Role of magnetic resonance imaging in the diagnosis of osteomyelitis in diabetic foot infections

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Purpose: **The role of magnetic resonance imaging (MRI) in the diagnosis of osteomyelitis in foot infections in diabetics was investigated. The accuracy, sensitivity, and specificity of MRI, plain radiography, and nuclear scanning were determined for diagnosing osteomyelitis, and a cost comparison was made.**
Methods: **Twenty-seven patients with diabetic foot infections were studied prospectively. All patients underwent MRI and plain radiography. Twenty-two patients had technetium bone scans, and 19 patients had Indium scans. Nineteen patients had all four tests performed. Patients with obvious gangrene or a fetid foot were excluded.**
Results: **The diagnosis of osteomyelitis was established by pathologic specimen (n = 18), bone culture (n = 3), or successful response to medical management (n = 6). Osteomyelitis was confirmed in nine of the pathologic specimens. The diagnostic sensitivity, specificity, and accuracy for MRI was 88%, 100%, and 95%, respectively, for plain radiography it was 22%, 94%, and 70%, respectively, for technetium bone scanning it was 50%, 50%, and 50%, respectively, and for Indium leukocyte scanning it was 33%, 69%, and 58%, respectively. The data were analyzed statistically with the two-tailed Fisher's exact test. MRI was the only test that was statistically significant ($p < 0.01$).**
Conclusions: **MRI appeared to be the single best test for the diagnosis of osteomyelitis associated with diabetic foot infections. It had a better diagnostic accuracy than conventional modalities and appeared to be more cost-effective than the frequently used Indium scan. (J Vasc Surg 1996;24:266-70.)**

Diabetic foot infections account for 20% of hospital admissions among patients with diabetes and 80% of infectious amputations each year.[1] Currently, approximately 15 million diabetic patients are in the United States, and this number increases by 6% annually.[2] Diabetic foot infections represent a significant problem, causing disability, suffering, and medical expense. Although Eckman et al.[3] have recommended empiric treatment of suspected osteomyelitis in diabetics, a precise diagnosis is preferable when a prolonged course of therapy or amputation is advised.

Prevention still remains the best means to preserve the diabetic foot. However, once infection is present, debridement of devitalized tissue with preservation of the uncompromised tissue is of paramount importance. Exploration of a foot that does not have osteomyelitis can lead to needless amputation with attendant morbidity and disability. Traditionally, plain radiography and nuclear scanning were the standard for diagnosing osteomyelitis. These tests, however, can be falsely positive and negative.[4-7] Recently, magnetic resonance imaging (MRI) has been successful in diagnosing diabetic foot infections.[5-11] The goal of this study was to determine the accuracy of MRI for diagnosing osteomyelitis in diabetic patients' feet and compare this with traditional modalities. A cost comparison was also made.

METHODS

Between November 1991 and December 1992, 27 patients (19 men and 8 women) admitted to the Lehigh Valley Hospital with diabetic foot infections were enrolled in the study group. Patients underwent complete history and physical examination, and per-

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tinent laboratory studies were performed. Patients with obvious gangrene or a fetid foot who required immediate surgery were excluded from the study.

Initial broad-spectrum antibiotics were narrowed according to subsequent bacterial sensitivity determinations. Limbs were evaluated for ischemia by physical examination and Doppler studies. Seven patients underwent arteriographic evaluation. The subsequent treatment of patients was based on clinical judgment of the attending physician, who was not blinded to the results of the previously mentioned studies. Successful medical management was defined as a 5- to 10-day course of antibiotics and local care that resulted in a healed or improved ulcer at the time of follow-up (2 to 6 months).

The cost of each study was determined by the hospital accounting office and included the cost of performing the study and the reimbursement for reading the study by the hospital-based physicians.

Bone scanning was performed with a gamma camera and three-phase technique. Technetium-99_m-MDP was used in a dose of 20 μCi. Flow images, blood pool, and delayed images were then obtained.

Leukocyte scanning was performed according to the method of Thakur et al.[12] Leukocytes were obtained from a 50 ml blood sample. After separation, washing, and resuspension of the leukocytes were performed, labeling was performed with 500 to 600 μCi of Indium-111 Oxine, and the cells were reinjected. Plantar and lateral or medial images of the infected foot were obtained the next day (18 to 24 hours after reinjection) with a large field of view gamma camera fitted with a medium-energy collimator and were centered on the 173 kev and 247 kev photopeaks of Indium-111. Images were acquired for 10 minutes in each projection.

All patients underwent MRI scanning with a 1.5 tesla Signa system (General Electric Medical Systems, Milwaukee, Wis.). Scans were obtained with a dedicated extremity coil. All patients underwent scanning in the axial oblique and coronal oblique planes. T1-weighted images were obtained with spin-echo technique with TR/TE = 700/13 msec, slice thickness = 4 mm, 256 × 256 matrix, 2 excitations, and field of view = 16 to 20 cm. T2-weighted images were also obtained in both planes, and spin-echo technique was used with TR/TE = 3000/45, 90 msec, 256 × 125 matrix, 2 excitations, and field of view = 16 to 20 cm. In all cases an inversion recovery scan was obtained in the axial oblique plane (TR/TE = 2000/40 msec, TI = 165 msec, 256 × 128 matrix, 2 excitations, 4 mm slice thickness).

All patients in the series (27) had loss of skin integrity with either ulceration or eschar formation. Patients with cellulitis only were not included in the study. The bone submitted for pathologic examination was determined by the surgeon on the basis of clinical examination and the results of the diagnostic studies performed. Repeat MRI and scintigraphy were not performed to confirm the removal of the involved bone. Gross and microscopic evaluations were performed on all bone and soft tissue excised or amputated. The diagnosis of osteomyelitis was based on histologic findings of subperiosteal new bone formation, lytic areas of bone loss, the presence of fibrosis, and infiltration of polymorphonuclear leukocytes and lymphocytes.

Interpretation of the studies was done by staff radiologists and nuclear medicine specialists and was reviewed by the clinicians. The physicians were not specifically blinded to the results of the other diagnostic studies, but none was aware of the pathologic end point of the presence or absence of osteomyelitis before submitting their reports.

RESULTS

A total of 27 patients were (19 men and 8 women) entered in this study. Their mean age was 66 years (range 34 to 82 years), and the mean duration of diabetes was 20 years. One patient had his diabetes diagnosed at the time of entrance into the study. Fifty-nine percent of patients controlled their diabetes with insulin, 30% used oral agents, and the remainder used dietary control alone. The mean hemoglobin A_1C was 8.1% with a range of 5.1% to 13%. Seven patients had undergone previous vascular bypass procedures. Six patients were active smokers. Presenting signs included cellulitis (70%), seropurulent drainage (67%), leukocyte count greater than 10,000/mm^3 (33%), absent dorsalis pedis and posterior tibial pulses (44%), and neuropathy (67%). Patients with cellulitis only were not included in the study.

All 27 patients underwent MRI and plain radiography. Twenty-two patients received triple-phase bone scans (^{99m}Tc-MDP), and 19 patients received Indium-labeled leukocyte scans (^{111}In-WBC). The accuracy of each modality for diagnosing osteomyelitis was determined, and a cost comparison was made (Table I). The diagnosis of osteomyelitis was confirmed or refuted by pathologic specimen (n = 18, 67%) or bone culture (n = 3, 11%) or was excluded by response to medical management (n = 6, 22%). Osteomyelitis was present in 9 of the 21 specimens of bone examined as part of open debridements, biopsies, or amputations. There were five positive specimens from open debridement, one from bone biopsy,

Table I. Diagnostic test results for osteomyelitis in 27 patients

	n	*Sensitivity (%)*	*Specificity (%)*	*Accuracy (%)*	*Cost ($)*
MRI	27	89	100	95	785
Plain radiographs	27	22	94	70	76
Technetium bone scan	22	50	50	50	235
Indium leukocyte scan	19	33	69	58	1045

and three from amputations. The data were analyzed statistically for overall diagnostic precision with a two-tailed Fisher's exact test. MRI was the only test that was statistically significant ($p < 0.01$).

Nine patients underwent open debridement with bone resection; five had pathologic report positive for osteomyelitis, and four specimens were negative. One (11%) false-negative MRI result was found in these nine patients. Seven patients also had ^{99m}Tc-MDP scans performed; two (29%) were false-positive, and three (43%) were false-negative. Five of the nine patients had ^{111}In-WBC scans performed; two (40%) were false-positive, and three (60%) were false-negative. The plain radiographs of these nine patients revealed one (11%) false-positive result and three (33%) false-negative results. One patient had an abscess diagnosed by MRI that was confirmed at the time of operation. Three patients in this group subsequently required revascularization procedures.

Three patients had bone cultures performed; two were negative, and one was positive. Both patients with negative bone cultures responded to a brief course of antibiotics and local care. The patient with the positive bone culture responded to 6 weeks of intravenous antibiotics. All three patients had MRI, ^{99m}Tc-MDP, and ^{111}In-WBC scans. The three MRIs agreed with the cultured results. Two false-positive ^{99m}Tc-MDP scans and one false-positive ^{111}In-WBC scan occurred. The plain radiographs revealed one false-negative result.

Nine patients had amputations; seven had two amputations, and two had transmetatarsal amputations. Three patients had pathologically confirmed osteomyelitis, and the remaining six specimens were negative. The MRI scans agreed with the pathologic specimens in all nine patients, and two of the scans showed abscesses that were confirmed at operation. Seven of the nine patients received ^{99m}Tc-MDP scans; one (14%) was false-negative, and one (14%) was false-positive. Six of the nine patients also received ^{111}In-WBC scans, of which one (17%) was false-positive, and one (17%) was false-negative. There were also three (33%) false-negative (33%) plain radiographs in this group. Four of these patients had subsequent revascularization procedures. All nine of the patients' amputation sites ultimately healed.

In six patients successful medical treatment excluded the diagnosis of osteomyelitis. Their plain radiographs and MRIs were negative for osteomyelitis. Two (33%) ^{99m}Tc-MDP scans were false-positive. Five of the six patients had ^{111}In-WBC scans performed, and all of these were negative for osteomyelitis. Exclusion of the six medically treated patients from the analysis revealed eight true-positive results, zero false-positive results, 18 true-negative results, and one false-negative result with a sensitivity of 88.8%, specificity of 100%, and an overall accuracy of 96.3%.

DISCUSSION

Foot infections in diabetic patients are often the precursor to the loss of multiple digits or major amputation and therefore should be recognized and treated promptly. Clinical evaluation of foot infections in diabetic patients is valuable. The presence of a fetid wound or extensive gangrene precludes the need for more sophisticated studies, because surgical debridement is inevitable. In addition, the finding of palpable exposed bone at the base of an open wound in a diabetic's foot has been shown to correlate well with the presence of osteomyelitis, and therefore more expensive diagnostic studies may be unnecessary.[3]

Pedal osteomyelitis is a common complication of diabetes, occurring in up to 15% of patients.[13] Because of superimposed abnormalities such as neuropathic joint disease, trauma, and chronic soft-tissue changes, an accurate diagnosis of osteomyelitis based on plain radiographs or ^{99m}Tc-MDP scans is difficult.[5-7,13,14] Radiographic findings may be normal or present only as soft-tissue swelling at the time of initial presentation in acute osteomyelitis, because any radiographic changes are not apparent for 10 to 14 days.[5,13] When radiographic abnormalities are seen, they may be difficult to interpret, because similar changes may occur with diabetic osteopathy or minor trauma.[5,13] Therefore plain radiographic evaluation for osteomyelitis in the diabetic foot is fraught with error.[13]

The ^{99m}Tc-MDP scan gives less anatomic detail than radiographs but provides more functional information. Commonly, the bone scan will be positive before there is enough bone mineral loss to be seen on routine radiographs.[15] Localization of ^{99m}Tc-MDP is related both to osteoblastic activity and skeletal vascularity. The accuracy of these scans for the diagnosis of osteomyelitis is also limited in the diabetic patient because of the previously noted superimposed abnormalities. The sensitivity of ^{99m}Tc-MDP scans for diagnosing osteomyelitis in diabetic patients ranges from 75% to 100%, with specificity ranging from 25% to 77%.[6,14,16] This study had a sensitivity of 33%, which is lower than that reported by others. The specificity in our study was 50%, and this is consistent with previous reported series.

^{111}In-WBC scans have been used with varying results for the diagnosis of osteomyelitis in diabetic patients. Sensitivities ranging from 50% to 100% and specificities ranging from 29% to 100% have been reported.[6,7,16-18] In this study the sensitivity for ^{111}In-WBC scans was 33%, and the specificity was 69%. Inconsistencies in ^{111}In-WBC scans may be due to the fact that Indium-labeled white blood cells localize at noninfected acute fracture sites, and stress fractures frequently occur at sites of neuropathic osteoarthropathy and may not be seen on plain radiographs.[19,20] In addition, the poor spacial resolution afforded by scintigraphic technique can make it difficult to determine whether osteomyelitis is present at sites with adjacent soft-tissue infection.[14,19,20] In addition, diabetic patients frequently have impaired circulation to their feet, which can lead to false-negative results, if the isotope does not reach the area of infection.[4,14] Our poor results on ^{111}In-WBC scans may be attributed to the previously mentioned difficulties. Reader error, however, must be considered as a possible cause, because the same group of nuclear medicine physicians read both the ^{99m}Tc-MDP scans and the ^{111}In-WBC scans, and the reported sensitivities of both of these tests were lower than results reported by others. Other studies have evaluated combined ^{111}In-WBC/^{99m}Tc-MDP scans to differentiate soft-tissue infection from bony involvement. Results have been successful, but the tests can take up to 48 hours to perform and at a significant cost.[17,18,20] In one study leukocyte scans with ^{111}In in 12 patients yielded a sensitivity of 100% and a positive predictive value of 100% when results were compared with those of bone biopsy. However, 11 other patients with foot ulcers seen in the same time interval were excluded from the study, and this weakens any conclusions drawn regarding the value of ^{111}In scanning.[21]

Recently, MRI has demonstrated good diagnostic accuracy in the evaluation of diabetic foot infections.[6,7,9-11,22] Sensitivities and specificities ranging from 77% to 100% and 81% to 100%, respectively, have been reported in diabetic patients.[6,11,12] With contrast-enhanced T1-weighted MRIs, a sensitivity of 88% and specificity of 93% were noted in a series of 51 cases. These results were superior to the three-phase bone scans performed in the same patients.[23] In this study we found a sensitivity of 89% and a specificity of 100%.

MRI appears to be more accurate than plain radiography, ^{99m}Tc-MDP scanning, and ^{111}In-WBC scanning. It also appears to be equal to or superior to combined ^{111}In-WBC/^{99m}Tc-MDP scanning.[17,18,20] Weinstein et al.[24] noted MRI to be superior to both technetium-99 and gallium-67 bone scans ($p < 0.01$) in a series of 14 patients with pathologic tissue diagnosis. MRI offers several distinct advantages including a shorter performance time (approximately 1 hour vs 48 hours for the ^{111}In-WBC/^{99m}Tc-MDP scans). Ionizing radiation is also avoided. The excellent soft-tissue detail demonstrated on MRI scans helps identify the extent of cellulitis and localization of abscess, thereby directing surgical exploration of an already tenuous foot.[9-11] Although MRI is more cost-effective than combined ^{111}In-WBC/^{99m}Tc-MDP scans ($785 vs $1280), Eckman et al. state that the cost of MRI would need to be less than $185 to make the imaging more cost-effective than empiric therapy with antibiotics and debridement.[3]

The indications for the nine amputations performed in our study included not only osteomyelitis but extensive soft-tissue necrosis with loss of digital skin and exposure of tendons and joint capsule. Seven patients required revascularization. It is our protocol to perform early debridement amputations so that a closed healed wound may be obtained with a patent bypass graft.

Shortcomings of this study include the end point of successful medical management as documentation of the absence of osteomyelitis. This is not as accurate as the bacteriologic and pathologic confirmation of the diagnosis of osteomyelitis. Defining the absence of osteomyelitis based on the response to medical management is a soft end point when compared with pathologic diagnosis. The definition, however, was made conservatively by requiring continued wound healing for the 2- to 6-month follow-up period after a brief, not ongoing course of antibiotics. Even with those six patients excluded, the value of MRI was still clearly demonstrated (sensitivity, 88.9%, specificity, 100%). Because all six patients met the end point of absence of osteomyelitis as defined previously, they were therefore all considered true-negative studies. The exclusion of patients from this study who entered the hospital with advanced gangrene and foot sepsis also limits the generalization of these results. Clinical judgment mandated immediate surgical intervention, and there was no utility to further diagnostic studies. Each clinician will have a somewhat different threshold in selecting patients for immediate surgical treatment.

The reliability of the diagnostic studies is also dependent on the site of bony involvement. All of the positive pathologic specimens for osteomyelitis and positive MRI studies were for bones from the forefoot (phalanges or distal metatarsals). No specimens were obtained from the midfoot or hindfoot. The findings on bone biopsy may also on occasion be spurious because of sampling error or previous antibiotic therapy. However, in our study, if the three cases diagnosed by bone biopsy are excluded, the sensitivity of MRI is still 87.5%, and the specificity remains 100%.

This study demonstrated the advantage of MRI over nuclear scanning and plain radiography. We have altered our clinical algorithm for the care of similar patients to recommend MRI evaluation early in their clinical course. In conclusion, we showed that MRI was a sensitive and specific test for the diagnosis of osteomyelitis in diabetic foot infections. It had a better diagnostic accuracy than the conventional modalities of plain radiography, ^{99m}Tc-MDP scanning, or ^{111}In-WBC scanning. It was also more cost-effective than the frequently used ^{111}In-WBC scanning or combined ^{111}In-WBC/^{99m}Tc-MDP scanning.

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