CLINICAL NUCLEAR MEDICINE
Volume 26, Number 6, pp 491–494

Subcutaneous Whole-Body Radionuclide Venography Using Tc-99m In Vivo Tagged Red Blood Cells

DAVID C. YANG, M.D.,* RITA S. RATANI, M.D.,* JIM KALANI, M.D.,* YU-WEN JOYCE CHEN, M.D.,‡ YING-FONG HUANG, M.D.,‡ PAUL MAGZADEH, M.D.,† AND RAHMAN ILKHANIZADEH, M.D.†

Purpose: The accurate diagnosis of deep vein thrombosis (DVT) is essential to prevent its complications and to initiate appropriate treatment. Doppler ultrasound (DUS), contrast venography, and intravenous radionuclide venography have been used for many years to detect DVT. However, obtaining venous access in the foot for injection of contrast agent can be difficult.

Methods: The authors introduce the technique of subcutaneous radionuclide venography using Tc-99m in vivo tagged red blood cells and compare it with DUS, a widely used method. Sixty patients (120 lower extremities) underwent subcutaneous radionuclide venography and DUS.

Results: The concordance rate was 94% in the femoral veins and 95% in the popliteal veins. Subcutaneous radionuclide venography revealed 10 iliac vein thromboses and 2 inferior vena cava thromboses that were not detected by DUS.

Conclusions: Subcutaneous radionuclide venography is a useful alternative method for detecting DVT. It is particularly valuable for evaluating DVT in the iliac veins and in the inferior vena cava.

Key Words: Deep Vein Thrombosis, Subcutaneous Radionuclide Venography, Doppler Ultrasound, Tc-99m Red Blood Cells.

From the Departments of Radiology and Surgery,† New York Methodist Hospital and Weill Medical College of Cornell University, New York, New York, and Department of Nuclear Medicine,‡ Kaohsiung Medical University, Taiwan*

THE CONSEQUENCES OF untreated deep vein thrombosis (DVT), namely pulmonary embolism and postphlebitic syndrome, have high mortality and morbidity rates. Therefore, the accurate diagnosis of DVT is crucial to initiate appropriate therapy.

Several imaging methods have been used to detect venous thrombosis. Conventional contrast venography has been the reference procedure for detecting venous thrombosis. However, the test may not be feasible or definitive in 10% to 20% of patients (1,2). Systemic allergic reaction, dislodgment of the thrombus, and local chemical phlebitis induced by the intravenous contrast agent are potential complications of this procedure. Doppler ultrasound (DUS) is a widely used method for detecting DVT. However, it is operator dependent and its reliability for the diagnosis of isolated calf vein thrombosis is not well established (3). The iliac veins and inferior vena cava are not routinely evaluated by DUS.

In nuclear imaging, intravenous radionuclide venography has been used for many years to evaluate DVT. However, frequently intravenous administration of a radiopharmaceutical into the foot is difficult or impossible in the presence of edema associated with DVT.

In this article, we introduce the technique of subcutaneous radionuclide venography (SCRV) using Tc-99m in vivo tagged red blood cells using a whole-body imaging approach. The results of SCRV and DUS are compared.

Materials and Methods

Equipment

We used a dual-head whole-body imaging system (Siemens Medical Systems, Issaquan, WA) and a Genesys dual-head gamma camera system (ADAC Laboratories, Milpitas, CA). We used a 140-KeV energy peak with a 15% window and a matrix size of 1,024 × 1,024 × 8. The ADAC system used collimators with a 15″ × 20″ field of view and the Siemens a 15.25″ × 24″ field of view. We used a Siemens Microlot imager to obtain hard copy analog images. ADAC Scopix and Codonix imagers interfaced with a Pegasys computer produced digital images.

Subcutaneous Radionuclide Venography Technique

For in vivo tagging of the red blood cells, 15 mg of Mallinckrodt stannous pyrophosphate mixed with 4 ml saline was administered into an antecubital vein. Approximately 15 minutes

Received for publication July 10, 2000. Revision accepted January 22, 2001.

Correspondence: David C. Yang, M.D., Department of Radiology, New York Methodist Hospital, 506 Sixth Street, Brooklyn, New York 11215. E-mail: dcydavidyang@netscape.net

later, the patient was placed on a whole-body imaging table in the supine position. Elastic tourniquets were applied above both ankles to occlude the superficial venous system. Highly specific activity Tc-99m pertechnetate (5 to 8 mCi; approximate volume, 0.2 ml) was injected subcutaneously using a 25-gauge needle into the dorsum of each foot. After the injection, the feet were covered with rubberized lead sheets to eliminate the interfering scattered radiation at the sites of injection. The dual-detector heads were centered at the level of the feet. When radioactivity appeared in the acquisition monitor (usually in 3 to 5 minutes), the first-pass anterior and posterior whole-body images were obtained from the feet to the head with a moving detector head speed set at 15 cm/minute. The first-pass whole-body image took approximately 10 to 15 minutes to complete, depending on the patient's height. The tourniquets were released and the second-pass whole-body images were obtained from the feet to the head to evaluate the superficial and deep venous systems. The entire procedure took approximately 30 minutes (Fig. 1).

Interpretation Criteria of Subcutaneous Radionuclide Venography

Deep vein thrombosis was diagnosed based on diminished or absent venous blood flow in the affected segments of the deep veins with or without development of collaterals.

The first-pass whole-body images showed the occlusive processes of the deep venous system, whereas the second-pass whole-body images showed abnormalities of the superficial and deep veins.

Subcutaneous radionuclide venography can differentiate DVT from venous insufficiency. In DVT, in addition to diminution or absence of flow in the deep veins during the first pass, the superficial collaterals and soft tissue swelling are usually visualized during the second pass (Figs. 2 and 3). In the postphlebitic syndrome with venous insufficiency, destruction of the valves in the deep veins and perforators allows the radiotracer to enter the superficial varicose veins during the first pass.

Results

Comparison of Subcutaneous Radionuclide Venography and Doppler Ultrasound

To determine the accuracy of SCRV, we examined 60 patients (ages 33 to 96 years; mean age, 64.5 years; male:female ratio, 22:38) who underwent SCRV and DUS of each limb (120 limbs) at New York Methodist Hospital, New York, New York, between July and December 1998. Two nuclear medicine physicians conducted the review using a double-blind method. In the femoral veins, 35 of 38 segments showed concordant positive results, whereas 75 of 78 segments had concordant negative results by both methods. Three femoral vein segments were diagnostically inconclusive for comparison. In popliteal veins, 32 of 36 segments showed concordant positive results, and 82 of 84 segments had concordant negative results. The concordance rate was 94% in the femoral veins and 95% in the popliteal veins. In addition, SCRV revealed 10 iliac vein DVTs and 2 inferior vena cava obstructions that were not detected by DUS.

The coauthors at Koahsiung Medical University Hospital, Taiwan, examined 25 patients (ages 15 to 84 years; mean age, 59.1 years; male:female ratio, 13:17) who underwent SCRV and DUS of each limb (50 limbs) from September 1998 to January 1999. Nine patients were diagnosed as DVT involving the femoral veins (n = 7) and left popliteal veins (n = 2) by SCRV and by DUS. Sixteen patients did not show evidence of DVT by either of these methods.

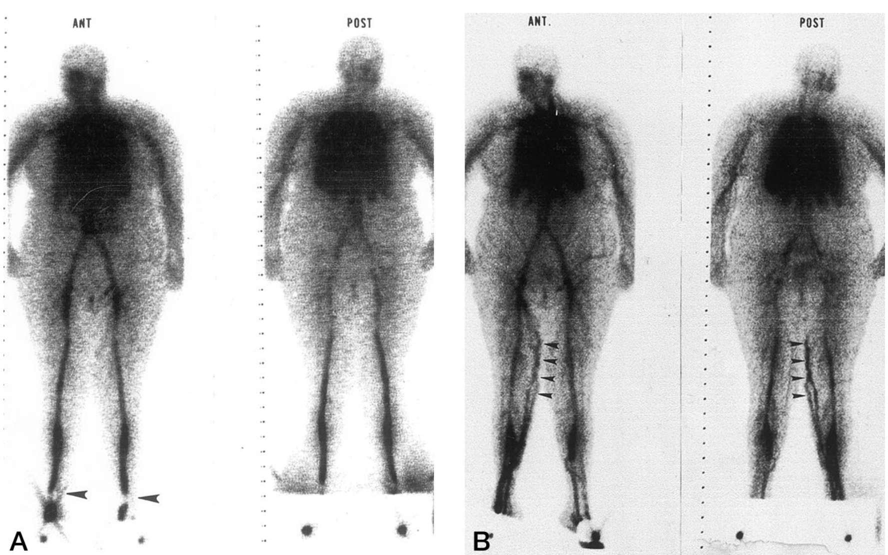

Fig. 1. A normal result in a 61-year-old woman with acute onset of swelling and redness in her left calf. (A) The whole-body anterior and posterior body images were obtained during the first pass with tourniquets applied at the ankles (arrowheads). Patent popliteal, femoral, and iliac veins are visualized. (B) The second-pass images after release of the tourniquet show the greater saphenous vein along the medial aspect of the right lower extremity (arrowheads). Doppler ultrasound showed no evidence of thrombosis.

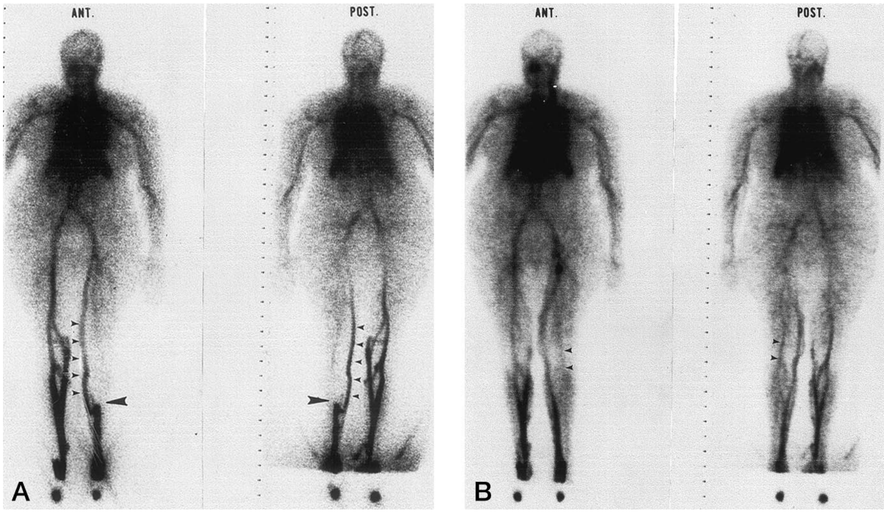

Fig. 2. Deep vein thrombosis in the left femoropopliteal veins is apparent in a 92-year-old woman with pain and swelling of the left lower extremity. (A) The first-pass images show an abrupt obstruction at the left upper calf vein (arrowhead) associated with collateral circulation into the great saphenous vein (arrowheads). In the right lower extremity, there is no evidence of venous obstruction. However, flow into the superficial veins on the medial aspect of the right lower leg is compatible with venous insufficiency. (B) The second-pass images show persistent diminished blood-pool activity in the left femoropopliteal veins. Faintly visualized activity in the left popliteal region (arrowheads) is possibly a result of the overlapping arterial phase.

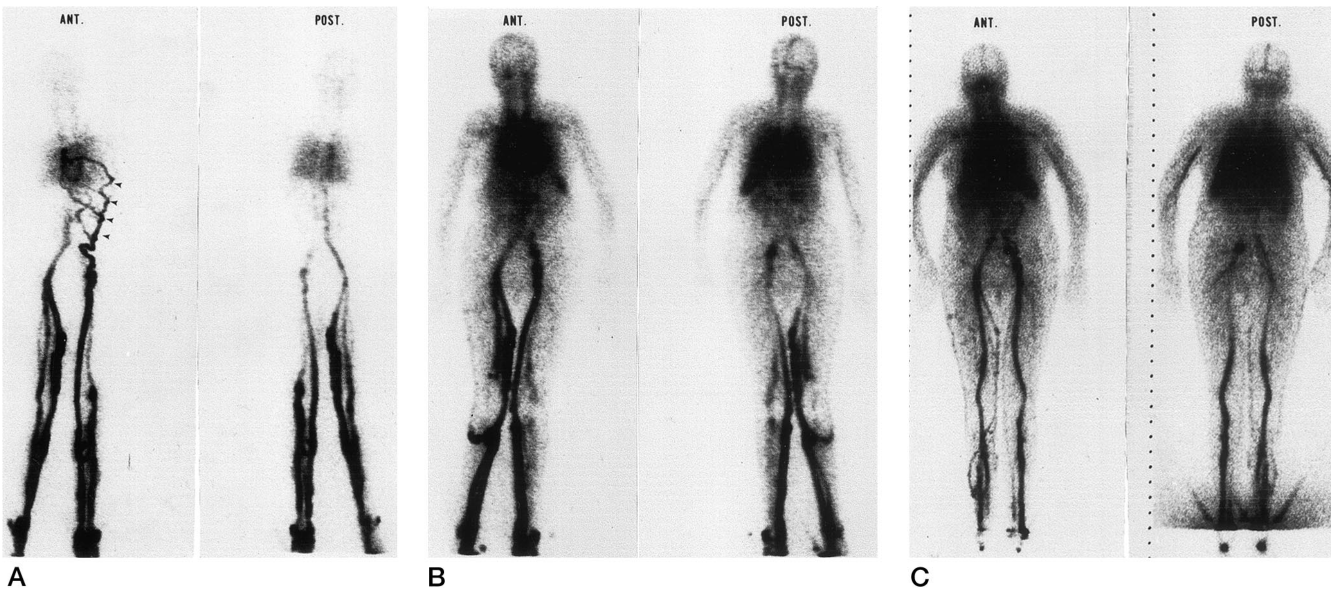

Fig. 3. Extensive DVT is apparent in the bilateral femoral veins, the left iliac vein, and the inferior vena cava in a 57-year-old woman with a history of varicose veins and phlebitis. (A) Initial intravenous radionuclide venography showed obstruction of the left iliac vein associated with the collateral circulation (arrowheads) extending from the proximal femoral vein upward to the left lateral portion of the abdomen and chest. Varicose veins are visualized along the medial aspect of both lower extremities. (B) Subcutaneous radionuclide venography performed 2 days later shows segmental obstruction in the right popliteal vein. Irregular narrowing of the left femoral and iliac veins with collaterals along the left side of the abdomen are evident. (C) Subcutaneous radionuclide venography at the 1-year follow-up shows improvement in the femoropopliteal DVT. Persistent narrowing and collaterals are visualized along the left iliac vein.

Discussion

Venography of the lower limbs by the subcutaneous approach was first introduced by Wu and Jong (4), who injected Tc-99m pertechnetate subcutaneously into the acupuncture points at the ankle and obtained regional images. The mechanism of venography after subcutaneous administration at acupuncture points was thought to be diffusion of the Tc-99m pertechnetate ion into the veins (5).

Tc-99m pertechnetate has the disadvantage of high background activity in the soft tissue, which obscures venous details. We have used the blood-pool agent Tc-99m in vivo tagged RBCs, which shows the venous structures more clearly. It is likely that after subcutaneous injection, Tc-99m pertechnetate diffuses into the subcutaneous soft tissue and veins. The pertechnetate ion diffuses across the red blood cell membranes, where it is reduced by the stannous pyrophosphate ions administered previously. The Tc-99m label binds to the beta chain of hemoglobin.

The application of tourniquets above the ankles during the first pass preferentially directs the radioactivity into the deep veins, thus facilitating their visualization. The first-pass and second-pass images are complementary in the interpretation of venographs. The first-pass whole-body images show the deep venous system of the lower extremities, iliac veins, and inferior vena cava. The second-pass whole-body images show varicose veins or superficial venous abnormalities. Because there are no superficial and deep venous systems in the upper extremities, the use of tourniquets is not necessary for the SCRV of the upper extremities.

Subcutaneous injection at the acupuncture points is not essential. Although it has been suggested that absorption of radioisotopes through acupuncture points is better than via nonacupuncture points (5), in our experience subcutaneous injection can be made at any point on the dorsum of the feet without adversely affecting the quality of the study. Subcutaneous radionuclide venography can also be used to visualize the venous system of the upper extremities and the superior vena cava. In addition, SCRV can be performed in amputees with injection at the amputation stump.

We used whole-body images instead of obtaining regional spot view images of the venous sections. This allowed us to view the entire venous tree of the lower extremities, iliac veins, and the inferior vena cava in one image and helped us to identify the continuous anatomic segments of both the superficial and deep veins. The whole-body images are technically easier to obtain than the regional images, which require manual repositioning of the camera heads.

Intravenous radionuclide venography and radiographic contrast venography often do not allow venous access for pedal intravenous administration, particularly in patients who are obese or have edema or small veins. Subcutaneous injections are much easier to perform. A subcutaneous injection can be made in a few seconds. Subcutaneous radionuclide venography can be particularly helpful when intravenous access is difficult.

The radiation dose to the skin at the site of subcutaneous injection is approximately 0.02 Gy/mCi (G. Kocheril, written personal communication, 1991), which is far less than the permissible safety level of radiation.

Recently, Tc-99m apcitide (Acutect, Diatide, Londonderry, NH) (6) was introduced to detect acute venous thrombosis in the lower extremities. Spiral computed tomography (7) and magnetic resonance imaging (8) angiography are evolving methods. Their roles in the diagnosis and management of venous and pulmonary thromboembolism are being investigated.

Subcutaneous radionuclide venography is a simple and accurate technique with high concordance to Doppler ultrasonography. Therefore, SCRV may be an ideal substitute in the evaluation of possible DVT. Subcutaneous radionuclide venography can detect thrombosis in the iliac veins and inferior vena cava, which are difficult to evaluate by DUS. The subcutaneous technique is particularly useful in patients with edema of the extremities or those who are obese, when obtaining pedal venous access is difficult or impossible. Subcutaneous venography also can be performed in the upper extremities and in amputation stumps.

Acknowledgments

The authors thank George Kocheril, Ph.D., for his help in calculating the estimated dose of skin radiation and the staff members of our departments for their technical support.

References

1. McLachlan MS, Thomson JG, Taylor DW, et al: Observer variations in the interpretation of lower limb venograms. AJR Am J Roentgenol 132:227, 1979.
2. Lensing AW, Prandoni P, Buller HR, et al: Lower extremity venography with iohexol: results and complications. Radiology 177: 503, 1990.
3. Gotway MB, Edinburgh KJ, Feldstein VA, et al: Imaging evaluation of suspected pulmonary embolism. Curr Probl Diagn Radiol 28:131, 1999.
4. Wu CC, Jong SB: Radionuclide venography of lower limbs by subcutaneous injection: comparison with venography by intravenous injection. Ann Nucl Med 3:125, 1989.
5. Wu CC, Chen MF, Lin CC: Absorption of subcutaneous injection of Tc-99m pertechnetate via acupuncture points and non-acupuncture points. Am J Chin Med 22:111, 1994.
6. Carretta RF: Scintigraphic imaging of the lower-extremity acute venous thrombosis. Advances in Therapy 15:315, 1998.
7. Loud PA, Grossman ZD, Klippenstein DI, Ray CE: Combined CT venography and pulmonary angiography: a new diagnostic technique for suspected thromboembolic disease. AJR Am J Roentgenol 170:951, 1998.
8. Evans AJ: Detection of DVT: prospective comparison of MRI and sonography. J Magn Reson Imaging 1:44, 1996.