ORIGINAL ARTICLE

Analysis of radiological parameters associated with decreased fractional anisotropy values on diffusion tensor imaging in patients with lumbar spinal stenosis

Xiandi Wang[1] · Hongli Wang[1] · Chi Sun[1] · Shuyi Zhou[2] · Tao Meng[3] · Feizhou Lv[1] · Xiaosheng Ma[1] · Xinlei Xia[1] · Jianyuan Jiang[1]

Abstract

Purpose Previous studies have indicated that decreased fractional anisotropy (FA) values on diffusion tensor imaging (DTI) are well correlated with the symptoms of nerve root compression. The aim of our study is to determine primary radiological parameters associated with decreased FA values in patients with lumbar spinal stenosis involving single L5 nerve root.

Methods Patients confirmed with single L5 nerve root compression by transforaminal nerve root blocks were included in this study. FA values of L5 nerve roots on both symptomatic and asymptomatic side were obtained. Conventional radiological parameters, such as disc height, degenerative scoliosis, dural sac cross-sectional area (DSCSA), foraminal height (FH), hypertrophic facet joint degeneration (HFJD), sagittal rotation (SR), sedimentation sign, sagittal translation and traction spur were measured. Correlation and regression analyses were performed between the radiological parameters and FA values of the symptomatic L5 nerve roots. A predictive regression equation was established.

Results Twenty-one patients were included in this study. FA values were significantly lower at the symptomatic side comparing to the asymptomatic side (0.263 ± 0.069 vs. 0.334 ± 0.080, $P = 0.038$). DSCSA, FH, HFJD, and SR were significantly correlated with the decreased FA values, with $r = 0.518$, 0.443, 0.472 and -0.910, respectively ($P < 0.05$). DSCSA and SR were found to be the primary radiological parameters related to the decreased FA values, and the regression equation is $FA = -0.012 \times SR + 0.002 \times DSCSA$.

Conclusions DSCSA and SR were primary contributors to decreased FA values in LSS patients involving single L5 nerve root, indicating that central canal decompression and segmental stability should be the first considerations in preoperative planning of these patients.

Xiandi Wang and Hongli Wang contributed equally to this article.

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Key points

[List your key words here]

1. Diffusion Tensor Imaging
2. Fractional Anisotropy
3. Nerve Roots
4. Lumbar Spinal Stenosis
5. Radiological Parameters

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1. Diffusion Tensor Imaging of lumbar spinal nerve roots has the potential to assist the diagnosis and surgical planning of lumbar spinal stenosis

2. Sagittal rotation is more related to nerve root compression than sagittal translation

3. Central canal decompression and segmental stability should be the first considerations in preoperative planning of patients with lumbar spinal stenosis involving single L5 nerve

[Citation]

Keywords Diffusion tensor imaging · Fractional anisotropy · Nerve roots · Lumbar spinal stenosis · Radiological parameters

Introduction

Lumbar spinal stenosis (LSS), defined as narrowing of the central, lateral spinal canal or intervertebral foramen, leads to substantial functional disability [1]. Degeneration of the intervertebral discs, facet joints and ligaments surrounding the vertebral canal together causes nerve root compression, resulting in the symptoms of neurogenic claudication [1]. LSS, with an estimated incidence of 9% in general populations and 47% in populations over 60 years [2], is considered the most common reason for spinal surgery in patients over 65 years [3]. Mechanical compression, ischemia and chemical irritations of the nerve roots are important mechanisms of neurologic symptoms in LSS [4]. The diagnosis of LSS depends on neurologic symptoms, physical examination, and significant imaging changes.

X-ray radiography, CT, MRI or their combinations remain standard imaging tools for the diagnosis of LSS [5]. However, clinical presentations and radiological findings are not always consistent. Therefore, researchers have endeavored to explore novel techniques to improve the accuracy of LSS diagnosis. Diffusion tensor imaging (DTI) with fiber tracking is a new MRI-based imaging technique [6] and has been widely used to demonstrate the functional connections of the central nervous system [7]. Unlike CT and conventional MRI, DTI can identify microstructures in nervous tissues by describing variations in water diffusion directions, known as diffusion anisotropy [8]. In nervous tissues, diffusion anisotropy is primarily caused by cellular membranes, with contributions from myelination and the packing of the axons. A fractional anisotropy (FA) value ranging from 0 to 1 is the most commonly used quantitative diffusion value to reflect the directionality of molecular diffusion [8]. A greater FA value indicates anisotropic diffusion, while a lower FA value indicates more isotropic diffusion in tissues [9].

Recently, increasing numbers of studies have reported the use of DTI in peripheral nerves, including median nerves, trigeminal nerves and lumbar spinal nerve roots [10, 11]. In LSS patients, FA values were found to be significantly lower in compressed nerve roots, and studies illustrated that decreased FA values were significantly associated with clinical symptoms in LSS patients [12]. However, no study has been performed to explore the possible correlation between radiological parameters and decreased FA values. Therefore, we designed this study to identify primary radiological parameters related to a decreased FA value in LSS patients with single L5 nerve root involvement, in an attempt to improve the diagnostic accuracy and surgical strategies of LSS.

Materials and methods

Patient population

We recruited our study subjects in a 1-year period from December 2015 to December 2016. Patients who were initially recruited to our study met the following criteria: (1) typical symptoms of neurogenic intermittent claudication on the unilateral side, (2) negative straight-leg raising signs on physical examination, and (3) radiological clues of limited L5/S1 spinal canal stenosis. Patients with previous histories of spinal trauma, surgery, infection, claustrophobia or other psychological problems were excluded from the study. All patients were given DTI scan after admission and were arranged for unilateral transforaminal L5 nerve root block at the symptomatic side. Those who responded well to the nerve root block were finally included in this study, and their radiological data were retrieved for further analysis. This study was approved by the Institutional Review Board of Huashan Hospital of Fudan University (Shanghai, China),

and all participating patients singed informed consent for the study.

DTI protocol

All included patients received DTI scan in a supine position using the 3-T scanner (Siemens Magnetom Verio, Erlangen, Germany with a six-channel body coil. DTI was performed using echo-planar imaging (EPI) sequence with a free-breathing scanning technique. The imaging parameters were as follows: b value: 0 and 800 s/mm^2; MPG, 30 directions; 6000/76 ms for TR/TE, respectively; axial section orientation, 3/0.9-mm slice thickness/gap; 320×255 mm^2 FOV; 128×102 matrix; $2.5 \times 2.0 \times 3.0$ mm^3 actual voxel size; 25 total slices; and 6 min 21 s scan time. Axial T2-weighted anatomical images were also obtained by using the following protocol: T2 turbo-spin-echo (TSE) sequence with variable flip angle RF excitations (SPACE: sampling perfection with application optimized contrasts using different flip angle evolutions): TR/TE 3200/335 ms, FOV 90×200 mm, and section thickness/gap 3/1 mm.

Post-processing of DTI data

Data post-processing, such as determining the independent elements of the diffusion tensor, deriving the corresponding eigenvalues and eigenvectors, and reconstructing was performed using dedicated software (Neuro 3D; Siemens Healthcare AG). Axial T2-weighted anatomical images were overlaid on the DTI data to permit the anatomical correlation. FA values were measured on both symptomatic side and asymptomatic side along the path of L5 spinal nerve root at three levels, where the spinal nerve root passed: intraspinal, intraforaminal and extraforaminal regions (Fig. 1). Free-hand regions of interest (ROI) tools were used to manually outline the nerve root on axial T2 TSE anatomical images, and correspondent ROIs were synchronized to the fused anatomic-tensor mapping images (Fig. 2). FA values within the ROIs could be read in the software and averaged FA values were used in our statistical analysis.

Radiological parameter measurement

Radiological parameters were measured by two experienced spine surgeons who were blind to the patients' information except for the side of the symptoms. X-ray radiography and CT were performed using the picture-archiving and communication system (PACS). In the anterior–posterior (AP) view, the following radiological parameters were obtained: disc height (DH), defined as the mean of anterior and posterior heights [13]; foraminal height (FH), measured as the maximum distance between the inferior margin of the pedicle of the superior vertebra and the superior margin of the pedicle
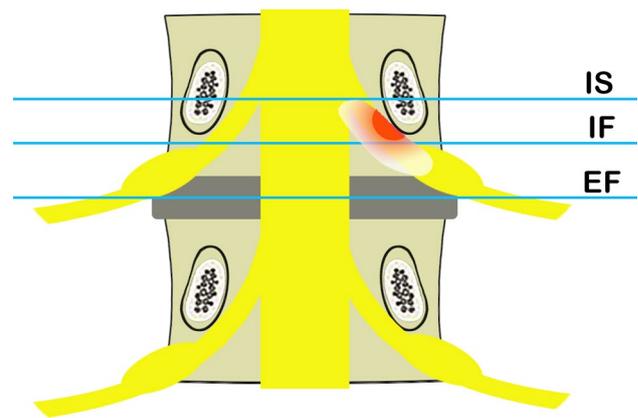

Fig. 1 Diagram showing that the regions of interest (ROIs) were placed along the path of L5 spinal nerve root at three levels [intraspinal (IS), intraforaminal (IF) and extraforaminal (EF)] regions where the spinal nerve root passed

of the inferior vertebra [14]. Whether the patients had traction spur (TS) or degenerative scoliosis (DS) was recorded as 0 for negative findings, and 1 for positive findings. In the flexion–extension X-rays, sagittal translation (ST) and sagittal rotation (SR) were measured using the method described in previous articles [15]. In CT scans with coronal and sagittal plane reconstruction, hypertrophic facet joint degeneration (HFJD) was evaluated on the symptomatic side. HFJD is a four-degree grading system ranging from 0 to 3, where 0 represents no obvious degeneration, and 3 represents severe degeneration. Grading criteria were as follow: grade 0: normal facet joint space (2–4 mm width); grade 1: narrowing of the facet joint space (< 2 mm) and/or small osteophytes and/or mild hypertrophy of the articular processes; grade 2: narrowing of the facet joint space and/or moderate osteophytes and/or moderate hypertrophy of the articular processes and/or mild subarticular bone erosions; grade 3: narrowing of the facet joint space and/or large osteophytes and/or severe hypertrophy of the articular processes and/or severe subarticular bone erosions and/or subchondral cysts [16]. MRI assessments were performed on Siemens work station (Magic View 1000; Erlangen, Germany). Sedimentation sign (SS), which refers to the sedimentation of the cauda equina to the dorsal part of the dural sac [17], was evaluated on T1- and T2-weighted sequences. Dural sac cross-sectional area (DSCSA) was measured at L5/S1 intervertebral disc level, using the method described in previous studies [18].

Statistical analysis

Statistical analyses were performed using SPSS 17.0 statistics software (SPSS Inc., Chicago, IL). Descriptive statistics were listed in the form of mean and standard deviation (SD). Student t test was used in the comparison of FA
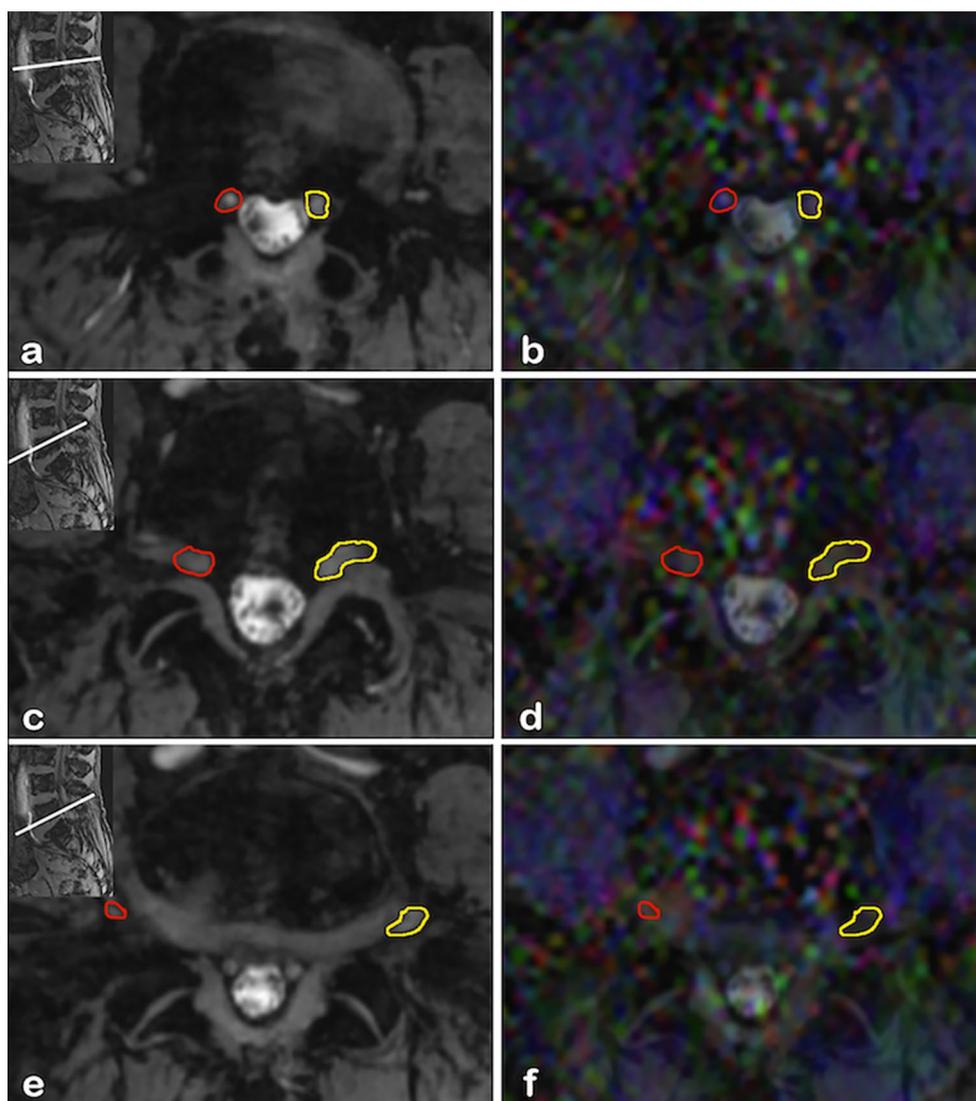
Fig. 2 A 73-year-old man with a 1-year history of left-leg intermittent claudication. Selective nerve root block confirmed the patient with single left L5 nerve root involvement. Regions of interest (ROIs) of the symptomatic side (yellow) and asymptomatic side (red) were selected manually on T2-TSE anatomical images (**a**–**c**). Colored fractional anisotropy (FA) maps were overlapped to the anatomical images, and ROIs were automatically synchronized to the fused images (**b**, **d**, **f**). The FA values of the L5 nerve root at symptomatic side versus asymptomatic side were as follow: intraspinal region (**a**, **b**): 0.224 vs. 0.301, intraforaminal region (**c**, **d**): 0.161 vs. 0.324, and extraforaminal region (**e**, **f**): 0.223 vs. 0.332. Mean FA value of L5 spinal nerve root at symptomatic versus asymptomatic side is 0.203 vs. 0.319

values between the symptomatic and asymptomatic side. The correlation of decreased FA values and radiological parameters was analyzed by correlation coefficient test: $r < 0.2$: a very weak correlation; $0.2 \leq r < 0.4$: a weak correlation; $0.4 \leq r < 0.6$: a moderate correlation; $0.6 \leq r < 0.8$: a very good correlation; $r \geq 0.8$: an excellent correlation. Multiple linear regression analysis was conducted to find out the independent association between potential parameters and decreased FA values, and then regression equation was established. Furthermore, paired t test was also conducted to test the significance of correlation and the regression equation. $P < 0.05$ was considered statistically significant.

Results

Forty-five patients were initially recruited to our study. Twenty-one patients were confirmed with single L5 nerve root compression by transforaminal selective nerve root block and were finally included in this study. Mean age of these patients was 66.6 (range 50–79) years with a male/

female ratio of 10:11. FA value was significantly lower on the symptomatic side comparing to the asymptomatic side, with 0.263 ± 0.069 and 0.334 ± 0.080, respectively ($P = 0.038$). Lumbar X-ray A–P view showed that DH and FH were 8.9 ± 2.5 and 12.4 ± 4.0 mm, respectively. TS was observed in 12 (57.1%) patients and DS in 11 (52.4%) patients. X-ray with the extension and flexion position showed that ST was 1.9 ± 1.1 mm and SR $12.8° \pm 4.9°$ in these patients. CT scan assessing the facet joint on the symptomatic side using HFJD grading system showed: grade 0 in 5 (23.8%) cases, grade 1 in 5 (23.8%) cases, grade 2 in 5 (23.8%) cases, and grade 3 in 6 (28.6%) cases. Central canal and cauda equina were observed on MRI which indicated DSCSA was 64.5 ± 16.1 mm^2 and 16 (76.2%) patients were positive for SS (Table 1.).

Pearson correlation coefficient test indicated an excellent correlation between decreased FA values and SR ($r = -0.91$, $P = 0.001$); a moderate correlation between decreased FA values and DSCSA ($r = 0.518$, $P = 0.016$), FH ($r = 0.443$, $P = 0.044$), and HFJD ($r = 0.472$, $P = 0.031$) (Fig. 3). No significant correlation was observed between decreased FA values and DH, TS, DS, ST and SS (all $P > 0.05$) in these patients. All the data are shown in Table 2. Multiple

Table 1 General characteristics of the included subjects

	Maximum	Minimum	Mean	SD
Demographic parameters				
Age (years)	79	50	66.6	9.1
BMI (kg/m^2)	25	19	22.1	1.9
Gender (M/F)	10/11			
X-ray parameters				
Plain X-ray parameters				
DH (mm)	13.0	5.6	8.9	2.5
FH (mm)	20.4	4.7	12.4	4.0
TS (±)	12/9			
DS (±)	11/10			
Flexion–extension X-ray parameters				
ST (mm)	4.0	0.0	1.9	1.1
SR (°)	20.2	4.0	12.8	4.9
CT parameters				
HFJD (0/1/2/3)		5/5/5/6		
MRI parameters				
DSCSA (mm^2)	88.9	25.0	64.5	16.1
SS (±)	16/5			
FA value				
Symptomatic	0.416	0.134	0.263	0.069
Asymptomatic	0.459	0.198	0.334	0.080

BMI body mass index, *DH* disc height, *DS* degenerative scoliosis, *DSCSA* dural sac cross-sectional area, *DTI* diffusion tensor imaging, *FA* fractional anisotropy, *FH* foraminal height, *HFJD* hypertrophic facet joint degeneration, *SR* sagittal rotation, *SS* sedimentation sign, *ST* sagittal translation, *TS* traction spur

linear regression analysis was conducted by using parameters found to be significantly correlated with decreased FA values. The results showed that SR ($P = 0.005$) and DSCSA ($P = 0.018$) were the primary contributors to decreased FA values in LSS patients. FA values in LSS could be predicted by the regression equation: $FA = -0.012 \times SR + 0.002 \times DSCSA$ (Table 3). Furthermore, the paired t test showed no significant difference between the actual and predicted FA values using our equation ($P = 0.300$).
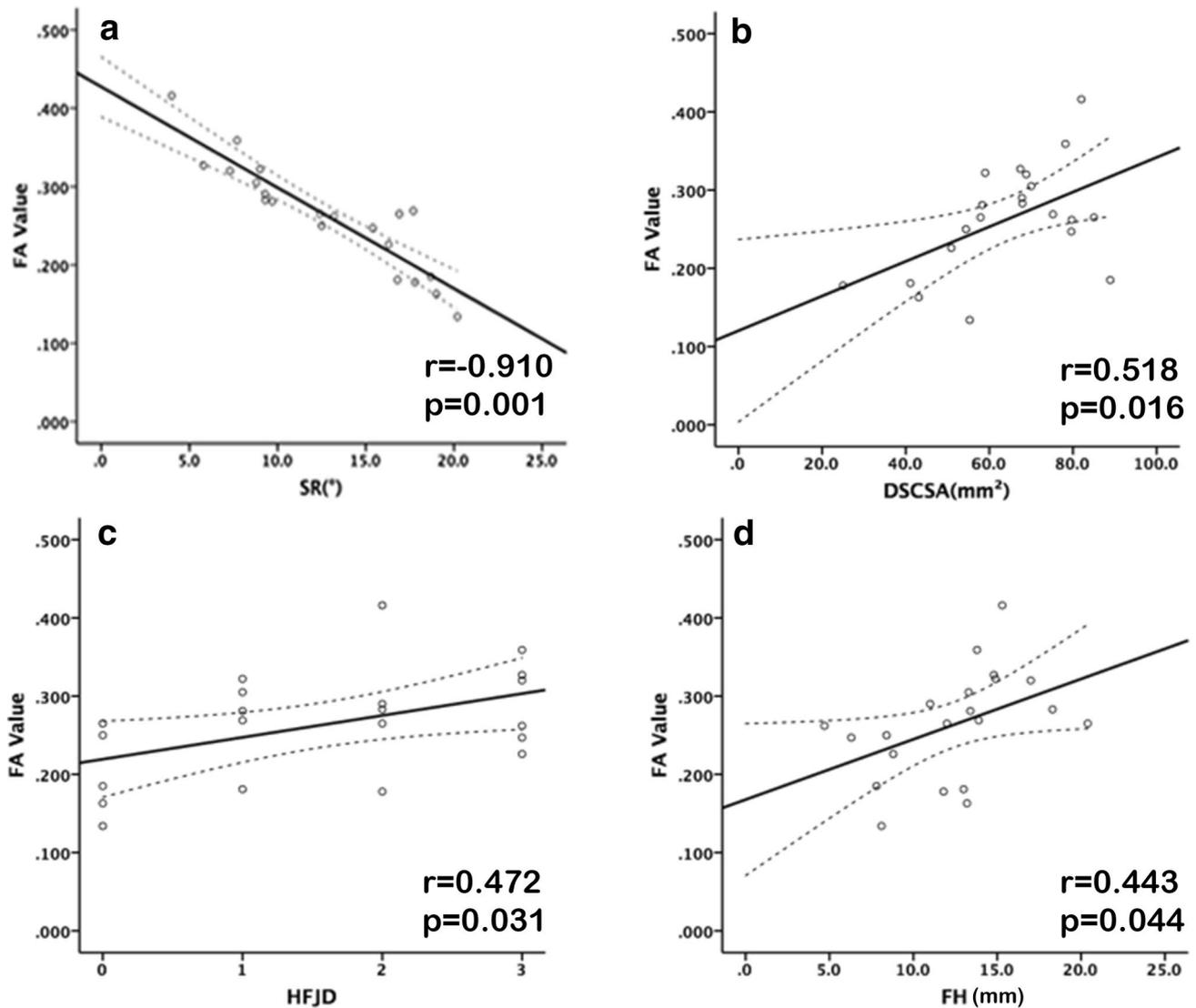
Discussion

Diagnosis of LSS requires the combination of clinical symptoms, physical examinations and imaging (including X-ray radiography, CT, and MRI). However, there is no substantive relationship between the neurological symptoms and levels or ranges of stenosis on radiographs [18]. Some methods have been proposed to improve the diagnostic accuracy of patients with LSS, such as selective nerve root block, semi-quantitative and quantitative radiological measurements [17], electromyography (EMG) and computed tomography myelography (CTM) [19]. In recent years, the importance of DTI as a complementary method in the diagnosis of nerve root compression in LSS is gaining increasing attention [20, 21]. Some studies reported normal FA values in healthy individuals and decreased values in patients with LSS [12]. However, no study has been performed to explore the correlation between radiological parameters and decreased FA values in these patients. Therefore, we conducted this study to determine the primary radiological parameters associated with decreased FA values in patients with LSS, aiming to improve the accuracy of diagnosis and provide references for surgical strategies.

Our results showed that FA values in LSS patients involving single L5 nerve root ranged from 0.134 to 0.416, which was significantly lower than the asymptomatic side and those reported in asymptomatic subjects [12, 22]. Some reasons could explain this phenomenon. On the one hand, mechanical compression and inflammations can lead to decreased blood flow and ischemia of the spinal nerve roots, consequently resulting in Wallerian degeneration and endoneurial fibrosis. These microstructural changes may affect water diffusion within the nerve roots by increasing the diffusion distance, leading to increased diffusion perpendicular to the largest eigenvalue and decreased FA values [23]. On the other hand, inflammation caused by immunochemical factors as well as mechanical compression could lead to a series of pathophysiological changes of the compressed lumbar spinal nerve, including edema, congestion and accelerated vascular permeability [24]. Olmarker et al. [25] found that lumbar spinal nerve roots were more likely to develop intraneural edema than peripheral nerves. Thus, water molecule

Fig. 3 Graphs showing the correlations between fractional anisotropy (FA) values and radiological parameters. **a** An excellent correlation between decreased FA values and SR ($r = -0.910$, $P = 0.001$), **b–d** a moderate correlation between decreased FA values and DSCSA ($r = 0.518$, $P = 0.016$), HFJD ($r = 0.472$, $P = 0.031$) and FH ($r = 0.443$, $P = 0.044$). *DSCSA* dural sac cross-sectional area, *FH* foraminal height, *HFJD* hypertrophic facet joint degeneration, *SR* sagittal rotation

diffusion in edematous tissues might become more isotropic. Fluid trapped in such tissues may create an isotropic environment to decrease the FA value [26]. Furthermore, the decrease in the FA value was reported to be significantly correlated with the decreased number of axons in animal experiments [12].

Correlation coefficient test indicated that decreased FA value was correlated with FH, while there was no significant correlation between decreased FA values and other parameters on plain X-rays (including DH, TS, and DS). Hasegawa et al. [23] evaluated 100 foramens from 18 cadavers and found that FH less than 15 mm was related to lumbar spinal nerve compression. Our results were similar to their

findings with an average FH of 12.4 mm. Based on our findings, we recommend that it should be an important concern to restore FH and gain a sufficient foraminal decompression of the nerve roots with significantly decreased FA. A significant correlation was also observed between SR and decreased FA values in our study. SR is regarded as primary evaluation of lumbar spinal stability. Lumbar spine degeneration begins at an early stage as hypermobility of the motion segmentation due to the intervertebral disc degeneration and followed by hypomobility when degeneration becomes more severe. With a larger range of extension in the instable lumbar spine, the ligamentum flavum bulges into the lumbar spinal canal posteriorly which leads to dynamic

Table 2 Correlation between FA values and radiological parameters

		DH	FH	TS	DS	ST	SR	HFJD	DSCSA	SS	FA
	P										
DH	r	1									
	P	–									
FH	r	0.031	1								
	P	0.894	–								
TS	r	− 0.147	0.202	1							
	P	0.525	0.381	–							
DS	r	0.289	− 0.337	− 0.055	1						
	P	0.204	0.135	0.813	–						
ST	r	− 0.121	0.121	− 0.074	− 0.168	1					
	P	0.601	0.602	0.749	0.467	–					
SR	r	− 0.14	0.508*	0.070	− 0.154	0.122	1				
	P	0.546	0.019	0.763	0.506	0.599	–				
HFJD	r	0.289	0.102	0.012	0.395	− 0.108	0.209	1			
	P	0.204	0.661	0.959	0.076	0.641	0.363	–			
DSCSA	r	− 0.274	0.062	− 0.008	− 0.237	− 0.12	0.153	0.273	1		
	P	0.230	0.788	0.973	0.300	0.605	0.509	0.231	–		
SS	r	0.188	− 0.244	− 0.258	0.362	− 0.149	− 0.053	0.084	− 0.258	1	
	P	0.415	0.287	0.258	0.106	0.52	0.821	0.716	0.259	–	
FA	r	− 0.194	0.443*	− 0.188	− 0.203	0.09	− 0.910*	0.472*	0.518*	− 0.036	1
	P	0.399	0.044	0.413	0.377	0.697	0.001	0.031	0.016	0.876	–

DH disc height, *DS* degenerative scoliosis, *DSCSA* dural sac cross-sectional area, *DTI* diffusion tensor imaging, *FA* fractional anisotropy, *FH* foraminal height, *HFJD* hypertrophic facet joint degeneration, *SR* sagittal rotation, *SS* sedimentation sign, *ST* sagittal translation, *TS* traction spur

$*P<0.05$

Table 3 Multiple linear regression analysis between FA values and FH, SR, HFJD and DSCSA

	B	Standard error	T	P
Constant	0.018	0.046	0.395	0.698
FH	0.002	0.003	0.873	0.395
SR	− 0.012	0.002	− 8.800 s	0.005
HFJD	0.015	0.008	1.803	0.090
DSCSA	0.002	0.001	2.628	0.018

Regression equation: FA = − 0.012 × SR + 0.002 × DSCSA

DSCSA dural sac cross-sectional area, *FA* fractional anisotropy, *FH* foraminal height, *HFJD* hypertrophic facet joint degeneration, *SR* sagittal rotation

compression of the nerve roots. This may explain why SR was found to be significantly correlated with decreased FA values in patients with LSS. However, ST, another radiological parameter for lumbar stability in flexion–extension X-ray, was not found to be significantly correlated with decreased FA values in our study. Our study also illustrated that HFJD was correlated with decreased FA values. Facet joint degeneration is characterized by facet joint arthritis and hypertrophy, resulting in an excessive formation of osteophytes and may cause compression of lumbar spinal nerve roots.

Therefore, it is reasonable to deduce that the more severe the degeneration of facet joints is, the lower the FA value of the affected spinal nerve roots would be. Furthermore, we found that DSCSA was another important parameter associated with decreased FA values in LSS patients. DSCSA is a parameter related to central spinal canal stenosis, and it is a comprehensive reflection of disc herniation, hypertrophy of the facet joint, and inward folding of the ligamentum flavum. All these potential factors mentioned above may also cause nerve root compression, resulting in decreased FA values. Our study did not show any significant correlation between SS and decreased FA values. SS was first reported by Barz et al. [17] and has proven to be sensitive and efficient in patients with LSS. However, SS was reported to be inaccurate and not sensitive in predicting the compression of nerve roots at the L5/S1 level, due to the distribution and tension of the cauda equina [27].

Finally, we performed a multiple linear regression analysis and calculated the regression equation of FA values. The results indicated that SR and DSCSA were the most important factors that may result in the compression of nerve roots and decrease the FA value in LSS with single L5 nerve root involvement. FH and HFJD that were omitted in the regression analysis. This may be because that decreased FH and

higher grade HFJD could have a direct impact on DSCSA, which then indirectly affects FA values.

Although we found that the primary radiological parameters were associated with the decreased FA values in LSS patients with single L5 nerve root compression, there are still some limitations that should be addressed. First, all LSS patients recruited in our study had single L5 nerve root compression, and patients with severe LSS and nerve compression at other levels were excluded. Further studies on different spinal nerve roots and different ranges of spinal stenosis are required to get more comprehensive results. Second, the sample size in our study was relatively small. Studies with larger sample size should be performed in the future to yield more accurate results.

Conclusions

DSCSA and SR were primary radiological parameters associated with decreased FA values in LSS patients involving a single L5 nerve root, which indicates that central canal decompression and segmental stability should be first considerations of preoperative planning in these patients.

Compliance with ethical standards

Conflict of interest None of the authors has any potential conflict of interest.

Human and animal right statement We declare that all human and animal studies have been approved by — University and — Hospital and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent We declare that all patients gave informed consent prior to inclusion in this study.

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Affiliations

Xiandi Wang[1] · Hongli Wang[1] · Chi Sun[1] · Shuyi Zhou[2] · Tao Meng[3] · Feizhou Lv[1] · Xiaosheng Ma[1] · Xinlei Xia[1] · Jianyuan Jiang[1]

✉ Jianyuan Jiang
jjy@fudanspine.com

[1] Department of Orthopedic Surgery, Huashan Hospital, Fudan University, No. 12 Middle Urumqi Road, Shanghai 210000, People's Republic of China

[2] Department of Radiology, Huashan Hospital, Fudan University, No. 12 Middle Urumqi Road, Shanghai 210000, People's Republic of China

[3] Department of MRI Application, Siemens Healthcare Ltd, Shang, No. 278, Zhouzhu Road, Shanghai 210031, People's Republic of China