Technetium-99m Red Blood Cell Venography in Patients with Clinically Suspected Deep Vein Thrombosis: A Prospective Study

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We have compared technetium-99m (^{99m}Tc) red blood cell (RBC) venography to serial impedance plethysmography (IPG) in 110 consecutive patients with a first episode of clinically suspected deep vein thrombosis (DVT). IPG was performed at Day 0 and, if abnormal, contrast venography was also performed to rule out a falsely positive result. Patients with an initially normal IPG had the test repeated at Days 1, 3, 5 to 7, and 10 to 14. Contrast venography was not performed and anticoagulant treatment was withheld in all patients who remained normal during repeated IPG testing. Technetium-99m RBC venography was performed at Day 0 in patients with an initially abnormal IPG and during the period of serial IPG testing in those with an initially normal IPG. The sensitivity of [^{99m}Tc]RBC venography for proximal DVT was 0.68, with 95% confidence limits (CL) from 0.48 to 0.89. Specificity was 0.88 (95% CL from 0.81 to 0.95). When the findings of [^{99m}Tc]RBC venography for the entire lower extremity were compared to the reference method, the sensitivity increased to 0.90 (95% CL from 0.82 to 0.97) but the specificity decreased to 0.56 (95% CL from 0.51 to 0.62). Technetium-99m RBC venography is a sensitive but less specific method for detecting DVT of the entire lower extremity. An abnormal [^{99m}Tc]RBC venogram, particularly in the calf region, should always be confirmed by another diagnostic method.

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Although it has been available for a number of years (*1–4*), the technique of technetium-99m red blood cell ([^{99m}Tc]RBC) venography has never been validated in a study which fulfilled all the essential methodologic criteria required in the evaluation of a diagnostic test. These methodologic requirements are: (a) consecutive patients should undergo both the test under evaluation and the reference test, (b) both tests should be interpreted blindly and without knowledge of each other in order to avoid the diagnostic suspicion bias, and (c) the test should be evaluated in a broad spectrum of patients with a variety of symptoms (e.g., duration, severity) and other co-morbid conditions (e.g., varicose veins, non-thrombotic causes of leg swelling) (*5*). Avoidance of these methodologic features often leads to an exaggerated optimism during the early evaluation of a diagnostic test, followed by subsequent disillusionment when more rigorous investigation is undertaken.

We have incorporated these methodologic features in a prospective study comparing [^{99m}Tc]RBC venography to serial impedance plethysmography (IPG) in patients with clinically suspected first episode of deep vein thrombosis (DVT). Previous studies have shown that serial IPG testing is equivalent to contrast venography for making management decisions in patients with clinically suspected first DVT episode (*6,7*). IPG is highly (95%) sensitive and specific to thrombosis of the popliteal or more proximal veins (*8*), and, when performed serially, will detect any extension of isolated calf DVT into the proximal deep venous system (*7,9*). We have chosen serial IPG testing for our reference method because in our center it has a better outpatient availability and a lower frequency of inadequate tests results than contrast venography.

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METHODS

Patient Population

Consecutive patients referred to the Montreal General Hospital Division of Hematology noninvasive vascular laboratory between September 20, 1985 and October 25, 1986 with a first episode of clinically suspected DVT were studied prospectively.

Study Protocol

Each patient was evaluated at the time of initial referral. Details pertaining to their symptoms and signs, past history of DVT, risk factors for DVT and other co-morbid conditions were recorded in a standard fashion. Following the clinical evaluation, an IPG was performed and if abnormal, contrast venography was performed in order to rule out a false-positive test result (Fig. 1). Patients with venographically confirmed proximal DVT (thrombosis of the popliteal or more proximal veins) were treated with anticoagulants. Patients with an initially abnormal IPG who did not undergo contrast venography (because of allergy to the contrast material or due to refusal of the treating physician) were also treated with anticoagulants. In these patients, we felt that the potential complications of untreated proximal DVT outweighed the risks of anticoagulant treatment. Patients with an initially normal IPG had the test repeated the next day (Day 1) and then at Days 3, 5 to 7, and, 10 to 14. Anticoagulant treatment was withheld in all patients who remained normal during serial IPG testing. Symptomatic patients who met the eligibility criteria underwent [^{99m}Tc]RBC venography. Patients were considered eligible if they were age 18 yr or greater, had no history of DVT, had no history of allergy to radiographic contrast material, were able to lie in the prone position, were not pregnant or breast feeding, were geographically accessible for repeated IPG testing, were not receiving anticoagulants and gave informed consent. Technetium-99m RBC venography was performed at day 0 in patients with an initially abnormal IPG and during the period of serial testing in those with an initially normal IPG.

Diagnostic Tests

Occlusive cuff impedance plethysmography (IPG 200, Codman, Peterborough, Ontario) with sequential testing and a variable occlusion time was performed and interpreted according to a method which has been previously published (*10,11,12*). Contrast venography was performed with the patient in the supine position and nonweight bearing (*13*). The diagnostic criterion for DVT was a constant intraluminal filling defect seen in two or more projections. For [^{99m}Tc]RBC venography, 5 ml of blood was withdrawn into a heparinized syringe and added to a Brookhaven kit (Cadema Medical Products, Middletown, NY). After centrifugation, 2 ml of red blood cells were labeled with 20 mCi of [^{99m}Tc]pertechnetate. The labeled red blood cells were injected in a peripheral arm vein. One million counts per image were obtained on a large field-of-view Siemens gamma camera. Anterior views of the lower abdomen and upper thighs as well as anterior and posterior views of the lower thighs, knees and calves were obtained. Each [^{99m}Tc]RBC venogram was assessed visually and assigned to one of the three following categories: normal, abnormal or possible. The possible category was devised in order to account for adjacent arterial cross-talk and various degrees of occlusion by the thrombus. A scan was considered normal if there was a normal and symmetrical concentration of the radioactivity throughout the entire deep venous system (Fig. 2). A scan was considered abnormal if there was a 50% or greater decrease in the visual assessment of radioactivity in a deep vein compared to the same vein in the other leg or to the activity in the same vein bordering the defect (Fig. 3). A scan was considered possible if there was a less than 50% decrease in radioactivity in a deep vein compared with the same vein in the other leg or to the activity in the same vein bordering the defect (Figs. 4 and 5).

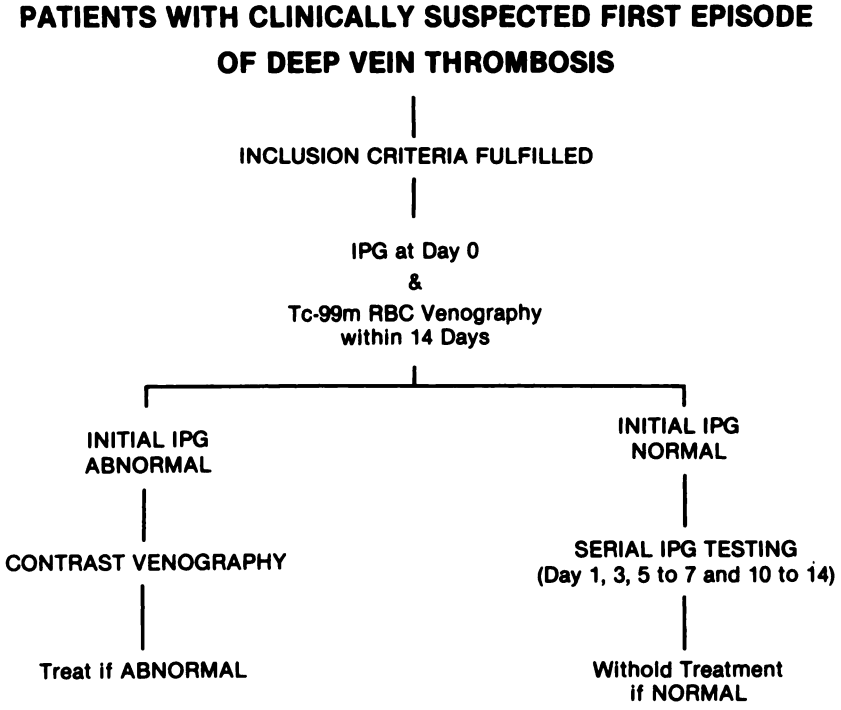

FIGURE 1
Diagnostic process of 302 consecutive patients with clinically suspected DVT. Patients who did not fulfill the inclusion criteria and therefore did not undergo [^{99m}Tc]RBC venography were submitted to the same protocol of IPG testing shown in this figure.

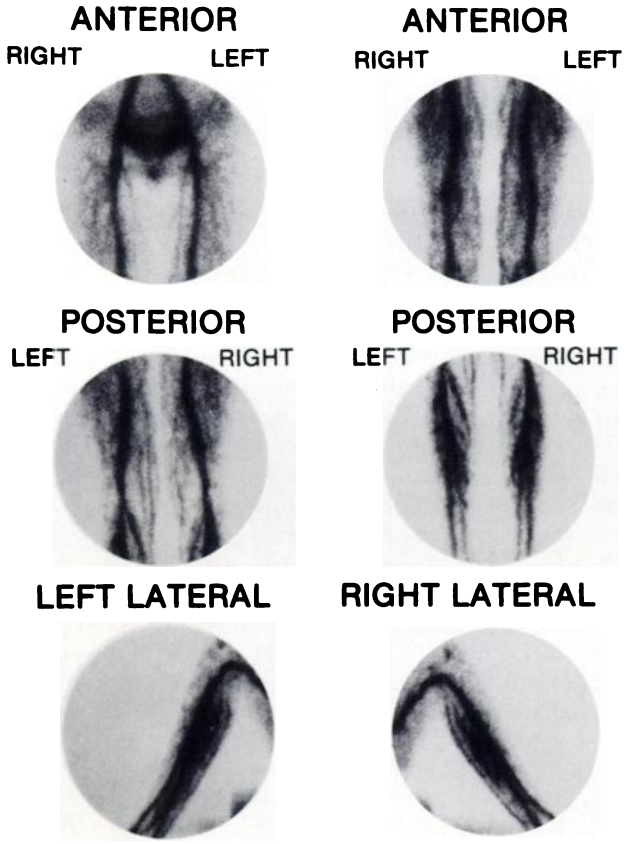

FIGURE 2
Normal [^{99m}Tc]RBC venogram. There is a normal and symetrical distribution of the radionuclide concentration throughout the entire deep venous system.

Methodologic Considerations

The results of contrast venography and [^{99m}Tc]RBC venography were intrepreted blindly by panels of three experienced radiologists and nuclear physicians respectively, without knowledge of clinical findings or of each others' results. In each panel, the interpretation sessions were held with the three observers together and each nuclear scan or contrast venogram was assigned to one of the various categories by concensus agreement. Occasional cases in which uniform agreement could not be reached were adjudicated by the third observer. For [^{99m}Tc]RBC venography, both legs were interpreted but only the symptomatic one was included in the analysis. Management decisions were made solely on the basis of the results of IPG (and contrast venography if abnormal), irrespective of the results of [^{99m}Tc]RBC venography.

Statistical Methods

The data on the clinical characteristics of patients (Table 1) were analyzed by chi-square for comparing proportions and by Student's t-test for comparing means. The diagnostic efficacy of [^{99m}Tc]RBC venography was measured by calculating the sensitivity, specificity, positive and negative predictive values. The 95% confidence limits (CL) on the observed sensitivity and specificity of [^{99m}Tc]RBC venography were calculated from the binomial distribution.

RESULTS

During the study period, 302 patients with clinically suspected first episode of DVT were recorded. The clinical characteristics of these patients are shown in Table 1. One hundred and ten patients (36%) underwent [^{99m}Tc]RBC venography and 192 (64%) did not. There were no statistically significant differences in the baseline characteristics among these two patients groups, except in the proportion of inpatients/outpatients ($p < 0.001$). This difference is due to the fact that many postoperative patients could not assume the prone position, required for proper assessment of the calf region, and, several ill patients refused to sign the consent form. The age of the 110 patients who underwent [^{99m}Tc]RBC venography ranged from 19 to 87 yr (mean 59 yr); 52 were males and 58 were women. Technetium-99m RBC venography was performed at: Day 0 in 19 patients (17%), Day 1 in 36 patients (33%), Day 2 in 14 patients (13%), Day 3 in nine patients (8%), Day 4 in nine patients (8%), Day 5 in five patients (5%), Day 6 in eight patients, and, between Day 7 and 13 in ten patients (7%). [^{99m}Tc]RBC venography was not performed in: 95 patients (31%) who refused to sign the consent form, 40 patients (13%) who were unable to lie in the prone position, 14 patients (5%) who did not keep their appointment, 14 patients (4%) who were unable to given informed consent, ten patients (3%) who were pregnant, eight patients who were critically ill (3%), five patients (2%) who were geographically inaccessible for repeated IPG testing, four patients (1%) who were on anticoagulants, one patient <18 yr, one patient who died before the test could be performed.

Outcome During IPG Testing

Thirty (27.2%) of the 110 patients who underwent [^{99m}Tc]RBC venography had an initially abnormal IPG (Fig. 6). Proximal DVT was confirmed by contrast venography in seventeen patients (15%). Contrast venography was normal in 7 patients. It was not performed in 6 patients due to refusal of the treating physician. Two of the 80 patients (2.5%) with an initially normal IPG became abnormal, at day 1, during serial testing. These two patients had proximal DVT confirmed by both contrast venography and [^{99m}Tc]RBC venography on that day.

Forty-nine (25.5%) of the 192 patients who did not undergo [^{99m}Tc]RBC venography had an initially abnormal IPG (Fig. 7). Proximal DVT was confirmed by contrast venography in 25 patients (13%). Contrast venography was normal in 11 patients. It was not performed in 13 patients due to refusal of their treating physician. Two of the 143 patients (1.3%) with an initially normal IPG became abnormal during serial testing. One patient became abnormal at Day 1 and the other at Day 3. Both patients had venographically confirmed proximal DVT.

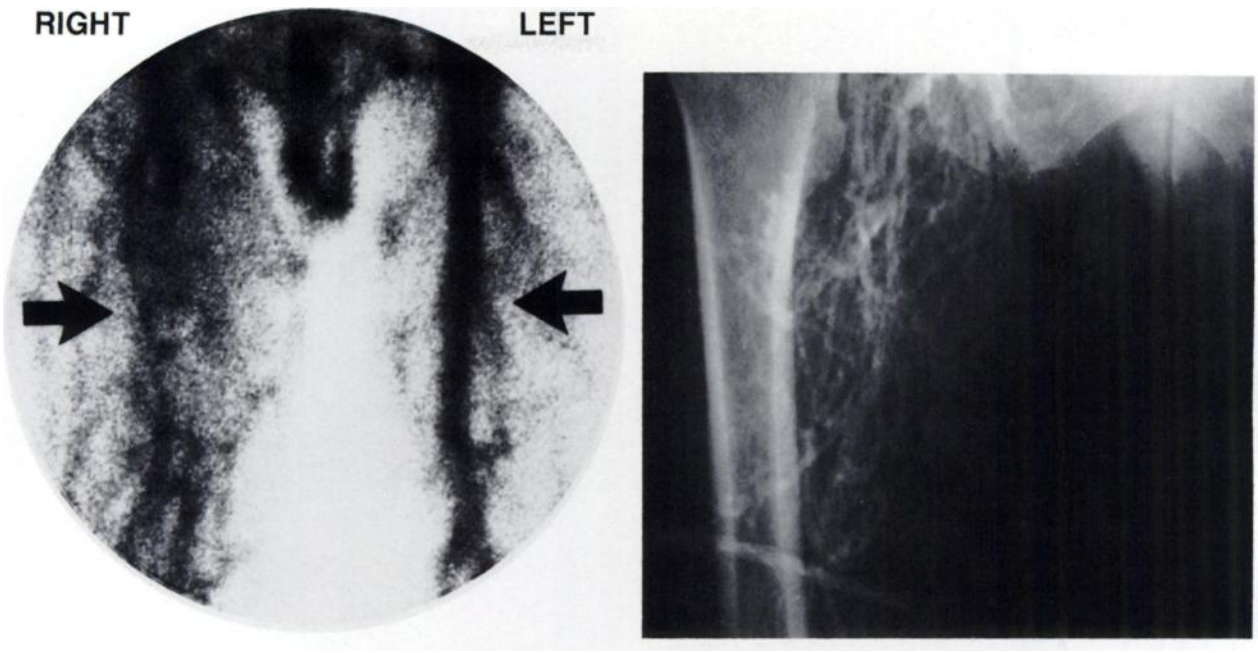

FIGURE 3
Abnormal [^{99m}Tc]RBC venogram of the right leg. There is a >50% decrease in radionuclide concentration in the right superficial femoral vein compared with the left superficial femoral vein (left). Contrast venography disclosed an intraluminal filling defect in the right popliteal vein (view not shown) and a nonvisualized right superficial femoral vein (right).

Thus, in our entire study population, four of 223 patients (1.7%) with an initially normal IPG became abnormal during serial testing. One patient (0.4%) developed symptoms and signs of pulmonary embolism during serial IPG testing. Ventilation-perfusion lung scanning was read as low probability for pulmonary embolism and contrast venography disclosed a nonocclusive thrombus of the popliteal vein. The positive predictive value of IPG for proximal DVT in our entire study population was 55%. If one excludes the 19 patients who did not undergo contrast venography, it increased to 72%. Twelve of 18 patients (67%) with an abnormal IPG and normal contrast had muscle tension due to pain or anxiety (causing a constriction of the underlying deep vein), three patients (17%) had congestive cardiac failure (causing a decrease in venous return), and three patients (17%) had severe peripheral arterial insufficiency (causing a decrease in arterial inflow).

Diagnostic Efficacy of [^{99m}Tc]RBC Venography

The results of [^{99m}Tc]RBC venography for the detection of proximal DVT (thrombosis of the popliteal or more proximal veins) are shown in Tables 2 and 3. The prevalence of proximal DVT was 17%. These results represent 110 limbs in 103 patients. Seven patients had bilateral symptoms in the lower extremity and the seven patients with an initially abnormal IPG who did not undergo contrast venography were excluded from the analysis. Nine patients had a possible [^{99m}Tc]RBC venogram result. Four of these patients (44%) had venographically confirmed proximal DVT (Fig. 4). The other five patients had a normal contrast venogram (Fig. 5). One of the patients with a possible [^{99m}Tc]RBC venogram and an abnormal IPG died from massive pulmonary embolism, proven at autopsy, after the treating physician had prematurely discontinued anticoagulant treatment. With the possible results included in the normal category, the sensitivity was 0.47 (95% CL from 0.25 to 0.70) and the specificity was 0.93 (95% CL from 0.88 to 0.99) (Table 2). Positive and negative predictive values were 0.60 and 0.90, respectively. With the possible results included in the abnormal category, the sensitivity rose to 0.68 (95% CL from 0.48 to 0.89) and the specificity decreased to 0.88 (95% CL from 0.81 to 0.95) (Table 3). Positive and negative predictive values were 0.54 and 0.93, respectively.

The results of [^{99m}Tc]RBC venography for the entire lower extremity for the detection of DVT by serial IPG testing are shown in Tables 4 and 5. One hundred and six limbs in 103 patients were available for analysis. Seven of the initial 110 patients had bilateral symptoms and the seven patients with an initially abnormal IPG who did not undergo contrast venography were excluded from the analysis. Twenty patients had a possible [^{99m}Tc]RBC venogram result. Five patients (25%) had

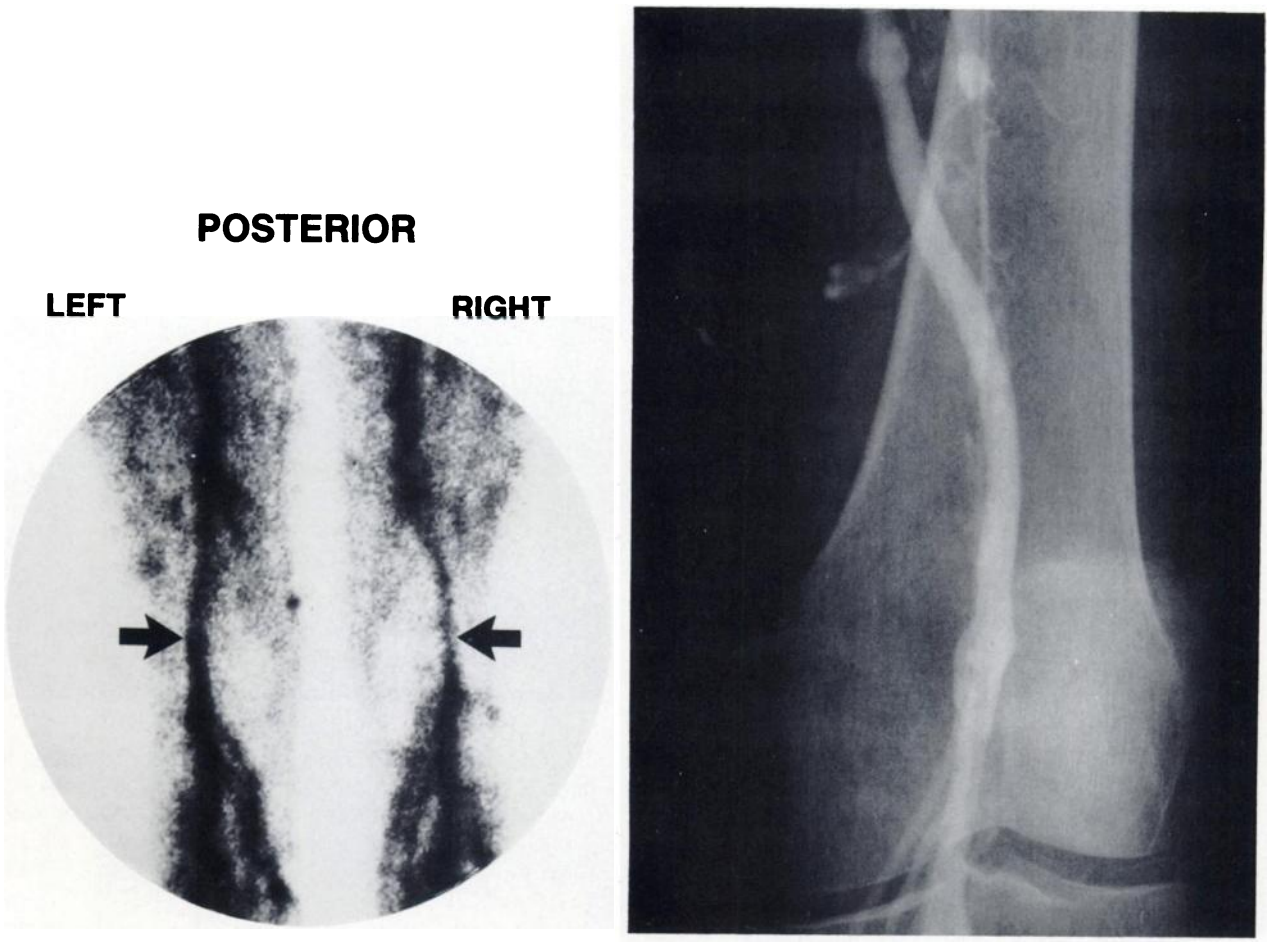

FIGURE 4
Technetium-99m RBC venogram in the possible category. There is a <50% decrease in radionuclide concentration in the right popliteal vein compared to the left popliteal vein (left). Contrast venography of the right leg was normal and showed no intraluminal filling defect in the popliteal vein (right).

venographically confirmed proximal DVT. Contrast venography was normal in the other 15 patients. With the possible results included in the normal category, the sensitivity was 0.63 (95% CL from 0.41 to 0.85) and the specificity was 0.74 (95% CL from 0.64 to 0.83) (Table 4). Positive and negative predictive values were 0.34 and 0.90, respectively. With the possible results included in the abnormal category, the sensitivity rose to 0.90 (95% CL from 0.82 to 0.97). The specificity decreased to 0.56 (95% CL from 0.51 to 0.62) (Table 5). Positive and negative predictive values were 0.31 and 0.96, respectively.

DISCUSSION

We have evaluated prospectively [^{99m}Tc]RBC venography in a broad spectrum of patients with clinically suspected first episode of deep vein thrombosis. All [^{99m}Tc]RBC venograms were assessed visually and scans with a 50% or greater decrease in radioactivity were classified as abnormal. We chose this 50% cutoff level because it was easy to assess visually and allowed scans with incompletely occlusive thrombi to be classified in the abnormal category. Our reference method had two components: contrast in patients with an abnormal IPG, and, serial IPG testing in patients with an initially normal IPG. We performed contrast venography in patients with an abnormal IPG in order to rule out a false-positive test result. The majority of patients with a falsely abnormal IPG had muscle tension due to pain or anxiety. We did not perform contrast venography in patients with normal IPGs in view of the very high negative predictive value of serial IPG testing. The negative predictive value of serial IPG testing in patients with a first episode of clinically suspected DVT has been demonstrated in one retrospective (*14*) and two prospective studies (*7,9*). In the two prospective studies, the negative predictive value of serial IPG testing was determined by clinical outcome. In the study by Hull and co-workers, only six of 311 patients with suspected DVT (2%) who had an initially normal IPG and re-

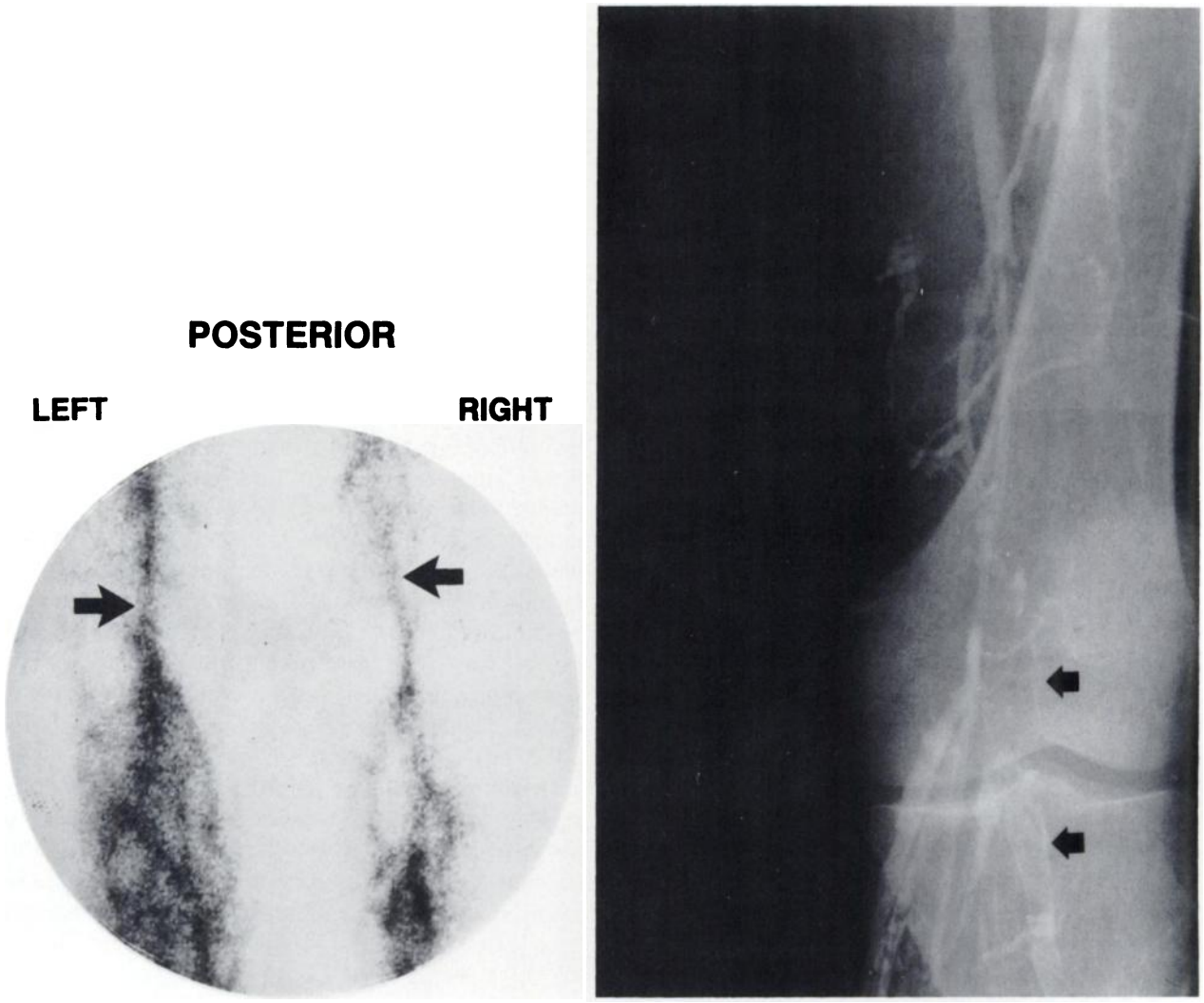

FIGURE 5
Technetium-99m RBC venogram in the possible category. There is a <50% decrease in radionuclide concentration in the right popliteal vein compared to the left popliteal vein (left). Contrast venography disclosed an intraluminal filling defect in the right popliteal vein (right).

mained normal during serial testing, returned during a follow-up period of 1 yr with objectively documented venous thromboembolism (*7*). Similarly, in the Amsterdam General Practitioner study, one of 289 patients (0.3%) who had an initially normal IPG and normal serial testing, returned with objectively documented venous thromboembolism during a 6 mo follow-up period (*9*).

Our results of [^{99m}Tc]RBC venography for the detection of proximal DVT show a sensitivity of 0.47 (95% CL from 0.25 to 0.70) and a specificity of 0.93 (95% CL from 0.88 to 0.99), with the possible results included in the normal category (Table 2). With the possible results included in the abnormal category, the sensitivity rises to 0.68 (95% CL from 0.48 to 0.89) and the specificity decreases to 0.88 (95% CL from 0.81 to 0.95) (Table 3). These results indicate that a possible [^{99m}Tc] RBC venogram result cannot be used to rule out proximal DVT.

When the findings of the entire lower extremity by [^{99m}Tc]RBC venography are compared with our reference method, with the possible results included in the abnormal category (Table 5), the sensitivity increases further to 0.90 (95% CL from 0.82 to 0.97). This is because all patients with proximal DVT by contrast venography also had calf DVT and all these were detected by [^{99m}Tc]RBC venography. The negative predictive value of [^{99m}Tc]RBC venography for the entire lower extremity was very high, at 0.96, indicating that a normal result rules out DVT. On the other hand, the specificity decreases sharply to 0.56 (95% CL from 0.51 to 0.62). This is because several patients who remained normal by serial IPG testing had either a possible (15 patients) or abnormal (23 patients) [^{99m}Tc]RBC veno-

TABLE 1
Clinical Characteristics of 302 Patients with Clinically Suspected Deep Vein Thrombosis*

	RBC venography performed	RBC venography not performed
Patients, n	110	192
Male : female, n	52 : 58	74 : 118
Age, yr	59.3 ± 8.3*	58.9 ± 18.0*
Days since onset of symptoms, n	10.5 ± 10.1*	9.8 ± 10.1*
Days in bed during last month, n	7.8 ± 6.7*	10.3 ± 8.7*
Hospital status, n		
Inpatient	39	105†
Outpatient	71	87†
History of, n		
Surgery within 6 mo	34	71
Hospitalization within 6 mo	61	122
Cancer	14	36
Heart disease	35	43
Liver disease	7	7
Lung disease	15	28
Clinical symptoms, n		
Pain and swelling	30	52
Pain only	54	90
Swelling only	47	88
Leg signs observed, n		
Swelling	65	127
Tenderness	82	136
Positive Homan's sign	27	40

* Values are mean ± s.d., where indicated.
† p value < 0.001.

gram result. In other words, 44% of symptomatic patients with a false-positive diagnosis of DVT (i.e., false positive = 1 − specificity) would have been unnecessarily treated with anticoagulants on the basis of the results of [^{99m}Tc]RBC venography alone.

One may argue that the majority of patients with normal serial IPG and either a possible or abnormal [^{99m}Tc]RBC venogram result had bona fide isolated calf DVT. We think this is an unlikely finding. It is well established that 20% of cases of isolated calf DVT undergo extension in the popliteal or more proximal veins (*7,9,15*), at which point they become readily detectable during serial IPG testing. This extension occurs during the 10 to 14 days following initiation of the thrombotic process, before the thrombi become firmly adherent to the vessel wall. In our entire study population, only four of 223 patients (1.7%) with an initially normal IPG became abnormal during the period of serial testing. This implies that the true frequency of isolated calf DVT in our study population is ~8.5% (i.e. 8.5%, with a 20% frequency of proximal extension = 1.7%). Also, recent studies using contrast venography, in patients with clinically suspected DVT, have indicated a frequency of isolated calf DVT of ~10% in these patients (*6,7,9,16*).

In summary, we have compared [^{99m}Tc]RBC venography to a method which reliably differentiates between those patients with clinically suspected DVT who should receive anticoagulant treatment from those in whom it can be safely withheld. Our results indicate

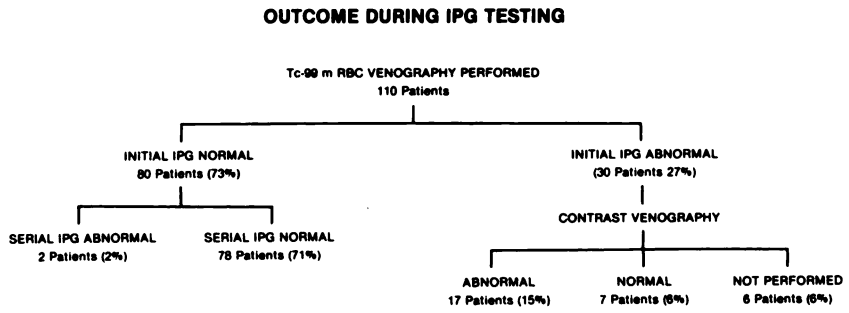

FIGURE 6
Outcome during IPG testing of the 110 patients who underwent [^{99m}Tc] RBC venography.

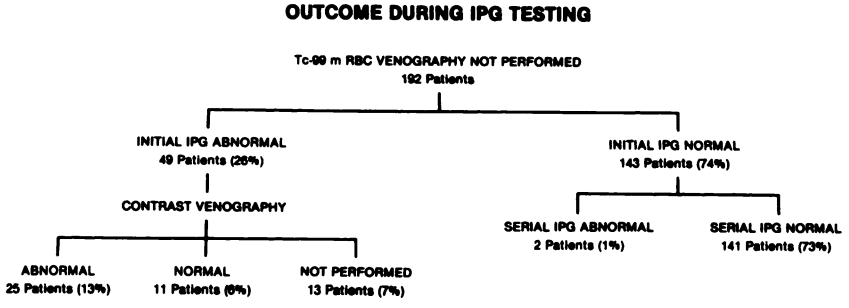

FIGURE 7
Outcome during IPG testing of the 192 patients who did not undergo [^{99m}Tc]RBC venography.

TABLE 2
Proximal DVT by [^{99m}Tc]RBC Venography, with the Possible Results Included in the Normal Category

		Serial IPG	
		Abnormal*	Normal
	Abnormal	9	6
Results of [^{99m}Tc]RBC venography for proximal DVT	Possible	4	5
	Normal	6	80

* Confirmed by contrast venography.
Sensitivity = 0.47 (0.25–0.70). Specificity = 0.93 (0.88–0.99). Positive predictive value = 0.60. Negative predictive value = 0.90.

TABLE 3
Proximal DVT by [^{99m}Tc]RBC Venography, with the Possible Results Included in the Abnormal Category

		Serial IPG	
		Abnormal*	Normal
	Abnormal	9	6
Results of [^{99m}Tc]RBC venography for proximal DVT	Possible	4	5
	Normal	6	80

* Confirmed by contrast venography.
Sensitivity = 0.68 (0.48–0.89). Specificity = 0.88 (0.81–0.95). Positive predictive value = 0.54. Negative predictive value = 0.93.

TABLE 4
DVT of the Lower Extremity by [^{99m}Tc]RBC Venography, with the Possible Results Included in the Normal Category

		Serial IPG	
		Abnormal*	Normal
	Abnormal	12	23
Results of [^{99m}Tc]RBC venography for the entire lower extremity	Possible	5	15
	Normal	2	49

* Confirmed by contrast venography.
Sensitivity = 0.63 (0.41–0.85). Specificity = 0.74 (0.64–0.83). Positive predictive value = 0.34. Negative predictive value = 0.90.

that a normal [^{99m}Tc]RBC venogram result in the entire lower extremity rules out DVT. However, the safety of withholding anticoagulant treatment in patients with a normal [^{99m}Tc]RBC venogram result in the entire lower extremity should be confirmed in future studies. Our results also indicate that a possible [^{99m}Tc]RBC venogram result does not rule out DVT and therefore should be considered as abnormal. An abnormal [^{99m}Tc]RBC venogram result, particularly in the calf region, should always be confirmed by another method such as IPG or contrast venography in view of its low positive predictive value. If the IPG is used and is normal, it should be repeated serially as per our study protocol; anticoagulant treatment can be withheld if the patient remains normal during repeated IPG testing. If contrast venography is used and is abnormal, even in the calf region only, the patient should be treated with anticoagulants. This is because contrast venography cannot be repeated serially to detect any extension in the proximal deep venous system.

TABLE 5
DVT of the Lower Extremity by [^{99m}Tc]RBC Venography, with the Possible Results Included in the Abnormal Category

		Serial IPG	
		Abnormal*	Normal
	Abnormal	12	23
Results of [^{99m}Tc]RBC venography for the entire lower extremity	Possible	5	15
	Normal	2	49

* Confirmed by contrast venography.
Sensitivity = 0.90 (0.82–0.97). Specificity = 0.56 (0.51–0.62). Positive predictive value = 0.31. Negative predictive value = 0.96.

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REFERENCES

1. Beswick W, Chmiel R, Booth R, et al. Detection of deep venous thrombosis by scanning of ^{99m}technetium-labelled-red-cell venous pool. *Br Med J* 1979; 1:82–84.
2. Lisbona R, Stern J, Derbekyan D. Tc-99m red blood cell venography in deep vein thrombosis of the leg: a correlation with contrast venography. *Radiology* 1982; 143:771–773.
3. Singer I, Royal HD, Uren RF, et al. Radionuclide plethysmography and Tc-99m red blood cell venography in venous thrombosis: comparison with contrast venography. *Radiology* 1984; 150:213–217.

4. Littlejohn Go, Brand CA, Ada A, et al. Popliteal cysts and deep venous thrombosis: Tc-99m red blood cell venography. *Radiology* 1985; 155:237–240.
5. Ransohoff DF, Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. *N Engl J Med* 1978; 299:926–930.
6. Hull RD, Hirsh J, Sackett DL, et al. Replacement of venography in suspected venous thrombosis by impedance plethysmography and ^{125}I-fibrinogen leg scanning. *Ann Intern Med* 1981; 94:12–15.
7. Hull RD, Hirsh J, Carter C, et al. Diagnostic efficacy of impedance plethysmography for clinically suspected deep vein thrombosis: a randomized trial. *Ann Intern Med* 1985; 102:21–28.
8. Hull RD, Raskob GE, Leclerc JR, et al. The diagnosis of clinically suspected venous thrombosis. *Clin Chest Med* 1984; 5:43–56.
9. Huisman MV, Buller HR, Ten Cate JW, et al. Serial impedance plethysmography for suspected deep venous thrombosis in outpatients. The Amsterdam general practitioner study. *N Engl J Med* 1986; 314:823–828.
10. Hull Rd, Van Aken WG, Hirsh J, et al. Impedance plethysmography using the occlusive cuff technique in the diagnosis of venous thrombosis. *Circulation* 1976; 52:696–700.
11. Hull RD, Taylor DW, Hirsh J, et al. Impedance plethysmography: the relationship between venous filling and sensitivity and specificity for proximal vein thrombosis. *Circulation* 1978; 58:898–902.
12. Taylor DW, Hull RD, Sackett DL, et al. Simplification of the sequential impedance plethysmography technique without loss of accuracy. *Thromb Res* 1980; 17:561–565.
13. Coel MN, Dodge W. Complication rate with supine phlebography. *Am J Roentgenol* 1978; 131:821–822.
14. Wheeler HB, Anderson FA, Cardullo, PA, et al. Suspected deep vein thrombosis. management by impedance plethysmography. *Arch Surg* 1982; 117:1206–1209.
15. Kakkar VV, Flanc C, Howe CT, et al. Natural history of post-operative deep vein thrombosis. *Lancet* 1969; 2:230–233.
16. Hull RD, Hirsh J, Sackett DL, et al. Replacement of venography in suspected venous thrombosis by impedance plethysmography and ^{125}I fibrinogen leg scanning: a less invasive approach. *Ann Intern Med* 1981; 94:12–15.