Critical Review Form

Meta-analysis

Magnetic Resonance Imaging for Diagnosing Foot Osteomyelitis: *A Metaanalysis, Arch Intern Med* 2007; 167:125-132

Objective: **To conduct "a comprehensive meta-analysis of the test performance of MRI for the diagnosis of osteomyelitis of the foot and ankle". (p. 126) The investigators also performed a subset analysis to explore the reason for variability among included studies and compared the accuracy of MRI with ^{99m}Tc bone scanning, plain radiography and WBC scanning.**

Methods: **Investigators conducted an electronic search of MEDLINE and EMBASE for English-language articles since 1966. They also performed a hand-search of selected articles and contacted Surgery/Radiology specialists to identify additional published literature not identified by the electronic searches. Included studies had to evaluate mostly adults (> 80% over age 16) suspected of having osteomyelitis of the foot or ankle. Studies had to report sufficient detail for the meta-analysis authors to re-construct 2x2 tables.**

Once the studies were identified, meta-analysis authors extracted data using the STARD checklist via two independent reviewers. Investigators also extracted information about blinding and criterion standard(s) employed "to understand better the quality of the sensitivity and specificity estimates reported". (p. 126) Original study investigators were not contacted for details except to ensure duplicate patients were not reported when more than one publication existed.

Data were abstracted to compute diagnostic odds ratios [(true positive*true negative) / (false positive*false negatives)] to derive a summary receiver operating characteristics curve. In order to evaluate the stability of the estimates for sensitivity and specificity, the DOR was computed for 13 subsets (not reported in the manuscript but obtained via personal communication with the lead author): all full text studies; sample size ≥ 20; Charcot prevalence low or not reported; diabetes prevalence >90%; not hospitalized or hospitalization not specified; gadolinium not used or not reported; site count greater than patient count by 10% or less; prospective design; non-consecutive enrollment or not specified; no or unspecified blinding; criteria used to judge positive MRI described; appropriate disease-positive criterion standard

used >90% of cases; inappropriate disease-negative criterion standard employed; published after 1998.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes. What is the diagnostic accuracy of MRI for potential osteomyelitis of the foot or ankle compared with x-rays, bone scans or tagged-WBC scans.
2.	Was the search for relevant studies details and exhaustive?	No. The authors did not assess non-English manuscripts or contact diagnostic experts within primary care, emergency medicine, or industry for additional published or unpublished data.
3.	Were the primary studies of high methodological quality?	No. As reported in Table 1 (p. 127) 7/16 included studies were not prospective in design, 11/16 did not enroll consecutive patients, and 10/16 did not blind MRI assessors to other clinical data.
4.	Were the assessments of the included studies reproducible?	Uncertain. No validated instrument to appraise that evidence quality was used. The meta-analysis authors do not report any disagreements or adjudication for study quality or inclusion criteria.
II.	***What are the results?***	

1.	What are the overall results of the study?	• 16 studies of 496 patients published between 1990 and 2006 were included in this analysis. The mean age of patients was > 55 years in all but 5 studies and 11studies had a 100% prevalence of diabetes. • MRI criteria for osteomyelitis was generally defined as focally decreased marrow signal intensity in T1-weighted images and a focally increased signal intensity in fat-suppressed T2-weighted or short tau inversion recovery images. • Osteomyelitis prevalence averaged ~ 50% (range 32% - 89%). • MRI sensitivity ranged 77 – 100% and specificity 40% - 100% with overall DOR 42.1 (95% CI 14.8 – 119.9) with higher performance noted in studies that did not use bone histology for gold standard (DOR 67.4) and lower estimates for studies published after 1998 that generally used a prospective design and blinded MRI reviewers (DOR 25.3). • Summary LR^+ of MRI was 3.8 (95% CI 2.5 – 5.8) and LR^- 0.14 (0.08 – 0.26). • Using a clinically significant sensitivity cut-point of 90% the following diagnostic test characteristics were noted. Test — Sen — Spec — LR+ — LR- MRI — 90% — 82.5% — 5.1 — 0.12 Triple phase bone scan — 90% — 28.5% — 1.3 — 0.35 WBC scan — 90% — N/A — N/A — N/A X-ray — 90% — N/A — N/A — N/A • The investigators provided the following adjustments to disease probability for MRI +/- and Tc^{99m} +/- possibilities.

Posttest Probability Stratified by Imaging Test Result Across a Spectrum of Pretest Probabilities				
	Posttest Probability, %			
Pretest Probability, %	**MRI Positive***	**MRI Negative**	**Tc 99m Positive†**	**Tc 99m Negative**
10.0	36.2	1.3	11.2	3.4
25.0	63.0	3.8	27.4	9.6
50.0	83.6	10.7	53.1	24.2
75.0	93.9	26.5	77.2	49.0
90.0	97.9	51.9	91.1	74.2

*Using the all-studies estimate, which was lower than that calculated from studies that also had technetium Tc 99m data. The 90% sensitivity and 82.5% specificity translate to a positive likelihood ratio of 5.1 and a negative likelihood ratio of 0.12.

†Using a higher sensitivity threshold of 95%, which decreases the negative likelihood ratio to 0.32; the specificity at this threshold is 16% and the positive likelihood ratio is 1.13.

The DOR and sensitivities did not vary significantly for various subsets of MRI patients as reported by the authors:

MRI Study Subset	# Studies	DOR (95% CI)	Specificity @ 90% Sensitivity
Full text studies	16	42.1 (15-112)	82.5
Sa ple size ≥ 20	12	42.9 (12-150)	82.5
Charcot prevalence low or not reported	14	48.4 (19-127)	84
Diabetes prevalence > 90%	11	45.2 (12-172)	83.5
Not hospitalized (or not stated)	10	53.0 (11-257)	85.5
Gadolinium not used (or not stated)	11	55.1 (12-256)	86.0
Site count > patient count by 10% or less	9	29.1 (6-139)	76.5
Prospective design	9	25.3 (4-168)	73.5
Nonconsecutive enrollment	11	52.5 (21-181)	72.5
No blinding (or not specified)	9	47.9 (13-181)	72.5
MRI positive criteria defined	13	33.4 (10-112)	78.5
Appropriate + criterion standard used	14	42.1 (13-137)	82.5
Inappropriate – criterion standard used	12	67.4 (18-248)	88.5
Published after 1998	9	25.3 (5-117)	73.5

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		• If a patient has 25% pre-test probability of osteomyelitis, for every 100 patients who have a bone scan 12/13 would have the diagnosis correctly excluded but only 24/87 with a positive result would be correctly identified as having osteomyelitis.
2.	How precise are the results?	Fairly wide 95% CI's are noted for the DOR's. <u>MRI vs. Bone scan</u> <u>DOR (95% CI)</u> MRI 149.9 (54.6 – 411.3) Bone scan 3.6 (1.0 – 13.3) <u>MRI vs. X-ray</u> MRI 81.5 (14.2 – 466.1) X-ray 3.3 (2.2 – 5.0) <u>MRI vs. WBC scan</u> MRI 120.3 (61.8 – 234.3) WBC scan 3.4 (0.2 – 62.2)
3.	Were the results similar from study to study?	No, for MRI sensitivity ranged 77 – 100% and specificity ranged 40 – 100%. Similar variability was noted in the ranges for Tc^{99m}, x-ray, and WBC scans.
III.	***Will the results help me in caring for my patients?***	
1.	How can I best interpret the results to apply them to the care of my patients?	Across studies MRI is highly sensitive to detect osteomyelitis and should be the preferred diagnostic test to rule-in or rule-out the diagnosis. Unlike x-ray bone scan, or WBC scan MRI also assists with surgical planning by visualizing deep collections of necrotic tissue or prevalence.
2.	Were all patient important outcomes considered?	No patient-oriented outcomes (time to diagnosis, functional recovery) were assessed.
3.	Are the benefits worth the costs and potential risks?	Probably since 3-phase bone scan costs $288 by 2006 Medicare figures compared with $416 for extremity MRI. " Given the small difference in cost (which is approximated by Medicare reimbursement) between MRI

Limitations

1) **Small number of non-ED based methodologically heterogeneous studies upon which to base a meta-analysis including few using a well-accepted criterion standard.**

2) **Insufficient reporting of sensitivity, specificity LR^+ and LR^- for x-rays and tagged WBC scans.**

Bottom Line

MRI is the diagnostic test of choice to rule-out the diagnosis of (mostly diabetic) foot or ankle osteomyelitis with vastly superior negative likelihood ratios compared with x-rays, bone scans, or WBC scans. At 90% sensitivity the specificity for MRI is fairly stable across various subsets of study subjects, including the studies that did not provide the prevalence of Charcot arthropathy patients amongst their subjects.