

Magnetic Resonance Imaging for Diagnosing Foot Osteomyelitis

A Meta-analysis

Alok Kapoor, MD; Stephanie Page, MD; Michael LaValley, PhD; Daniel R. Gale, MD; David T. Felson, MD, MPH

Background: Uncertainty exists regarding the optimal workup of patients with suspected osteomyelitis of the foot, many of whom have diabetes mellitus. We conducted a meta-analysis to determine the diagnostic test performance of magnetic resonance imaging (MRI) for osteomyelitis of the foot and compared this performance with that of technetium Tc 99m bone scanning, plain radiography, and white blood cell studies.

Methods: We searched MEDLINE (from 1966 to week 3 of June 2006) and EMBASE (from 1980 to week 3 of June 2006) for English-language studies in which adults suspected of having osteomyelitis of the foot or ankle were evaluated by MRI. We then extracted data using a standard form derived from the Cochrane Methods Group. To summarize the performance of diagnostic tests, we used the summary receiver operating characteristic curve analysis, which relies on the calculation of the diagnostic odds ratio (DOR). We also examined subsets of studies defined by the presence or absence of particular design flaws or populations.

Results: Sixteen studies met inclusion criteria. In all studies combined, the DOR for MRI was 42.1 (95% confidence interval, 14.8-119.9), and the specificity at a 90% sensitivity cut point was 82.5%. The DOR did not vary greatly among subsets of studies. In studies in which a direct comparison could be made with other technologies, the DOR for MRI was consistently better than that for bone scanning (7 studies—149.9 vs 3.6), plain radiography (9 studies—81.5 vs 3.3), and white blood cell studies (3 studies—120.3 vs 3.4).

Conclusions: We found that MRI performs well in the diagnosis of osteomyelitis of the foot and ankle and can be used to rule in or rule out the diagnosis. Magnetic resonance imaging performance was markedly superior to that of technetium Tc 99m bone scanning, plain radiography, and white blood cell studies.

Arch Intern Med. 2007;167:125-132

OSTEOMYELITIS OF THE FOOT and ankle is the primary or secondary reason for 75 000 hospitalizations in the United States each year.¹ By far the most common group at risk is persons with diabetes mellitus. In terms of diagnostic evaluations, history and routine laboratory tests, including the erythrocyte sedimentation rate, are not particularly informative.^{2,3} Although bone biopsy serves as a gold standard diagnostic test and is generally safe, the fear of introducing infection and the need for a surgical practitioner to perform the biopsy make development of diagnostic algorithms using noninvasive imaging strategies attractive.

Plain radiography is the traditional and often the initial modality used for evaluating bone infections in the foot. Radiographic changes are often not visible until 2 to 4 weeks after onset of infection, accounting in part for the low sensitivity

of plain radiography.^{4,6} The specificity of plain radiography tends to be higher than its sensitivity but can be compromised by posttraumatic reactions, nonspecific periosteal reactions as seen in chronic venous stasis, and most commonly Charcot osteoarthropathy. Charcot osteoarthropathy, or Charcot foot, is a disruption in foot architecture that results from microtrauma to an insensate foot. It is often indistinguishable from osteomyelitis.

Bone scanning with technetium Tc 99m [^{99m}Tc]-labeled diphosphonate can detect early changes of osteomyelitis but suffers from lack of specificity. White blood cell (WBC) scanning, usually with indium In 111, is more specific but lacks sensitivity.⁵ In addition, WBC scanning requires the inconvenient and time-consuming process of drawing and incubating patient blood before reinjecting and obtaining images.

Diagnostic findings of pedal osteomyelitis on MRI include a focal area of de-

Author Affiliations: Division of General Internal Medicine and Clinical Epidemiology Research and Training Unit, Boston University (Drs Kapoor, Page, LaValley, and Felson), Boston, and Commonwealth Radiology Group, Salem (Dr Gale), Mass. Dr Page is now with the Department of Hospitalist Medicine, Mount Auburn Hospital, Cambridge, Mass.

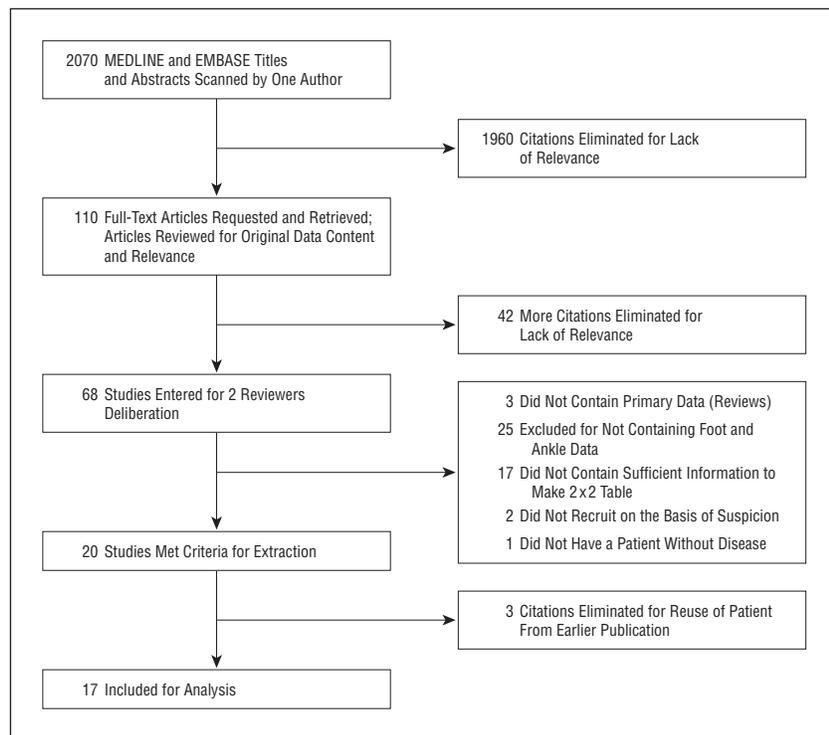


Figure 1. Flowchart of article selection.

creased marrow signal intensity on T1-weighted images and a focally increased signal intensity on fat-suppressed T2-weighted or short tau inversion recovery images.⁷ The MRI changes seen in osteomyelitis may be confused with changes seen in bony infarcts, fractures, and Charcot foot.

Accurate estimates of MRI test performance for osteomyelitis of the foot are difficult to establish. Most studies have reported on small cohorts, combined persons with suspected osteomyelitis of the foot and those with suspected osteomyelitis of other body sites, included persons both with and without diabetes, and left unstated the prevalence of Charcot foot. Studies have drawn different conclusions about the value of MRI alone (or compared with other technologies) and have reported vastly different estimates of diagnostic specificity (0%-100%). Previous systematic reviews⁸⁻¹⁰ were limited by the number of publications they analyzed or the lack of foot-specific information.

We conducted a comprehensive meta-analysis of the test performance of MRI for the diagnosis of osteomyelitis of the foot and ankle. We then conducted subset analyses to explore the reason for variability among included studies. We

also compared the accuracy of MRI with ^{99m}Tc bone scanning, plain radiography, and WBC scanning.

METHODS

STUDY IDENTIFICATION

We searched MEDLINE (from 1966 to week 3 of June 2006) and EMBASE (from 1980 to week 3 of June 2006) for English-language articles. (The complete search strategy is available from the authors on request.) We also searched the bibliographies of included studies and asked specialists within the fields of surgery and radiology to recommend citations.

STUDY SELECTION

We included studies that evaluated the diagnostic test performance of MRI in adult patients suspected of having osteomyelitis of the foot or ankle or who had foot infection and were systematically examined for osteomyelitis. Specifically, studies were enrolled when information from the usual diagnostic performance 2 × 2 table (index diagnostic test result positive or negative vs true disease state present or absent) could be extracted about discrete foot and ankle cases, when 80% or more of the patients were 16 years or older, and when at least one site with the disease and one without were identified by the

reference standard (eg, bone biopsy). Two authors (A.K. and S.P.) evaluated each study for inclusion, and a third author (D.T.F.) refereed ties.

STUDY EXTRACTION AND QUALITY ASSESSMENT

Once studies were selected, we used a data extraction instrument derived from the Cochrane Methods Group checklist on Systematic Review of Screening and Diagnostic Tests.¹¹ Two independent reviewers (A.K. and S.P.) extracted data that pertained to study population characteristics. The prevalence of diabetes in each study was noted. To understand better the quality of the sensitivity and specificity estimates reported in each study, we also extracted information about blinding and the type of reference standard used. Specifically, we calculated the frequency that a bone biopsy–based reference standard was used to determine or exclude osteomyelitis. For a positive disease determination, positive histologic analysis or culture results (however it was determined by the study authors) from a bone specimen were recorded. For the negative reference standard, we recorded the percentage of patients in whom osteomyelitis was excluded by negative histologic analysis results (however it was determined by the authors). If an individual study characteristic was not explicitly documented, no determination was made regarding the study status and a “not specified” label was assigned to the study for that characteristic. No attempt was made to contact study authors except to determine whether the same patients were enrolled more than once by authors with multiple publications.

COMPARISON OF DIAGNOSTIC IMAGING TESTS

We extracted data on the diagnostic performance of bone scan, plain radiography, and WBC studies if a 2 × 2 diagnostic performance table could be derived from a study that was already included for its MRI data.

DATA SYNTHESIS AND ANALYSIS

For each study, we constructed a 2 × 2 contingency table that consisted of true-positive, false-positive, false-negative, and true-negative results according to the reference standard used in each case. We then calculated the sensitivity and specificity in the usual fashion and the diagnostic odds ratio (DOR), as determined by the formula (true positive × true negative)/(false positive × false negative). We

Table 1. Characteristics of Included Studies

Source	Enrollment Criteria	No. of Sites in the Study (No. of Patients)*	Mean Age of Patients, y	Prevalence of Diabetes, %	Prospective Design	Consecutive Enrollment	MRI Assessors†
Craig et al, ¹⁴ 1997	Diabetic patients scheduled for partial amputation	57 (13)	57.0	100.0	Yes	NS	NS
Croll et al, ¹⁵ 1996	Patients admitted with nongangrenous diabetic foot infections	27 (27)	66.0	100.0	Yes	NS	No
Enderle et al, ¹⁶ 1999	Diabetic patients suspected of having chronic osteomyelitis from random surgery and medicine clinics	19 (19)	60.7	100.0	Yes	Yes	Yes
Ertugrul et al, ¹⁷ 2006	Diabetic patients with ulcers at Wagner grade ≥ 3 ‡	31 (31)	62.0	100.0	Yes	NS	NS
Horowitz et al, ¹⁸ 1993	Patients admitted with diabetic foot infections	47 (41)	54.4	100.0	Yes	NS	No
Kearney et al, ¹⁹ 1999	Diabetic outpatients suspected of having osteomyelitis	13 (13)	59.0	100.0	Yes	NS	NS
Ledermann et al, ²⁰ 2002	Diabetic and nondiabetic patients suspected of osteomyelitis	84 (72)	NS	NS	NS	NS	Yes
Levine et al, ²¹ 1994	Diabetic patients with suspected osteomyelitis complicating soft tissue infection	29 (27)	51.6	100.0	No	NS	No
Lipman et al, ²² 1998	Patients with peripheral neuropathy and high clinical suspicion	20 (20)	46.0	85.0	Yes	Yes	Yes
Maas et al, ²³ 2002	Patients with neuropathy and inflammation in addition to leprosy	18 (12)	63.0	0	No	Yes	Yes
Morrison et al, ²⁴ 1998	Patients suspected of having osteomyelitis of the foot	73 (62)	56.0	84.9	No	NS	Yes
Nigro et al, ²⁵ 1992	Patients with foot inflammation and possible osteomyelitis	47 (44)	55.0	70.5	NS	NS	NS
Remedios et al, ²⁶ 1998	Diabetic patients with peripheral neuropathy, chronic foot ulcers, and signs of osteomyelitis	9 (9)	57.0	100.0	Yes	NS	NS
Seabold et al, ²⁷ 1990	Patients highly suspected of having osteomyelitis in and around Charcot joint	12 (11)	50.6	91.7	No	No	No
Vesco et al, ²⁸ 1999	Diabetic patients with foot ulcers	24 (24)	59.0	100.0	Yes	Yes	NS
Weinstein et al, ²⁹ 1993	Diabetic patients admitted with suggestion of osteomyelitis, nonhealing ulcer, or soft tissue infection	75 (47)	49.6	100.0	Yes	Yes	Yes
Yuh et al, ³⁰ 1989	Patients suspected of having osteomyelitis or nonhealing ulcer	44 (24)	58.2	100.0	NS	Yes	Yes

Abbreviations: MRI, magnetic resonance imaging; NS, not specified.

*Site refers to site in the body. If each patient had 1 site suggestive of osteomyelitis, the number of sites would equal the number of patients. Because the included studies typically did not document performance estimates at the patient level, we calculated the summary estimate of performance at the level of the site. Later, we examined the summary estimate in a subset of studies in which the number of multiple sites for the same patient was low or nil. In addition, the number of sites listed corresponds to that for the entire study. Individual imaging tests may not have been performed in all cases. Please see "Comparison of Diagnostic Imaging Tests" subsection in the "Results" section.

†Blinded to other tests and to reference standard.

‡Wagner grading system is a clinical tool for evaluating diabetic foot ulcers. Scoring ranges from 1 to 5 for progressively deeper ulcers and less salvageable feet; grade 3 lesions are associated with osteomyelitis and/or abscess. Stage 4 and 5 ulcers indicated gangrenous lesions.

then conducted a summary receiver operating characteristic curve analysis as our meta-analytic method. This method has been described before.^{12,13} We repeated this analysis in 13 subsets that represented different study populations (eg, low or unspecified prevalence of Charcot foot) and the presence or absence of design flaws (eg, no blinding).

COMPARISON OF DIAGNOSTIC IMAGING TESTS

We compared the head-to-head test performance of MRI with 3 other imaging tests. Because we had collected data on all MRI diagnostic studies, we evaluated

these other technologies compared with MRI, which was our focus in this study. We included only studies in which 1 of the 3 diagnostic modalities was compared with MRI. To make comparisons, we used the same summary receiver operating characteristic method mentioned earlier. In certain studies not every patient underwent each test being compared, perhaps because a diagnosis was reached when the patient underwent the first diagnostic test, making the next one unnecessary. To account for this bias, we also measured the performance of the subset of studies in which all (or nearly all) patients underwent both diagnostic tests being compared. All sta-

tistical procedures were performed using SAS statistical software, version 9.1.3 (SAS Institute Inc, Cary, NC).

RESULTS

Our search strategy yielded 2070 titles with and without abstracts. One author (A.K.) reviewed them and requested 110 articles for full-text review. After eliminating those that did not meet the inclusion criteria (**Figure 1**), we were left with the 17 studies described in **Table 1**.¹⁴⁻³¹ One study²⁷ examined only patients with

Table 2. MRI Diagnostic Criteria, Frequency of Biopsy Use, and MRI Performance

Source	Signs on MRI Used to Determine Positive Result*	Biopsy Reference Standard, %		Prevalence of Osteomyelitis, %	MRI Performance	
		Positive†	Negative‡		Sensitivity, %	Specificity, %
Craig et al, ¹⁴ 1997	Primary, half of patients getting T1 with gadolinium, and soft tissue mass or ulcer	100.0	100.0	36.8	90.5	65.0
Croll et al, ¹⁵ 1996	NS	100.0	55.6	33.3	88.9	100.0
Enderle et al, ¹⁶ 1999	Increased uptake on STIR with ulcer or soft tissue mass and T1 with gadolinium§	100.0	100.0	73.7	100.0	75.0
Ertugrul et al, ¹⁷ 2006	Decreased T1, turboinversion recovery magnitude, and T1 with gadolinium	100.0	100.0	74.2	78.2	60.0
Horowitz et al, ¹⁸ 1993	Increased TR/TE or increased T2 and some gadolinium, with or without cortical disruption	100.0	NS	31.9	100.0	100.0
Kearney et al, ¹⁹ 1999	NS	NS	0	69.2	100.0	50.0
Ledermann et al, ²⁰ 2002	Primary, T1 with gadolinium, and many secondary signs	100.0	100.0	63.1	90.6	83.9
Levine et al, ²¹ 1994	Standard primary	100.0	31.3	44.8	76.9	100.0
Lipman et al, ²² 1998	Primary and many secondary	100.0	20.0	75.0	77.3	40.0
Maas et al, ²³ 2002	Standard primary, T1 with gadolinium, and many secondary	50.0	0	88.9	100.0	50.0
Morrison et al, ²⁴ 1998	Standard primary, T1 with gadolinium for most patients, and many secondary signs	100.0	0	58.9	91.3	83.2
Nigro et al, ²⁵ 1992	NS	92.3	NS	55.3	100.0	95.2
Remedios et al, ²⁶ 1998	Standard primary	100.0	20.0	44.4	100.0	80.0
Seabold et al, ²⁷ 1990	Standard primary	100.0	0	36.4	100.0	0¶
Vesco et al, ²⁸ 1999	Standard primary, T1 with gadolinium, and ulcer, sinus tract, or soft tissue mass	0	0	54.2	100.0	81.8
Weinstein et al, ²⁹ 1993	Standard primary	100.0	55.2	61.3	100.0	79.3
Yuh et al, ³⁰ 1989	Standard primary	100.0	21.1	61.4	100.0	89.5

Abbreviations: MRI, magnetic resonance imaging; NS, not specified; STIR, short tau inversion recovery; TR/TE, repetition time/echo time.

*Standard primary refers to the presence of focally decreased marrow signal on T1-weighted images and focally increased marrow signal on T2-weighted images or STIR images. T1 with gadolinium refers to use of enhancement with gadolinium contrast in fat suppressed T1-weighted images. Secondary signs include cortical disruption and adjacent cutaneous ulcer or soft tissue mass plus the presence of a sinus tract and in some cases adjacent soft tissue inflammation or edema.

†The frequency of the use of positive bone histologic analysis results or bone culture (however it was determined by the study authors) as the reference standard to confirm disease was calculated.

‡The frequency of the use of negative bone histologic analysis results (however it was determined by the study authors) as the reference standard to exclude disease was calculated.

§T1 with gadolinium was recorded but not included in determination of positive scan result.

¶In these cases, authors did not provide a single composite sensitivity and specificity, so only primary signs were analyzed.

¶¶All of the study subjects had Charcot joint; this may explain the low specificity.

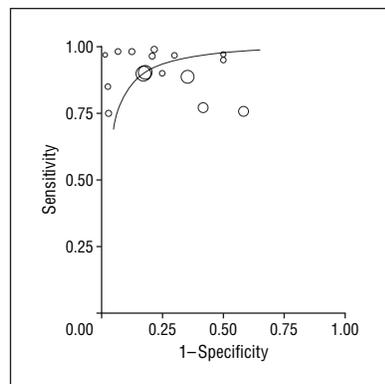


Figure 2. Summary receiver operating characteristic curve of magnetic resonance imaging performance in 16 studies. Bubble size represents sample size.

suspected osteomyelitis in or around a Charcot joint. Although this was not an a priori exclusion criterion, we believed the study was not consistent with the intent of our analysis. We chose to provide a summary estimate of the performance of MRI in a typical patient population at risk rather than one in which the population is artificially enriched with problem cases, and so the study was eliminated from analysis.

Eleven of the 16 studies involved almost exclusively diabetic patients. Nine of 16 recruited patients prospectively (ie, study authors en-

rolled patients before any imaging tests were recorded). Most studies did not specify or standardize the exact reason for diagnostic suspicion of osteomyelitis. In many cases, it was implied by the presence of a complicated or infected foot ulcer. Indeed, foot ulcer was required or uniformly present in 6 studies. In most instances, the number of cases with Charcot disease was not reported.

Most studies judged an MRI scan to be positive by the same criterion: a lesion in the bone that showed focally decreased marrow signal intensity in T1-weighted images and

Table 3. Diagnostic Performance of 4 Technologies in Studies That Compared MRI With Another Imaging Test

Source	MRI		Technetium Tc 99m Bone Scan		Plain Radiography		WBC Scan	
	Sensitivity, %	Specificity, %	Sensitivity, %	Specificity, %	Sensitivity, %	Specificity, %	Sensitivity, %	Specificity, %
Croll et al, ¹⁵ 1996	88.9	100.0	50.0	50.0	22.2	94.4	33.3	69.2
Enderle et al, ¹⁶ 1999	100.0	75.0	83.3	75.0	71.4	80.0		
Horowitz et al, ¹⁸ 1993	100.0	100.0			43.8	100.0		
Kearney et al, ¹⁹ 1999	100.0	50.0	88.9	100.0	66.7	100.0		
Levine et al, ²¹ 1994	76.9	100.0	100.0	25.0	60.0	81.3	80.0	28.6
Lipman et al, ²² 1998	77.3	40.0			73.3	40.0		
Nigro et al, ²⁵ 1992	100.0	95.2	90.5	33.3	69.6	33.3		
Remedios et al, ²⁶ 1998	100.0	81.8	100.0	0	38.5	100.0	90.9	84.6
Yuh et al, ³⁰ 1989	100.0	89.5	94.4	18.2	75.0	60.0		

Abbreviations: MRI, magnetic resonance imaging; WBC, white blood cell.

a focally increased signal intensity in fat-suppressed T2-weighted or short tau inversion recovery images. Eight studies^{14,16,18,20,22-24,28} evaluated other diagnostic signs that were sometimes termed *secondary signs*, including cortical disruption, adjacent cutaneous ulcer, soft tissue mass, presence of a sinus tract, and, in some cases, adjacent soft tissue inflammation or edema. See **Table 2** for further details.¹⁴⁻³¹

The prevalence of criterion standard–defined osteomyelitis averaged approximately 50%, with a range of 32% to 89%. Most authors reported results according to the number of sites with potential osteomyelitis or number of at-risk bones imaged. We calculated a ratio of the number of patients to number of sites and compared MRI performance in studies with low and high ratios. Magnetic resonance imaging sensitivity was usually high and ranged from 77% to 100%; MRI specificity ranged from 40% to 100%.

Among all studies, the DOR for MRI was 42.1 (95% confidence interval [CI], 14.8-119.9). The specificity at a clinically relevant cut point of 90% sensitivity was 82.5%. We present the curve for diagnostic performance in **Figure 2**. We found no substantial or statistically significant differences in estimates of MRI diagnostic test performance among subsets of studies (available from the authors on request). The number of studies in certain subgroups was small (eg, subgroup with Charcot prevalence >10%), with small numbers of patients represented in each.

Small numbers in subsets prohibit robust conclusions. We therefore only discuss the subsets for which 8 or more studies were available for analysis. Studies that did not use bone histologic analysis to exclude disease tended to have higher performance (DOR, 67.4; 95% CI, 18.3-248.0). Studies published in 1998 or afterward reported lower performance (DOR, 25.3; 95% CI, 5.5-116.8). Most of the later studies had a prospective design and documented assessment of MRI blinded to other results.

COMPARISON OF DIAGNOSTIC IMAGING TESTS

We compared the diagnostic performance of 4 technologies in studies that compared MRI with another imaging test (**Table 3**). We found 7 studies that directly compared MRI with ^{99m}Tc bone scanning, all using the triple-phase technique. Magnetic resonance imaging performance was markedly superior (DOR, 149.9; 95% CI, 54.6-411.3) vs bone scan (DOR, 3.6; 95% CI, 1.0-13.3) (**Figure 3**). At the 90% sensitivity cut point, the specificity for MRI was 98% compared with 28.5% for technetium. Similarly, in 9 studies that compared plain radiography with MRI, MRI outperformed plain radiography (DOR, 81.5; 95% CI, 14.2-466.1 compared with DOR, 3.3; 95% CI, 2.2-5.0). In 3 studies in which MRI was compared with WBC study, the DOR for MRI was 120.3 (95% CI, 61.8-234.3) compared with 3.4 (95% CI, 0.2-62.2) for WBC studies.

COMMENT

This meta-analysis demonstrated that MRI performs well in the diagnosis of osteomyelitis of the foot and ankle in adults. Good diagnostic performance was consistent across a subset of studies of different designs and different patients. Moreover, MRI outperformed technetium, plain radiography, and WBC studies.

Although the performance of MRI was strong, our review revealed many flaws in the published literature concerning imaging tests for osteomyelitis in the foot or ankle. Few studies prospectively followed up a cohort of patients in which assessment of MRI was blinded to other imaging tests and reference standard results, and few verified the diagnosis in all cases with a biopsy. Although the estimate of performance did not change substantially within study subsets, the relatively small number of studies did not permit exploring the combined effect of multiple design issues.

In addition, the frequency of Charcot foot was not typically documented in our studies. Performance estimates could vary significantly among studies of varying prevalence of Charcot foot. In the 13 studies in which prevalence was not documented, the prevalence of Charcot foot was probably low. However, in diabetic patients with coexistent diabetic foot infection, prevalence is uncertain. Although it may be uncommon in the general diabetic

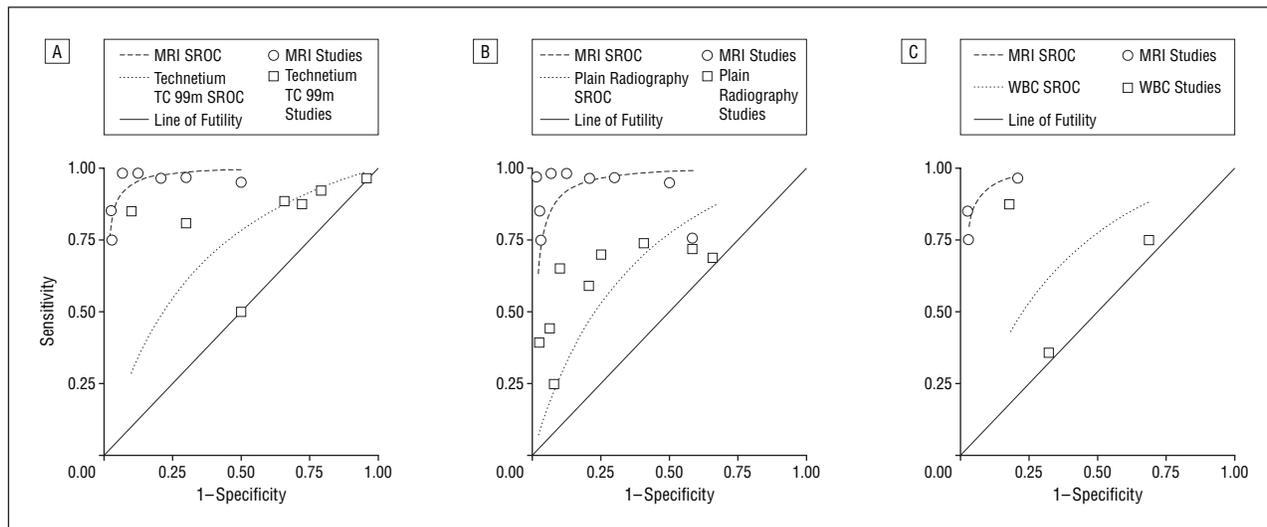


Figure 3. Head-to-head performance of magnetic resonance imaging (MRI) and technetium Tc 99m bone scanning (A), MRI and plain radiography (B), and MRI and white blood cell (WBC) scanning (C). SROC indicates summary receiver operating characteristic curve.

Table 4. Posttest Probability Stratified by Imaging Test Result Across a Spectrum of Pretest Probabilities

Pretest Probability, %	Posttest Probability, %			
	MRI Positive*	MRI Negative	Technetium Tc 99m Positive†	Technetium Tc 99m Negative
10.0	36.2	1.3	11.2	3.4
25.0	63.0	3.8	27.4	9.6
50.0	83.6	10.7	53.1	24.2
75.0	93.9	26.5	77.2	49.0
90.0	97.9	51.9	91.1	74.2

Abbreviation: MRI, magnetic resonance imaging.

*Using the all-studies estimate, which was lower than that calculated from studies that also had technetium Tc 99m data. The 90% sensitivity and 82.5% specificity translate to a positive likelihood ratio of 5.1 and a negative likelihood ratio of 0.12.

†Using a higher sensitivity threshold of 95%, which decreases the negative likelihood ratio to 0.32; the specificity at this threshold is 16% and the positive likelihood ratio is 1.13.

population, Charcot foot is likely much more prevalent among patients with peripheral neuropathy.³² Given that the management strategies for Charcot foot and osteomyelitis are vastly different (offloading and contact casting vs long-term antibiotics), making an accurate diagnosis is essential.

This meta-analysis has 2 major implications. First, this study confirms that MRI is a strong test to aid in both confirming and excluding osteomyelitis of the foot. Using the clinically relevant cut point of 90% sensitivity, the positive likelihood ratio is 5.1 and the negative likelihood ratio is 0.12. Assuming a pretest probability of 50% (not far from the 55% calculated from all studies), a patient with a positive MRI would have an 84% chance of hav-

ing the diagnosis (**Table 4**). If any other features or examination findings favor the diagnosis of osteomyelitis, such as substantial depth of ulcer or positive probe to bone, the addition of a positive MRI virtually clinches the diagnosis. A negative MRI study in our baseline hypothetical patient results in a posttest probability of 11%. Combined with absence of substantial ulcer depth or a negative probe to bone, MRI effectively rules out osteomyelitis.

The second major implication is that there should be a diminished use of ^{99m}Tc bone scanning in the diagnosis of osteomyelitis of the foot. Although bone scanning has been proposed for ruling out the disease (given its purported high sensitivity), the lack of adequate specificity creates many false-positive re-

sults.^{4,6,33} Using a hypothetical prevalence of osteomyelitis of 25%, for every 100 patients subjected to bone scanning, 12 of 13 with a negative result would have the diagnosis correctly excluded (negative predictive value, 91%), but only 24 of 87 with a positive result would be correctly identified as having osteomyelitis (positive predictive value, 27%). A diagnostic algorithm that includes bone scanning would thereby result in the ordering of numerous second imaging tests or biopsies. At a lower prevalence of osteomyelitis (eg, 5%-15%), ^{99m}Tc scanning may successfully rule out disease (Table 4). However, clinicians often underestimate the prevalence of osteomyelitis, particularly in patients with a diabetic foot infection; this finding suggests that an assumption of low prevalence may be risky.³⁴ In addition, MRI permits detection of deep collections of pus or necrotic tissue and visualization of foot anatomy, which helps the surgeon plan surgery when indicated. The Infectious Disease Society of America has already recognized that MRI is the preferred advanced imaging test for suspected osteomyelitis but recommends performing serial plain radiography before ordering an MRI.³⁵ We are unaware of any study that has formally evaluated serial plain radiography vs early MRI. Such an investigation and/or cost-effectiveness analysis would likely clarify better the place for MRI in the diagnostic algorithm of os-

teomyelitis of the foot.³⁵ Clinicians should, of course, consider history, physical examination findings, and imaging test results before deciding on therapeutic interventions.

In this meta-analysis, we chose to focus on osteomyelitis of the foot and ankle, because disease of the foot and ankle is a distinct entity that affects a particular patient population, that is, patients with diabetes and/or peripheral neuropathy. We did not analyze non-English-language articles. We are unaware of any evidence of bias in English language studies that assessed technology.

We did not exclude studies on the basis of date of publication or advent of innovation or variation in interpretation of MRI. Although MRI evaluation of osteomyelitis has evolved, with gadolinium now often used, subset analysis based on gadolinium use did not reveal any substantial variation in performance. Secondary diagnostic signs (such as cortical breaks) appeared to be incorporated into the diagnostic algorithm for osteomyelitis more frequently in recent publications. Ahmadi et al³¹ recently published a retrospective analysis of additional criteria for use in assessing osteomyelitis superimposed on Charcot foot, but this work is still largely untested.

As for the comparison of diagnostic tests, we focused on comparing MRI with plain radiography and radionuclide scanning, making 3 discrete head-to-head comparisons with MRI. A recent review by the Health Technology Assessment group supports this approach, suggesting that heterogeneity of diagnostic test comparisons will be less of a problem in head-to-head comparisons.³⁶ We did not analyze other imaging modalities, such as combined bone scanning and WBC study, computed tomography, immunoglobulin tagged tracer scanning, or positron emission tomography, because 2 or fewer studies directly compared them to MRI. We did not compare the performance of biopsy with MRI. A biopsy affords information regarding the exact pathogen responsible for infection, something that imaging tests cannot do.

According to 2006 figures, Medicare reimburses \$288 for a 3-phase bone scan and \$416 for a lower-

extremity MRI without contrast (\$451 with contrast).^{37,38} We calculated these values on the basis of how our center bills Medicare, which is the sum of the reimbursement to our facility when providing the service to an outpatient and the reimbursement to the radiologist interpreting the film (the professional component alone). For an inpatient, Medicare reimburses the relevant diagnosis-related code; therefore, unique MRI payment information is not available. Given the small difference in cost (which is approximated by Medicare reimbursement) between MRI and ^{99m}Tc bone scan and the large difference in diagnostic performance between these technologies, MRI would be more cost-effective except when the probability of disease was low. Local availability and cost of each test must also be considered when selecting the appropriate test. Formal decision modeling is needed to fully characterize the place of MRI in the diagnostic algorithm of osteomyelitis of the foot and ankle.

In summary, MRI has a strong performance in the diagnosis of osteomyelitis of the foot and ankle in adults. It outperforms 3-phase ^{99m}Tc bone scanning and plain radiography. The role of bone scanning is probably eclipsed by that of MRI except in cases in which MRI is contraindicated or the probability of disease is low.

Accepted for Publication: September 15, 2006.

Correspondence: Alok Kapoor, MD, Division of General Internal Medicine, Boston University, 91 E Concord St, MAT 200, Second Floor, Boston, MA 02118 (alok.kapoor@bmc.org).

Author Contributions: Dr Kapoor had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Kapoor and Felson. *Acquisition of data:* Kapoor. *Analysis and interpretation of data:* Kapoor, Page, LaValley, Gale, and Felson. *Drafting of the manuscript:* Kapoor, Page, and Felson. *Critical revision of the manuscript for important intellectual content:* Kapoor, Page, LaValley, and Gale. *Statistical analysis:*

LaValley. *Obtained funding:* Felson. *Administrative, technical, and material support:* Kapoor, Page, Gale, and Felson. *Study supervision:* Felson. **Financial Disclosure:** None reported.

Funding/Support: This study was supported by National Research Service Award T-32 HP 10028-08 and by grant AR47785 from the National Institutes of Health.

Acknowledgment: We thank Gary Gibbons, MD, Charles Foster, MD, and Jorge Medina, MD, for their consultation on this project. Special thanks also to Louise Falzon, MLIS, and Joseph Harzbecker, MLS, for the guidance in preparation of search strategies.

REFERENCES

1. Agency for Healthcare Research Quality. Health Care Utilization Project (HCUP). <http://hcup.ahrq.gov/HCUPnet.asp>. Accessed November 9, 2005.
2. Jude EB, Selby PL, Mawer EB, Burgess J, Boulton AJM. Inflammatory and bone turnover markers in Charcot arthropathy and osteomyelitis of the feet in diabetic patients. *Diabetologia*. 2002;45(suppl 2):A341-A342.
3. Eneroth M, Larsson J, Apelqvist J. Deep foot infections in patients with diabetes and foot ulcer: an entity with different characteristics, treatments, and prognosis. *J Diabetes Complications*. 1999;13:254-263.
4. Black ER, Bordley DR, Tape TG, Panzer RJ. *Diagnostic Strategies for Common Medical Problems*. 2nd ed. East Peoria, Ill: Versa Press; 1999.
5. Jeffcoate WJ, Lipsky BA. Controversies in diagnosing and managing osteomyelitis of the foot in diabetes. *Clin Infect Dis*. 2004;39(suppl 2):S115-S122.
6. Becker W. Imaging osteomyelitis and the diabetic foot. *Q J Nucl Med*. 1999;43:9-20.
7. Karchevsky M, Schweitzer ME, Morrison WB, Parellada JA. MRI findings of septic arthritis and associated osteomyelitis in adults. *AJR Am J Roentgenol*. 2004;182:119-122.
8. Eckman MH, Greenfield S, Mackey WC, et al. Foot infections in diabetic patients: decision and cost-effectiveness analyses. *JAMA*. 1995;273:712-720.
9. Matowe L, Gilbert FJ. How to synthesize evidence for imaging guidelines. *Clin Radiol*. 2004; 59:63-68.
10. Termaat MF, Raijmakers PGHM, Scholten HJ, Bakker FC, Patka P, Haarman HJTM. The accuracy of diagnostic imaging for the assessment of chronic osteomyelitis: a systematic review and meta-analysis. *J Bone Joint Surg Am*. 2005; 87:2464-2471.
11. Bossuyt PM, Reitsma JB, Bruns DE, et al. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Ann Intern Med*. 2003;138:W1-W12.
12. Littenberg B, Moses LE. Estimating diagnostic accuracy from multiple conflicting reports: a new meta-analytic method. *Med Decis Making*. 1993; 13:313-321.
13. Moses LE, Shapiro D, Littenberg B. Combining in-

- dependent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. *Stat Med*. 1993; 12:1293-1316.
14. Craig JG, Amin MB, Wu K, et al. Osteomyelitis of the diabetic foot: MR imaging—pathologic correlation. *Radiology*. 1997;203:849-855.
 15. Croll SD, Nicholas GG, Osborne MA, Wasser TE, Jones S. Role of magnetic resonance imaging in the diagnosis of osteomyelitis in diabetic foot infections. *J Vasc Surg*. 1996;24:266-270.
 16. Enderle MD, Coerper S, Schweizer HP, et al. Correlation of imaging techniques to histopathology in patients with diabetic foot syndrome and clinical suspicion of chronic osteomyelitis: the role of high-resolution ultrasound. *Diabetes Care*. 1999; 22:294-299.
 17. Ertugrul MB, Baktiroglu S, Salman S, et al. The diagnosis of osteomyelitis of the foot in diabetes: microbiological examination vs. magnetic resonance imaging and labelled leucocyte scanning. *Diabet Med*. 2006;23:649-653.
 18. Horowitz JD, Durham JR, Nease DB, Lukens ML, Wright JG, Smead WL. Prospective evaluation of magnetic resonance imaging in the management of acute diabetic foot infections. *Ann Vasc Surg*. 1993;7:44-50.
 19. Kearney T, Pointin K, Cunningham D, Gedroyc W, Robinson S, Elkeles RS. The detection of pedal osteomyelitis in diabetic patients. *Pract Diabetes Int*. 1999;16:98-100.
 20. Ledermann HP, Schweitzer ME, Morrison WB. Nonenhancing tissue on MR imaging of pedal infection: characterization of necrotic tissue and associated limitations for diagnosis of osteomyelitis and abscess. *AJR Am J Roentgenol*. 2002; 178:215-222.
 21. Levine SE, Neagle CE, Esterhai JL, Wright DG, Dalinka MK. Magnetic resonance imaging for the diagnosis of osteomyelitis in the diabetic patient with a foot ulcer. *Foot Ankle Int*. 1994;15:151-156.
 22. Lipman BT, Collier BD, Carrera GF, et al. Detection of osteomyelitis in the neuropathic foot: nuclear medicine, MRI and conventional radiography. *Clin Nucl Med*. 1998;23:77-82.
 23. Maas M, Slim EJ, Heekema AF, et al. MR imaging of neuropathic feet in leprosy patients with suspected osteomyelitis. *Int J Lepr Other Mycobact Dis*. 2002;70:97-103.
 24. Morrison WB, Schweitzer ME, Batte WG, Radack DP, Russel KM. Osteomyelitis of the foot: relative importance of primary and secondary MR imaging signs. *Radiology*. 1998;207:625-632.
 25. Nigro ND, Bartyński WS, Grossman SJ, Kruljac S. Clinical impact of magnetic resonance imaging in foot osteomyelitis. *J Am Podiatr Med Assoc*. 1992; 82:603-615.
 26. Remedios D, Valabhji J, Oelbaum R, Sharp P, Mitchell R. 99mTc-nanocolloid scintigraphy for assessing osteomyelitis in diabetic neuropathic feet. *Clin Radiol*. 1998;53:120-125.
 27. Seabold JE, Flickinger FW, Kao SC, et al. Indium-111-leukocyte/technetium-99m-MDP bone and magnetic resonance imaging: difficulty of diagnosing osteomyelitis in patients with neuropathic osteoarthropathy. *J Nucl Med*. 1990;31: 549-556.
 28. Vesco L, Boulahdour H, Hamissa S, et al. The value of combined radionuclide and magnetic resonance imaging in the diagnosis and conservative management of minimal or localized osteomyelitis of the foot in diabetic patients. *Metabolism*. 1999;48:922-927.
 29. Weinstein D, Wang A, Chambers R, Stewart CA, Motz HA. Evaluation of magnetic resonance imaging in the diagnosis of osteomyelitis in diabetic foot infections. *Foot Ankle*. 1993;14:18-22.
 30. Yuh WT, Corson JD, Baraniewski HM, et al. Osteomyelitis of the foot in diabetic patients: evaluation with plain film, 99mTc-MDP bone scintigraphy, and MR imaging. *AJR Am J Roentgenol*. 1989;152:795-800.
 31. Ahmadi ME, Morrison WB, Carrino JA, Schweitzer ME, Raikin SM, Ledermann HP. Neuropathic arthropathy of the foot with and without superimposed osteomyelitis: MR imaging characteristics. *Radiology*. 2006;238:622-631.
 32. Horden LD. UpToDate. <http://www.uptodate.com/>. Accessed November 9, 2005.
 33. Mushlin AI, Littenberg B. Diagnosing pedal osteomyelitis: testing choices and their consequences. *J Gen Intern Med*. 1994;9:1-7.
 34. Newman LG, Waller J, Palestro CJ, et al. Unsuspected osteomyelitis in diabetic foot ulcers: diagnosis and monitoring by leukocyte scanning with indium In 111 oxyquinoline. *JAMA*. 1991;266: 1246-1251.
 35. Lipsky BA, Berendt AR, Deery G, et al; Infectious Diseases Society of America. Diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2004;39:885-910. <http://www.journals.uchicago.edu/CID/journal/issues/v39n7/34365/34365.html>. Accessed August 22, 2006.
 36. Dinnes J, Deeks J, Kirby J, Roderick P. A methodological review of how heterogeneity has been examined in systematic reviews of diagnostic test accuracy. *Health Technol Assess*. 2005;9(12): 1-113, iii.
 37. Centers for Medicare & Medicaid. Hospital Outpatient PPS Addendum B. July 2006. <http://www.cms.hhs.gov/HospitalOutpatientPPS/AU/list.asp#TopOfPage>. Accessed August 24, 2006.
 38. Centers for Medicare & Medicaid. Physician fee schedule relative value files: RVU06A. July 2006. <http://www.cms.hhs.gov/PhysicianFeeSched/PFSRVF/list.asp#TopOfPage>. Accessed August 24, 2006.