Original Article

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Quantitative Analysis in Cervical Spinal Cord Injury Patients Using Diffusion Tensor Imaging and Tractography

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Objective To investigate the clinical usefulness of diffusion tensor imaging (DTI) and tractography in the prediction of outcomes after traumatic cervical spinal cord injury (SCI) and to assess whether the predictability is different between DTI and tractography administered before and after surgery.

Methods Sixty-one subjects with traumatic cervical SCI were randomly assigned to preop or postop groups and received DTI accordingly. Among the patients who had DTI before surgery, we assigned 10 patients who had received repeated DTI examinations at 8 weeks after injury to the follow-up group. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values were obtained from DTI, and imaginary fiber and crossing fiber numbers were calculated from the tractography. Neurological status and functional status were assessed at 4 and 8 weeks after SCI.

Results The neurologic and functional statuses of both groups improved after 4 weeks. Out of the initial 61 patients who were enrolled in the study, the failure rate of DTI image analysis was significantly higher in the postop group (n=17, 41.5%) than in the preop group (n=6, 20%). The FA values and fiber numbers in the preop group tended to be higher than those in the postop group, whereas ADC values were lower in the preop group. When comparing the tractographic findings in the follow-up group, imaginary fiber numbers at the C6 and C7 levels and crossing fiber numbers from the C3 to C6 levels were significantly decreased after surgery. Several DTI and tractographic parameters (especially the ADC value at the C4 level and imaginary fiber numbers at the C6 level) showed significant correlations with neurologic and functional statuses in both the preop and postop groups. These findings were most prominent when DTI and physical examination were simultaneously performed.

Conclusion Preoperative DTI and tractography demonstrated better FA and ADC values with lower interpretation failure rates than those obtained after surgery, whereas postoperative data significantly reflected the patient's clinical state at the time of evaluation. Therefore, DTI and tractography could be useful in predicting clinical outcomes after traumatic cervical SCI and should be interpreted separately before and after spine surgery.

Keywords Spinal cord injuries, Diffusion tensor imaging, Tractography, Prognosis

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INTRODUCTION

Spinal cord injury (SCI) is one of the most life-changing neurological conditions affecting individuals and the health care system [1]. In recent studies, the prognoses of patients with SCI have been predicted to some extent by using magnetic resonance imaging (MRI) findings, such as the intensity of the intramedullary hemorrhagic signal and the degree of cord compression [2,3].

Conventional MRI is routinely used to evaluate damage to spinal cord tissue. However, MRI provides little information on the health and integrity of the spinal cord tissue itself and the white matter; thus, it has limitations in reflecting neurological and functional statuses [4]. Diffusion tensor imaging (DTI) is an MRI technique for estimating the directional diffusivity of water that correlates with axonal integrity [5]. DTI has been used for the quantitative anatomical evaluation of white matter tracts, and the relationship between DTI and clinical statuses or outcomes has been previously studied [6,7]. However, DTI has important technical limitations that can result in images with low signals and artifacts due to the minute size of the spinal cord or motion artifacts due to swallowing, respiratory motion, and cerebrospinal fluid pulsation [8].

Surgical intervention is performed in many patients with SCI to re-establish and prevent secondary injury. These interventions may affect the image sensitivities of MRI and DTI due to artifacts, and their effects on the neurologic and functional prognoses are still unclear.

We aimed to demonstrate the utility of DTI and tractography in predicting the outcomes of patients after cervical SCI and to determine whether the prediction accuracy differs between DTIs performed before and after surgical intervention.

MATERIALS AND METHODS

Subjects

We performed a prospective randomized clinical trial involving acute stage cervical SCI patients resulting in an American Spinal Injury Association impairment scale (AIS) of B, C, and D. This study was approved by the Dankook University Hospital Institutional Review Board (No. 2018-05-037). Written informed consents were obtained. The inclusion criteria were (1) age ≥18-years-old; (2) incidences of acute traumatic injuries; (3) AIS B, C, and D; (4) neurological levels of injury (NLI) corresponding to C7 or higher; and (5) those patients who received surgical management. Patients with any of the following conditions were excluded: (1) combined or preexisting brain lesions; (2) combined peripheral nerve injuries; and (3) patients in which artifact-laden images were obtained.

Of the 89 patients with SCI, 28 patients were excluded, and a total of 61 patients were enrolled in this study. Fig. 1 shows the flowchart of the patients and a schematic representation of the clinical trial design. These patients were randomly assigned to the preop or postop groups, with those patients who received DTI before surgery being assigned to the former group and the latter group being examined at 4 weeks after surgery. The patients who had DTI before surgery and had a repeated DTI examination at 8 weeks after injury were assigned to the follow-up group (Fig. 1).

A portion of the echo-planar images (EPIs) was of low quality due to metal interference, patient movement during imaging, and/or other unknown reasons, thus failing to produce meaningful DTI and tractography data. The failure rate of the DTI image analysis was significantly higher in the postop group (n=17; 41.5%) than in the preop group (n=6; 20%) (p=0.017, chi-square test).

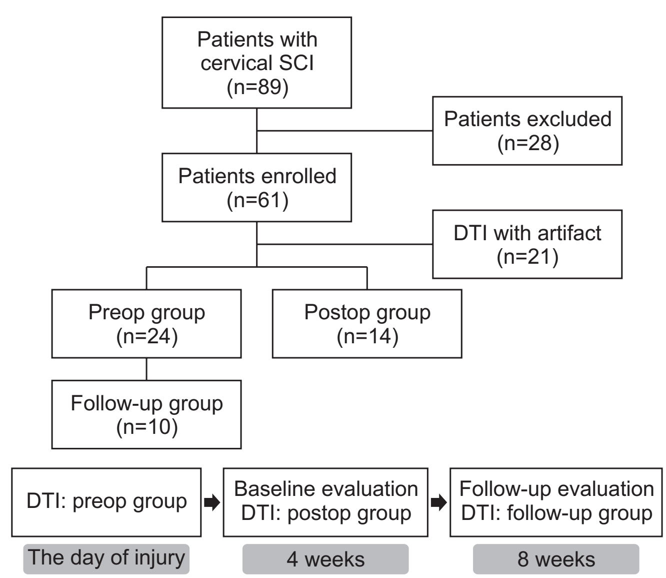


Fig. 1. Flowchart of a schematic representation of the clinical study design. SCI, spinal cord injury; DTI, diffusion tensor imaging.

After excluding these cases, we used data from 38 patients with cervical SCI in this study (preop, n=24; postop, n=14; follow-up, n=10). Due to the loss to follow-up and DTI analysis failure rates (n=21; 34.4%), 10 patients were finally included as the follow-up group. When a power calculation was conducted by using G*Power version 3.1.9.2 (http://www.gpower.hhu.de/) and after setting the alpha to 0.05 and beta to 0.20 based on the tractographic values, the required sample size for the follow-up study was calculated to be nine subjects per group; thus, the sample size for this study ensured adequate power to detect statistical significance. All of the patients received conventional physical and occupational therapy, including gait training, strengthening exercises, and activities of daily living (ADL) training. Physical and occupational therapy was administered for 1 hour, 5 days per week for 4 weeks each.

Methods

Neurological assessment

The neurological assessment was performed according to the International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI) developed by the American Spinal Injury Association (ASIA) [9]. The baseline evaluation was performed at 4 weeks after injury when the patients were transferred to the Department of Rehabilitation Medicine, and a follow-up evaluation was performed 8 weeks later. The AIS and NLI were determined for all of the patients. The upper extremity motor scores (UEMSs) and the lower extremity motor scores (LEMSs) were evaluated in 10 key muscle groups (C5, C6, C7, C8, T1, L2, L3, L4, L5, and S1). Light touch (LT) and pinprick (PP) sensory scores were separately recorded in upper (UE; in C5 to T1) and lower extremity dermatomes (LE; in L2 to S1).

Functional assessment

ADL performance was evaluated by using the Korean version of the Modified Barthel Index (K-MBI) and Functional Independence Measure (FIM) at 4 weeks (baseline evaluation) and 8 weeks after injury (follow-up evaluation). The K-MBI consists of 10 items and ranges from a score of 0 (completely dependent) to 100 (independent in basic ADLs) [10]. The FIM has 18 items that assess function in six areas. Each item is graded based on the level of independence from 1 (requiring total assistance) to 7 (completely independent). Three independent FIM scores can be generated by summing individual items for each category: a total score (FIM total: 18 items), a motor score (FIM motor: self-care, sphincter control, and transfer/locomotion), and a cognitive score (FIM cognitive: communication and social cognition) [10]. In this study, a total K-MBI score, a total FIM score, and three FIM motor item scores were selectively used.

Diffusion tensor imaging and tractography

For SCI patients who satisfied the inclusion criteria, their inclusion in either test group was randomly determined. Preop groups had DTI performed on the day of the injury, whereas the postop patients had DTI administered 4 weeks after the injury.

Multiplanar MRI of the cervical spine was acquired on a 1.5T MR scanner (Signa; GE, Milwaukee, WI) by using a T2-weighted fast spin-echo (FSE) sequence in all of the patients. Diffusion tensor imaging was obtained via diffusion-weighted single-shot EPIs between the spinal levels of C2 and T1.

The imaging parameters were as follows: image matrix=256×256; voxel dimensions=0.9375×0.9375 mm; section thickness=4 mm with no intersection gap; FOV=240 mm; NEX=1; scan time=4 minutes and 9 seconds; and number of slices=24–28 (according to the length of the entire cervical spine in each patient). Diffusion encoding was performed in 25 noncollinear gradient directions with 2 b values (b=0 and 500 s/mm^2). Each EPI cervical level was determined by using axial and sagittal T2-weighted images of the same subject.

The investigator who analyzed the DTI images was blinded to the clinical statuses of the patients. We determined the spinal cord levels C3 to C7 on DTI by contrasting the sagittal view of the T2-weighted MRI. Rotationally invariant parameters, such as the fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values, were calculated on a voxel-by-voxel basis by using the Diffusion Toolkit (version 0.6.4) and were visualized by using TrackVis software (version 0.6.1; Massachusetts General Hospital, Boston, MA, USA, available free at http://www.trackvis.org) for the quantitative analysis. Anisotropy refers to the preferential diffusion of molecules in a single direction, with white matter tracts being highly anisotropic structures and thus having high FA values. ADC values, which are also known as the mean

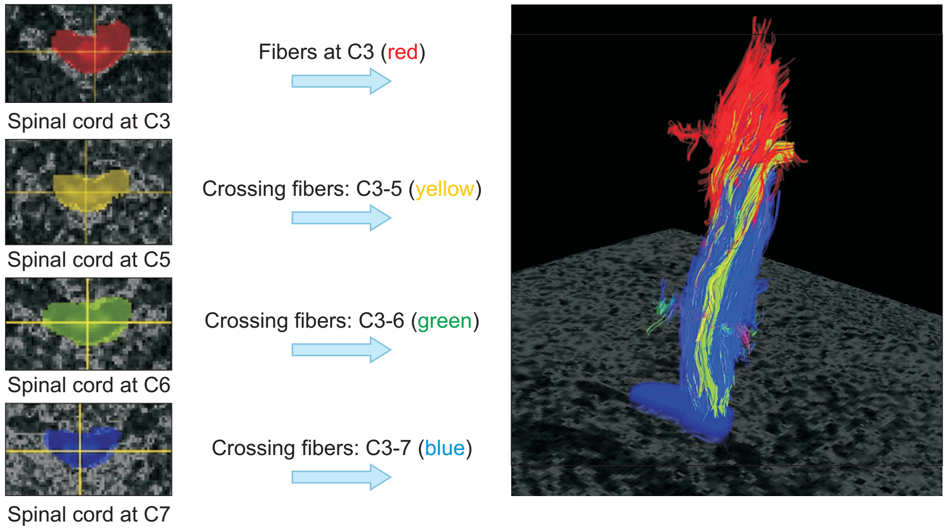


Fig. 2. Example of tractographic analysis.

diffusivity, were obtained by averaging diffusivities along the three principal axes for each voxel, thus reflecting the degree of myelination/fiber organization [5]. For the FA and ADC analyses, two axial EPIs at each cervical cord level from C3 to C7 (C3, C4, C5, C6, and C7) were selected, and a total of 16 voxels in four directions (anterior, posterior, right, and left lateral directions) at each level were chosen based on a previous study [7].

Tractography, which reconstructs fiber projections throughout the white matter, produces a voxelwise map of fiber orientation [11]. The number of fiber projections is the number of reconstructed streamlines penetrating the specified region of interest (ROI) in the axial plane from C3 to C7. The number of imaginary fibers crossing the ROIs of the two cervical levels (C3 and C5, C3 and C6, and C3 to C7) was calculated (Fig. 2).

Statistical analysis

Statistical analyses were performed by using PASW Statistics version 23 (IBM Corp, Armonk, NY, USA). The Mann-Whitney U test was used to compare the numerical data between the two groups. The Pearson chi-square test was used to analyze the baseline categorical data, such as sex, cause, initial NLI and AIS, and the failure rate of the DTI analysis between the preop and postop groups. A Wilcoxon signed-rank test was performed to compare the changes in the neurologic scores, functional scores, and quantitative DTI parameters between the initial and follow-up statuses of patients in the follow-up group. A Spearman correlation analysis was performed to delineate the relationships between the neurologic and functional assessments and the quantitative DTI parameters (FA, ADC, fiber numbers, and connection rate) at each cervical level. A p-value less than 0.05 was considered to be statistically significant.

RESULTS

In this study, we analyzed whether neurologic, functional, and DTI parameters changed after surgery compared to preoperative statuses. Between the preop and postop groups, there were no differences in age, sex, cause of trauma, initial NLI, or AIS scores. The most common NLI was C5, and the severity of most of the subjects' impairments according to the ISNCSCI was AIS D. Patients underwent anterior cervical discectomy and fusion (ACDF), lateral mass fixation, laminectomy, or laminoplasty surgeries. In addition, ACDF was the most common treatment among patients, whereas there was no difference in surgical treatment approaches between the two groups (Table 1). Both groups showed significant improvements on the UEMS, K-MBI, the three motor subscales (self-care, sphincter control, and transfer/locomotion), and total FIM scores after 4 weeks. In addition, there was a significant improvement in the LT sensory score and the total sensory score of UE in the preop group. There were no significant differences between the preop and postop groups (Table 2).

When comparing the quantitative DTI parameters of the two groups, there were significant differences in several parameters. FA values at the C3 and C4 levels were significantly higher in the preop group than in the postop

Table 1. Baseline characteristics of the preop and postop groups

	Preop group (n=24)	Postop group (n=14)	p-value
Age (yr)	57.71±13.49	55.71±9.83	0.431[a)]
Sex, male	23 (95.8)	11 (78.6)	0.132[b)]
Cause			0.407[b)]
Traffic accident	14 (58.3)	7 (50.0)	
Slip down	6 (25.0)	3 (21.4)	
Direct trauma	3 (12.5)	1 (7.1)	
Fall down	1 (4.2)	3 (21.4)	
Initial NLI			0.114[b)]
C2	5 (20.8)	1 (7.1)	
C3	6 (25.0)	2 (14.3)	
C4	5 (20.8)	4 (28.6)	
C5	4 (16.7)	5 (35.7)	
C6	0 (0)	2 (14.3)	
C7	4 (16.7)	0 (0)	
Initial AIS			0.525[b)]
B	2 (8.3)	0 (0)	
C	4 (16.7)	3 (21.4)	
D	18 (75.0)	11 (78.6)	
Surgery type			0.058[b)]
ACDF	13 (54.2)	12 (85.7)	
Lateral mass fixation	6 (25.0)	1 (7.1)	
Laminectomy	0 (0)	1 (7.1)	
Laminoplasty	5 (20.8)	0 (0)	

Values are presented as mean±standard deviation or number (%).
NLI, neurological level of injury; AIS, American Spinal Injury Association impairment scale; ACDF, anterior cervical discectomy, and fusion.
[a)]Mann-Whitney test, [b)]Pearson chi-square test.

group, and ADC values at the C3, C4, C5, and C7 levels were significantly lower in the preop group than in the postop group. When comparing FA and ADC values at each patient's level of injury, ADC values at the level of injury were significantly lower in the preop group than in the postop group. Moreover, fiber numbers at all levels (C3, C4, C5, C6, and C7 levels) were significantly higher in the preop group than in the postop group, but there were no differences in crossing fiber counts (Table 3).

Spearman correlation coefficients between preoperative DTI parameters and the patients' baseline ISNCSCI motor/sensory scores and K-MBI and FIM scores (at 4 weeks after injury) demonstrated that FA at the C7 level correlated with LEMS (r=-0.601). In addition, the ADC values at the C4 level and fiber numbers at the C3 and C7 levels were significantly correlated with the baseline PP sensory score of the UE (r=-0.471, r=0.442, and r=0.417, respectively). Moreover, the FA and ADC values at the C7 level before surgery correlated with the LEMS (r=-0.601 and r=0.722, respectively). The FA values at the C3 level were associated with the baseline total FIM score (r=0.476), and the fiber numbers at the C3 level were associated with the baseline sphincter control subscale of FIM (r=0.474).

When comparing the preoperative DTI parameters and the follow-up clinical statuses (at 8 weeks after the injury), FA values at the C4 level before surgery were associated with the LT sensory score of UE after 8 weeks. ADC values at the C4 level before surgery were also significantly correlated with LT and the total sensory score of UE (r=-0.622 and r=-0.561, respectively). In addition, ADC values at the C5 and C7 levels before surgery were associated with LEMS. Moreover, fiber counts at the C6 level were associated with the self-care subscale and total FIM scores, and fiber numbers at the C7 level were correlated with the same items and K-MBI (Table 4).

When comparing the postoperative DTI parameters and baseline clinical statuses, which were performed at similar periods (at 4 weeks after the injury), many values showed significant associations (Table 5). The FA values at the C3 level after surgery were highly associated with UEMS (r=0.736). Additionally, the ADC values at the C4 and C5 levels, fiber numbers at the C3, C4, C5, and C6 levels, and crossing fiber numbers from the C3 to C5 levels after surgery were associated with LEMS. Many of the postoperative fiber numbers and crossing fiber numbers were associated with the functional scores. Furthermore, the fiber numbers at the C4 to C6 levels and crossing fiber numbers from the C3 to C5 and C3 to C6 levels after surgery were correlated with the K-MBI score. Additionally, the crossing fiber numbers from C3 to C7 after surgery were related to the self-care subscale of the FIM score. The fiber numbers at the C3 to C6 levels (r=0.61, r=0.694, r=0.804, and r=0.632, respectively) and the crossing numbers from the C3 to C5 and C3 to C6 levels (r=-0.676 and r=0.628, respectively) correlated with the sphincter control subscale of the FIM score. Moreover, the fiber

Table 2. Neurologic and functional changes between the preop and postop groups

	Preop group (n=24)			Postop group (n=14)			p-value[b)] (preop vs. postop)	
	Baseline	Follow-up	p-value[a)]	Baseline	Follow-up	p-value[a)]	Baseline	Follow-up
Upper extremity								
Motor	29.25±13.53	36.78±13.44	0.000*	31.29±12.29	39.57±9.14	0.001*	0.422	0.851
Sensory								
Light touch	14.04±3.98	15.87±4.33	0.012*	12.79±4.34	14.43±4.60	0.068	0.220	0.301
Pinprick	15.58±4.38	16.78±4.38	0.100	12.86±4.29	14.43±4.60	0.109	0.045*	0.118
Total	29.63±7.82	32.65±8.20	0.012*	25.64±8.63	28.86±9.21	0.144	0.104	0.314
Lower extremity								
Motor	39.88±17.19	40.52±17.41	0.440	44.00±10.55	48.21±3.73	0.068	0.363	0.321
Sensory								
Light touch	16.96±4.39	16.87±5.29	0.888	14.64±4.99	14.64±4.99	1.000	0.168	0.145
Pinprick	17.21±4.13	16.78±5.55	0.750	14.64±4.99	14.64±4.99	1.000	0.128	0.145
Total	34.17±8.30	33.65±10.77	0.888	29.29±9.97	29.29±9.97	1.000	0.161	0.185
K-MBI	30.13±28.82	53.41±34.76	0.000*	47.36±38.23	71.44±31.28	0.028*	0.113	0.184
FIM								
Self-care	12.46±7.18	18.73±12.11	0.001*	18.64±13.77	28.67±14.97	0.042*	0.314	0.052
Sphincter control	8.88±5.09	11.27±4.59	0.008*	9.64±4.80	12.44±3.13	0.039*	0.705	0.532
Transfer/locomotion	10.71±7.17	17.91±11.23	0.001*	17.86±12.37	23.78±12.12	0.042*	0.123	0.203
Total	65.58±19.99	82.23±27.60	0.000*	81.36±29.10	98.56±30.35	0.043*	0.130	0.191

Values are presented as mean±standard deviation.
K-MBI, Korean version of the Modified Barthel Index; FIM, Functional Independence Measure.
[a)]Mann-Whitney test, [b)]Wilcoxon sum rank test.
*$p<0.05$.

numbers at the C5 and C6 levels and crossing numbers from the C3 to C5 and C3 to C7 levels correlated with the transfer/locomotion subscale of the FIM score. The fiber number at the C4 and C5 levels and all of the crossing fiber numbers (C3 to C5, C3 to C6, and C3 to C7 levels) were associated with the total FIM scores.

In a comparison of the postoperative DTI parameters and the follow-up clinical scales (8 weeks after injury), there were a limited number of correlations. The ADC values at the C4 level (r=0.572) and fiber numbers at the C5 and C6 levels were significantly correlated with the follow-up LEMS (r=-0.658 and r=0.575, respectively).

In the follow-up group who underwent initial DTI and follow-up DTI, the UEMS and LT sensory scores of the UE and all of the functional scores were significantly improved after 4 weeks. When comparing initial and follow-up tractography data, the fiber numbers at C6 and C7 levels and the crossing fiber numbers from C3 to C6 levels were significantly higher in initial values than in follow-up values. Fig. 3 shows the fiber tractography of 10 patients in the follow-up group. Furthermore, imaginary fibers at the C3 and C6 levels and crossing fibers from the C3 to the C6 levels were compared before and after surgery. Four weeks after surgery, all of the patients showed improvements in UEMS, K-MBI, and FIM compared to the baseline values. However, the number of fibers at the C3 and C6 levels and the number of crossing fibers from the C3 to C6 levels in 8 patients were postoperatively decreased compared to pre-operation.

DISCUSSION

The UEMS and functional statuses of cervical SCI patients were significantly improved after 4 weeks, and there were no differences between the preop and postop groups. Preoperative FA values at the C3 and C4 levels

Table 3. DTI parameters between the preop and postop groups

	Preop group (n=24)	Postop group (n=14)	p-value
FA			
C3	0.772±0.078	0.606±0.112	0.000*
C4	0.700±0.102	0.568±0.136	0.006*
C5	0.664±0.102	0.612±0.120	0.066
C6	0.609±0.134	0.604±0.153	0.873
C7	0.676±0.125	0.573±0.173	0.085
Cinj	0.621±0.110	0.607±0.171	0.575
ADC			
C3	0.845±0.133	1.165±0.396	0.001*
C4	0.877±0.179	1.202±0.394	0.003*
C5	0.893±0.184	1.133±0.381	0.016*
C6	0.926±0.251	1.084±0.347	0.060
C7	0.777±0.346	1.134±0.372	0.009*
Cinj	0.902±.0241	1.178±0.432	0.015*
Fiber No.			
C3	1245.78±279.24	874.36±415.10	0.009*
C4	1267.48±294.06	736.36±477.08	0.001*
C5	1262.09±313.31	618.57±440.89	0.000*
C6	1157.04±293.19	432.79±373.51	0.000*
C7	813.65±430.23	288.71±299.86	0.000*
Crossing fiber No.			
C3-5	348.48±300.92	259.43±275.32	0.363
C3-6	235.70±275.26	143.93±236.59	0.137
C3-7	49.61±128.45	63.64±155.04	0.484

Values are presented as mean±standard deviation.
DTI, diffusion tensor imaging; FA, fractional anisotropy; Cinj, cervical spinal cord level of injury; ADC, apparent diffusion coefficient.
*p<0.05, Mann-Whitney test.

and fiber numbers at all levels were significantly higher than the postoperative values. In contrast, the ADC values at the C3, C4, C5, and C7 levels were significantly lower than the postoperative values. Fiber numbers and crossing fiber numbers after surgery were significantly decreased compared to before surgery.

FA measures the “magnitude” of total diffusion, and this effect has been attributed to anisotropic diffusion, with 0 indicating isotropic diffusion, and 1 denoting infinite anisotropy; in addition, FA values closer to 1 indicate a high degree of anisotropy. Any damage to the axonal membrane results in diffusion becoming unrestricted and isotropic. Moreover, the ADC or mean diffusivity is a measure of the average diffusion in all directions, with a low ADC value indicating that the nerve fibers are organized, whereas a high value indicates disorganization within the fiber tracts [12]. Previous studies have shown that SCI patients have lower FA values and higher ADC values than controls [7,13]. Physical trauma can lead to the disruption of axons, thus causing disorganization of the spinal cord white matter and creating barriers to the diffusivity of the water molecules [14].

In this study, the postoperative FA values were lower than the preoperative FA values, and the postoperative ADC values were higher than the preoperative ADC values. Therefore, this indicates that postoperative DTI has demonstrated axonal membrane damage and disorganization within fiber tracts compared to preoperative DTI. This may be influenced by the difficulty in analyzing postoperative DTI. Metallic implants located within

Table 4. Correlation analysis between follow-up (FU) neurologic and functional findings and DTI parameters in the preop group

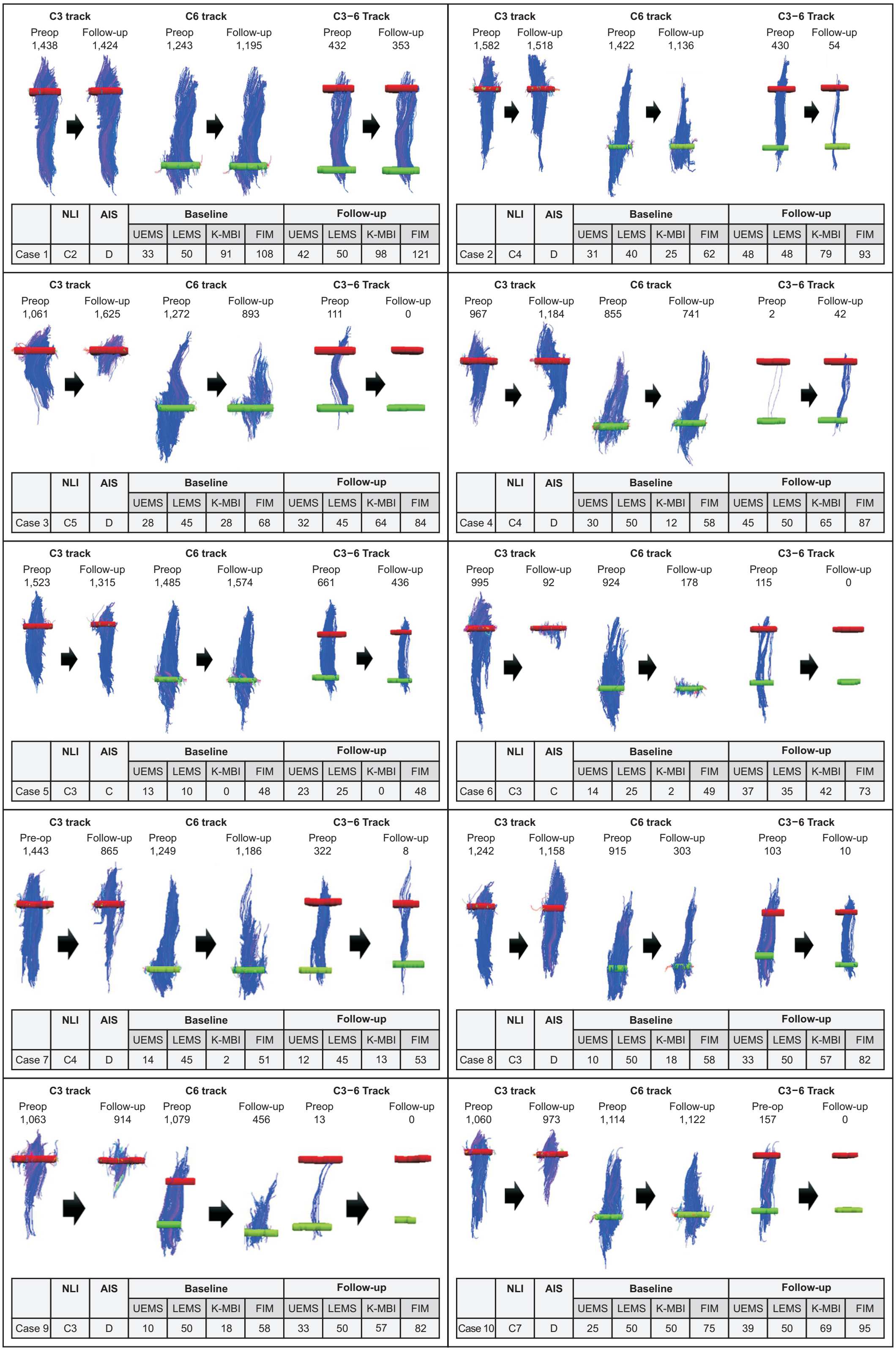
	Preop group (n=24)																	
	FA					ADC					Fiber No.					Crossing fiber No.		
	C3	C4	C5	C6	C7	C3	C4	C5	C6	C7	C3	C4	C5	C6	C7	C3-5	C3-6	C3-7
UE_FU																		
Motor	-0.021	0.079	-0.138	0.021	-0.172	0.004	0.075	0.207	0.011	0.338	0.296	0.101	0.219	0.042	0.387	0.221	0.130	0.165
Sensory																		
Light touch	0.161	0.571*	0.181	-0.142	-0.248	-0.142	-0.622*	-0.071	0.055	0.406	0.082	0.071	0.121	0.170	0.334	0.089	0.007	0.091
Pinprick	0.073	0.213	-0.003	-0.285	0.046	-0.121	-0.355	0.051	0.086	0.038	0.394	0.317	0.216	0.211	0.375	0.201	0.007	0.041
Total	0.084	0.466	0.206	-0.118	-0.108	-0.198	-0.561*	-0.051	0.006	0.025	0.191	0.148	0.127	0.125	0.345	0.071	-0.060	0.-007
LE_FU																		
Motor	-0.044	0.019	-0.258	-0.224	-0.441	0.192	0.207	0.504*	0.284	0.582*	0.124	0.143	0.116	-0.056	0.168	-0.004	0.007	0.016
Sensory																		
Light touch	0.113	-0.035	0.019	-0.146	-0.171	0.020	0.061	0.362	0.228	0.317	0.254	0.212	0.196	0.126	0.226	-0.038	-0.027	-0.135
Pinprick	0.078	0.017	0.106	0.045	-0.101	-0.101	-0.026	0.205	-0.014	0.213	0.364	0.378	0.257	0.077	0.288	0.072	-0.064	-0.135
Total	0.095	-0.032	-0.007	-0.075	-0.170	-0.018	0.007	0.324	0.105	0.025	0.364	0.319	0.215	0.097	0.200	-0.004	-0.010	-0.072
K-MBI_FU	0.280	0.128	0.149	0.060	0.035	-0.255	0.161	0.215	0.007	0.156	0.333	0.353	0.358	0.420	0.457*	0.233	0.211	0.152
FIM_FU																		
Self-care	0.190	0.053	0.142	0.126	0.089	-0.193	0.262	0.157	0.012	0.101	0.323	0.299	0.361	0.480*	0.461*	0.317	0.325	0.312
Sphincter control	0.002	0.037	0.081	-0.117	0.039	0.030	0.233	0.247	0.262	0.249	0.083	0.188	0.167	0.146	0.256	-0.080	-0.048	-0.076
Transfer	0.228	-0.006	-0.111	-0.210	0.048	-0.210	0.219	0.381	0.165	0.099	0.312	0.359	0.307	0.308	0.381	0.115	0.084	0.041
Total	0.331	0.106	0.110	-0.040	0.078	-0.278	0.172	0.275	0.065	0.093	0.310	0.342	0.329	0.454*	0.482*	0.195	0.213	0.186

DTI, diffusion tensor imaging; FA, fractional anisotropy; ADC, apparent diffusion coefficient; UE, upper extremity; LE, lower extremity; K-MBI, Korean version of the Modified Barthel Index; FIM, Functional Independence Measure.
*$p<0.05$, Spearman rank correlation analysis.

Table 5. Correlation analysis between baseline neurologic and functional findings and DTI parameters in the postop group

	Preop group (n=24)																	
	FA					ADC					Fiber No.					Crossing fiber No.		
	C3	C4	C5	C6	C7	C3	C4	C5	C6	C7	C3	C4	C5	C6	C7	C3-5	C3-6	C3-7
UE																		
Motor	0.736*	0.138	0.331	0.284	0.204	-0.366	0.325	0.096	0.185	-0.143	0.150	0.148	0.355	0.273	0.152	0.239	0.314	0.341
Sensory																		
Light touch	0.035	-0.334	-0.366	-0.174	0.016	-0.211	0.407	0.344	0.265	-0.006	0.095	0.116	0.198	0.044	0.054	0.142	0.059	0.123
Pinprick	-0.006	-0.391	-0.469	-0.253	-0.012	-0.126	0.295	0.228	0.156	0.000	-0.027	-0.027	0.059	-0.095	0.024	0.020	-0.032	0.071
Total	-0.006	-0.391	-0.469	-0.253	-0.012	-0.126	0.295	0.228	0.156	0.000	-0.027	-0.027	0.059	-0.095	0.024	0.020	-0.032	0.071
LE																		
Motor	0.007	-0.074	0.104	-0.026	-0.163	0.264	0.617*	0.576*	0.535	0.171	0.548*	0.496	0.690*	0.619*	-0.372	0.534*	0.491	0.396
Sensory																		
Light touch	-0.342	0.064	-0.150	0.257	0.321	0.150	-0.214	0.000	-0.235	-0.150	0.504	0.339	0.305	0.192	0.287	0.380	0.358	0.271
Pinprick	-0.342	0.064	-0.150	0.257	0.321	0.150	-0.214	0.000	-0.235	-0.150	0.504	0.339	0.305	0.192	0.287	0.380	0.358	0.271
Total	-0.342	0.064	-0.150	0.257	0.321	0.150	-0.214	0.000	-0.235	-0.150	0.504	0.339	0.305	0.192	0.287	0.380	0.358	0.271
K-MBI	0.366	0.149	0.292	0.022	-0.333	-0.033	0.311	0.096	0.245	0.426	0.460	0.535*	0.690*	0.563*	-0.099	0.599*	0.539*	0.522
FIM																		
Self-care	0.579*	0.096	0.202	0.094	-0.161	-0.348	0.305	0.136	0.296	0.283	0.246	0.336	0.434	0.442	0.232	0.444	0.419	0.550*
Sphincter control	0.150	0.252	0.402	0.122	-0.287	0.113	0.153	0.023	0.107	0.408	0.621*	0.694*	0.804*	0.632*	-0.119	0.676*	0.628*	0.501
Transfer	0.348	0.084	0.262	-0.042	-0.435	-0.095	0.318	0.117	0.295	0.510	0.413	0.528	0.662*	0.566*	-0.123	0.576*	0.516	0.577*
Total	0.338	0.132	0.264	-0.006	-0.360	-0.105	0.261	0.085	0.261	0.476	0.451	0.570*	0.697*	0.607	-0.011	0.608*	0.548*	0.564*

DTI, diffusion tensor imaging; FA, fractional anisotropy; ADC, apparent diffusion coefficient; UE, upper extremity; LE, lower extremity; K-MBI, Korean version of the Modified Barthel Index; FIM, Functional Independence Measure.
*p<0.05, Spearman rank correlation analysis.



	NLI	AIS	Baseline				Follow-up			
			UEMS	LEMS	K-MBI	FIM	UEMS	LEMS	K-MBI	FIM
Case 1	C2	D	33	50	91	108	42	50	98	121
Case 2	C4	D	31	40	25	62	48	48	79	93
Case 3	C5	D	28	45	28	68	32	45	64	84
Case 4	C4	D	30	50	12	58	45	50	65	87
Case 5	C3	C	13	10	0	48	23	25	0	48
Case 6	C3	C	14	25	2	49	37	35	42	73
Case 7	C4	D	14	45	2	51	12	45	13	53
Case 8	C3	D	10	50	18	58	33	50	57	82
Case 9	C3	D	10	50	18	58	33	50	57	82
Case 10	C7	D	25	50	50	75	39	50	69	95

Fig. 3. Fiber tractography and fibers numbers at the C3 and C6 levels and crossing fiber numbers from the C3 to C6 levels before surgery and after 4 weeks in the follow-up group (n=10). NLI, neurological level of injury; AIS, American Spinal Injury Association impairment scale; UEMS, upper extremity motor score; LEMS, lower extremity motor score; K-MBI, Korean version of the Modified Barthel Index; FIM, Functional Independence Measure.

the spine can cause geometric distortions that may cause inaccuracies in the measurement of DTI parameters and tractography [15]. This was also demonstrated in our study, wherein the failure rate of DTI analysis was more than doubled after surgery than before surgery.

Several animal studies have examined changes in quantitative DTI parameters of spinal cord tissue during the acute period [16-18]. One of these studies reported a decrease in axial diffusivity (AD), which is a measure of diffusion parallel to the spinal cord following injury, which could be used to distinguish SCI according to its severity. The reduction in AD was shown to be correlated with locomotor recovery [18]. Similarly, in this study, FA and ADC values at the C3 level were associated with the LEMS and the locomotion/transfer subscale of FIM.

In a study examining the optimal timing for obtaining DTI in SCI, several studies have shown that FA reductions in DTI performed within 3 hours or at the middle time point of 24 hours after SCI is the best time for identifying the injury severity [18,19]. However, in this study (and unlike in previous studies), the preoperative DTI performed on the same day as the SCI was not significantly better than the postoperative DTI in predicting the prognosis after SCI.

In a previous study, motor and sensory scores of the ISNCSCI were positively correlated with FA and negatively correlated with ADC values in chronic SCI patients [2]. The correlation between the reduction in diffusivity and the severity of SCI could help to quantify the amount of spared neural tissue in the spinal cord and to provide an estimate of functional recovery after injury [14]. In another study, crossing fiber numbers and connection rates calculated from tractography showed strong correlations with motor scores from C5 to T1 levels in cervical spinal cord injury patients [7]. In this study, as in previous studies, both motor and sensory scores and functional scores demonstrated the same trend. Additionally, fiber numbers and crossing fiber numbers were also positively correlated with clinical status. In both preoperative and postoperative DTI, many parameters showed a correlation with neurologic and functional statuses. However, this correlation was different between the preoperative and postoperative DTIs, and it was also different according to the clinical status at each time point. The most significant correlation was found when the DTI and clinical status were performed simultaneously. In particular, the postoperative fiber numbers at the C3 to C6 levels were most strongly correlated with the baseline K-MBI and FIM scores at 4 weeks after the injury. The postoperative DTI parameters significantly reflected the clinical state at the time of the evaluation.

This study had several limitations. First, the initial time of performing DTI and tractography was different in the preop and postop groups. The initial DTI of the preop group was performed on the same day as SCI, but the initial DTI of the postop group was performed at 4 weeks after SCI. In addition to metal implants, the pathological process of the injured spinal cord or surrounding tissues over 4 weeks in the spine may have affected DTI and tractographic findings. Second, the types of surgery performed with patients are diverse. Spine surgeons can use various methods, such as closed or open reduction, decompression, and anterior or posterior fixations, depending on the injury condition of the cervical spine. There was no significant difference according to the type of surgery between the two groups, but the surgery methods may affect DTI and the tractographic findings. Third, the sample size of each group was small, and the follow-up period was not long enough to delineate the long-term neurological and functional prognostic values of the DTI and the tractographic findings. Last, there were no accurate statistical data regarding the epidemiology of patients with spinal cord injury in Korea. Therefore, based on statistics in the United States, the most common AIS in incomplete cervical SCI patients was AIS D (58%) [20]. In our study, the most common AIS grade was AIS D (76%). The difference in the ratios could be considered a limitation.

Nevertheless, the most meaningful significance of this study is (to our knowledge) that it is the first study to clarify the relationship and prognostic power of DTI and tractography by individually analyzing preoperative and postoperative DTI in cervical SCI patients.

In conclusion, we performed DTI and tractography before and after surgery in cervical SCI patients and found correlations with their neurological and functional statuses. DTI and tractographic findings before surgery showed better FA and ADC values, more fiber numbers, and a lower failure rate for interpretation than those taken after surgery. However, the preoperative imaging findings could not reflect the neurological and functional prognoses better than the postoperative findings. The postoperative images showed better correlations with the neurological and functional statuses when both were executed at similar time frames. Therefore, DTI and tractography in cervical SCI patients should be separately interpreted before and after spine surgery.

CONFLICT OF INTEREST

No potential conflicts of interest relevant to this article were reported.

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AUTHOR CONTRIBUTION

Conceptualization: Kim SY. Methodology: Park GS, Kim SY. Formal analysis: Park GS, Kim TU, Hyun JK, Kim SY. Funding acquisition: Kim SY. Project administration: Kim SY. Visualization: Park GS, Lee SJ, Hyun JK, Kim SY. Writing - original draft: Park GS. Writing - review and editing: Park GS, Hyun JK, Kim SY. Approval of final manuscript: all authors.

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