



Q/ What's the best test for underlying osteomyelitis in patients with diabetic foot ulcers?

EVIDENCE-BASED ANSWER

A | **MAGNETIC RESONANCE IMAGING (MRI)** has a higher sensitivity and specificity (90% and 79%) than plain radiography (54% and 68%) for diagnosing diabetic foot osteomyelitis. MRI performs somewhat better than any of several common tests—probe to bone (PTB), erythrocyte sedimentation rate (ESR) >70 mm/hr, C-reactive protein (CRP) >14 mg/L, procalcitonin >0.3 ng/mL, and ulcer size >2 cm²—although PTB has the highest specificity of any test and is commonly

used together with MRI. No studies have directly compared MRI with a combination of these tests, which may assist in diagnosis (strength of recommendation [SOR]: **B**, meta-analysis of cohort trials and individual cohort and case control trial).

Experts recommend obtaining plain films when considering diabetic foot ulcers to evaluate for bony abnormalities, soft tissue gas, and foreign body; MRI should be considered in most situations when infection is suspected (SOR: **B**, evidence-based guidelines).

Evidence summary

One-fifth of patients with diabetes who have foot ulcerations will develop osteomyelitis.^{1,2} Most cases of diabetic foot osteomyelitis result from the spread of a foot infection to underlying bone.²

MRI has highest sensitivity, probe to bone test is most specific

A meta-analysis³ of 9 cohort trials (8 prospective, 1 retrospective) of 612 patients with diabetes and a foot ulcer examined the accuracy of diagnostic methods for osteomyelitis (TABLE^{3,4}). MRI had the highest sensitivity (90%), followed by bone scan (81%). Bone scan was the least specific (28%), however. Plain film radiography had the lowest sensitivity (54%). A PTB test was highly specific (91%) but had moderate sensitivity (60%). (PTB involves inserting a sterile, blunt stainless steel probe into an ulcerated lesion. If the probe comes to a hard stop, considered to be bone, the test is positive.)

A meta-analysis of 21 prospective and retrospective trials with 1027 diabetic patients with foot ulcers or suspected osteomyelitis found that ulcer size >2 cm², PTB, and ESR >70 mm/hr were helpful in making the diagnosis.⁴

Combining ESR with ulcer size increases specificity

A prospective trial of 46 diabetic patients hospitalized with a foot infection examined the accuracy of a combination of clinical and laboratory diagnostic features in patients with diabetic foot osteomyelitis that had been diagnosed by MRI or histopathology.⁵ (Twenty-four patients had osteomyelitis, and 22 didn't.)

ESR >70 mm/hr had a sensitivity of 83% and specificity of 77% (positive likelihood ratio [LR+]=3.6; negative likelihood ratio [LR-]=0.22). Ulcer size >2 cm² had a sensitivity of 88% and specificity of 77%

Morteza Khodaei, MD, MPH; Daniel Lombardo, MD; Linda C. Montgomery, MD; Corey Lyon, DO
University of Colorado School of Medicine, Denver

Cathy Montoya, MLS, AHIP
Houston Community College, Texas

DEPUTY EDITOR
Rick Guthmann, MD
Advocate Illinois Masonic Family Medicine Residency, Chicago

TABLE

Diagnosing osteomyelitis: How the tests stack up*

Type of evidence	Number of patients	Diagnostic test	Gold standard comparison	Pooled results
Meta-analysis of 9 cohort trials ³ (8 prospective, 1 retrospective)	Total N=612			
	4 trials; N=177	Plain film	Histopathology or bone culture	Sensitivity 54% Specificity 68% LR+=1.7 LR-=0.68
	4 trials; N=135	MRI	Histopathology or bone culture	Sensitivity 90% Specificity 79% LR+=4.3 LR-=0.13
	6 trials; N=185	Bone scan	Histopathology or bone culture	Sensitivity 81% Specificity 28% LR+=1.1 LR-=0.68
	2 trials; N=288	PTB	Histopathology or bone culture	Sensitivity 60% Specificity 91% LR+=6.7 LR-=0.44
Meta-analysis of 21 cohort trials ⁴ (8 prospective, 13 retrospective)	Total N=1027			
	1 trial; N=35	Ulcer >2 cm ²	Bone biopsy	LR+=7.2 LR-=0.48
	3 trials; N=75	PTB	Bone biopsy	LR+=6.4 LR-=0.39
	4 trials; N=108	ESR >70 mm/hr	Bone biopsy	LR+=11 LR-=0.34
	16 trials; N= 567 (data pooled for 7 trials; N=217)	Plain film	Bone biopsy	LR+=2.3 LR-=0.63

ESR, erythrocyte sedimentation rate; LR+, positive likelihood ratio; LR-, negative likelihood ratio; MRI, magnetic resonance imaging; PTB, probe to bone test.

* Numbers of trials and patients don't add up because multiple diagnostic tests were used in some trials.

† 10 trials were graded as a level II or III (included a blind comparison to the gold standard) and the rest were of low quality because they lacked blinding.

(LR+=3.8; LR-=0.16). Combined, an ESR >70 mm/hr and ulcer size >2cm² had a slightly better specificity than either finding alone, 82%, but a lower sensitivity of 79% (LR+=4.4; LR-= 0.26).

Serum markers accurately distinguish osteomyelitis from infection

An individual prospective cohort trial of 61 adult patients with diabetes and a foot infection, published after the meta-analysis⁴ described previously, examined the accuracy of serum markers (ESR, CRP, procalcitonin) for diagnosing osteomyelitis.⁶ A positive PTB test and imaging study (plain film, MRI, or

nuclear scintigraphy) were used as the diagnostic gold standard.

Thirty-four patients had a soft tissue infection and 27 had osteomyelitis. All markers were higher in patients with osteomyelitis than in patients with a soft tissue infection (ESR =76mm/hrvs66mm/hr; *P*<.001; CRP=25mg/Lvs 8.7 mg/L; *P*<.001; procalcitonin=2.4 ng/mL vs 0.71 ng/mL; *P*<.001). The sensitivity and specificity for each marker at its optimum points were: ESR >67 mm/hr (sensitivity 84%; specificity 75%; LR+=3.4; LR-=0.21); CRP >14 mg/L (sensitivity 85%; specificity 83%; LR+=5; LR-=0.18); and procalcitonin >0.3 ng/mL (sensitivity 81%; specificity 71%; LR+=2.8; LR-=0.27).

CONTINUED ON PAGE 321

CLINICAL INQUIRIES

CONTINUED FROM PAGE 310

Recommendations

The Infectious Diseases Society of America (IDSA) recommends performing the PTB test on any diabetic foot infection with an open wound (level of evidence: strong moderate).⁷ It also recommends performing plain radiography on all patients presenting with a new infection to evaluate for bony abnormalities,

soft tissue gas, and foreign bodies (level of evidence: strong moderate).

The IDSA, the American College of Radiology diagnostic imaging expert panel, and the National Institute for Health and Clinical Excellence recommend using MRI in most clinical scenarios when osteomyelitis is suspected (level of evidence: strong moderate).^{8,9} **JFP**

References

1. Gemechu FW, Seemant F, Curley CA. Diabetic foot infections. *Am Fam Physician*. 2013;88:177-184.
2. Lavery LA, Armstrong DG, Peters EJ, et al. Probe-to-bone test for diagnosing diabetic foot osteomyelitis: reliable or relic? *Diabetes Care*. 2007;30:270-274.
3. Dinh MT, Abad CL, Safdar N. Diagnostic accuracy of the physical examination and imaging tests for osteomyelitis underlying diabetic foot ulcers: meta-analysis. *Clin Infect Dis*. 2008;47:519-527.
4. Butalia S, Palda VA, Sargeant RJ, et al. Does this patient with diabetes have osteomyelitis of the lower extremity? *JAMA*. 2008;299:806-813.
5. Ertugrul BM, Savk O, Ozturk B, et al. The diagnosis of diabetic foot osteomyelitis: examination findings and laboratory values. *Med Sci Monit*. 2009;15:CR307-CR312.
6. Michail M, Jude E, Liaskos C, et al. The performance of serum inflammatory markers for the diagnosis and follow-up of patients with osteomyelitis. *Int J Low Extrem Wounds*. 2013;12:94-99.
7. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2012;54:e132-e173.
8. Schweitzer ME, Daffner RH, Weissman BN, et al. ACR Appropriateness Criteria on suspected osteomyelitis in patients with diabetes mellitus. *J Am Coll Radiol*. 2008;5:881-886.
9. Tan T, Shaw EJ, Siddiqui F, et al; Guideline Development Group. Inpatient management of diabetic foot problems: summary of NICE guidance. *BMJ*. 2011;342:d1280.

HELP DESK ANSWERS

CONTINUED FROM PAGE 315

N=231; mean difference [MD]=-0.54; 95% CI, -0.84 to -0.24) and conjunctival injection (4 trials, N=208; MD=-0.51; 95% CI, -0.97 to -0.05). NSAIDs weren't superior to placebo in treating other ocular symptoms of eyelid swelling, ocular burning, photophobia, or foreign body sensation, and they had a higher rate of stinging on application (odds ratio=4.0; 95% CI, 2.7-5.9).

Guideline recommends topical antihistamines or mast cell stabilizers

The American Academy of Ophthalmology's 2012 evidence-based guideline recommends treating allergic conjunctivitis with topical antihistamines (Level A-1 evidence, defined as important evidence supported by at least one RCT or a meta-analysis) and using topical mast cell stabilizers if the condition is recurrent.³ **JFP**

References

1. Owen CG, Shah A, Henshaw K, et al. Topical treatments for seasonal allergic conjunctivitis: systematic review and meta-analysis of efficacy and effectiveness. *Br J Gen Pract*. 2004;54:451-456.
2. Swamy BN, Chilov M, McClellan K, et al. Topical non-steroidal anti-inflammatory drugs in allergic conjunctivitis: meta-analysis of randomized trial data. *Ophthalmic Epidemiol*. 2007;14:311-319.
3. American Academy of Ophthalmology. Conjunctivitis summary benchmarks for preferred practice pattern guidelines. American Academy of Ophthalmology Web site. Available at: <http://one.aao.org/summary-benchmark-detail/conjunctivitis-summary-benchmark-october-2012>. Accessed October 18, 2013.



Visit us @ jfponline.com

THE JOURNAL OF
**FAMILY
PRACTICE**