Spinal Diffusion Tensor Imaging in Evaluation of Preoperative and Postoperative Severity of Cervical Spondylotic Myelopathy: Systematic Review of Literature

Rima S. Rindler[1], Falgun H. Chokshi[2], James G. Malcolm[1], Sheila R. Eshraghi[1], Mahmud Mossa-Basha[3], Jason K. Chu[1], Shekar N. Kurpad[4], Faiz U. Ahmad[1]

Key words
- Cervical spondylotic myelopathy
- Diffusion tensor imaging
- Modified Japanese Orthopaedic Score
- Neck Disability Index
- Spinal cord

Abbreviations and Acronyms
ADC: Apparent diffusion coefficient
AUC: Area under the curve
CSM: Cervical spondylotic myelopathy
DTI: Diffusion tensor imaging
FA: Fractional anisotropy
FTR: Fiber tract ratio
LMC: Level of maximal compression
mJOA: modified Japanese Orthopaedic Association
MRI: Magnetic resonance imaging
NDI: Neck Disability Index
OCEBM: Oxford Center for Evidence-Based Medicine
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
T2W: T2-weighted

From the Departments of [1]Neurological Surgery and [2]Radiology and Imaging Sciences, Emory University School of Medicine, Atlanta, Georgia; [3]Department of Radiology, University of Washington, Seattle, Washington; and [4]Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

To whom correspondence should be addressed: Faiz U. Ahmad M.D. [E-mail: faiz.ahmad@emory.edu]

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BACKGROUND: **Diffusion tensor imaging (DTI) is increasingly investigated as a potential diagnostic and prognostic tool for symptomatic degenerative cervical pathology; however, it is yet to be validated for this purpose.**

OBJECTIVE: **To investigate the association of preoperative DTI signal changes and postoperative outcomes in patients with cervical spondylotic myelopathy (CSM).**

METHODS: **We performed a systematic literature review using PubMed for clinical studies using DTI in adults undergoing operative management for CSM. Data on preoperative clinical status, preoperative DTI metrics, and postoperative clinical outcomes were abstracted. Preoperative DTI parameters were correlated with preoperative severity and postoperative outcomes and pooled across studies.**

RESULTS: **Nine studies met inclusion criteria for 238 patients who underwent operative management with mean follow-up time 310 days. Higher preoperative fractional anisotropy (FA) at the level of maximal compression correlates strongly with a higher preoperative modified Japanese Orthopaedic Association (mJOA) score ($n = 192$ patients, rho $= 0.62$, $P < 0.001$). Higher preoperative FA is associated with less postoperative mJOA change ($n = 27$, rho $= -0.42$, $P = 0.02$) but a greater recovery rate ($n = 93$, rho $= 0.32$, $P < 0.001$). Preoperative FA correlated with lower Neck Disability Index ($n = 15$, rho $= -0.61$, $P = 0.04$). Preoperative fiber tract ratio had a large positive correlation with a postoperative recovery rate ($n = 20$, rho $= 0.61$, $P = 0.005$). When reported, an apparent diffusion coefficient showed an inverse correlation compared with FA.**

CONCLUSION: **DTI is associated with preoperative severity and postoperative outcomes in CSM patients, suggesting that DTI may become useful in identifying those most likely to benefit from operative intervention (Level 3 Evidence). Prospective trials with standardized DTI acquisition techniques and patient selection are required for higher-level evidence.**

INTRODUCTION

Cervical spondylotic myelopathy (CSM) is a clinical entity of cervical spinal cord compression resulting from degeneration of bone, ligament, and intervertebral disks.[1] The clinical manifestation of myelopathy results from direct compression or ischemia.[2] Noncontrast magnetic resonance imaging (MRI) has long been the gold-standard imaging technique in evaluating and diagnosing cervical degeneration and its effects on the spinal canal and cord.[3] This is done typically with anatomic measurements of canal size, cord-to-canal ratios, or dynamic observation of canal size reduction with movement. Presence of T2-weighted (T2W) changes in cord parenchyma are also highly associated with advanced myelopathy.[4-6] Conventional MRI, however, is limited in predicting symptom severity, as patients may have a varying tolerance of spinal cord compression.[7] Patients may be significantly symptomatic with only "mild" cervical stenosis and no T2W hyperintensity, while others may have "severe" stenosis with myelomalacia and minimal, if any, symptoms. Furthermore, T2W changes are often a late finding and may predict worse outcome despite decompression.[8] These exceptions present diagnostic and therapeutic uncertainty to clinicians.

Diffusion tensor imaging (DTI) is being increasingly investigated as a potential diagnostic and prognostic tool for patients presenting with symptomatic cervical degenerative disease. DTI is thought to detect microstructural changes in tissue by

measuring the presence, strength, and directionality of water particles,[9] which are disrupted in cervical compression states. A recent systematic review and meta-analysis by Guan et al[10] noted significant differences in DTI parameters when comparing patients with CSM and healthy controls, specifically decreased fractional anisotropy (FA) and increased apparent diffusion coefficient (ADC) in patients. This suggested that DTI might be a useful tool in differentiating patients with symptomatic cervical stenosis from minimally or asymptomatic patients and assist in identifying candidates for operative intervention.

Therefore the purpose of this systematic review is to evaluate the association of DTI-related cord changes with preoperative severity and postoperative outcomes in patients with CSM.

MATERIALS AND METHODS

Data Sources

This retrospective investigation entails a systematic literature search that was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[11] The MeSh database system in PubMed was used to search for articles discussing the role of DTI in diagnosing and guiding treatment of cervical degenerative pathology in 3 separate searches. The first was ("Diffusion Tensor Imaging"[Mesh]) AND ("Spinal Cord"[Mesh]). The second was "diffusion tensor imaging" ([All Fields] and "spinal cord" [Title/Abstract]). The third was "DTI spine myelopathy." References of review articles were carefully evaluated for additional qualifying articles not identified in the first 3 searches.

Selection Criteria

Articles were limited to English language case reports, case series, and retrospective or prospective cohort studies of human patients published between January 1990 and October 2016. Only articles describing operative management of adult patients with CSM and use of DTI were included. Cervical degenerative pathology included any process causing symptomatic cervical stenosis or myelopathy, including spondylosis, ossification of the posterior longitudinal ligament, or intervertebral disk herniation. Specifically, articles detailing use of DTI in these patients and evaluating postoperative outcomes were included. Expert comments or general reviews were excluded. Articles that did not detail patient demographics or operative outcomes or that included nondegenerative cervical spine pathology (e.g., tumor) were excluded. Two reviewers (RSR and JGM) independently selected qualifying studies for inclusion to minimize the risk of selection bias. Disagreements were resolved by consensus. Duplicate studies were eliminated.

Study quality was assessed using the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence categorization.[12] Risk of bias for cohort studies was assessed by the Newcastle-Ottawa Scale, which is a 3-category, 9-point scale assessing case selection, comparability of groups, and exposure, with a higher grade indicating higher study quality.[13]

Data Extraction

The following data were extracted from each article according to inclusion criteria: patient demographics (age and gender), clinical pathology; radiographic data including DTI measures of interest, MRI protocols; use of other standardized clinical or radiographic measures; details of operative interventions, postoperative outcomes, and time to follow-up. Corresponding authors were contacted for additional information and missing data.

Statistical Methods

To estimate follow-up, the pooled mean and variance were calculated from studies only for patients who underwent operative management.* Correlations between DTI parameters (FA and ADC) and the modified Japanese Orthopaedic Association (mJOA)[14] score in Lee et al[15] (2011) were calculated by the authors using the Spearman rank correlation coefficient (rho) to measure the monotonic relationship between variables. Where possible, correlations between DTI parameters and clinical assessments were pooled. For these calculations, the correlation coefficients were first transformed to normal distributions using the Fisher Z-Transform ($z = \ln[(1+r)/(1-r)]/2$) with known standard error ($1/\sqrt{n-3}$). These were then pooled using the Mantel-Haenszel method with a fixed-effects model, unless Chi^2 and I^2 indicated significant heterogeneity, in which case a random-effects model was used.[16] Confidence intervals (CIs) are at 95%. A P value <0.05 was considered statistically significant in all analyses.

*Pooled variance (s_p^2) is estimated as the weighted average of sample variances (s_i^2) and counts (n_i): $s_p^2 = \Sigma([n_i-1]*s_i^2)/\Sigma(n_i-1)$.

RESULTS

Study Selection

A PRISMA flow chart of the screened articles is shown in Figure 1. The 3 PubMed queries resulted in 945 nonduplicated studies for screening according to described parameters. Seven additional studies were identified from a careful bibliography review. Thirty-seven studies from this initial screen underwent full text review. Twenty-five articles were excluded because no operative intervention was performed, 2 were review articles,[10,17] and 1 included other compressive cervical spine pathologies in averaged data.[18] The remaining 9 articles were included in this review (7 of these included preoperative assessment; 6 included postoperative outcome). One of these studies reported only 2 patients and was therefore not included in the pooled calculations.[19]

Study Characteristics

Table 1 provides characteristics of all 9 included studies. All studies were either case series (i.e., included >3 patients with detailed clinical and radiographic information, $n = 5$) or cohort studies (i.e., included both patients and healthy volunteers, $n = 4$). There were 276 patients with CSM, ossification of the posterior ligament, or combination, and 81 healthy controls. All studies reported a mean age and variably reported standard deviation and range, which only allowed for a pooled mean calculation. Two hundred thirty-eight patients (86%) underwent operative management and had a mean follow-up time of 310 days.

Risk of Bias of Individual Studies and Study Quality

Using the OCEBM criteria, the 4 cohort studies were Level of Evidence 3 and the

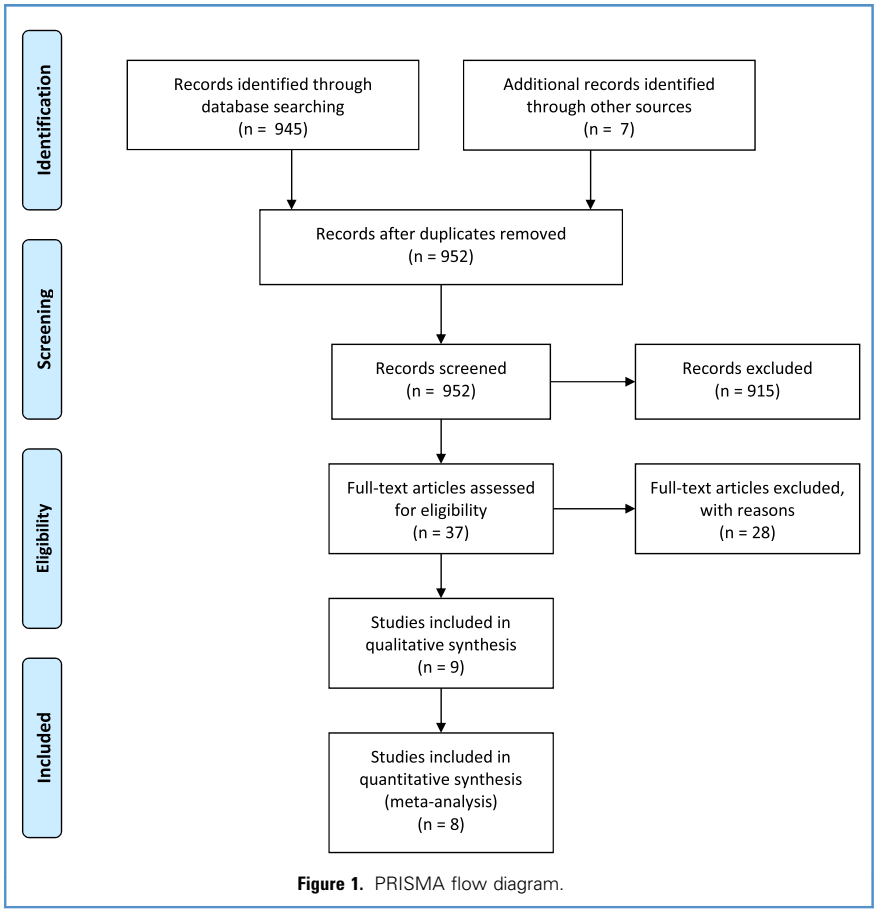

Figure 1. PRISMA flow diagram.

remaining 5 case series were Level of Evidence 4. The Newcastle-Ottawa Scale revealed a range of cohort study quality, from poor[24] to excellent.[15] Few of the cohort studies included well-matched controls. Other possible sources of bias include selection bias for patients included in case series and publication bias for studies reporting only on patients with good surgical outcome.

DTI Data Acquisition Techniques

The specific preoperative DTI measures obtained (e.g., FA, ADC, fiber tractography ratio [FTR]) and the reported cervical levels are listed in **Table 2**. All studies obtained raw FA data, but it was not reported by Nakamura et al[21] due to distortion artifact. ADC was reported in 3 articles.[15,22,25] Tractography data were qualitatively reported in one[15] and quantitatively in another using the FTR (FTR = number of fibers at compressed level/number of fibers at C2 level × 100%).[21]

The spinal cord cross-section at the level of maximum compression was included as a region-of-interest for DTI parameters in all but 2 studies, which reported lateral, posterior and anterior regions of interest in the axial cervical spinal cord.[24,25] For these studies, the lateral ROI was used in the analyses as it encompassed the corticospinal tracts. Some studies also analyzed the cervical cord level by level, averaged across multiple levels, or performed a combination. This study focused on DTI results obtained at the level of maximum compression, because it was the most commonly evaluated level across studies. Other important findings from levels other than level of maximum compression were noted.

Clinical Assessments and Operative Intervention

Several clinical tools were used to assess preoperative and postoperative clinical status. The mJOA[14] and Nurick clinical scale[27] were used to assess myelopathy severity. Both are obtained from physical examination. A higher mJOA score (0–17) or Nurick grade (0–5) indicates worse myelopathy. The Short Form-36 (SF-36)[28-30] and Neck Disability Index (NDI)[31] are self-completed questionnaires that assess pain and function. Lower SF-36 scores and higher NDI scores (0–50) indicate worse symptoms, function, and sense of well-being. The Oswestry Disability Index,[32] an additional patient questionnaire, was used by one article (data not shown).[19]

All studies reported correlation values between preoperative DTI with raw scores for preoperative clinical assessments. Studies varied in how they accounted for clinical change from the patient's own baseline status postoperatively. One study instead reported correlation with change between preoperative and postoperative values.[33] Another study transformed this change into a recovery rate equal to (postoperative − preoperative)/(17 − preoperative) × 100%, where 17 is the maximum mJOA score,[25] which essentially quantifies how much deficit a patient has recovered.[34]

Operative management was discussed differently in each study. Three studies reserved operations for patients with progressive or moderate-to-severe myelopathy and/or severe cord compression,[19,20,26] whereas the remaining 3 did not detail operative criteria.[15,21,24] Surgical decompression techniques included multilevel anterior cervical discectomy and fusion,[19,26] laminoplasty,[21,26] or were not described.[15,24]

Relationship of DTI Measures and Preoperative Clinical Assessments

Five studies used mJOA as a clinical assessment tool.[15,19,20,23,25,26] One did not specify whether the JOA tool that was used was the "modified" version; it was presumed to be "mJOA" for the purposes of this study.[21] Among the studies, 2 included SF-36,[20,24] 2 used NDI,[20,23] and 2 used Nurick.[20,22]

Pooled calculations revealed a strong positive correlation between FA and preoperative mJOA scores at the level of maximal compression (LMC) ($n = 5$ studies; rho = 0.62, 95% CI 0.53–0.71, $P < 0.001$) (**Table 3**A).[15,20,23,25,26] FA at the level of maximum compression did not correlate with the Nurick assessment (rho = −0.25, $P = 0.18$) but moderately correlated at the

Table 1. Demographics and Characteristics of Diffusion Tensor Imaging Studies Investigating Operative Outcomes in Cervical Spondylotic Myelopathy

Study	Study Design	OCEBM Level of Evidence	Newcastle-Ottawa Scale	Patients (Number Female)		Mean Age (Range or ± SD), Year		Pathology	Operative Intervention Number (%)	Follow-Up (Mean ± SD, days)
				Cases	Controls	Cases	Controls			
Jones 2011[19]	Ca	4	NA	3 (1)	0	63.7 (52–82)	NA	OPLL	2 (66.7%)	105 ± 21.2
Jones 2013[20]	Ca	4	NA	30 (16)	0	61.9 (±12.4)	NA	CSM	15 (50%)	180.7 ± 103.4
Lee 2011[15]	Co	3	8	20 (7)	20 (7)	49.6 (22–67)	"Matched"	CCM*	20 (100%)	90
Nakamura 2012[21]	Ca	4	NA	20 (5)	0	64.6 (44–82)	NA	CSM, OPLL	20 (100%)	401.5 ± 45
Rajasekaran 2016[22]	Ca	4	NA	35 (2)	0†	48 (35–82)	NA	CSM, OPLL	35 (100%)	365
Vedantam 2017[23]	Ca	4	NA	27 (15)	0	54.5 (±1.9)	NA	CSM	27 (100%)	90
Wang 2015[24]	Co	3	3	4 (0)	5 (2)	61.25 (53–73)	48 (39–53)	CSM	4 (100%)	180
Wang 2016[25]	Co	3	7	93 (45)	36 (14)	57.2 (42–69)	51.3 (20–77)	CSM	93 (100%)	365
Wen 2014[26]	Co	3	7	45 (19)	20 (10)	64 (43–86)	52 (41–62)	CSM	22 (48.9%)	455 ± 137.5
Totals	5 Ca 4 Co			276 (110)	81	57.0 (n/a)			238 (86%)	310.1

OCEBM, Oxford Center for Evidence-Based Medicine; SD, standard deviation; Ca, case series; NA, not applicable; OPLL, ossification of posterior longitudinal ligamen; CSM, cervical spondylotic myelopathy; Co, cohort study; CCM, cervical compressive myelopathy.
*Includes CSM, OPLL, os odontoideum.
†Controls were included in 1 table but never defined.

C2-3 (rho = −0.46, P = 0.01) and C7-T1 (rho = −0.38, P = 0.04) levels.[20] FA also did not correlate with NDI (rho = 0.19, P = 0.35) or SF-36 [Physical Component Score; pooled rho = 0.17, 95% (CI −0.20 to 0.49), P = 0.38[20,24]]. Within the CSM cohort, FA was also significantly lower in patients with a worse neurologic status in 2 of the studies[20,26]; however, these data could not be quantitatively pooled (data not shown).

Preoperative ADC in CSM had a strong negative correlation with mJOA (rho = −0.62, P < 0.001, see Table 3A).[15]

Preoperative FTR had a weak, nonsignificant correlation with mJOA (rho = 0.03, P = 0.90, see Table 3A).[21] There was no difference in the number of interrupted or intact fibers on tractography in patients with better (interrupted, n = 5; intact, n = 5) versus worse (interrupted, n = 3; intact, n = 7) symptoms.[15]

Predictive Ability for Operative Intervention

FA (area under the curve [AUC] 0.831) and mJOA (AUC 0.7578) were strongly accurate in identifying patients who underwent operative management in a single study; however, these values were not statistically different.[20]

Relationship of DTI Measures with Postoperative Outcome

Six studies reported correlation analyses between DTI measures and postoperative clinical outcome[20-25] in 194 patients with CSM. Differences in preoperative and postoperative clinical scores were not reported in 2 studies[15,20,26] or not calculated.[19,24] The remaining 3 studies were not incorporated in pooled analysis for the following reasons. Jones et al[19] reported only 2 patients, which precluded postoperative correlation calculations. Lee et al[15] reported a dichotomous postoperative outcome of "better or worse," defined as a ≥3-point increase in preoperative to postoperative mJOA score, but no raw mJOA scores that would allow for correlation with FA or ADC values. Similarly, Wen et al[26] reported dichotomous postoperative outcomes of "good or bad," defined as a recovery rate of >50% or ≥2 point mJOA improvement for good outcome. Raw postoperative mJOA scores were not available for calculating correlation.

Table 3B indicates some correlation between DTI and postoperative outcome. Three studies calculated the correlation between FA and postoperative mJOA.[20,23,25] One study correlated FA with raw mJOA scores and found no significant correlation (rho = 0.06, P = 0.84).[20] The second correlated with change from preoperative baseline finding that greater preoperative FA correlated with less postoperative improvement (rho = −0.42, P = 0.02).[23] The third study found that greater preoperative FA correlated with greater percent of recovered function (rho = 0.32, P < 0.001).[25] These varied correlation tactics precluded pooling.

For NDI, FA at the level of maximum compression had a strong negative correlation with postoperative NDI scores, with higher FA associated with improved level of function (rho = −0.61, P = 0.04)[20]. Preoperative FTR had a strong positive correlation with postoperative recovery rate (rho = 0.61, P = 0.005), where patients with FTR <60% correlated with

Table 2. Technical Details of Diffusion Tensor Imaging (DTI) Studies on Cervical Spondylotic Myelopathy; in Systematic Review

Study	DTI Measures					Scanner Make	Field Strength (T)	DTI Directions	Voxel Size (mm)	FOV (mm)	b (mm2/s)	TR (ms)	TE (ms)	Slice Thickness (mm)	Acquisition	ROI	C-Spine Levels Examined	DTI Processing
	FA	ADC	MD	Tr	FTR													
Jones 2011[19]	✓					NA	NA	NA	NA	NA	NA	NA	NA	NA	Axial	NA	C2/C3, C7/T1	NA
Jones 2013[20]	✓					General Electric	3	6	NA	180*180	1000	8100	94.1	4	Axial	Axial	LMC, C2/C3, C7/T1	GE Advantage
Lee 2011[15]	✓	✓		✓		Philips Achieva	3	15	1.95*1.95	250*224	600	3380	56	2	Sagittal	Axial	C1, C7, LMC	PRIDE (Philips)
Nakamura 2012[21]	✓	✓		✓	✓	NA	1.5	7	NA	300*300	1000	9000	84.9	4	Axial	Axial	C2, LMC	Volume-One
Rajasekaran 2016[22]	✓	✓				Siemens Magnetom	1.5	12	NA	220*220	500	6000	85	4	Axial	NA	NA	NA
Vedantam 2017[23]	✓					GE Signa Excite	1.5	15	3*3	128*128	600	5000	98.2	3	Axial	Axial	C1-2, LMC	Functional NeuroImages
Wang 2015[24]	✓		✓			Siemens Tim Trio	3	10 (Each Sag & Ax)	NA	200*200 (Each Sag & Ax)	750	3200 (Sag), 2500 (Ax)	73 (Sag), 90 (Ax)	2.5 (Sag), 5 (Ax)	Axial, Sagittal	Axial, Sagittal	C2-T1 (Axial), Lateral/ Anterior/ Posterior Margins of Cord (Sag)	Neuro 3D (Siemens)
Wang 2016[25]	✓	✓				General Electric	3	15	NA	180*180	1000	8000	87.6	4	Axial	Axial	C1/C2 reference, C3-C7 LMC	GE Functool
Wen 2014[26]	✓					Philips Achieva	3	15		80*80	600	NA	NA	7.5	Axial	Axial	C1-T1 (Axial)	DTI Studio

T, Tesla; FOV, field of view; TR, repetition time; TE, echo time; ROI, region of interest; FA, fractional anisotropy; ADC, apparent diffusion coefficient; MD, mean diffusivity; Tr, tractography; FTR, fiber tractography ratio; NA, not available; Sag, sagittal; Ax, axial; LMC, level of maximum compression.

Table 3. Relationship of Clinical Assessments and Radiographic Measures at Level of Maximal Compression

Study	FA				ADC	FTR/Tractography
	mJOA	NDI	Nurick	SF-36	mJOA	mJOA
A. Preoperative Diffusion Tensor Imaging (DTI) and Preoperative Clinical Assessment (Spearman Rank Correlation, rho)						
Jones 2013[20]	**0.47, *P* < 0.01**	0.19, $P = 0.35$	−0.25, $P = 0.18$	PCS: 0.21, $P = 0.29$		
Lee 2011[15]	0.03, $P = 0.90$*				0.08, $P = 0.75$*	
Nakamura 2012[21]						NS ($P = 0.95$)
Vedantam 2017[23]	**0.65, *P* < 0.001**	NS		NS		
Wang 2015[24]				PCS: −0.80, $P > 0.60$†		
Wang 2016‡,[25]	**0.763, *P* < 0.001**				**−0.703, *P* < 0.001**	
Wen 2014[26]	**0.327, *P* < 0.016**					
Pooled results [CI]	***0.62 [0.53–0.71], P < 0.001***			*0.16 [−0.20 to 0.49], P = 0.38*	**−0.62 [−0.72, −0.49], *P* < 0.001**	

Study	Patients	FA				ADC		FTR/Tractography
		mJOA	NDI	Nurick	SF-36	mJOA	Nurick	mJOA
B. Preoperative DTI and Postoperative Clinical Assessment (Spearman Rank Correlation, rho)								
Jones 2013[20]	15	0.06, $P = 0.84$	**−0.61; *P* = 0.04**	−0.22, $P = 0.44$	0.52, $P = 0.51$			
Nakamura 2012[21]	20							**0.61, *P* < 0.005**
Rajasekaran 2016[22]	35			−0.036, $P = 0.863$			−0.325, $P = 0.106$	
Vedantam 2017[23]	27	**−0.42, *P* = 0.02** (change)	NS		NS			
Wang 2015[24]	4				−0.40, $P > 0.60$†			
Wang 2016‡,[25]	93	**0.32, *P* < 0.001** (recovery rate)				**−0.293, *P* < 0.01** (recovery rate)		
Pooled results [CI]	*194*	NA		*−0.09 [−0.37, 0.21], P = 0.56*	*0.46 [−0.04, 0.78], P = 0.07*			

Bold values represents statistical significance at $P < 0.05$. Italics were the pooled results on the bottom row.
FA, fractional anisotropy; ADC, apparent diffusion coefficient; FTR, fiber tracking ratio (# fibers at compressed level/number of fibers at C2 level ×100%); mJOA, modified Japanese Outcome Assessment; NDI, Neck Disability Index; SF-36, Short Form-36; NA, not applicable, see text; NS, reported no significant difference but not quantified, unable to pool.
*Recalculated from reported data.
†Obtained from author correspondence.
‡Averaged over all regions, see text.

a recovery rate of <40%.[21] Of note, there was a trend for postoperative FTR to correlate with postoperative mJOA scores, but this did not reach significance (rho = 0.37, P = 0.05).[21]

Only 1 study directly evaluated the predictive ability of DTI measures at level of maximum compression in identifying patients with good postoperative outcome, reporting an AUC = 0.648 in a logistic regression model.[26] In this study, however, mean FA at C3-7 (AUC 0.743) and FA at C2 (AUC 0.781) independently predicted good surgical outcome (defined as recovery rate >50% or at least 2 points mJOA improvement) better than FA at the LMC and level of lowest FA value (AUC 0.648). In Lee et al[15] 2011, 80% of patients with intact fibers on tractography at LMC in the neurologically "worse" group improved at least 3 points on the mJOA

score postoperatively, compared with only 20% of patients with destroyed fibers; however, further sensitivity and specificity calculations were not performed.

DISCUSSION

This review found that FA values correlate with preoperative clinical severity and postoperative outcome in adult patients with cervical spondylotic myelopathy, suggesting that DTI measures may be useful tools in determining symptom severity and identifying operative candidates.

Relationship of DTI Measures and Preoperative Clinical Assessments

Some measures, particularly FA, correlated with preoperative clinical assessment tools measuring severity of myelopathy in some studies. FA at the level of maximum compression had a strong correlation with a single preoperative assessment (mJOA). ADC was found to have a similar inverse correlation.[15] Tractography (using FTR)[21] did not correlate with preoperative clinical assessment in a single study, which limits interpretation. Our review supports the findings reported in 2015 by Guan et al,[10] in their systematic review, that FA at LMC may be a useful diagnostic tool for identifying severity of myelopathy in patients with cervical spondylosis.

Although FA correlated strongly with mJOA across many studies, other clinical tools showed varied results. Several factors need to be considered when interpreting these results. The largest effects of compression on DTI may not occur at the LMC, especially in patients with multilevel disease.[26] FA values at other levels (e.g., C2-3, C7-T1) either more strongly correlated with mJOA or correlated better with other clinical assessments in some studies. FA (at C2-3) trended toward being the most accurate in identifying the need for operative intervention over other parameters.[20] Multilevel disease may have more complex effects on FA and DTI parameters than single-level disease, potentially increasing the variability of values at the level of maximum compression and therefore its diagnostic ability. Even when patients with "better" and "worse" symptoms were separated, significant differences in DTI between the 2 groups were inconsistent, particularly for FA. For example, FA (at LMC) was significantly lower in patients with more severe symptoms within the CSM cohort in some, but not all, studies. Additionally, DTI values vary by level even in healthy controls, with lower FA values found in lower cervical levels.[35] FA may also decrease with age,[36,37] though this is not a consistent finding.[38] One study found that using the ratio of LMC to C1-C2 had a stronger correlation with pathology and was robust to the effect of age.[25] These factors may complicate the diagnostic ability of DTI and FA across cervical levels and age groups. Although these data support the potential of FA as a biomarker or diagnostic tool for CSM severity, future studies are required to determine the optimal DTI measure and anatomic level of acquisition that best correlates with symptom severity.

Relationship of DTI Measures with Postoperative Outcome

The 2 studies that found moderate correlations with preoperative FA and postoperative mJOA each used a unique approach to incorporating mJOA using either change from baseline or recovery rate.[23,25] Since each patient has his or her own preoperative baseline score, it is important to predict on the basis of that, so more work should be done to explore these and similar approaches. Patients who improve postoperatively may have normalizing clinical assessment scores and may no longer correlate with preoperative DTI values. A more appropriate measure of postoperative outcome might be recovery rate or mean difference in assessment scores. This change might lead to a more accurate relationship between DTI measures and postoperative outcome. Additionally, as previously stated, the relationship may change according to the cervical level assessed, which should be further explored in future studies. Variable DTI acquisition techniques may also account for interstudy variability in defining a relationship between DTI and postoperative outcome.

It is important to note that postoperative improvement rates in this series were highly variable (20%–93%) and likely varied in accordance with symptom severity. There was a wide range of definitions for "improvement," which may certainly impact the predictive ability of DTI measures across the entire cohort of CSM patients. This variability is consistent with recovery rates reported in the literature, ranging from 54.5%–99.5% in the past 2 decades, not accounting for procedure type or definition of improvement.[39,40] This variability should certainly be taken into account in future studies by performing subgroup analyses according to myelopathy severity and operative approach, as well as providing consistent definitions for clinical improvement.

One future consideration is investigating the utility of DTI in the postoperative setting and the effect that surgical decompression might have on DTI measures and correlation with recovery. Only one study in this review performed postoperative DTI, which showed a trend in FA improvement postoperatively.[24] Imaging in this setting may, however, be significantly altered by high artifact from operative instrumentation, thus affecting accuracy of DTI measures.

Strengths and Limitations

This study reviewed a small number of qualifying articles, each of which had a unique study design, DTI acquisition techniques, and primary outcomes. All studies were Level of Evidence 3 or 4 and varied widely in quality, given that only 4 studies had a comparative control group (of varying quality) regarding initial DTI scores, and none had a comparative group for outcome. These factors make comparison across studies challenging. Furthermore, not all relevant data were reported for review and inclusion in a meta-analysis. Despite these limitations, periodic systematic reviews such as this help to evaluate the current state of new diagnostic techniques, exploring their potential clinical applications and providing guidance for future prospective studies.

CONCLUSION

DTI of the cervical spinal cord may become useful in predicting postoperative outcomes in patients with cervical spondylotic myelopathy. FA may play a particular role as a biomarker in predicting postoperative outcome, with a Level of Evidence 3 recommendation. Large,

controlled, prospective studies, however, are required for establishing standardized MRI acquisition protocols with appropriate DTI parameters, anatomic level of acquisition, and cut-off values for predicting need for operative intervention. Standardized clinical assessment tools, such as mJOA, should be used for detailed assessment of postoperative outcome in the context of considering preoperative baseline.[41]

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