Is Diffusion Anisotropy a Biomarker for Disease Severity and Surgical Prognosis of Cervical Spondylotic Myelopathy?[1]

Chun Yi Wen, PhD
Jiao Long Cui, BE
Harris S. Liu, BE
Kin Cheung Mak, MBBS
Wai Yuen Cheung, MBBS
Keith D. K. Luk, MBBS, FRCSEd
Yong Hu, PhD

Purpose: To explore the value of diffusion-tensor (DT) imaging in addressing the severity of cervical spondylotic myelopathy (CSM) and predicting the outcome of surgical treatment.

Materials and Methods: From July 2009 to May 2012, 65 volunteers were recruited for this institutional review board–approved study, and all gave informed consent; 20 volunteers were healthy subjects (age range, 41–62 years), and 45 were patients with CSM (age range, 43–86 years). Anatomic and DT 3.0-T magnetic resonance images were obtained. Surgical decompression was performed in 22 patients with CSM, and patients were followed up for 6 months to 2 years. The clinical severity of myelopathy and postoperative recovery were assessed by using the modified Japanese Orthopaedic Association (mJOA) score. A recovery ratio (comparison of postoperative with preoperative mJOA score) of more than 50% indicated a good clinical outcome of surgery. DT findings, patient age, T2 high signal intensity (HSI), and somatosensory evoked potential (SEP) were analyzed by using a logistic regression model to predict the surgical outcome of patients with CSM.

Results: A significant difference in cervical cord mean fractional anisotropy (FA) was found between healthy subjects and patients with CSM (0.65 ± 0.05 [standard deviation] vs 0.52 ± 0.13, $P < .001$). FA values were significantly correlated with the severity of neurologic dysfunction indicated by mJOA score ($r^2 = 0.327$, $P = .016$). Logistic regression analysis showed that mean FA ($P = .030$) and FA at the C2 vertebra ($P = .035$) enabled prediction of good surgical outcome; however, preoperative mJOA ($P = .927$), T2 HSI ($P = .176$), SEP amplitude ($P = .154$), and latency ($P = .260$) did not.

Conclusion: FA is a biomarker for the severity of myelopathy and for subsequent surgical outcome.

Online supplemental material is available for this article.

[1] From the Department of Orthopaedics and Traumatology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 12 Sandy Bay Rd, Pokfulam, Hong Kong. Received September 14, 2012; revision requested November 9; revision received February 22, 2013; accepted March 1; final version accepted June 6. Supported by the General Research Fund of the University Grant Council of Hong Kong (HKU 771608M/774211M) and AO East Asia Research Grant. **Address correspondence to** Y.H. (e-mail: *yhud@hku.hk*).

Cervical spondylotic myelopathy (CSM) is a chronic compressive spinal cord lesion in a narrow canal secondary to spondylosis or disk degeneration (1–3). Currently, spinal decompression surgery is the mainstay in the treatment of CSM (4); however, the debate persists regarding the factors affecting the surgical outcome of CSM, such as age (4–6), duration of symptoms (7–10), preoperative neurologic status (11), intramedullary signal intensity changes on T2-weighted magnetic resonance (MR) images (12,13), and somatosensory evoked potential (SEP) (14).

Diffusion-tensor (DT) imaging was developed to assess spinal cord microstructure by tracing water molecular diffusion at microscopic dimensions (15). The diffusion indexes, fractional anisotropy (FA) and diffusivity, are attributed to the densely packed axonal membranes in spinal cord parenchyma (16). Changes in the diffusion indexes reflect microstructural damages, such as demyelination or axon damage, in the spinal cord (17,18). Thus, DT imaging may be a promising tool with which to evaluate the severity of myelopathy and predict the surgical prognosis of CSM.

To date, previous studies have shown the feasibility of DT imaging in the evaluation of microstructural changes in the myelopathic cervical cord (19–28). The prognostic value of spinal cord DT imaging in patients with CSM has been addressed in several previous studies (29–31). Two of these previous studies examined the pattern of DT fiber tractography in patients with CSM (29,30). However, fiber tractography is a computerized simulation technique used to visualize the structural integrity, and it is not a standardized or well-received approach for quantitative assessment (15). Jones et al (31) reported correlations between the FA value at the most stenotic level and the surgical outcome of CSM in terms of the neck disability index. However, the clinical follow-up in the Jones et al (31) study was too short, so it remains difficult to draw conclusions from that work.

The objective of this study was to explore the value of DT imaging in addressing the severity of CSM and predicting the outcome of surgical treatment.

Advances in Knowledge

- Fractional anisotropy (FA) of the cervical spinal cord at the point of maximal compression correlates with the clinical severity of myelopathy; moreover, the FA value in patients with cervical spondylotic myelopathy (CSM) with a modified Japanese Orthopaedic Association (mJOA) score of 0–7 was lower than the FA value in patients with an mJOA score of 12–15 ($P = .014$).
- Logistic regression analysis showed that the mean FA value (score = 5.167, $P = .023$) is an indicator of good surgical outcome in comparison with age (score = 0.602, $P = .438$), mJOA score (score = 0.155, $P = .694$), and conventional T2 high signal intensity (score = 1.474, $P = .225$).
- Diffusion-tensor (DT) MR imaging of the myelopathic spinal cord is superior to current clinical and radiologic assessments in the prediction of surgical outcome.

Materials and Methods

Subjects

The institutional review board of research ethics approved all study procedures. A total of 65 subjects were recruited for this study from July 2009 to May 2012, including 20 healthy subjects (10 men, 10 women;, mean age, 52 years; age range, 41–62 years) and 45 patients with CSM (26 men, 19 women; mean age, 64 years; age range, 43–86 years). All subjects provided informed consent. Clinical diagnosis of CSM was based on the neurologic signs and symptoms of patients with compatible radiologic cervical cord compression in a stenotic canal. The criterion for inclusion in the CSM group was spinal canal stenosis, defined as narrowing in the anteroposterior diameter of the cervical canal to less than 13 mm, with clinical myelopathy. Patients with prior neurologic trauma, surgery, or both; other coexisting neurologic disorders (eg, multiple sclerosis); or claustrophobia were excluded. A consecutive series of 86 patients with CSM was referred from clinical outpatient services on the basis of inclusion and exclusion criteria. Eighteen patients refused to undergo additional DT imaging. One patient with CSM and claustrophobia and 12 other patients who had undergone previous lumbar surgery were excluded. The remaining 45 patients with CSM were recruited to this study. Decompression surgery in 22 patients with CSM and standard postoperative rehabilitation and follow-up ranged from 6 months to 2 years. Age-matched healthy volunteers were recruited as control subjects. The inclusion criteria for healthy subjects were intact sensory and motor function, negative Hoffman sign, no radiologic cervical

Implication for Patient Care

- DT imaging is a promising tool for use in the precise diagnosis and prognostication of CSM.

Published online before print
10.1148/radiol.13121885 **Content code:** NR

Radiology 2014; 270:197–204

Abbreviations:
CSM = cervical spondylotic myelopathy
DT = diffusion tensor
FA = fractional anisotropy
HSI = high signal intensity
mJOA = modified Japanese Orthopaedic Association
SEP = somatosensory evoked potential

Author contributions:
Guarantors of integrity of entire study, C.Y.W., J.L.C., Y.H.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, C.Y.W., J.L.C., K.C.M.; clinical studies, C.Y.W., J.L.C., K.C.M., K.D.K.L., Y.H.; statistical analysis, C.Y.W., J.L.C., H.S.L.; and manuscript editing, C.Y.W., J.L.C., W.Y.C., K.D.K.L., Y.H.

Conflicts of interest are listed at the end of this article.

stenosis, and no history of neurologic injury or surgery. Three neurologically intact subjects were excluded from the healthy group because of radiologic cervical stenosis.

Clinical Assessment

Senior spine surgeons (K.D.K.L., W.Y.C.; 30 and 10 years of experience, respectively) performed the clinical assessment. The modified Japanese Orthopaedic Association (mJOA) score was used for routine clinical assessment of the severity of myelopathy at our institute (32). The mJOA score is comprised of three categories; these are motor function of upper and lower limbs (7), sensory function (4), and sphincter function (33), with a full mJOA score of 17 (34). Recovery after surgical treatment was evaluated by using the recovery ratio of the Hirabayashi method, which is calculated by dividing the difference of postoperative mJOA score minus preoperative score by the difference of 17 minus preoperative score and then multiplying the result by 100%. A recovery ratio greater than 50% is considered indicative of a good outcome, whereas a recovery ratio less than 50% is indicative of a fair outcome (35).

Electrophysiologic Assessments

The functional integrity of the spinal cord was evaluated by using SEP (11). In brief, stimulation was applied to the median nerve in the wrists with a pulse duration of 0.2 msec at a rate of 5.1 Hz and a constant current of 10–30 mA. SEP signals were recorded from the C3 vertebra in response to right limb stimulation and from the C4 vertebra in response to left limb stimulation, with the reference electrode at front middle lead (or Fz) according to the International 10–20 system. After automatic artifact rejection, the mean signal over 200 consecutive sweeps was calculated. Further calculation with data from more than 500 sweeps was required if the waveform was not clearly identified. The data were inspected by an experienced electrophysiologist (Y.H., 16 years of experience) for the presence of the main peaks N19 and P22. The latency and amplitude of SEP signals in patients with CSM were compared with previously published criteria in healthy subjects (mean latency, 18.40 msec ± 0.71 [standard deviation]; amplitude, 1.23 μV ± 0.50). Abnormal SEPs were defined as delayed N19 latency (exceeding 2.5 standard deviations) or decreased peak-to-peak amplitude (<0.5 μV) (14).

MR Imaging

Anatomic and diffusion MR images were obtained within 1 month before treatment. All images were obtained by using a 3.0-T MR imager (Achieva; Philips Medical Systems, Best, the Netherlands). During the acquisition process, each subject was placed in the supine position with the sensitivity encoding neurovascular head and neck coil enclosing the cervical region, and the subject was instructed not to swallow to minimize motion artifacts.

Sagittal and axial T1- and T2-weighted images were acquired by using a fast spin-echo sequence. For sagittal imaging, the imaging parameters were as follows: repetition time msec/echo time msec, 530/7.2 for T1 imaging and 3314/120 for T2 imaging; field of view, 250 × 250 mm; section thickness, 3 mm; section gap, 0.3 mm; foldover direction, feet to head; two signals acquired; resolution, 0.92 × 1.16 × 3.0 mm for T1 imaging and 0.78 × 1.01 × 3.0 mm for T2 imaging; and resolution of reconstruction, 0.49 × 0.49 × 3.0 mm. A total of 11 sagittal images covering the cervical spinal cord from the C1 through C7 vertebrae were acquired. Each of these images was placed at the center of either each vertebra or each intervertebral disk. For axial imaging, the imaging parameters were as follows: 1000/8 for T1 imaging and 4000/120 for T2 imaging; field of view, 80 × 80 mm; section thickness, 7 mm; section gap, 2.2 mm; foldover direction, anterior to posterior; three signals acquired; resolution, 0.63 × 0.68 × 7.0 mm for T1 imaging and 0.63 × 0.67 × 7.0 mm for T2 imaging; resolution of reconstruction, 0.56 × 0.55 × 7.0 mm for T1 imaging and 0.63 × 0.63 × 7.0 mm for T2 imaging.

Cardiac vector cardiogram triggering was applied to minimize the pulsation artifact from cerebrospinal fluid. A total of 12 transverse images covering the cervical spinal cord from the C1 through C7 vertebrae were acquired. Each image was placed at the center of each vertebra or intervertebral disk. Diffusion MR images were acquired by using a pulsed sequence (single-shot spin-echo echo-planar imaging). Diffusion encoding occurred in 15 noncollinear and noncoplanar diffusion directions, with a b value of 600 sec/mm^2. The imaging parameters were as follows: five heartbeats/60; field of view, 80 × 80 mm; section thickness, 7 mm; section gap, 2.2 mm; foldover direction, anteroposterior; three signals acquired; resolution, 1.0 × 1.26 × 7.0 mm; and resolution of reconstruction, 0.63 × 0.63 × 7.0 mm. The image section planning was the same as that used to obtain the anatomic axial T1- and T2-weighted images, with 12 sections covering the cervical spinal cord from the C1 through C7 vertebrae. The duration of DT imaging was 24 minutes per subject on average, with a mean heart rate of 60 beats per minute. Spatial saturation with spectral presaturation with inversion recovery was applied to suppress the foldover effect. Cardiac vector cardiogram triggering was applied to minimize the pulsation artifacts caused by cerebrospinal fluid.

Image Analysis

Experienced researchers (C.Y.W., J.L.C.; both with 3 years of experience in DT image analysis; H.S.L., 1 year of experience) conducted the image analysis. Cervical cord compression was confirmed when the ratio of the sagittal diameter divided by the transverse diameter was less than 0.4 (36). The maximal compression level was determined by the lowest compression ratio. The presence of the T2 intramedullary high signal intensity (HSI) was recorded for subsequent analyses.

The diffusion measurements were performed with DTI Studio software (version 2.4.01 2003; Johns Hopkins University, Baltimore, Md). Image volume realignment and three-dimensional

Figure 1

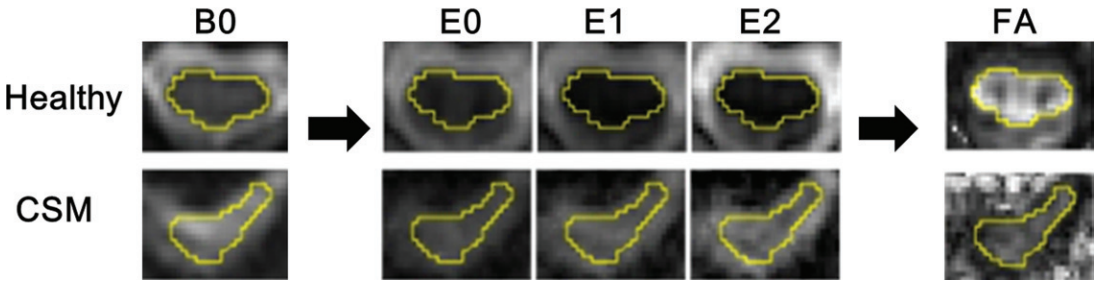

Figure 1: DT image analysis of the cervical cord. The region of interest was defined to cover the whole cord on axial *B*0 images. *E0*, *E1*, and *E2* represent the map of eigenvalues.

rigid body transformation were performed with the built-in algorithm of the software to reduce motion artifacts. The realigned and coregistered diffusion-weighted data sets were double checked for image quality and were then used to estimate DTs, including three eigenvalues (λ1, λ2, and λ3). As shown in Figure 1, the region of interest was defined on the basis of the non–diffusion-weighted image (b = 0 sec/mm^2; hereafter, *B*0 image) to cover the whole spinal cord and was adjusted according to the diffusion-weighted image to reduce cerebrospinal fluid contamination (37). Three eigenvalues (λ1, λ2, and λ3) were measured by averaging all selected voxels in the region of interest with ImageJ software (National Institutes of Health, Bethesda, Md). The diffusion indexes (eg, FA value), were calculated with the following formula:

$$\mathrm{FA} = \sqrt{\frac{3}{2}}\frac{\left[(\lambda 1-\lambda)^2+(\lambda 2-\lambda)^2+(\lambda 3-\lambda)^2\right]}{\lambda_1^2+\lambda_2^2+\lambda_3^2}.$$

Diffusion indexes of the cervical cord were measured at different anatomic locations. For example, we measured FA value at the level of the C2 vertebra, FA value at the maximal compression level, the lowest FA value along the myelopathic cervical cord, and the mean FA value from C3 through C7 vertebrae.

Statistical Analysis

Previous DT imaging studies have suggested FA of the cervical cord is the crucial parameter in the evaluation of myelopathy in patients with CSM (19). In this study, FA values in healthy subjects were compared with those in patients with CSM by using the Mann-Whitney *U* test. The relationship between the diffusion indexes of the myelopathic cervical cord and the mJOA score was examined by using the Spearman rank correlation. The results of clinical, electrophysiologic, and radiologic assessments were analyzed by using a logistic regression model to predict good or fair surgical outcomes and were depicted as receiver operating characteristic curves. The precision of clinical, electrophysiologic, and radiologic factors in the prediction of good or fair surgical outcomes was depicted by the area under the receiver operating characteristic curve. The level of significance was set at $P < .05$. All data analyses were performed by using SPSS analysis software (SPSS, version 16.0; SPSS, Chicago, Ill).

Results

No difference in age or sex was found between healthy subjects and patients with CSM. Among the 45 patients with CSM, 14 (31%) had a single-level compression and 31 (69%) had two or more levels of compression secondary to disk degeneration, spondylosis, or both. In addition, 13 (29%) patients had T2 HSI, and 20 (44%) had SEP abnormalities. Surgical decompression was performed in 22 patients with CSM by using either the anterior (n = 10 [45%]) or the posterior (n = 12 [55%]) approach.

The FA values in patients with CSM were significantly lower than those in healthy subjects at the C2 level (P = .003) and at the point of maximal spinal cord compression ($P < .001$); the lowest FA value ($P < .001$) and the mean FA values from C3 through C7 ($P < .001$) were also significantly lower in patients with CSM (Table 1). However, the lowest FA value did not necessarily appear at the maximal compression level. In 13 (93%) of 14 single-level compression cases, the lowest FA values were measured at the point of maximal compression or adjacent levels; however, these findings were not observed in 22 (71%) of 31 multilevel compression cases. In patients with CSM with multilevel compression, the FA value at the C2 vertebra correlated with the lowest FA value (r^2 = 0.254, $P < .001$), but it did not correlate with the FA value at the maximal compression level (r^2 = 0.053, P = .057) (Fig E1 [online]).

As shown in Figure 2, patients with a higher grade of clinical severity of CSM had lower FA values. For example, FA values at the maximal compression level in patients with mJOA scores of 0–7 were lower than those in patients with mJOA scores of 12–15 (P = .014).

In regard to the relationship between diffusion indexes and the severity of myelopathy, FA values at the maximal compression point were significantly correlated with the sum of the mJOA score (r^2 = 0.327, P = .016) and the upper limb category of the mJOA score (r^2 = 0.245, P = .046) (Fig E2 [online]). In contrast, in conventional MR imaging, the compression ratio of the myelopathic spinal cord (P = .479) and T2 HSI (P = .388) were

Figure 2

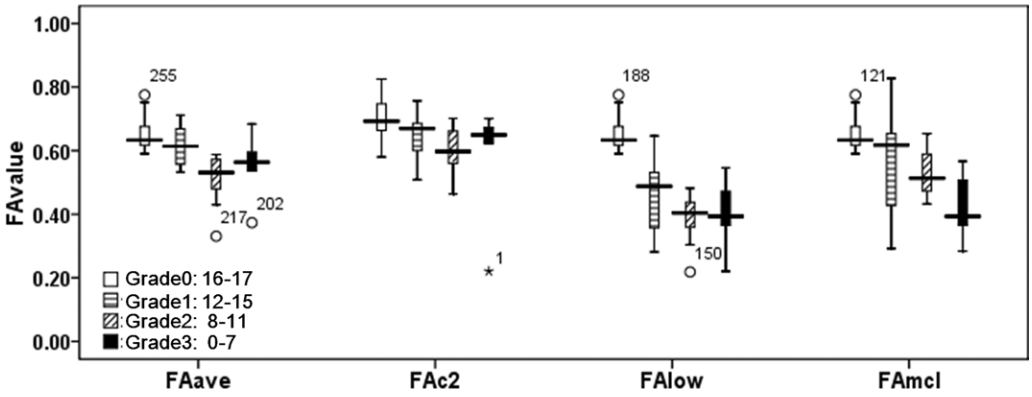

Figure 2: Box plot of FA values in patients with CSM with different severity grades of neurologic deficit classified by mJOA score. FA_{ave} = average FA value from the level of the C3 through C7 vertebrae, FA_{c2} = FA value at the level of the C2 vertebra, FA_{low} = lowest FA value along the myelopathic cervical cord, FA_{mcl} = FA value at maximal compression level.

Table 1

Diffusion Anisotropy of Cervical Cord between Healthy Subjects and Patients with CSM

Parameters and Group	Mean	95% Confidence Interval	Range	*P* Value*
FA_{C2}				.003
CSM	0.63 ± 0.10	0.60, 0.66	0.22–0.80	…
Healthy	0.70 ± 0.06	0.67, 0.73	0.58–0.82	…
FA_{mcl}				<.001
CSM	0.52 ± 0.13	0.48, 0.56	0.23–0.83	…
Healthy	0.65 ± 0.05	0.63, 0.67	0.59–0.78	…
FA_{low}				<.001
CSM	0.43 ± 0.10	0.40, 0.46	0.22–0.65	…
Healthy	0.65 ± 0.05	0.63, 0.67	0.59–0.78	…
$FA_{C3–C7}$				<.001
CSM	0.57 ± 0.08	0.55, 0.60	0.33–0.72	…
Healthy	0.65 ± 0.05	0.63, 0.67	0.59–0.78	…

Note.—Unless otherwise indicated, data are FA values. FA_{C2} = FA value at the level of the C2 vertebra, $FA_{C3–C7}$ = mean FA value at the level of the C3 through C7 vertebrae, FA_{low} = lowest FA value along the myelopathic cervical cord, FA_{mcl} = FA value at the maximal compression level.

* *P* values were calculated with the Mann-Whitney *U* test.

Figure 3

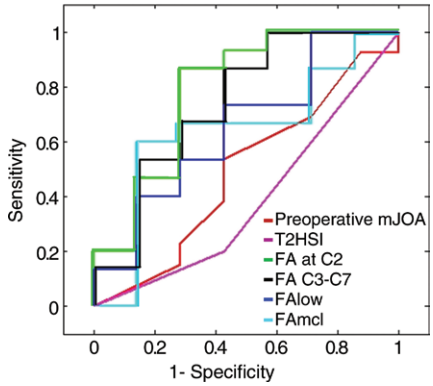

Figure 3: Receiver operating characteristic curves for the prognostic precision of surgical outcomes. Preoperative mJOA score (area = 0.489), T2 HSI (area = 0.386), FA value at the level of the C2 vertebra (0.781), mean FA value at the level of the C3 through C7 vertebrae (area = 0.743), the lowest FA value along the myelopathic cervical cord *(FAlow)* (area = 0.648), and FA value at the maximal compression level (area = 0.638) *(FAmcl)* are shown.

not associated with the clinical severity of myelopathy evaluated by using the mJOA score. Patients with more severe CSM tended to have abnormal SEPs, such as decreased amplitude and prolonged latency (r^2 = 0.236, P = .030).

When we compared the areas under the receiver operating characteristic curves (Fig 3), FA values at the C2 vertebra (FA = 0.781) and mean FA (FA = 0.743) were clearly higher than those for age (FA = 0.383), mJOA (FA = 0.386), SEP (FA = 0.662 for amplitude, FA = 0.595 for latency), and T2 HSI (FA = 0.386). The receiver operating characteristic curves show that FA values appeared to enable us to predict the surgical outcome with more precision than with preoperative mJOA, SEP, or T2 HSI. As shown in Table 2, mean FA from the C3 through C7 vertebrae correlates well with the clinical severity of myelopathy (r = 0.516, P = .014) but not with the age of the patients (r = 0.226, P = .311), mJOA score (r = 0.050, P = .836), T2 HSI (r = 0.239, P = .284) or SEP amplitude (P = .356) or latency (P = .410).

Discussion

In the current study, we showed that DT MR images correlate well with the clinical severity of myelopathy and

Table 2

Logistic Regression Analysis of Clinical, Electrophysiologic, and Radiologic Factors to Predict Surgical Outcome

Variable	Score	*P* Value
Age	0.602	.438
mJOA score	0.155	.694
T2 HSI	1.474	.225
SEP		
Amplitude	0.854	.356
Latency	0.678	.410
Diffusion index		
FA_{C2}	1.745	.186
FA_{mcl}	0.078	.779
FA_{low}	0.565	.452
$FA_{C3–C7}$	5.167	.023

Note.—Surgical outcome was quantified by comparing pre- and postoperative mJOA score. A difference in mJOA scores of more than 2 indicated a good outcome, while a difference in mJOA scores of 2 or less indicated a fair outcome. FA_{C2} = FA value at the level of the C2 vertebra, $FA_{C3–C7}$ = mean FA value at the level of the C3 through C7 vertebrae, FA_{low} = lowest FA value along the myelopathic cervical cord, FA_{mcl} = FA value at the maximal compression level.

the surgical prognosis of patients with CSM. This finding suggests that DT imaging results agree with the clinical imaging findings better than with the results of conventional imaging; therefore, DT imaging may improve confidence in the clinical diagnosis of CSM. Furthermore, the mean FA of the entire myelopathic cord enabled us to predict the response to surgical intervention. In fact, DT imaging was superior to the current clinical electrophysiologic and routine anatomic MR imaging assessment in terms of sensitivity and specificity in providing the prognosis of surgical outcomes. Our findings indicate the clinical utility of DT imaging in the diagnosis and prognostication of CSM by adding value to existing clinical and radiologic assessments.

Previous attempts have been made to investigate the relationship between DT indexes and various clinical scores in patients with CSM (22,30,33). The present study showed strong correlations between DT findings and the clinical severity of CSM in good agreement with the findings of previous studies (16,34); however, Lee et al (30) failed to detect this type of correlation. One possible reason for this disparity may be the heterogeneity of the patients. Lee and colleagues (30) recruited patients with various types of cervical myelopathy, including ossification of the posterior longitudinal ligament, atlantoaxial instability, and os odontoideum, skeletal dysplasia, and herniated intervertebral disk. In contrast, we enrolled only those patients who had cervical myelopathy secondary to spondylosis and disk degeneration, as was done in two other previous studies (22,33). Our findings support the notion that FA could be a radiologic marker for the severity of CSM (22,31).

Altered diffusion pattern in the myelopathic cervical cord was carefully observed in this study. A decrease in FA was observed not only at the point of the maximal compression level, but also at sites distant from the maximal compression level. These findings may reflect the fact that CSM-associated demyelination and axonal damage afflict both the myelopathic lesion site and the distal sites in the chronic course of the disease (38,39). Thus, the diffusion indexes from the whole cervical spinal cord should be selected to comprehensively reflect overall cervical cord damage in patients with CSM, a task that was not performed in the majority of previous DT imaging studies (22–29). In the present study, the mean FA value of the C3 through C7 vertebrae but not the mean FA value at the maximal spinal cord compression level was identified as the prognostic factor of decompression surgery for patients with CSM.

Conventional T1- and T2-weighted images were limited in their ability to provide macroscopic information, such as the degree of stenosis and the amount of edema or hemorrhage. It has been well documented that the severity of stenosis does not correlate with the symptoms of patients with CSM (36,40,41). T2 HSI in the myelopathic spinal cord is nonspecific, and the presence of T2 HSI does not reflect the severity of myelopathy (42–46). Thus, the prognostic value of T2 HSI in patients with CSM is controversial (42–46). The results of the present study are compatible with those of previous studies in that the prognostic value of T2 HSI was not significant in patients with CSM. Meanwhile, the hypointensity on T1-weighted images has been reported in patients with CSM (47,48). However, it is difficult to assess T1-weighted hypointensity in patients with severe spinal cord compression, and this assessment was not performed in the current study.

SEP is a clinically available tool used to monitor the functional integrity of the spinal cord during spinal surgery. In this study, we discovered that FA values still presented substantial alterations in patients with CSM and normal SEP (22). This finding implies that SEP is a less sensitive tool than diffusion indexes, although SEP has been reported to possess certain prognostic value (14).

There were a few limitations in the present study. First, the region of interest that we used in this study covered the whole spinal cord and did not distinguish white matter from gray matter; this might have introduced some bias. Van Hecke and colleagues (37) once tried to perform a thresholding procedure (FA = 0.2) to differentiate white matter from gray matter. This concept was borrowed from brain research and is fit for healthy subjects; however, it was not applicable to patients with CSM. In our experience, a thresholding procedure would cause the information loss of severely degenerated white matter (28). After we balanced the advantages and disadvantages of different approaches, we adopted the conventional approach to define a region of interest that covers the whole spinal cord in the present study. Moreover, the variation in the follow-up period (6 months to 2 years after surgery) might have introduced more variables that affected the comparison of surgical outcomes (32).

In summary, FA is suggested as a biomarker for the severity of myelopathy and enables one to predict the outcome of surgery in patients with CSM. Our findings suggest the need for a large-scale prospective study in the

near future to determine the threshold for FA values of the myelopathic spinal cord in which the function of the myelopathic cord is reversible so as to achieve a satisfactory recovery after surgery. In conjunction with existing clinical and radiologic assessments, the information garnered with DT imaging will be an integral part of diagnosis and prognostication in patients with CSM and it will help in the decision regarding surgical intervention.

Acknowledgment: The authors thank Xiang Li, MD, for clinical data and MR image scanning.

Disclosures of Conflicts of Interest: C.Y.W. No relevant conflicts of interest to disclose. **J.L.C.** No relevant conflicts of interest to disclose. **H.S.L.** No relevant conflicts of interest to disclose. **K.C.M.** No relevant conflicts of interest to disclose. **W.Y.C.** No relevant conflicts of interest to disclose. **K.D.K.L.** No relevant conflicts of interest to disclose. **Y.H.** No relevant conflicts of interest to disclose.

References

1. McCormick WE, Steinmetz MP, Benzel EC. Cervical spondylotic myelopathy: make the difficult diagnosis, then refer for surgery. Cleve Clin J Med 2003;70(10):899–904.
2. Ichihara K, Taguchi T, Sakuramoto I, Kawano S, Kawai S. Mechanism of the spinal cord injury and the cervical spondylotic myelopathy: new approach based on the mechanical features of the spinal cord white and gray matter. J Neurosurg 2003;99(3 Suppl):278–285.
3. Rao R. Neck pain, cervical radiculopathy, and cervical myelopathy: pathophysiology, natural history, and clinical evaluation. J Bone Joint Surg Am 2002;84-A(10):1872–1881.
4. Holly LT, Moftakhar P, Khoo LT, Shamie AN, Wang JC. Surgical outcomes of elderly patients with cervical spondylotic myelopathy. Surg Neurol 2008;69(3):233–240.
5. Matsuda Y, Shibata T, Oki S, Kawatani Y, Mashima N, Oishi H. Outcomes of surgical treatment for cervical myelopathy in patients more than 75 years of age. Spine (Phila Pa 1976) 1999;24(6):529–534.
6. Hasegawa K, Homma T, Chiba Y, Hirano T, Watanabe K, Yamazaki A. Effects of surgical treatment for cervical spondylotic myelopathy in patients > or = 70 years of age: a retrospective comparative study. J Spinal Disord Tech 2002;15(6):458–460.
7. Lee TT, Manzano GR, Green BA. Modified open-door cervical expansive laminoplasty for spondylotic myelopathy: operative technique, outcome, and predictors for gait improvement. J Neurosurg 1997;86(1):64–68.
8. Tanaka J, Seki N, Tokimura F, Doi K, Inoue S. Operative results of canal-expansive laminoplasty for cervical spondylotic myelopathy in elderly patients. Spine (Phila Pa 1976) 1999;24(22):2308–2312.
9. Suri A, Chabbra RP, Mehta VS, Gaikwad S, Pandey RM. Effect of intramedullary signal changes on the surgical outcome of patients with cervical spondylotic myelopathy. Spine J 2003;3(1):33–45.
10. Ebersold MJ, Pare MC, Quast LM. Surgical treatment for cervical spondylitic myelopathy. J Neurosurg 1995;82(5):745–751.
11. Emery E, Aldana P, Bunge MB, et al. Apoptosis after traumatic human spinal cord injury. J Neurosurg 1998;89(6):911–920.
12. Mehalic TF, Pezzuti RT, Applebaum BI. Magnetic resonance imaging and cervical spondylotic myelopathy. Neurosurgery 1990;26(2):217–226; discussion 226–227.
13. Okada Y, Ikata T, Yamada H, Sakamoto R, Katoh S. Magnetic resonance imaging study on the results of surgery for cervical compression myelopathy. Spine (Phila Pa 1976) 1993;18(14):2024–2029.
14. Hu Y, Ding Y, Ruan D, Wong YW, Cheung KM, Luk KD. Prognostic value of somatosensory-evoked potentials in the surgical management of cervical spondylotic myelopathy. Spine (Phila Pa 1976) 2008;33(10):E305–E310.
15. Thurnher MM, Law M. Diffusion-weighted imaging, diffusion-tensor imaging, and fiber tractography of the spinal cord. Magn Reson Imaging Clin N Am 2009;17(2):225–244.
16. Basser PJ, Jones DK. Diffusion-tensor MRI: theory, experimental design and data analysis—a technical review. NMR Biomed 2002;15(7-8):456–467.
17. DeBoy CA, Zhang J, Dike S, et al. High resolution diffusion tensor imaging of axonal damage in focal inflammatory and demyelinating lesions in rat spinal cord. Brain 2007;130(Pt 8):2199–2210.
18. Giorgio A, Palace J, Johansen-Berg H, et al. Relationships of brain white matter microstructure with clinical and MR measures in relapsing-remitting multiple sclerosis. J Magn Reson Imaging 2010;31(2):309–316.
19. Budzik JF, Balbi V, Le Thuc V, Duhamel A, Assaker R, Cotten A. Diffusion tensor imaging and fibre tracking in cervical spondylotic myelopathy. Eur Radiol 2011;21(2):426–433.
20. Demir A, Ries M, Moonen CT, et al. Diffusion-weighted MR imaging with apparent diffusion coefficient and apparent diffusion tensor maps in cervical spondylotic myelopathy. Radiology 2003;229(1):37–43.
21. Kara B, Celik A, Karadereler S, et al. The role of DTI in early detection of cervical spondylotic myelopathy: a preliminary study with 3-T MRI. Neuroradiology 2011;53(8):609–616.
22. Kerkovský M, Bednarík J, Dušek L, et al. Magnetic resonance diffusion tensor imaging in patients with cervical spondylotic spinal cord compression: correlations between clinical and electrophysiological findings. Spine (Phila Pa 1976) 2012;37(1):48–56.
23. Voss HU, Hartl R, Gamache FW, Heier LA, Ballon DJ, Ulug AM. Diffusion tensor imaging in cervical spondylotic myelopathy. World Spine J 2007;2(3):140–147.
24. Song T, Chen WJ, Yang B, et al. Diffusion tensor imaging in the cervical spinal cord. Eur Spine J 2011;20(3):422–428.
25. Xiangshui M, Xiangjun C, Xiaoming Z, et al. 3 T magnetic resonance diffusion tensor imaging and fibre tracking in cervical myelopathy. Clin Radiol 2010;65(6):465–473.
26. Mamata H, Jolesz FA, Maier SE. Apparent diffusion coefficient and fractional anisotropy in spinal cord: age and cervical spondylosis-related changes. J Magn Reson Imaging 2005;22(1):38–43.
27. Facon D, Ozanne A, Fillard P, Lepeintre JF, Tournoux-Facon C, Ducreux D. MR diffusion tensor imaging and fiber tracking in spinal cord compression. AJNR Am J Neuroradiol 2005;26(6):1587–1594.
28. Cui JL, Wen CY, Hu Y, Li TH, Luk KD. Entropy-based analysis for diffusion anisotropy mapping of healthy and myelopathic spinal cord. Neuroimage 2011;54(3):2125–2131.
29. Nakamura M, Fujiyoshi K, Tsuji O, et al. Clinical significance of diffusion tensor tractography as a predictor of functional recovery after laminoplasty in patients with cervical compressive myelopathy. J Neurosurg Spine 2012;17(2):147–152.
30. Lee JW, Kim JH, Park JB, et al. Diffusion tensor imaging and fiber tractography in cervical compressive myelopathy: preliminary results. Skeletal Radiol 2011;40(12):1543–1551.
31. Jones JG, Cen SY, Lebel RM, Hsieh PC, Law M. Diffusion tensor imaging correlates with the clinical assessment of disease severity

in cervical spondylotic myelopathy and predicts outcome following surgery. AJNR Am J Neuroradiol 2013;34(2):471–478.

32. Cheung WY, Arvinte D, Wong YW, Luk KD, Cheung KM. Neurological recovery after surgical decompression in patients with cervical spondylotic myelopathy: a prospective study. Int Orthop 2008;32(2):273–278.

33. Mann NH 3rd, Brown MD, Hertz DB, Enger I, Tompkins J. Initial-impression diagnosis using low-back pain patient pain drawings. Spine (Phila Pa 1976) 1993;18(1):41–53.

34. Yonenobu K, Abumi K, Nagata K, Taketomi E, Ueyama K. Interobserver and intraobserver reliability of the Japanese orthopaedic association scoring system for evaluation of cervical compression myelopathy. Spine (Phila Pa 1976) 2001;26(17):1890–1894; discussion 1895.

35. Chung SS, Lee CS, Chung KH. Factors affecting the surgical results of expansive laminoplasty for cervical spondylotic myelopathy. Int Orthop 2002;26(6):334–338.

36. Bednarik J, Kadanka Z, Dusek L, et al. Presymptomatic spondylotic cervical myelopathy: an updated predictive model. Eur Spine J 2008;17(3):421–431.

37. Van Hecke W, Leemans A, Sijbers J, Vandervliet E, Van Goethem J, Parizel PM. A tracking-based diffusion tensor imaging segmentation method for the detection of diffusion-related changes of the cervical spinal cord with aging. J Magn Reson Imaging 2008; 27(5):978–991.

38. Urakawa T, Matsuzawa H, Suzuki Y, Endo N, Kwee IL, Nakada T. Analysis of ascending spinal tract degeneration in cervical spondylotic myelopathy using 3D anisotropy contrast single-shot echo planar imaging on a 3.0-T system. J Neurosurg Spine 2011;15(6):648–653.

39. Fehlings MG, Skaf G. A review of the pathophysiology of cervical spondylotic myelopathy with insights for potential novel mechanisms drawn from traumatic spinal cord injury. Spine (Phila Pa 1976) 1998;23(24): 2730–2737.

40. Matsumoto M, Toyama Y, Ishikawa M, Chiba K, Suzuki N, Fujimura Y. Increased signal intensity of the spinal cord on magnetic resonance images in cervical compressive myelopathy: does it predict the outcome of conservative treatment? Spine (Phila Pa 1976) 2000;25(6):677–682.

41. Kadanka Z, Kerkovsky M, Bednarik J, Jarkovsky J. Cross-sectional transverse area and hyperintensities on magnetic resonance imaging in relation to the clinical picture in cervical spondylotic myelopathy. Spine (Phila Pa 1976) 2007;32(23):2573–2577.

42. Kohno K, Kumon Y, Oka Y, Matsui S, Ohue S, Sakaki S. Evaluation of prognostic factors following expansive laminoplasty for cervical spinal stenotic myelopathy. Surg Neurol 1997;48(3):237–245.

43. Ohshio I, Hatayama A, Kaneda K, Takahara M, Nagashima K. Correlation between histopathologic features and magnetic resonance images of spinal cord lesions. Spine (Phila Pa 1976) 1993;18(9):1140–1149.

44. Wada E, Ohmura M, Yonenobu K. Intramedullary changes of the spinal cord in cervical spondylotic myelopathy. Spine (Phila Pa 1976) 1995;20(20):2226–2232.

45. Yone K, Sakou T, Yanase M, Ijiri K. Preoperative and postoperative magnetic resonance image evaluations of the spinal cord in cervical myelopathy. Spine (Phila Pa 1976) 1992;17(10 Suppl):S388–S392.

46. Mastronardi L, Elsawaf A, Roperto R, et al. Prognostic relevance of the postoperative evolution of intramedullary spinal cord changes in signal intensity on magnetic resonance imaging after anterior decompression for cervical spondylotic myelopathy. J Neurosurg Spine 2007;7(6):615–622.

47. Vedantam A, Jonathan A, Rajshekhar V. Association of magnetic resonance imaging signal changes and outcome prediction after surgery for cervical spondylotic myelopathy. J Neurosurg Spine 2011;15(6):660–666.

48. Mummaneni PV, Kaiser MG, Matz PG, et al. Preoperative patient selection with magnetic resonance imaging, computed tomography, and electroencephalography: does the test predict outcome after cervical surgery? J Neurosurg Spine 2009;11(2):119–129.