Clinical Features and Diagnosis of Venous Thrombosis

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The clinical diagnosis of venous thrombosis is inaccurate because the clinical findings are both insensitive and nonspecific. The sensitivity of clinical diagnosis is low because many potentially dangerous venous thrombi are clinically silent. The specificity of clinical diagnosis is low because the symptoms or signs of venous thrombosis all can be caused by nonthrombotic disorders. For these reasons, a practical approach for the diagnosis of venous thrombosis is important. A current approach to the diagnosis of clinically suspected venous thrombosis favors the use of impedance plethysmography over Doppler ultrasonography as the main test for this disorder. This is because impedance plethysmography is precise and objective, whereas the interpretation of Doppler ultrasonography is subjective and requires considerable skill and experience to form reliable diagnoses.

The use of serial impedance plethysmography has been evaluated recently in a prospective study. The rationale of repeated impedance plethysmography evaluation is based on the premise that calf vein thrombi are only clinically important when they extend into the proximal veins, at which point detection with impedance plethysmography is possible. Therefore, by performing repeated examinations with impedance plethysmography in patients with clinically suspected venous thrombosis, it is possible to identify patients with extending calf vein thrombosis who can be treated appropriately. Impedance plethysmography is performed immediately on referral; if it is positive in the absence of clinical conditions that are known to produce falsely positive results, the diagnosis of venous thrombosis is established, and the patient is treated accordingly. If the result of the initial impedance plethysmography evaluation is negative, anticoagulant therapy is withheld, and impedance plethysmography is repeated the following day, again on day 5 to 7 and on day 10 to 14. If impedance plethysmography becomes positive during this time, a diagnosis of venous thrombosis is made and anticoagulant therapy is commenced.

Positive impedance plethysmography in the presence of conditions known to produce a false positive result (for example, congestive cardiac failure) should be confirmed by venography. If noninvasive tests for the diagnosis of venous thrombosis are not available, a clinical suspicion of venous thrombosis should be objectively confirmed or excluded by performing ascending venography.

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Clinical Diagnosis

Patients who present with a possible clinical diagnosis of deep vein thrombosis fall into three categories. The first and largest group consists of patients whose clinical manifestations are compatible with but not diagnostic of venous thrombosis. These patients should be investigated by reliable objective tests. In patients in the second group, a diagnosis of venous thrombosis can be excluded by careful history and examination, either because the clinical features clearly indicate the presence of another disorder (for example, arthritis, nerve compression, cellulitis) or the features are totally inconsistent with a diagnosis of deep vein thrombosis. The third group is the smallest, consisting of patients who present with phlegmasia cerulea dolens, whose

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Clinical features are so characteristic of venous thrombosis that a diagnosis can be confidently made on clinical grounds.

The unreliability of clinical diagnosis has been demonstrated by numerous studies (1-7) comparing clinical findings with the results of objective testing. We have now evaluated more than 1,000 patients with clinically suspected venous thrombosis by venography at our institution. Approximately 70% of all patients investigated did not have venous thrombosis and 30% had deep vein thrombosis. The prevalence of venous thrombosis was lower (only 20%) in patients who were not hospitalized at the time of presentation. Ninety percent of those patients who had venous thrombosis had thrombi in the proximal venous segments, and in only 10% were thrombi confined to the deep calf veins. The most common clinical symptoms were pain, tenderness and swelling. Pain occurred in 50% of the patients with thrombosis and in the same percent without; tenderness occurred in 75% of patients with thrombosis, but was not a useful differentiating sign because it also occurred in 50% of patients who did not have thrombosis. Other clinical features including night cramps, redness or cyanosis and dilated veins were relatively uncommon and occurred with approximately equal frequency in patients with and without thrombosis. Of interest was the finding that some patients with calf vein thrombosis had pain and tenderness that extended above the knee, and many patients with proximal vein thrombosis had symptoms confined to the calf.

Evaluation of Symptoms and Signs of Venous Thrombosis

Pain and tenderness. The severity of these clinical features bear no relation to the size or extent of thrombosis. Pain and tenderness associated with calf vein thrombosis is usually localized to the calf, but may extend along the anterior and medial aspects of the thigh and into the groin. Patients with proximal vein thrombosis may have pain that is localized to the calf, thigh or buttock. Patients with proximal vein thrombosis may also have more diffuse pain and tenderness of the calf and thigh.

Pain and tenderness is localized to the posterior tibial veins and the peroneal, popliteal, superficial femoral, common femoral and iliac veins. Pain and tenderness located away from these regions suggests that these features are not due to venous thrombosis.

Swelling. Swelling is due to edema, which may be caused either by obstruction of large proximal veins or by inflammation of perivascular tissues. The swelling may be marked and associated with obvious pitting edema or it may be mild and only detected as increased tissue turgor of calf muscles, which can be appreciated by carefully palpating the relaxed calf.

Homan's sign. Discomfort in the upper calf on forced dorsiflexion of the foot (Homan's sign) is a time-honored sign of venous thrombosis. It is both insensitive and nonspecific, being present in less than one-third of symptomatic patients with objectively documented deep vein thrombosis and in more than 50% of symptomatic patients who do not have venous thrombosis.

Venous distension and prominence of subcutaneous vessels. Venous dilation is a relatively uncommon and nonspecific manifestation of acute venous thrombosis. Prominence of superficial veins was recorded in 17% of symptomatic patients studied with venographically proved thrombosis and in approximately 20% of patients without thrombosis.

Discoloration. In patients with venous thrombosis, the leg may be pale, cyanosed or a reddish purple color. Marked pallor is an uncommon sign that may occur in the early stages of acute iliofemoral vein thrombosis; it is thought to be caused by arterial spasm. Cyanosis is caused by impaired venous return and stagnant anoxia and occurs in patients with obstructive iliofemoral vein thrombosis. Rarely, the leg may be diffusely red, hot and inflamed as a result of marked perivascular inflammation, and when this occurs, it may be difficult to differentiate from cellulitis.

Phlegmasia alba dolens. This is a term used to describe the "milk" leg or white leg caused by iliofemoral vein thrombosis with associated arterial spasm. The pulses may be weak or absent, and the leg is cold. There may be relatively little swelling in the early stages, but as the spasm wears off, the leg becomes swollen and takes on a mottled blue appearance.

Phlegmasia cerulea dolens. This is the term used to describe the marked swelling and cyanosis that occurs with obstructive iliofemoral vein thrombosis. The cyanosis is caused by extensive venous obstruction that in its most severe form not only involves most of the deep veins of the leg including the iliofemoral, superficial femoral and popliteal veins, but also the long saphenous veins and the venous tributaries that drain into the deep venous system. The obstruction to flow caused by venous occlusion and severe edema may impair arterial inflow and produce marked tissue ischemia. The leg is very painful, swollen, cyanosed and frequently covered with multiple petechial hemorrhages. The patient may be hypotensive due to marked pooling of blood in the affected leg, and there may be a mild thrombocytopenia probably due to platelet consumption. These features usually gradually subside when the patient is treated with heparin and confined to bed with the leg elevated.

Occasionally, however, the cyanosis may progress to venous gangrene, and rarely the affected leg may require amputation unless the obstruction is rapidly removed by thrombectomy or thrombolytic therapy.

Palpable cord. When a vessel that is easily palpable becomes thrombosed, it may be felt as an obvious cord.
The palpable cord of superficial phlebitis is readily distinguished from that found in deep vein thrombosis by its immediate subcutaneous location or its anatomic site, or both. This is an uncommon sign, and it may be difficult to differentiate a venous cord from edema or hemorrhage of the calf muscle.

**Differential Diagnosis of Symptoms and Signs of Venous Thrombosis**

Careful clinical documentation and follow-up study often uncover one of the following alternative diagnoses in approximately 70% of patients with clinically suspected venous thrombosis who have normal findings by objective tests (7). In many of these, the clinical diagnosis of the alternative condition only becomes obvious on follow-up examination after venous thrombosis has been excluded by objective testing.

**Differential diagnosis of pain or tenderness, or both.**

**Muscle strain or trauma.** Muscle ache may occur when the leg muscles have been subjected to unusual types or amounts of activity. Pain usually occurs in the calf, but also may involve the thigh. There may be tenderness, which at times can be quite severe. There is usually no swelling, but occasionally after very marked muscle exertion, the leg muscles may feel tense, heavy and turgid and may be associated with some calf and ankle swelling.

**Muscle tear.** Fibers of the gastrocnemius or plantaris muscle may be torn as a result of sudden contraction of calf muscles during plantar flexion. Typically, the muscle tear occurs when the foot is suddenly flexed against resistance (for example, when the individual begins to run). There is a sudden severe pain in the back of the leg, which may simulate a direct blow to the calf muscles. Examination reveals local tenderness, and it may be possible to palpate the localized swelling caused by hematoma. If there is a complete muscle tear or muscle avulsion at its attachment to the tendon or tendon rupture, it may be possible to palpate the gap produced by the tear.

After a number of days, a bruise may appear either in the posterior aspect of the medial malleolus or in the anteromedial part of the leg, but this is not invariable. Pain and tenderness may continue for a number of days or even weeks and may be very severe, particularly during any activity involving plantar flexion.

**Direct muscle or leg trauma.** Direct muscle trauma sustained during a vigorous sporting activity or during an accident may produce delayed pain and swelling due to hematoma and inflammation. This can present considerable diagnostic difficulty because venous thrombosis is a well recognized complication of leg trauma.

**Spontaneous muscle hematoma.** Occasionally, patients who are being treated with anticoagulants develop pain and swelling of the leg without obvious trauma or after mild trauma. It may be difficult to decide if these symptoms are caused by hemorrhage or recurrent venous thrombosis.

**Arterial insufficiency.** Arterial insufficiency is not usually confused with venous thrombosis because the clinical features of the two conditions are sufficiently distinctive.

**Neurogenic pain.** Compression of the sciatic nerve or lateral cutaneous nerve of the thigh produces leg pain, which is easily differentiated from venous thrombosis.

**Ruptured Baker’s cyst.** When a Baker’s cyst or popliteal cyst ruptures, the fluid contents track down the tissue planes between the calf muscle and produce an inflammatory response of pain, tenderness, heat and swelling, which may simulate the clinical features of acute venous thrombosis. In most cases, there is a history of arthritis of the knee or of traumatic or operative injury to the knee. Occasionally, this condition may occur without a past history of knee trauma or arthritis or there may be intermittent pain or swelling in the region of the popliteal fossa months or years preceding the acute episode. On examination of the knee, there may be evidence of arthritis or previous surgery or trauma and there may be a fullness of the popliteal fossa on the affected side. The diagnosis can be readily established by arthrography, but because venous thrombosis and ruptured Baker’s cyst may occur in the same patient, it may be necessary to specifically exclude venous thrombosis before attributing the acute clinical features to a ruptured Baker’s cyst.

**Arthritis of the knee or ankle joint or Achilles tendonitis.** Deep pain and swelling produced by arthritis of the knee or ankle or by inflammation of Achilles tendon may occasionally be confused with venous thrombosis.

**Inflammation of other tissues in the legs.** Cellulitis, lymphangitis, vasculitis, myositis and panniculitis may produce pain and tenderness of the leg. These conditions can usually be differentiated from venous thrombosis on clinical grounds alone when they are fully developed, but they may occasionally be confused with venous thrombosis in their early stages or if they are atypical.

**Varicose veins.** Patients with varicose veins frequently have pain and tenderness in the calf when they have been standing for a period of time. Occasionally, an obvious superficial varicose vein becomes inflamed and thrombosed and the pain is more severe. When these clinical features occur in association with more diffuse pain in the calf or with edema of the leg, it may be difficult to exclude an associated deep vein thrombosis without performing objective diagnostic tests.

**Pregnancy and patients taking an oral contraceptive pill.** Pain and tenderness in the leg may occur in pregnancy or in individuals taking an estrogen-containing oral contraceptive pill. Occasionally, the pain and tenderness in pregnant patients are associated with quite marked swelling of the calf or thigh, which may be unilateral. In many cases, these symptoms and signs are not due to venous thrombosis. The
cause of pain and tenderness is uncertain, but may be due to venous dilation caused by estrogens, inflammation of the vein wall without associated thrombosis or muscle cramps. Unilateral leg swelling occurring in pregnancy may also be caused by compression of the iliac vein by the enlarged uterus.

**Differential Diagnosis of Leg Swelling With or Without Associated Pain and Tenderness**

A number of conditions other than venous thrombosis can produce edema or swelling of the leg with or without associated pain and tenderness.

**Compression of the iliac vein.** External compression of the iliac vein by tumor, hematoma or abscess may be impossible to differentiate from acute iliofemoral vein thrombosis on clinical grounds alone. The noninvasive tests such as plethysmography and Doppler ultrasound are frequently positive, and even a venogram may be misinterpreted as being positive (falsely) if either a cutoff or abnormal collateral vessels are accepted as evidence of deep venous thrombosis. Definitive differentiation between acute venous thrombosis and external compression can be made when the venogram shows either a characteristic smooth symmetric indentation characteristic of the external compression or an intraluminal filling defect characteristic of acute thrombosis.

Compression of the left common iliac vein by the right common iliac artery may produce chronic swelling that is usually painless or it may produce acute exacerbations of swelling that last for hours or days and then either completely or only partly subside. The leg swelling, which may be intermittent, is thought to be due to impaired venous return that occurs as a result of fibrosis and narrowing of the left common iliac vein where it is crossed by the iliac artery.

**The postphlebitic syndrome.** Typically, patients with the postphlebitic syndrome have long-standing symptoms of swelling associated with an ache in the calf that occurs on standing or leg exercise. Some of these patients present with repeated episodes of more severe swelling and pain, which may be associated with calf tenderness, and in these, it may be difficult to exclude a complicating acute venous thrombosis as the cause of the symptoms. The majority of episodes of acute pain, tenderness and swelling that occur in patients with the postphlebitic syndrome are not caused by acute venous thrombosis and do not require anticoagulant treatment. These acute exacerbations are probably caused by progressive venous dilation, which produces further valvular incompetence and so results in a sudden increase in venous pressure in the calf veins.

**Leg immobilization.** Swelling may occur in patients who have their leg immobilized in a plaster cast for a number of weeks or months or who have limb paralysis either because of stroke, paralytic poliomyelitis or spinal cord injury. Not all of the episodes of swelling are caused by venous thrombosis, although it is well recognized that thrombosis frequently complicates leg immobilization. The mechanism of swelling is uncertain but may be due to alterations in venous tone or capillary permeability.

**Leg inflammation.** Inflammatory conditions of the leg such as cellulitis, panniculitis, erythema nodosum and severe myositis may cause diffuse swelling, but these can usually be differentiated from venous thrombosis because of other associated characteristic features.

**Lymphedema.** Leg swelling is a characteristic feature of impaired lymphatic drainage. In its severest form, lymphedema is nonpitting and brawny, but milder forms of lymphedema may be pitting. When lymphedema occurs as a result of a congenital defect in the lymphatic channels, it is rarely difficult to differentiate from venous thrombosis, but when it is acquired as a result of trauma to the lymphatic vessels (for example, after hip surgery, leg fracture or from compression of major lymphatic channels by leg plaster), it may be impossible to distinguish from edema caused by venous obstruction without performing objective tests.

**Lipedema.** This condition occurs in female patients often becoming obvious in adult life. The leg swelling is due to accumulation of subcutaneous fat and is, therefore, chronic and not associated with pitting or signs of inflammation. It is readily distinguished from edema caused by venous thrombosis by examination of the legs.

**Self-induced edema.** Occasionally, factitious syndromes may simulate venous thrombosis. Pain, tenderness and swelling may be produced by self-inflicted injury to the legs, application of a venous tourniquet or other bizarre mechanisms.

**Diagnosis of Venous Thrombosis Using Objective Tests**

**Venography**

Venography is accepted as the reference standard for the diagnosis of venous thrombosis. Ascending venography outlines the entire deep venous system of the legs, including the external and common iliac veins in most patients. However, common femoral or iliac venography may be needed if the external and common iliac veins are not properly visualized by the ascending technique or if the inferior vena cava must be outlined.

**Ascending venography.** The aim of venography is to outline the deep venous system of the legs by injecting radiopaque contrast medium into a dorsal foot vein. The quality of venography can be improved by injecting a large volume of dye and by careful attention to a number of technical details. Filling of the calf veins is improved if the patient is examined while tilting the table foot to 40° from the horizontal and by avoiding weight-bearing on the leg.
being examined. The use of fluoroscopic monitoring during injection makes it possible to identify suspicious areas and so reduce the risk of confusing a filling defect due to a thrombus with a flow artifact produced when opacified blood in the major venous channel is mixed with nonopacified blood flowing in from a tributary. This type of artifact can often be distinguished from an intraluminal defect by performing a Valsalva maneuver while contrast agent is being injected under fluoroscopy.

The use of an ankle tourniquet to promote filling of the deep venous system by obstructing the superficial veins is controversial. Some authorities consider that it may prevent adequate filling of the deep veins and that it is unnecessary when a tilt table is used. The profunda femoral vein and the internal iliac veins are not usually adequately visualized by ascending venography, even when a Valsalva maneuver is performed.

**Iliac venography.** Visualization of the external and common iliac veins and the inferior vena cava can be achieved by injecting contrast medium directly into the common femoral vein (13), by intrasosseous injection (13) or by retrograde injection by means of a catheter passed through the right atrium and inferior vena cava (14). The simplest of these techniques is femoral vein puncture, which is usually performed by entering the femoral vein on the unaffected side and passing a catheter into the common iliac vein of the affected side using the Seldinger technique. The intrasosseous technique is very painful and requires a general anesthetic; it has been reported to produce fatal fat embolism (15). Retrograde catheterization is more complex than femoral vein puncture, but allows the internal iliac system to be examined and may be combined with pulmonary angiography.

In practice, ascending venography with careful attention to technique provides adequate visualization of the deep veins of the calf, the popliteal vein, the femoral vein and the external and common iliac veins. In occasional patients, direct puncture of the femoral vein is required to clarify the nature of a suspicious defect in the common femoral or iliac veins.

**Normal anatomy of venous system.** The venous system in the leg consists of three pairs of deep calf veins; the posterior tibial, the peroneal and anterior tibial veins, the soleal and gastrocnemius plexus of veins and the superficial venous system (Fig. 1). The soleal plexus drains into the posterior tibial vein, and the gastrocnemius plexus drains into the popliteal vein. The popliteal vein becomes the superficial femoral vein at the junction of the proximal part of the popliteal fossa and the adductor canal in the thigh. The superficial femoral vein is joined by the deep femoral vein in the upper thigh to form the common femoral vein, which becomes the external iliac vein at the level of the inguinal ligament. The external iliac vein is joined by the internal iliac vein in the pelvis to form the common iliac vein, and the common iliac veins converge to form the inferior vena cava. The superficial venous system consists of two major veins, the long and short saphenous veins, which drain into the common femoral and popliteal veins, respectively. The superficial system is connected with the deep venous system by communicating veins that contain valves that direct flow from the superficial into the deep system. A number of variations of the deep venous system are recognized, the most common of which are accessory popliteal veins, bifid superficial femoral veins and an abnormally high or low origin of the popliteal vein.

**Criteria for the diagnosis of venous thrombosis.** The most reliable criterion for the diagnosis of acute deep vein thrombosis is the presence of an intraluminal filling defect that is constant in all films and is seen in a number of
of a segment of the deep venous system, with abrupt termination of the column of contrast medium at a constant site below the segment and reappearance of the contrast medium at a constant site above the segment, and 2) nonfilling of the deep venous system above the knee, despite adequate venographic technique. The likelihood that these appearances are due to venous thrombosis is increased if the abnormality is associated with the presence of abnormal collateral vessels. The presence of a constant intraluminal filling defect is usually considered diagnostic of acute venous thrombosis, while the other two abnormalities or variations thereof may be caused by incomplete mixing of contrast medium with blood, external compression of a vein or injecting the contrast medium too far proximally in the foot.

**Pitfalls of venography.** Venography is a difficult technique that requires considerable experience to execute and interpret adequately. Unless care is taken to inject the dye into the dorsal foot vein, there may be nonfilling of calf veins, which is incorrectly interpreted either as caused by a thrombus because the vein in not filled or as normal because a filling defect is not seen. Also, the common femoral, external iliac and common iliac veins may be inadequately filled by ascending venography; once again, there are two common errors: 1) failure to detect even a large nonobstructive thrombus in the common femoral region because flow into the external iliac or common iliac vein appears to be adequate, although filling of the common femoral vein is suboptimal; and 2) incorrectly diagnosing venous thrombosis because of a streaming effect in the common femoral or iliac veins caused by inadequate opacification. Misinterpretation of an inadequate venogram (usually in the direction of a falsely positive diagnosis) is becoming an important problem with the increasing use of venography in centers without a special interest or expertise in this technique.

**Side effects of venography.** Venography may produce pain in the foot while the dye is being injected or delayed pain in the calf 1 or 2 days after the injection (9). Both the early and delayed pain associated with injection of contrast medium are probably related to direct damage of the venous endothelium by hyperosmolar radiopaque contrast medium (9). This may produce superficial phlebitis, but in our experience, only 1 to 2% of patients with a negative venogram develop clinically significant venous thrombosis. Others (16) reported a higher frequency of postvenography positive fibrinogen leg scan findings; these differences could be due to differences in venographic technique or in the patient population under study. The frequency of postvenography positive leg scan results is reduced by diluting the contrast material from 70 to 45% or by using isotonic contrast material.

**Other less common complications of venography** include hypersensitivity reactions to the radiopaque dye and local skin and tissue necrosis due to extravasation of contrast at the site of injection (9).

**Noninvasive Tests for the Diagnosis of Venous Thrombosis**

A large number of noninvasive or less invasive techniques for the diagnosis of venous thrombosis have recently been introduced. Of these, three have been most carefully evaluated: iodine-125–fibrinogen leg scanning, (17,18), impedance plethysmography (4,19–22) and Doppler ultrasonography (23–26). Each of these tests has different applications, depending on whether the patient has clinically suspected venous thrombosis or is being screened because of a high risk of developing venous thrombosis. Other diagnostic techniques have been evaluated to a limited extent, including other forms of plethysmography (8), thermography (27) and various isotopic methods (28,29). Sensitive blood tests that detect intravascular fibrin formation and lysis are currently also undergoing clinical evaluation.

**Iodine-125–Fibrinogen Leg Scanning**

**Principles.** The diagnosis of venous thrombosis by radiiodine-labeled fibrinogen scanning depends on incorporation of circulating labeled fibrinogen as fibrin into the thrombus, which is then detected by measuring the increase in overlying surface radioactivity with an isotope detector (30,31). Fibrinogen scanning can be used for screening patients who are at a high risk of developing venous thrombosis. It can also be used to complement impedance plethysmography to confirm or exclude the diagnosis of clinically suspected venous thrombosis (33,34). Fibrinogen leg scanning detects over 90% of acute calf vein thrombi (17,18,35,36), but only between 60 and 80% of proximal vein thrombi, depending on their location. Fibrinogen scanning is relatively insensitive in the upper thigh and insensitive to venous thrombi in the pelvis (35,36).

The use of radiofibrinogen carries a theoretical risk of transmitting serum hepatitis, but this risk has been eliminated for practical purposes by preparing fibrinogen from a small number of carefully selected donors who have not transmitted hepatitis during years of frequent blood donations and who are hepatitis-associated antigen-free.

**Scanning technique.** Patients are scanned with an isotope detector probe with their legs elevated 15° above the horizontal to minimize venous pooling in the calf veins. Readings are taken over both legs and recorded as a percent of the surface radioactivity measured over the heart. The surface radioactivity is recorded over the femoral vein at 7 to 8 cm intervals, starting below the inguinal ligament, and then at similar intervals over the medial and posterior aspects of the popliteal fossa and calf. Venous thrombosis is sus-
pected if there is an increase in the radioactive reading of more than 20% at any point compared with the readings over the adjacent points on the limb, with the same point on the previous day or with the readings over the corresponding point on the opposite leg. Venous thrombosis is diagnosed if the scan remains abnormal at repeated examination and the abnormality persists for more than 24 hours. The technique is simple and rapid so that up to 15 to 20 patients can be scanned each day by one technologist. Scanning time is limited by the in vivo survival of fibrinogen; after a single injection of 100 μCi, counting is possible for about 7 days. The thyroid gland is first blocked by potassium iodide (100 mg), which is given orally to prevent excessive uptake of radioactive iodide. If the patient is still at risk for developing venous thrombosis after 7 days, the injections can be repeated at intervals to extend the scanning time for the period of high risk.

Potential limitation of iodine-125-fibrinogen test. As mentioned, the test is insensitive to thrombi in the pelvic veins (35, 36) because iodine-125 is a relatively low energy gamma emitter and is unreliable in the upper thigh because of the close proximity of the bladder, which frequently contains radioactive urine, and because of the presence of large veins and arteries that produce an increase in the background count. Iodine-125-fibrinogen is contraindicated during pregnancy and lactation and should not be used in young patients unless very definite indications exist. It crosses the placenta and a small amount enters the fetal circulation (36). A study (36) in postpartum women has shown that radioactivity also appears in breast milk.

Causes of discrepancy between results of leg scanning and venography. A leg scan abnormality in the presence of a normal venogram may be due to hematoma, inflammation, uptake of radioactivity by a surgical wound or nonvisualization of the thrombus by the venogram. A false negative scan may occur in patients with an old venous thrombus that is no longer taking up fibrinogen, if a thrombus forms after most of the radioactive fibrinogen has been cleared from the circulation, if the thrombus is too small to be detected by leg scanning or if the thrombus is isolated in a common femoral or iliac vein. Iodine-125-fibrinogen leg scanning should never be used as the only diagnostic test in patients with clinically suspected venous thrombosis because it fails to detect many high proximal vein thrombi and because there may be a delay of hours or even days before sufficient amounts of fibrinogen accumulate in the thrombus to make the test positive.

Impedance Plethysmography

Principles. Plethysmography is a noninvasive method that detects volume changes in the leg. Several plethysmographic techniques, including impedance plethysmography (19–21), strain gauge plethysmography (8) and air cuff plethysmography (37) have been used to detect venous thrombi; impedance plethysmography has been the most thoroughly evaluated.

Impedance plethysmography is sensitive and specific for thrombosis of the popliteal, femoral or iliac veins (proximal veins), but is relatively insensitive to calf vein thrombosis. The principle of the method is based on the observation that blood volume changes in the calf, produced by maximal respiratory effort or inflation and deflation of a pneumatic thigh cuff, result in changes in electrical resistance (impedance). These changes are reduced in patients with obstruction (for example, by thrombosis) of the popliteal or more proximal veins. The original method (22) which used maximal respiratory effort to produce venous occlusion, had shortcomings because sick patients were frequently unable to cooperate sufficiently for the test to be reliable. Therefore, the test was modified by using a pneumatic cuff to temporarily occlude the venous outflow (occlusive impedance plethysmography) (19, 21). This modified test is sensitive and specific for proximal vein thrombosis.

Technique. Occlusive impedance plethysmography is performed with the patient supine and with the lower limb elevated 25 to 30°, the knee flexed 10 to 20° and the ankle 8 to 15 cm higher than the knee. A pneumatic cuff, 15 cm in width, is applied to the midthigh and inflated to 45 cm H₂O, thereby occluding venous return. After a predetermined period of time, the cuff is rapidly deflated and the changes in electrical resistance (impedance) resulting from alterations in blood volume distal to the cuff are detected by circumferential calf electrodes and recorded on an electrocardiographic paper strip. The changes in impedance during cuff inflation and deflation are measured, and both the total increase during cuff inflation and the decrease occurring in the first 3 seconds of deflation are plotted on a two-way impedance plethysmographic graph. The graph includes a “discriminant line” that was developed by discriminant function analysis to provide optimal separation of the impedance plethysmographic results in the normal and abnormal in terms of proximal vein thrombosis (Fig. 2(19).

The accuracy of impedance plethysmography is critically dependent on the degree of venous filling during cuff occlusion (38). Venous filling is frequently suboptimal after only 45 seconds of cuff occlusion (as was originally recommended), and this may compromise the accuracy of the test. Venous filling is improved by prolonging the period of cuff occlusion from 45 seconds to 2 minutes and by introducing repeated sequential testing. These maneuvers increase venous filling and the sensitivity and specificity of the test. It was noted that as venous filling increased, there was a corresponding increase in venous emptying in normal legs, but not in legs with proximal vein thrombosis, so that...
the regression lines relating venous filling and emptying (Fig. 3) in normal and abnormal legs diverged significantly (p < 0.001). Thus, increased venous filling increases the separation between normal and abnormal impedance plethysmographic results and enhances the accuracy of the test.

Unrecognized contraction of leg muscles in patients who are apprehensive or have postoperative pain is a recognized cause of falsely positive impedance plethysmographic results. The inexperienced technician may have difficulty in distinguishing an abnormal impedance plethysmographic result caused by venous thrombosis from that caused by isometric muscle contraction, which can be detected directly by electromyography. The use of an electromyographic device in conjunction with the impedance plethysmograph is clinically feasible and should be a helpful addition when the test is performed by an inexperienced technician (39).

Causes of discrepancy between impedance plethysmography and venography. Impedance plethysmography only detects thrombi that produce obstruction to venous outflow and, therefore, will not detect most calf vein thrombi. It may also overlook small, nonocclusive proximal vein thrombi. The test may also be negative when proximal vein thrombosis is associated with well developed collateral vessels.

The impedance test does not distinguish between thrombotic and nonthrombotic obstruction to venous outflow. Thus, falsely positive results may be obtained if a patient is positioned incorrectly or inadequately relaxed with constriction of veins by contracting leg muscles, if the vein is compressed by an extravascular mass or if venous outflow is impaired by raised central venous pressure. Reduced arterial inflow to the limb because of severe obstructive arterial disease can also lead to reduced outflow and, hence, produce a falsely positive result.

Clinical results. A number of studies (8,12,39) have evaluated impedance plethysmography in patients with clinically suspected venous thromboembolism. Wheeler et al. (22) compared results of impedance plethysmography with results from venography in 168 legs. Impedance plethysmographic findings were normal in 106 of 108 legs that were normal by venography, and abnormal in 40 of 41 legs with venographically demonstrated recent thrombi of the popliteal, femoral or iliac veins (proximal vein thrombosis). There were 19 calf vein thrombi detected by venography, but plethysmography identified only 3. Johnston et al. (20), using a similar technique, detected all 20 proximal vein thrombi with impedance plethysmography, which was normal in 40 of 44 legs without thrombosis and abnormal in only 5 of 15 legs with calf vein thrombi. In a study of 346 patients with suspected venous thrombosis, Hull et al. (38) reported that impedance plethysmographic results were abnormal in 124 of 133 limbs with proximal vein thrombosis (sensitivity 93%). Seventy-three of 88 limbs with calf vein thrombosis had normal impedance plethysmography. Abnormal impedance plethysmography was found in the absence of thrombosis in 11 of 397 legs, the majority of which had clearly recognizable clinical conditions known to produce falsely positive results.

Other investigators have reported similar high values for sensitivity and specificity of impedance plethysmography for symptomatic venous thrombosis (Table 1). Thus, in patients with clinically suspected venous thrombosis, a positive impedance plethysmographic result can be used to make therapeutic decisions in the absence of clinical conditions that are known to produce falsely positive results (for example, congestive heart failure, severe peripheral vascular disease and local leg muscle tension). A normal result essentially excludes a diagnosis of proximal vein thrombosis, but does not exclude diagnosis of calf vein thrombosis.

Causes of discrepancy between impedance plethysmography and venography. Impedance plethysmography only detects thrombi that produce obstruction to venous outflow and, therefore, will not detect most calf vein thrombi. It may also overlook small, nonocclusive proximal vein thrombi. The test may also be negative when proximal vein thrombosis is associated with well developed collateral vessels.

The impedance test does not distinguish between thrombotic and nonthrombotic obstruction to venous outflow. Thus, falsely positive results may be obtained if a patient is positioned incorrectly or inadequately relaxed with constriction of veins by contracting leg muscles, if the vein is compressed by an extravascular mass or if venous outflow is impaired by raised central venous pressure. Reduced arterial inflow to the limb because of severe obstructive arterial disease can also lead to reduced outflow and, hence, produce a falsely positive result.

Clinical results. A number of studies (8,12,39) have evaluated impedance plethysmography in patients with clinically suspected venous thromboembolism. Wheeler et al. (22) compared results of impedance plethysmography with results from venography in 168 legs. Impedance plethysmographic findings were normal in 106 of 108 legs that were normal by venography, and abnormal in 40 of 41 legs with venographically demonstrated recent thrombi of the popliteal, femoral or iliac veins (proximal vein thrombosis). There were 19 calf vein thrombi detected by venography, but plethysmography identified only 3. Johnston et al. (20), using a similar technique, detected all 20 proximal vein thrombi with impedance plethysmography, which was normal in 40 of 44 legs without thrombosis and abnormal in only 5 of 15 legs with calf vein thrombi. In a study of 346 patients with suspected venous thrombosis, Hull et al. (38) reported that impedance plethysmographic results were abnormal in 124 of 133 limbs with proximal vein thrombosis (sensitivity 93%). Seventy-three of 88 limbs with calf vein thrombosis had normal impedance plethysmography. Abnormal impedance plethysmography was found in the absence of thrombosis in 11 of 397 legs, the majority of which had clearly recognizable clinical conditions known to produce falsely positive results.

Other investigators have reported similar high values for sensitivity and specificity of impedance plethysmography for symptomatic venous thrombosis (Table 1). Thus, in patients with clinically suspected venous thrombosis, a positive impedance plethysmographic result can be used to make therapeutic decisions in the absence of clinical conditions that are known to produce falsely positive results (for example, congestive heart failure, severe peripheral vascular disease and local leg muscle tension). A normal result essentially excludes a diagnosis of proximal vein thrombosis, but does not exclude diagnosis of calf vein thrombosis.
Doppler Ultrasonography

Principles. Doppler ultrasound flowmeter examination has been evaluated as a noninvasive diagnostic test in patients with clinically suspected deep vein thrombosis (1,25,26). In expert hands, Doppler ultrasound is a sensitive method for detecting proximal vein thrombosis, but is less sensitive to calf vein thrombosis.

The Doppler ultrasound flow velocity detector contains an oscillator that activates a piezoelectric crystal in a handheld probe so that it emits an ultrasound beam at a frequency of 5 MHz. This beam is directed percutaneously at an underlying vein, where it is reflected from blood cells. If the blood is stationary, the frequency of the reflected beam is identical with that of the incident beam and no sound is recorded. On the other hand, if the particles of blood are moving, the beam is reflected at a changed frequency (the Doppler shift), which is proportional to the velocity of flow. This difference in frequency between the incident and reflected ultrasound beam is received by a second piezoelectric crystal in the probe and amplified into an audible signal or flow sound (25,26).

Evolution of the positive impedance plethysmogram.

Knowledge of the frequency with which abnormal impedance plethysmographic result returns to normal is of practical clinical importance because patients with proximal vein thrombosis frequently develop symptoms in the affected leg during or after long-term anticoagulant therapy. In patients who return with recurrent leg symptoms after an episode of deep vein thrombosis, objective testing is required to differentiate acute recurrent deep vein thrombosis from the postphlebitic syndrome or nonthrombotic causes for leg symptoms. A normal baseline impedance plethysmogram before presentation greatly simplifies the diagnostic process (see the section on Diagnosis of Acute Recurrent Deep Vein Thrombosis).

We recently completed a prospective cohort study (40) of 131 patients with proximal vein thrombosis who had an abnormal impedance plethysmographic result returns to normal is of practical clinical importance because patients with proximal vein thrombosis frequently develop symptoms in the affected leg during or after long-term anticoagulant therapy. The impedance plethysmographic result returns to normal is of practical clinical importance because patients with proximal vein thrombosis frequently develop symptoms in the affected leg during or after long-term anticoagulant therapy. The impedance plethysmographic result returns to normal at the end of 3 months (long-term) anticoagulant therapy. On the basis of these findings, we perform a baseline impedance plethysmogram at the time of discontinuing anticoagulant therapy. The impedance plethysmogram at the time of discontinuing anticoagulant therapy at 3 months in all patients with proximal vein thrombosis.

Table 1. Sensitivity and Specificity of Occlusive Impedance Plethysmography for Proximal Vein Thrombosis in Patients With Symptomatic Venous Thrombosis

<table>
<thead>
<tr>
<th>Investigator, Year (Reference)</th>
<th>Sensitivity* (%)</th>
<th>Specificity† (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hull et al., 1976 (19)</td>
<td>93 (124 of 133)</td>
<td>97 (386 of 397)</td>
</tr>
<tr>
<td>Hull et al., 1977 (85)</td>
<td>98 (59 of 60)</td>
<td>95 (108 of 114)</td>
</tr>
<tr>
<td>Toy and Schrier, 1978 (88)</td>
<td>94 (15 of 16)</td>
<td>100 (9 of 9)</td>
</tr>
<tr>
<td>Flanagan et al., 1978 (89)</td>
<td>96 (52 of 54)</td>
<td>95 (93 of 98)</td>
</tr>
<tr>
<td>Hull et al., 1978 (38)</td>
<td>92 (155 of 169)</td>
<td>96 (305 of 317)</td>
</tr>
<tr>
<td>Gross and Burney, 1979 (90)</td>
<td>100 (9 of 9)</td>
<td>94 (32 of 34)</td>
</tr>
<tr>
<td>Cooperman et al., 1979 (91)</td>
<td>87 (20 of 23)</td>
<td>96 (72 of 75)</td>
</tr>
<tr>
<td>Wheeler, 1980 (92)</td>
<td>98 (88 of 90)</td>
<td>92 (191 of 209)</td>
</tr>
<tr>
<td>Hull et al., 1981 (87)</td>
<td>95 (74 of 78)</td>
<td>98 (157 of 160)</td>
</tr>
<tr>
<td>Peters et al., 1982 (93)</td>
<td>92 (36 of 39)</td>
<td>93 (115 of 124)</td>
</tr>
</tbody>
</table>

*Proportion of patients with positive venograms who had a positive impedance plethysmogram. †Proportion of patients with normal venograms who had a normal impedance plethysmogram. (Adapted from Hull R, et al. [1].)

Technique

The Doppler ultrasound examination is performed with the patient lying comfortably in bed in the semiupright position. Care should be taken to remove garments that constrict venous outflow because they may interfere with venous return. The common femoral vein is located by first placing the probe over the common femoral artery, which can be easily identified, and then moving it medially until the low pitched sound typical of venous flow is heard. The intensity of this low pitched sound changes with respiration and has been described as a "wind storm." When the abdomen is compressed above the inguinal ligament, respiratory variation in the flow sound is abolished; when abdominal compression is released, there is an augmented sound as blood flow in the veins suddenly increases. The thigh and calf are gently squeezed, both maneuvers producing an augmented sound due to sudden acceleration of venous flow. Patency of the superficial femoral vein can be demonstrated by moving the probe distally along this vein and repeating calf and distal thigh compression. Augmentation of flow is also produced by sudden release of thigh compression proximal to the probe. The probe is then placed over the posterior tibial vein, which is located by identifying the posterior tibial artery. Augmentation of flow is produced by squeezing the foot and by suddenly releasing proximal calf compression.

Positive Doppler examination. The Doppler flowmeter is highly sensitive to occluding thrombi in the popliteal and more proximal veins, but less sensitive to nonocclusive proximal thrombi and calf thrombi. Obstruction to venous outflow may result in loss of phasicity of the venous signal, and may produce a continuous venous signal due to loss of the normal respiratory fluctuation. In addition, augmentation of the venous signal, which normally occurs as a result of compression of the limb distal to the probe, or to release of compression proximal to the probe, may be either absent, diminished, or high-pitched and of short duration.

Clinical results. Several carefully performed studies (25,26) comparing Doppler flowmeter examination with
venography show that this technique, as mentioned, is sensitive to proximal vein thrombosis but less sensitive to calf vein thrombosis. Advantages of this technique are that it can be performed more conveniently and rapidly than can impedance plethysmography and that it is less expensive. The disadvantages of Doppler ultrasonography are that its interpretation is subjective and the test requires considerable skill and experience to perform reliably. Although this is a major limitation, in skilled hands, it is almost as sensitive to symptomatic proximal vein thrombosis as is impedance plethysmography and it is more sensitive to symptomatic calf vein thrombosis, detecting approximately 50% of such patients.

Doppler ultrasonography is more reliable than impedance plethysmography for detecting proximal vein thrombosis in patients with raised central venous pressure or arterial insufficiency, and has the advantage that it can be used in patients who have their legs in plaster or who are in traction.

Other Isotopic Techniques for the Diagnosis of Venous Thrombosis

A number of radioisotopic techniques have been used in the last 15 years to assist in the diagnosis of deep vein thrombosis, including radionuclide venography using technetium-99m-labeled macroaggregated albumin or human albumin microspheres (40–57), technetium-99m-labeled red blood cells (58–61), streptokinase, urokinase and plasmin, each labeled with technetium-99m (62–68), technetium-99m sulfur colloid (69–71) and indium-111-labeled platelets (72–78).

Radionuclide venography-technetium-99m macroaggregated human albumin or human albumin microspheres. The isotope, technetium-99m, is widely available. Kits are available commercially for labeling both macroaggregated albumin and human albumin microspheres. The technetium-99m macroaggregated albumin is injected in the dorsal veins of the feet on each side, tourniquets are usually used and a variety of imaging techniques have been described in relation to various schedules of injection. Images of the passage of the isotope up the legs, thighs and pelvis are made, followed by static imaging looking for “hot spots.” Exercising the legs is done to encourage unattached collections of the technetium-99m macroaggregated albumin to be cleared from the veins.

Normal studies show a continuous flow of the tracer from the ankle to the inferior vena cava. The static images obtained after exercising the limbs show only background activity. Abnormal studies with thrombi show delay in flow of the tracer up the limb. With occlusion of the deep venous system of the legs or pelvis, passage of the tracer through the superficial veins or collateral veins can be seen. Static images show “hot spots.”

Other causes of increased radioactivity in the legs have been identified. These include venous stasis in varicose veins, trapping of tracer behind large valves or by venous occlusion with poor collateral flow, recent venous injury, venous catheterization, the use of contrast venography, superficial isotope contamination and bladder accumulation from excretion of tracer (42,43).

Early studies (41,44,48,50,52,55–57) comparing radionuclide venography with contrast venography showed sensitivities of 84 to 92%, specificities of 67 to 97%, positive predictive values of 64 to 91% and negative predictive values of 90 to 93%.

Recent studies comparing radionuclide venography with contrast venography carried out prospectively and interpreted “blindly” have helped clarify the clinical use of radionuclide venography. The reliability of this test in diagnosing venous thrombosis in the calf and popliteal veins is so poor that it should not be considered for this purpose. However, for thromboses in the thigh and, particularly for those in the iliac veins, reliability is much improved. For thromboses in the veins in the thigh, sensitivity was 75% and specificity was 99%; for thromboses in the iliac veins sensitivity was 100% and specificity 100% (41).

Technetium-99m-labeled red blood cells. Red blood cells are readily labeled in vivo with technetium-99m pertechnetate by giving a few (3.4 mg) milligrams of stannous phosphate 30 minutes earlier intravenously: 15 to 20 mCi of technetium-99m are then injected for the study. Images are obtained of the distribution of blood volume in the limbs, and veins are more visible than the arteries. A diagnosis of venous thrombosis is made by evidence of failure to visualize an entire vein or segment of vein, asymmetry and poor definition of a vein compared with its companion in the opposite limb.

This isotope technique was compared with venography in 35 patients (60); however the selection of patients, whether the readings were blinded and the time between the radioisotope study and venography were not mentioned. Sensitivity was 95% and specificity was 78%. In an earlier study by Beswick et al. (58), readings were blind, the sensitivity was 100% and the specificity was 89% (positive predictive value of 96% and a negative predictive value of 100%). An unspecified number of patients with negative scans did not have venography performed.

More recently, Singer et al. (61) studied the use of radionuclide plethysmography as an adjunct to imaging the venous system with technetium-99m-labeled red blood cells. In a small prospective study of 21 patients with clinically suspected deep vein thrombosis, they compared radionuclide plethysmography, radionuclide venography using technetium-99m-labeled red blood cells and contrast venography. Radionuclide plethysmography was performed 30 minutes after the intravenous injection of the labeled red blood cells, with the legs elevated 27 cm above the examination table and positioned over a gamma camera. The
Figure 4. Practical noninvasive approach for the diagnosis of clinically suspected deep vein thrombosis using serial impedance plethysmography (IPG). *In the absence of clinical conditions known to produce false positive impedance plethysmographic results (for example, congestive heart failure). DVT = deep vein thrombosis.

The sensitivity was 93% and specificity was 100% for iliofemoral vein thrombosis.

Other isotopic techniques, particularly indium-111 platelet scintigraphy (79), are evolving with a promising future.

Other Techniques for the Diagnosis of Venous Thrombosis

Other diagnostic techniques have been less intensively evaluated for the diagnosis of venous thrombosis. These include phleborrheography (air cuff plethysmography) (37), strain gauge plethysmography (8), thermography (27) and blood tests that reflect intravascular fibrin formation and fibrin proteolysis. Initial studies showed that phleborrheography has the disadvantage of a subjective interpretation. Promising initial results have been reported with thermography, but further studies are required before its value and limitations can be adequately assessed. Sensitive tests for intravascular fibrin formation and fibrin proteolysis are promising, but technically difficult. They include immunoassays of fibrinopeptide A (80), fragment E of fibrin/fibrinogen (81) and d dimer of fibrin. The fibrinopeptide A assay is only positive if the test is performed while the thrombus is being laid down, while tests for fibrin degradation products may remain positive for days after the thrombotic process has been arrested. The standard tests for fibrin degradation products such as latex agglutination, tanned red blood cell hemagglutination inhibition assay and staphylococcal clumping are not sufficiently responsive to be useful for excluding a diagnosis of acute venous thrombosis. Because both the fibrinopeptide A assay and the radioimmunoassay for fibrin/fibrinogen degradation products detect intravascular fibrin formation, they are not specific for the diagnosis of acute venous thrombosis. Either of these tests have potential to be used in combination with other noninvasive diagnostic tests. Their major drawbacks at present include

<table>
<thead>
<tr>
<th>Diagnostic Approach</th>
<th>Total Cost per Patient With Correct Diagnosis and Treatment</th>
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<tbody>
<tr>
<td></td>
<td>Proximal Vein Thrombosis</td>
</tr>
<tr>
<td></td>
<td>Canada*</td>
</tr>
<tr>
<td>Clinical diagnosis</td>
<td></td>
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<tr>
<td>Venography Outpatient</td>
<td>4,107</td>
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<tr>
<td>Elective inpatient</td>
<td>5,651</td>
</tr>
<tr>
<td>Impedance plethysmography plus venography</td>
<td>4,155</td>
</tr>
<tr>
<td>Impedance plethysmography plus leg scanning</td>
<td>3,986</td>
</tr>
<tr>
<td>Impedance plethysmography alone</td>
<td>2,995</td>
</tr>
</tbody>
</table>

*Dollar cost in Ontario in 1980 Canadian dollars (87) †Dollar cost in an urban New England hospital in 1980 U.S. dollars (87)
are that they are technically difficult, not readily available and their clinical utility has never been formally tested in a broad spectrum of patients.

The objective noninvasive diagnostic tests that have been adequately evaluated in patients with clinically suspected venous thrombosis are impedance plethysmography, Doppler ultrasound and iodine-125-fibrinogen leg scanning. None of these tests used alone is as accurate as venography. In appropriate combinations, however, these tests can replace venography in patients with symptoms or signs suggestive of venous thrombosis. Venography may still be required when the patient has a clinical condition known to produce a falsely positive result with one of the noninvasive tests. These include arterial insufficiency or congestive cardiac failure, which can give a falsely positive impedance plethysmogram, and trauma to the leg, which may produce a false positive iodine-125-fibrinogen leg scan.

A Practical Noninvasive Approach for the Diagnosis of Venous Thrombosis

Our current approach to the diagnosis of clinically suspected venous thrombosis favors the use of impedance plethysmography over Doppler ultrasonography as the main test for this disorder (82,83). This is because impedance plethysmography is precise and objective, whereas the interpretation of Doppler ultrasonography is subjective and requires considerable skill and experience to form reliable diagnoses. The use of serial impedance plethysmography has been evaluated recently in a prospective study (82) in which the safety of withholding anticoagulant therapy in patients with a negative test on repeated impedance plethysmography was documented by careful long-term follow-up study. To date, the effectiveness and safety of using Doppler ultrasonography alone have not been formally evaluated.

Repeated impedance plethysmography. The rationale of repeated impedance plethysmography evaluation is based on the premise that calf vein thrombi are only clinically important when they extend into the proximal veins, at which point detection with impedance plethysmography is possible (84). Therefore, by performing repeated examinations with impedance plethysmography in patients with clinically suspected venous thrombosis, it is possible to identify patients with extending calf vein thrombosis who can be treated appropriately. Since extension occurs only in a minority (approximately 20%) of patients with calf vein thrombosis, by detecting only those patients with extension, treatment is confined to those patients who are most likely to benefit. An alternative approach is to detect and treat all calf vein thrombi by adding leg scanning in the diagnostic approach (85,86), but this may be more harm than good because the potential benefit of anticoagulant therapy may be outweighed by the risk of bleeding.

Comparison of impedance plethysmography and iodine-125-fibrinogen scanning. We have recently completed a randomized clinical trial (82) comparing combined impedance plethysmography and iodine-125-fibrinogen leg scanning with serial impedance plethysmography alone for the diagnosis of clinically suspected venous thrombosis. The results of that study indicate that impedance plethysmography performed on the day of referral and, if negative, repeated the next day, again on day 5 to 7 and on day 10 is as effective as the combined approach of impedance plethysmography and leg scanning for the diagnosis of clinically suspected venous thrombosis. Furthermore, the clinical outcomes observed on long-term follow-up indicate that it is safe to withhold anticoagulant therapy in patients who remain negative by serial impedance plethysmography.

Diagnostic protocol. A diagnostic algorithm for the noninvasive diagnosis of clinically suspected venous thrombosis is shown in Figure 4. Impedance plethysmography is performed immediately on referral; if it is positive in the absence of clinical conditions that are known to produce falsely positive results, the diagnosis of venous thrombosis is established, and the patient is treated accordingly. If the result of the initial impedance plethysmography evaluation is negative, anticoagulant therapy is withheld and impedance plethysmography is repeated the next day, again on day 5 to 7 and on day 10 to 14. If the impedance plethysmogram becomes positive during this time, a diagnosis of venous thrombosis is made, and anticoagulant therapy is commenced. A positive impedance plethysmogram in the presence of conditions known to produce a false positive result (for example, congestive heart failure) should be confirmed by venography.

If noninvasive tests for the diagnosis of venous thrombosis are not available, a clinical suspicion of venous thrombosis should be objectively confirmed or excluded by performing ascending venography. Impedance plethysmography alone is the most cost-effective diagnostic approach (Table 2) (82,87).

References


