies, and clinical outcome. Three patterns of platelet localization emerged as the best predictors of active DVT: (a) focal or (b) linear 4-hr localization, or (c) an asymmetric blood-pool pattern on 4-hr imaging that evolved into a focal or linear pattern by 16 to 24 hr. All false-positive studies had abnormal patterns confined to the inguinal region at 24 hr. All patients with false-negative studies had received heparin between 4 and 24 hr. The potential pitfalls encountered in the evaluation of the iliac, femoral, and popliteal veins are reviewed and the importance of delayed imaging in selected cases is emphasized.

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Indium-111 platelet scintigraphy (In-PS) is a useful alternative to contrast venography for demonstrating acute deep venous thrombophlebitis (DVT) (*1–4*). In-PS is particularly useful for evaluating patients who have relative contraindications for contrast venography, such as known allergy to contrast media, cardiac or renal impairment, marked obesity, edema, or severe illness precluding standard venography. In-PS is also valuable for monitoring high-risk, postoperative patients (*1,3*) and appears to be useful for evaluating patients with chronic venous disease who develop signs and symptoms of acute thrombophlebitis (*4*). The diagnosis of acute DVT can be established as early as 4 hr after i.v. injection of autologous-labeled platelets (*3,4*).

This retrospective analysis was performed in an attempt to optimize the scintigraphic criteria necessary to establish the diagnosis of active DVT and to identify any factors that might influence the results of In-PS. We were particularly interested in evaluating any potential influence of heparin and warfarin therapy in our patient population, since the effect of anticoagulants on the diagnostic efficacy of In-PS has not been firmly established (*1–6*).

MATERIALS AND METHODS

Patient Selection

During a 2-yr period, a total of 60 patients with suspected acute thrombophlebitis underwent In-PS. All of these patients had noted onset of pain, swelling, and erythema in an upper and/or lower extremity for 1 wk or less in duration. Sufficient clinical and diagnostic documentation was available to evaluate the results of In-PS in 47 of these 60 cases. Informed consent was obtained from each patient.

Contrast venography was available to document the presence or absence of DVT in 38 of the 47 cases. Contrast venography was performed within 24 hr of In-PS in every case. Contrast-enhanced computed tomography (CT) of the abdomen-pelvis had been performed and was also utilized in six of these 38 cases. When contrast venography revealed evidence of deep venous thrombosis, the referring physicians were notified and heparin therapy was initiated.

In the remaining nine cases, confirmation of In-PS was obtained from the results of other diagnostic studies or procedures. These included Doppler sonography in five cases, tissue biopsy and culture in three cases, CT in three cases, and magnetic resonance imaging (MRI) in two cases.

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For reprints contact: James E. Seabold, MD, Div. of Nuclear Medicine, Dept. of Radiology, The University of Iowa Hospitals and Clinics, Iowa City, IA 52242.

Thirteen of the 60 patients who underwent In-PS did not have sufficient documentation to verify the presence or absence of venous thrombophlebitis and were not included in the final tabulation. This group included three patients who had nondiagnostic contrast venograms due to incomplete filling of the deep venous system in the symptomatic extremities. There were four patients with prior DVT who had Doppler sonography as the only supporting diagnostic test for active DVT. Among the six remaining cases, relative contraindications had precluded contrast venography and/or the results of In-PS had supported the clinical impression and no further diagnostic studies were performed.

Preparation of ^{111}In Platelets

Autologous platelets were labeled with [^{111}In]oxine by a technique modified from Hawker et al. (*7*). The platelets were separated from 50 ml of acid-citrate-dextrose-anticoagulated whole blood by a two-step centrifugation process. The platelet pellet was resuspended in modified Tyrode's solution (*8*) and incubated with 0.5–0.9 mCi (18.5–33.3 MBq) of [^{111}In]oxine (Amersham Corporation, Arlington Heights, IL) for 5 min. For each preparation 1×10^9 platelets were labeled yielding an efficiency of 30–80% (mean 63%). Each patient received between 0.25 and 0.5 mCi (9.25–18.5 MBq) of i.v. autologous labeled platelets.

Platelet Scintigraphy

Ten-minute images were obtained of the anterior pelvis, thighs, and calves and posterior mid-legs (knees) and calves. Lateral views were obtained as needed. Images of the chest and upper extremities were obtained when clinically indicated (Fig. 1). All images were acquired using a large field-of-view gamma camera fitted with a medium-energy collimator. The counts ranged from 3,000 to 6,000 per min. Imaging was performed 3–4 and 16–24 hr after i.v. administration of the labeled platelets and, in some cases, was repeated at 28–48 hr. Fifteen-minute images were obtained if the count rate was <5,000 cts per min for the entire field of view at the time of interpretation. Each study was interpreted by two nuclear medicine physicians (JES and GRC) who were unaware of the patients' identities or results of other diagnostic studies. Each study was reviewed and classified according to one of five patterns of platelet localization (Table 1). In order to obtain a consensus interpretation, any inter-observer disagreements were resolved by joint review.

Contrast Venography and Doppler Sonography

Contrast venography was performed using standard tilt-table technique with tourniquets at the ankle and above the knee (*9–11*). Either 100 ml of Renografin 60 or 80 ml of Renografin 60 diluted with 20 ml of normal saline was manually injected through a 21- or 23-gauge butterfly needle placed in a dorsal pedal vein. Normal saline (100–200 ml) was then infused to flush out residual contrast medium. Radiographs of the upper extremities, calves (anterior and oblique), knees (anterior and oblique), thighs, and pelvis were obtained as indicated. Contrast venograms were re-interpreted by two radiologists (GRC and DAK) who were unfamiliar with the results of the other studies at the time of evaluation. Inter-observer disagreements were resolved by joint review of the study in consultation with a third observer.

The venograms were interpreted as positive for the presence of deep venous thrombosis if a persistent intraluminal filling defect with or without collaterals was identified. For the purpose of data tabulation, equivocal or uncertain sites were treated as negative. Computed tomography was interpreted as positive for acute venous thrombosis if an intraluminal filling defect was identified on contrast-enhanced images. Magnetic resonance imaging was considered positive for venous thrombosis if increased signal intensity was identified within a deep vein.

The results of Doppler flow sonography were also compared with In-PS, but only in patients with no history of thrombophlebitis and no evidence of pelvic or abdominal malignancy. Except in one case, where the upper extremities were involved, only sites between the knee and inguinal ligament were evaluated. Doppler flow sonography was interpreted as positive if no deep venous flow was detected. It was presumed that patients with radiographic or MRI evidence of deep venous thrombosis and *acute* clinical symptoms had *active* thrombophlebitis. Clinical follow-up was used to exclude non-thrombotic causes for the acute symptoms.

RESULTS

Three patterns of platelet localization correlated with active DVT: (a) well-defined or "discrete" increase in tracer localization at the site of a deep vein (focal pattern); (b) sharp or "abrupt" increase in tracer localization along the course of a deep vein on 4- and 24-hr images, relative to adjacent background activity (linear pattern); and (c) asymmetric blood-pool pattern on 4-hr images that evolved into a focal or linear pattern of localization by 16–24 hr. For the purpose of tabulation of the results and identification of problem cases, In-PS was considered positive if one of these three patterns was identified. Adherence to these criteria yielded 16 true-positive, 19 true-negative, six false-positive, and six false-negative In-PS studies (Table 1). The "false-positive" studies were based on findings related to the inguinal region (Group V, Table 1). Ten of the 24 patients with evidence of active thrombophlebitis, who had "false-negative" or equivocal 4-hr In-PS studies, had received anticoagulants (Table 2). All six of the patients with false-negative 24-hr In-PS received heparin between 4 and 24 hr.

Group I

Thirteen of the 47 In-PS studies showed a symmetric blood-pool pattern on 4- or 24-hr images (Fig. 1). On final analysis, ten of these patients had no evidence of active DVT (Table 1), but three patients had venographically proved deep venous thrombosis. Each of these three patients received heparin therapy within 24 hr of In-PS (Table 2). Patient 1 received i.v. heparin as late as 4 hr before In-PS and then received 6,000 units of subcutaneous (s.c.) heparin 10 hr before delayed imaging. Patient 4 received continuous i.v. heparin therapy until 8 hr before In-PS, which was re-instituted after 4-hr imaging. Patient 39 received 5,000 units of subcutaneous heparin 10 hr before 4-hr imaging and was

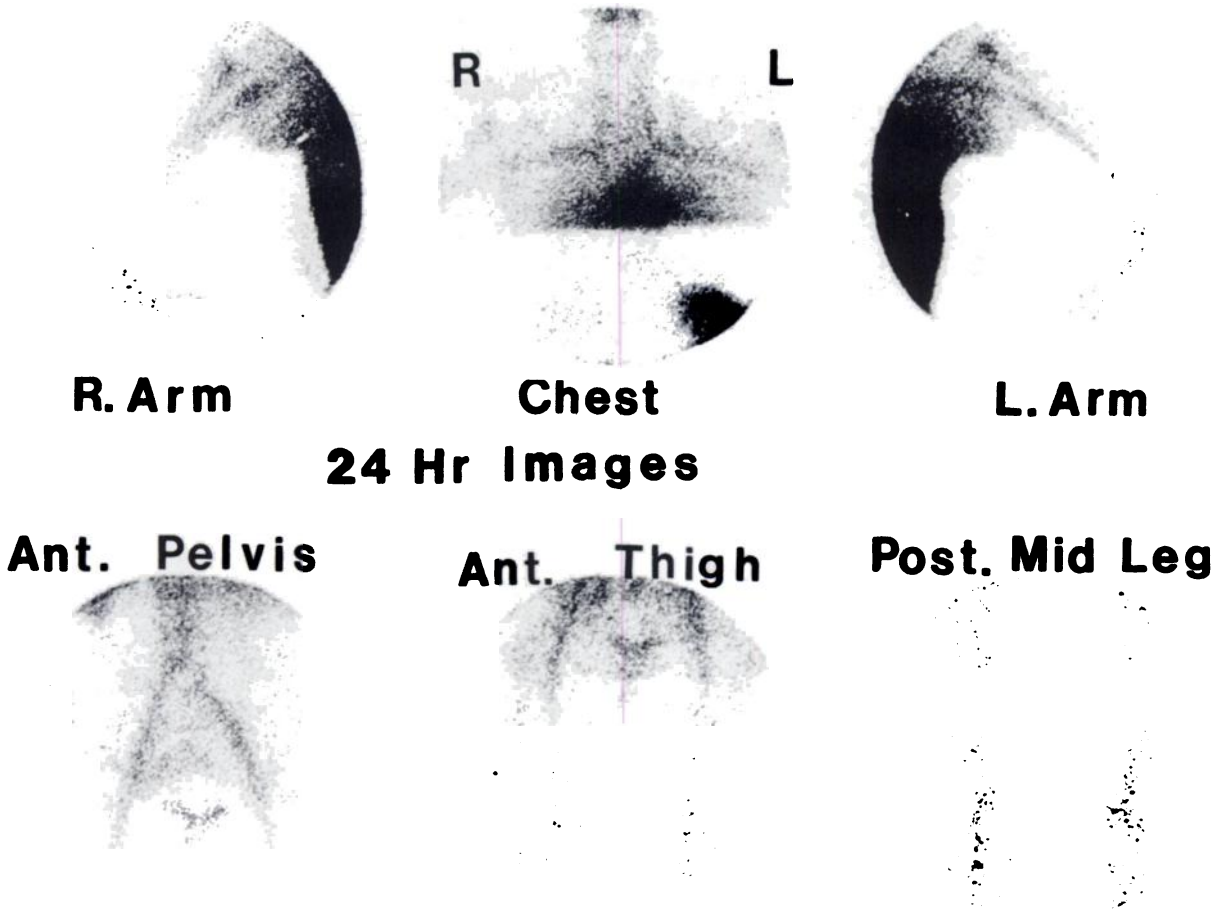


FIGURE 1
36-yr-old with documented episodes of upper and lower extremity thrombophlebitis presented with acute right arm pain and swelling. Contrast venography was negative. In-PS: Normal symmetric blood-pool pattern in upper and lower extremities at 4 and 24 hr.

TABLE 1
Patterns of ^{111}In-Platelet Localization

	4 hr	16–24 hr	No. of patients	DVT	No DVT
Group I	Symmetric blood pool	Symmetric	13	3*	10
Group II	Discrete focal	Discrete focal	6	5	1†
	Abrupt linear	Abrupt linear	3	3	—
Group III	Asymmetric blood pool	More symmetric	10	3*	7
Group IV	Asymmetric blood pool	Discrete focal	4	4	—
	Asymmetric blood pool	Abrupt linear	5 9‡	4	1†
Group V	Increased inguinal (only)	Bilat increased	3	0	3§
		Unilat increased	3	0	3§
		Total	47	22	25

24-hr In-PS results: 16 true-positives, 19 true-negatives, six false-positives, six false-negatives, sensitivity* = 16/22 (73%), specificity = 19/25 (75%).

* False-negative 24-hr In-PS; heparin therapy given between 4- and 24-hr imaging (see text). All six false-negative cases received anticoagulant therapy before 4-hr and between 4- and 24-hr imaging (see Table 2).

† Superficial thrombophlebitis by In-PS confirmed by clinical findings. Contrast venography was nondiagnostic for DVT.

‡ Four of nine cases received anticoagulants before In-PS (see Table 2).

§ False-positive 24-hr In-PS.

TABLE 2
In-PS Results in Patients Receiving Anticoagulants

	Case No.*	Drug	Route	Time stopped before imaging (hr)	PT (10–13) (sec)	PTT (22–33) (sec)	Platelet imaging: Image pattern	Platelet imaging: Time after injection (hr)	Tabulation
	1	Heparin	i.v.	4	12	36	Sym	4	FN
		Heparin	s.c.	10	13	52	Sym	16	FN
	4	Heparin	i.v.	8	10	30	Sym	4	FN
		Heparin	i.v.	— (CPI)	12	150	Sym	20	FN
Group I	39†	Heparin	s.c.	10	11	28	Sym	4	FN
		Heparin	i.v.	— (CPI)	12	101	Sym	22	FN
	3‡	Warfarin	p.o.	16	17	74	Asym	4	FN
		Heparin	i.v.	— (CPI)	18	114	More sym	20	FN
	8	Warfarin	p.o.	15	15	28	Asym	4	FN
		Heparin	i.v.	— (CPI)	14	60	More sym	22	FN
Group III	13§	Heparin	i.v.	4	12	45	Asym	4	FN
		Heparin	i.v.	8	11	52	More sym	21	FN
	6	Warfarin	p.o.	16	21	42	Asym	4	FN
		(2 wk)		36	17	37	Focal	24	TP
				43	13	38	Focal	31	TP
	15	Heparin	i.v.	14	12	48	Asym	4	FN
Group IV					12	23	Linear	22	TP
	30	Heparin	i.v.	4	13	69	Asym	4	FN
					13	24	Linear	21	TP
	43¶	Heparin	s.c.	15	13	30	Asym	4	FN
					13	31	Sl focal	24	TP
					—	—	Focal	28	TP

CPI = Constant pump infusion, Sym = symmetric, Asym = asymmetric, FN = false-negative, TP = true-positive, p.o. = per oral, s.c. = subcutaneous, Sl = slight.

* Contrast venography (CV) demonstrated deep venous thrombi in all but one case (43; see below).

† CT revealed no evidence of venous thrombosis or recurrent pelvic lymphoma. Venography showed clots in the saphenous and common femoral veins and nonvisualization of the inferior vena cava and iliac veins.

‡ CT revealed 4 × 4 cm left para-aortic mass, obstructed left ureter, and intraluminal filling defect in left common iliac vein and inferior vena cava to level of left renal vein.

§ CV revealed intraluminal filling defects in the right greater saphenous vein and nonvisualization of the remaining deep venous system.

¶ 19-yr-old female with no prior thrombophlebitis, swollen left thigh, and tender "palpable cord"; plethysmography and Doppler sonography of the left upper leg were positive.

started on continuous i.v. heparin therapy between 4- and 24-hr imaging. Interestingly, at the time of 4-hr imaging none of the patients had partial thromboplastin times (PTT) that exceeded twice the upper limit of the normal range. In fact, at the time of 16-hr imaging, Patient 1 still did not have a PTT exceeding twice the normal value. Nevertheless, all three patients showed a symmetric pattern of platelet activity on early and delayed images.

Group II

Nine studies demonstrated either a focal or linear pattern of platelet localization along the course of a vein on 4-hr images (Table 1). In six studies one or more foci increased in number, size, and/or intensity between 4 and 24 hr (Fig. 2). Two studies showed a linear pattern of localization at 4 hr that increased by 24 hr (Fig. 3). One study showed platelet localization along a shorter segment of the superficial femoral vein on 24-hr images compared with 4-hr images. All but one of these studies were true-positive for DVT. The remaining study correctly identified superficial thrombophlebitis and was a true-negative for DVT.

Group III

Ten studies showed an asymmetric blood-pool pattern on 3- 4-hr images that appeared more symmetric by 16–24 hr (Fig. 4). Venous stasis with slow clearance of blood-pool activity explained this pattern in seven cases. Deep venous thrombi were demonstrated by contrast venography in the remaining three patients, each of whom had received anticoagulants (Table 2). Patient 3 had been receiving warfarin therapy for 5 days before In-PS. Warfarin was stopped 16 hr before 4-hr imaging and a constant i.v. heparin infusion was initiated between the 4- and 20-hr images. In Patient 8,

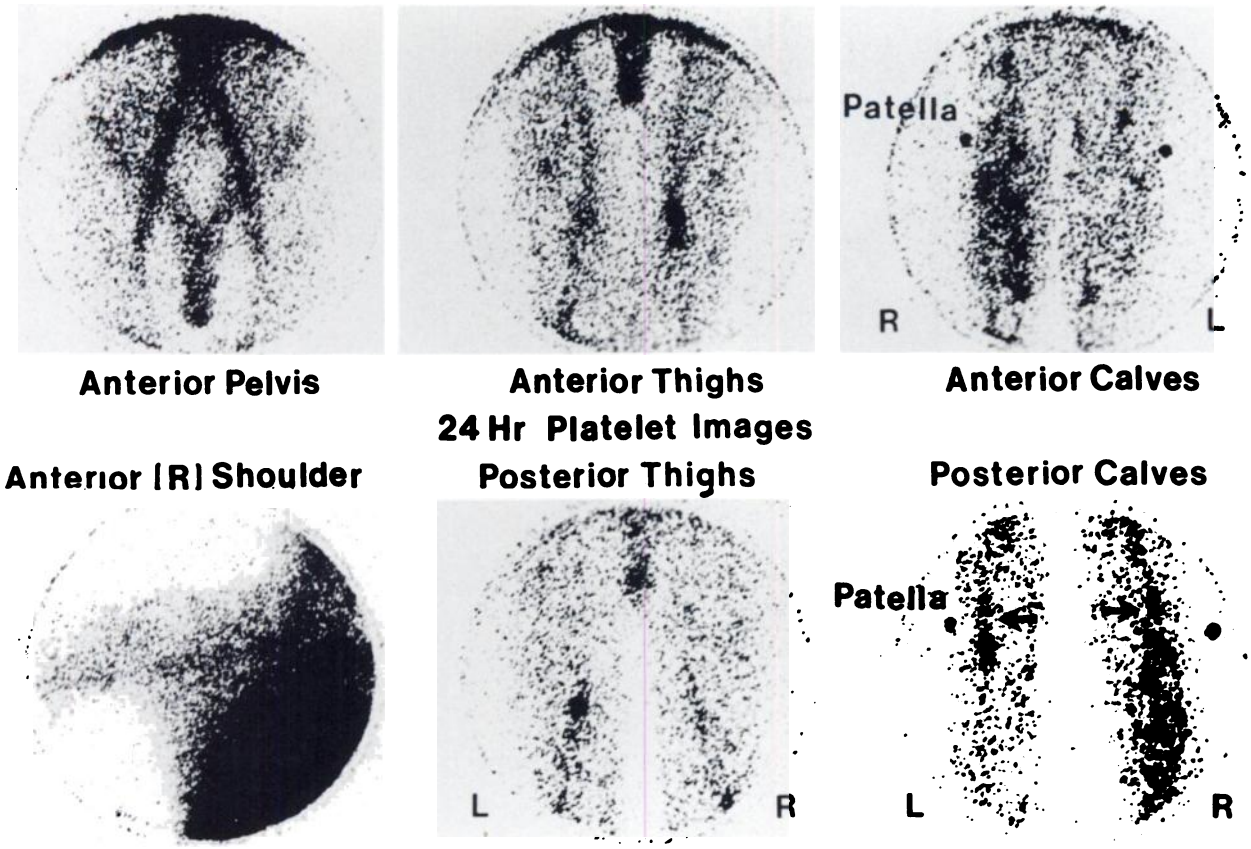


FIGURE 2
49-yr-old with prior episodes of lower extremity DVT evaluated for acute right arm and persistent leg pain and swelling. Contrast venography of right arm was negative, but showed acute thrombi in popliteal and deep calf veins of the right leg. In-PS: Focal platelet localization in left thigh, both calves, and both popliteal regions (arrow).

warfarin therapy had been stopped 15 hr before 4-hr imaging, but constant i.v. heparin infusion was also started before 22-hr imaging. Patient 13 had received i.v. heparin until 4 hr before early imaging and an i.v. heparin bolus (5,000 units) 8 hr before 21-hr In-PS. The patient's PTT was not greater than twice the normal range at the time of the 21-hr false-negative In-PS (Table 2).

Group IV

Nine studies showed an asymmetric blood-pool pattern on the 4-hr images that evolved into either a focal or linear pattern by 16–24 hr (Fig. 5A). Eight of the nine patients had DVT confirmed by contrast venography; all had abnormal tracer localization at the site of a deep vein. One patient had convincing clinical evidence of superficial thrombophlebitis despite a nondiagnostic contrast venogram. The In-PS on this patient showed a linear pattern of platelet localization confined to a superficial vein. This study was classified as negative for active DVT (Fig. 5B). Among the nine patients in Group IV, Patient 6 received warfarin therapy for more than 2 wk before imaging (Table 2), which was discontinued 16 hr before imaging. Patients 15, 30, and 43 received heparin as late as 4 hr before In-PS; however, heparin therapy was not re-instituted until after 21–28-hr images. The five remaining patients in Group IV did not have heparin re-instituted until after delayed imaging.

Group V

Six patients demonstrated an abnormal pattern of tracer activity confined to the inguinal region, which did not decrease on 16–24 hr images. All six were classified as false-positive (Table 1). In three of the six cases a unilateral pattern of increased inguinal activity was observed. One of these three patients had cellulitis involving the right foot and a renal transplant in the contralateral iliac fossa. The second had a nonunited femoral fracture involving the contralateral extremity and a negative venogram. A third patient had prior episodes of thrombophlebitis, but had no evidence of femoral or iliac thrombosis on venography. Delayed images showed gradual reduction of the linear pattern over time (Fig. 6).

The remaining three patients had a bilateral pattern of abnormal inguinal activity. Two of the three had an irregular pattern in the region of the femoral veins on In-PS (Fig. 7), while the third showed a nearly symmetric pattern of enhanced localization extending distally

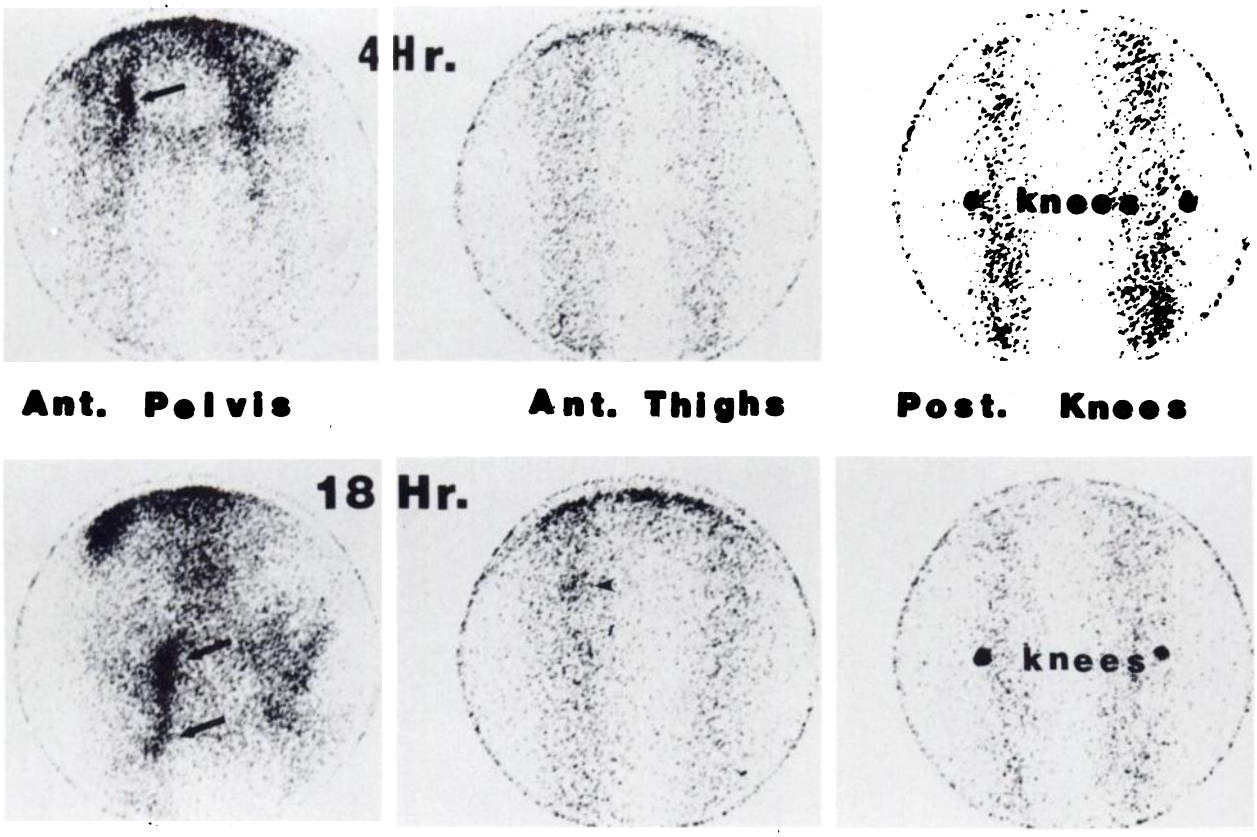


FIGURE 3
72-yr-old presented 3 mo after hip fracture with progressive right leg pain and swelling for 5 days. Contrast venography demonstrated an thrombus in right iliac vein. In-PS: Abrupt increased tracer localization along the course of right common iliac vein at 4 hr (arrow) with progression by 18 hr (arrows) and a new focus in right thigh (arrowhead).

from the level of the iliac veins. This latter patient had a clinically unsuspected recurrent pelvic lymphoma, resulting in bilateral compression of the iliac veins with marked deep venous stasis, thereby giving a false impression of platelet deposition.

Soft-Tissue Infections

Nine patients had superficial cellulitis, with six of nine In-PS studies demonstrating diffuse platelet localization at soft-tissue sites persisting as long as 16–24 hr after injection (Fig. 8). One additional patient had mild diffuse platelet localization at the level of the knee 2 days after removal of a noninfected prosthesis. The platelet localization was correctly identified as a diffuse inflammatory process and all 10 studies were categorized as true-negatives.

Two additional patients had localized soft-tissue infections involving a lower extremity. The first patient had diffusely increased tracer localization in the region of the gluteus maximus and hamstring muscle groups corresponding to a pyogenic myositis. The second patient was an obese diabetic whose platelet scintigram showed an intense focus of localization in the right calf corresponding to a pyogenic abscess (Fig. 9). In both cases, the abnormality was correctly identified as an inflammatory or infectious process other than active DVT.

DISCUSSION

Contrast venography is the standard diagnostic modality for demonstrating deep venous thrombosis (*9–11*). While the complication rate of contrast venography has decreased with the use of nonionic contrast media and saline infusion after contrast injection, it is still an invasive procedure (*12,13*). Satisfactory visualization of the deep venous system cannot always be achieved with contrast venography, particularly in patients with chronic venous disease. This often precludes an accurate assessment of acute thrombus formation in these patients. Furthermore, the repeated use of contrast venography in patients with recurrent episodes of clinically suspected thrombophlebitis is not highly efficacious (*14*).

Several noninvasive modalities have been developed as alternatives to contrast venography to identify patients who are at risk for venous thromboembolism (*15*). These noninvasive modalities can be divided into

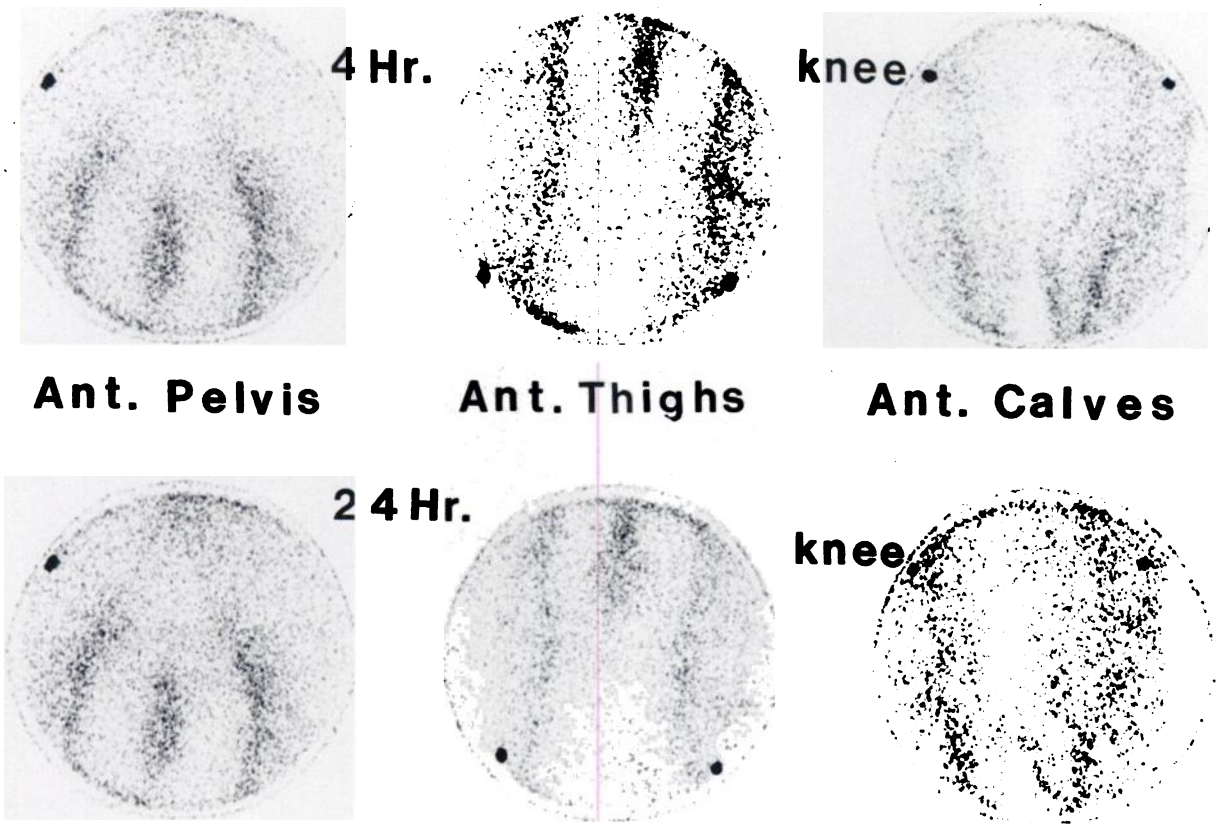


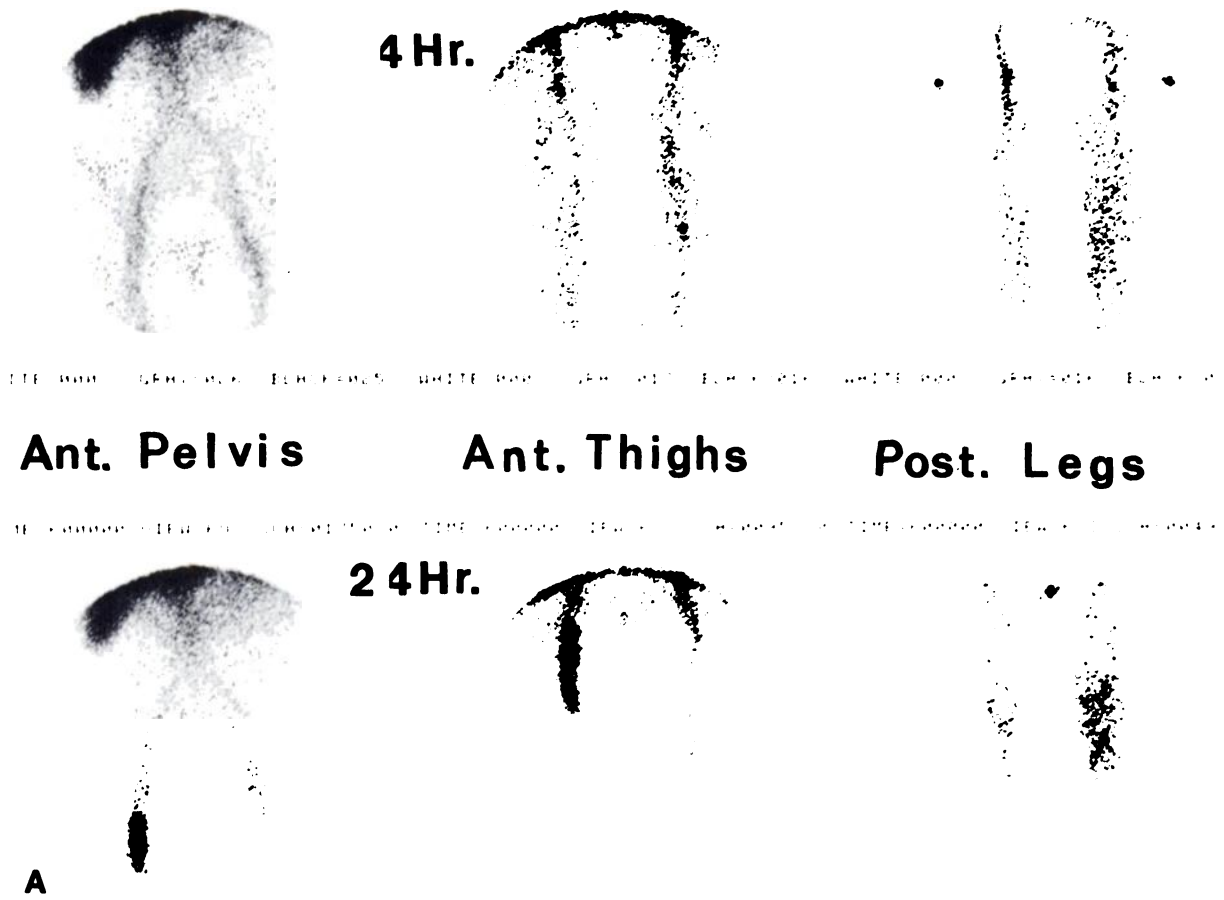
FIGURE 4
55-yr-old with documented prior DVTs, who presented with left leg pain and swelling of 5 days' duration. Contrast venography showed chronic venous changes with varicosities and incompetent perforating veins, but no evidence of deep venous thrombosis. In-PS: Asymmetric 4-hr blood-pool pattern in thighs and calves, becoming more symmetric by 24 hr. Example of true-negative study in patient with chronic venous insufficiency.

two basic groups: (a) those capable of detecting deep venous disease in the proximal extremity, such as impedance plethysmography, Doppler ultrasound, and radionuclide venography (*14–19*), and (b) those capable of detecting active thrombus formation, such as radiolabeled fibrinogen or fibrin fragments radiolabeled antibodies, and platelet scintigraphy (*1–4, 20–23*). Each modality in the first group has achieved fairly good sensitivity and specificity in selected groups of patients without prior history of DVT. However, these diagnostic procedures are limited in their ability to distinguish between thrombo-occlusive disease and non-thrombotic causes of venous obstruction (*14–19*). Since radiolabeled fibrinogen and platelets are incorporated directly into the thrombus, these procedures offer potentially greater specificity for the detection of acute or active thrombophlebitis in patients with pre-existing venous disease.

The iodine-125- (^{125}I) labeled fibrogen study has been utilized to detect acute DVT in postsurgical and posttraumatic patients as well as patients with prior thrombosis and recurrent symptoms (*16–18*). However, accumulation of dissociated ^{125}I in the bladder decreases its sensitivity and specificity for proximal thrombi. The clinical applicability of iodine-123-labeled fibrinogen, radiolabeled fibrin fragments, and radiolabeled antibodies will depend upon the commercial availability of these tracers (*20–23*). In-PS, on the other hand, can potentially be performed at any facility capable of imaging ^{111}In leukocytes.

In-PS is an accurate test for detection of acute DVT in high-risk postoperative patients (*1,3*). The utility of labeled platelets in this clinical setting is not surprising considering the data published from animal models of cardiac and venous thrombi (*24–26*). These models demonstrate that acute thrombi have the greatest affinity for fresh thrombi with optimal localization within 24 hr of thrombus induction (*24–26*). Nevertheless, the data from this and other clinical studies indicate that In-PS can detect the presence of active DVT in patients who develop symptoms more than 24 hr before imaging (*1–4*). All the mechanisms contributing to diagnostic platelet localization in this setting are not fully understood.

Most of the patients with positive In-PS in our series had the onset of symptoms within 2 to 6 days of labeled



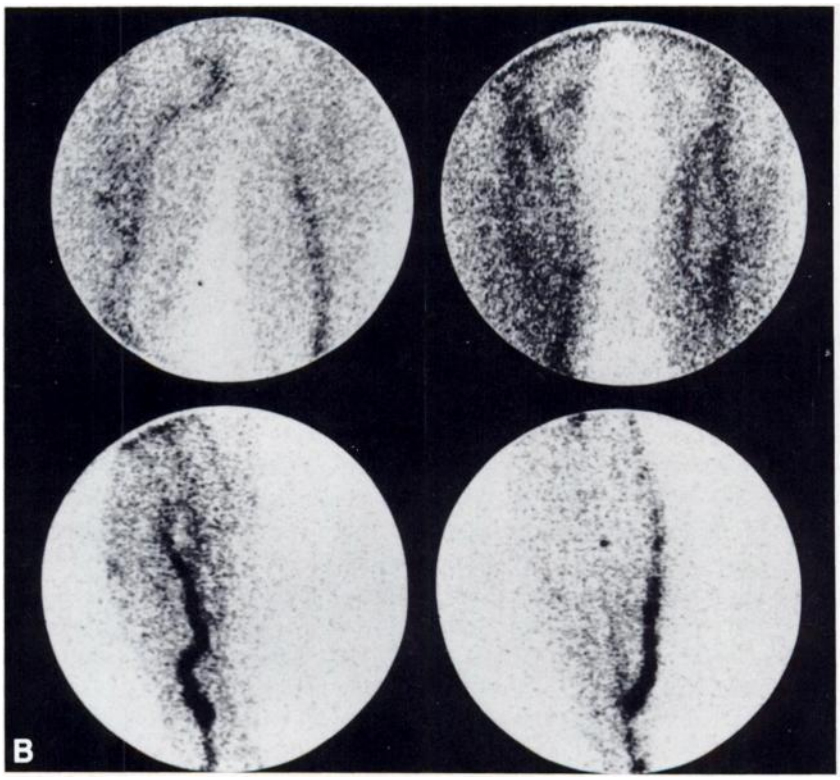


FIGURE 5
A: 50-yr-old with painful swollen right calf. Contrast venography showed intraluminal clot almost occluding the femoral vein. In-PS: Asymmetric blood-pool pattern in thighs at 4 hr evolving into a linear pattern in right thigh by 24 hr, plus diffusely increased localization in right calf by 24 hr. Example of an equivocal 4-hr In-PS in a patient who was receiving i.v. heparin up to 4 hr before imaging. B: 24-yr-old with documented recurrent thrombophlebitis presented with progressive left leg pain and swelling of 6 days' duration. Contrast venography showed non-filling of left common iliac and femoral veins, and incomplete filling of left deep calf veins associated with dilated superficial varicosities. In-PS: Asymmetric blood-pool pattern of both thighs and calves at 4 hr (upper images) evolving into a linear pattern (arrowheads) along a superficial left calf vein by 24 hr (lower images: medial and posterior views of left calf). Example of positive In-PS at a site of acute superficial thrombophlebitis.

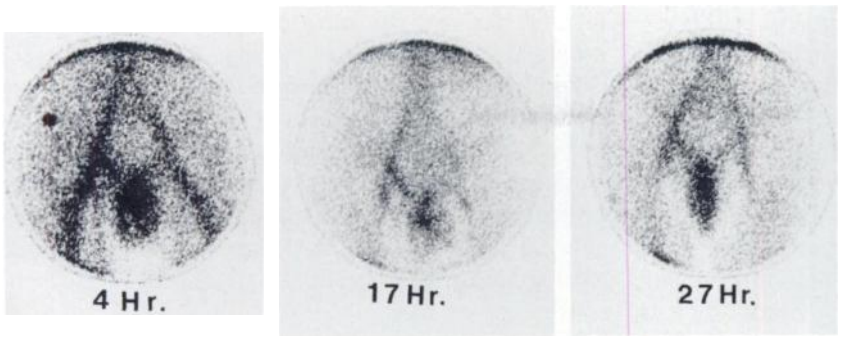


FIGURE 6
34-yr-old presented 1 mo after a small cerebral infarct with cellulitis of the right calf. Contrast venography: No evidence of acute DVT. In-PS: Slightly asymmetric blood-pool pattern in the pelvis at 4 hr. Linear pattern of increased activity in the right inguinal region (common femoral vein) at 17 hr that becomes more symmetric by 27 hr. Example of unilateral increased inguinal activity not related to active thrombophlebitis, but probably reflecting venous stasis.

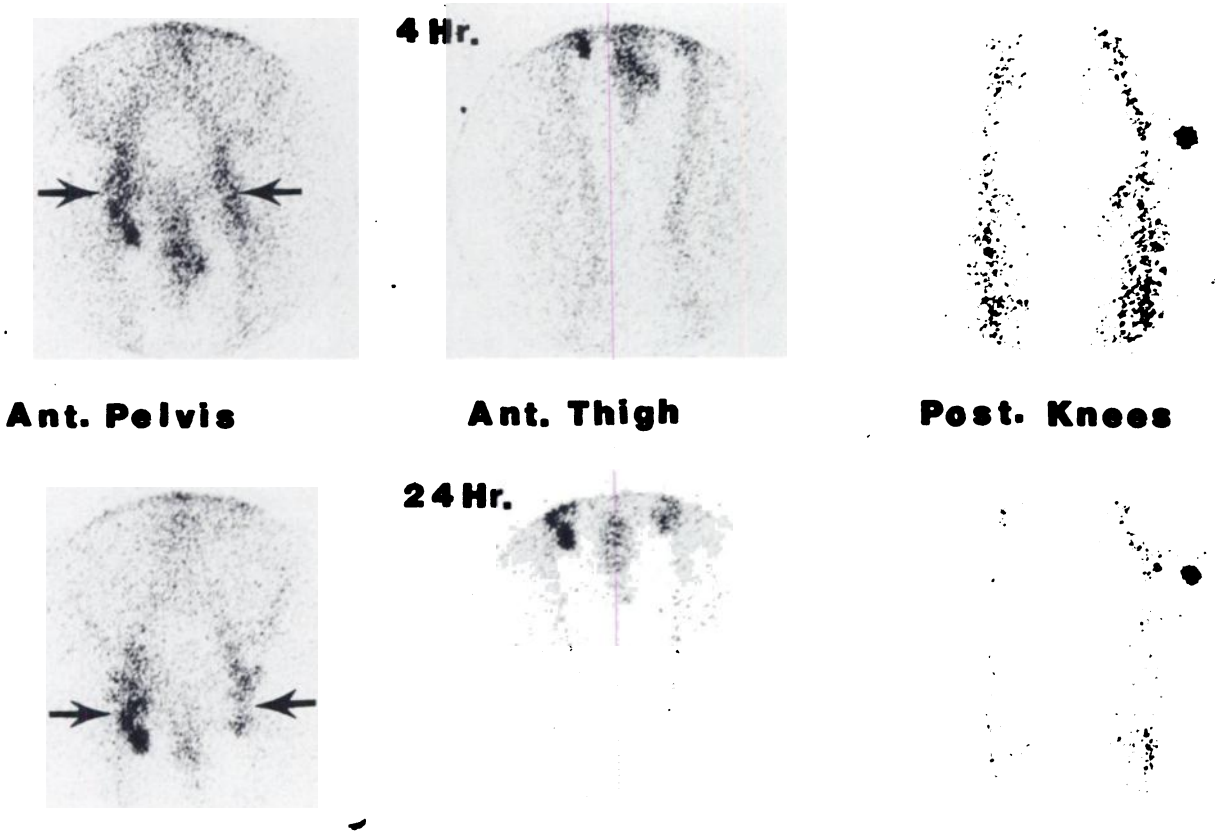


FIGURE 7
42-yr-old with acute onset of right leg erythema, swelling, and tenderness that responded promptly to antibiotic therapy. Contrast venography was negative for thrombosis, venous stasis or dilatation. In-PS: 4- and 24-hr images showing an irregular pattern of increased radioactivity confined to both inguinal regions (arrows). Midline blood-pool activity in external genitalia. Example of bilateral increased inguinal activity.

platelet injection. In addition, 15 of the 16 true-positive cases of active DVT had greater platelet localization on 24-hr than on 4-hr images. The degree of platelet localization is affected by the nature of the thrombogenic stimulus, degree of stasis, extent of endothelial injury, and degree of trauma to adjacent tissue (*27–29*). These and other observations suggest that the degree of active phlebitis and endothelial injury play an important role in continued platelet localization (*27,29*).

Some investigators have reported that heparin therapy had no effect on the results of In-PS (*1,5,6*), but others have subsequently noted decreased sensitivity following systemic heparinization (*2–4,30*). In this series, systemic heparin therapy had been administered to seven patients within 24 hr of early imaging. None of these seven patients had diagnostic 4-hr In-PS (Table 2). In-PS became positive by 16–20-hr images in three of the seven patients who received no additional heparin

therapy. In the remaining four patients, heparin therapy was re-instituted after 4-hr imaging and the 14-24-hr images remained negative. The optimal time for stopping heparin prior to In-PS has not been established. Furthermore, rapid reversal of heparin's anticoagulant effect with protamine sulfate might increase the risk of embolic complication.

There also have been conflicting reports of the effect of warfarin therapy on In-PS (*1,2*). Warfarin inhibits synthesis of clotting factors II, VII, IX, and X, and should inhibit platelet accumulation indirectly by limiting thrombus propagation (*31*). Our experience is limited, but suggests that warfarin therapy does reduce the sensitivity of early In-PS. Three patients with false-negative 4-hr In-PS had received warfarin and had prolonged prothrombin times (PT) at the time of early imaging. The 24-hr images became positive in one patient as the PT became normal. The other two patients were started on heparin infusion after early imaging (Table 2). Since tabulation of this series, we have studied a symptomatic patient with venographically proved venous thrombosis who was receiving warfarin. Four- and 24-hr In-PS was negative, but 48-hr In-PS was positive despite an elevated PT of 32 sec. Our data are inconclusive as to the effect of warfarin therapy on In-PS, but suggest that delayed imaging should be performed in these cases. Aspirin therapy had no apparent effect on In-PS results in four cases.

Total thrombotic occlusion of a vein is another potential cause for a false-negative In-PS study. Only one patient in this series had complete deep venous occlusion documented by contrast venography (Case 13, Table 2). In addition, intraluminal filling defects (clots) were also demonstrated within the greater saphenous vein. Platelet localization should have been present at these sites, but the patient had also received heparin therapy. Fenech et al. (*1*) have reported two cases of ^{111}In-platelet localization at the proximal end of a thrombus completely occluding a deep vein. These thrombi also caused negative defects in the venous blood-pool pattern.

Venous activity may affect the appearance of the blood-pool pattern. The inguinal region appears to be the most difficult anatomic site to interpret. Two of six false-positive studies showed bilateral irregularly increased inguinal activity that persisted at 24 hr (Fig. 7). The basis for this increased inguinal activity is not fully understood. Such findings might have resulted from prior venous or arterial femoral punctures, but this could not be substantiated. Contrast venography did not demonstrate venous dilatation, tortuosity, or stasis in these regions. One possibility is that inguinal venous blood-pool activity appears accentuated due to the superficial location of the femoral vein and the relative increased soft-tissue attenuation proximally and distally. A third case showing abrupt bilateral increased inguinal activity was most likely due to stasis from proximal compression of both iliac veins by recurrent pelvic lymphoma. This increased blood-pool activity gradually decreased on delayed images obtained after 24 hr. Regardless of the pattern observed, 24-hr bilateral increased inguinal localization is unlikely to represent active thrombophlebitis. Delayed imaging is repeated after 24 hr to look for the appearance of increasing focal localization or gradually decreasing blood-pool activity.

The three false-positive 24-hr studies showing unilateral increased inguinal activity were most likely due to altered venous blood-pool on one side of the pelvis. In these cases, a more symmetric blood-pool pattern was observed on delayed images acquired more than 24 hr after platelet injection (Fig. 6). One patient had undergone renal transplantation, one had received a hip prosthesis, and the third had unilateral stasis from chronic venous disease. Thus, unilateral increased activity confined only to the inguinal region also requires delayed imaging.

Technical factors are also important in the performance of In-PS. Active thrombophlebitis involving the popliteal and/or posterior tibial veins can be missed if only anterior images of the lower extremities are obtained. In three studies, abnormal platelet localization along the popliteal and/or deep calf veins could be identified only on posterior views. Failure to identify localization along these veins on anterior views probably results from photon attenuation by overlying tissue. In addition, when there are multiple abnormal sites, popliteal localization can be difficult to identify on anterior views alone (Fig. 2). For these reasons, routine posterior views of the calf and mid-leg are recommended.

As in the inguinal region, the popliteal blood-pool activity can appear accentuated on posterior views due to the superficial location of the vein. Lateral or medial views of the legs can also help distinguish between deep and superficial localization (Fig. 5B). Finally, image quality can be improved by placing the detector immediately adjacent to the extremity rather than beneath the imaging table. All these factors can be used to advantage when differentiating soft-tissue infection (*32*) from active DVT (Figs. 8 and 9).

In summary, In-PS is a useful alternative to contrast venography for detecting acute or recurrent active DVT, but potential pitfalls should be recognized. An asymmetric 4-hr blood-pool pattern is an indeterminate finding and delayed images at 24 hr or later are required, particularly in patients who have received anticoagulants. Regardless of pattern, increased platelet activity confined only to the inguinal region must be interpreted with caution, and is unlikely to represent active thrombophlebitis. Posterior views of the knees and calves should be obtained routinely and supplemented with

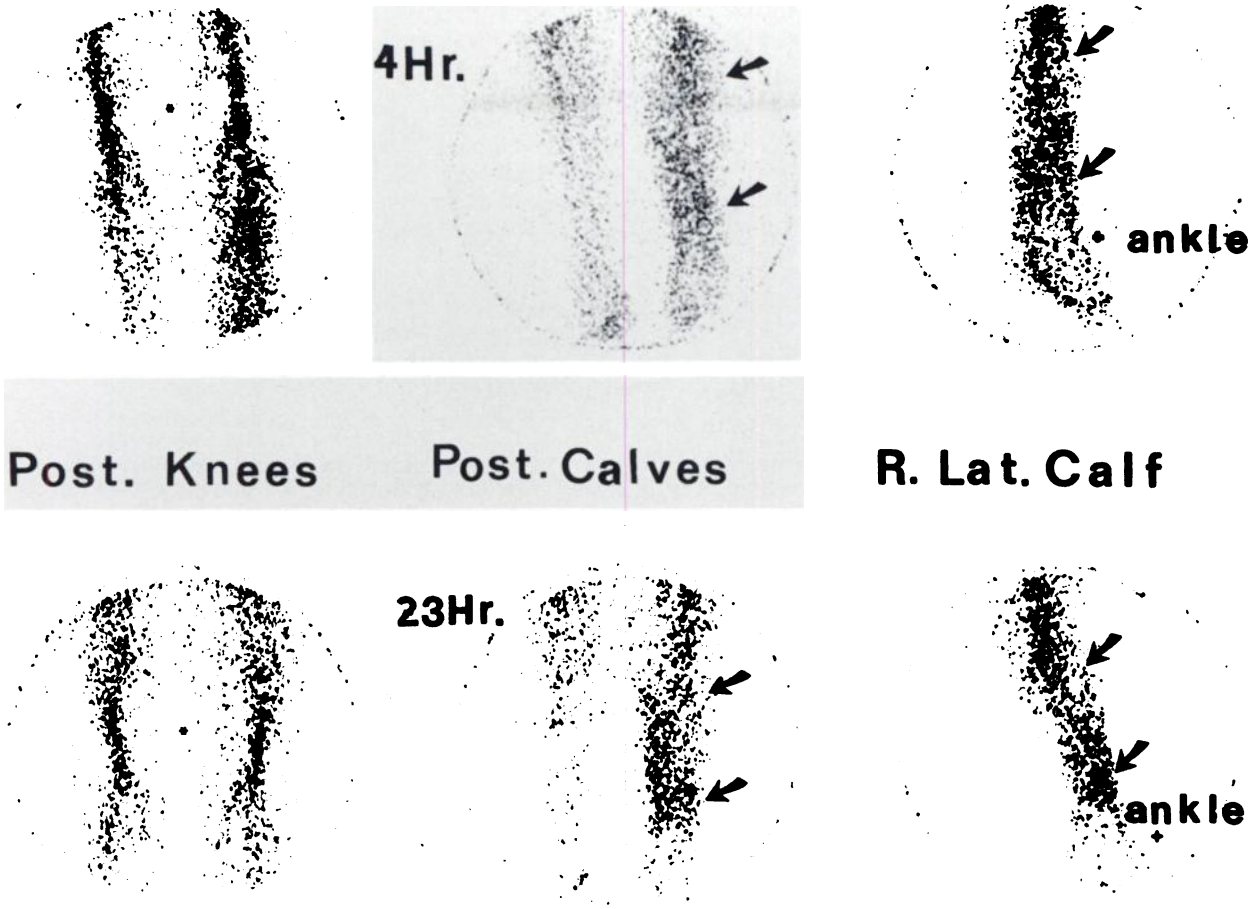


FIGURE 8
41-yr-old diabetic with right calf pain, swelling, and erythema. Doppler sonography was negative. In-PS: Diffuse superficial localization in the right calf at 4 and 23 hr from cellulitis (arrows) that responded to antibiotic therapy.

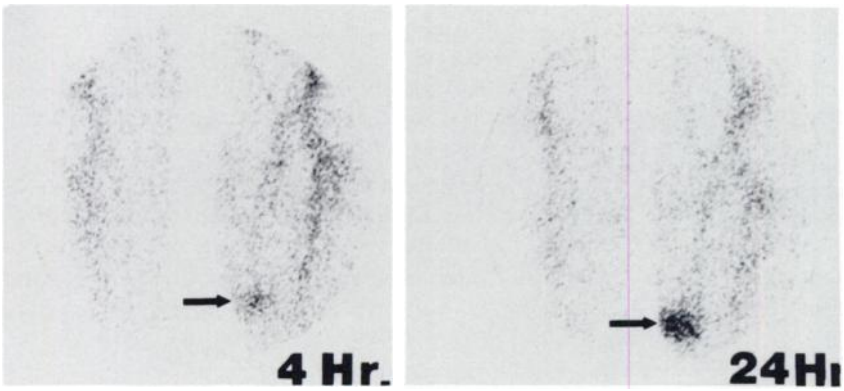


FIGURE 9
62-yr-old diabetic presented 1 yr after internal fixation of right ankle fracture with right calf pain, swelling, and erythema of 6 days' duration. Subcutaneous pyogenic abscess of right calf surgically drained 1 day after platelet imaging. In-PS: Large focus of increased localization in the medial aspect of the right calf (arrow) not confined to a deep vein.

images that can best identify the site of platelet localization.

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