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Diffusion Tensor Imaging in Diagnosing and Evaluating Degenerative Cervical Myelopathy: A Systematic Review and Meta-Analysis

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Abstract

Study Design: Systematic review.

Objective: Degenerative cervical myelopathy (DCM) is a common spinal cord disorder necessitating surgery. We aim to explore how effectively diffusion tensor imaging (DTI) can distinguish DCM from healthy individuals and assess the relationship between DTI metrics and symptom severity.

Methods: We included studies with adult DCM patients who had not undergone decompressive surgery and implemented correlation analyses between DTI parameters and severity, or compared healthy controls and DCM patients.

Results: 57 studies were included in our meta-analysis. At the maximal compression (MC) level, fractional anisotropy (FA) exhibited lower values in DCM patients, while apparent diffusion coefficient (ADC), mean diffusivity (MD), and radial diffusivity

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(RD) were notably higher in the DCM group. Moreover, our investigation into the diagnostic utility of DTI parameters disclosed high sensitivity, specificity, and area under the curve values for FA (.84, .80, .83 respectively) and ADC (.74, .84, .88 respectively). Additionally, we explored the correlation between DTI parameters and myelopathy severity, revealing a significant correlation of FA (.53, 95% CI:0.40 to .65) at MC level with JOA/mJOA scores.

Conclusion: Current guidelines for DCM suggest decompressive surgery for both mild and severe cases. However, they lack clear recommendations on which mild DCM patients might benefit from conservative treatment vs immediate surgery. ADC's role here could be pivotal, potentially differentiating between healthy individuals and DCM. While it may not correlate with symptom severity, it might predict surgical outcomes, making it a valuable imaging biomarker for clearer management decisions in mild DCM.

Keywords
diffusion tensor imaging, degenerative cervical myelopathy, diagnosis, meta-analysis

Introduction

Degenerative cervical myelopathy (DCM) is the most prevalent spinal cord disorder resulting in significant neurologic dysfunctions and is a leading cause of cervical spine surgical procedures.[1,2] Despite progress in medical knowledge, there remains a critical need for non-invasive, reliable measures for evaluating the condition of the spinal cord in patients with DCM.[3,4] While magnetic resonance imaging (MRI) is the established imaging technique for diagnosing DCM and aids in guiding treatment strategies, it predominantly identifies anatomical compression factors like the intervertebral disc, ligamentum flavum, vertebral osteophytes, facet joints, and ossification of the posterior longitudinal ligament.[5] It also detects T2-weighted hyperintensity within the spinal cord. However, MRI's efficacy is limited by its inability to consistently align with clinical symptoms, as it often fails to reveal microscopic changes in the spinal cord, which are crucial in DCM.[6]

Emerging in the field of neuroimaging, diffusion tensor imaging (DTI) has offered new insights into the pathology of the central nervous system disorders, particularly in DCM.[7] DTI's ability to trace water molecule diffusion at microscopic scales provides for the assessment of spinal cord microstructure. DTI has revealed significant variations in the cervical spinal cord at the point of maximal compression in DCM cases.[8] A key measurement in DTI is Fractional Anisotropy (FA), which ranges from 0 to 1, indicating the directionality of water diffusion.[9] High FA values in a healthy spinal cord suggest a uniform direction of axonal paths, similar to aligned straws. In contrast, conditions like DCM disrupt this uniformity, leading to decreased FA.[9] DTI also tracks other indices such as Mean Diffusivity (MD), Apparent Diffusion Coefficient (ADC), Axial Diffusivity (AD), and Radial Diffusivity (RD). These indices measure the average rate and direction of water diffusion in tissue.

Although initial studies have linked DTI parameters to preoperative clinical evaluations, the full diagnostic potential of DTI in differentiating between DCM patients and healthy individuals remains largely uncharted. Recent studies highlight the significance of preoperative FA in correlating with postoperative myelopathy severity measured by the Japanese Orthopedic Association (JOA) or modified JOA (mJOA) scores, particularly in older individuals and those with longer follow-up periods.[10] Notably, recovery rates showed a substantial correlation with ADC across various age groups. Nevertheless, no significant correlations were identified between other DTI parameters (MD, AD) and postoperative outcomes.

This systematic review and meta-analysis was designed to explore these areas. The goal is to define the effectiveness of DTI to distinguish DCM from healthy individuals and to assess the relationship between DTI metrics and symptom severity, as indicated by JOA and mJOA.

Methods

Protocol Registration and Compliance

The protocol for this systematic review was formally registered with PROSPERO, the International Prospective Register of Systematic Reviews, under the identifier CRD42023417303. Details of the protocol are accessible via the PROSPERO database (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023417303). Adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines was maintained throughout the study to ensure a rigorous and transparent methodology.

Literature Search Strategy

A methodical and comprehensive literature search was conducted across several electronic databases, namely PubMed, Web of Science, and EMBASE, to identify relevant studies. The search, performed in December 2023 by author FF, was not limited by language constraints. The search strategy was meticulously designed using specific keywords such as "degenerative cervical myelopathy", "cervical spondylotic myelopathy", "diffusion tensor imaging", and "fractional

anisotropy". Each database search was customized with a unique combination of these terms to maximize retrieval efficiency. Additionally, manual searches were conducted within the reference lists of key articles to uncover further applicable studies.

Inclusion and Exclusion Criteria

The systematic review encompassed primary studies of any design. For inclusion in this systematic review, manuscripts needed to meet the following eligibility criteria: (1) Enrolment of adult patients diagnosed with DCM who have not undergone any form of decompressive surgery for the condition, (2) Evaluation of the impact of DTI parameters on patient symptoms or comparing them to healthy subjects, (3) Reporting symptom severity by JOA or mJOA, (4) Implementation of any correlation analysis between DTI parameters and severity, or comparing them between healthy and DCM (5) Reporting of a correlation coefficient or mean and *P*-value or 95% CI for it. Studies failing to adhere to these specifications were excluded. No restrictions on the publication dates of the potential studies were imposed.

Study Selection Process

The study selection was executed via a systematic and rigorous approach. Initially, 2 independent reviewers, MM and FR, conducted a preliminary screening by examining titles and abstracts, thereby eliminating unrelated studies. Subsequently, these reviewers performed a detailed assessment of the full texts against the predefined inclusion and exclusion criteria. Discrepancies were resolved through discussion or, if necessary, consultation with a third reviewer, FF, to reach a consensus.

Data Extraction Methodology

Data extraction was independently carried out by 2 reviewers (FF and MM), using a pre-tested, standardized template in MS Excel. EndNote software facilitated reference management. Extracted data encompassed demographic information, radiographic data including DTI measures, MRI protocols, clinical or radiographic measurements, JOA or mJOA scores, diagnostic accuracy data (e.g., AUC, specificity, sensitivity), and correlation or comparison metrics. Discrepancies in data extraction were addressed through discussion and consensus.

Risk of Bias Assessment

The QUADAS-2 tool, recommended for bias assessment in systematic reviews of diagnostic accuracy studies, was employed. This tool evaluates 4 domains: patient selection, index test, reference standard, and flow and timing. Two researchers (FF and FR) independently applied this tool to each study, with their assessments exhibiting complete agreement, underscoring the consistency of the evaluation process.

Data Analysis Techniques

A variety of statistical methods were employed for data synthesis. Initially, pooled mean and mean difference meta-analyses were conducted to compare various DTI parameters between DCM patients and healthy controls. For correlation data between DTI parameters and JOA/mJOA scores, Spearman and Pearson correlations were first transformed to z-scores using the inverse variance method to calculate pooled effect sizes and then back-transformed for reporting. We acknowledge the distinction between Spearman and Pearson correlations in assessing different types of relationships, yet both measures quantify the strength and direction of associations between variables. By integrating both Spearman and Pearson correlations, we aimed to capture a wider range of associations and provide a more nuanced understanding of the underlying relationships within the dataset.

To pool diagnostic accuracy data (sensitivity, specificity, AUC) for DTI parameters distinguishing between healthy and DCM subjects, a proportional meta-analysis was initially performed. Additionally, for AUC analysis, pooled means and 95% confidence intervals of DTI parameters were utilized, especially when direct diagnostic accuracy tests were less prevalent in the studies. This analysis assumed a binormal distribution for DTI parameters, with pooled standard errors reflecting the combined variability in control and DCM groups. Z-scores were calculated to quantify the distinction between the mean DTI values of both groups, and subsequently transformed into AUC values using the standard normal distribution's cumulative distribution function.

All meta-analyses were also subgrouped based on levels used for DTI indices measurements and based on age. An age of 65 was used as the cut-off point for the age subgroup as this age defines the elderly subgroup, and we wanted to see if DTI indices could be valuable in both age groups.[10] Heterogeneity among studies was quantified using the I2 statistic. The pooled effect size is reported as a pooled correlation coefficient with a 95% confidence interval. All statistical analyses were conducted using R version 4.2.3.

Results

Literature Search

With our initial search, 1115 records were identified, of which 302 duplicates were removed. Then, after screening titles and abstracts, 715 were further excluded. After reviewing full texts an additional 41 articles were excluded. Finally, 57 eligible studies were used for data extraction and quality assessment (Figure 1).

Quality Assessment

The risk of bias for each study can be found in Tables 1 and 2. Most studies had a high risk of bias for patient selection as

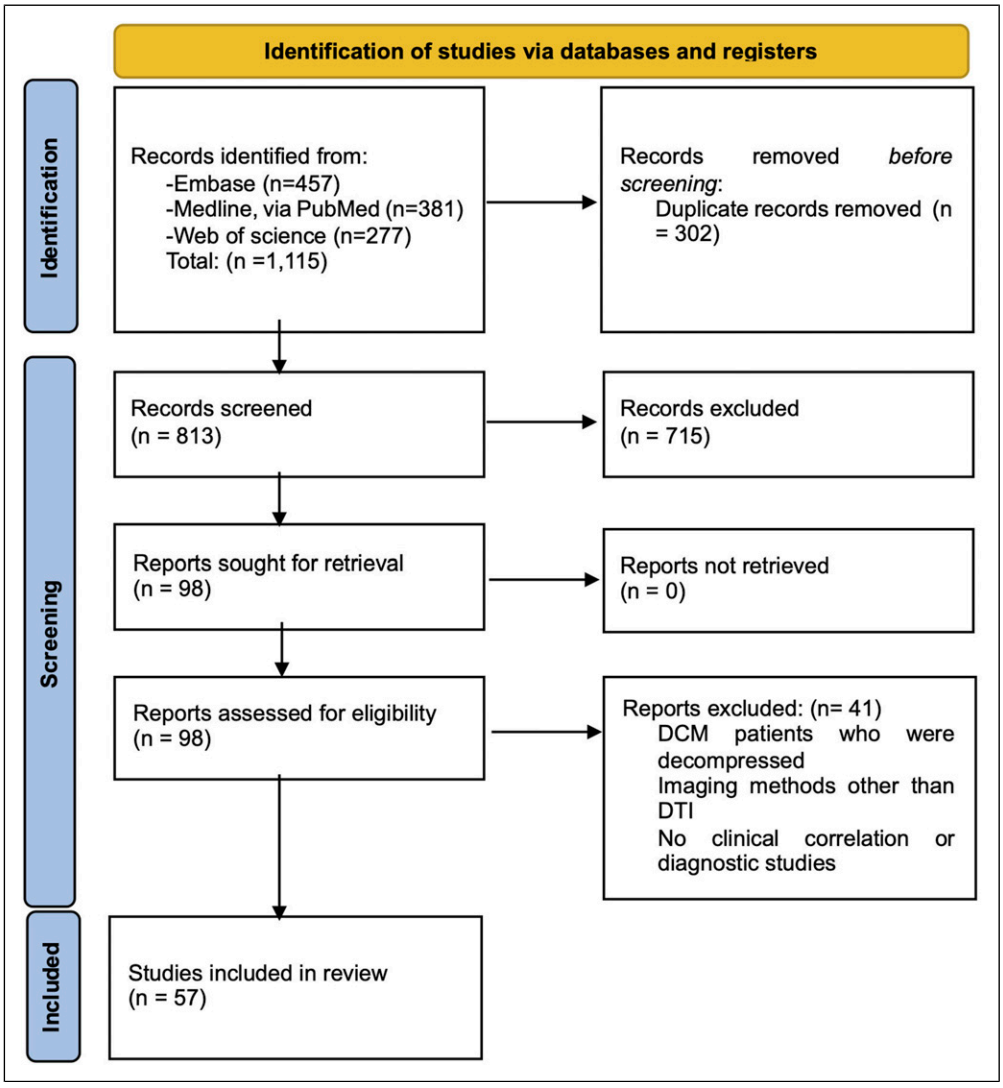

Figure 1. PRISMA flow chart for this review.

they had small sample sizes. Also, since the diagnostic tests didn't have predefined cut-off points for diagnostic studies, they all had a high risk of bias for the index test domain of the QUADAS 2 bias assessment tool.

Comparison of DTI Parameters Between DCM and Healthy Subjects

We identified 40 studies that compared DTI parameters between subjects with DCM and healthy individuals. These studies spanned from 2005 to 2023 and were conducted in 13 countries across Europe,[11-20] Asia,[8,21-43] North America,[44-48] with only 1 in Africa.[49] In total, these studies encompassed 1503 DCM patients and 1141 healthy subjects (Table 3).

The DTI parameters analyzed included FA, ADC, AD, RD, and MD. FA and ADC were the most frequently measured parameters. Among these studies, 24 utilized DTI parameters from the maximal compression level of the cervical spine (MC),[11-13,16,18,20,22,23,25,26,28-30,33,34,37,38,40,42,44-47,49] 15 calculated the mean DTI values from several cervical spine levels,[8,14,15,21,24,27,31,32,35,36,39-41,43,48] and 2 focused on the C2/C3 level.[17,19]

We performed a meta-analysis to compare the mean differences in FA values between DCM patients and healthy subjects. This analysis was conducted separately for studies measuring FA at MC,[11-13,16,18,20,22,23,25,26,28,30,33,34,37,38,40,42,44-47,49] and for those assessing the mean across several levels.[8,14,15,21,24,27,31,32,35,36,39-41,43,48] The results, depicted in Figure 2 forest plots, indicate that FA values are significantly lower in DCM patients at both MC and the averaged levels. Subgroup analysis for elderly (aged 65 years and older) and non-elderly populations showed significant differences in both subgroups (Figure 2).

ADC was the second most studied DTI parameter. Meta-analyses were conducted separately for studies examining ADC values at MC[11,13,16,18,20,22,23,26,28,33,42,49] and those averaging

Table 1. Quality Assessment of Studies Which Compared the DTI Parameters Between DCM and Healthy Subjects.

Study	Risk of Bias				Applicability Concerns		
	Patients Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standards
Facon, 2005 [10]	High	High	Low	Low	Low	Low	Low
Budzik, 2011 [11]	High	High	Low	Low	Low	Low	Low
Cui, 2011 [20]	High	High	Low	Low	High	Low	Low
Lee, 2011 [21]	High	High	Low	Low	Low	Low	Low
Song, 2011 [22]	High	High	Low	Low	Low	Low	Low
Hori, 2012 [23]	High	High	Low	Low	Low	Low	Low
Keřkovský, 2012 [12]	High	High	Low	Low	Low	Low	Low
Lindberg, 2012 [13]	High	High	Low	Low	Low	Low	Low
Uda, 2013 [24]	High	High	Low	Low	Low	Low	Low
Wen, 2013 [25]	High	High	Low	Low	High	Low	Low
Yoo, 2013 [26]	High	High	Low	Low	High	Low	Low
Banaszek. 2014 [14]	High	High	Low	Low	Low	Low	Low
Cui, 2014 [27]	High	High	Low	Low	Low	Low	Low
Ellingson, 2014 [43]	Low	High	Low	Low	Low	Low	Low
Rajasekaran, 2014 [28]	High	High	Low	Low	Low	Low	Low
Wen, 2014 (1) [29]	High	High	Low	Low	Low	Low	Low
Wen, 2014 (2) [30]	High	High	Low	Low	Low	Low	Low
Ellingson, 2015 (1) [44]	Low	High	Low	Low	Low	Low	Low
Lee, 2015 [31]	Low	High	Low	Low	Low	Low	Low
Maki, 2016 [32]	High	High	Low	Low	Low	Low	Low
Suetomi, 2016 [33]	High	High	Low	Low	High	Low	Low
Tu, 2016 [34]	High	High	Low	Low	Low	Low	Low
Ying, 2016 [35]	High	High	Low	Low	Low	Low	Low
Keřkovský, 2017 [15]	High	High	Low	Low	Low	Low	Low
Liu, 2017 [36]	High	High	Low	Low	Low	Low	Low
Martin, 2017 [45]	High	High	Low	Low	Low	Low	Low
Dong, 2018 [37]	Low	High	Low	Low	Low	Low	Low
Maki, 2018 [38]	High	High	Low	Low	Low	Low	Low
Rao, 2018 [46]	High	High	Low	Low	Low	Low	Low
Gohmann, 2019 [16]	High	High	Low	Low	Low	Low	Low
Iwasaki, 2019 [7]	High	High	Low	Low	Low	Low	Low
Schatlo. 2019 [17]	High	High	Low	Low	High	Low	Low
Han, 2020 [39]	High	High	Low	Low	Low	Low	Low
Wu, 2020 [40]	High	High	Low	Low	Low	Low	Low
Vallotton, 2021 [18]	High	High	Low	Low	Low	Low	Low
Skotarczak, 2022 [19]	High	High	Low	Low	Low	Low	Low
Yang, 2022 [41]	High	High	Low	Low	High	Low	Low
Mostafa, 2023 [48]	High	High	Low	Low	Low	Low	Low
Wang, 2023 [42]	High	High	Low	Low	Low	Low	Low
Zhang, 2023 [47]	High	High	Low	Low	Low	Low	Low

across multiple levels.[14,15,24,31,32,36,43,48] In both analyses, ADC values were significantly higher in DCM patients compared to healthy controls. However, nearly all studies, except 1, included participants with a mean age below 65 years; thus, we could not report pooled results for the elderly subgroup (Figure 3).

For MD, AD, and RD, separate meta-analyses were conducted for MC and averaged levels. The meta-analysis for MD, focusing on studies at MC,[12,25,29,30,37,38,45] revealed higher MD values in DCM patients in both elderly and non-elderly subgroups. However, only 2 studies compared MD as an average of several levels, rendering the pooled results less reliable due to their limited number and it's not reported here. AD, when pooled, included more studies that assessed the average of several levels[14,27,35,41,48]; however, no significant difference was found between DCM and healthy groups. Pooled results on AD difference in MC levels are also not reported here as the number of studies was limited. Conversely, RD, which also had a greater number of studies assessing averages,[14,27,35,41,48] showed a significantly higher mean in DCM patients in both meta-analyses and age subgroups (Figure 4).

We also explored the pooled results of studies investigating either MC or the average of several levels as the measurement

Table 2. Quality Assessment of Studies Which Assessed the Correlation of DTI Parameters With Myelopathy Severity.

Study	Risk of Bias				Applicability Concerns		
	Patients Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standards
Lee, 2011 [22]	High	High	Low	Low	Low	Low	Low
Gao, 2013 [65]	Low	High	Low	Low	Low	Low	Low
Jones, 2013 [51]	Low	High	Low	Low	Low	Low	Low
Ellingson, 2014 [44]	Low	High	Low	Low	Low	Low	Low
Wen, 2014 (1) [40]	Low	High	Low	Low	Low	Low	Low
Ellingson, 2015 (2) [52]	High	High	Low	Low	Low	Low	Low
Ying, 2016 [32]	Low	High	Low	Low	Low	Low	Low
Liu, 2017 [43]	Low	High	Low	Low	Low	Low	Low
Maki, 2017 [53]	Low	High	Low	Low	Low	Low	Low
Vedantam, 2017 [54]	High	High	Low	Low	Low	Low	Low
Yang, 2017 [55]	High	High	Low	Low	Low	Low	Low
Dong, 2018 [33]	Low	High	Low	Low	Low	Low	Low
Maki, 2018 [34]	High	High	Low	Low	Low	Low	Low
Okita, 2018 [56]	High	High	Low	Low	Low	Low	Low
Rao, 2018 [47]	Low	High	Low	Low	Low	Low	Low
Yang, 2018 [57]	High	High	Low	Low	Low	Low	Low
Zheng, 2018 [58]	High	High	Low	Low	Low	Low	Low
Cui, 2019 [59]	High	High	Low	Low	Low	Low	Low
Shabani, 2019 [60]	Low	High	Low	Low	Low	Low	Low
d'Avanzo, 2020 [61]	High	High	Low	Low	Low	Low	Low
Han, 2020 [35]	Low	High	Low	Low	Low	Low	Low
Iwama, 2020 [66]	High	High	Low	Low	Low	Low	Low
Kitamura, 2020 [67]	High	High	Low	Low	Low	Low	Low
Wu, 2020 [36]	High	High	Low	Low	Low	Low	Low
Zhang, 2020 [68]	Low	High	Low	Low	Low	Low	Low
Han, 2021 [62]	Low	High	Low	Low	Low	Low	Low
Valošek, 2021 [63]	Low	High	Low	Low	Low	Low	Low
Zhao, 2022 [64]	Low	High	Low	Low	Low	Low	Low

points for DTI parameters. The mean difference in FA between the 2 groups was −.11 (95% Confidence Interval [CI]: −.14 to −.08) in MC studies, −.09 (95% CI: −.11 to −.07) in averaged level studies, and −.10 (95% CI: −.12 to −.08) when all studies were pooled. For ADC, the mean differences were .22 (95% CI: .12 to .32) in MC studies, .22 (95% CI: .07 to .36) in averaged level studies, and .22 (95% CI: .14 to .30) when pooled. The mean differences in MD were .27 (95% CI: .15 to .39) in MC studies, .27 (95% CI: −.02 to −.55) in averaged level studies, and .25 (95% CI: .16 to .35) when pooled. For AD, the mean differences were .14 (95% CI: −.05 to .33) in MC studies, .18 (95% CI: .04 to .40) in averaged level studies, and .15 (95% CI: .04 to .26) when pooled. Lastly, the mean differences in RD were .15 (95% CI: .07 to .24) in MC studies, .21 (95% CI: .13 to .30) in averaged level studies, and .18 (95% CI: .12 to .23) when pooled (Figure 5).

Diagnostic Ability of DTI for DCM

To assess the diagnostic capabilities of DTI parameters, our initial step involved identifying studies that reported specificity, sensitivity, or AUC values for these parameters in differentiating between DCM patients and healthy subjects. A total of 8 studies[11,13,25,29,36,44,46,49] meeting these criteria were identified, as detailed in Table 4. Specificity, sensitivity, and AUC values for both FA and ADC from these studies were aggregated. The aggregated results for FA including 370 participants showed a sensitivity of .84, specificity of .80, and AUC of .83. In contrast, for ADC, the sensitivity, specificity, and AUC resulting from 258 participants were .74, .84, and .88, respectively.

Furthermore, attempted calculation of the AUC by using the pooled mean of DTI parameters from all studies that measured them in both healthy individuals and DCM patients. This approach enabled us to estimate the overall diagnostic utility of each parameter, focusing solely on AUC in the absence of specificity or sensitivity data. As presented in Table 5, the calculated AUC values for all measured parameters were greater than .9, except AD.

Correlation of DTI Parameters with Myelopathy Severity Based on JOA or mJOA

In our analysis, we identified 28 studies[22,32-36,40,43,44,47,50-67] that explored the correlation between DTI parameters and the severity of myelopathy, as assessed by JOA or mJOA (Table 6). These studies spanned from 2011 to 2022 and were primarily conducted in Asian countries,[22,32-36,40,43,52-58,61,63-67]

Table 3. Study Characteristics of Studies Which Compared the DTI Parameters Between DCM and Healthy Subjects.

Study	Country	DTI Parameters	Levels	DCM (n)	Healthy (n)
Facon, 2005[11]	France	FA, ADC	MC	15	11
Budzik, 2011[12]	France	FA, MD	MC	20	15
Cui, 2011[21]	Hong Kong	FA	Mean of several levels	5	15
Lee, 2011[22]	South Korea	FA, ADC	MC	20	20
Song, 2011[23]	China	FA, ADC	MC	50	20
Hori, 2012[24]	Japan	FA, ADC	Mean of several levels	18	15
Keřkovský, 2012[13]	Czech Republic	FA, ADC	MC	52	32
Lindberg, 2012[14]	France	FA, ADC, AD, RD	Mean of several levels	15	10
Uda, 2013[25]	Japan	FA, MD	MC	19	7
Wen, 2013[39]	Hong Kong	FA	Mean of several levels	7	15
Yoo, 2013[26]	South Korea	FA, ADC	MC	15	5
Banaszek. 2014[15]	Poland	FA, ADC	Mean of several levels	132	25
Cui, 2014[27]	Hong Kong	FA, AD, RD, MD	Mean of several levels	23	20
Ellingson, 2014[44]	USA	FA, RD	MC	32	16
Rajasekaran, 2014[28]	India	FA, ADC	MC	35	40
Wen, 2014 (1)[40]	Hong Kong	FA	MC, mean of several levels	45	20
Wen, 2014 (2)[41]	Hong Kong	FA, AD, RD	Mean of several levels	15	25
Ellingson, 2015 (1)[45]	USA	FA, MD	MC	21	6
Lee, 2015[29]	South Korea	FA, AD, RD, MD	MC	14	50
Maki, 2016[30]	Japan	FA, MD	MC	40	10
Suetomi, 2016[31]	Japan	FA, ADC	Mean of several levels	10	11
Tu, 2016	China	FA, ADC	MC	40	20
Ying, 2016[32]	China	FA, ADC	Mean of several levels	32	21
Keřkovský, 2017[16]	Czech Republic	FA, ADC	MC	74	186
Liu, 2017[43]	China	FA, ADC	Mean of several levels	40	42
Martin, 2017[46]	Canada	FA	MC	58	40
Dong, 2018[33]	China	FA, ADC	MC	60	50
Maki, 2018[34]	Japan	FA	MC	20	10
Rao, 2018[47]	USA	FA	MC	44	24
Gohmann, 2019[17]	Germany	FA	C2/C3	20	18
Iwasaki, 2019[8]	Japan	FA	Mean of several levels	28	13
Schatlo, 2019[18]	Switzerland	FA, ADC	MC	11	16
Han, 2020[35]	China	FA, AD, RD, MD	Mean of several levels	55	20
Wu, 2020[36]	China	FA, ADC	Mean of several levels	29	29
Vallotton, 2021[19]	Switzerland	FA, AD, RD, MD	C2/C3	24	24
Skotarczak, 2022[20]	Poland	FA, ADC	MC	128	37
Yang, 2022[37]	South Korea	FA, AD, RD, MD	MC	8	12
Mostafa, 2023[49]	Egypt	FA, ADC	MC	134	150
Wang, 2023[38]	China	FA, AD, RD, MD	MC	53	21
Zhang, 2023[48]	USA	FA, ADC, AD, RD	Mean of several levels	42	20

Abbreviations: DCM; degenerative cervical myelopathy, DTI; diffusion tensor imaging, MC; maximum compression, FA; fractional anisotropy, ADC; apparent diffusion coefficient, AD; axial diffusivity, MD; mean diffusivity, RD; radial diffusivity.

with additional research carried out in the USA[11,44,47,50,51,59] and Europe.[11,60,62] Collectively, these studies encompassed 1002 subjects with DCM. Among them, 9 studies[22,34,52,55,57,63-66] utilized JOA for evaluating myelopathy severity, while 19[32,33,35,36,40,43,44,47,50,51,53,54,56,58-62,67] adopted mJOA for the same purpose. In terms of DTI metrics, FA emerged as the most frequently investigated parameter, followed by ADC and others.

For correlation studies, our analysis was limited to pooling results for MC level DTI parameters due to the scant number of studies at other levels. FA was again the predominant measure used and demonstrated a significant correlation with JOA/mJOA across all subjects and in both age subgroups r = .53 (95% CI: .40-.65). Although ADC was the second most commonly used parameter, it did not exhibit a notable correlation with JOA/mJOA. The sole study focusing on ADC, conducted on a group with an average age of 65, reported an r = −.11 (95% CI: −.31 to .10). Similarly, MD, another parameter for which sufficient data was available for meta-analysis, did not show a significant pooled correlation r = −.23 (95% CI: −.55 to .14). Due to the limited number of studies,

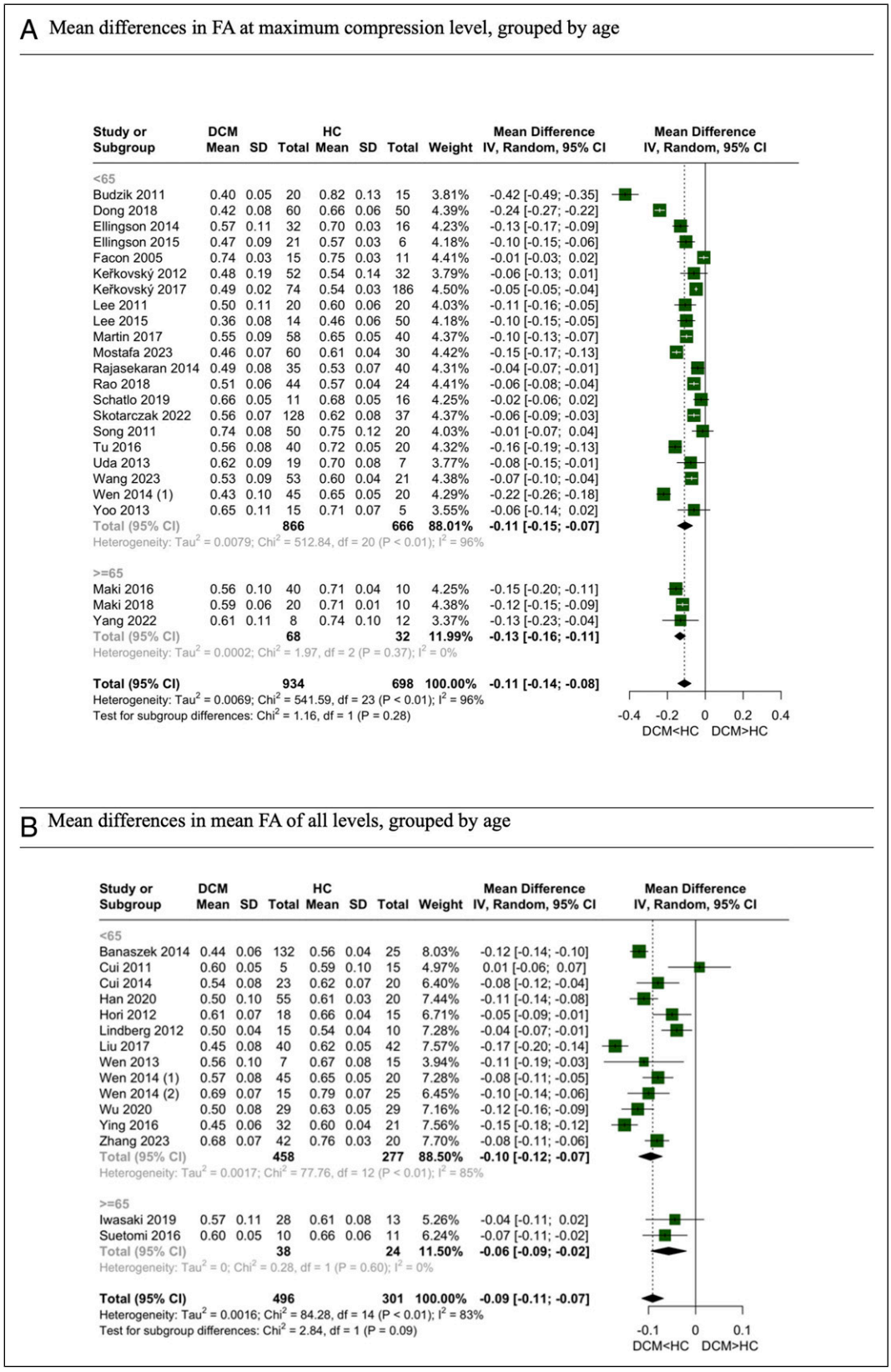

Figure 2. Meta-analysis for comparison of FA between DCM and healthy subjects. (A) Mean differences in FA at maximum compression level, grouped by age. (B) Mean differences in mean FA of all levels, grouped by age.

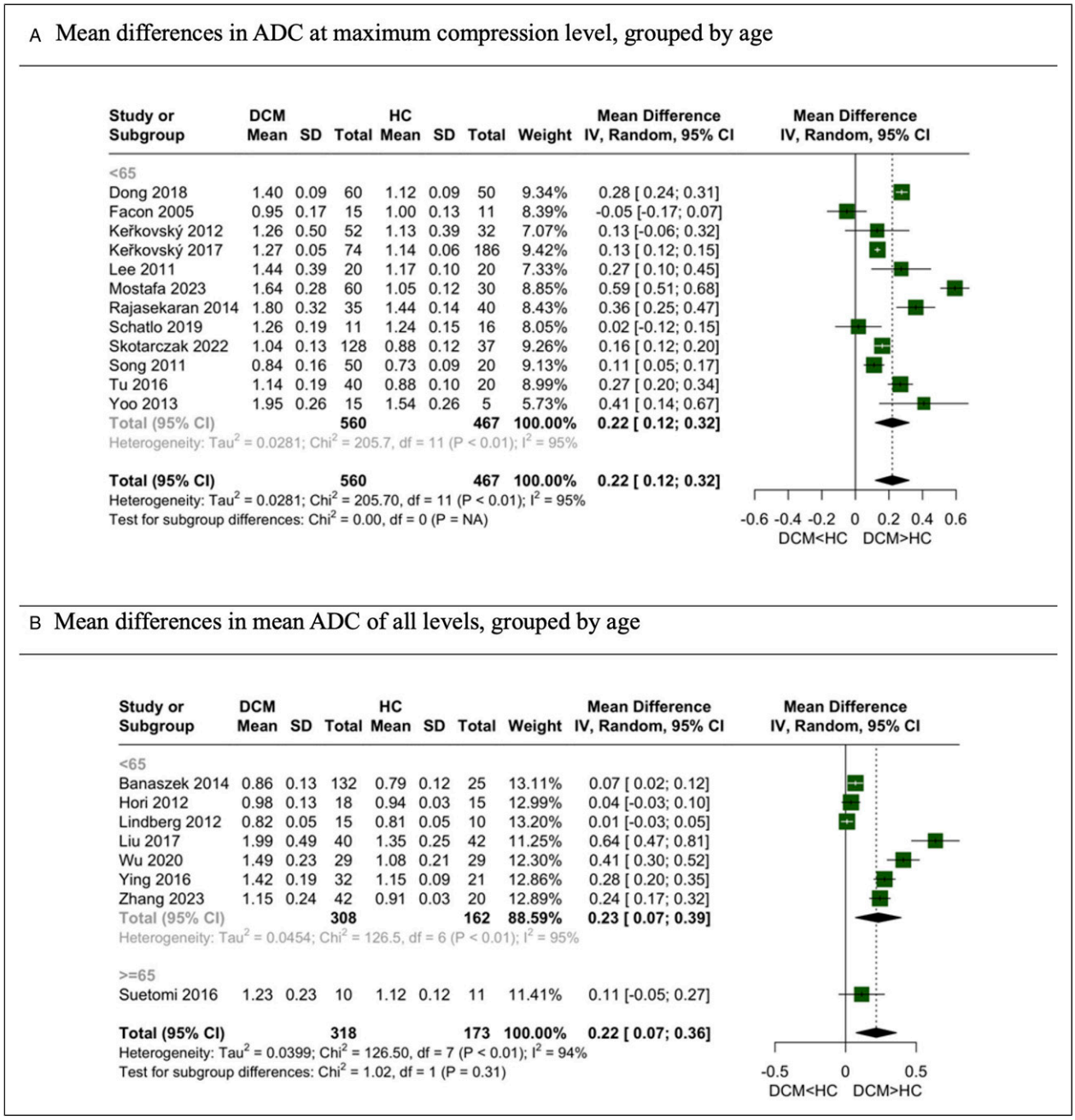

Figure 3. Meta-analysis for comparison of ADC between DCM and healthy subjects. (A) Mean differences in ADC at maximum compression level, grouped by age. (B) Mean differences in mean ADC of all levels, grouped by age.

results for AD could not be pooled. However, the correlation between RD and JOA/mJOA, analyzed from 3 studies involving samples with an average age below 65 years, revealed a notable correlation r = −.20 (95% CI: −.37 to −.01) (Figure 6).

Discussion

This systematic review and meta-analysis synthesize the literature and offer an advancement in understanding DTI's role in diagnosing and evaluating DCM. A total of 57 studies were included that involved more than 1000 DCM patients, providing a comprehensive assessment of the utility of DTI parameters for diagnosis and correlation with severity. Our findings underscore DTI's diagnostic reliability, particularly through FA and ADC parameters. The consistent observation of lower FA and higher ADC values in DCM patients across various study populations and methodologies highlights DTI's potential as a diagnostic tool. This shows promise for clinical use in DCM, where traditional imaging often is limited in early and accurate detection. The high diagnostic accuracy,

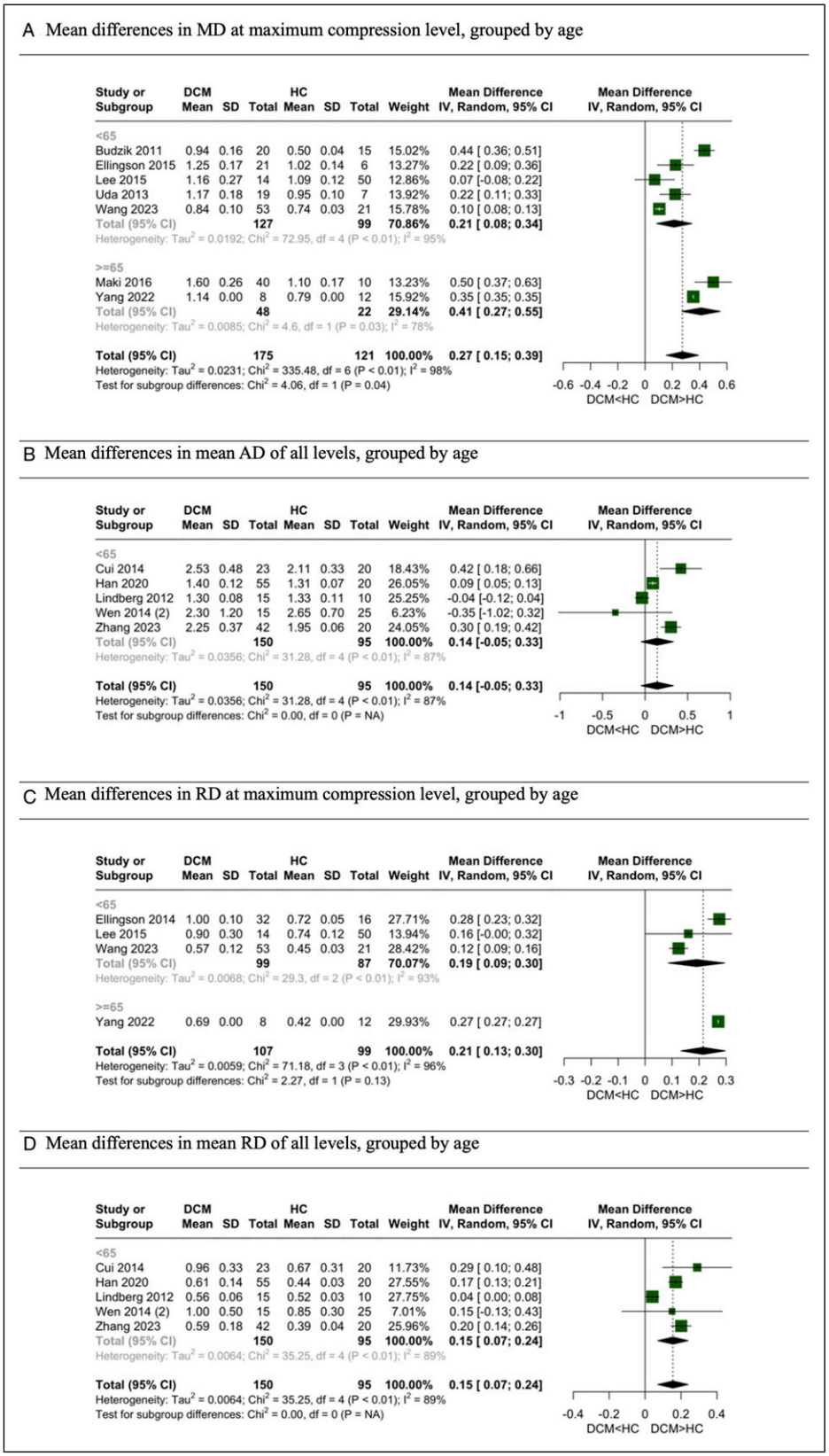

Figure 4. Meta-analysis for comparison of MD, AD and RD between DCM and healthy subjects. (A) Mean differences in MD at maximum compression level, grouped by age. (B) Mean differences in mean AD of all levels, grouped by age. (C) Mean differences in RD at maximum compression level, grouped by age. (D) Mean differences in mean RD of all levels, grouped by age.

Table 4. Diagnostic Ability of DTI for DCM.

Author	Control (n)	DCM (n)	Level	DTI Parameter	Sensitivity	Specificity	AUC
Facon, 2005[11]	11	15					
			MC	FA	.733	1	
				ADC	.134	0.8	
Keřkovský, 2012[13]	13	52					
			MC	FA	.65	.719	.68
				ADC	0.7	.75	.73
Uda, 2013[25]	30	26					
			MC	MD	1	.75	.903
				FA			.76
Ellingson, 2014[44]	9	48					
			MC	RD			.8944
				FA	.72	.75	.77
Lee, 2015[29]	50	14					
			MC	MD	1	.448	
				FA	1	.276	
Martin, 2017[46]	40	58					
			MC	FA			.813
Wu, 2020[36]	29	29					
			Mean of several levels	FA	.7586	.8966	.899
				ADC	.9655	.7241	.895
Mostafa, 2023 [49]	30	60					
			Mean of several levels	FA	.97	.927	.969
				ADC	.881	.98	.958
Pooled	212	302					
				FA	.84	0.8	.83
				ADC	.74	.84	.88

Abbreviations: DCM; degenerative cervical myelopathy, DTI; diffusion tensor imaging, AUC; area under the ROC Curve, MC; maximum compression, FA; fractional anisotropy, ADC; apparent diffusion coefficient, MD; mean diffusivity, RD; radial diffusivity.

Table 5. Pooled AUC Calculated by Using the Pooled Mean of DTI Parameters.

	Control (n)	Pooled Mean Control	95% CI	DCM (n)	Pooled Mean DCM	95% CI	AUC
ADC	467	1.1	.97-1.23	560	1.33	1.14-1.52	.9961
FA	698	.65	.61-.68	934	.54	.5-.58	.9977
MD	121	.88	.72-1.04	175	1.16	.97-1.34	.9986
AD	33	1.49	1.15-1.84	61	1.67	1.1-2.23	.731
RD	99	.58	.41-.75	107	.78	.59-.98	.9833

Abbreviations: DCM; degenerative cervical myelopathy, CI; confidence interval, AUC; area under the ROC Curve, FA; fractional anisotropy, ADC; apparent diffusion coefficient, AD; axial diffusivity, MD; mean diffusivity, RD; radial diffusivity.

indicated by aggregated sensitivity, specificity, and AUC values, illustrates the consistent findings and accuracy of DTI and supports the greater integration of DTI into clinical practice.

Studies comparing DTI parameters between healthy individuals and DCM patients assessed these parameters through MC, an average across several levels, or at the C2/C3 space. We aimed to subgroup the mean difference meta-analyses of different parameters based on whether they were measured at MC or averaged across multiple levels (Figure 5). The objective was to determine which measurement type (MC or average of several levels) leads to a larger mean difference when comparing DTI indices between healthy individuals and DCM patients, potentially making it a superior choice for differentiating between healthy and DCM subjects. Upon subgrouping the pooled results by these measurement levels, the pooled difference between healthy and DCM patients indicated that the difference for almost all DTI parameters is equivalent or nearly so across different levels. This significant finding suggests that both methods might possess comparable diagnostic capabilities when differentiating between healthy and DCM subjects or employing DTI for DCM diagnosis.

The correlation between DTI parameters, especially FA, and myelopathy severity assessed by JOA or mJOA scores, is

Table 6. Study Characteristics of Studies Which Assessed the Correlation of DTI Parameters With Myelopathy Severity.

Study	Country	DCM (n)	Age (Mean)	Gender (% Female)	Myelopathy Scale	Type of MRI(T)	DTI Parameter	Levels	Type of Correlation
Lee, 2011[22]	South Korea	20	50.6	35	JOA	3	FA, ADC	MC	Spearman
Gao, 2013[64]	China	104	53	49	JOA	3	FA	MC	Spearman
Jones, 2013[50]	USA	30	62	53.3	mJOA	3	FA	MC	Spearman
Ellingson, 2014[44]	USA	48	60		mJOA	3	FA, RD	MC	Regression
Wen, 2014 (1)[40]	Hong Kong	45	64	42.2	mJOA	3	FA	MC	Spearman
Ellingson, 2015 (2)[51]	USA	27	62	51.9	mJOA	3	FA, MD	MC	Pearson
Ying, 2016[32]	China	32	54.3	37.5	mJOA	3	FA	MC, mean of several levels	Spearman
Liu, 2017[43]	China	40	55.6	45	mJOA	1.5	FA, ADC	MC	Spearman
Maki, 2017[52]	Japan	26	63.8	30.8	JOA	3	FA, MD	MC	Spearman
Vedantam, 2017[53]	USA	27	54.5	66.6	mJOA	1.5	FA	MC, C1-C2	Pearson
Yang, 2017[54]	South Korea	20	52.8	15	mJOA	3	FA, ADC	MC, level below MC	Pearson
Dong, 2018[33]	China	60	55	35	mJOA	3	FA	MC	Pearson
Maki, 2018[34]	Japan	20	67.6	45	JOA	3	FA	MC	Spearman
Okita, 2018[55]	Japan	27	70.5	22.2	JOA	3	FA, ADC	MC	Pearson
Rao, 2018[47]	USA	44	53.9	59	mJOA	1.5	FA	MC	Regression
Yang, 2018[56]	South Korea	20	52.8	15	mJOA	3	FA, ADC	MC, level below MC	Pearson
Zheng, 2018[57]	China	61	62.4	36	JOA	3	ADC, MD, AD, RD	MC	Regression
Cui, 2019[58]	China	40	55.6	45	mJOA	3	FA, ADC	MC, lumbosacral enlargement	Spearman
Shabani, 2019[59]	USA	46	53.6	58.6	mJOA	1.5	FA	MC	Regression
d'Avanzo, 2020[60]	Italy	11	57.6	54.5	mJOA	1.5	FA	MC, levels above and below MC	Spearman
Han, 2020[35]	China	55	58.6	38.2	mJOA	3	FA, MD, AD, RD	MC, mean of several levels, C2	Spearman
Iwama, 2020[65]	Japan	28	69.7	25	JOA	3	FA	MC	Pearson
Kitamura, 2020[66]	China	15	71.5	33.3	JOA	3	FA	MC	Spearman
Wu, 2020[36]	China	29	47.5	41.4	mJOA	3	FA, ADC	MC	Pearson
Zhang, 2020[67]	China	36	54.9	63.9	mJOA	3	FA	MC	Spearman
Han, 2021[61]	China	37	55	62.2	mJOA	3	FA	MC	Spearman
Valošek, 2021[62]	Austria	21	58.2	57.1	mJOA	3	FA, AD	C3	Spearman
Zhao, 2022[63]	China	33	48.2	57.6	JOA	3	FA, ADC	MC	Pearson

Abbreviations: DCM; degenerative cervical myelopathy, MRI; Magnetic resonance imaging, DTI; diffusion tensor imaging, JOA; the Japanese Orthopedic Association, mJOA; the modified Japanese Orthopedic Association, MC; maximum compression, FA; fractional anisotropy, ADC; apparent diffusion coefficient, AD; axial diffusivity, MD; mean diffusivity, RD; radial diffusivity.

noteworthy. This correlation justifies using DTI not just for diagnosis but also for assessing disease progression and treatment efficacy. Given that the JOA and mJOA assessments have numerous limitations on assessing severity, such as being subjective, non-linear, coarse, and easily confounded by other physical disabilities, DTI offers the distinct advantage of providing a direct measure of spinal cord tissue injury and has potential use in future guidelines to help more accurately quantify severity. However, the lack of significant correlation in other parameters like ADC and MD suggests a more complex interaction between DTI metrics and myelopathy, warranting a multifaceted approach in future studies.

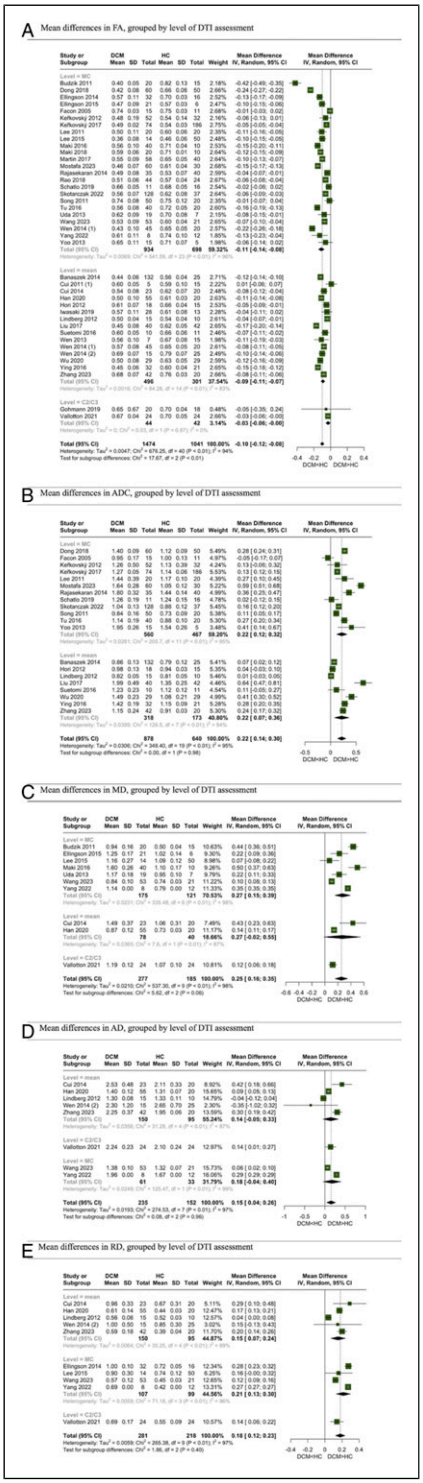

Figure 5. Meta-analysis for comparison of DTI parameters of different levels between DCM and healthy subjects. (A) Mean differences in FA, grouped by level of DTI assessment. (B) Mean differences in ADC, grouped by level of DTI assessment. (C) Mean differences in MD, grouped by level of DTI assessment. (D) Mean differences in AD, grouped by level of DTI assessment. (E) Mean differences in RD, grouped by level of DTI assessment.

An intriguing finding is the significant correlation between FA and RD, calculated at MC, with JOA/mJOA. While the number of studies investigating RD is still limited, the pooled results show FA's significant correlation with symptom severity. The number of studies on ADC, the second most studied parameter, indicates it did not correlate with symptom severity. These findings are interesting because another recent systematic review and meta-analysis investigating the correlation between preoperative DTI parameters and decompressive surgery outcomes based on myelopathy severity like JOA/mJOA showed FA significantly correlated with outcomes in some age subgroups but not all. In contrast, ADC was correlated with surgery outcomes across different age groups and all age groups together.[10]

The findings of this review, which investigates the correlation of DTI parameters with disease severity in patients who have not undergone surgery, and the previous review that examined the correlation between preoperative DTI parameters and decompressive surgery outcomes, shed light on the complex association between DTI metrics and myelopathy.[10] These findings suggest that FA might be a good indicator of symptom severity, but not necessarily of decompressive surgery outcomes. The complex association of FA with preoperative severity and decompression outcomes is also evident in studies included in this review that investigated the correlation of DTI parameters in both preoperative and postoperative periods.[33,35,40,47,50,53,55,56,59,61,65,66] Most of these studies focus primarily on FA and reveal complex results. They mostly show that FA can be correlated with preoperative disease severity, but not all studies were able to demonstrate a correlation between FA and postoperative disease severity or recovery rate.[47,53,55,59,65] This again suggests that while FA may be better used for assessing disease severity, it may not always be a reliable indicator of decompression outcomes.

Conversely, ADC seems to correlate with decompressive surgery outcomes but not preoperative symptom severity. From a surgical standpoint, these findings are significant. They suggest that patients with higher FA might have more severe myelopathy symptoms, but it's unclear if the severity improves post-surgery. For predicting improvement after surgery, ADC might be a more reliable DTI parameter. Not only does it show no uniform correlation with symptom severity, but other systematic reviews also indicate its correlation with postoperative outcomes in DCM patients.[10]

The findings of this systematic review on preoperative symptom severity and DTI, coupled with the recent study on postoperative outcomes and DTI in DCM patients,[10] could significantly impact patient selection for decompressive surgery. Current guidelines for DCM suggest decompressive surgery for both moderate and severe cases.[68] However, there is a lack of precise recommendations for mild DCM ranging from non-operative treatment such as physical therapy to

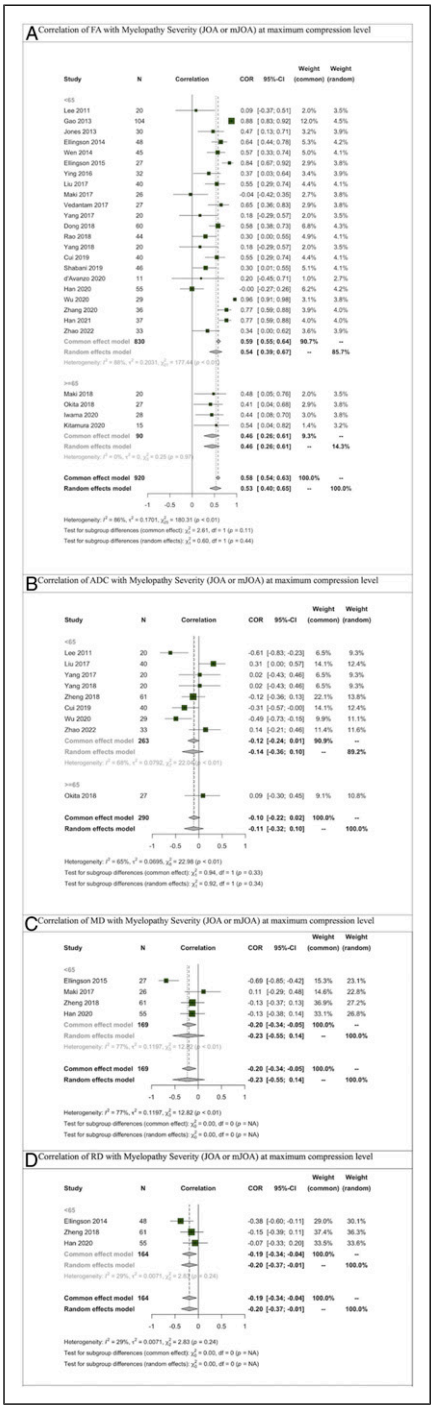

Figure 6. Meta-analysis for Correlation of DTI Parameters with Myelopathy Severity Based on JOA or mJOA at maximum compression level. (A) Correlation of FA with Myelopathy Severity (JOA or mJOA) at maximum compression level. (B) Correlation of ADC with Myelopathy Severity (JOA or mJOA) at maximum compression level. (C) Correlation of MD with Myelopathy Severity (JOA or mJOA) at maximum compression level. (D) Correlation of RD with Myelopathy Severity (JOA or mJOA) at maximum compression level.

immediate surgery. ADC's role here could be pivotal, potentially differentiating between healthy and DCM patients. While it may not correlate with symptom severity, it might predict surgical outcomes, making it a valuable imaging biomarker for future management decisions in mild DCM.

Limitations

This review, while comprehensive, does highlight several significant research gaps and limitations that must be acknowledged. Firstly, the prevalent risk of bias, especially in patient selection and the absence of uniform diagnostic thresholds, is a critical concern that requires immediate attention in future research endeavors. The small sample sizes and the geographical concentration of studies, primarily in Asia, potentially limit the broader applicability and generalizability of our findings.

Additionally, a notable limitation of this study is the pooling of the diagnostic ability of DTI parameters across the entire myelopathy severity spectrum. This approach raises questions about the specificity of DTI parameters in differentiating between healthy individuals and patients with mild DCM. The ability of DTI to distinguish between these 2 groups is crucial, as it directly impacts clinical decision-making, particularly in the early stages of the disease. Therefore, further investigation is needed to determine whether DTI parameters can effectively differentiate between healthy and mild DCM cases.

Furthermore, the variability in measuring DTI parameters across different cervical spine levels poses a significant challenge. This inconsistency hampers the development of a standardized diagnostic approach and complicates the interpretation of results across studies.

Future Directions

Addressing these limitations is imperative in future research. Future studies should aim for larger, more diverse cohorts with harmonized DTI measurement protocols, enhancing the generalizability and applicability of DTI in diagnosing and monitoring DCM. Establishing clear, evidence-based diagnostic cut-offs will be crucial for improving diagnostic accuracy and reliability. Additionally, further research should focus on the specific diagnostic capabilities of DTI parameters in differentiating mild DCM from healthy states. Integrating advanced data analysis techniques, such as machine learning, could provide significant insights and refine the diagnostic capabilities of DTI.

Conclusion

In conclusion, while this systematic review and meta-analysis provide valuable insights into the utility of DTI in DCM, the

highlighted limitations underscore the need for continued and focused research to fully understand and leverage DTI's potential in clinical practice, particularly in early-stage DCM diagnosis.

Declaration of Conflicting Interests

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References

1. Boogaarts HD, Bartels RH. Prevalence of cervical spondylotic myelopathy. *Eur Spine J*. 2015;24(Suppl 2):139-141. doi:10.1007/s00586-013-2781-x
2. Wilson JR, Tetreault LA, Kim J, et al. State of the art in degenerative cervical myelopathy: an update on current clinical evidence. *Neurosurgery*. 2017;80(3s):S33-S45. doi:10.1093/neuros/nyw083
3. Badhiwala JH, Ahuja CS, Akbar MA, et al. Degenerative cervical myelopathy - update and future directions. *Nat Rev Neurol*. 2020;16(2):108-124. doi:10.1038/s41582-019-0303-0
4. Theodore N. Degenerative cervical spondylosis. *N Engl J Med*. 2020;383(2):159-168. doi:10.1056/NEJMra2003558
5. Takamiya S, Iwasaki M, Yokohama T, Oura D, Niiya Y, Fujimura M. The prediction of neurological prognosis for cervical spondylotic myelopathy using diffusion tensor imaging. *Neurospine*. 2023;20(1):248-254. doi:10.14245/ns.2244708.354
6. He B, Sheldrick K, Das A, Diwan A. Clinical and research MRI techniques for assessing spinal cord integrity in degenerative cervical myelopathy-a scoping review. *Biomedicines*. 2022;10(10):2621. doi:10.3390/biomedicines10102621
7. Shabani S, Kaushal M, Budde MD, Wang MC, Kurpad SN. Diffusion tensor imaging in cervical spondylotic myelopathy: a review. *J Neurosurg Spine*. 2020;33:65-72. doi:10.3171/2019.12.Spine191158
8. Iwasaki M, Yokohama T, Oura D, Furuya S, Niiya Y, Okuaki T. Decreased value of highly accurate fractional anisotropy using 3-tesla ZOOM diffusion tensor imaging after decompressive surgery in patients with cervical spondylotic myelopathy: aligned fibers effect. *World Neurosurg X*. 2019;4:100056. doi:10.1016/j.wnsx.2019.100056
9. Ellingson BM, Cohen-Adad J. Chapter 3.1 - diffusion-weighted imaging of the spinal cord. In: J Cohen-Adad, CAM Wheeler-Kingshott, eds. *Quantitative MRI of the Spinal Cord*. San Diego: Academic Press; 2014:123-145.
10. Mohammadi M, Roohollahi F, Mahmoudi MM, et al. Correlation between pre-operative diffusion tensor imaging indices and post-operative outcome in degenerative cervical myelopathy: a systematic review and meta-analysis. *Global Spine J*. 2024. Online first. doi:10.1177/21925682231225634
11. 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. doi:10.1055/s-0042-1751068
12. 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. doi:10.1007/s00330-010-1927-z
13. 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. doi:10.1097/BRS.0b013e31820e6c35
14. Lindberg PG, Feydy A, Sanchez K, Rannou F, Maier MA. Measures of spinal canal stenosis and relationship to spinal cord structure in patients with cervical spondylosis. *J Neuroradiol*. 2012;39(4):236-242. doi:10.1016/j.neurad.2011.09.004
15. Banaszek A, Bladowska J, Szewczyk P, Podgórski P, Sąsiadek M. Usefulness of diffusion tensor MR imaging in the assessment of intramedullary changes of the cervical spinal cord in different stages of degenerative spine disease. *Eur Spine J*. 2014;23(7):1523-1530. doi:10.1007/s00586-014-3323-x
16. Keřkovský M, Bednařík J, Jurová B, et al. Spinal cord MR diffusion properties in patients with degenerative cervical cord compression. *J Neuroimaging*. 2017;27(1):149-157. doi:10.1111/jon.12372
17. Gohmann RF, Blume C, Zvyagintsev M, et al. Cervical spondylotic myelopathy: changes of fractional anisotropy in the spinal cord and magnetic resonance spectroscopy of the primary motor cortex in relation to clinical symptoms and their duration. *Eur J Radiol*. 2019;116:55-60. doi:10.1016/j.ejrad.2019.04.009
18. Schatlo B, Remonda L, Gruber P, et al. Cervical spine prospective feasibility study: dynamic flexion-extension diffusion-tensor weighted magnetic resonance imaging. *Clin Neuroradiol*. 2019;29(3):523-532. doi:10.1007/s00062-018-0686-0
19. Vallotton K, David G, Hupp M, et al. Tracking white and gray matter degeneration along the spinal cord axis in degenerative cervical myelopathy. *J Neurotrauma*. 2021;38(21):2978-2987. doi:10.1089/neu.2021.0148
20. Skotarczak M, Dzierżanowski J, Kaszubowski M, et al. Diagnostic value of diffusion tensor imaging in patients with clinical signs of cervical spondylotic myelopathy. *Neurol Neurochir Pol*. 2022;56(4):341-348. doi:10.5603/PJNNS.a2022.0031
21. 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. doi:10.1016/j.neuroimage.2010.10.018
22. 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. doi:10.1007/s00256-011-1161-z

23. Song T, Chen WJ, Yang B, et al. Diffusion tensor imaging in the cervical spinal cord. *Eur Spine J*. 2011;20(3):422-428. doi:10.1007/s00586-010-1587-3
24. Hori M, Fukunaga I, Masutani Y, et al. New diffusion metrics for spondylotic myelopathy at an early clinical stage. *Eur Radiol*. 2012;22(8):1797-1802. doi:10.1007/s00330-012-2410-9
25. Uda T, Takami T, Tsuyuguchi N, et al. Assessment of cervical spondylotic myelopathy using diffusion tensor magnetic resonance imaging parameter at 3.0 tesla. *Spine (Phila Pa 1976)*. 2013;38(5):407-414. doi:10.1097/BRS.0b013e31826f25a3
26. Yoo WK, Kim TH, Hai DM, et al. Correlation of magnetic resonance diffusion tensor imaging and clinical findings of cervical myelopathy. *Spine J*. 2013;13(8):867-876. doi:10.1016/j.spinee.2013.02.005
27. Cui JL, Li X, Chan TY, Mak KC, Luk KD, Hu Y. Quantitative assessment of column-specific degeneration in cervical spondylotic myelopathy based on diffusion tensor tractography. *Eur Spine J*. 2015;24(1):41-47. doi:10.1007/s00586-014-3522-5
28. Rajasekaran S, Yerramshetty JS, Chittode VS, Kanna RM, Balamurali G, Shetty AP. The assessment of neuronal status in normal and cervical spondylotic myelopathy using diffusion tensor imaging. *Spine (Phila Pa 1976)*. 2014;39(15):1183-1189. doi:10.1097/brs.0000000000000369
29. Lee S, Lee YH, Chung TS, et al. Accuracy of diffusion tensor imaging for diagnosing cervical spondylotic myelopathy in patients showing spinal cord compression. *Korean J Radiol*. 2015;16(6):1303-1312. doi:10.3348/kjr.2015.16.6.1303
30. Maki S, Koda M, Saito J, et al. Tract-specific diffusion tensor imaging reveals laterality of neurological symptoms in patients with cervical compression myelopathy. *World Neurosurg*. 2016;96:184-190. doi:10.1016/j.wneu.2016.08.129
31. Suetomi Y, Kanchiku T, Nishijima S, et al. Application of diffusion tensor imaging for the diagnosis of segmental level of dysfunction in cervical spondylotic myelopathy. *Spinal Cord*. 2016;54(5):390-395. doi:10.1038/sc.2015.192
32. Ying J, Zhou X, Zhu M, et al. The contribution of diffusion tensor imaging to quantitative assessment on multilevel cervical spondylotic myelopathy. *Eur Neurol*. 2016;75(1-2):67-74. doi:10.1159/000443270
33. Dong F, Wu Y, Song P, et al. A preliminary study of 3.0-T magnetic resonance diffusion tensor imaging in cervical spondylotic myelopathy. *Eur Spine J*. 2018;27(8):1839-1845. doi:10.1007/s00586-018-5579-z
34. Maki S, Koda M, Ota M, et al. Reduced field-of-view diffusion tensor imaging of the spinal cord shows motor dysfunction of the lower extremities in patients with cervical compression myelopathy. *Spine (Phila Pa 1976)*. 2018;43(2):89-96. doi:10.1097/brs.0000000000001123
35. Han X, Ma X, Li D, et al. The evaluation and prediction of laminoplasty surgery outcome in patients with degenerative cervical myelopathy using diffusion tensor MRI. *AJNR Am J Neuroradiol*. 2020;41(9):1745-1753. doi:10.3174/ajnr.A6705
36. Wu W, Yang Z, Zhang T, et al. Microstructural changes in compressed cervical spinal cord are consistent with clinical symptoms and symptom duration. *Spine (Phila Pa 1976)*. 2020;45(16):E999-E1005. doi:10.1097/brs.0000000000003480
37. Yang HE, Kim WT, Kim DH, Kim SW, Yoo WK. Utility of diffusion and magnetization transfer MRI in cervical spondylotic myelopathy: a pilot study. *Diagnostics (Basel)*. 2022;12(9):2090. doi:10.3390/diagnostics12092090
38. Wang C, Han X, Ma X, et al. Spinal cord perfusion is associated with microstructural damage in cervical spondylotic myelopathy patients who underwent cervical laminoplasty. *Eur Radiol*. 2024;34:1349. doi:10.1007/s00330-023-10011-9
39. Wen CY, Cui JL, Lee MP, Mak KC, Luk KD, Hu Y. Quantitative analysis of fiber tractography in cervical spondylotic myelopathy. *Spine J*. 2013;13(6):697-705. doi:10.1016/j.spinee.2013.02.061
40. Wen CY, Cui JL, Liu HS, et al. Is diffusion anisotropy a biomarker for disease severity and surgical prognosis of cervical spondylotic myelopathy? *Radiology*. 2014;270(1):197-204. doi:10.1148/radiol.13121885
41. Wen CY, Cui JL, Mak KC, Luk KD, Hu Y. Diffusion tensor imaging of somatosensory tract in cervical spondylotic myelopathy and its link with electrophysiological evaluation. *Spine J*. 2014;14(8):1493-1500. doi:10.1016/j.spinee.2013.08.052
42. Tu C, Wang JH, Liao HB, et al. [The value of diffusion tensor imaging and fiber tractography in cervical spondylotic myelopathy]. *Zhongguo Gu Shang*. 2016;29(3):200-204. doi:10.1002/jmri.25109
43. Liu Y, Kong C, Cui L, et al. Correlation between diffusion tensor imaging parameters and clinical assessments in patients with cervical spondylotic myelopathy with and without high signal intensity. *Spinal Cord*. 2017;55(12):1079-1083. doi:10.1038/sc.2017.75
44. Ellingson BM, Salamon N, Grinstead JW, Holly LT. Diffusion tensor imaging predicts functional impairment in mild-to-moderate cervical spondylotic myelopathy. *Spine J*. 2014;14(11):2589-2597. doi:10.1016/j.spinee.2014.02.027
45. Ellingson BM, Salamon N, Woodworth DC, Holly LT. Correlation between degree of subvoxel spinal cord compression measured with super-resolution tract density imaging and neurological impairment in cervical spondylotic myelopathy. *J Neurosurg Spine*. 2015;22(6):631-638. doi:10.3171/2014.10.Spine14222
46. Martin AR, De Leener B, Cohen-Adad J, et al. A novel MRI biomarker of spinal cord white matter injury: T2*-weighted white matter to gray matter signal intensity ratio. *AJNR Am J Neuroradiol*. 2017;38(6):1266-1273. doi:10.3174/ajnr.A5162
47. Rao A, Soliman H, Kaushal M, et al. Diffusion tensor imaging in a large longitudinal series of patients with cervical spondylotic myelopathy correlated with long-term functional outcome. *Neurosurgery*. 2018;83(4):753-760. doi:10.1093/neuros/nyx558
48. Zhang JK, Jayasekera D, Song C, et al. Diffusion basis spectrum imaging provides insights into cervical spondylotic myelopathy pathology. *Neurosurgery*. 2023;92(1):102-109. doi:10.1227/neu.0000000000002183
49. Mostafa NSA-A, Hasanin OAM, Al Yamani Moqbel EAH, Nagy HA. Diagnostic value of magnetic resonance diffusion tensor imaging in evaluation of cervical spondylotic myelopathy. *EJRNM*. 2023;54(1):175. doi:10.1186/s43055-023-01124-8
50. 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. doi:10.3174/ajnr.A3199

51. Ellingson BM, Salamon N, Hardy AJ, Holly LT. Prediction of neurological impairment in cervical spondylotic myelopathy using a combination of diffusion MRI and Proton MR spectroscopy. *PLoS One*. 2015;10(10):e0139451. doi:10.1371/journal.pone.0139451
52. Maki S, Koda M, Kitamura M, et al. Diffusion tensor imaging can predict surgical outcomes of patients with cervical compression myelopathy. *Eur Spine J*. 2017;26(9):2459-2466. doi:10.1007/s00586-017-5191-7
53. Vedantam A, Rao A, Kurpad SN, et al. Diffusion tensor imaging correlates with short-term myelopathy outcome in patients with cervical spondylotic myelopathy. *World Neurosurg*. 2017;97: 489-494. doi:10.1016/j.wneu.2016.03.075
54. Yang YM, Yoo WK, Yoo JH, et al. The functional relevance of diffusion tensor imaging in comparison to conventional MRI in patients with cervical compressive myelopathy. *Skeletal Radiol*. 2017;46(11):1477-1486. doi:10.1007/s00256-017-2713-7
55. Okita G, Ohba T, Takamura T, et al. Application of neurite orientation dispersion and density imaging or diffusion tensor imaging to quantify the severity of cervical spondylotic myelopathy and to assess postoperative neurologic recovery. *Spine J*. 2018;18(2):268-275. doi:10.1016/j.spinee.2017.07.007
56. Yang YM, Yoo WK, Bashir S, Oh JK, Kwak YH, Kim SW. Spinal cord changes after laminoplasty in cervical compressive myelopathy: a diffusion tensor imaging study. *Front Neurol*. 2018;9:696. doi:10.3389/fneur.2018.00696
57. Zheng W, Chen H, Wang N, et al. Application of diffusion tensor imaging cutoff value to evaluate the severity and postoperative neurologic recovery of cervical spondylotic myelopathy. *World Neurosurg*. 2018;118:e849-e855. doi:10.1016/j.wneu.2018.07.067
58. Cui L, Kong C, Chen X, Liu Y, Zhang Y, Guan Y. Changes in diffusion tensor imaging indices of the lumbosacral enlargement correlate with cervical spinal cord changes and clinical assessment in patients with cervical spondylotic myelopathy. *Clin Neurol Neurosurg*. 2019;186:105282. doi:10.1016/j.clineuro.2019.02.014
59. Shabani S, Kaushal M, Budde M, Schmit B, Wang MC, Kurpad S. Comparison between quantitative measurements of diffusion tensor imaging and T2 signal intensity in a large series of cervical spondylotic myelopathy patients for assessment of disease severity and prognostication of recovery. *J Neurosurg Spine*. 2019;31:473-479. doi:10.3171/2019.3.Spine181328
60. d'Avanzo S, Ciavarro M, Pavone L, et al. The functional relevance of diffusion tensor imaging in patients with degenerative cervical myelopathy. *J Clin Med*. 2020;9(6):1828. doi:10.3390/jcm9061828
61. Han CF, Hai Y, Liu YZ, et al. [A long-term follow up study of cervical spondylotic myelopathy using diffusion tensor imaging]. *Zhonghua Yi Xue Za Zhi*. 2021;101(43):3594-3599. doi:10.3760/cma.j.cn112137-20210429-01030
62. Valošek J, Labounek R, Horák T, et al. Diffusion magnetic resonance imaging reveals tract-specific microstructural correlates of electrophysiological impairments in non-myelopathic and myelopathic spinal cord compression. *Eur J Neurol*. 2021; 28(11):3784-3797. doi:10.1111/ene.15027
63. Zhao G, Zhang C, Zhan Y, He L. The correlation between functional connectivity of the primary somatosensory cortex and cervical spinal cord microstructural injury in patients with cervical spondylotic myelopathy. *Dis Markers*. 2022;2022: 2623179. doi:10.1155/2022/2623179
64. Gao SJ, Yuan X, Jiang XY, et al. Correlation study of 3T-MR-DTI measurements and clinical symptoms of cervical spondylotic myelopathy. *Eur J Radiol*. 2013;82(11):1940-1945. doi:10.1016/j.ejrad.2013.06.011
65. Iwama T, Ohba T, Okita G, et al. Utility and validity of neurite orientation dispersion and density imaging with diffusion tensor imaging to quantify the severity of cervical spondylotic myelopathy and assess postoperative neurological recovery. *Spine J*. 2020;20(3):417-425. doi:10.1016/j.spinee.2019.10.019
66. Kitamura M, Maki S, Koda M, et al. Longitudinal diffusion tensor imaging of patients with degenerative cervical myelopathy following decompression surgery. *J Clin Neurosci*. 2020; 74:194-198. doi:10.1016/j.jocn.2019.05.018
67. Zhang H, Guan L, Hai Y, Liu Y, Ding H, Chen X. Multi-shot echo-planar diffusion tensor imaging in cervical spondylotic myelopathy. *Bone Joint J*. 2020;102-b(9):1210-1218. doi:10.1302/0301-620x.102b9.Bjj-2020-0468.R1
68. Fehlings MG, Tetreault LA, Riew KD, et al. A clinical practice guideline for the management of patients with degenerative cervical myelopathy: recommendations for patients with mild, moderate, and severe disease and nonmyelopathic patients with evidence of cord compression. *Global Spine J*. 2017;7(3 Suppl): 70s-83s. doi:10.1177/2192568217701914