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Clinical Study

Diffusion tensor imaging predicts functional impairment in mild-to-moderate cervical spondylotic myelopathy

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Abstract

BACKGROUND CONTEXT: Magnetic resonance imaging (MRI) is the standard imaging modality for the assessment of cervical spinal cord; however, MRI assessment of the spinal cord in cervical spondylotic myelopathy patients has not demonstrated a consistent association with neurologic function or outcome after surgical or medical intervention. Thus, there is a need for sensitive imaging biomarkers that can predict functional impairment in patients with advanced cervical spondylosis.

PURPOSE: To implement diffusion tensor imaging (DTI) as an imaging biomarker for microstructural integrity and functional impairment in patients with cervical spondylosis.

STUDY DESIGN: Nonrandomized, single institution study.

PATIENT SAMPLE: Forty-eight cervical spondylosis patients with or without spinal cord signal change underwent DTI of the spinal cord along with functional assessment.

OUTCOME MEASURES: Functional measures of neurologic function via modified Japanese Orthopedic Association (mJOA) score.

METHODS: A zoomed-echoplanar imaging technique and two-dimensional spatially selective radiofrequency excitation pulse were used for DTI measurement. Fractional anisotropy (FA), mean diffusivity (MD), radial and axial diffusion (AD) coefficient, AD anisotropy, ψ, defined as AD-MD, and the standard deviation (SD) of primary eigenvector orientation were evaluated at the site of compression.

RESULTS: Results suggest average FA, transverse apparent diffusion coefficient, ψ, and SD of primary eigenvector orientation at the spinal level of highest compression were linearly correlated with mJOA score. Receiver-operator characteristic analysis suggested FA and ψ could identify stenosis patients with mild-to-moderate symptoms with a relatively high sensitivity and specificity.

FDA device/drug status: Not applicable.

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CONCLUSIONS: The results of this study support the potential use of DTI as a biomarker for predicting functional impairment in patients with cervical spondylosis.

Keywords: Diffusion tensor imaging; DTI; Spinal cord; Cervical spondylotic myelopathy; Biomarker; CSM; Stenosis; mJOA

Introduction

Cervical spondylosis is a spinal disorder characterized by degeneration of vertebral bodies, intervertebral discs, facet joints, and associated ligaments typically resulting in formation of bony spurs and, in some cases, myelopathy. Cervical spondylosis, with or without myelopathy, occurs more frequently with increasing age and is seen in as many as 95% of men and 70% of women, aged 60 to 65 years [1]. Myelopathy from cervical spondylosis is the most common diagnosis for patients with spinal cord disorders older than 64 years [2] and is thought to occur primarily from spinal canal stenosis, resulting in the compromise of spinal cord tissue. Studies have shown that a prolonged duration of symptoms may be associated with a poor surgical outcome [3,4], and therefore, early surgical intervention is commonly advocated based on imaging features before severe symptoms manifest.

Magnetic resonance imaging (MRI) is the standard imaging modality for the assessment of cervical spinal cord health. Assessment of the spinal cord for cervical spondylotic myelopathy (CSM) often includes morphology measurements, such as canal size or Torg-Pavlov ratio [5] and T1/T2-weighted MRI signal changes; however, morphometry [6–8] and abnormal MRI signal change [9–16] have not demonstrated consistent associations with neurologic function or outcome after surgical intervention. Thus, there is a need for reliable radiologic criteria and imaging biomarkers for identifying patients who will benefit from surgical intervention [17].

Diffusion tensor imaging (DTI), an MRI technique sensitive to the magnitude and orientation of water self-diffusion, is sensitive to spinal cord tissue microarchitecture [18] and superior to routine T2-weighted MRI in detecting subtle changes in spinal cord integrity after injury [19–21]. Preliminary reports have found differing diffusion characteristics between normal volunteers and patients with cervical spondylosis and myelopathy, suggesting that this technique might be of diagnostic utility [10,19,20,22]. Although studies have explored the use of DTI as a tool to study CSM and DTI has shown promise in characterizing other spinal cord pathologies, there remains a need for systematic evaluation of DTI metrics and potential neurologic correlations to move DTI from the benchtop into clinical practice.

In the present study, we performed axial DTI through the upper cervical spinal cord in 9 healthy, neurologically intact control subjects and 48 patients with cervical spondylosis, with or without mild-to-moderate myelopathy, to determine whether DTI provides information about spinal cord integrity and neurologic impairment beyond conventional MRI examination.

Materials and methods

Patients

A prospective study was carried out to describe the DTI characteristics observed throughout the cervical spinal cord. A series of 48 patients (n=48; age range, 38–78 years; mean=60 years) diagnosed with cervical spondylosis, with (n=32) or without (n=16) neurologic symptomatology, with homogeneous DTI acquisition parameters were examined as part of a prospective NIH-funded study. (Note that this study was funded by the NIH and there are no perceived biases associated with this funding source.) Fifteen patients underwent two or more scans during the period of observation. Nine healthy volunteers underwent the same cervical imaging and served as a control group. All procedures complied with the principles of the Declaration of Helsinki and were approved by the institutional review board at our institution.

Conventional MRI

Imaging procedures consisted of both routine conventional MRI and DTI scans performed on a 3.0 T MRI scanner (3T TrioTim; Siemens Healthcare, Erlangen, Germany), using a standard whole body coil array for radiofrequency (RF) reception (with only two neck coil elements covering the cervical spinal cord activated). Routine clinical MRI scans consisted of T1- and T2-weighted sequences in the sagittal plane and T2-weighted images in the axial plane. The presence of T2-weighted signal change and spinal cord morphometry defined by the anteroposterior diameter of the cord at the level of highest compression was documented and used for subsequent comparisons with DTI metrics.

Diffusion tensor imaging

Axial diffusion-weighted images were collected through the level of most significant canal narrowing. Excitation consisted of a custom two-dimensional (2D), spatially selective RF excitation pulse (2D-RF) and the resulting MRI signals were acquired using a reduced field of view EPI (echoplanar imaging) readout, with ramp sampling (zoomed-EPI). Echo time/repetition time was set to 67 ms/5 s, slice thickness was set to 4 mm with no gap, number of excitations=15, and six diffusion sensitizing directions were collected at b=500 s/mm^2, along with a single T2-weighted (b=0 s/mm^2) image.

After acquisition of diffusion-weighted images, eddy-current and motion correction was performed using FSL

(Functional Magnetic Resonance Imaging of the Brain Software Library; Oxford, UK; http://www.fmrib.ox.ac.uk/fsl/). The diffusion tensor was then constructed in Analysis of Functional NeuroImages (available at http://afni.nimh.nih.gov). The eigenvalues and eigenvectors were extracted from the diffusion tensor and fractional anisotropy (FA) [23]; axial diffusivity, AD (corresponding to the largest eigenvalue); radial diffusivity, RD (corresponding to the average of the two smallest eigenvalues); mean diffusivity (MD, average of all three eigenvalues); and AD anisotropy (ψ, corresponding to AD-MD [24,25]) were calculated. The measures of AD and RD were chosen because they are believed to reflect the degree of axonal and myelin damage, respectively [26–29]. Additionally, the standard deviation (SD) of the primary eigenvector orientation, std (θ), defined as the angle between the primary eigenvector, v_1, and the z-axis or $\theta = \tan^{-1}\left(\frac{\sqrt{\left(\frac{\partial v_{1,x}}{\partial z}\right)^2 + \left(\frac{\partial v_{1,y}}{\partial z}\right)^2}}{v_{1,z}}\right)$, within the level of highest compression was calculated as a measure of white matter disorganization and tract disruption. For instance, if white matter tracts are tightly packed and organized in a single direction, the SD will be low because the eigenvectors for all voxels will be oriented in the same general direction. Alternatively, if white matter tract orientation is disrupted because of compression or damage, the eigenvector orientation for voxels within the cord at the site of compression will likely be less coherent, resulting in a larger SD of primary eigenvector orientation.

Regions of interest

Manual segmentation of spinal cord regions of interest was performed for the whole cord (no gray/white matter distinction) at each axial image slice location, using the T2-weighted anatomical images, similar to previous techniques [30,31]. Regions of interest were placed within the spinal cord at each image location such that at least two voxels around the edge of the cord were excluded to assure no partial volume contamination from surrounding cerebrospinal fluid. Data from all voxels in the region of interest were pooled and averaged across each vertebral level (2–3 slices) and the space between each level (ie, space commonly exhibiting compression in CSM patients, usually 2–3 slices). Diffusion tensor imaging measurements at the site of compression were used for subsequent analysis.

Functional assessment

The present study used the modified Japanese Orthopedic Association (mJOA) score, the most commonly used functional outcome assessment instrument in CSM patients [32] that has been demonstrated to be a valid and reliable outcome measurement in this population [33]. Moderate symptomatology was defined as having an mJOA score between 11 and 14 and mild symptomatology was a score between 15 and 17.

EVIDENCE & METHODS

Context

While MRI is considered the imaging modality of choice for the detection of cervical spondylotic myelopathy (CSM), there is limited correlation between MRI findings and neurological function as well as outcomes following treatment. The authors sought to evaluate whether the use of diffusion tensor imaging (DTI) could improve diagnostic capabilities in the setting of CSM.

Contribution

The authors performed a prospective analysis of 48 patients with different levels of neurologic compromise associated with CSM. Furthermore, 9 healthy controls also underwent the imaging protocol. DTI results were correlated with severity of CSM as measured on the mJOA scale. DTI appeared to have relatively high sensitivity and specificity for detecting patients with symptomatic CSM.

Implications

The authors' findings demonstrate that DTI can be applied to the evaluation of patients with CSM. How this would change surgeon management at present is not clear. Certainly, physical examination findings may be correlated with the results of imaging studies and this is typically the way in which decisions are made for surgical intervention. Relatively few patients (n=15) in the current work underwent DTI multiple times and the ''prognostic'' capacity of this modality cannot truly be addressed. Furthermore, the design of this study obviates the possibility of determining how DTI may be used to predict response to surgical intervention. These are clearly important issues that should be addressed in future work.

—The Editors

Statistics

Conventional MRI measures of anteroposterior diameter and T2 hyperintensity were explored as predictors of functional impairment. A Student *t* test was used to determine whether there was a significant difference in spinal cord compression between patients with spondylosis and healthy volunteers. Linear regression was used to determine whether the anteroposterior spinal cord diameter was correlated with mJOA score. An analysis of variance (ANOVA) was used to test whether there was a relationship between spinal cord diameter at the site of compression between patients with no neurologic impairment (mJOA=18), mild impairment (mJOA=15–17), and moderate impairment (mJOA=10–14).

Next, the signal-to-noise ratio (SNR) of the spinal cord at various spinal cord segments in healthy controls were compared with historic data [31] using a two-way ANOVA.

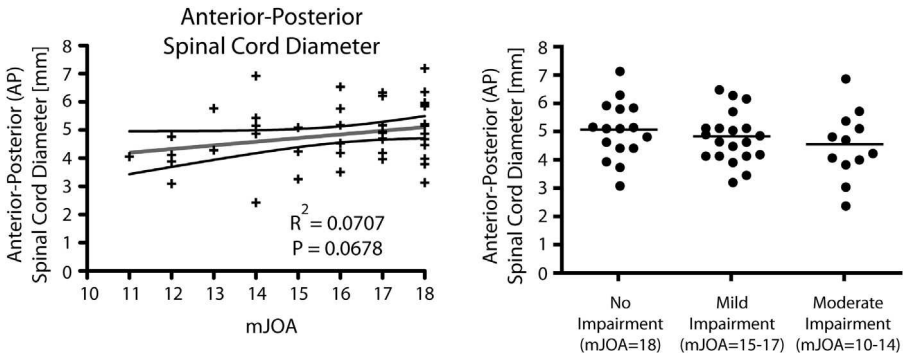

Fig. 1. Conventional magnetic resonance imaging measures of spinal cord compression. (Left) Linear regression results comparing mJOA score with anteroposterior (AP) spinal cord diameter (R^2=0.0707, p=.0678). (Right) Comparison of AP spinal cord diameter between patients without neurologic impairment (mJOA=18), patients with mild impairment (mJOA=15–17), and patients with moderate impairment (mJOA=10–14). Results show no significant difference in spinal cord diameter between these groups (analysis of variance, p=.4146). mJOA, modified Japanese Orthopedic Association.

The repeatability of DTI measurements within the spinal cord were examined in a subset of 15 patients with minimal neurologic impairment (mJOA0 17) by calculating the median coefficient of variation for both FA and MD.

A one-way ANOVA was used to determine whether there was a significant difference in FA at the site of compression between patients with no neurologic impairment, mild impairment, or moderate impairment. Tukey test for multiple comparisons was used to test difference between these individual groups. Linear regression was then used to test whether FA, MD, AD, RD, ψ or std (θ) at the level of compression correlated with mJOA score. A Bonferroni-corrected p value ! .0083 was considered statistically significant for linear regression analysis (corrected p value=.05/6).

Additionally, receiver-operator characteristic (ROC) analysis was used to determine the sensitivity and specificity for DTI indices to differentiate spondylosis patients with neurologic symptoms (mJOA! 18) from spondylosis patients without symptoms (mJOA=18), and distinguish between moderately affected patients (mJOA! 15) and those with mild or no impairment. The area under the ROC curve (AUC) was used as a measure of DTI metric performance. A two-way ANOVA was used to test whether the ROC performance differed across the various DTI metrics and between detecting any impairment (mJOA=18 vs. mJOA! 18) or moderate impairment (mJOA! 15 vs. mJOA≥15).

Results

Clinical symptoms

The majority of the cervical spondylosis cohort with neurologic symptoms presented with gait and/or hand coordination difficulty. The mean mJOA score in this cohort

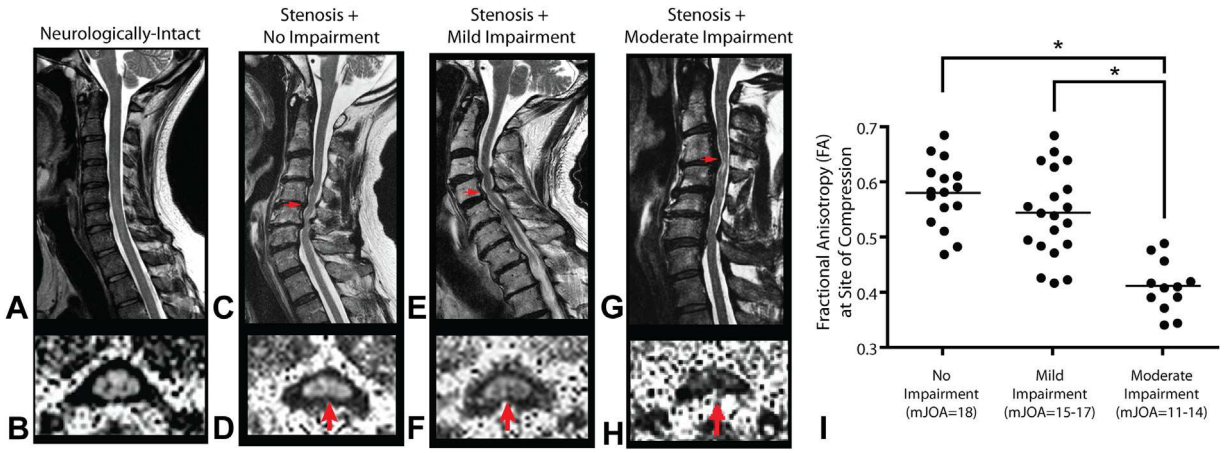

Fig. 2. FA at the site of spinal cord compression. (A, C, E, G) Sagittal T2-weighted and (B, D, F, H) FA images of a neurologically intact (A, B) control subject, (B) showing high FA in spinal cord white matter, (C, D) a patient with cervical spondylosis without neurologic impairment (mJOA=18), (E, F) a patient with cervical spondylosis with mild impairment (mJOA=15), and (G, H) a patient with cervical spondylosis with moderate impairment (mJOA=12). Note that patients demonstrate a decreasing FA at the site of most severe compression with increasing neurologic impairment, suggestive of increasing microstructural damage. Note on axial images, posterior=top, anterior=bottom. (I) Comparison of FA at the site of compression between patients without neurologic impairment (mJOA=18), patients with mild impairment (mJOA=15–17), and patients with moderate impairment (mJOA=10–14). Results show a significant difference between patients with moderate impairment and those with mild or no impairment (analysis of variance, p! .0001; Tukey test, p! .05 for moderate vs. mild or no impairment). The arrows show region of spinal cord compression. *p! .05. mJOA, modified Japanese Orthopedic Association.

was 15.1, with a range from 11 to 17. Neck pain was the most common clinical presentation in the cohort of cervical spondylosis patients without neurologic symptomatology. All 16 patients without symptoms had a mJOA score of 18.

Conventional MRI

The mean anteroposterior spinal cord diameter in cervical spondylosis patients was significantly narrower in cervical spondylosis patients than healthy controls (4.56±1.02 [SD] mm vs. 7.00±0.75 [SD] mm; *t* test, p! .0001). Within the cervical spondylosis cohort, there was a slight trend between spinal cord diameter and neurologic impairment. In particular, we observed a trend between anteroposterior diameter and mJOA (Fig. 1, Left; R^2=0.0707, p=.0678; Power=0.53%); however, there was no relationship observed between neurologic impairment and presence of intraspinal T2 hyperintensity. Additionally, no relationship between spinal cord diameter and severity of neurologic impairment (none, mild, and moderate) within the cervical spondylosis cohort was observed (Fig. 1, Right; ANOVA, p=.4146).

Reproducibility and quality of DTI data

High quality b=0 s/mm^2 and b=500 s/mm^2 images, reaching a maximum SNR of nearly 20 and an SNR full-width, half-max of approximately 80 mm for b=0 s/mm^2 images, were acquired using the 2D-RFþ zoomed-EPI sequence. When compared with historic controls [31], axial FA measurements from C2 through the C6–C7 level in the nine neurologically intact volunteers in the present study showed no significant differences, suggesting the pulse sequence used in the present study may provide comparable results with previous studies (two-way ANOVA, p=.129 between studies, p=.128 across spinal levels, p=.410 interaction). To test the repeatability of spinal cord DTI measurements, we examined a subset of 15 patients with spinal stenosis, minimal neurologic impairment (mJOA≥17), no change in impairment during observation, and more than two scans over an average duration of 200 days (±13 days standard error of the mean [SEM]). Evaluations of MD and FA at C2 in these patients (average distance from site of compression=37.0±3.5 mm) demonstrated a median coefficient of variation for MD and FA of 8.7% and 4.6%, respectively.

Fractional anisotropy changes at the site of compression

Fractional anisotropy images demonstrated high diffusion anisotropy within regions of white matter in neurologically intact control subjects, consistent with healthy, densely packed axon tracts (Fig. 2, A–B). In contrast with the high diffusion anisotropy in neurologically intact volunteers, patients with symptomatic spondylosis showed significant narrowing of the spinal canal and a reduction in FA

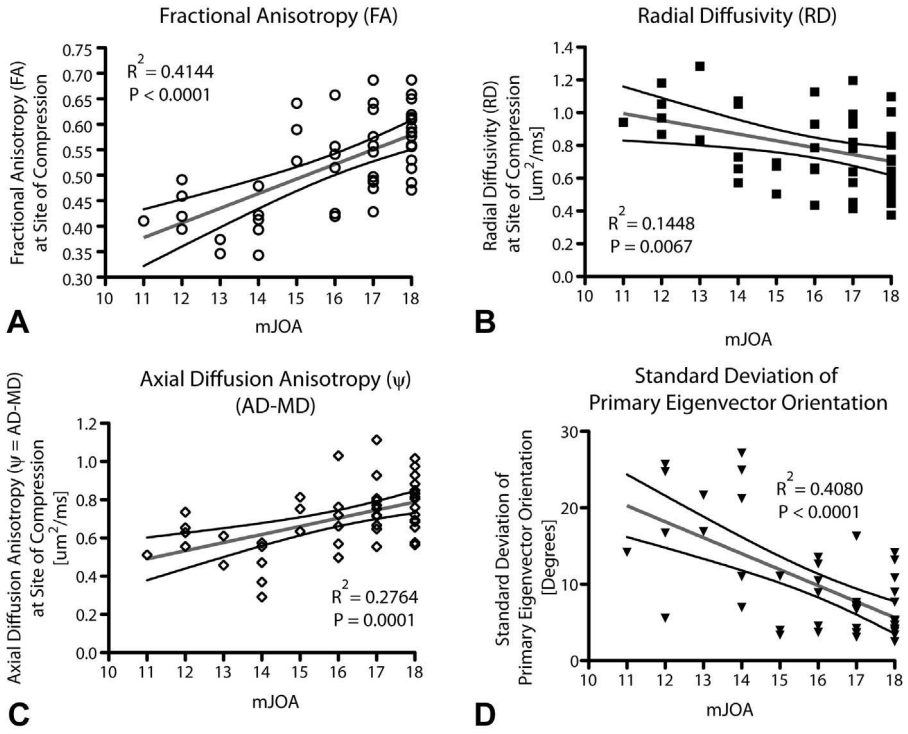

Fig. 3. Correlation between diffusion tensor imaging and neurologic impairment. Linear regression results comparing mJOA with (A) FA (R^2=0.4144, p! .0001), (B) RD (R^2=0.1448, p=.0067), (C) ψ (R^2=0.2764, p=.0001), and (D) standard deviation of primary eigenvector orientation or std (θ) (R^2=0.4080, p! .0001). All measurements were made at the level of highest spinal cord compression. mJOA, modified Japanese Orthopedic Association.

(Fig. 2, C–D). A closer examination of our patient cohort revealed a pattern of decreased FA at the site of compression with increasing neurologic impairment (decreasing mJOA). Fractional anisotropy measurements at the site of compression could significantly stratify patients based on categorical severity of neurologic impairment (Fig. 2, E; ANOVA, p! .0001). For example, patients showing spondylosis without neurologic symptoms demonstrated a relatively high FA measurement at the site of compression compared with adjacent levels. In patients with relatively mild neurologic impairment, for example, mJOA=15 to 17, FA values at the site of compression were slightly decreased relative to adjacent levels, although not significantly different from patients without neurologic impairment (Tukey test for multiple comparisons, p0 .05 for mild vs. no impairment). In patients with moderate myelopathy, for example, mJOA=11 to 14, FA values were markedly reduced compared with adjacent levels and patients with mild or no neurologic impairment (Tukey test, p! .05 for moderate vs. mild & moderate vs. no impairment).

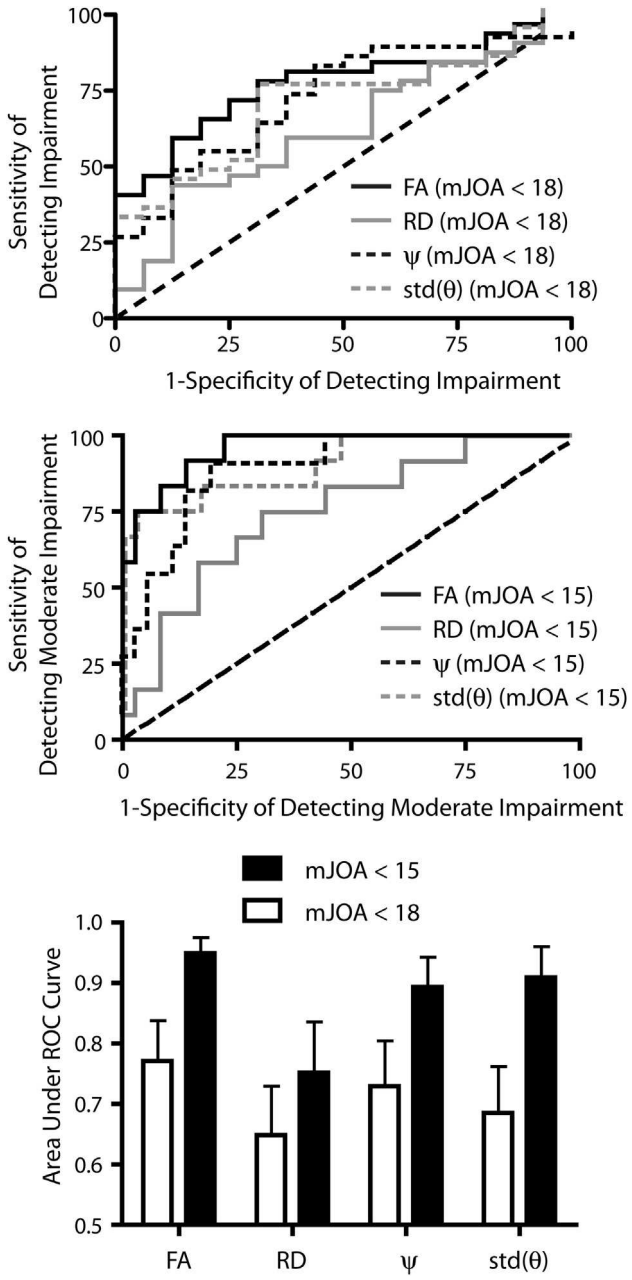

Fig. 4. ROC results for diffusion tensor imaging (DTI) metrics. (Top) ROC curves showing the sensitivity and specificity of different DTI metrics to spondylosis patients with mJOA! 18. (Middle) ROC curves showing the sensitivity and specificity of different DTI metrics to stenosis patients with moderate impairment. (Bottom) Area under the ROC curve as a measure of performance for DTI metrics for mJOA! 15 (solid black bars) and mJOA! 18 (white bars). ROC, receiver-operator characteristic; mJOA, modified Japanese Orthopedic Association; FA, fractional anisotropy; RD, radial diffusivity.

DTI correlates of neurologic impairment

Consistent with more qualitative observations, a significant positive linear correlation was found between FA measurements at the site of compression and mJOA score (Fig. 3, A; Pearson, R^2=0.4144, p! .0001; Power=93%). No significant linear correlation was observed between MD or AD and mJOA score (R^2! 0.03, p0 .25, Power0 60% for both MD and AD). A significant, although rather weak, negative correlation was observed between RD and mJOA (Fig. 3, B; R^2=0.1448, p=.0067, Power=51%). Although neither MD nor AD was considered statistically significant predictor of mJOA score, ψ, or the difference between AD and MD, showed a positive linear correlation with mJOA (Fig. 3, C; R^2=0.2764, p=.0001, Power=52%). To test whether displacement in the orientation of white matter tracts at the site of compression is a significant predictor of neurologic impairment, we examined the variance in the primary eigenvector orientation that should be relatively small in the intact spinal cord, suggesting all white matter tracts are oriented in the same direction (ie, rostral-caudal). Our results demonstrate a strong negative correlation between the SD of primary eigenvector orientation and mJOA (Fig. 3, D; R^2=0.4080, p! .0001, Power0 90%), suggesting disorganization in white matter tract orientation at the site of compression is higher in patients with more neurologic impairment.

Receiver-operator characteristic analysis aimed at differentiating spondylosis patents with and without neurologic impairment suggested that FA, ψ, and SD in primary eigenvector orientation could identify symptomatic patients with significant sensitivity and specificity. Specifically, an average FA value, measured at the site of highest compression, less than 0.55 resulted in a 72% sensitivity and 75% specificity of detecting patients with mJOA ! 18 (Fig. 4, Top and Bottom; AUC=0.77±0.07 SEM, p=.0024) and an 81% sensitivity and 92% specificity of detecting patients with moderate impairment (Fig. 4, Middle and Bottom; mJOA! 15; AUC=0.95±0.03 SEM, p! .0001). Average ψ, RD, and SD of primary eigenvector orientation at the site of compression were not significant predictors of symptomatic patients (mJOA! 18) after Bonferroni correction

(Fig. 4, Top and Bottom; p0 .0083), but were all significant predictors of moderate impairment (mJOA! 15) (Fig. 4, Middle; p! .0095). A side-by-side comparison of the AUC for all DTI metrics suggested no significant difference in metrics performance (ANOVA; DTI metric, p=.1064); however, there was a significant increase in ROC performance when identifying stenosis patients with moderate neurologic impairment (mJOA! 15) compared with identification of patients with only slight neurologic impairment (mJOA! 18; Fig. 4, Bottom; ANOVA, severity of impairment, p=.0004).

Discussion

Cervical spondylosis and stenosis are pathological conditions of the spinal column that affect the vast majority of older individuals with increasing age. The diagnosis of CSM typically includes static or dynamic X-rays, computed tomography, myelography, or conventional MRI. Despite the significant advancement of conventional MRI technology since its inception, the value of traditional imaging technologies in diagnosing and predicting early response to treatment remains controversial. Results from the present study suggest a trend may exist between anteroposterior spinal cord diameter and mJOA; however, the study did not have adequate statistical power (53%) to make a definitive conclusion. However, the low correlation coefficient (R^2=0.0707) and slope associated with this relationship suggests that traditional MRI measures are not likely to be predictive of neurologic impairment.

Chronic compression of the spinal cord produces pathological changes in the tissue microstructure that can be detected using DTI. For example, results from the present study clearly demonstrate an increase in MD and decrease in FA at the site of chronic compression in patients with chronic stenosis relative to neurologically intact control subjects, consistent with previous studies [10,19,20,22]. Additionally, we observed a decrease in FA in CSM patients proportional to the degree of neurologic impairment as measured with mJOA score, consistent with a recent study by Jones et al. [34]. Our results also suggest, FA measurements at the site of compression are a strong biomarker for identifying symptomatic stenosis patients (mJOA! 18 or mJOA! 15), which is a trend also observed by other investigators [35,36].

Inconsistent with our present findings is the hypothesis that MD is a significant predictor of myelopathy. Data from a study published by Demir et al. [19] suggested MD measurements at the site of compression had a relatively high sensitivity and specificity for identifying symptomatic patients. Additionally, data from Uda et al. [37] suggested MD was the best predictor of myelopathy when compared with FA; however, this study compared healthy control subjects directly with symptomatic patients and did not compare symptomatic and nonsymptomatic patients with cervical stenosis. Our results clearly demonstrated no significant correlation between MD and mJOA score when examining a cohort of cervical spondylosis composed of symptomatic and asymptomatic individuals.

Results support the hypothesis that AD and RD may be sensitive biomarkers to axonal dysfunction and demyelination, respectively [26–29]. Previous studies by Song et al. [27,28] have eloquently demonstrated that dysmyelination results in an increased RD, without a change in AD. Conversely, the studies by Ellingson et al. [26] and Budde et al. [29] have demonstrated a strong correlation between the decrease in AD and a decrease in axonal function. Further supporting this hypothesis is the observation that changes in AD and RD follow distinctly different temporal profiles [30], where the decrease in AD occurs much quicker than the increase in RD. In the present study, we observed a negative linear correlation between RD and mJOA, suggesting a decrease in neurologic function may accompany an increase in demyelination in patients with chronic spinal cord compression. Although we did not observe a significant correlation between AD or MD and mJOA, AD anisotropy (ψ), defined as the difference between AD and MD, was significantly correlated with functional impairment. In the context of the present study, we hypothesized that ψ would allow for assessment of AD independent of MD because MD was thought to fluctuate as a result of spinal cord compression. Taken together, these results may imply that some degree of both axonal dysfunction (myelopathy) and demyelination may be present in patients with spinal cord compression.

Results from the present study demonstrated a strong correlation between the SD in primary eigenvector orientation and mJOA score. Consistent with our findings, a recent study by Song et al. [38] showed abnormal deflection in primary eigenvector orientation, illustrated using FA color maps, in approximately three-fourth of patients with myelopathy. In another recent study, Cui et al. [39] documented a high degree of "entropy," or disorganization, in primary eigenvector orientation at the compression site in patients with CSM compared with healthy controls. These results appear to be consistent with the hypothesis that primary eigenvector orientation, which is thought to be a surrogate of white matter tract orientation, dendritic orientation, or interneuron orientation, becomes more disorganized with increasing neurologic impairment. Future studies aimed at exploring the role of axon and cell body morphological changes in mild-to-moderate CSM may provide more insight into the influence of these mechanisms on DTI measurements.

Clinical relevance

One of the strengths of this study is that in contrast to some of the other published DTI studies, both neurologically symptomatic and asymptomatic patients with severe cervical spondylosis were analyzed, rather than just symptomatic CSM patients. The inclusion of a spectrum of patients with advanced cervical stenosis and spondylosis mirrors what is encountered in practice by many spine surgeons

and represents an area of clinical management controversy and challenge. As demonstrated in Fig. 2, it can be very difficult to discern neurologic status based on standard MRI because each of the study patients has significant stenosis, yet very different neurologic status.

Although none of the standard MRI parameters (spinal cord diameter, signal change) were able to discern clinical condition between patients with similar appearing MRI scans, DTI was clearly able to discriminate neurologic condition. As such, this novel imaging technology may be able to serve as a potential noninvasive biomarker and help play a role in the treatment algorithm of patients with advanced cervical spondylosis and myelopathy.

Study limitations

A potential limitation to the present study was the use of only six diffusion sensitizing directions to estimate the diffusion tensor. Although previous spinal cord DTI studies have suggested that white matter integrity in the spinal cord does not require a full tensor, only longitudinal (axial) and transverse (radial) diffusion sensitivities [40], DTI studies in the brain suggest an increase in accuracy of diffusion tensor estimation with increasing number of diffusion directions [41,42]. Despite this potential limitation, our results in neurologically intact control subjects were consistent with historical data performed with many more diffusion sensitizing directions. Furthermore, since we performed DTI with a large number of averages, it is likely this signal-to-noise advantage was sufficient to maintain a highly accurate estimate of the diffusion tensor.

Conclusions

Results from the present study support the use of DTI as an imaging biomarker for predicting neurologic impairment in patients with mild-to-moderate CSM.

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