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Diagnosis of Lower-Limb Deep Venous Thrombosis: A Prospective Blinded Study of Magnetic Resonance Direct Thrombus Imaging

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Background: **Current magnetic resonance techniques generate high signal from venous blood and show thrombi as filling defects. Magnetic resonance direct thrombus imaging (MRDTI) directly visualizes acute thrombus.**

Objective: **To determine the accuracy of MRDTI for diagnosis of acute symptomatic deep venous thrombosis (DVT) below and above the knee.**

Design: **Prospective, blinded study.**

Setting: **A 1355-bed university hospital.**

Patients: **101 patients with suspected DVT who had had routine venography. Participants were recruited from a cohort of patients with suspected DVT. All patients with a positive venogram and one quarter of patients with a negative venogram were selected by using a random sequence.**

Intervention: **MRDTI was performed within 48 hours of venography and was interpreted by two reviewers.**

Measurements: **Diagnosis of DVT overall; isolated calf, femoropopliteal, and ileofemoral DVT; and thrombus in the calf, femoropopliteal, and iliac segments.**

Results: **The reports from two readers had sensitivities of 96% and 94% and specificities of 90% and 92% for diagnosis of DVT. Sensitivities were 92% and 83% for isolated calf DVT, 97% and 97% for femoropopliteal DVT, and 100% and 100% for ileofemoral DVT. Specificities were 94% and 96% for isolated calf DVT and 100% and 100% for both femoropopliteal and ileofemoral DVT. Similarly, sensitivity and specificity within each of the venous segments ranged from 91% to 100%. Interobserver variability measured by using a weighted κ statistic ranged from 0.89 to 0.98 for these measures.**

Conclusion: **Magnetic resonance direct thrombus imaging is an accurate noninvasive test for diagnosis of DVT, and its accuracy is maintained below the knee. Comparison of individual venous segments showed that results of MRDTI agreed strongly with findings on venography. Scanning was well tolerated, and interpretation was highly reproducible.**

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Despite considerable recent advances in diagnostic techniques for lower-limb deep venous thrombosis (DVT), current methods have disadvantages. Ultrasonography, the most accurate noninvasive test, is widely available and cheap. As such, it has largely replaced venography as the test of first choice for symptomatic DVT. In a recent meta-analysis, the sensitivity of ultrasonography was 89% overall for symptomatic DVT and 97% for above-knee thrombosis (1). Large outcome studies have shown that patients may be safely left untreated after a negative result on ultrasonography if they have a low clinical risk score, a low D-dimer level, or a negative result on repeated ultrasonography at 1 week (2–4). However, these strategies may be complex and still require 3% to 34% of outpatients and most inpatients to undergo repeated ultrasonography at 1 week (2–4). In practice, retesting after 1 week is inconvenient, and physicians often rely on a single test or request immediate venography (5). Other problems with ultrasonography include poor sensitivity for asymptomatic disease, difficulties in diagnosing DVT recurrence, and limited visualization in the pelvis (1, 6, 7).

Impedance plethysmography is also commonly used; however, it has a lower diagnostic accuracy than ultrasonography and has similar weaknesses in the setting of recurrent thrombosis, asymptomatic DVT, and DVT below the knee or in the pelvis (1, 4, 6). Computed tomography and magnetic resonance imaging techniques can visualize DVT above the knee and in the pelvis but in general are unsuccessful below the knee (8–10). The ability of these techniques to diagnose DVT recurrence and asymptomatic disease has not been tested.

Venography is the reference standard diagnostic test, but it has in large part been replaced by noninvasive tests. In clinical practice, it is the most reliable test for the diagnosis of asymptomatic thrombosis and thrombosis isolated within the calf or pelvis. However, imaging in the pelvis is inadequate in up to 24% of normal studies, and the proximal extent of thrombosis is fre-

quently not delineated in patients with above-knee DVT (11). Underfilling of vessels and vessels overlying one another also create problems with venography below the knee. Studies have shown that interobserver variability for venography is high (10% to 16%), especially below the knee ($\kappa = 0.46$ to 0.73 below the knee and 0.46 to 0.84 above the knee) (12, 13). In addition, a high proportion of studies are nondiagnostic for possible DVT recurrence (1, 6).

A noninvasive test is needed that accurately diagnoses above-knee DVT and thrombus below the knee, in the pelvis, and in asymptomatic limbs. Unlike most imaging techniques, which identify thrombus as filling defects, magnetic resonance direct thrombus imaging (MRDTI) visualizes thrombus against a suppressed background (14). In an unblinded comparison with venography, we previously showed that MRDTI precisely visualizes acute deep venous thrombus (14, 15). In the current study, we sought to assess prospectively whether MRDTI is a reliable diagnostic test for suspected acute symptomatic DVT.

METHODS

The ethics committee at our institution granted approval for the study, and all participants gave written informed consent. With the exceptions of pregnant women, patients with known contrast allergy, and those with renal failure, all patients with DVT suspected on the basis of lower limb symptoms are investigated by using venography at our institution. Participants were recruited after routine venography was done between May 1998 and September 1999. During this time, 338 consecutive patients underwent routine contrast venography. Consecutive patients with positive venograms were selected, along with one quarter of those with negative venograms, according to a predetermined random sequence. This protocol was chosen to equalize the numbers of positive and negative cases and was based on a 6-month audit of venograms in our institution that found that 22% of venograms were positive. Clinical diagnostic criteria were not used, and the decision to request investigation for suspected DVT had been made by the attending clinician; however, patients who did not have leg symptoms were not recruited. Other exclusion criteria were failed or inconclusive venography, failed or inconclusive MRDTI, contraindications to MRI, and claustrophobia (**Figure 1**). Individual venous segments that were nondiagnostic at venography were also excluded from analysis.

Magnetic resonance direct thrombus imaging was performed on all patients recruited within 48 hours of venography. The scans were interpreted by an experienced radiologist (reviewer A) and by a nonradiologist (reviewer B) trained to read MRDTI scans. For venograms and MRDTI scans, the reviewers noted the presence or absence of DVT; the diagnostic classification of DVT, divided into isolated calf DVT, femoropopliteal DVT, and ileofemoral DVT; and the presence of thrombus in the calf, femoropopliteal, and iliac venous segments. Venograms were obtained and initially reported by the radiologists on duty. This initial report was used to make recruitment decisions; if the results were discordant with those of MRDTI, ultrasonography was also performed. However, ultrasonography was not used in the calculations of the accuracy of MRDTI. After completion of the study, venograms were interpreted by an independent radiologist, and these results were used as the gold standard against which MRDTI was compared. Results of MRDTI and venography were reported without knowledge of the results of other tests and the other readings. The D-dimer level was measured in all patients at the time of the MRDTI scan by using the Nycocard (Nycomed Pharma AS, Asker, Norway) technique (normal level < 0.3 mg/L).

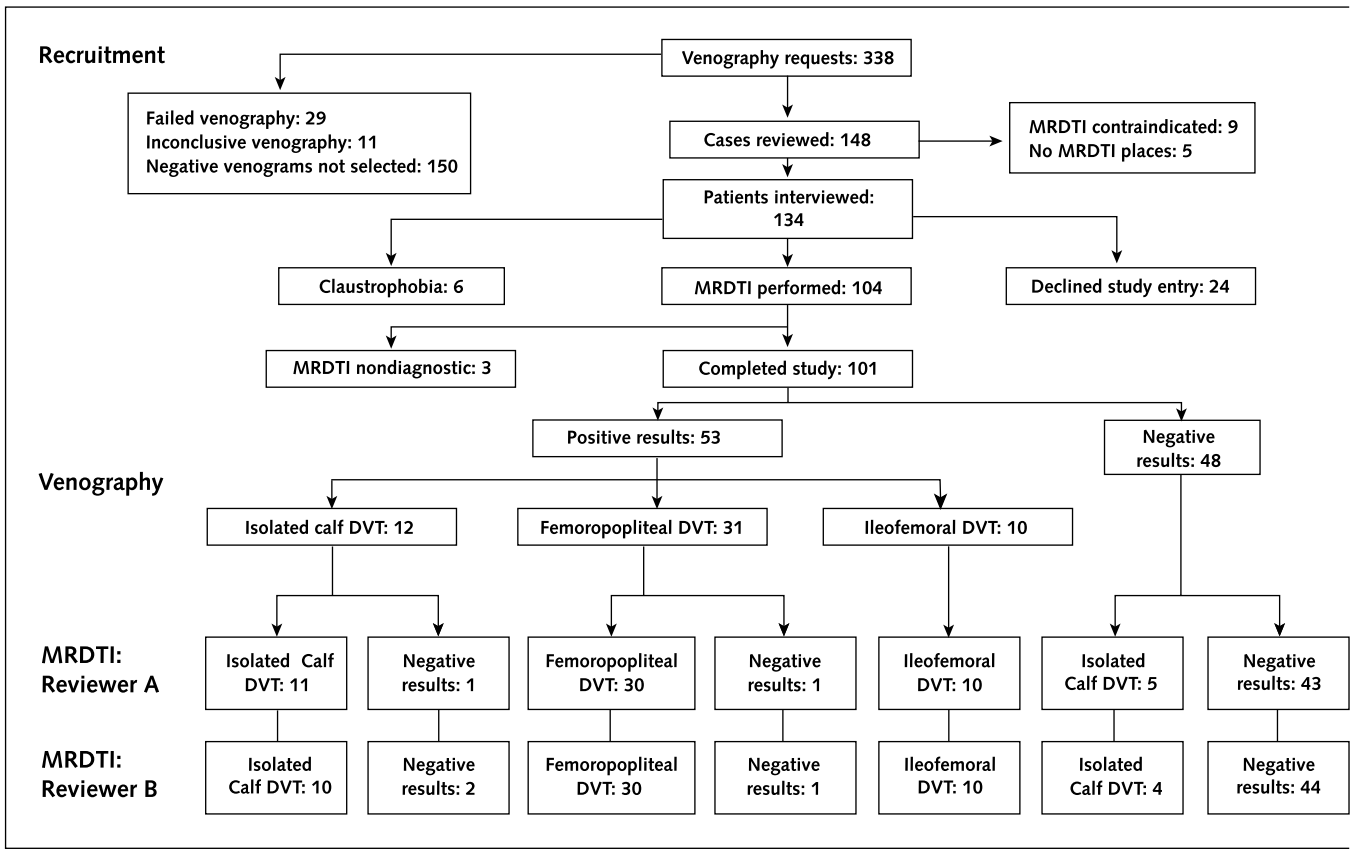
Venography

Venography was performed by cannulating a dorsal pedal vein with a 21-gauge needle and rapidly injecting 50 to 100 mL of iodinated contrast medium (I_2, 300 mg/mL), with the patient supine and tilted 30 degrees with his or her feet downward. A tourniquet was applied above the ankle. Anteroposterior and two oblique views of the deep calf and popliteal veins were obtained. Views of the femoral and iliac veins were then obtained. The study result was considered positive if intraluminal filling defects were seen or persistent nonfilling of veins with a sharp cut-off was detected.

Magnetic Resonance Imaging

Magnetic resonance imaging was performed by using a 1.5-Tesla unit (Siemens Vision, Erlangen, Germany) with a T1-weighted magnetization-prepared

Figure 1. **Outline of the study.**



DVT = deep venous thrombosis; MRDTI = magnetic resonance direct thrombus imaging.

three-dimensional gradient-echo sequence. The sequence included a water-only excitation radiofrequency pulse to abolish the fat signal, and the effective inversion time was chosen to nullify the blood signal. Imaging was performed from the ankle to the inferior vena cava in two imaging blocks with a total acquisition time of 12 minutes by using a 55-cm body coil. Both legs were imaged simultaneously. Scanning was performed by radiographers in all cases. Image assessment involved reading of coronal source data and standard image reconstruction techniques. Acute thrombus was diagnosed on the basis of its high signal against the suppressed background (**Figure 2**).

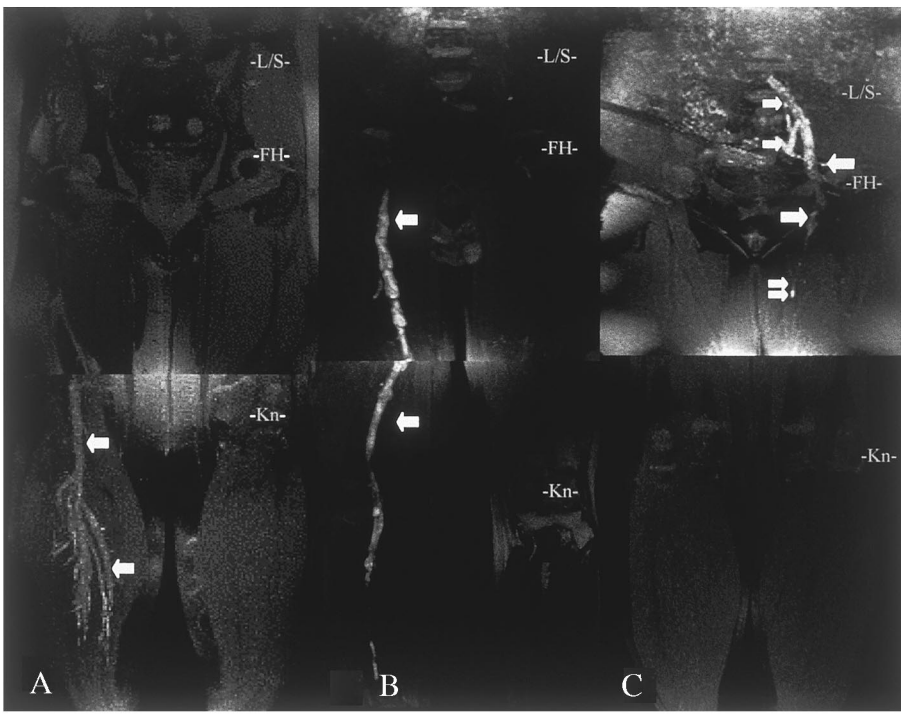
Ultrasonography

Color flow and compression ultrasonographic images of the symptomatic limb from the common femoral vein distally were obtained by using a 5-MHz linear array transducer. As much of the superficial femoral vein as possible was imaged, together with the popliteal vein and the calf veins. Augmentation of flow was used to verify patency. Examinations were performed by senior radiologists, and DVT was confirmed in all cases by noncompressibility on gray-scale images. The sonographer was unaware of the other test results, but in cases of possible isolated calf thrombosis, he or she was told to concentrate the examination below the knee to maximize accuracy in this region.

Statistical Analysis

Sensitivity and specificity were calculated for the overall diagnosis of DVT; diagnosis of isolated calf DVT, femoropopliteal DVT, and ileofemoral DVT; and presence of thrombus in the calf, femoropopliteal vein, and iliac vein. Exact CIs were calculated. Interobserver error was calculated for these observations by us-

Figure 2. **Magnetic resonance direct thrombus imaging in three patients.**



A. Extensive below-knee deep venous thrombosis (DVT) extending into the right popliteal vein (*arrows*). **B.** Large above-knee DVT extending up to the right common femoral vein (*arrows*). Poor fat suppression is seen in the left knee. **C.** Pelvic thrombosis in the left common and internal and external iliac veins, with extension into the common femoral vein (*single arrows*) and long saphenous vein (*double arrow*). FH = femoral head; Kn = knee joint; L/S = lumbosacral joint.

ing the weighted κ statistic with equally spaced weights for positive, nondiagnostic, and negative studies. Confidence intervals for the κ statistic were calculated from asymptotic estimations of the standard error. Calculations were performed by using SPSS software (SPSS, Inc., Chicago, Illinois).

RESULTS

One hundred four patients were recruited according to our protocol (**Figure 1**). The time between venography and MRDTI was less than 8 hours in 28 patients, 8 to 24 hours in 44 patients, and 24 to 48 hours in 32 patients. Age ranged from 20 to 95 years, and symptom onset varied from 1 to 35 days. Ninety-five patients were referred from medical specialties and 9 from surgical specialties; 47 were inpatients and 57 were outpatients. Both reviewers reported that 3 of 5 patients with ipsilateral total hip replacements had nondiagnostic MRDTI scans. Venography diagnosed femoropopliteal DVT in 1 of these patients and was negative in 2 patients. These 3 patients were excluded from further analysis, leaving 101 patients in the study. One patient could tolerate only the first scanning block from ankle to thigh level owing to claustrophobia; however, femoropopliteal DVT could still be diagnosed. All other patients tolerated MRI.

Eighteen of 148 patients (12%) were excluded from the study. Fifteen patients could not undergo MRI because of contraindications (9 patients) or claustrophobia (6 patients), and 3 patients had inconclusive results on MRDTI. Venography failed (29 patients) or was inconclusive (11 patients) in 12% of patients (40 of 338). Venography was inconclusive because of incomplete filling of vessels and difficulties in differentiating acute thrombus from other causes of filling defects. Venography failed owing to unsuccessful venous cannulation,

which was related to lower-limb edema or obesity in most cases.

The overall sensitivities of reviewers A and B in diagnosing DVT were 96% (95% CI, 89% to 99%; 51 of 53 tests) and 94% (CI, 86% to 98%; 50 of 53 tests). Corresponding specificities were 90% (CI, 79% to 96%; 43 of 48 tests) and 92% (CI, 82% to 97%; 44 of 48 tests). The overall interobserver error according to the weighted κ statistic was 0.94 (CI, 0.88 to 1.00).

The **Table** shows the sensitivity and specificity of MRDTI for diagnosing isolated calf DVT, femoropopliteal DVT, and ileofemoral DVT. There were two MRDTI tests that both reviewers reported as falsely negative and four MRDTI tests that both reviewers reported as falsely positive compared with venography. On venography, one of the two false-negative MRDTI studies was diagnosed as isolated calf DVT, and one was diagnosed as isolated popliteal vein thrombosis. The patient with isolated calf DVT had a D-dimer level that was not elevated (0.1 mg/L), and ultrasonography found no evidence of thrombosis. Anticoagulation was withheld, and no clinical events were recorded after 9 months. The patient with isolated popliteal vein thrombosis had a D-dimer level that was undetectable on our assay (<0.1 mg/L), but ultrasonographic findings concurred with those on venography. This patient had had a large ipsilateral above-knee DVT 6 months earlier. The false-positive MRDTI studies had all been classified as isolated calf vein thrombosis. Magnetic resonance MRDTI detected a 1-mL thrombus in one of these patients, and ultrasonography was negative. In the remaining three patients, MRDTI diagnosed thrombosis in the gastrocnemius veins (**Figure 3**). Ultrasonography also diagnosed isolated gastrocnemius vein thrombosis in these patients. At 1 week, one of the three patients was breathless; magnetic resonance pulmonary angiography detected multiple pulmonary emboli, and repeated MRDTI diagnosed thrombus progression in the leg. A fifth false-positive result, reported by reviewer A, was a superficial short saphenous vein thrombus misdiagnosed as being within a deep calf vein.

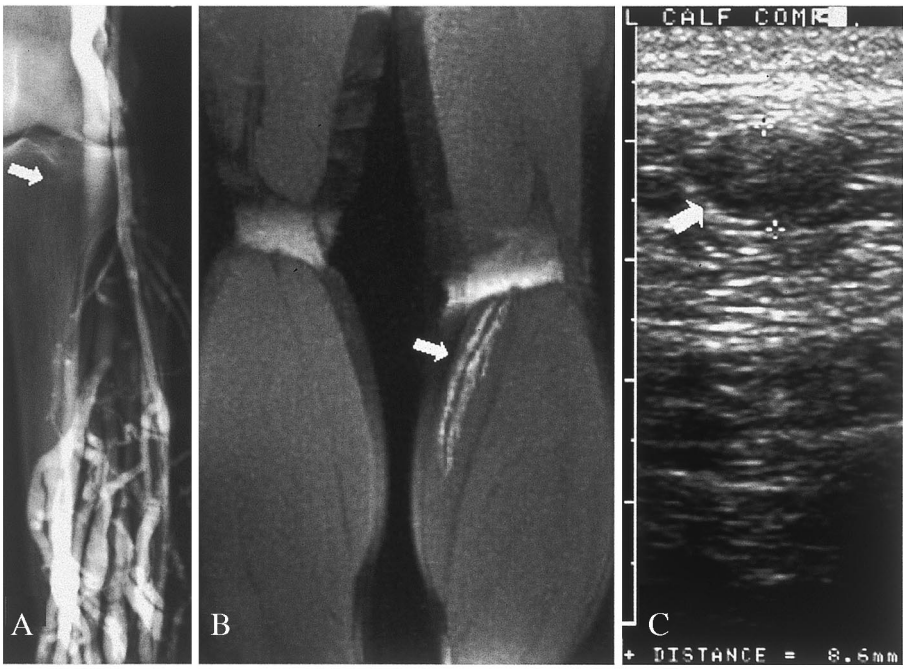
The sensitivity and specificity of MRDTI for the presence of thrombus in the calf and in the femoropopliteal and iliac segments are shown in the **Table**. Venography showed calf thrombosis in 48 patients. Twelve of these patients (described above) had isolated calf DVT. In 36 patients, venography diagnosed calf vein thrombosis associated with above-knee thrombosis. Magnetic resonance direct thrombus imaging diagnosed calf and above-knee thrombosis in 35 of these patients and diagnosed femoropopliteal thrombosis but not calf vein thrombosis in 1 patient. The latter patients had had symptoms for more than 4 weeks before diagnosis. Magnetic resonance direct thrombus imaging correctly iden-

Table. **Sensitivity and Specificity of Magnetic Resonance Direct Thrombus Imaging for Diagnosis of Deep Venous Thrombosis in Different Locations and Segments***

Disease or Segment	Sensitivity [95% CI]†		Specificity [95% CI]†		Interobserver Error [95% CI]‡
	Reviewer A	Reviewer B	Reviewer A	Reviewer B	
	% (n/n)				
Diagnosis					
Isolated calf DVT	92 [66–100] (11/12)	83 [56–97] (10/12)	94 [88–98] (84/89)	96 [90–98] (85/89)	0.89 [0.78–1.0]
Femoropopliteal DVT	97 [85–100] (30/31)	97 [85–100] (30/31)	100 [95–100] (70/70)	100 [95–100] (70/70)	0.98 [0.94–1.0]
Ileofemoral DVT	100 [74–100] (10/10)	100 [74–100] (10/10)	100 [97–100] (91/91)	100 [97–100] (91/91)	0.94 [0.82–1.0]
Segment					
Calf veins	96 [87–99] (46/48)	94 [84–98] (45/48)	91 [81–96] (48/53)	93 [84–97] (49/53)	0.94 [0.91–1.0]
Femoropopliteal	98 [89–100] (40/41)	98 [89–100] (40/41)	100 [95–100] (60/60)	100 [95–100] (60/60)	0.98 [0.94–1.0]
Iliac veins	100 [74–100] (10/10)	100 [74–100] (10/10)	100 [96–100] (77/77)	100 [96–100] (77/77)	0.94 [0.82–1.0]

* Venography was used as the gold standard. DVT = deep venous thrombosis.
† The number of patients used to calculate the percentage is shown in parentheses.
‡ Weighted κ statistic.

Figure 3. **Venography, magnetic resonance direct thrombus imaging, and ultrasonography in a patient with gastrocnemius thrombus.**



A. Venogram. The gastrocnemius veins have not been visualized (*arrow*). **B.** Magnetic resonance direct thrombus imaging. The technique demonstrates high-signal filling paired gastrocnemius veins (*arrow*). **C.** Ultrasonographic image. This image under compression shows a gastrocnemius vein filled with thrombus (*arrow*).

tified femoropopliteal thrombosis in 30 of 31 cases of femoropopliteal DVT. In 14 of these patients, venography failed to visualize the iliac veins. These cases were categorized as femoropopliteal DVT, and the iliac segments were excluded from the segmental comparison with MRDTI. Both iliac and femoropopliteal thrombosis were correctly identified in 10 patients with ileofemoral DVT.

The four false-positive cases of isolated calf vein thrombosis were the only false-positive venous segments. However, the iliac veins were not visualized on venography in several cases diagnosed as femoropopliteal thrombosis (see below).

The iliac veins were not visualized on venography in 14 patients with femoral thrombosis. Magnetic resonance direct thrombus imaging demonstrated extension into the iliac veins in 3 of these patients and extension into the inferior vena cava as far as the renal veins in 1 patient. In addition, venography did not define the upper extent of thrombosis in 9 of 10 patients with ileofemoral DVT. Magnetic resonance direct thrombus imaging showed extension into the inferior vena cava in 3 of these patients. Greater proximal extension into the iliac vein or inferior vena cava was therefore demonstrated by MRDTI in 7 of 41 (17%) patients with above-knee DVT. These findings are observational only and were not validated by using any other technique.

Magnetic resonance direct thrombus imaging also diagnosed asymptomatic contralateral thrombosis in 9 of 53 (17%) patients with DVT and 1 postoperative patient with no thrombus in the symptomatic leg. In the latter patient, venography of the asymptomatic leg was performed and below-knee DVT was confirmed.

DISCUSSION

In unselected patients presenting with suspected acute symptomatic DVT, MRDTI was highly sensitive and specific for diagnosis of DVT overall and for the

individual diagnoses of isolated calf DVT, femoropopliteal DVT, and ileofemoral DVT. Similarly, a separate comparison of the venous segments showed that MRDTI reliably diagnosed thrombosis in the calf, femoropopliteal, and iliac vessels. Interpretation of MRDTI was highly reproducible between observers, and κ values were significantly higher than those reported for venography (12, 13).

Patients were drawn from consecutive venogram requests made by clinicians who suspected DVT on the basis of leg symptoms. Exclusion criteria were designed only to exclude patients who could not undergo MRI and those who had nondiagnostic test results. Symptom duration and age range varied widely, and the case-mix included representative proportions of inpatients and surgical patients. Magnetic resonance direct thrombus imaging was compared with the accepted reference standard of venography, and venograms were read by an independent radiologist. Magnetic resonance direct thrombus imaging scans were reported by both a radiologist and a nonradiologist, without knowledge of other test results. Exact CIs were calculated in all instances.

Selection of one quarter of patients with negative venograms allowed us to include more patients with positive results and to separately assess isolated below-knee DVT, femoropopliteal DVT, and ileofemoral DVT. The overall specificity for the diagnosis of DVT is valid. However, the higher proportion of positive cases than in the recruitment population affected the assessment of specificity for the diagnoses of isolated calf, femoropopliteal, and ileofemoral DVT and for the individual venous segments.

The small numbers of patients with isolated calf thrombosis and ileofemoral thrombosis produced wide CIs for these diagnoses. However, calf thrombosis associated with above-knee thrombosis was accurately diagnosed. In addition, further analysis suggests that the venographic diagnosis was erroneous in three patients in whom MRDTI diagnosed thrombosis in the gastrocnemius veins and venography was negative. Noncompressibility was clearly demonstrated by ultrasonography in the gastrocnemius veins in these patients, whereas venographic contrast had failed to fill these vessels. Although ultrasonography has poor sensitivity below the knee, its specificity remains high (90% to 100%), and the gastrocnemius veins, which are near the skin surface, are not difficult to image (6). Poor filling of the gastrocnemius veins is common in venography, especially if ankle tourniquets are used, and may occur in up to 75% of studies (11, 16). Moreover, thrombus progression and pulmonary embolism occurred at 1 week in one of these patients. Although venography is considered the most reliable test below the knee, its inaccuracies are well known, and error rates are most pronounced below the knee because of inadequate filling and overlying vessels (12, 13, 17).

Above-knee MRDTI was falsely negative compared to venography in one patient. Ultrasonography confirmed the venographic diagnosis of isolated popliteal vein thrombosis. However, the patient had had ipsilateral femoropopliteal thrombosis 6 months earlier, and both ultrasonography and venography discriminate poorly between acute and chronic thrombus. The low D-dimer level may suggest that ultrasonography and venography demonstrated persistent filling defects from the previous DVT that would not have been visualized on MRDTI.

Assessment of the accuracy of a new diagnostic test against an imperfect gold standard is problematic. The accuracy of the new test will be underestimated if its errors are independent of those of the reference test and will be overestimated if the errors are not independent (18). Thrombus is visualized by venography as filling defects in veins that are opacified by using contrast; inaccuracies are caused by incomplete filling of vessels with contrast, overlying vessels, and difficulties in differentiating acute thrombus from other causes of filling defects (principally chronic thrombus). Magnetic resonance direct thrombus imaging visualizes thrombus directly; venous blood is not imaged, and thrombus more than 6 months old is not visualized. Therefore, the errors of MRDTI and venography are likely to be independent, and our study probably underestimated the accuracy of MRDTI.

Consideration of the results of ultrasonography and D-dimer measurement is therefore relevant when results of MRDTI and venography are discordant. Revision of the reference diagnosis according to results of ultrasonography in the discordant cases would increase the overall sensitivity to 98% (54 of 55 tests interpreted by reviewer A) and 96% (53 of 55 tests interpreted by reviewer B), with an overall specificity of 96% (44 of 46 tests interpreted by reviewer A) and 98% (45 of 46 tests

interpreted by reviewer B). The reported sensitivity of MRDTI for isolated calf thrombosis increases to 100% (14 of 14 tests interpreted by reviewer A) and 93% (13 of 14 tests interpreted by reviewer B), and the reported specificity increases to 98% (85 of 87 tests by reviewer A) and 99% (86 of 87 tests by reviewer B) The estimated accuracy for femoropopliteal and ileofemoral thrombosis would remain unchanged. However, the use of a second reference test only in the discordant cases and the poor sensitivity of ultrasound in the calf veins would tend to overestimate the sensitivity of MRDTI for isolated calf vein thrombosis in this analysis. We therefore used venography as the reference standard and discussed the discordant cases in full. A limitation of our study is the lack of D-dimer and ultrasonography results in the cases in which results of MRDTI and venography were concordant.

Venography was inconclusive in 11 patients, again principally owing to inadequate filling of vessels and problems in differentiating acute from chronic thrombus. Venography failed in 29 patients in whom unsuccessful venous cannulation was related to tissue oedema and obesity. Because MRDTI would not be expected to be less reliable in these cases, their exclusion probably did not affect the estimated accuracy of MRDTI.

The sensitivity and specificity of MRDTI, a noninvasive test, were high below the knee and in the pelvis. Current MRI techniques have high accuracy in the ileofemoral veins but cannot image vessels with slow flow below the knee. They are also susceptible to flow artifacts, and imaging times may be long (19, 20). More invasive computed tomography and MRI techniques that use injection into the symptomatic foot visualize the deep veins below and above the knee but share many of the problems of conventional venography (21, 22).

Most current imaging techniques require all of the deep veins to be visualized so that thrombus in them can be excluded. This is most straightforward for the superficial and common femoral veins and the popliteal vein, which are usually single vessels; accuracy is high in these veins. However, sensitivity is much lower for the multiple small veins below the knee and for the more inaccessible pelvic and deep femoral veins (7, 11). Impedance plethysmography has similar problems, but for different reasons. Magnetic resonance direct thrombus imaging differs fundamentally from these techniques because acute thrombus is directly visualized. Interpretation of studies involves a search for regions of high signal and does not require visualization of unaffected veins. Thus, a nonradiologist can interpret MRDTI scans accurately and rapidly. Signal generation does not depend on blood flow or filling of vessels with contrast. Flow artifacts, low flow rates in small veins, and venous occlusion due to extrinsic compression or chronic thrombus thus do not affect the technique. However, other causes of high signal must be distinguished from DVT; these include thrombus in other structures (hematomas or arterial thrombus); failure of the water excitation pulse to remove fat signal; and fast inflow of blood at the edge of the imaging block, which can also generate high signal for several centimeters within arteries. The use of standard multiplanar reconstruction techniques allows differentiation of these other causes of high signal from venous thrombosis.

Visualization of thrombus depends on the T1 shortening that occurs after blood clots. This T1 shortening is caused by methemoglobin production (23). The onset of the T1 reduction in intracranial hematomas is delayed by up to 7 days, and we were concerned that very fresh thrombosis may have been missed in the acute phase. However, we did not observe this in the current study, and it has been shown that high signal is visible within 8 hours of the onset of symptoms (14). Intravascular methemoglobin production is probably much more rapid than in hematomas. Similarly, high signal in DVT lasts from several weeks to several months, whereas high signal in intracranial hematomas may last more than 1 year (23). In the current study, above-knee DVT only was diagnosed by using MRI in one patient who presented at 33 days, but venography also demonstrated filling defects below the knee. This below-knee thrombus may have lost its high signal by the time of scanning. However, the duration of symptoms in the two false-negative cases was not notably long or short, and MRDTI diagnosed DVT despite wide variation in the duration of symptoms.

Access and cost of MRI may limit widespread use of MRDTI at present. Typical commercial charges for ultrasonography and unilateral venography are $300 (range, $200 to $500) and $450 (range, $250 to $800), respectively (24). The cost of MRI depends on the duration of the scan and the use of contrast. A typical commercial charge for an MRI scan without contrast that requires a scanning time of 40 to 60 minutes would be $1000,

whereas more rapid sequences may cost considerably less (25–27). Magnetic resonance direct thrombus imaging is performed on a standard clinical scanner, requires no special patient preparation, does not require contrast, and had a scanning time of 12 minutes in our study. Scanning time may be reduced to 7 minutes without degradation of image quality. Therefore, the cost of MRDTI should be similar to that of venography. Magnetic resonance direct thrombus imaging cannot be done in patients with contraindications to MRI, those with claustrophobia, and those who cannot lie flat.

Magnetic resonance direct thrombus imaging may have a specific role in several scenarios. Deep venous thrombosis in pregnancy is frequently pelvic in origin, and in our experience, MRDTI is both successful and well tolerated in pregnancy (28). The full extent of thrombosis can be assessed noninvasively in patients with ileofemoral DVT who may be candidates for thrombolysis (**Figure 2**). Magnetic resonance imaging can be done without difficulty in patients with full-length leg plaster casts. In addition, because it is noninvasive, carries no exposure to ionizing radiation or contrast agents, and provides comprehensive imaging of the full extent of thrombosis, MRDTI is well suited for repeated testing to monitor thrombus progression or for use in natural history or therapeutic trials.

The time course of the high signal in MRDTI allows confident diagnosis of acute thrombus and may also allow exclusion of fresh thrombosis in cases of DVT recurrence. Conventional tests are often inconclusive in this setting because the age of filling defects cannot be determined. At 6 months, 43 of the patients in this study with initially positive MRDTI scans were rescanned; no patient had remaining regions of high signal, despite persistent deep venous occlusion on ultrasonography in some of these patients (data not shown). Therefore, the presence of high signal from thrombus indicates that the thrombus is less than 6 months old. In addition, we have shown that changes in the pattern of high signal during the first few weeks after formation allows accurate determination of thrombus age (29).

Asymptomatic DVT was detected in the contralateral leg in 10 patients. Conventional noninvasive tests have poor sensitivity for asymptomatic thrombosis, which is frequently small and localized and does not obstruct the lumen (1, 6). Magnetic resonance direct thrombus imaging can image small-volume thrombi and does not depend on filling of the lumen or obstruction to blood flow. Therefore, MRDTI would probably be a reliable test for asymptomatic thrombosis. Combined with magnetic resonance pulmonary embolus imaging, MRDTI could therefore be an important research tool (30). Because imaging times are becoming shorter, the cost of MRDTI could soon be similar to that of other noninvasive tests (31, 32). Current protocols allow at least four patients to be scanned per hour.

In summary, current imaging methods for the diagnosis of DVT have disadvantages. Magnetic resonance direct thrombus imaging is noninvasive, does not require contrast agent, and is highly accurate and reproducible. Its accuracy is maintained both in the calf and pelvis, and sensitivity and specificity below the knee are high. Magnetic resonance direct thrombus imaging has promising roles in the diagnosis of DVT in pregnancy and demonstration of the full extent of thrombosis in high-risk patients. It is also well suited for diagnosis of recurrent thrombosis and asymptomatic disease and as a powerful research tool. Lack of widespread availability of MRI and cost limit use of MRDTI at present. However, as scanners become more plentiful and scanning speed increases, costs will decrease and may become similar to those of other noninvasive tests.

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