



Negative Correlation Between Fractional Anisotropy on Diffusion Tensor Imaging and Neck Disability Index in Cervical Spondylotic Radiculopathy After Percutaneous Cervical Nucleoplasty: A Cross-Sectional Study

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Purpose: This study aimed to examine the correlation between diffusion tensor imaging (DTI) parameters (fractional anisotropy, FA; apparent diffusion coefficient, ADC) and clinical outcomes (neck disability index, NDI; visual analog scale, VAS) in cervical spondylotic radiculopathy (CSR) patients following percutaneous cervical nucleoplasty (PCN), respectively.

Methods: This is a cross-sectional study. We collected clinical data from 30 patients with CSR who underwent DTI before and 3 months after PCN. The FA and ADC were derived from DTI. The NDI and VAS were used to evaluate the clinical symptoms preoperatively, at 3 months postoperatively, and at the final follow-up. By setting multiple region of interest areas, the cervical nerve roots were delineated using fiber tractography. The Pearson correlation analysis was used to investigate the relationship between DTI values and clinical severity.

Results: NDI and VAS scores after PCN were significantly improved compared with preoperative scores ($P < 0.05$). The FA and ADC values after PCN were significantly different from the preoperative values ($P < 0.001$). The Pearson correlation revealed that preoperative FA values were strongly correlated with preoperative NDI scores ($r = -0.802$, $P < 0.001$), whereas postoperative FA values were strongly correlated with postoperative NDI scores ($r = -0.804$, $P < 0.001$). Furthermore, postoperative FA values were strongly correlated with NDI scores at the final follow-up ($r = -0.805$, $P < 0.001$). However, no significant difference was observed between the DTI and VAS scores. Similarly, no significant correlations were observed between ADC values and NDI scores pre- and postoperatively.

Conclusion: DTI is an imaging method that helps identify the clinical functional status of patients with CSR after PCN. The FA value can be used as a potential predictor of patient prognosis and are strongly negatively correlated with NDI scores. However, the long-term predictive effect warrants further investigation.

Keywords: cervical spondylotic radiculopathy, percutaneous cervical nucleoplasty, diffusion tensor imaging, fractional anisotropy, apparent diffusion coefficient, clinical outcome

Introduction

Cervical spondylotic radiculopathy (CSR) is the common form of cervical spondylosis, constituting approximately 60%–70% of cases.¹ It primarily manifests clinically as unilateral or bilateral sensory and motor disorders within the nerve root innervation area.² After failure of conservative treatment, surgery may be considered as a primary option. With the increasing popularity of the minimally invasive concept, percutaneous cervical nucleoplasty (PCN) has been gradually



applied for treating CSR. In current research, Kim et al³ and de Rooij et al⁴ have demonstrated that PCN treatment for radiculopathy caused by cervical disc herniation has satisfactory clinical efficacy. Under intraoperative fluoroscopy guidance, the herniated disc is ablated using low-temperature plasma technology, aiming to alleviate the direct compression of the intervertebral disc on peripheral nerve tissue.⁵ Compared with traditional open surgery, PCN offers the advantages of local anesthesia, reduced trauma, shorter surgical duration, and faster recovery under surgical indications.⁴

Currently, conventional magnetic resonance imaging (MRI) and computed tomography (CT) are commonly used in the clinical diagnosis of CSR, which identifies whether or not the herniation of the soft tissue of the spinal canal and bony spinal stenosis compress the nerve root.^{6,7} However, MRI and CT only indirectly identify compression or injury in the nerve root and provide no direct evidence of nerve root injury. Furthermore, in clinical practice, the MRI results sometimes do not match the clinical signs and symptoms, which makes the prompt determination of nerve root compression severity challenging.^{7,8} Therefore, an urgent concern remains on the need for a noninvasive test that qualitatively and quantitatively reflects the degree of nerve root injury to provide more detailed imaging parameters to help clinical treatment.

Diffusion tensor imaging (DTI) and fiber tractography (FT) are innovative MRI techniques developed based on diffusion-weighted imaging and are considered to be the main examination methods to exhibit nerve fiber bundle arrangements and changes.⁹ DTI quantifies water molecule diffusion in living tissues, thereby accurately demonstrating the morphological characteristics of the spinal cord and nerve fiber bundles. Hence, theoretically, this approach can help in the clinical diagnosis and prognostic monitoring of cervical spondylosis.⁶ In 2023, Atchut et al⁹ demonstrated that DTI has good discriminatory ability in distinguishing cervical spinal stenosis from non-stenosis. In 2024, Wang et al¹⁰ reported that dynamic DTI can predict postoperative outcomes in cervical spondylotic myelopathy and has predictive value for poor postoperative neurological recovery. DTI parameters include fractional anisotropy (FA) and apparent diffusion coefficient (ADC). FA reflects the diffusion of water molecules along the axis, while ADC reflects the diffusion pattern of water molecules.^{6,7} Current research has proved that as nerve injury becomes more severe, the FA value is lower and the ADC value is higher.⁶⁻¹⁰ However, to the best of our knowledge, few studies have investigated the use of DTI in nerve root compression assessment and analyzed the association between DTI use and patient prognosis in CSR.

In the present study, we analyzed the correlation between DTI parameters and postoperative clinical functional status in patients with CSR to evaluate the potential monitoring role of DTI in patients with CSR after PCN. Furthermore, PCN application for CSR in this study reduces the interference of DTI artifacts by effectively avoiding internal fixation, thereby enabling us to more accurately analyze the role of DTI.

Materials and Methods

Patient Population

We conducted a pre-experiment to calculate the appropriate sample size required. With a power level of 0.80 and a significance level of 0.05, our pre-experiment concluded that at least 25 cases were needed. This study included 30 consecutive patients with CSR deemed suitable for PCN from June 1, 2020 to December 31, 2021. All patients were from Beijing Chaoyang Hospital. The diagnostic criteria of CSR were based on the North American Spine Society (NASS) guidelines for the diagnosis and treatment of CSR (2010) and the expert consensus on the standardization of diagnosis and treatment of CSR in 2015.^{11,12} The inclusion criteria were (1) unilateral CSR confirmed by clinical examination (radicular pain/paresthesia/muscle weakness/abnormal reflexes in the arm) and MRI concordance; (2) failure of ≥ 12 weeks conservative therapy; and (3) indication for PCN per NASS guidelines. The exclusion criteria were (1) cervical spondylotic myelopathy; (2) surgical history of the planned segment; (3) herniated intervertebral disc or free intervertebral disc calcification; (4) severe or localized cervical spinal stenosis; (5) intolerance or noncooperation with the treatment, paralysis, or partial paralysis; and (6) obvious surgical contraindications or otherwise unsuitable for surgery. All patients were followed up for at least 1 year, using methods such as outpatient services and telephone call surveys. The study adhered to the principles of the Declaration of Helsinki and was approved by ethics committee of the Beijing Chaoyang Hospital (2020-4-22-2, 2020-04-22). All participants provided written informed consent.

Surgical Technique

All surgeries were performed by a senior surgeon with experience in performing >100 PCN procedures. PCN was performed under local anesthesia in the supine position. The ablation procedure was performed using a low-temperature plasma multifunctional surgical system (Model: SM-D380C; Manufacturer: Xi'an Surgical Medical Technology Co., Ltd., China). The surgical segments and puncture points were guided by C-arm fluoroscopy in the anteroposterior and lateral planes. Intraoperative ultrasound was employed to locate the space between the sheaths, and a spinal needle was used to puncture the right side of the neck, passing into the disc space (Figure 1). The inner stylet in the introducer needle was then removed. The fiber was threaded through the introducer needle, and the specialized radiofrequency (RF) probe was connected to the power generator. Fluoroscopy confirmed the position of the RF probe approximately 3 mm from the posterior edge of the intervertebral disc. A safety test was conducted at Level 1 power for 1 second to assess proximity to neural structures. Patients were monitored for immediate adverse reactions (eg, radicular pain, muscle twitching). Absence of symptoms confirmed safe probe positioning prior to ablation. The patient exhibited no adverse reactions after the safety test. The ablation then shifted to level 2 for 6 s and three cycles. Following the safety test for vaporization, the vaporization then shifted to level 1 for 6 s and two cycles. Afterward, the vaporization shifted to level 2 for 6 s and two cycles. The puncture needle was then pulled out 5 mm along with the probe, and the tip was confirmed to be in the intervertebral disc by fluoroscopy. Vaporization was set to level 2 for 6 s, and annulus fibroplasty was performed for two cycles. Thereafter, the RF probe and introducer needle were removed.

Clinical Assessment

Data on the demographic characteristics of all participants, including sex, age, symptom duration, compressed segment, and follow-up duration, were obtained. The visual analog scale (VAS)¹³ and neck disability index (NDI)¹⁴ were used to examine patients before surgery, at 3 months after surgery, and at the final follow-up (at least 12 months). The VAS scores ranged from 0 to 10, with 0 indicating no pain and 10 indicating the most severe pain. The NDI score was used to quantify the degree of pain and the life status of patients. The total score ranged from 0 (no disability) to 50 (complete disability).

DTI Acquisition, Processing, and Measurements

Imaging was performed using a Philips Ingenia 3.0T CX MRI system (Software Version: R5.6) equipped with a 16-channel Spine Matrix coil three days prior to surgery and 3 months postoperatively (Figure 2). The patients were in the supine position. The scanning sequence included localization scan, T1-weighted imaging, T2-weighted imaging (T2WI), and DTI. DTI data were acquired using multishot echo planar imaging (MS-EPI). DTI post-processing and fiber tractography were performed using DTI Studio v3.0 (Laboratory of Brain Anatomical MRI, Johns Hopkins University, Baltimore, MD) on the Philips IntelliSpace Portal v12.1 workstation (ISP; Philips Healthcare, Best, Netherlands). Plain MRI scanning was performed for

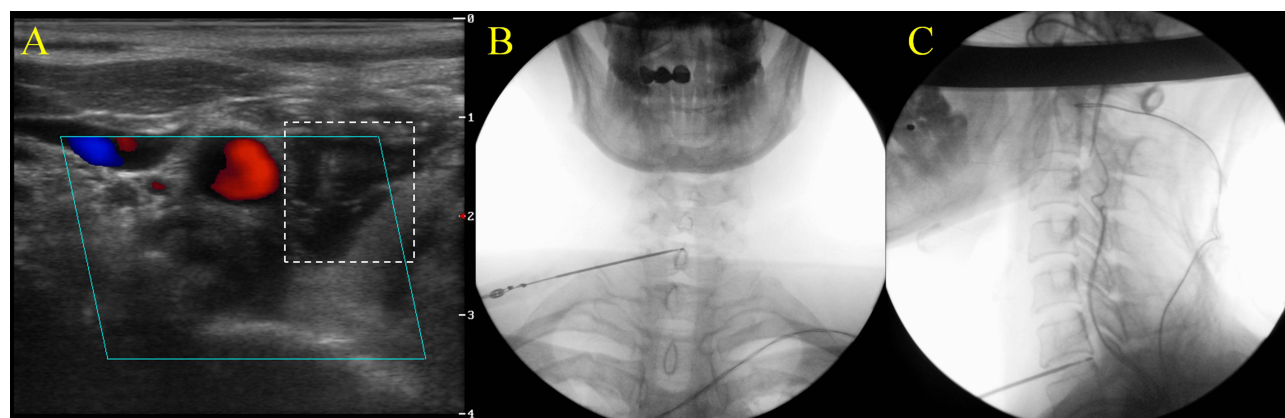


Figure 1 Ultrasonic and fluoroscopic images during surgery. **(A)** The space between the carotid and thyroid sheaths is separated by the ultrasonic-assisted injection of normal saline. The white dotted box indicates the saline injection site. The blue box displays the blood flow signal within the area. Intraoperative anteroposterior **(B)** and lateral **(C)** fluoroscopy images showing the introducer needle passing through the narrowed space.

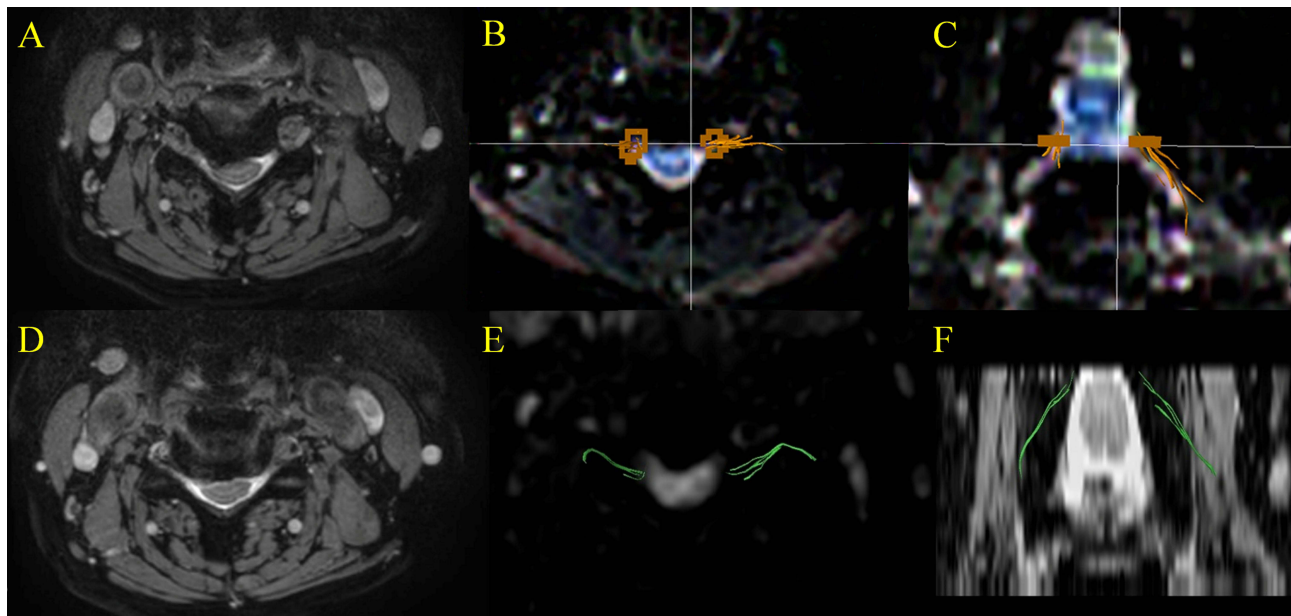


Figure 2 A 49-year-old woman with CSR underwent PCN for C6/C7 disc herniation. The integrity of postoperative nerve root fibers was significantly improved in FT images, with a normal shape and uniform fiber bundle distribution. (A) Preoperative DTI scanning. Preoperative cross (B) and coronal (C) sections of FT imaging. (D) DTI scanning and cross (E) and coronal (F) sections of FT imaging 3 months postoperatively. The Orange boxes in (B and C) represent region of interest (ROI), and the orange lines represent nerve root fibers. The green lines in (E and F) represent nerve root fibers.

sagittal plane positioning. The T2WI settings included the following: repetition time, 2,420 ms; time to echo, 69 ms; matrix, 112×112 ; field of view, 140.0×140.0 mm; slice thickness, 2 mm; flip angle, 90° ; voxel, $1.25 \times 1.25 \times 2.00$ mm; diffusion sensitivity coefficient B, 0; b value, $800 \text{ mm}^2/\text{s}$; diffusion sensitivity gradient direction, 32; and number of excitations, 4.

DTI tensor images were uploaded to the Philips workstation. First, we corrected the original DTI images to reduce the influence of motion artifacts and, thus, improve the DTI image quality and fiber tracking results. The required DTI images were generated by the diffusion software package. A region of interest (ROI) of approximately 4 mm^2 was manually drawn in the nerve root traversing area. The FA and ADC values of the region were displayed and clicked for fiber bundle tracking at the same time. The FA and ADC values were measured blinded by three radiologists, and the average value was taken as the final measurement result.

Statistical Analysis

SPSS (version 27.00; Chicago, Illinois, USA) was used for statistical analysis. In this study, continuous variables (VAS, NDI, FA and ADC) followed a normal distribution and were expressed as mean \pm standard deviation. For VAS and NDI, there were three time points before and after surgery, therefore, repeated measures ANOVA was used to compare the differences between time points, and the Bonferroni method was used for multiple calibrations. For FA and ADC, there are two time points before and after surgery, and the difference follows a normal distribution, therefore, a paired *t*-test was used to compare the differences between the two time points. DTI parameters (FA and ADC) and clinical scores (VAS and NDI) were obtained from the same patients, and there was a linear relationship between the two with no obvious outliers. Therefore, the Pearson correlation analysis was used to delineate the correlation between the DTI values and VAS or NDI scores. Correlation coefficients (*r*) were considered strong when their absolute value was ≥ 0.8 .¹⁵ A *P* value of <0.05 indicated statistical significance. The figures were created using GraphPad Prism version 9 and Photoshop software (Adobe Photoshop version 2023).

Results

A total of 30 patients, including 12 males and 18 females, were enrolled in this study, with a mean age of 60.63 ± 8.64 years (range of 45–74 years, 95% CI: 57.41–63.86) and symptom duration of 22.93 ± 8.75 months (range of 10–38

months, 95% CI: 19.67–26.20). Based on the preoperative localization of the compressed nerve roots, all patients were divided into four groups with damaged C4 (n = 2, 6.7%), C5 (n = 10, 33.3%), C6 (n = 13, 43.3%), and C7 (n = 5, 16.7%) nerve roots. The follow-up duration was 17.03 ± 3.58 months (range of 12–23 months, 95% CI: 15.70–18.37).

All surgeries were successfully completed. No vascular or nerve injury occurred during the procedure. Table 1 shows the clinical and DTI parameters between the pre- and post-operation. The preoperative VAS and NDI scores were 5.65 ± 1.04 and 25.53 ± 5.16 , respectively. After PCN, the VAS score decreased to 2.35 ± 0.75 at 3 months and 2.19 ± 0.78 at the final follow-up, and the NDI score decreased to 13.00 ± 3.42 at 3 months and 11.73 ± 5.58 at the final follow-up. All postoperative scores were significantly lower than the preoperative ones ($P < 0.001$). The preoperative and postoperative FA values were 0.39 ± 0.030 and 0.44 ± 0.025 , respectively. Meanwhile, the preoperative and postoperative ADC values were 1.48 ± 0.101 and 1.23 ± 0.076 , respectively. The postoperative DTI values were significantly different from the preoperative ones ($P < 0.001$).

The Pearson correlation coefficient between the DTI quantitative values and clinical function scores showed that preoperative FA values were strongly correlated with preoperative NDI ($r = -0.802$, $P < 0.001$). Postoperative FA values were strongly correlated with postoperative NDI ($r = -0.804$, $P < 0.001$). Postoperative FA values were strongly associated with NDI scores at the final follow-up ($r = -0.805$, $P < 0.001$) (Figure 3). We revealed no significant correlations between DTI and VAS scores (Table 2). Similarly, no significant correlations were observed between ADC and NDI scores pre- and postoperatively. Therefore, we indicate the use of postoperative FA values in predicting patient prognosis after PCN.

Discussion

DTI has been reported predominantly as an adjunctive test for degenerative cervical diseases to diagnose disease severity and recovery prognosis.^{16–18} However, literature investigating the association between DTI and CSR remains limited. FA and ADC values are important indicators for assessing neurophysiological status.^{6,8} In the present study, we revealed higher FA and lower ADC values postoperatively than preoperatively, which was similar to the results of previous studies.^{7,19} Furthermore, we revealed a strong association between NDI scores and FA values, including preoperative NDI scores with preoperative FA and postoperative NDI scores with postoperative FA values. However, notably, no strong correlation was observed between DTI and VAS scores. Therefore, the association between NDI scores and FA values is a potential predictor of patient prognosis and provides auxiliary information for postoperative rehabilitation.

Traditional anterior cervical discectomy and fusion is the gold standard for treating CSR, which requires the placement of internal fixation devices during surgery.²⁰ However, the presence of internal fixation devices greatly increases DTI artifact interference. In the present study, 30 patients with CSR consecutively underwent minimally invasive PCN, which has the advantage of avoiding the effects of implants on DTI.²¹ Before PCN, FT imaging was performed, which is a rare noninvasive imaging method for the visualization of white matter fibers. The images showed that the nerve roots on the affected side were displaced, thinning, and tortuous and the arrangement of nerve fibers was sparse and broken, which was consistent with previous studies involving fiber tracing technology.²² When MRI demonstrates inconsistent imaging features with the patient's symptoms, DTI and tractography further improve the diagnosis by visualizing and accurately locating the area of nerve root compression without the option of invasive neurophysiology or nerve root block.⁶ Currently, several studies have explored the comparison between multiple

Table 1 Comparison of the Clinical and DTI Parameters Between the Pre- and Post-Operation

Scores and Parameters	Preoperative	3 Months Postoperative	P	Preoperative	Final Follow-up	P
VAS	5.65 ± 1.04	2.35 ± 0.75	$<0.001^*$	5.65 ± 1.04	2.19 ± 0.78	$<0.001^*$
NDI	25.53 ± 5.16	13.00 ± 3.42	$<0.001^*$	25.53 ± 5.16	11.73 ± 5.58	$<0.001^*$
FA	0.39 ± 0.030	0.44 ± 0.025	$<0.001^*$	-	-	-
ADC	1.48 ± 0.101	1.23 ± 0.076	$<0.001^*$	-	-	-

Notes: *Statistically significant at $p < 0.05$.

Abbreviations: VAS, visual analog scale; NDI, neck disability index; FA, fractional anisotropy; ADC, apparent diffusion coefficient.

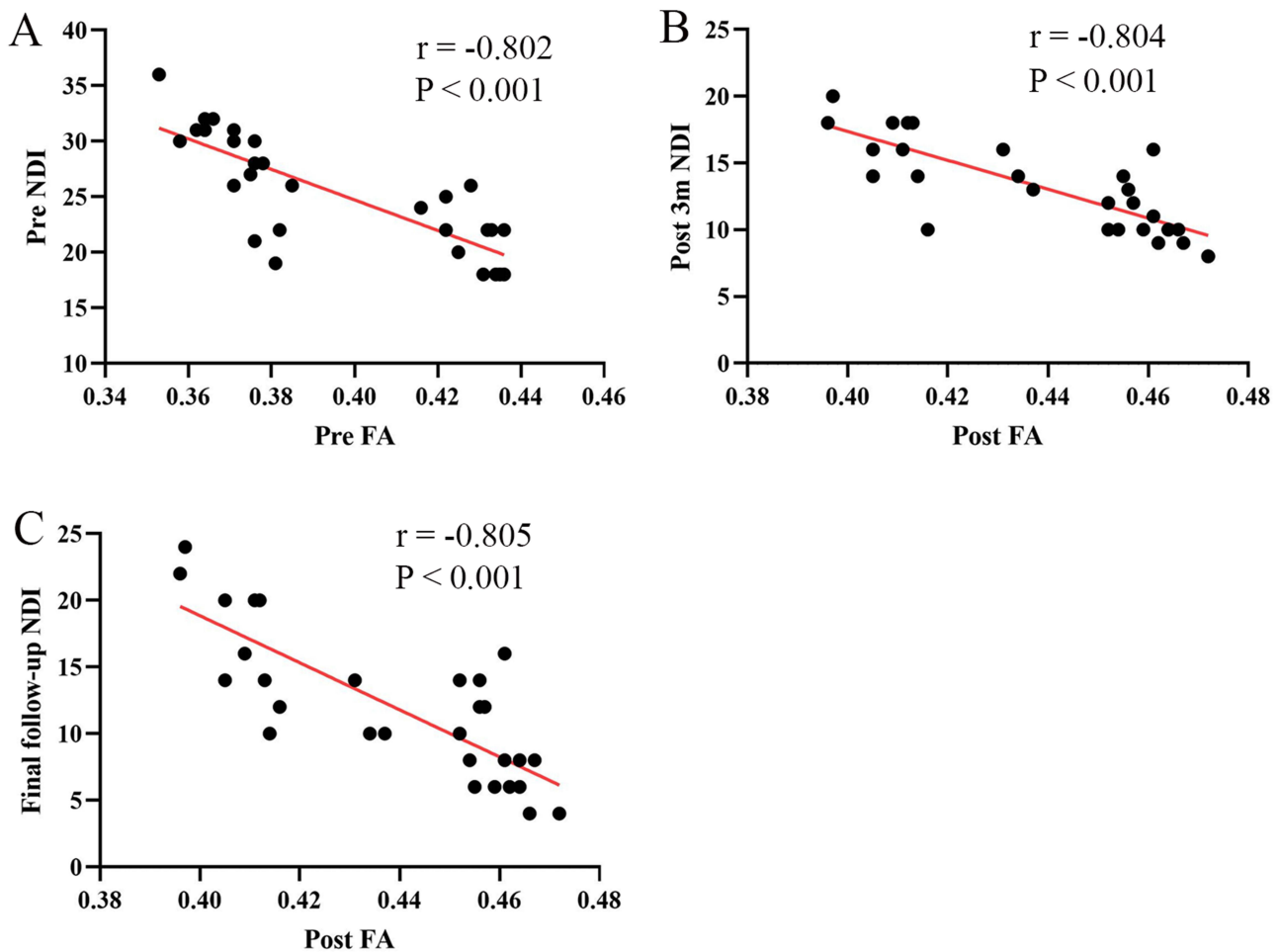


Figure 3 The Pearson correlation coefficient between the FA values and NDI scores. FA values were negatively associated with NDI scores preoperatively (A) and postoperatively (B). Furthermore, postoperative FA values were negatively associated with NDI scores at the final follow-up (C).

treatments and PCN for patients with CSR, such as PCN,²³ anterior discectomy,²⁴ and pulsed RF.²⁵ The aforementioned studies have concluded that PCN demonstrate advantages in terms of reduced trauma, decreased blood loss, and faster recovery. Accurate diagnosis of CSR combined with minimally invasive treatment can avoid extensive decompression

Table 2 Correlation Between DTI Parameters and Clinical Scores

	Clinical Scores	DTI Parameters	r	P
VAS	Preoperative	Preoperative FA	-0.031	0.869
		Preoperative ADC	0.145	0.444
	3 months postoperative	Postoperative FA	-0.677	<0.001*
		Postoperative ADC	0.358	0.052
	Final follow-up	Postoperative FA	-0.651	<0.001*
		Postoperative ADC	0.436	0.016*
NDI	Preoperative	Preoperative FA	-0.802	<0.001*
		Preoperative ADC	0.153	0.420
	3 months postoperative	Postoperative FA	-0.804	<0.001*
		Postoperative ADC	0.346	0.061
	Final follow-up	Postoperative FA	-0.805	<0.001*
		Postoperative ADC	0.451	0.012*

Notes: *Statistically significant at p<0.05.

Abbreviations: DTI, diffusion tensor imaging; VAS, visual analog scale; NDI, neck disability index; FA, fractional anisotropy; ADC, apparent diffusion coefficient; r, The correlation coefficient.

common in conventional open surgery and reduce the complexity and risk of surgical procedures.²⁶ In this study, we revealed that the patient's postoperative clinical function scores were significantly improved compared with the preoperative scores, and no serious postoperative complications, such as hematoma and spinal cord injury, were reported, indicating that PCN treatment for CSR achieved satisfactory clinical efficacy.

In general, once a transition from moderate to high T2WI signal is observed on conventional MRI, the nerve root is in a long-term injury state, indicating an unsatisfactory prognosis even after surgical treatment.^{27,28} Therefore, early accurate diagnosis of CSR is particularly important for improving patients' quality of life. Kara²⁹ enrolled 16 patients with neurological signs but without hyperintensity in the spinal cord on T2WI. This finding shows that DTI may indicate abnormalities in the spinal cord before the hyperintensity of conventional T2WI. Kerkovský³⁰ suggested that DTI has a higher potential to distinguish clinical subtypes than conventional MRI and electrophysiological examination. Compared with traditional MRI, DTI shows more sensitivity and specificity for subtle cervical nerve lesions. Liang³¹ compared 30 patients with CSR with 24 healthy volunteers and found that the FA values of C5–C8 in healthy volunteers and heterolateral nonstenotic nerve of patients with CSR were both significantly higher than those of the stenotic cervical segments of patients with CSR, with lower ADC values. In this study, we observed similar changes in FA and ADC after nerve root decompression after PCN.

FA is the most commonly used diffusion tensor index, which represents the direction of the diffusion of water molecules. A decrease in the FA value is considered to be due to the impairment of the cell membrane and myelin barrier function of nerve fibers, and the diffusion of water molecules tends to be isotropic.³² Previous studies have shown that both mechanical compression and microenvironment changes can affect the DTI quantitative values.³³ We found that the FA values were negatively correlated with the NDI scores. This result agrees with Chen et al³⁴ suggesting that disease severity in patients can be assessed by DTI to some extent. Furthermore, we revealed that NDI scores at 3 months postoperatively and the last follow-up remained strongly associated with postoperative FA levels, indicating a correlation between NDI scores and FA values as a potential prognostic predictor in patients with CSR. However, we did not find a strong correlation between FA values and VAS scores, which may be related to the following reasons: VAS assessments are easily influenced by patient subjectivity, and chronic pain perception is affected by physiological, psychological, and social factors.³⁵ Since FA primarily reflects microscopic changes in neural structures,³⁴ the incomplete overlap in mechanisms between the two may weaken the strength of the association. Therefore, future studies should integrate objective pain assessment tools such as quantitative sensory testing (QST), and explore multi-parameter models (eg, FA combined with T2WI signals) to enhance predictive performance.¹⁸

Few studies have focused on the relationship between changes in DTI indicators and improvement in clinical symptoms after surgery. Traditional MRI can only reflect the cervical disc that is no longer herniated after surgery. However, the compressed nerve root can still maintain a high signal on T2WI, even enhanced in a short period of time; therefore, it is difficult to evaluate the recovery of patients.³⁶ In addition, when dealing with complex cervical disc herniation, PCN sometimes fails to adequately decompress the compressed nerve root, resulting in the residue continuing to compress or irritate the nerve root, which manifests as incomplete symptom relief. Thus, there is an urgent need for effective tools to assist in the assessment of postoperative recovery of patients. DTI is an effective auxiliary assistant for postoperative evaluation of efficacy to some extent. The improvement in the FA value is closely related to axon regeneration, as the axonal membrane of nerve fibers plays a major limiting role in the anisotropic movement of water molecules, and the formation of myelin sheath can assist in regulating the anisotropic diffusion of water molecules.³⁷ If the FA value shows no significant improvement after surgery, it may reflect the persistence of nerve root injury and poor prognosis. Under these circumstances, reoperation should be considered as soon as possible to improve the prognosis of patients.

The ADC value reflects the diffusion rate of water molecules in the microenvironment of biological tissues without directionality.³⁸ Higher ADC values are usually associated with severe tissue damage, which may affect the recovery and prognosis of patients after surgery.³⁹ The lower the ADC quantization value, the less severe the spinal degenerative disease and the better the postoperative recovery of the nervous system. However, in this study, we revealed no strong association between ADC and clinical function scores. Therefore, further studies are warranted to investigate the correlation between ADC and patient prognosis in the future. Our study selected an MS-EPI sequence for DTI imaging.

Although the scanning time is longer and the patient needs to strictly brake, this imaging method has a higher image signal-to-noise ratio and spatial resolution; therefore, it is more beneficial for tracking nerve fiber tracts.⁴⁰

In addition, our study has some limitations. First, this is a retrospective study with a small sample size, providing limited clinical evidence. A multicenter study with a large sample size may be needed in the future. Second, the follow-up time of this study was short, and the long-term imaging data of some patients were incomplete. We will further investigate the long-term changes in the DTI quantitative values. Finally, the ROI region in this experiment was selected manually, which had a certain subjectivity. It is expected to improve the accuracy by assisting the algorithm in the determination of DTI values.

Conclusion

PCN is an effective surgical procedure for treating patients with CSR. DTI is an imaging method that helps identify the clinical functional status of patients with CSR after PCN. The FA value can be used as a potential predictor of patient prognosis and are strongly negatively correlated with NDI scores. However, the long-term predictive effect warrants further investigation. In the future, large-scale, multi-center studies will need to be conducted, and it is hoped that the accuracy of predictions can be improved through the application of auxiliary algorithms.

Abbreviations

DTI, diffusion tensor imaging; CSR, cervical spondylotic radiculopathy; PCN, percutaneous cervical nucleoplasty; FA, fractional anisotropy; ADC, apparent diffusion coefficient; NDI, neck disability index; VAS, visual analog scale; MRI, magnetic resonance imaging; CT, computed tomography; FT, fiber tractography; MS-EPI, multishot echo planar imaging; ROI, region of interest; T2WI, T2-weighted imaging.

Data Sharing Statement

The original contributions presented in the study are included in the article, further inquiries can be made available by the corresponding authors without undue reservation.

Ethics Approval and Consent to Participate

The studies involving humans were approved by the institutional review board at Beijing Chaoyang Hospital, Capital Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Disclosure

The authors report no conflicts of interest in this work.

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