Probe-to-Bone Test for Diagnosing Diabetic Foot Osteomyelitis

Reliable or relic?

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OBJECTIVE — We sought to assess the accuracy of the probe-to-bone (PTB) test in diagnosing foot osteomyelitis in a cohort of diabetic patients with bone culture proven disease.

RESEARCH DESIGN AND METHODS — In this 2-year longitudinal cohort study, we enrolled 1,666 consecutive diabetic individuals who underwent an initial standardized detailed foot assessment, followed by examinations at regular intervals. Patients were instructed to immediately come to the foot clinic if they developed a lower-extremity complication. For all patients with a lower-extremity wound, we compared the results of the PTB test with those of a culture of the affected bone. We called PTB positive if the bone or joint was palpable and defined osteomyelitis as a positive bone culture.

RESULTS — Over a mean of 27.2 months of follow-up, 247 patients developed a foot wound and 151 developed 199 foot infections. Osteomyelitis was found in 30 patients: 12% of those with a foot wound and 20% in those with a foot infection. When all wounds were considered, the PTB test was highly sensitive (0.87) and specific (0.91); the positive predictive value was only 0.57, but the negative predictive value was 0.98.

CONCLUSIONS — The PTB test, when used in a population of diabetic patients with a foot wound among whom the prevalence of osteomyelitis was 12%, had a relatively low positive predictive value, but a negative test may exclude the diagnosis.

Diabetes Care 30:270–274, 2007

Individuals with diabetes have an ~25% lifetime risk of developing a foot complication (1), the most common of which is skin ulceration. Over half of these foot wounds may eventually become infected, which greatly increases the risk of lower-extremity amputation (2–5). While most diabetic foot infections involve only the soft tissue, bone involvement occurs in 20–66% of cases (6–8). Furthermore, foot infections complicated by osteomyelitis generally have a worse outcome and often require surgical resection and prolonged antibiotic therapy (6,7).

While diagnosing osteomyelitis is important, it is unfortunately also difficult. Clinical and laboratory signs and symptoms are generally unhelpful (6,7). Bone infection may not show up on plain radiographs in the first 2 weeks, and any X-ray abnormalities detected may be caused by the neuropathic bone disorders that frequently occur in diabetes. More accurate imaging studies, such as radionuclide scans or magnetic resonance imaging, are expensive and not universally available (9–21). In 1995, Grayson et al. (22) described a clinical technique they used in diabetic patients with a foot infection consisting of exploring the wound for palpable bone with a sterile blunt metal probe. Their most important finding was that the probe-to-bone (PTB) test had a positive predictive value of 89%, leading them to conclude that a positive test usually made imaging studies for diagnosing osteomyelitis unnecessary (22). Since then, many have considered a positive PTB sufficient evidence for osteomyelitis. In the study by Grayson et al., however, the prevalence of osteomyelitis in their population with "severe limb-threatening infections" was 66%. Furthermore, the investigators did not obtain a bone specimen for analysis, the criterion standard for the diagnosis, from all patients and used histopathological rather than microbiological confirmation to diagnose osteomyelitis. To assess the value of the PTB test in an unselected population of individuals with diabetes, we conducted the test as part of a prospective cohort study of foot complications in diabetic patients and confirmed the presence of osteomyelitis by bone culture.

RESEARCH DESIGN AND METHODS

— As part of a diabetes disease management program to study and prevent lower-extremity complications and in cooperation with two large primary care physician groups in south Texas, we prospectively enrolled 1,666 patients in an observational trial over an 8-month period. As part of a systematic screening program, we documented each patient's medical history for all potential foot complications and screened them for established risk factors (23). Patients were then seen at regular intervals (i.e., every 2–12 months, depending on their foot risk classification) for routine foot care and repeat evaluations (24). In addition, all patients were instructed to immediately return to the foot clinic if they developed any foot complication. We followed the patients for an average of 27.2 months (range 4–32) and tracked all pertinent clinical outcomes, verifying all hospital

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Received for publication 26 July 2006 and accepted in revised form 19 October 2006.

Abbreviations: PTB, probe to bone.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-1572

Table 1—*Characteristics of patients with diabetic foot wound by osteomyelitis status*

	Osteomyelitis				
	Yes (n = 30)	No (n = 217)	P value	Relative risk	95% CI
Age >70 years	51.3	52.6	0.85	0.99	0.97–1.01
Male	58.6	52.1	0.51	1.26	0.63–2.53
Diabetes duration (years)	17.0 ± 10.1	13.0 ± 9.6	0.03	1.03	1.00–1.06
BMI (kg/m^2)	28.7 ± 6.2	29.6 ± 7.3	0.53	0.98	0.93–1.04
Peripheral neuropathy	83.3	72.4	0.2	1.79	0.71–4.47
Peripheral vascular disease	43.3	37.8	0.6	1.22	0.62–2.40
Wound depth					
Full thickness skin	10.0	73.7		1.00	
To fascia or tendon	3.3	17.1	0.75	1.43	0.15–13.37
To bone/joint	86.7	9.2	<0.001	30.71	9.73–96.93
Ulcer duration (days)	267 ± 284	169 ± 268	0.06	1.001	1.000–1.001

Data are percent or means ± SD.

admissions and lower-extremity amputations with claims data. The disease management program's foot clinic was the primary source for foot care, as well as for referral and consultation for diabetes-related lower-extremity complications. This project was approved by our institutional review board.

We defined a foot wound as a full thickness lesion involving any portion of the foot or ankle (25–27). We excluded wounds characterized as blisters, minor lacerations, or abrasions (n = 16). We defined a wound infection clinically, by criteria consistent with the International Working Group guidelines (28), i.e., the presence of wound purulence or at least two signs or symptoms of local inflammation or systemic symptoms of infection with no other apparent cause. We evaluated all wounds to determine the extent of soft tissue involved and for any evidence of bone infection (osteomyelitis) (6,29,30). As part of this evaluation, each patient underwent the PTB test, conducted by one of two experienced podiatrists using a sterile probe to gently explore the wound. We defined a positive test as palpating a hard or gritty substance that was presumed to be bone or joint space. Each patient with a clinically infected wound also underwent a series of plain radiographs and had additional imaging studies as indicated. If, based on the clinical examination (other than the PTB test) and imaging studies, we thought bone infection was possible, the patient underwent bone biopsy. Using aseptic techniques, we obtained specimens for culture, either in the clinic or operating room, following standard surgical skin preparation with betadiene. We obtained bone specimens by needle aspirate, curettage, or rongeur at the time of debridement or through sites that were noncontiguous with the wound. Specimens were transferred to a sterile container or transport tube with culture media and quickly transported to the clinical microbiology laboratory. We used the results of bone culture to determine the presence or absence of bone infection. A positive culture was defined as growth of any organism from the bone specimen. Although our data forms did not specifically record information on antimicrobial treatment in all cases, most patients presented with an acute wound and were not receiving any antibiotic therapy. We followed all patients with a foot wound until it either healed or required surgical intervention.

To assess the value of PTB in diagnosing osteomyelitis, we calculated the sensitivity, specificity, and positive and negative predictive values of the test using the results of the bone culture as the criterion standard. We calculated statistical values using SPSS version 11.0 for Macintosh (SPSS, Chicago, IL) and Diagnostic and Agreement Statistics DAG Software (Mental Health Research Institute, Parkville, Victoria, Australia).

RESULTS — The demographic and clinical characteristics of the patients we enrolled are shown in Table 1. Over a mean of 27.2 months of follow-up, 247 (14.8%) of the 1,666 enrolled patients developed a foot wound and 151 (9.1%) developed 199 foot infections. One patient with cellulitis did not have a wound, precluding conducting the PTB test. All of the patients with osteomyelitis presented with signs and symptoms of a soft tissue foot infection. Bone infection was documented in 30 patients, representing 20% of the 150 infected patients and 12% of all 247 with a foot wound.

The PTB test was performed in all of the 247 patients with a wound; it was positive in 46 (18.6%), 26 (56.5%) of whom had osteomyelitis. The test was positive in 26 (86.7%) of the 30 with culture-proven bone infection, as well as in 20 (9.2%) of the 217 without osteomyelitis. Among the 150 patients with a clinically infected wound, the test was positive in 46 (30.7%). There were no complications attributable to the PTB test.

The values for sensitivity, specificity, and positive and negative predictive values of the PTB test for all patients with a foot wound and for the patients with a clinically infected foot wound are shown in Table 2. The sensitivity was 87% for both groups (i.e., all wounds and infected wounds), while the specificity was 91% for all wounds and 87% for infected wounds. The negative predictive value was extremely high (96–98%), but the positive predictive value was only 57–62%. The positive likelihood ratio was 9.4 for all wounds and 6.5 for infected wounds, similar to the values for the negative likelihood ratios for both populations.

CONCLUSIONS — Osteomyelitis of the foot in individuals with diabetes is often difficult to diagnose. Bone biopsy is considered the criterion standard for the diagnosis. While histopathological definitions may be useful for diagnosing osteomyelitis, most prefer microbiological methods (6,31). Many clinicians (and patients) are hesitant to undertake this invasive and rather expensive procedure. Thus, clinicians have sought clinical evi-

Table 2—*Statistical analysis of the PTB test for diagnosing osteomyelitis in all foot wounds and in clinically infected wounds*

Statistic	All wounds value (n = 247)	Infected wounds value (n = 150)
Sensitivity	0.87 (0.71–0.96)	0.87 (0.69–0.96)
Specificity	0.91 (0.89–0.92)	0.87 (0.79–0.92)
Positive predictive value	0.57 (0.46–0.62)	0.62 (0.46–0.76)
Negative predictive value	0.98 (0.96–0.99)	0.92 (0.91–0.99)
Positive likelihood ratio	9.40 (6.05–14.61)	6.50 (4.03–10.48)
Negative likelihood ratio	6.81 (2.73–16.97)	6.50 (2.60–16.23)

Data in parentheses are 95% CI.

dence to help them determine what patients were likely to have diabetic foot osteomyelitis. Unfortunately, local inflammatory signs and symptoms may be blunted because of diabetes-related vascular insufficiency, peripheral neuropathy (32), and leukocyte dysfunction (33). While clinical findings (34) or elevations in hematological inflammatory markers (e.g., white blood cell count, erythrocyte sedimentation rate [35], or C-reactive protein [36]) may be helpful (37,38), these are not sufficiently accurate for diagnosis (3,4,35,39–45). Furthermore, evaluating published reports of the sensitivity, specificity, and predictive value of various diagnostic methods is complicated by inconsistent operational definitions and outcome measures, as well as the variability in the prevalence of osteomyelitis in the populations studied (46). It is not surprising, therefore, that the clinical assessment for diagnosing osteomyelitis has a reported sensitivity ranging from 0 to 54% (9,20,47,48). Various imaging studies, especially magnetic resonance, certainly enhance the accuracy of diagnosing osteomyelitis, but these are expensive, time-consuming, and not universally available (49,50). Thus, clinicians have sought a simple inexpensive bedside test to help determine which patients should undergo more extensive evaluations.

Since its introduction, the PTB technique has been widely used for evaluating diabetic patients with a foot wound. Palpation of bone with a metal probe is a simple bedside procedure predicated on the concept that if the probe can reach the bone, so can infectious bacteria. In the report by Grayson et al. (51) on 76 hospitalized patients enrolled in a diabetic foot infection antibiotic trial, 66% were found to have osteomyelitis, defined by histology on bone biopsy (in most subjects) and by surgical exploration or radiological imaging (in the rest). They calculated that the PTB test had a sensitivity of 66%, specificity of 85%, positive predicative value of 89%, and a negative predictive value of 56% (22). Our study evaluated more than three times as many patients with a foot wound and more than twice as many with a foot infection. Unlike in the study by Grayson et al., our patients were identified (and largely treated) in an outpatient setting. Furthermore, in all of our patients, osteomyelitis was defined exclusively by a positive bone culture. We found very little difference in positive and negative predictive values when we compared PTB results in all patients who had a wound with the subset who had clinical signs of infection. In our patient population, the PTB had high sensitivity and specificity, but because of the lower prevalence of osteomyelitis, our positive predictive value was only 57–62%. Thus, a positive PTB only slightly increased the probability of osteomyelitis over tossing a coin. The negative predictive value, however, was considerably higher, at 96–98%. A negative test, therefore, argues strongly against the diagnosis of osteomyelitis. These results confirm the importance of disease prevalence in assessing any test for making the diagnosis of diabetic foot osteomyelitis (46).

At least three factors may have contributed to the apparent disparity in outcomes between our study and that of Grayson et al. (51). First, the lower positive predictive value in our population may be attributable to their lower prevalence of osteomyelitis (20 vs. 66%) (46). Second, all of the patients in the Grayson et al. study required hospitalization for severe foot infections, which required parental antibiotics. Our study population was derived from patients who mostly presented in a clinic setting, and only 61% of patients with a foot wound had evidence of infection. Third, when bone biopsy was performed by Grayson et al., they histologically defined osteomyelitis (in 46 of 50 cases by the presence of inflammatory cells, fibrosis, necrosis, and reactive bone), while we defined it microbiologically (by a positive culture of a bone specimen). Because most of our patients presented with an acute foot wound, we believe that few were receiving antibiotic therapy, enhancing the value of a microbiologically based diagnosis. Thus, it is possible that they missed cases of osteomyelitis that did not have histological changes (false negatives) or that we included cases that represented microbial contamination (false positives) of the bone specimen. Our patient population is probably more representative of those in a typical clinical practice where the PTB would be most commonly used.

Our study had several potential limitations. First, we did not perform histological examination of the bone specimens to compare against the culture results. Rather, we elected to use a positive bone culture as our criterion standard. We did so because it is often difficult to obtain an adequate core of bone from the small bones of the feet (especially toes) to allow histopathological analysis and because the criteria for histologically diagnosing osteomyelitis are not well-defined. Furthermore, because we believe that most of our patients were not receiving antibiotic therapy at the time the bone biopsy was taken and they underwent careful wound cleansing and debridement before the procedure, we thought that the risk of false negative or positive results was low. Additionally, for samples collected in this study and in our greater clinical experience, readings of histological specimens often refer to signs of inflammation or inflammatory cells but do not specifically describe osteomyelitis. Second, we did not conduct a bone biopsy on patients with a foot wound in whom there was no suspicion of bone involvement. While work in this area suggests that bone biopsy is both safe (52,53) and helpful (49), we believed it would be unethical to do this procedure on patients with no suspicion of osteomyelitis. As previously stated, none of the patients who did not undergo a biopsy were later found to have developed osteomyelitis. Because the average follow-up for patients in this population was 27 months and our group was the sole source of diabetic foot referral, it was unlikely that we missed any cases of bone infection. Third, the PTB was con-

ducted by one of two podiatrists, but we did not test the interrater reliability.

We were only able to find two other studies in the literature of the PTB test in patients with a diabetic foot wound. In a recent brief report, Shone et al. (54) described 81 patients with 104 foot wounds on whom they did the PTB test. They did not diagnose osteomyelitis by bone biopsy but rather clinically (mostly by physical examination and plain X-rays, with bone histology in a minority). Their patients included both those in whom the diagnosis had already been made and those in whom it was made later. Interestingly, their results were similar to ours, i.e., PTB had a positive predictive value of 53% and a negative predictive value of 85%. They diagnosed osteomyelitis in 19 (24%) of their patients, a prevalence similar to that in our study (20%). Balsells et al. (55) performed a PTB test in a series of 33 episodes of foot ulceration (on 28 diabetic patients) that required the patient to be hospitalized. Among the 21 who had osteomyelitis (defined by either positive nuclear medicine scans or characteristic X-ray changes associated with a foot ulcer), only 7 (33%) had a positive PTB. Unfortunately, they reported no data on the results of PTB in the 12 patients who did not have bone infection, limiting the ability to evaluate the test's accuracy in this study.

If we are to use the PTB test in clinical practice, we must understand both its value and limitations. Unfortunately, some have inappropriately generalized the results from the study by Grayson et al. to all foot (and even other) wounds in various clinical settings (56,57). We have also observed clinicians using devices and methods for the test that are quite different from those described in the original study. Furthermore, there are no data on the interrater or intrarater reliability of the test. Perhaps most importantly, clinicians must realize that the prior prevalence of osteomyelitis greatly affects the usefulness of the PTB test. In a population with "limb-threatening" infections and a high prevalence of osteomyelitis, a positive PTB is probably quite helpful in diagnosing bone infection. In more typical clinical settings, however, this is less likely to be true, and the PTB test is a better tool to exclude osteomyelitis. We need further studies on this test to answer the remaining questions and to help understand its value in different settings.

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