Diffusion-Weighted Magnetic Resonance Imaging and Apparent Diffusion Coefficient Mapping for Diagnosing Infectious Spondylodiscitis: A Preliminary Study

Tai-Yuan Chen, MD, Te-Chang Wu, MD, Yu-Kun Tsui, MD, Hou-Hsun Chen, MD, Chien-Jen Lin, MD, Huey-Jen Lee, MD, Tai-Ching Wu, MD

From the Section of Neuroradiology, Department of Medical Imaging, Chi-Mei Medical Center, Tainan, Taiwan (TYC, TCW, YKT, HHC, CJL, TCW); Central Taiwan University of Science and Technology, Taichung, Taiwan (TYC); Chia Nan University of Pharmacy and Science, Tainan, Taiwan (TYC); Shu Zen College of Medicine and Management, Kaohsiung, Taiwan (TYC); and Departments of Radiology and Neuroradiology, University Hospital, University of Medicine and Dentistry of New Jersey, Newark, NJ (HJL).

Keywords: Apparent diffusion coefficient, degenerative disc disease, diffusion-weighted imaging, infectious spondylodiscitis, magnetic resonance imaging.

ABSTRACT

BACKGROUND AND PURPOSE
Though diffusion-weighted (DW) magnetic resonance imaging (MRI) is useful for diagnosing many pathologies, its use in infectious spondylodiscitis is unclear. We aimed to evaluate the use of DW MRI and apparent diffusion coefficient (ADC) mapping for the diagnosis of infectious spondylodiscitis.

METHODS
In this retrospective study, 17 patients with confirmed infectious spondylodiscitis were matched by age and level of infected disc with 17 patients with degenerative disc disease (DDD) and 17 healthy controls. All patients received conventional MRI and diffusion-weighted imaging (DWI) in the same imaging session. ADC values of the 3 groups of patients were compared.

RESULTS
The mean age of each group was 67.4 ± 11.6 years. The mean ADCs of the normal control, DDD, and infectious spondylodiscitis groups were 1.76 ± 0.19 × 10⁻³, 1.12 ± 0.22 × 10⁻³, and 1.27 ± 0.38 × 10⁻³ mm²/second, respectively. The ADCs of the DDD and infectious spondylodiscitis groups were both significantly lower than that of the normal control group (both, P < 0.001).

CONCLUSION
These data suggest that DWI/ADC MRI may be useful in the early diagnosis of infectious spondylodiscitis.

Introduction
Early diagnosis and prompt initiation of adequate treatment are essential for good clinical outcomes in patients with infectious spondylodiscitis. Many imaging techniques, including conventional plain radiography, computed tomography (CT), magnetic resonance imaging (MRI), and radionuclide studies have been used to diagnose spinal infections. Of these, MRI is the most sensitive (93-96%) and specific (92.5-97%) modality for early detection of spinal infections.

Several MRI characteristics have been described in pyogenic vertebral osteomyelitis and spondylodiscitis including decreased signal intensity on T1-weighted images, increased signal intensity on T2-weighted images, enhancement on contrast-enhanced MR images in the disc and adjacent vertebral bodies, erosion or destruction of at least 1 vertebral endplate, decreased disc height, an absent intranuclear cleft, paraspinal and/or epidural inflammatory soft tissue, and abscess formation. However, early detection of infection can be challenging.

Diffusion-weighted imaging (DWI) is based on the random motion of water protons. As a radiographic technique, it has successfully been used as an important diagnostic tool in the

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Fig 1. Flowchart of subject selection.

The water mobility and microscopic diffusion motion of water molecules are heavily impeded in an abscess and lead to a decrease of ADC in the abscess center. These phenomena have been extensively described with brain abscesses and other intracranial infectious processes. We proposed that this phenomenon could be detected in an infected intervertebral disc and hypothesized that infected discs will restrict diffusion more than normal intervertebral discs.

Thus, the aim of this preliminary study was to evaluate patients with infectious spondylodiscitis with DWI using ADC analysis to enhance early detection.

Materials and Methods

Subjects

We retrospectively reviewed the medical records of 168 consecutive patients who received MR scanning for the evaluation of spinal pathology from May 2010 to April 2011. The study was approved by the Institutional Review Board of Chi-Mei Medical Center and because of the retrospective nature of the study the requirement of informed consent was waived.

Patients were included if their initial clinical presentation was consistent with infectious spondylodiscitis. Patients were excluded if they had a history of spinal surgery. All patients received conventional MRI and DWI in the same
Table 1. Demographic and Clinical Characteristics of the 3 Study Groups

|                      | Normal Control | DDD           | Infectious Spondylodiscitis | P-value |
|----------------------|----------------|---------------|----------------------------|---------|
| Age, years           | 67.4 ± 11.6    | 67.4 ± 11.6   | 67.4 ± 11.6                | -       |
| Gender (male)        | 10 (58.8%)     | 10 (58.8%)    | 14 (82.4%)                 | .319a   |
| WBC, ×10³/uL         | 6.36 ± 1.44    | 7.24 ± 1.18†  | 10.31 ± 2.95†‡             | < .001b*|

Data presented as mean ± SD or number (percentage).

\( ^a \)Cochran's Q test.

\( ^b \)Repeated measures ANOVA.

\( ^{< .05} \) indicates a significant difference among the 3 groups.

\( ^∗ \)Significant difference as compared to the normal control group (\( P < .05 \)).

\( ^{< .001} \)Significant difference as compared to the DDD (\( P < .05 \)).

**Fig 2.** Comparison of the ADC among the 3 groups. Data are presented as mean ± SD.

\( ^{< .001} \)Significant difference as compared to the normal group (\( P < .001 \)).

\( ^{< .001} \)Significant difference as compared to the DDD group (\( P < .001 \)).

A diagnosis of infectious spondylodiscitis/discitis was confirmed by either microbiological or histological studies or by laboratory findings such as elevated erythrocyte sedimentation rate, leukocytosis, elevated C-reactive protein, or clinical response to antimicrobial therapy. A separate group of patients with DDD was included for comparison due to the high prevalence of DDD in the patient population, as well as DDD being in the differential diagnosis of infectious spondylodiscitis.

A group of patients with normal clinical and imaging findings from the original cohort were also included. Seventeen patients from the DDD group and normal control groups were then selected (Fig 1) such that all patients in the 3 groups were matched in terms of age and involved disc level.

**MRI**

Regions of interest (ROI) were drawn in the affected intervertebral discs for ADC calculation. ADC values were measured and compared with those of the healthy control and the DDD groups. Imaging was carried out using a 1.5-T Siemens Avanto MR scanner (Siemens Healthcare, Erlangen, Germany). A phased-array spine CTL coil was used for anatomical high-resolution imaging and diffusion measurements. The conventional MR protocol consisted of sagittal T1-weighted imaging (T1WI; TR/TE/NEX, 576/10/3), sagittal T2-weighted imaging (T2WI; TR/TE/NEX, 3,500/106/3), and sagittal T2WI with fat suppression. Sections (4-mm thick) with 1-mm intersection gaps, 30-cm field of view (FOV), and 448 × 314 matrix were used for all scans. Axial T1WI and axial T2WI with fat-suppression images were also included. DWI was performed as single-shot spin-echo echo-planar imaging (TR/TE, 2,500/72 with diffusion sensitivities; \( b = 0 \) seconds/mm², \( b = 400 \) seconds/mm², and \( b = 800 \) seconds/mm²). The diffusion gradients were applied sequentially in 3 orthogonal directions to generate 3 sets of sagittal diffusion-weighted images. Sections (4-mm thick) without intersection gaps, a 40-cm FOV, and a 192 × 192 matrix were used for all scans. The scanning time was 153 seconds. Analysis of diffusion changes was performed by “in-line” calculation of the ADC based on the Stejskal and Tanner equation as the negative slope of the linear regression line best fitting the points for \( b \) versus ln (SI), where SI is the signal intensity from an ROI of the images acquired at the 3 \( b \) values.

The data from the diffusion-weighted images were transferred to a Numaris 4 workstation (Siemens). ADC maps were generated by automatically performing this calculation on a pixel-by-pixel basis. ROI measurements were performed by 2 neuroradiologists with experience in DWI. The physicians reviewed the images independently and without prior knowledge of other laboratory results. When discrepancies were identified, the images were re-reviewed and a final diagnosis was reached by consensus.

**Statistical Analysis**

Continuous variables (eg, white blood cell count [WBC] and ADC) were presented as means and SD. Categorical variables (eg, gender) were expressed as counts and percentages. Since
Fig 3. A 62-year-old female with infectious spondylodiscitis of L3-L4. (A) Sagittal T2WI showed hyperintense changes in the L3-L4 intervertebral disc and adjacent bone marrow, associated with endplate destruction. (B) Sagittal DWI (b = 400 seconds/mm$^2$) showed hyperintense changes in the L3-L4 intervertebral disc, and the corresponding ADC map (C) revealed hypointense changes with an ADC value ($1.40 \times 10^{-3}$ mm$^2$/second) lower than the mean value of normal controls. The arrows had pointed to infected intervertebral disc.

this was an age-matched study, the comparisons between age-matched groups are not independent. Hence, for comparisons of the 3 groups, continuous variables were examined by repeated measures analysis of variance (ANOVA), and the difference in gender distributions was examined by Cochran’s Q test. When a significant difference among groups was apparent, multiple comparisons were performed by the use of the Bonferroni procedure for type I error adjustment. The SAS software package version 9.2 (SAS Institute Inc., Cary, NC, USA) was used for performing all statistical analyses. All statistical assessments were evaluated at a 2-sided significance level ($\alpha$ level) of .05, but $P$ value will be specified if greater significant level had been reached.

Results

In this age-matched study, there were 17 patients in each group, ie, infectious spondylodiscitis, DDD, and normal control groups. The mean age in each group was 67.4 ± 11.6 years. The demographic and clinical characteristics of the 3 groups are shown in Table 1. There was no significant difference in gender distributions among the 3 groups ($P = .319$). The mean WBC counts of the normal control, DDD, and infectious spondylodiscitis groups were $6.36 \pm 1.44 \times 10^3$/uL, $7.24 \pm 1.18 \times 10^3$/uL, and $10.31 \pm 2.95 \times 10^3$/uL, respectively, and the WBC count of the infectious spondylodiscitis group was significantly higher than that of the normal control group and the DDD group (both, $P < .001$).

The mean ADCs of the normal control, DDD, and infectious spondylodiscitis groups were $1.76 \pm 0.19 \times 10^{-3}$, $1.12 \pm 0.22 \times 10^{-3}$, and $1.27 \pm 0.38 \times 10^{-3}$ mm$^2$/second, respectively. As with the mean WBC, significant differences in the mean ADC between the 3 groups were also found ($P < .001$; Fig 2). The ADCs of the DDD and infectious spondylodiscitis groups were both significantly lower than that of the normal control group (both, $P < .001$).

Representative images of spondylodiscitis and DDD are shown in Figures 3 and 4, respectively.

Discussion

Infectious spondylodiscitis can lead to devastating sequelae if not managed promptly; thus early detection is critical for obtaining good outcomes. The results of this study showed that the mean ADC of the infectious spondylodiscitis group was significantly lower than that of normal controls, but higher than that of patients with DDD. Thus, combined with other clinical factors, DW MRI may aid in the early diagnosis of infectious spondylodiscitis.

The lumbar disc is the largest avascular tissue in the adult human body. The nucleus pulposus is avascular throughout its life, the blood supply to the annulus fibrosus discontinues during the second decade of life, and cells in the disc can be farther than 5 mm away from the nearest blood vessel. The transport of metabolites occurs through the matrix of the disc by molecular diffusion in response to concentration gradients and, to some degree, by fluid that is pumped in and out when the volume of the disc changes during activity. Changes in diffusion are thought to be an early marker of disc degeneration or other conditions, and have been shown to be potentially useful in the clinical diagnosis of DDD. MRI is the only in vivo method for imaging diffusion; it images the translational motion of protons at the microscopic level. Diffusion into the intervertebral disc has been demonstrated in
animals\textsuperscript{27} and humans\textsuperscript{28} using MRI with a gadolinium contrast medium. Quantitative studies of normal and degenerate intervertebral discs have also been performed by measuring the T1 and T2 relaxation times\textsuperscript{29–32}; however, these measurements have not been shown to be reliable for the monitoring of biochemical alterations associated with lumbar disc pathology.\textsuperscript{33} DWI, however, may prove to play an important role in the clinical evaluation of vertebral disc infectious pathologies.

Proton diffusion in tissues is restricted by both permeable and nonpermeable barriers due to cellular and fibrous structures. Tissue fluid is contained in multiple compartments, and the physical quantity, accessible by MR DWI, is the ADC. The largest ADC is observed when the diffusion-sensitizing gradient is parallel to the fiber-tract direction, and the smallest when the gradient is perpendicular to the fiber-tract direction. Kerttula et al.\textsuperscript{34} were the first to measure the ADC values of the nucleus pulposus in vivo in 3 orthogonal directions in the thoracolumbar spines of healthy young people, and reported that ADC values of the thoracolumbar discs varied from 1.27 to 1.9 × 10\textsuperscript{−3} mm\textsuperscript{2}/second. The ADC values obtained in our study are similar to those reported by Kerttula et al. Interestingly, Kerttula et al.\textsuperscript{34} showed an increasing trend of ADC values toward lower positioned discs. The matrix of the nucleus pulposus can be thought of as a network of thin, randomly oriented collagen fibers packed with proteoglycans. The proteoglycans interpenetrate and divide the space between the collagen fibers into small pores through which water and small solutes can move. The pore size and the swelling pressure depend on the proteoglycan concentration. The more proteoglycans that are present, the more water the disc can hold and the better it can resist a mechanical load. During aging, the amount of proteoglycans decreases, the water content of the nucleus falls dramatically, and the thickness of collagen fibers increases.\textsuperscript{34} Based on the aforementioned findings, we matched patients by age and disc level to minimize the effects of these variables on the results.

Though characteristic MRI findings of vertebral osteomyelitis and spondylodiscitis have been described,\textsuperscript{5–9} early detection remains challenging. Our finding that infected discs (with or without epidural abscess) were markedly hyperintense relative to the surrounding tissues on DWI is consistent with those of previously published articles that have described a similar appearance in abscess cavities in the brain, liver, and orbit.\textsuperscript{12–16,24} Additionally, the present finding that both infected discs and epidural abscesses were dark on the ADC maps also agrees with those of published articles that have described low ADC values within abscesses.\textsuperscript{12,14,22} Conventional MRI findings in infectious spondylodiscitis and the vacuum phenomenon of DDD often have considerable overlap, making a definite diagnosis difficult without a pathological specimen. The hyperintensity of T2WI in infected discs and vacuum discs can overlap, and differentiating the 2 may be challenging. The results of our study showed that the mean ADC of the infectious spondylodiscitis group (1.27 ± 0.38 × 10\textsuperscript{−3} mm\textsuperscript{2}/second) was significantly lower than that of the normal group (1.76 ± 0.19 × 10\textsuperscript{−3} mm\textsuperscript{2}/second), but higher than that of the DDD group (1.12 ± 0.22 × 10\textsuperscript{−3} mm\textsuperscript{2}/second). This finding agrees with that of a published report suggesting that dehydration mostly precedes clinical degeneration, ie, there may be less water available for measurement of anisotropy in a degenerative vacuum disc.\textsuperscript{34}

We acknowledge that this study has some limitations. The first limitation is the relatively small number of subjects in each group, and second, repeat scans and long-term follow-up were not performed. Therefore, larger prospective studies are warranted to validate our preliminary findings.
Conclusions
Our results showed that mean ADC of infectious spondylodiscitis was significantly lower than that of normal intervertebral discs, but higher than that of patients with DDD. These data suggest that DWI/ADC MRI may be useful in the early diagnosis of infectious spondylodiscitis, which may result in more favorable outcomes.

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