Does This Patient With Diabetes Have Osteomyelitis of the Lower Extremity?

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CLINICAL SCENARIOS

Case 1
A 52-year-old woman is referred from the emergency department with a diabetic foot ulcer. She has type 1 diabetes mellitus that was first diagnosed at age 12 years. Her condition is complicated by nephropathy, retinopathy, and peripheral vascular disease. She has recently noticed erythema, swelling, and pain over the left foot. On physical examination, she has a pulse of 90/min, blood pressure of 136/84 mm Hg, and temperature of 36.1°C. Pedal pulses are diminished. There is a 2.2 × 1.5-cm ulcer in the toe webbing that probes to underlying bone. Investigations reveal a white blood cell count of 9500/µL and an erythrocyte sedimentation rate (ESR) of 75 mm/h. Wound swab Gram stain reveals gram-positive cocci and gram-negative bacilli. Radiographs of the foot identify soft tissue swelling and cortical erosion in the area of the ulcer. Should magnetic resonance imaging (MRI) of the foot be ordered?

Case 2
A 64-year-old man is referred with a nonhealing ulcer. He has a small wound overlying the fourth metatar-
inadequately treated, osteomyelitis in-
tation is reported to be 7.4%.6

...patients having lower extremity amputa-
ulcer care in the United States alone.2

...on diabetic foot
1995 to 1996 revealed that US $1.45 bil-
...infections begins with an assess-
...patient to skin breakdown. The history taking should

...myelitis?

WHY IS THIS DIAGNOSIS IMPORTANT?

Foot-related complications account for
up to 20% of all diabetes-related ad-
missions in the North American dia-
abetic population.1 Medicare data from
1995 to 1996 revealed that US $1.45 bil-
...of these cases.4 When

...ostomyelitis in-creases the risk of amputation.3 The

...mortality of pa-
tients having lower extremity amputa-
...to be 7.4%.6

The diagnosis of lower limb osteo-
myelitis in patients with diabetes
remains a challenge. The classic signs
and symptoms of infection may be
absent or masked by the coexistence
of vascular disease and neuropathy.
The gold standard for the diagnosis of
osteomyelitis is a bone biopsy and
culture. This invasive procedure is
not always practical7 and may be con-
traindicated in patients with diabetes
and severe peripheral vascular dis-
ease. It is therefore important to
determine the features of the history,
physical examination, and prelimi-
nary investigations that aid in the
diagnosis of osteomyelitis to minimize
costly and invasive investigations and
initiate appropriate and timely
therapy. Herein, we summarize the
test characteristics of the history,
physical examination, routinely avail-
able laboratory measurements and
radiographs, and MRI for evaluating
lower extremity osteomyelitis in
patients with diabetes.

CLINICAL EVALUATION OF THE LOWER EXTREMITY
IN PATIENTS WITH DIABETES

History

The evaluation for osteomyelitis and
other infections begins with an assess-
ment of a patient’s diabetes and the risk
factors that predispose a patient to skin
breakdown. The history taking should
include duration of diabetes, glycemic
control, microvascular or macrovascular
disease, and presence of peripheral
neuropathy and peripheral vascular dis-
ease. In addition, the clinician should
inquire about recent trauma and his-
tory of ulcers.

Physical Examination

On physical examination, the clinician
should assess for local and systemic
features of infection such as fever,
chills, hypotension, and presence and
appearance of wound or ulcer (ery-
thema, swelling, purulence, size, and
depth).7-10 The clinician should note
the presence of foot deformities, ten-
derness, neuropathy, and venous or
arterial insufficiency.7,11,12 Because of
neuropathy, patients may not perceive
foreign bodies within the ulcer.

It is sometimes difficult to distin-
guish between lower extremity ulcers
due to diabetes and those caused pri-
marily by venous or arterial insuffi-
ciency. Venous ulcers are typically
found above the medial or lateral malleoli
and frequently have irregular bor-
ders. Arterial ulcers often affect the toes
or the shins, with the borders of the ul-
cer being pale and appearing as if they
have been punched out. These ulcers
may lack granulation tissue and are
typically painful in the absence of co-
existing neuropathy. Diabetic ulcers
usually occur at areas of increased
pressure, such as the sole of the foot, or
areas where shoes have rubbed against the
skin.13 Although any ulcer is a risk fac-
tor for osteomyelitis, the traumatized
skin in a patient with vascular insuffi-
ciency is also prone to this disease pro-
cess.14

Ulcer Area. One method for quan-
tifying ulcer size is to multiply the long-
est and widest diameters of the le-
sion.9 This may not be a completely
accurate estimation of ulcer area, as
some ulcers may be round or irregu-
larly shaped.

Probe-to-Bone Test. The probe-to-
bone test of a foot ulcer is performed
at the bedside with a sterile, blunt, stain-
less steel probe. The examiner gently
probes the wound for the presence of
a rock-hard, gritty structure at the
wound base in the absence of any in-
tervening soft tissue. The presence of
such a finding indicates a positive
probe-to-bone result, whereas the in-
ability to probe the base of a wound to
periosteum or bone is a negative re-
result.10

Wagner Grade. Wagner8 developed
a scale to grade foot ulcers based on ob-
servations. Foot ulcers are graded from
0 to 5 based on depth of lesion and pres-
ence or absence of features of infec-
tion and/or gangrene (Box 1). A limi-
tation of the Wagner grading scale is

Box 1. Wagner Grading Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No open lesions; may have evidence of healed lesions or deformities</td>
</tr>
<tr>
<td>1</td>
<td>Superficial ulcer</td>
</tr>
<tr>
<td>2</td>
<td>Deeper ulcer to tendon, bone, or joint capsule</td>
</tr>
<tr>
<td>3</td>
<td>Deeper tissues involved, with abscess, osteomyelitis, or tendinitis</td>
</tr>
<tr>
<td>4</td>
<td>Localized gangrene of toe or forefoot</td>
</tr>
<tr>
<td>5</td>
<td>Gangrene of foot (partial or total)</td>
</tr>
</tbody>
</table>

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that all deep tissue infections (including abscess, tendinitis, and osteomyelitis) are accounted for in a single grade.

METHODS
Search Strategy and Study Selection
We searched the MEDLINE electronic database for English-language articles between 1966 and March 2007 using the following search terms: osteomyelitis, diabetes, signs and symptoms, physical examination, diagnosis, diagnostic tests, and “sensitivity and specificity.” We identified additional references by modifying a previously published search strategy.15 This strategy combined 9 exploded Medical Subject Headings (physical examination, medical history taking, professional competence, “sensitivity and specificity,” reproducibility of results, observer variation, “diagnostic tests, routine,” decision support techniques, and Bayes theorem). We then took the intersection of this set with osteomyelitis and diabetes mellitus (exploded). We identified additional articles through a hand search of references from retrieved articles, previous reviews, and polling experts. The titles and abstracts (when available) of the articles retrieved were evaluated to determine their eligibility for our review. Publications in abstract and letter form were included to minimize publication bias.

Articles were included for review if they fulfilled all of the following criteria: (1) they were original studies describing historical features, physical examination, laboratory investigations, or plain radiograph in the diagnosis of lower extremity osteomyelitis in patients with diabetes mellitus, (2) data could be extracted to construct 2×2 tables or the article reported operating characteristics of the diagnostic measure, and (3) the diagnostic test was compared with a reference standard. Studies in pediatric populations or mixed populations of patients with and without diabetes were excluded. Data from a single high-quality meta-analysis, not conforming to the prespecified search criteria and data extraction, were used to summarize the test characteristics of MRI in patients with diabetes who were thought to have osteomyelitis.

Reference Standard
Bone biopsy is the gold standard for the diagnosis of osteomyelitis. Ideally, bone specimens should have both microbiological and histological analysis; however, we required the gold standard for osteomyelitis to be culture or histological results because patients had often received antibiotic therapy before bone biopsy or surgical intervention, thus lowering the yield of bone culture.

Quality Review
One author (S.B.) identified potential articles by screening the retrieved articles and by searching through the bibliographies of these articles. Two authors independently reviewed articles for quality and extracted the operating characteristics of the diagnostic tests. Each article was rated using a topic-specific quality rating scale that used published principles16 as well as a modified quality checklist specific to the Rational Clinical Examination series17 (Box 2).

Data Analysis
Likelihood ratios (LRs) predicting the presence of osteomyelitis, given a positive test result (sensitivity/specificity) and a negative test result (1–sensitivity/specificity) were calculated for each outcome of interest using published raw data.18 Where 2 or more studies examined the same clinical variable, we calculated summary LRs and 95% confidence intervals (CIs) using the DerSimonian and Laird random-effects approach.19 Estimated variances of LRs were computed using the usual methods for ratios of proportions,20 with their reciprocals used as study weights. In studies with a zero cell count, the value 0.5 was added to each cell count to permit use of this variance estimation. All analyses were performed using R software, version 2.0.1.21

RESULTS
Study Characteristics
The electronic literature search identified 279 studies, of which 21 met our inclusion criteria and form the basis of our review (TABLE 1 and FIGURE).9,10,22-40 The included studies accounted for a total of 1027 patients. Three studies reported sensitivity or specificity but not both.23,32,36 Eight studies prospectively...
evaluated patients. One meta-analysis of the test performance of MRI for the diagnosis of osteomyelitis of the foot and ankle included 11 studies in patients with diabetes and accounted for a total of 275 patients.41

### Prior Probability of Osteomyelitis

The prevalence of osteomyelitis in the selected studies ranged from 12%

## Table 1. Studies Addressing Diagnosis of Lower Extremity Osteomyelitis in Patients With Diabetes Mellitus

<table>
<thead>
<tr>
<th>Source</th>
<th>Level of Evidence</th>
<th>Study Type</th>
<th>Population</th>
<th>Prevalence of Osteomyelitis, %</th>
<th>Biopsy, %</th>
<th>Methods of Reaching a Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newman et al, 19919</td>
<td>II</td>
<td>Prospective</td>
<td>Inpatients and outpatients with foot ulcer (n = 35)</td>
<td>68&lt;sup&gt;a&lt;/sup&gt;</td>
<td>100&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Histology and/or culture</td>
</tr>
<tr>
<td>Grayson et al, 1995&lt;sup&gt;10&lt;/sup&gt;</td>
<td>III</td>
<td>Prospective</td>
<td>Inpatients with severe limb-threatening foot infections (n = 75)</td>
<td>66&lt;sup&gt;a&lt;/sup&gt;</td>
<td>61&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Histology or radiological evidence of bone destruction in association with an infected ulcer and/or purulent, friable, nonviable bone</td>
</tr>
<tr>
<td>Wang et al, 1990&lt;sup&gt;22&lt;/sup&gt;</td>
<td>III</td>
<td>Prospective</td>
<td>Inpatients with suspected osteomyelitis (n = 32)</td>
<td>74&lt;sup&gt;b&lt;/sup&gt;</td>
<td>100&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Histology</td>
</tr>
<tr>
<td>Johnson et al, 1996&lt;sup&gt;23&lt;/sup&gt;</td>
<td>III</td>
<td>Prospective</td>
<td>Suspected osteomyelitis (n = 22)</td>
<td>NA</td>
<td>72</td>
<td>Culture and histology or clinical follow-up</td>
</tr>
<tr>
<td>Enderle et al, 1999&lt;sup&gt;24&lt;/sup&gt;</td>
<td>III</td>
<td>Prospective</td>
<td>Suspected osteomyelitis and indication for minor amputation (n = 19)</td>
<td>74</td>
<td>100</td>
<td>Histology</td>
</tr>
<tr>
<td>Lee et al, 1986&lt;sup&gt;25&lt;/sup&gt;</td>
<td>III</td>
<td>Retrospective</td>
<td>Cellulitis or foot ulcers (n = 90)</td>
<td>27</td>
<td>Not stated</td>
<td>Surgical and pathologic “proof” or a positive bone scan with clinical response to therapy</td>
</tr>
<tr>
<td>Shone et al, 2006&lt;sup&gt;26&lt;/sup&gt;</td>
<td>III</td>
<td>Retrospective</td>
<td>Outpatients (n = 81)</td>
<td>20&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Not stated</td>
<td>Clinical in association with radiological evidence and, when necessary, MRI or deep tissue samples</td>
</tr>
<tr>
<td>Park et al, 1982&lt;sup&gt;27&lt;/sup&gt;</td>
<td>III</td>
<td>Retrospective</td>
<td>Variety of ischemic infections and/or ischemic problems (n = 59)</td>
<td>67</td>
<td>100</td>
<td>Histology</td>
</tr>
<tr>
<td>Weinstein et al, 1993&lt;sup&gt;28&lt;/sup&gt;</td>
<td>III</td>
<td>Retrospective</td>
<td>Inpatients with suspected osteomyelitis, nonhealing ulcer, or soft tissue infection (n = 32)</td>
<td>74&lt;sup&gt;b&lt;/sup&gt;</td>
<td>100&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Histology</td>
</tr>
<tr>
<td>Yuh et al, 1989&lt;sup&gt;29&lt;/sup&gt;</td>
<td>III</td>
<td>Retrospective</td>
<td>Suspected osteomyelitis and/or nonhealing foot ulcers (n = 14)</td>
<td>86&lt;sup&gt;b&lt;/sup&gt;</td>
<td>100&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Histology</td>
</tr>
<tr>
<td>Lavery et al, 2007&lt;sup&gt;30&lt;/sup&gt;</td>
<td>IV</td>
<td>Prospective</td>
<td>Outpatients (n = 247)</td>
<td>12</td>
<td>NA</td>
<td>Culture</td>
</tr>
<tr>
<td>Shults et al, 1989&lt;sup&gt;31&lt;/sup&gt;</td>
<td>IV</td>
<td>Prospective</td>
<td>Foot ulcers or infection limited to forefoot (n = 32)</td>
<td>72</td>
<td>100</td>
<td>Culture</td>
</tr>
<tr>
<td>Croll et al, 1996&lt;sup&gt;32&lt;/sup&gt;</td>
<td>IV</td>
<td>Prospective</td>
<td>Inpatients with foot infections (n = 27)</td>
<td>33</td>
<td>78</td>
<td>Histology, bone culture, or response to medical management</td>
</tr>
<tr>
<td>Keenan et al, 1989&lt;sup&gt;33&lt;/sup&gt;</td>
<td>IV</td>
<td>Retrospective</td>
<td>Suspected osteomyelitis (n = 77)</td>
<td>44&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Culture and/or histology or clinical evidence</td>
</tr>
<tr>
<td>Larcos et al, 1991&lt;sup&gt;34&lt;/sup&gt;</td>
<td>IV</td>
<td>Retrospective</td>
<td>Suspected osteomyelitis (n = 51)</td>
<td>27</td>
<td>55</td>
<td>Bone biopsy or culture or deep-wound culture during debridement or clinical follow-up as outpatient</td>
</tr>
<tr>
<td>Seldin et al, 1985&lt;sup&gt;35&lt;/sup&gt;</td>
<td>IV</td>
<td>Retrospective</td>
<td>Suspected osteomyelitis (n = 30)</td>
<td>60&lt;sup&gt;d&lt;/sup&gt;</td>
<td>60</td>
<td>Histology and/or culture or clinical resolution of symptoms without prolonged antibiotic therapy</td>
</tr>
<tr>
<td>Keal et al, 2001&lt;sup&gt;36&lt;/sup&gt;</td>
<td>IV</td>
<td>Retrospective</td>
<td>Inpatients (n = 29)</td>
<td>66</td>
<td>53</td>
<td>Histology, positive results of at least 2 imaging modes (bone scan, MRI, radiograph), or positive probe to bone</td>
</tr>
<tr>
<td>Levine et al, 1994&lt;sup&gt;37&lt;/sup&gt;</td>
<td>IV</td>
<td>Retrospective</td>
<td>Suspected osteomyelitis complicating a soft tissue infection (n = 27)</td>
<td>45&lt;sup&gt;c&lt;/sup&gt;</td>
<td>62&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Histology, surgical observation of lack of communication between infected region and bone, or clinical resolution</td>
</tr>
<tr>
<td>Ouen et al, 1992&lt;sup&gt;38&lt;/sup&gt;</td>
<td>IV</td>
<td>Retrospective</td>
<td>Suspected osteomyelitis (n = 16)</td>
<td>44</td>
<td>56</td>
<td>Histology or clinically</td>
</tr>
<tr>
<td>Armstrong et al, 1996&lt;sup&gt;39&lt;/sup&gt;</td>
<td>V</td>
<td>Retrospective</td>
<td>Inpatients (n = 28)</td>
<td>100</td>
<td>100</td>
<td>Intraoperative bone cultures at time of admission and/or histological evidence of osteomyelitis</td>
</tr>
<tr>
<td>Vesco et al, 1999&lt;sup&gt;40&lt;/sup&gt;</td>
<td>V</td>
<td>Retrospective</td>
<td>Inpatients (n = 24)</td>
<td>54</td>
<td>0</td>
<td>Clinical bone involvement (ie, the ability to probe to bone), radiologic evidence of bone involvement, positive combined radionuclide imaging and MRI, or clinical evidence of bone involvement during follow-up</td>
</tr>
</tbody>
</table>

**Abbreviations:** MRI, magnetic resonance imaging; NA, could not be determined with data provided.

<sup>a</sup>Calculations based on number of ulcers.

<sup>b</sup>Calculations based on number of bone specimens.

<sup>c</sup>Calculations based on number of cases.

<sup>d</sup>Calculations based on number of radiographs.
to 100%. A retrospective cohort study of 8905 patients with diabetes found that 15% of those with a foot ulcer developed osteomyelitis at or after diagnosis.22 The prior probability that a leg ulcer in a patient with diabetes will end up being osteomyelitis is more likely to reflect this value than the values found in the highly selected group of patients in the included studies.

**Precision of Symptoms, Signs, and Investigations for Osteomyelitis**

There were no studies identified that addressed the precision of symptoms, signs, or investigations in the diagnosis of lower extremity osteomyelitis.

**Accuracy of Symptoms and Signs for Osteomyelitis**

No studies were identified that addressed the utility of any component of the history in the diagnosis of osteomyelitis.

Seven studies assessed physical examination findings in the diagnosis of lower extremity osteomyelitis.9,10,24,26,30,39,40 The 7 studies included a total of 509 patients. No studies examined the test characteristics of a combination of findings. Temperature was examined in a single study, which received a level V quality rating (nonindependent comparisons of test results with a standard of uncertain validity) and demonstrated a poor sensitivity of 19%; patients without osteomyelitis were not included, so specificity and LRs could not be calculated.39

“Bone exposure” as a single finding suggests osteomyelitis (LR, 9.2; 95% CI, 0.57-146; Table 2). While the absence of bone exposure, defined as visualization of bone either directly or after probing, has a much narrower CI and lowers the likelihood of osteomyelitis, the LR of 0.70 (95% CI, 0.53-0.92) is not low enough to rule out osteomyelitis unless the pretest probability is already very low.

Good-quality evidence5 suggests that an ulcer area larger than 2 cm² (calculated as described above) makes osteomyelitis more likely (LR, 7.2; 95% CI, 1.1-49), while an ulcer area smaller than 2 cm² decreases the likelihood of osteomyelitis by about half (LR, 0.48; 95% CI, 0.31-0.76). The presence or absence of ulcer inflammation (erythema, swelling, purulence) does not modify the probability of disease (positive LR, 1.5; 95% CI, 0.51-4.7; negative LR, 0.84; 95% CI, 0.56-1.3).9

The probe-to-bone test has been evaluated in 3 studies.10,26,30 Shone et al26 and Lavery et al30 studied the probe-to-bone test in an outpatient setting, while Grayson et al10 prospectively evaluated the probe-to-bone test in 75...
patients with suspected severe limb-threatening infection. A positive probe-to-bone test result increases the likelihood of osteomyelitis (summary LR, 6.4; 95% CI, 3.6-11). A negative probe-to-bone test result has a summary LR of 0.39 (95% CI, 0.20-0.76).

Three studies described the diagnostic accuracy of clinical gestalt.9,24,40 One study described the diagnostic accuracy of “clinical judgment”9 and 2 studies used the Wagner grading scale.24,40 Because the Wagner grade is a subjective assessment, we elected to summarize the data together with clinical judgment. The clinical impression of osteomyelitis, without formal rules or weighting of the findings, increases the likelihood of osteomyelitis about 5-fold (summary LR, 5.9; 95% CI, 1.8-17). When a clinician judges that osteomyelitis is absent, the likelihood decreases (summary LR, 0.54; 95% CI, 0.30-0.97) (Table 2). These data suggest that clinicians might be more proficient at detecting the presence of osteomyelitis than at detecting its absence.

Accuracy of Laboratory Investigations for Osteomyelitis

Four studies evaluated the utility of laboratory investigations in the diagnosis of osteomyelitis.9,36,38,39 (Table 2). The 4 studies included a total of 108 patients, a rather small number. Three studies of varying quality evaluated the utility of ESR.9,36,38 The cutoff used to define an elevated ESR varied among the studies. An ESR of more than 70 mm/h increases the probability of the diagnosis of osteomyelitis with a summary positive LR of 11 (95% CI, 1.6-79.0), while an ESR of less than 70 mm/h has a summary LR of 0.34 (95% CI, 0.06-1.90).9,36 (Table 2) with a 95% CI that crosses 1.0.

The value of an elevated white blood cell count was examined in a single study and demonstrated poor sensitivity (range, 14%-54%) regardless of the cutoff studied.39 Patients without osteomyelitis were not included in this study, so specificity and LRs could not be calculated.39

### Table 3. Diagnostic Accuracy of Plain Radiographs for Lower Extremity Osteomyelitis in Patients with Diabetes Mellitus

<table>
<thead>
<tr>
<th>Source</th>
<th>Definition Used to Interpret Radiographs</th>
<th>Positive LR (95% CI)</th>
<th>Negative LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newman et al, 1991</td>
<td>Cortical erosion in the area of the foot ulcer</td>
<td>3.4 (0.46-24)</td>
<td>0.79 (0.58-1.1)</td>
</tr>
<tr>
<td>Yuh et al, 1989</td>
<td>Permeated radiolucencies, destructive changes, and/or periosteal new bone formation</td>
<td>3.0 (0.54-17)</td>
<td>0.33 (0.14-0.82)</td>
</tr>
<tr>
<td>Weinstein et al, 1993</td>
<td>Permeated radiolucencies, destructive changes, cortical defects, and periosteal reaction</td>
<td>2.8 (0.97-8.0)</td>
<td>0.59 (0.40-0.86)</td>
</tr>
<tr>
<td>Oyen et al, 1992</td>
<td>Soft tissue swelling, osteoporosis, osteitis, and/or medullary destruction and sequestration</td>
<td>2.7 (0.92-8.0)</td>
<td>0.54 (0.22-1.3)</td>
</tr>
<tr>
<td>Larcos et al, 1991</td>
<td>Bone destruction alone or in combination with soft tissue swelling, osteopenia, or periosteal reaction</td>
<td>2.5 (0.97-6.4)</td>
<td>0.69 (0.43-1.1)</td>
</tr>
<tr>
<td>Park et al, 1982</td>
<td>Cortical defects associated with soft tissue swelling or subcutaneous gas</td>
<td>2.0 (0.84-4.8)</td>
<td>0.56 (0.30-1.0)</td>
</tr>
<tr>
<td>Seldin et al, 1985</td>
<td>Focal cortical and/or medullary destruction or destruction of opposing joint space surfaces</td>
<td>1.9 (0.99-3.5)</td>
<td>0.13 (0.02-0.98)</td>
</tr>
</tbody>
</table>

Summary LR

<table>
<thead>
<tr>
<th></th>
<th>Positive LR (95% CI)</th>
<th>Negative LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.3 (1.56-3.3)</td>
<td>0.63 (0.51-0.78)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LR, likelihood ratio.

*Only studies that clearly defined what constitutes an abnormal radiograph are included.

Calculations based on number of ulcers.

Calculations based on number of bone specimens.

Calculations based on number of radiographs.

Swab culture39 was examined in a single study and had no diagnostic utility, with positive and negative LRs of 1.0 (95% CI for positive LR, 0.65-1.5; 95% CI for negative LR, 0.08-13) (Table 2), suggesting that in patients with suspected osteomyelitis, a positive swab was equally common in patients with and without biopsy-proven osteomyelitis.

Accuracy of Plain Radiographs for Osteomyelitis

Sixteen studies that included 567 patients assessed the accuracy of plain radiographs in the diagnosis of lower extremity osteomyelitis.9,22-24,31,32 Some studies used 3 views9,28,35 and others used 2 views,24,31 but for the most part it was unclear how many views were taken.9

The characteristic signs of osteomyelitis on plain radiograph include focal loss of trabecular pattern, periosteal reaction, and frank bone destruction, often accompanied by soft tissue swelling.43 The studies that clearly stated a definition for a positive radiographic result incorporated 1 or more of these features and were used to calculate summary LRs (Table 3).

Radiographic results alone appear to be marginally useful if positive, with a summary LR of 2.3 (95% CI, 1.6-3.3), and less useful when negative for osteomyelitis (summary LR, 0.63; 95% CI, 0.51-0.78) (Table 3). We found no studies that address the utility of serial radiographs in the diagnosis of osteomyelitis.

*References 9, 22-25, 27-29, 31-35, 37, 38, 40.

†References 22, 23, 25, 27, 29, 32-35, 37, 38, 40.
**Other Clinical Considerations**

**Soft Tissue Culture.** We identified 3 studies\(^44-46\) that compared superficial swab culture with bone culture. Swab culture identified the identical pathogens as bone culture in only 19% to 36% of isolates. Superficial swab cultures do not reliably predict bone microorganisms.

**Other Radiological Modes Including MRI.** A comprehensive review of all radiological modes in the evaluation and diagnosis of lower extremity osteomyelitis is beyond the scope of this review. The utility of nuclear scans and MRI in the diagnosis of osteomyelitis have been recently reviewed elsewhere.\(^41,47\) A recent meta-analysis reported that nuclear imaging (technetium, indium, and white blood cell scans) lacks specificity (62%-88.5%) in the diagnosis of osteomyelitis.\(^47\) Kapoor et al\(^41\) recently summarized the test characteristics of MRI in foot osteomyelitis. Eleven of the 16 MRI studies included exclusively patients with diabetes. Magnetic resonance imaging was shown to have a sensitivity of 90% (range, 77%-100%) and a specificity of 83% (range, 40%-100%) in all patients and a summary positive LR of 3.8 (95% CI, 2.5-5.8) and a summary negative LR of 0.14 (95% CI, 0.08-0.26) in patients with diabetes.\(^41\) Magnetic resonance imaging was also shown to be more accurate than technetium Tc 99m bone scan, plain radiography, and white blood cell scan. The overall accuracy (ie, the weighted average of the sensitivity and specificity) of MRI is 89% (95% CI, 83.0-94.5).

**Limitations of the Literature**

There are several important limitations to consider when interpreting the presented studies. We identified only 10 studies that attained a level II or III quality rating, with the remainder considered to be of overall poor quality. The majority of studies evaluated were of retrospective design and had unblinded protocols. Aside from study design, the physical examination findings and maneuvers were often described in a single study\(^48,49\) and the precision was not addressed.\(^48,49,26,40\)

The accuracy of combinations of variables is unknown. Patients were studied most often in tertiary care centers, thus resulting in a selection bias. For example, 1 study that evaluated the probe-to-bone test was in patients with severe limb-threatening infection.\(^10\) The study by Newman et al\(^9\) that discussed the diagnostic accuracy of clinical impression did not clearly define what this entailed, thus limiting reproducibility.

In the studies that addressed the utility of plain radiographs, details of the definition used to interpret the radiograph were missing in more than half of the studies.\(^22-25,31-33,37,40\) Also not defined was the time between clinical presentation and the time the radiograph was performed. Bony changes associated with osteomyelitis may take 7 to 15 days after the onset of the infectious process before they are identified on plain radiographs.\(^29\)

Patients who lacked features commonly suggestive of osteomyelitis were less likely to have a bone biopsy. This form of bias, referred to as verification bias, occurs when the decision to perform the gold standard test (bone biopsy or culture) is influenced by the results of clinical variables or screening test being studied. This will in turn inappropriately increase the apparent sensitivity of the test and decrease its apparent specificity.

**SCENARIO RESOLUTION**

**Case 1**

While there is some uncertainty about the pretest probability of osteomyelitis in a patient with diabetes and a lower extremity ulcer, our best estimate is 15%. Using each clinical predictor individually, an ulcer area of larger than 2 cm\(^2\) with an LR of 7.2 (95% CI, 1.1-49) increases the likelihood of osteomyelitis to 56%, and the positive finding of probing to bone (LR, 6.4; 95% CI, 3.6-11) increases the probability of osteomyelitis to 53%. The elevation in ESR with a positive LR of 11 (95% CI, 1.6-79) increases the probability of osteomyelitis from 15% to 66%. While most clinicians believe that the presence of these 3 variables together would make the diagnosis of osteomyelitis certain, the literature does not speak to the accuracy of combinations of variables (as noted in the aforementioned limitations). At this point, most clinicians would treat as osteomyelitis. Those who are uncomfortable with the uncertainties in these data might choose to order an MRI. A positive MRI result in combination with any one of these clinical variables increases the probability of osteomyelitis to greater than 80% (assuming independence of the LRs).

**Case 2**

The physical examination features and laboratory and radiographic results are not helpful in this case presentation to make a diagnosis of osteomyelitis. As indicated herein, ulcer area larger than 2 cm\(^2\), a positive probe to bone, an ESR greater than 70 mm/h, or an abnormal radiographic finding are more likely to be associated with osteomyelitis, but none of the testing modes in our review, with the exception of MRI, displayed clinically useful negative LRs for ruling out osteomyelitis. Assuming a prevalence of 15%, a negative MRI finding decreases the probability of osteomyelitis to 2.4%, thus effectively excluding the diagnosis. The elevated white blood cell counts and positive wound swab cultures are not diagnostically helpful.

**CLINICAL BOTTOM LINE**

Osteomyelitis of the foot causes significant morbidity in patients with diabetes, with a significant financial burden to patients and the institutions caring for these patients. Although there is no substitute for a detailed history, its utility in the diagnosis of osteomyelitis in patients with diabetes has not been well studied. The available evidence suggests that an ulcer that measures more than 2 cm\(^2\) or a positive probe-to-bone finding may be helpful to establish the diagnosis. An ESR greater than 70 mm/h or positive plain radiograph findings appear to be help-
ful in increasing the likelihood of osteomyelitis. Magnetic resonance imaging results should be interpreted in the context of the pretest probability. Temperature, ulcer inflammation, white blood cell count, and swab culture do not appear to be helpful in establishing the diagnosis or directing therapy in patients with diabetes and a lower extremity ulcer.

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