Published in final edited form as:

Infect Dis Clin Pract (Baltim Md). 2012 September 1; 20(5): 326–329. doi:10.1097/IPC.0b013e3182639f6a.

Association Between Follow-Up Magnetic Resonance Imaging and Clinical Status Among Patients With Spinal Infections

Sanjiv Baxi, MD, MS^{*}, Preeti N. Malani, MD, MSJ^{†,‡,§,||}, Diana Gomez-Hassan, MD, PhD[¶], and Sandro K. Cinti, MD^{‡,||}

^{*}Department of Internal Medicine, University of California San Francisco, San Francisco, CA

[†]Division of Geriatric Medicine, Department of Internal Medicine, University of Michigan Health System, Ann Arbor, MI

[‡]Division of Infectious Diseases, Department of Internal Medicine, University of Michigan Health System, Ann Arbor, MI

[§]Geriatric Research, Education, and Clinical Center (GRECC), Ann Arbor, MI

^{||}Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, MI

[¶]Division of Neuroradiology, Department of Radiology, University of Michigan Health System, Ann Arbor, MI

Abstract

Background—Spinal infections, including paraspinal and/or epidural abscesses and vertebral discitis and osteomyelitis, can have devastating consequences. The diagnostic imaging modality of choice has traditionally been magnetic resonance imaging (MRI) given the very high sensitivity and specificity, although the role of MRI in follow-up of spinal infections and how this relates to follow-up clinical status is poorly understood. We sought to understand the relationship between follow-up MRI and clinical status.

Methods—We conducted a retrospective review of adults with spinal infection to assess the relationship between follow-up MRI and clinical course. The degree of agreement between MRI and clinical follow-up was assessed using the Cohen kappa coefficient. A multinomial logistic regression model was applied to assess the impact of covariates in affecting the clinical outcome and MRI at follow-up independently.

Results—Ninety-eight patients met inclusion criteria during a 13-year period. We observed a lack of correlation between clinical follow-up status and MRI ($\kappa = 0.065$, $P = 0.322$). The McNemar-Bowker test for symmetry revealed that this disagreement was asymmetric ($P < 0.001$). Notably, clinical worsening was never associated with an improved MRI, and clinical improvement was overall not predictive of MRI result and vice versa.

Conclusions—Routine follow-up MRI does not seem to correlate with clinical follow-up among patients with spinal infections. The use of MRI without new clinical indications in routine follow-up testing should be interpreted with caution.

Keywords

spinal infections; magnetic resonance imaging; vertebral osteomyelitis; discitis

Although spinal infections including discitis, osteomyelitis, and paraspinal or epidural abscesses are relatively uncommon, these infections can be associated with potentially devastating neurological sequelae including cord compression, residual neurologic deficits, and severe chronic pain.^{1,2} The incidence of spinal infections is rising and may be related in part to an aging population, increasing use of immunosuppressive agents, a larger number of spinal surgeries, and intravenous drug use. Additionally, part of this epidemiological shift is related to improved modalities for diagnosis, namely, magnetic resonance imaging (MRI).^{2,3}

Magnetic resonance imaging is the diagnostic modality of choice for evaluating the spine and surrounding tissues in patients with suspected spinal infection. Although in the evaluation of epidural abscess, vertebral osteomyelitis, and discitis, MRI has a reported sensitivity of 96% and specificity of 93%,^{2,4-6} the role of follow-up imaging in the clinical management of spinal infections is less well established. The impact of MRI results on clinical decision making deserves careful attention, particularly in the context of rising health care costs and the increasing availability of MRI units, which have resulted in proportional increases in the number of MRIs performed.⁷

When follow-up MRI suggests worsening spinal infection, patients may undergo additional interventions including biopsies, operations, and extended courses of parenteral or oral therapy regardless of clinically observed improvement. This approach can result in increased morbidity and adverse events in addition to direct costs. Some previous studies have suggested that follow-up imaging may not in fact correlate with clinical outcome in patients with spinal infections. However, these investigations have been limited by relatively small sample sizes.⁸⁻¹⁰ We sought to better understand the relationship between follow-up MRI and clinical outcomes among patients with spinal infection by reviewing the experience of a large academic medical center.

MATERIALS AND METHODS

Study Setting

We conducted a retrospective cohort study of patients with spinal infections admitted to the University of Michigan Health System (UMHS), a 914-bed tertiary care center, from January 1995 through October 2007. Patients were identified using a key word search through the UMHS CareWeb® patient record system, which includes MRI reports and clinical notes. The key word search included the following terms: *vertebral osteomyelitis*, *vertebral discitis*, *spinal infection* and/or *epidural abscess*.

Case Ascertainment

We included adult patients (18 years or older) who had an initial and follow-up vertebral MRI consistent with spinal infection and initial and follow-up clinical features consistent with spinal infection that were documented at UMHS in the electronic medical record (EMR). Relevant laboratory data were also reviewed to corroborate this determination. An attending Infectious Diseases physician (S.K.C.) confirmed that each patient's clinical history met inclusion criteria. This determination was further corroborated by a review of Infectious Diseases consultation reports when available in the EMR. These cases were further classified as having definite, probable, or possible spinal infection as follows. Definite cases required microbiological confirmation by positive spinal or cerebrospinal fluid culture. Probable cases demonstrated histopathological findings suggestive, but not diagnostic, of infection on direct biopsy or had patients with positive blood cultures. Possible cases had clinical and radiographic data consistent with infection without confirmatory microbiological or histopathological data (modified from Kowalski et al⁸).

Clinical features suggestive of spinal infection included back pain, fever, and neurological symptoms such as altered mental status, headache, weakness, paresthesias, and bowel or bladder incontinence. Laboratory support for spinal infection included elevated erythrocyte sedimentation rate and/or C-reactive protein, anemia, leukocytosis, positive microbiology culture from an appropriate site (blood and/or spinal aspiration), or pathologic specimens including bone and/or tissue biopsy. Changes in clinical status at follow-up were assessed by review of clinical notes from infectious disease consultation reports in the EMR along with other providers' reports as well as trends in laboratory studies. Specifically, the words *improved*, *improving*, or *improvement* were screened for and identified in the follow-up infectious diseases clinic notes, as well as equivalent terminology referencing no change and/or worsening.

Magnetic resonance imaging protocols included sagittal and axial T2, short T1 inversion recovery, T1 fluid-attenuated inversion recovery images with and without gadolinium contrast enhancement. Criteria used to identify potential changes associated with discitis and osteomyelitis included abnormal signal and enhancement within a disc and associated surrounding end plate irregularity, loss of cortical definition, and abnormal increased T2 signal with enhancement of the adjacent marrow space. Close inspection for potential epidural abscesses or intradural extension was performed. The neural foramina and the paraspinal soft tissues were also evaluated for spread of infection or inflammation in these areas. Changes in MRI appearance were assessed by attending neuroradiologists and existing radiology reports were analyzed by the study team.

Statistical Analysis

A multinomial logistic regression model was used to assess the impact of variables with a priori significance on MRI or clinical follow-up outcomes independently. The comparative outcome was follow-up clinical and MRI outcomes, and these were reported as improved, no-change, or worse and a Cohen J coefficient was determined to assess the degree of agreement among these categorical outcomes. In addition, the McNemar-Bowker test was used to assess whether the disagreement or agreement was symmetric. A two-tailed alpha =

0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 16.0 (IBM, SPSS, Chicago, Ill). This study was approved by the Institutional Review Board of the University of Michigan.

RESULTS

We initially identified 831 patients with potential spinal infection, of which 98 patients met the inclusion criteria. Table 1 describes the demographics of the study population. The mean $\pm$ SD age was 54.5 ± 14.0 years; 61.2% were men, and most of the patients were white (85.7%). The most common clinical characteristics at presentation were back pain (89.8%) and fever (29.6%), and neurologic abnormalities (including motor or sensory deficits, altered mental status, and headache) accounted for 25.5%. The most common comorbidities were diabetes mellitus (15.3%) and end-stage renal disease (9.2%). 12.2% of patients reported use of intravenous drugs, 2% of the patients were HIV positive, 7.1% had an autoimmune condition, and 12.2% were recently or currently on chronic steroids with another 11.2% on some non-steroid-based immunosuppressive therapy. Regarding classification, 40.8% of the patients had definite spinal infection, 56.1% had probable spinal infection, and 3.1% had possible spinal infection.

Median laboratory parameters at presentation included a white blood cell count of 7.8 thousand cells per millimeter³ and 6.6 thousand cells per millimeter³ at clinical follow-up (normal laboratory range, 4.0–10.0 thousand cells per millimeter³, which is equivalent to 10⁹ cells per liter), erythrocyte sedimentation rate of 65.0 mm/h and 32.5 mm/h at clinical follow-up (normal laboratory range, 0–20 mm/h), C-reactive protein of 10.5 mg/L (normal laboratory range, 0.0–0.6 mg/L), and hematocrit of 33.1% (normal laboratory range, 36%–46%).

Initial MRI at diagnosis revealed epidural involvement (frank abscess, phlegmon, or fluid collection) in 52.0% and paraspinal abscess in 26.5% of the patients. The most common site of infection was the lumbar region (39.8%), followed by the thoracic (22.4%) and lumbosacral (17.3%) regions. The remainder of infections involved the cervical spine in 13.3%, sacrococcygeal region in 2.0%, and multiple levels either contiguous (2.0%) or noncontiguous (3.1%).

Identification of an infectious agent was attempted in all patients, often using a combination of modalities. Diagnostic results were identified in blood culture (55.1%), open biopsy (27.6%), needle aspiration (17.3%), computed tomography-guided aspiration (10.2%), and cerebrospinal fluid culture (2.0%). Table 2 lists the organisms identified and their relative frequency. Overall, gram-positive organisms were noted in 61 individuals (62.2%). The most common gram-positive organism was *Staphylococcus aureus*, which was identified in 39 patients (39.8%); 33.3% (13/39) of these isolates demonstrated methicillin resistance. Gram-negative organisms were seen alone in 4 cases and in total in 7 patients (7.1% including polymicrobial) and included *Acinetobacter*, *Escherichia coli*, *Enterobacter cloacae*, *Haemophilus paraprothophilus*, *Serratia marcescens*, and 2 cases of *Stenotrophomonas maltophilia*. Other organisms included *Candida* species, *Aspergillus*, and one patient with *Mycobacterium tuberculosis* infection. No organism was identified in 23

patients (23.5%). All patients were treated with antimicrobial therapy, and the duration of therapy varied greatly from 4 weeks to years, with a median of 18.5 weeks and an interquartile range of 20 weeks. Therapy included various combinations of oral and intravenous antibiotics.

The median time to MRI follow-up was 47.5 days from the time of the original MRI study. The median time of clinical follow-up from the day of diagnosis was 35.0 days. Table 3 demonstrates the distribution of patients according to their follow-up clinical result tabulated against follow-up MRI result. The κ coefficient for this relationship was 0.065 ($P = 0.322$), demonstrating a lack of correlation in the outcomes; and the McNemar-Bowker test of symmetry had a value of $\chi^2 = 20.714$ ($P < 0.001$), indicating that the lack of correlation in the tabulated results is not weighted symmetrically across each of the relationships. A multinomial logistic regression was applied to each of the demographic factors in Table 1 and none of them were predictive of MRI follow-up outcome ($P > 0.9$ for all factors). Interestingly, none of the factors were associated with clinical improvement either ($P > 0.9$).

Overall, 69 (70.4%) of 98 patients had improved clinically at the time of follow-up; 45 of the 98 patients demonstrated improvement on MRI. Of the 69 patients who had clinical improvement, 33 (47.8%) had an improved MRI, 16 (23.2%) had no change in the MRI appearance, and 20 (29%) had a worsened appearance on MRI. Eight (8.2%) of the 98 patients had worsened clinical status, and none of these patients demonstrated improvement on their follow-up MRI; 5 (62.5%) of the 8 patients had a worsened MRI, and 3 patients (37.5%) had no change on their follow-up study. Overall, 29 of the 98 patients had worsening on MRI, although 20 (69%) of the 29 patients were noted to have clinically improved at follow-up. Three (10.3%) of these 29 patients subsequently underwent surgical intervention. Of the remaining 69 patients in the study, 7 patients (10.1%) underwent surgical intervention.

We were unable to systematically assess changes in therapy given that many patients were transitioned to suppressive antibiotic therapy or came off parenteral therapy during their follow-up visits for reasons unrelated to clinical presentation.

DISCUSSION

We evaluated the relationship between follow-up MRI and clinical status among 98 patients with spinal infections, and the preceding results offer additional evidence regarding the lack of clinical use of routine MR imaging to evaluate the response to treatment of spinal infections. Our patients were medically diverse with a variety of comorbid medical conditions, none of which seemed to be predictive of clinical or MRI outcome. Our study supports many of the findings that have been previously reported in the spinal infection literature including a disproportionate male tendency, staphylococcal predominance, highest frequency in the lumbar region, and having a highly variable clinical presentation.^{2,3,8,11} Most notably, our study failed to demonstrate a relationship between follow-up MRI and clinical outcome, which is consistent with previous work. Among the patients who have improved clinically (or have shown clinical stability), the role of MRI in follow-up remains unclear, as 52.2% of these 69 patients had either no change or worsening on follow-up MRI.

In contrast, among those patients with clinical worsening, follow-up MRI may help confirm an abnormality and provide an anatomical correlate, as none of the 8 patients who were clinically worse at follow-up demonstrated an improvement in MRI.

Despite very high sensitivity and specificity, the role of MRI in the routine follow-up of patients with spinal infections has been incompletely established. Prior investigations have raised questions about the clinical use of routine imaging. Kowalski and colleagues^{8,9} demonstrated a lack of correlation between follow-up MRI and clinical status in 2 separate studies. The first study included 79 patients and failed to demonstrate a clear association, although there seemed to be some use in predicting treatment failure among patients who had a worsening demonstrated on follow-up MRI or computed tomography.⁹ The second study, which looked at 33 patients with pyogenic spine infections, concluded that soft tissue findings were more predictive of outcome than bony findings.⁸ In a prospective study of 29 patients, Zarrouk et al¹⁰ failed to find predictive use of MRI among patients with bacterial vertebral osteomyelitis. Much like the present findings, these and other authors noted that abnormalities may persist on MRI irrespective of clinical and/or biological response.^{10,12,13}

Our results can help inform the optimal approach to the clinical management of patients with spinal infections. First, if patients have clinical worsening, our findings suggest that these patients will not have improved MRI findings and most of the time will in fact demonstrate worsening on their follow-up imaging. This observation supports the belief that some change in a patient's clinical state has resulted in clinical worsening that can be correlated to some change on repeat MRI (e.g., progression of disease). The same cannot be said for patients with clinical improvement or a lack of change at follow-up. Given that these patients have clinically improved or stabilized, routine follow-up imaging in such patients may be difficult to interpret and could lead to additional testing or unnecessary interventions.

Several limitations to our study exist, including its retrospective nature. In addition, the referral nature of our hospital may indicate that our patients may have had more complicated or atypical cases, potentially limiting the generalizability of these results. Furthermore, patients who require a follow-up MRI may be inherently different from patients who do not require one. The attending physicians in the infectious disease clinic were not always the same person who evaluated the patient in the inpatient hospital setting, which may or may not have affected the follow-up provider's decision making and tendency to order follow-up imaging, although this may more accurately represent the current state of clinical practice in large tertiary referral centers. Finally, it is unclear to what degree worsened clinical status may have influenced the radiologist's read and vice versa when follow-up MRI was available before the patient's clinical follow-up or an MRI was ordered out of concern for clinical worsening. Despite these shortcomings, our findings provide important additional confirmation of the limitation of routine follow-up MRI in patients with spinal infections and is supported by this study's relatively large sample of patients with both clinical and MRI follow-up.

In conclusion, our results support the notion that routine follow-up MRI of spinal infections does not correlate meaningfully with clinical status and that the indiscriminate and routine

use of such imaging may complicate and confound clinical decision-making. Although we do advocate for imaging in situations where patients have a change or progression in clinical status (eg, recurrent fever, new neurological deficit, worsening back pain, abnormal lab parameters, etc...), we suggest that routine follow-up MRI be pursued with caution. Further study, specifically a large prospective randomized trial, is needed to better delineate the optimal role of MRI in the routine follow-up of patients with spinal infections.

Acknowledgments

This work was supported by the University of Michigan Multidisciplinary Clinical Researchers in Training (MCRiT) program (grant number UL1RR024986).

REFERENCES

1. Osenbach RK, Hitchon PW, Menezes AH. Diagnosis and management of pyogenic vertebral osteomyelitis in adults. *Surg Neurol.* 1990; 33:266–275. [PubMed: 2326732]
2. Gouliouris T, Aliyu SH, Brown NH. Spondylodiscitis: update on diagnosis and management. *J Antimicrob Chemother.* 2010; 65S3:S11–S24.
3. Cottle L, Riordan T. Infectious spondylodiscitis. *J Infect.* 2008; 56:401–412. [PubMed: 18442854]
4. Ledermann HP, Schweitzer ME, Morrison WB, et al. MR imaging findings in spinal infections: rules or myths? *Radiology.* 2003; 228:506–514. [PubMed: 12802004]
5. Stabler A, Reiser MF. Imaging of spinal infection. *Radiol Clin North Am.* 2001; 39:115–135. [PubMed: 11221503]
6. Carragee EJ. The clinical use of magnetic resonance imaging in pyogenic vertebral osteomyelitis. *Spine.* 1997; 22:780–785. [PubMed: 9106320]
7. Baker LC, Atlas SW, Afendulis CC. Expanded use of imaging technology and the challenge of measuring value. *Health Aff.* 2008; 27:1467–1478.
8. Kowalski TJ, Layton KF, Berbari EF, et al. Follow-up MR imaging in patients with pyogenic spine infections: lack of correlation with clinical features. *AJNR Am J Neuroradiol.* 2007; 28:693–699. [PubMed: 17416823]
9. Kowalski TJ, Berbari EF, Huddleston PM, et al. Do follow-up imaging examinations provide useful prognostic information in patients with spine infection? *Clin Infect Dis.* 2006; 43:172–179. [PubMed: 16779743]
10. Zarrouk V, Feydy A, Salles F, et al. Imaging does not predict the clinical outcome of bacterial vertebral osteomyelitis. *Rheumatology.* 2007; 46:292–295. [PubMed: 16877464]
11. Carragee EJ. Pyogenic vertebral osteomyelitis. *J Bone Joint Surg Am.* 1997; 79:874–880. [PubMed: 9199385]
12. Modic MT, Feiglin Dh, Piraino DW, et al. Vertebral osteomyelitis: assessment using MR. *Radiology.* 1985; 157:157–166. [PubMed: 3875878]
13. Korvin De B, Provensol T, Le Dantec P, et al. Aspects and value of MRI in the diagnosis and follow-up of common microbes in infectious spondylodiscitis. Apropos of 25 clinically and biologically suspected patients. *J Radiol.* 1994; 75:267–277. [PubMed: 8051677]

TABLE 1

Demographics and Clinical Characteristics of the Study Population (n = 98)

Characteristic	Number (%)
Age, mean, yrs	54.5
Female	38 (38.8)
Race	
White	84 (85.7)
African American	12 (12.2)
Hispanic	1 (1.0)
Not available	1 (1.0)
Smoking status	
Never	56 (57.1)
Former	21 (21.4)
Current	19 (19.4)
Not available	2 (2.0)
Diabetes mellitus	15 (15.3)
End-stage renal disease	9 (9.2)
Cirrhotic liver disease	6(6.1)
Intravenous drug use	12 (12.2)
Congestive heart failure	8 (8.2)
HIV positive	2 (2.0)
Active malignancy*	9 (9.2)
Autoimmune condition [†]	7 (7.1)
Chronic steroid use, recent	12 (12.2)
Prior XRT	0 (0.0)
On chemotherapy	2 (2.0)
On immunosuppression, non-steroid	11 (11.2)
Disease likelihood	
Definite	40 (40.8)
Probable	55 (56.1)
Possible	3 (3.1)
Epidural involvement	51 (52.0)
Paraspinal abscess	26 (26.5)
Neurological deficit present	16 (16.3)
Surgical intervention	10 (10.2)
Avg WBC (n = 81) [‡]	−2.3 cells per microliter
Avg ESR (n = 65) [§]	−38.1 mm/h
Median days to MRI follow-up	47.5
Median days to clinical follow-up	35

Avg indicates average; ESR, erythrocyte sedimentation rate; HIV, human immunodeficiency virus; WBC, white blood cell count; XRT, x-ray radiation therapy.

* Confirmed conditions included renal cell carcinoma, multiple myeloma, esophageal adenocarcinoma, and chronic lymphocytic leukemia.

[†] Confirmed conditions included sarcoidosis, rheumatoid arthritis, primary biliary cirrhosis, nonspecific connective tissue disorder, Sjogren syndrome, and chronic inflammatory demyelinating polyneuropathy.

[‡] WBC is the change in the WBC from the time of diagnosis until clinical follow-up.

[§] ESR is the change in the ESR from the time of diagnosis until clinical follow-up.

TABLE 2

Isolated Pathogens From 98 Patients With Spinal Infections

Organism	Number (%)
Gram Positive (n = 61)	
<i>Staphylococcus</i>	44 (44.9)
Methicillin-susceptible <i>Staphylococcus aureus</i>	26 (26.5)
Methicillin-resistant <i>Staphylococcus aureus</i>	13 (13.3)
Methicillin-susceptible <i>Staphylococcus epidermidis</i>	2 (2.0)
Methicillin-resistant <i>Staphylococcus epidermidis</i>	3 (3.1)
<i>Streptococcus</i> species	13 (13.2)
<i>Enterococcus</i> species	2 (2.0)
<i>Corynebacterium diphtheriae</i>	1 (1.0)
<i>Peptostreptococcus prevotii</i>	1 (1.0)
Gram negative (n = 4)	
<i>Escherichia coli</i>	1 (1.0)
<i>Enterobacter cloacae</i>	1 (1.0)
<i>Haemophilus paraphrophilus</i>	1 (1.0)
<i>Serratia marcescens</i>	1 (1.0)
Other (n = 33)	
<i>Mycobacteria tuberculosis</i>	1 (1.0)
<i>Aspergillus fumigatus</i>	1 (1.0)
<i>Candida glabrata</i>	1 (1.0)
Polymicrobial	7 (7.1)
No organism identified	23 (23.5)

TABLE 3

Follow-Up Clinical and MRI Results for 98 Study Patients

	Improved Clinically	No Change Clinically	Worse Clinically	Total
MRI improved	33 (33.7%)	12 (12.2%)	0 (0.0%)	45 (45.9%)
MRI unchanged	16 (16.3%)	5 (5.1%)	3 (3.1%)	24 (24.5%)
MRI worse	20 (20.4%)	4 (4.1%)	5 (5.1%)	29 (29.6%)
Total	69 (70.4%)	21 (21.4%)	8 (8.2%)	98 (100%)