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

Rima S. Rindler1, Falgun H. Chokshi2, James G. Malcolm1, Sheila R. Eshraghi1, Mahmud Mossa-Basha3, Jason K. Chu1, Shekar N. Kurpad4, Faiz U. Ahmad1

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.
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 al10 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 literature 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.18 Correlations between DTI parameters (FA and ADC) and the modified Japanese Orthopaedic Association (mJOA)14 score in Lee et al15 (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\(z = \ln((1+t)/(1−t))/2\) with known standard error \(1/(\sqrt{n−3})\). These were then pooled using the Mantel-Haenszel method with a fixed-effects model, unless Chi² and F 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.

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,16,17 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
remaining 5 case series were Level of Evidence 4. The Newcastle-Ottawa Scale revealed a range of cohort study quality, from poor to excellent. 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 due to distortion artifact. ADC was reported in 3 articles. Tractography data were qualitatively reported in one and quantitatively in another using the FTR (FTR = number of fibers at compressed level/number of fibers at C2 level × 100%). 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. For these studies, the lateral ROI was used in the analyses as it encompassed the corticospinal tracts. Some studies also analyzed cervical levels 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 and Nurick clinical scale 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) and Neck Disability Index (NDI) are self-completed questionnaires that assess pain and function. Lower SF-36 scores and higher NDI scores indicate worse symptoms, function, and sense of well-being. The Oswestry Disability Index, an additional patient questionnaire, was used by one article (data not shown).

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. Another study transformed this change into a recovery rate equal to (postoperative – preoperative)/17 × 100%, where 17 is the maximum mJOA score, which essentially quantifies how much deficit a patient has recovered.

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, whereas the remaining 3 did not detail operative criteria. Surgical decompression techniques included multilevel anterior cervical disectomy and fusion, laminoplasty, or were not described.

Relationship of DTI Measures and Preoperative Clinical Assessments
Five studies used mJOA as a clinical assessment tool. 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. Among the studies, 2 included SF-36, 2 used NDI, and 2 used Nurick. 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 3A). 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
C2-3 (r = −0.46, P = 0.01) and C7-T1 (r = −0.38, P = 0.04) levels.29 FA also did not correlate with NDI (r = 0.19, P = 0.35) or SF-36 [Physical Component Score; pooled r = 0.17, 95% (CI −0.20 to 0.49), P = 0.3820,24]. Within the CSM cohort, FA was also significantly lower in patients with a worse neurologic status in 2 of the studies26,28; however, these data could not be quantitatively pooled (data not shown).

Preoperative ADC in CSM had a strong negative correlation with mJOA (r = −0.62, P < 0.001, see Table 3A).15 Preoperative FTR had a weak, nonsignificant correlation with mJOA (r = 0.03, P = 0.90, see Table 3A).29 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.30

### Relationship of DTI Measures with Postoperative Outcome

Six studies reported correlation analyses between DTI measures and postoperative clinical outcome20–25 in 194 patients with CSM. Differences in preoperative and postoperative clinical scores were not reported in 2 studies20,24 or not calculated.19–24 The remaining 3 studies were not incorporated in pooled analysis for the following reasons. Jones et al19 reported only 2 patients, which precluded postoperative correlation calculations. Lee et al25 reported a dichotomous postoperative outcome of “better or worse,” defined as a 2-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 al26 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 (r = 0.06, P = 0.84).20 The second correlated with change from preoperative baseline finding that greater preoperative FA correlated with less postoperative improvement (r = −0.42, P = 0.02).15 The third study found that greater preoperative FA correlated with greater percent of recovered function (r = 0.32, P < 0.001).15 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 (r = −0.61, P = 0.04)20. Preoperative FTR had a strong positive correlation with postoperative recovery rate (r = 0.61, P = 0.005), where patients with FTR <60% correlated with

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Design Type</th>
<th>OCEBM Level of Evidence</th>
<th>Newcastle-Ottawa Scale</th>
<th>Patients (Number Female)</th>
<th>Mean Age (Range or ± SD, Year)</th>
<th>Operative Intervention</th>
<th>Pathology</th>
<th>Number (%)</th>
<th>Follow-Up (Mean ± SD, days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones 2011</td>
<td>Ca</td>
<td>4</td>
<td>NA</td>
<td>3 (1)</td>
<td>63.7 (52–82)</td>
<td>NA</td>
<td>OPLL</td>
<td>2 (66.7%)</td>
<td>105 ± 21.2</td>
</tr>
<tr>
<td>Jones 2013</td>
<td>Ca</td>
<td>4</td>
<td>NA</td>
<td>30 (16)</td>
<td>61.9 (±12.4)</td>
<td>NA</td>
<td>CSM</td>
<td>15 (50%)</td>
<td>180.7 ± 103.4</td>
</tr>
<tr>
<td>Lee 2011</td>
<td>Ca</td>
<td>3</td>
<td>8</td>
<td>20 (7)</td>
<td>49.6 (22–67)</td>
<td>Matched</td>
<td>CCM</td>
<td>20 (100%)</td>
<td>90</td>
</tr>
<tr>
<td>Nakamura 2012</td>
<td>Ca</td>
<td>4</td>
<td>NA</td>
<td>20 (5)</td>
<td>64.6 (44–82)</td>
<td>NA</td>
<td>CSM, OPLL</td>
<td>20 (100%)</td>
<td>401.5 ± 45</td>
</tr>
<tr>
<td>Rajasekaran 2018</td>
<td>Ca</td>
<td>4</td>
<td>NA</td>
<td>35 (2)</td>
<td>48 (35–82)</td>
<td>NA</td>
<td>CSM, OPLL</td>
<td>35 (100%)</td>
<td>365</td>
</tr>
<tr>
<td>Vaidantam 2017</td>
<td>Ca</td>
<td>3</td>
<td>8</td>
<td>27 (15)</td>
<td>54.5 (±1.9)</td>
<td>NA</td>
<td>CSM</td>
<td>27 (100%)</td>
<td>90</td>
</tr>
<tr>
<td>Wang 2015</td>
<td>Co</td>
<td>3</td>
<td>4</td>
<td>4 (0)</td>
<td>61.25 (53–73)</td>
<td>48 (39–53)</td>
<td>CSM</td>
<td>4 (100%)</td>
<td>180</td>
</tr>
<tr>
<td>Wang 2016</td>
<td>Co</td>
<td>3</td>
<td>7</td>
<td>93 (45)</td>
<td>57.2 (42–69)</td>
<td>51.3 (20–77)</td>
<td>CSM</td>
<td>93 (100%)</td>
<td>365</td>
</tr>
<tr>
<td>Wen 2014</td>
<td>Co</td>
<td>3</td>
<td>7</td>
<td>45 (19)</td>
<td>64 (43–86)</td>
<td>52 (41–62)</td>
<td>CSM</td>
<td>22 (48.9%)</td>
<td>455 ± 137.5</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td></td>
<td>276 (110)</td>
<td>57.0 (n/a)</td>
<td></td>
<td></td>
<td>238 (86%)</td>
<td>310.1</td>
</tr>
</tbody>
</table>

OCEBM, Oxford Center for Evidence-Based Medicine; SD, standard deviation; Ca, case series; NA, not applicable; OPLL, ossification of posterior longitudinal ligament; CSM, cervical spondylotic myelopathy; Co, cohort study; CCM, cervical compressive myelopathy.

*Includes CSM, OPLL, CSM, os odontoideum.
| Controls were included in 1 table but never defined.
Table 2. Technical Details of Diffusion Tensor Imaging (DTI) Studies on Cervical Spondylotic Myelopathy; in Systematic Review

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

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.
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 al15 2011, 80% of patients with intact fibers on tractography at LMC in the neurologically “worse” group improved at least 3 points on the mJOA

<table>
<thead>
<tr>
<th>Study</th>
<th>FA</th>
<th>ADC</th>
<th>FTR/Tractography</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Preoperative Diffusion Tensor Imaging (DTI) and Preoperative Clinical Assessment (Spearman Rank Correlation, rho)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jones 201320</td>
<td>0.47, P &lt; 0.01</td>
<td>0.19, P = 0.35</td>
<td>–0.25, P = 0.18</td>
</tr>
<tr>
<td>Lee 201115</td>
<td>0.03, P = 0.90*</td>
<td>NS</td>
<td>0.08, P = 0.75*</td>
</tr>
<tr>
<td>Nakamura 201221</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Vedantam 201723</td>
<td>0.65, P &lt; 0.001</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Wang 201524</td>
<td>NS</td>
<td>PCS: –0.80, P &gt; 0.60†</td>
<td></td>
</tr>
<tr>
<td>Wang 201625</td>
<td>0.763, P &lt; 0.001</td>
<td>–0.703, P &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Wen 201426</td>
<td>0.327, P &lt; 0.016</td>
<td>0.16 [–0.20 to 0.49], P = 0.38</td>
<td>–0.62 [–0.72, –0.49], P &lt; 0.001</td>
</tr>
<tr>
<td>Pooled results [CI]</td>
<td>0.62 [0.53–0.71], P &lt; 0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>mJOA</th>
<th>NDI</th>
<th>Nurick</th>
<th>SF-36</th>
<th>mJOA</th>
<th>Nurick</th>
<th>mJOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Preoperative DTI and Postoperative Clinical Assessment (Spearman Rank Correlation, rho)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jones 201320</td>
<td>15</td>
<td>0.06, P = 0.84</td>
<td>–0.61; P = 0.04</td>
<td>–0.22, P = 0.44</td>
<td>0.52, P = 0.51</td>
<td>0.61, P &lt; 0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nakamura 201221</td>
<td>20</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Rajasekaran 201622</td>
<td>35</td>
<td>–0.42, P = 0.02 (change)</td>
<td>–0.036, P = 0.863</td>
<td>NS</td>
<td>NS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vedantam 201723</td>
<td>27</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Wang 201524</td>
<td>4</td>
<td>–0.40, P &gt; 0.60†</td>
<td></td>
<td></td>
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<tr>
<td>Wang 201625</td>
<td>93</td>
<td>0.32, P &lt; 0.001 (recovery rate)</td>
<td>–0.08 [–0.37, 0.21], P = 0.56</td>
<td>0.46 [–0.04, 0.78], P = 0.07</td>
<td>–0.293, P &lt; 0.01 (recovery rate)</td>
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<tr>
<td>Pooled results [CI]</td>
<td>194</td>
<td>NA</td>
<td>–0.09 [–0.37, 0.21], P = 0.56</td>
<td>0.46 [–0.04, 0.78], P = 0.07</td>
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Bold values represent 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 x 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.
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. Tractography (using FTR) 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, in their systematic review, that FA at LMC may be a useful diagnostic tool for identifying severity of myelopathy in patients with cervical spondylodiscitis.

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. 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 LMC tended toward being the most accurate in identifying the need for operative intervention over other parameters. 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. FA may also decrease with age, though this is not a consistent finding. 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. 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. 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%–99.3% in the past 2 decades, not accounting for procedure type or definition of improvement. 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. 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, anatomical 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.\textsuperscript{41}

REFERENCES


Conflict of interest statement: Faiz U. Ahmad M.D. M.Ch., has consulting agreements with Depuy-Synthes and Medtronic, Inc. All authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.