SCCEP 2013 LLSA Course Article 3
Does this Patient With Diabetes Have Osteomyelitis of the Lower Extremity?

Butalia S, et al. JAMA. Feb 2008;299(7):806-813.

Article: A "Rational Clinical Examination" paper from JAMA, presents a clinical scenario and scours the literature for EB studies to answer the above question. **Conficts: None reported.**

Clinical Scenarios:

Case 1:
- 52 y.o. Woman with IDDM for 12 years and CC of 2.2 X 1.5 cm foot ulcer that probes to bone
- Pt has neuropathy, retinopathy and peripheral vascular disease
- Pt has erythema, swelling and pain over left foot, diminished pedal pulses and normal VS.
- Culture shows Gram + Cocci and Gram - Bacilli, Sed Rate 75, X-Ray shows cortical erosion
- **Does this patient require an MRI of foot?**

Case 2:
- 64 y.o. Man with NIDDM with CC non-healing ulcer over 4th MC head right foot x 3 weeks
- Pt has neuropathy, retinopathy and nephropathy. He completed 10 days of ABX
- Pt has erythema, swelling over 1 cm round ulcer that does not probe to bone
- Culture shows Gram + Cocci and Gram - Bacilli, Sed Rate 25, WBC 14,500, X-Ray is normal
- **How likely is osteomyelitis?**

Why is the Diagnosis of Osteomyelitis Important (and Challenging)?:

1. Foot -related Complications account for up to 20% of all diabetes-related admissions
2. Diabetic foot problems (mostly infections) are most common cause of non-traumatic amputations
3. Inadequately treated Osteo increases risk of amputation peri-0perative mortality is 7.4%
4. **Diagnosis of Osteo of lower limb in DM is challenging:**
    1. Classic Signs and Symptoms masked by Neuropathy and PVD
    2. Definitive test of bone biopsy in invasive and may be contraindicated
    3. **This paper will concentrate on H&P, labs X-Rays and MRI findings**

History

1. Risk Factors:
    a. Duration of diabetes and degree of glycemic control
    b. PVD: both micro and macro-vascular
    c. Presence of peripheral neutropathy
2. Recent trauma or history of prior ulcers.:

Physical Exam

1. VS, F/C/S, presence of wound or ulcer
2. Presence of foot deformities, tenderness, neuropathy and venous or arterial insufficiency
3. **Differentiating different causes of leg ulcers by their location and appearance**
    a. **Venous**: Above malleoli irregular borders, edema, dermatitis, hyper-pigmentation
    b. **Arterial**: Affect toes and shin, with pale borders and a punched out appearance
    c. **Diabetic:** Affect areas of increased pressures like soles, or where shoes rub
4. **Ulcer area:** Multiply width x length
5. **Probe to bone** test: Use sterile stainless steel and probe for hard gritty surface

6. **Wagner Grade**: Grade 0-5

    a. Grade 0: No open lesion, may be healed lesion or deformity
    b. Grade 1: Superficial ulcer
    c. Grade 2: Deep, to tendon, bone or joint capsule
    d. Grade 3: Abscess, osteomyelitis or tendonitis
    e. Grade 4: Gangrene of toe or forefoot
    f. Grade 5: Gangrene of foot

Study Methods:

- Medline from 1966-2007 for English language with appropriate keywords
- Two investigators reviewed all articles independently
- Additional studies gleaned from articles' references, previous reviews and expert polling
- Abstracts and letter publications were accepted to minimize publication bias
- Only 21 out of 279 articles (total of 1027 patients) met inclusion/exclusion criteria

Inclusion Criteria:

- Articles reporting original studies on H&P, Lab, Plain X-Rays in the diagnosis of Osteo in DM
- Data could be extracted to constructed 2 X 2 tables or article reported operating characteristics
- **Diagnostic test was compared with a reference standard (Bone Biopsy for Mirco or Histo**)
- **MRI Test characteristics were based on a single high quality Meta-Analysis of Osteo in DM**

Exclusion Criteria:

- Pediatrics
- Mixed populations of diabetics and non-diabetics

Prior Probability of Osteomyelitis (Reasonable "pre-test" probablity)

1. 12 to 100% in selected Studies
2. **One large restrospective cohort study: found 15% of DM with foot ulcer had or got Osteo**

Accuracy of Symptoms and Signs for Osteo

1. **"Bone Exposure"** defined as seeing or probing bone:
    a. Highly suggests Osteo if Present: LR 9.2
    b. **Doesn't R/O osteo if absent** : LR 0.7 (95% CI 0.5-0.92)
2. **Ulcer Size > 2 cm^2**
    a. Suggests osteo: LR 7.2
    b. < 2 cm^2 lowers but doesn't R/O osteo LR .7
    c. **presence or absence of erythema, swelling or purulence doesn't change prob of Osteo**
3. **"Probe to Bone"** evaluated in three studies
    a. Positive test: LR 6.4 (95% CI 3.6-11)
    b. Negative test: LR 0.39 (95% CI 0.2-0.76) **Bad at R/O Osteo**
4. **Clinical Gestalt:** three studies, two incorporating the subjective Wagner scale
    a. Clinical impression of Osteo: LR 5.5 (95% CI: 1.8-17)
    b. Clinical judgement Osteo absent: LR 0.54 5 (95% CI: 0.3-0.97) **Bad at R/O Osteo**

Accuracy of Lab for Osteo: 4 studies including a total of only 108 patients, 3 on ESR, one on WBC

5. ESR > 70
    a. Positive test: LR 11 (95% CI 6.6-179)
    b. Negative test: LR 0.34 **(95% CI 0.06-1.9**) **Bad at R/O Osteo**
6. **WBC and Swab culture both performed poorly at diagnosing Osteo**

Accuracy of Plain Radiographs for Osteo: 16 studies and 567 patients. Characteristics signs of Osteo on plain film include **focal loss of trabecular pattern, periosteal reaction and frank bone destruction, often with tissue swelling.**

1. Positive Findings: LR 2.3 (95% CI 1.6-3.3) Minimally useful
2. Negative Findings: LR 0.63 (95% CI 0.51-0.78) **Bad at R/O Osteo**

Other Imaging Modalities including MRI:

1. Nuclear imaging with Tech99, tagged WBC, etc. lack specificity
2. **MRI:**
   a. **Positive MRI in ALL patient (not just DM) LR 3.8** (95% CI 2.5-5.8)
   b. **Negative MRI in Diabetics LR 0.14 (95% CI 0.08-0.26)**

Limitations of the Literature: Only 10 higher quality studies were found, most studies were retrospective, tertiary care centered based which results in selection bias. Finally, patients who lack the classical features of Osteo were less likely to get a bone biopsy, which may cause "verification bias" and make the tests appear more sensitive than they are.

Scenario Resolution:
Case 1:

- 52 y.o. Woman with IDDM for 12 years and CC of:
- 2.2 X 1.5 cm foot ulcer (LR 7.2)
- Probes to bone (LR 6.4)
- Sed Rate 75 (LR 11)
- Most Clinicians would treat as Osteo without an MRI
- An positive MRI would increase probability to 80%

Case 2:

- 64 y.o. Man with NIDDM with CC non-healing ulcer over 4th MC head right foot x 3 weeks
- Over 1 cm round ulcer that does not probe to bone (Both decrease likelihood of Osteo)
- **How likely is osteomyelitis? Assumming prevalence of 15%, none of the above finding lower the probability enough to exclude the disease. A Negative MRI decrease the post-test probability to 2.4%**

Clinical Bottom Line

1. Clinical utility of history has not been studied
2. **Ulcer Size > 2 $cm^{2,}$ and + probing to bone are helpful in establishing Osteo**
3. Sed Rate >70 and positive plain films **May Be** helpful in establishing Osteo
4. **No test reliably rule out Osteo**, except MRI in a low probability patient
5. MRI should be interpreted in light of pre-test probabilities
6. Swab (surface) cultures, WBC and sign of inflammation around ulcer are useless