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CLINICAL INVESTIGATIVE STUDY

T1 mapping in patients with cervical spinal canal stenosis with and without decompressive surgery: A longitudinal study

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Abstract

Background and Purpose: Cervical spinal canal stenosis (cSCS) is a common cause of spinal impairment in the elderly. With conventional magnetic resonance imaging (MRI) suffering from various limitations, high-resolution single-shot T1 mapping has been proposed as a novel MRI technique in cSCS diagnosis. In this study, we investigated the effect of conservative and surgical treatment on spinal cord T1 relaxation times in cSCS.

Methods: T1-mapping was performed in 54 patients with cSCS at 3 Tesla MRI at the maximum-, above and below the stenosis. Subsequently, intraindividual T1-differences (ΔT1) intrastenosis were calculated. Twenty-four patients received follow-up scans after 6 months.

Results: Surgically treated patients showed higher ΔT1 at baseline (154.9 ± 81.6 vs. 95.3 ± 60.7), while absolute T1-values within the stenosis were comparable between groups (863.7 ± 89.3 milliseconds vs. 855.1 ± 62.2 milliseconds). In surgically treated patients, ΔT1 decreased inverse to stenosis severity. After 6 months, ΔT1 significantly decreased in the surgical group (154.9 ± 81.6 milliseconds to 85.7 ± 108.9 milliseconds, $p = .021$) and remained unchanged in conservatively treated patients. Both groups showed clinical improvement at the 6-month follow-up.

Conclusions: Baseline difference of T1 relaxation time (ΔT1) might serve as a supporting marker for treatment decision and change of T1 relaxation time might reflect relief of spinal cord narrowing indicating regenerative processes. Quantitative T1-mapping represents a promising additional imaging method to indicate a surgical treatment plan and to validate treatment success.

KEYWORDS
decompressive surgery, outcome measurement, spinal canal stenosis, T1 mapping

INTRODUCTION

Degenerative cervical spinal myelopathy is the most common cause of spinal impairment in the elderly, with a steadily increasing prevalence in individuals over the age of 50,[1] and spinal degeneration affecting up to 90% of people above 60 years of age.[2–4] Subsequent cervical spinal canal stenosis (cSCS) with resulting spinal cord narrowing and potential cord compression shows a strong variability in clinical presentation and disease course, and can be associated with severe clinical morbidity.

Due to the variability of clinical presentation and lack of pathognomonic findings, diagnosis of spinal canal stenosis (SCS) can be difficult.[5] Notably, the severity of clinical presentation not necessarily correlates with the degree of the stenosis, further complicating diagnosis and treatment decisions.[6,7] Additionally, recommendations regarding necessary diagnostic measures[8,9] and favorable therapeutic regimen (eg, conservative or surgical treatment) are inconsistent.[10]

A necessary measure in SCS diagnosis, besides clinical history and examination, is spinal neuroimaging. Conventional magnetic resonance imaging (MRI), including T1- and T2-weighted imaging (T1w and T2w), remains the method of choice for diagnosing cSCS and potential cord compression, reflecting not only the width of the compressed regions of the spinal cord but also irreversible changes like gliosis or myelomalacia.[11] MRI is not only able to quantify the SCS extent but is suitable to exclude various differential diagnoses by allowing evaluation of vertebrae, spinal cord, and surrounding tissue. However, early and mild-stage SCS might not be visible in conventional T1w and T2w images. Moreover, microstructural abnormalities of the spinal cord, indicated by T1w-hypointensities and T2w-hyperintensities,[12] often cannot be attributed to a specific pathophysiology (eg, acute edema vs. chronic gliosis and demyelination), especially in advanced SCS. This emphasizes a possible lack of correlation between imaging results and clinical presentation, accelerating the difficulties in streamlining therapeutic recommendations. Further limitations of spinal cord evaluation with conventional MRI are operator-dependency and associated inter-rater variability[13] as well as the missing potential for functional studies, for example, visualization of intermittent posture-dependent spinal cord compression in low-grade SCS. Furthermore, T2 signal intensity changes (ISI, increased signal intensity) in the spinal cord may only appear in advanced SCS stages. However, in these stages, surgical therapy often only results in minor clinical improvement.[13–15]

Recent developments in imaging modalities, such as dynamic cervical MRI,[16,17] as well as ultra-high-field structural MRI, seek to improve the diagnostic process in SCS.[18] However, these techniques are not widely available and require prolonged imaging protocols. High-resolution single-shot T1 mapping at a 3 Tesla was implicated as a fast, sensitive, and reproducible imaging biomarker, allowing for early diagnosis of spinal cord narrowing and outcome prediction.[19,20] T1 relaxation times depend on various parameters, such as myelin and nonmyelin water content, iron concentration, axonal size, and axonal density.[12,21–24] In T1 mapping studies, clinically mildly affected patients without detection of spinal cord compression on conventional MRI showed decreased T1 relaxation times within the maximum of the stenosis. Moreover, these findings were translatable to patients with severe (grade 3) SCS,[25] indicating the difference in T1 relaxation time to be more sensitive for spinal cord compression compared to absolute T1 values.[20] Additionally, single-shot T1 mapping with the use of T1FLASH is very fast and less susceptible to motion artifacts,[19,26,27] therefore, it could potentially be integrated in routine MRI protocols without significant prolongation of the scanning time.

The aim of this study is the investigation of T1 relaxation times as a potential marker for treatment decisions and success in patients with cSCS receiving decompressive surgery or conservative treatment.

METHODS

Study design and patient inclusion

Patients with symptomatic cSCS undergoing decompressive spinal surgery or conservative treatment have been included in this prospective, single-center, observational study. Recruitment took place in the Department of Neurology and Neurosurgery at the University Medical Center Goettingen (Germany) between 2019 and 2022. Treatment decisions were made by the treating clinicians (neurologist, neurosurgeons) according to current best practice principles and guidelines. Clinical history and examination as well as conventional MRI and electrophysiological studies were performed at baseline. All patients were invited for follow-up MRI scans and clinical examination after 6 months. Figure 1 shows a graphical display of the study and MRI protocol.

The severity of SCS was assessed according to the graduation system developed by Kang et al.,[28] sorting the patients into severity groups 0-3 depending on sagittal T2-weighted MRI of the spinal cord. While grade 0 equals a normal result without any narrowing of the spinal canal, grade 1 is defined by a partial narrowing of the ventral or dorsal subarachnoid cavity. Grade 2 in turn is defined by the full narrowing of the subarachnoid cavity accompanied by a compression of the spinal cord without detection of ISI. Grade 3 refers to stenosis with ISI in the compressed part of the spinal cord in T2-weighted MRI, referred to as myelopathy signal.

Patients included in the study needed to give informed consent and be able to partake in the examinations specified in the study protocol. Therefore, exclusion criteria contained contraindications for MRI (eg, implanted pacemaker), diseases affecting the central nervous system (eg, multiple sclerosis, Parkinson's disease) due to possible confounding of study results, as well as a bodyweight of > 120 kg and abdominal circumference of > 90 cm, due to size limitations of the MRI scanner.

The study protocol was approved by the ethics committee of the University Medical Center Goettingen (Protocol number 6/6/17). Informed consent was obtained from all participants. Patient data were accessed using electronic patient records and clinical information systems (ixserv, ixmid Software Technology GmbH).

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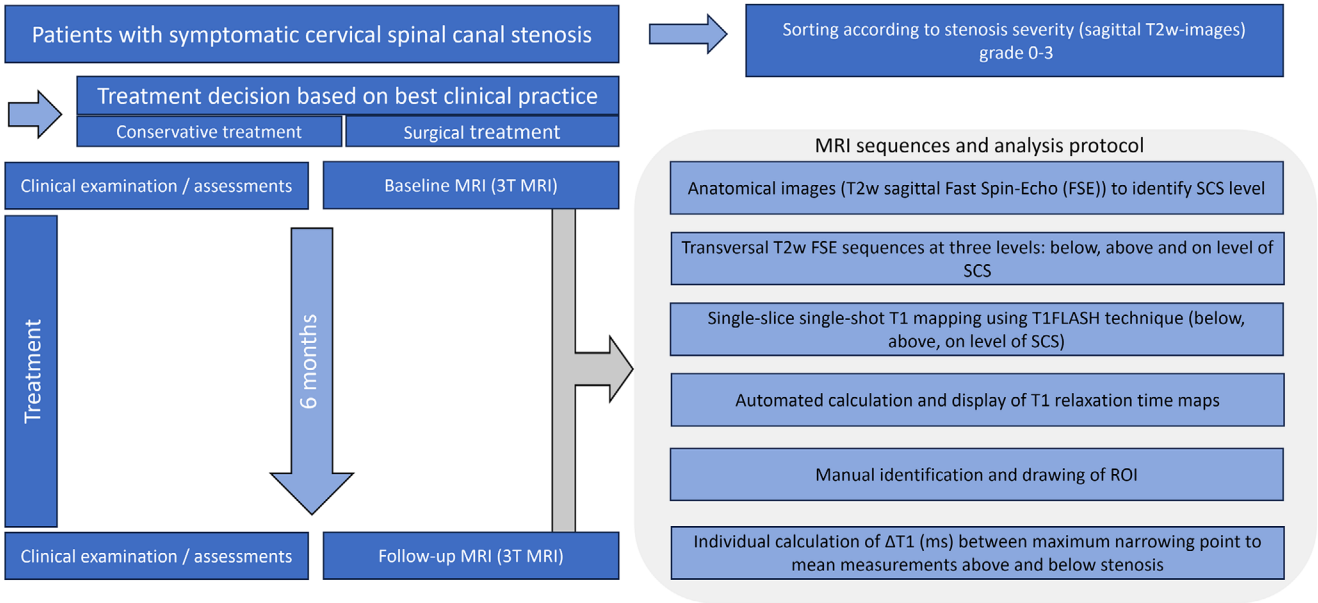

FIGURE 1 Study and MRI protocol: After study inclusion, patients received clinical assessments and 3T MRI at baseline as well as at follow-up after 6 months. A step-wise MRI protocol was implemented to determine spinal canal stenosis maximum and calculate ΔT1 individually at both timepoints. ms, milliseconds; ROI, regions of interest; SCS, spinal canal stenosis; T2w, T2-weighted images; 3T MRI, 3 Tesla MRI; ΔT1, T1 differences.

MRI protocol and T1-mapping

MRI studies were conducted using a 3-Tesla-MRI (Magnetom Prisma fit, Siemens Healthineers) with a 64-channel head and neck coil. MRI scans were performed using the imaging method detailed in our two previous articles on T1-mapping in SCS.[20,25] Anatomical images were based on a T2-weighted sagittal Fast Spin-Echo (FSE) scan of the cervical and upper thoracal spine, identifying levels of the SCS. Transversal T2-weighted FSE sequences with an in-plane resolution of 0.7 mm and a slice thickness of 3 mm (repetition time TR = 4280 milliseconds, echo time TE = 98 milliseconds, flip angle = 120°) were obtained at three levels: below, above, and on the level of the spinal canal narrowing. Subsequently, single-slice single-shot T1 mapping using the T1FLASH technique was performed at the most severe narrowing of the spinal canal in the stenosis, as well as above, and below at a physiological width of the spinal canal. T1-mapping of the spinal column was performed at 0.5 mm in-plane resolution and 4 mm slice thickness in multiple axial sections perpendicular to the spinal cord. T1FLASH is based on a single inversion-recovery experiment with a leading slice-selective 180° inversion pulse, a highly undersampled radial gradient-echo readout and a nonlinear inverse image reconstruction technique (for protocol details, see reference Wang et al., 2015).[29] To summarize, a low-flip angle gradient-echo sequence (TR 3.81 milliseconds, TE 2.60 milliseconds, flip angle = 6°) with a small golden-angle radial trajectory (angle = 20.89°) and radiofrequency spoiling by random phase alterations[30] was employed. For optimization of computational speed, data binning involved 17 spokes per frame, resulting in a temporal resolution of 65 milliseconds for sampling the inversion-recovery process. Scan time for one T1 map equaled 4 seconds; including scout and localizer (each 14 seconds), cervical T2w (sagittal and transversal, each 1.49 minutes) overall scan time including the three acquired T1 maps was 4.30 minutes (= 258 seconds). After completion of data acquisition, maps of T1 relaxation times are calculated automatically and immediately displayed on the MRI system. Quantitative values are obtained by pixelwise fitting of the exponential signal model[31] to the set of reconstructed serial images. The parametric results are the equilibrium magnetization (M0), the steady-state magnetization (Mss), and the effective relaxation rate 1/T1* yielding T1 = T1* [(Mss – M0)/Mss – 1]. For the follow-up scan, an equal location was achieved by an anatomical localizer and a visual inspection of relevant MRI scans.

Determination of mean T1-values of the spinal cord ensued by the manual drawing of a region of interest (ROI) using both grayscale T1 maps and corresponding T2-weighted anatomical images. Partial volume effects of the cerebrospinal fluid, which has a prolonged T1 value in comparison, can be minimized through the high spatial resolution of the T1 maps, making it easily distinguishable from the spinal cord and bone structures. The difference of T1-relaxation time (= ΔT1) has been determined as follows: ΄T1 (ms) = $\frac{(T1\ (ms)\ above\ stenosis + T1\ (ms)\ below\ stenosis)}{2} - T1\ (ms)\ within\ maximum\ stenosis$. Fiji (Fiji Is Just ImageJ v2.15.0, https://imagej.net/software/fiji/)[32] was used for data analysis and ROI determination.

Clinical examinations

Clinical examination was performed at baseline and after 6 months. Pain was assessed using the Numeric Rating Scale (NRS) as a patient-reported outcome measure, with patients describing their current level of pain on a semiquantitative scale between 0 (= no pain) and

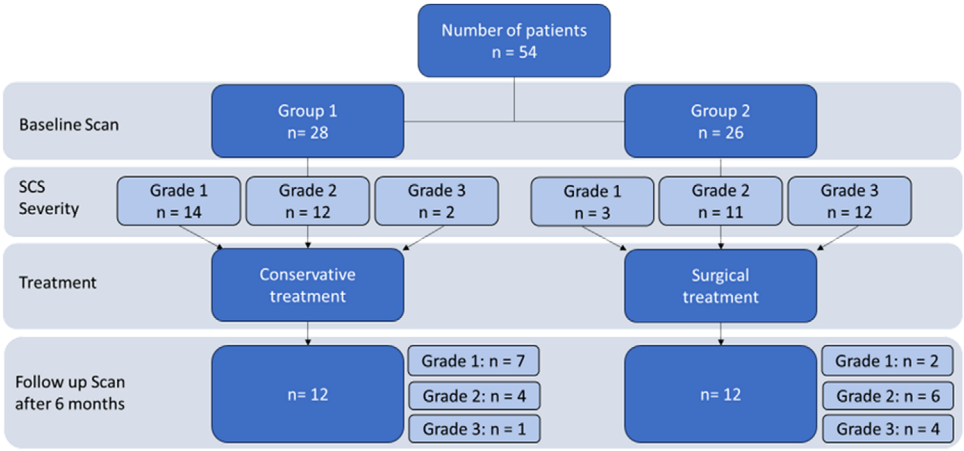

FIGURE 2 Study design and patient distribution to treatment arms, referencing severity grades of cervical spinal canal stenosis. *n*, number of patients.

10 (= maximum possible pain). The modified Japanese-Orthopedic-Association-Score (mJOA-Score) was used to quantify clinical impairment, including parameters like muscle strength and function, sensory function, and bladder control.[33,34] Grip strength and fatigue-able weakness were evaluated by the Grip and Release-Test; patients were asked to open and close their fists as often as possible in 10 seconds, the number of movements was counted, and 20 cycles or more were deemed normal.[35] Walking ability was assessed using the Nurick scale, categorizing patients into six groups (grade 0 = normal gait, grade 5 = complete immobility, patient is bedbound), and the 30-meter walking test (30MWT).[36]

Statistical analysis

Statistical analysis was performed using SPSS 28 (IBM SPSS Statistics, Armonk, NY, USA, https://www.ibm.com/products/spss-statistics/). Baseline characteristics of all patients and controls are shown as mean ± standard deviation (SD), if normally distributed, and as median with interquartile range (IQR), if unnormal distribution occurred. Statistical differences were analyzed using unpaired *t*-test or Mann-Whitney U-test, respectively. T1 relaxation times were compared using one-way ANOVA with repeated measurements and post-hoc Bonferroni correction for multiple comparisons at a threshold of $p < .05$. Categorial variables were described as number with percentage (*n*, %), and correlations were calculated using the Chi-Square Test. Correlations between clinical or radiological scores and T1 relaxation times were determined by a bivariate Pearson-correlation. *p*-Values below .05 were considered statistically significant.

RESULTS

Baseline characteristics

In Figure 2, the overall study design and patient distribution into different treatment arms are referenced. Baseline MRI scans were performed in 54 patients, with 28 (51.9%) patients receiving conservative and 26 (48.1%) patients receiving surgical treatment. Follow-up scans after 6 months were available in 12 patients in each group. Baseline characteristics are shown in Table 1. There were no significant differences in age, weight, or height. There was a significant difference in gender distribution with more males in the surgical versus the conservative treatment group (76.9% vs. 42.9%, $p = .011$).

Moreover, the severity of cSCS differed between the groups. Whereas at baseline, both groups included nearly equal numbers of patients with a grade 2 stenosis (12 [42.9%] and 11 [42.83%], respectively), in the conservative treatment group, only two patients (7.1%) had severe (grade 3) stenosis with the majority of patients ($n = 14$, 50%) showing a mild stenosis, compared to the surgical treatment group including 12 patients (46.2%) with severe (grade 3) and only three patients (11.5%) with low-grade (grade 1) stenosis. On average, patients in the surgical treatment group showed a higher-grade stenosis (median [IQR] = 2 [2-3]) compared to the patients with conservative treatment (median [IQR] = 1.5 [1-2]; $p = .001$). The most common location of stenosis was at C5/6 in both groups, with 57.1% and 42.3% of patients in each group, respectively.

The surgical group showed significantly higher clinical deficits caused by the SCS at baseline. The JOA-Score was lower in the surgical group (conservative: median [IQR] = 16 [12.8-17], surgical: median [IQR] = 13 [10.9-14.6], $p = .001$), the Nurick scale was correspondingly higher (conservative: median [IQR] = 0 [0-1.5], surgical: median [IQR] = 2 [1-2.3], $p = .007$). The average level of pain was higher in the surgically treated group, but no statistically significant difference was detected (conservative: median [IQR] = 0 [0-3], surgical: median [IQR] = 2 [0-5], $p = .179$). For the grip and release test, the mean value between repeated measures of the right and left hand was calculated without detection of relevant differences between groups ($p = .627$). Similarly, no significant differences in the results of the 30-meter walking tests were found ($p = .863$).

TABLE 1 Baseline characteristics.

	SCS conservative treatment ($n = 28$)	SCS surgical treatment ($n = 26$)	p-value
Age (mean ± SD)	62.4 ± 13.8	65.0 ± 12.8	.470
Sex male *n* (%)	12 (42.9)	20 (76.9)	.011*
Height (mean cm ± SD)	171.9 ± 9.7	174.1 ± 8.4	.381
Weight (mean kg ± SD)	80.1 ± 14.2	80.0 ± 14.4	.989
Spinal level of stenosis			.648
C2/3 *n* (%)	1 (3.6)	0	
C3/4 *n* (%)	3 (10.7)	4 (15.4)	
C4/5 *n* (%)	6 (21.4)	8 (30.8)	
C5/6 *n* (%)	16 (57.1)	11 (42.3)	
C6/7 *n* (%)	2 (7.1)	3 (11.5)	
C7/Th1 *n* (%)	0	0	
SCS severity median (IQR)	1.5 (1-2)	2 (2-3)	.001*
Grade 1 *n* (%)	14 (50.0)	3 (11.5)	
Grade 2 *n* (%)	12 (42.9)	11 (42.3)	
Grade 3 *n* (%)	2 (7.1)	12 (46.2)	
Clinical examinations			
Pain NRS median (IQR)	0 (0-3)	2 (0-5)	.179
mJOA score median (IQR)	16 (12.8-17.0)	13 (10.9-14.6)	.001*
Nurick scale median (IQR)	0 (0-1.5)	2 (1-2.3)	.007*
Grip and Release Mean (mean ± SD)	20.8 ± 7.7	19.8 ± 7.8	.627
30MWT (mean ± SD)	19.3 ± 12.6	18.7 ± 7.7	.863

Abbreviations: C, cervical; cm, centimeter; IQR, interquartile range; kg, kilograms; mJOA, modified Japanese-Orthopedic-Association-Score; *n*, number of patients; NRS, numeric rating scale; SD, standard deviation; Th, thoracic; 30MWT, 30-meter walking test.
*Significance level of $p < .05$.

TABLE 2 Comparison of longitudinal T1-measurements between treatment groups.

	Baseline	Follow up	p-value
Conservative treatment	$n = 12$		
T1 intrastenosis(ms)	855.1 ± 62.2	863.5 ± 42.2	.654
ΔT1 (T1-Differences)(ms)	95.3 ± 60.7	118.6 ± 43.2	.233
Surgical treatment	$n = 12$		
T1 stenosis(ms)	863.7 ± 89.3	931.7 ± 106.5	.064
ΔT1(ms)	154.9 ± 81.6	85.7 ± 108.9	.021*

Note: All the data are represented as mean ± standard deviation unless otherwise indicated.
Abbreviations: ms, milliseconds; *n*, number of patients.
*Significance level of $p < .05$.

Longitudinal analysis of T1 relaxation times in patients with conservative and surgical treatment

Pooling all SCS severity grades together, longitudinal changes of the absolute T1 relaxation time and ΔT1 were analyzed in both treatment groups (Table 2). Overall, ΔT1 and absolute T1 values at SCS maximum remained unchanged in the group with a conservative treatment approach. In contrast, in the patient group receiving spinal surgery, absolute T1 values at the SCS level showed a trend toward an increase from 863.7 milliseconds ± 89.3 to 931.7 milliseconds ± 106.5 ($p = .064$) with significant reduction of ΔT1 6 months after surgery (mean ± SD [milliseconds]: baseline: 154.9 ± 81.6 vs. long-term: 85.7 ± 108.9, $p = .021$). Overall, surgical intervention resulted in a significant decrease of ΔT1 in T1 mapping, whereas a conservative approach did not lead to statistically significant changes in T1 values.

Cross-sectional assessment of T1 relaxation time at baseline and follow-up

T1 relaxation time was measured for all scanned levels (below, within, and above the stenosis) and the ΔT1 was calculated (Table 3) and compared between different grades of SCS and between conservative and surgical treatment groups. Representative T1 maps are shown in Figure 3. Absolute T1 relaxation times at the maximum spinal cord narrowing were comparable between the surgical and conservative group at baseline. However, ΔT1 was higher in the surgical group compared to the conservative group in all three SCS severity categories. In both

TABLE 3 T1 mapping results at baseline and follow-up.

	Conservative treatment			Surgical treatment		
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Baseline, $n = 54$	$n = 14$	$n = 12$	$n = 2$	$n = 3$	$n = 11$	$n = 12$
T1 stenosis (ms)	875.5 ± 48.8	828.8 ± 67.9	889.4 ± 61.2	785.6 ± 77.1	884.2 ± 73.7	892.4 ± 62.8
T1 above stenosis (ms)	984.4 ± 72.7	941.5 ± 100.3	906.5 ± 56.9	941.6 ± 88.3	1032.9 ± 105.9	963.7 ± 79.4
T1 below stenosis (ms)	942.2 ± 60.6	931.0 ± 100.6	919.2 ± 118.5	950.9 ± 138.5	1001.9 ± 117.5	1028.6 ± 70.9
T1 mean above/below (ms)	963.3 ± 53.8	936.2 ± 77.7	912.8 ± 87.7	946.3 ± 112.8	1017.4 ± 93.8	996.1 ± 63.3
ΔT1 (T1-Differences, ms)	87.8 ± 66.6	107,5 ± 71.5	23.5 ± 149.0	160.6 ± 114.2	133.3 ± 83.9	103.8 ± 64.4
Follow up ($n = 24$)	$n = 7$	$n = 4$	$n = 1$	$n = 2$	$n = 6$	$n = 4$
T1 stenosis (ms)	879.9 ± 39.0	830.1 ± 35.6	882.4	947.5 ± 111.9	882.2 ± 111.5	998.5 ± 75.6
T1 above stenosis (ms)	1027.2 ± 40.6	1015.0 ± 48.7	945.3	959.2 ± 52.9	1001.9 ± 81.1	1053.6 ± 55.7
T1 below stenosis (ms)	940.6 ± 48.1	941.3 ± 124.8	1023.0	1029.0 ± 134.3	1000.1 ± 138.0	1054.3 ± 41.4
T1 mean above/below (ms)	983.9 ± 25.9	978.2 ± 73.3	984.2	994.1 ± 93.6	1001.0 ± 105.8	1054.0 ± 41.0
ΔT1 (ms)	104.1 ± 36.3	148.1 ± 49.6	101.8	46.6 ± 205.5	118.8 ± 87.0	55.5 ± 111.3

Note: T1 mapping results with mean T1 relaxation times within, above, and below the spinal canal stenosis as well as ΔT1 in both patients with conservative and surgical treatment. All T1 relaxation times are given in milliseconds. All the data represent mean ± standard deviation unless otherwise indicated. Abbreviations: ms, milliseconds; *n*, number of patients.

treatment groups, ΔT1 was lower in grade 3 stenosis compared to grade 1 and 2 stenosis; however, result interpretation in the conservative group is limited due to the reduced sample size (grade 3 $n = 2$). Patients in the surgical treatment group overall had a higher ΔT1 compared to the conservative treatment group. In the surgical treatment arm, ΔT1 decreased inverse to stenosis severity, with mean ΔT1-values (mean ± SD [milliseconds]) of 160.6 ± 114.2, 133.3 ± 83.9, and 103.8 ± 64.4 in the SCS grades 1-3, respectively. Absolute T1-mapping values within the stenosis increased from grade 1 to 3 SCS accordingly, from 785.6 ± 77.1 in grade 1 SCS to 884.2 ± 73.7 and 892.4 ± 62.8 in grade 2 and 3 stenosis.

Absolute T1 values at the maximum level of the stenosis and ΔT1 were reevaluated after 6 months in both treatment groups (Table 2). In the conservatively treated group, comparison of SCS-severity groups after 6 months showed a similar dynamic to the baseline scan, with increasing ΔT1 between grade 1 and 2 (mean ± SD [milliseconds], 1: 104.1 ± 36.3, 2: 148.1 ± 49.6). A follow-up was only performed in one patient in the grade 3 SCS group with conservative treatment. In the surgically treated group, follow-up scans 6 months after operative decompression were performed in 12 patients. As in the baseline scans, ΔT1 increased between grade 1 and grade 2 stenosis (mean ± SD [milliseconds], 1: 46.4 ± 205.5, 2: 118.8 ± 87.0) and decreased again in grade 3 stenosis (mean ± SD [milliseconds]: 55.5 ± 111.3).

Clinical assessments and functional implications

Results from clinical assessments are shown in Table 4. Improvements of clinical tests were found in both treatment groups. In the surgical group, there was a slight, nonsignificant improvement in Pain NRS, JOA scale, and 30MWT as well as a trend toward an improved grip and release test (21.2 ± 8.5 and 25.4 ±10.9, $p = .059$). Only patients with complete datasets for the individual parameter/test at baseline and follow-up visit were included, leading to different case numbers for each assessment. In the group with a conservative treatment plan, patients showed a significant increase in repetitions in the Grip and Release-Test (mean ± SD: baseline: 22.5 ± 5.4, follow up 29.7 ± 5.6, $p = .002$), testing upper extremity functions, as well as a significant improvement in the 30-meter walking test (mean ± SD, baseline: 16.9. ± 5.7, follow up 13.8 ± 7.0, $p = .023$) after 6 months. Congruously, answers in the NRS for pain revealed a reduction of subjective pain level. The results of the Nurick scale and mJOA score remained unchanged. No significant correlation of

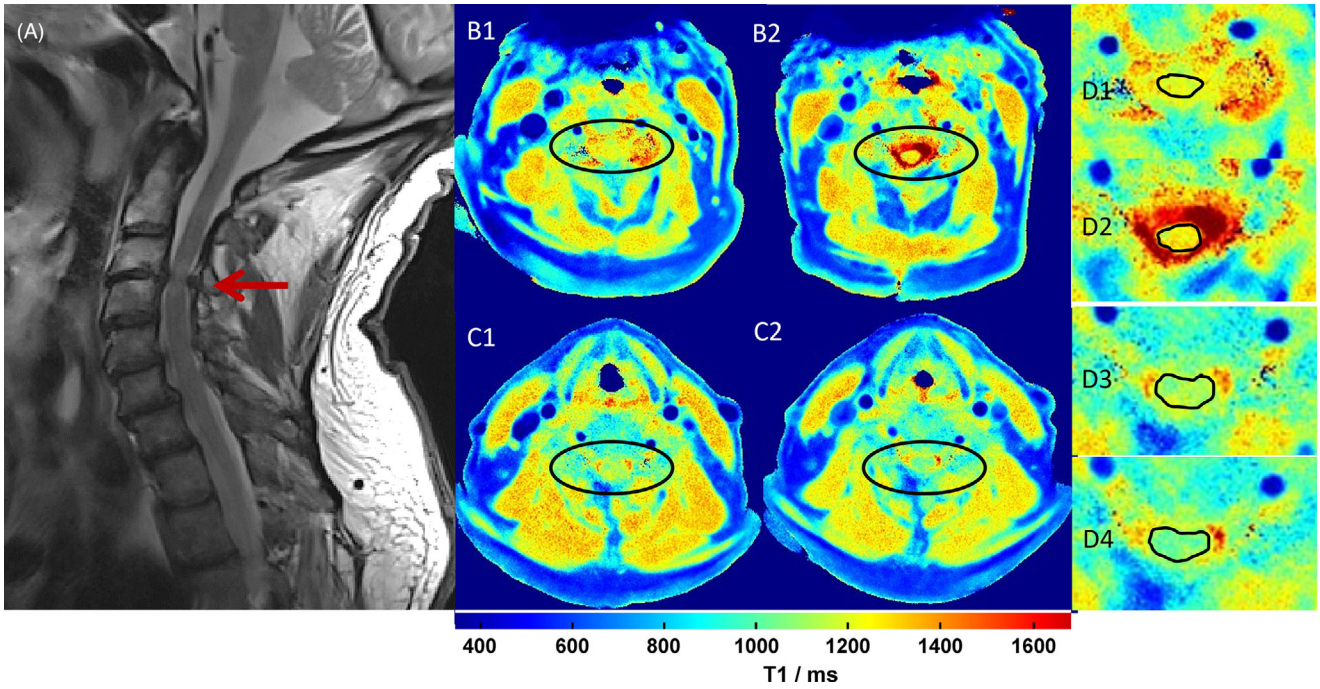

FIGURE 3 Representative case of a patient with a grade 2 spinal canal stenosis (SCS): (A) sagittal plane T2-weighted MRI with punctum maximum SCS at C3/4 (red arrow); (B1) color-coded axial T1 map before and (B2) 6 months post-decompressive surgery. Note the increase in T1 relaxation time (region marked with ellipsis) from baseline (B1) to follow-up scan (B2). (C1) and (C2) show a representative case with a grade 2 SCS managed conservatively at baseline and follow-up, respectively. Note no change in T1 relaxation times in this patient. The measured regions of interest are indicated with black in the enlarged exemplary images displayed in column D (D1-D4). ms, milliseconds.

TABLE 4 Comparison of longitudinal clinical assessments between treatment groups.

	Conservative treatment			Surgical treatment		
	Baseline	6 months follow up	*p*-value	Baseline	6 months follow up	*p*-value
n (SCS grade)	*n* = 12 (1.5 ± 0.7)			*n* = 12 (2.2 ± 0.7)		
ΔT1	95.3 ± 60.7	118.6 ± 43.2	.233	154.9 ± 81.6	85.7 ± 108.9	.021*
n (SCS grade)	*n* = 10 (1.6 ± 0.7)			*n* = 12 (2.2 ± 0.7)		
Pain (NRS)	1.7 ± 2.8	1.0 ± 2.2	.343	2.3 ± 2.5	1.0 ± 1.9	.142
n (SCS grade)	*n* = 9 (1.4 ± 0.5)			*n* = 12 (2.2 ± 0.7)		
mJOA score	16.3 ± 1.3	16.1 ± 1.3	.195	12.5 ± 2.4	13.5 ± 2.5	.297
n (SCS grade)	*n* = 6 (1.3 ± 0.5)			*n* = 11 (2.1 ± 0.6)		
Nurick scale	0.2 ± 0.4	0.7 ± 1.0	.203	1.6 ± 0.9	1.9 ± 0.8	.341
n (SCS grade)	*n* = 10 (1.6 ± 0.7)			*n* = 12 (2.2 ± 0.7)		
Grip and Release	22.5 ± 5.4	29.7 ± 5.6	.002*	21.2 ± 8.5	25.4 ±10.9	.059
n (SCS grade)	*n* = 6 (1.3 ± 0.5)			*n* = 9 (2.0 ± 0.7)		
30MWT	16.9 ± 5.7	13.8 ± 7.0	.023*	18.2 ± 8.2	16.3 ± 9.3	.260

Note: All the data represent mean ± standard deviation unless otherwise indicated.
Abbreviations: mJOA, modified Japanese-Orthopedic-Association-Score; *n*, number or patients; NRS, numeric rating scale; 30MWT, 30-meter walking test.
*Significance level of $p < .05$.

changes in clinical severity and functional tests between baseline visit and follow-up with T1 measurements (ΔT1) for the evaluated parameters was found (Table 5). Nevertheless, it must be noted that the average severity of SCS was higher in the patient group receiving surgical treatment (mean ± SD: 2.2 ± 0.7) compared to conservatively treated patients (1.5 ± 0.7), which is reflected in the average severity grade of SCS for each individual clinical test (Table 4).

TABLE 5 Results of correlation analysis between ΔT1-changes and clinical progression in both treatment groups.

	Conservative ΔT1 LT−ΔT1 BL	Surgical ΔT1 LT−ΔT1 BL
Pearson-correlation "*r*"	*n* = 10	*n* = 12
ΔGrip and Release mean (LT-BL)	0.068	0.194
Significance value of correlation	0.851	0.546
Pearson-correlation "*r*"	*n* = 6	*n* = 9
Δ30MWT (LT-BL)	0.295	(−)0.424
Significance value of correlation	0.570	0.225
Kendall-Tau-correlation	*n* = 10	*n* = 12
ΔPain (NRS) (LT-BL)	(−)0.447	0.134
Significance value of correlation	0.117	0.566

Abbreviations: BL, baseline; LT, long-term follow up; *n*, number of patients; NRS, numeric rating scale; 30MWT, 30 meter walking test.

DISCUSSION

Spinal decompression surgery reduces ΔT1 in longitudinal follow-up

In this study, the longitudinal changes of ΔT1 between a surgical and a conservative treatment approach in cervical SCS were evaluated to assess the feasibility of T1 mapping as an imaging biomarker. Patients receiving a surgical intervention showed a significant decrease in ΔT1 at the 6-month follow-up scan, with a corresponding trend toward increased absolute T1 values intrastenosis. This might reflect the reduction of spinal cord narrowing after surgery, since lower T1 relaxation times within the SCS correspond with the SCS severity.[20] Contrasting, conservatively treated patients did not show a relevant change in absolute T1 values or ΔT1 after 6 months. Overall, changes in T1 mapping might correlate with a beneficial impact of spine surgery, with a decreased ΔT1 possibly associated with recovery of the spinal cord. This correlation emphasizes the impact of surgical decompression on T1 relaxation times, showing reversibility of conspicuous T1 mapping results even in severe SCS, whereas the traditionally used ISI may remain irreversible after surgical treatment, complicating assessment of post-surgery symptoms.[37] This implicates the applicability of T1 mapping as a follow-up parameter in spinal surgery to evaluate structural improvement, especially in patients experiencing residual or even progressive symptoms. Additionally, with further evaluation, T1 mapping might be of assistance explaining residual symptoms in patients with high presurgical impairment.

ΔT1-values depend on the SCS severity and might be influenced by spinal cord edema

A nonsignificant increase in ΔT1 was observed between grade 1 and 2 SCS in the conservatively treated cohort. In grade 3 stenosis, as well as the surgical intervention group, ΔT1 slightly decreased with aggravation of spinal canal narrowing, without the detection of statistically significant changes. This observation differs from results in previous publications, where a grade-dependent difference in ΔT1 from grade 1 to grade 3 stenosis has been detected,[20] indicating ΔT1 as a more sensitive spinal cord compression marker than absolute T1 values.[25] Notably, only patients receiving conservative treatment recommendations were included in these previous studies. Naturally, this approach excluded more severely affected patients receiving surgical treatment. Fittingly, in this study, patients with comparable characteristics (conservative treatment, grade 1 and 2 SCS) display the previously described trend, whereas imaging results diverge in high-grade stenosis as well as patients with severe clinical manifestation prompting surgical intervention. This suggests pathophysiological differences in high-grade stenosis contributing to changes in T1 mapping imaging results as well as clinical presentation. A major contributor might be spinal cord edema. Water is known to possess a relatively long T1 relaxation time. Therefore, edema formation might majorly influence T1 relaxation time and subsequently calculation of ΔT1. Additional studies including a larger and more diverse patient cohort are required to verify this effect and further analyze the reliability of T1 mapping in severity assessment of SCS.

With no relevant differences in absolute T1 values at baseline between treatment groups, absolute T1 relaxation time at stenosis level seems to not be a good predictor of treatment. However, at baseline, patients in the surgically treated group showed overall higher ΔT1 compared to the conservatively treated cohort, either in group-wise comparison (comparison of grade 1 to 1, grade 2 to 2, and grade 3 to 3) as well as in pooled results. These differences might correspond to pathophysiological differences prompting a more severe clinical presentation with significant symptoms subsequently resulting in a recommendation for surgery. A possible explanation could be a more acute onset of spinal canal narrowing with reduced development of compensatory measures in this cohort. Therefore, with further investigation, ΔT1 might provide a supportive diagnostic measure for treatment determination in borderline cases in the future.

Improvement of clinical function in both treatment groups after 6 months

In the conservatively treated cohort, the 6MWT and the Grip and Release test improved significantly after 6 months. However, most other functional assessments showed trends toward improvement, without significant differences between the conservative and surgical treatment group. Interestingly, the detected significant changes in ΔT1 between timepoints in surgically treated patients did not correlate with the clinical outcome changes. Nevertheless, the improvement of clinical parameters in both treatment groups might complicate the determination of relevant correlations between imaging results and functional outcome measures. Notably, conservative treatments can include different therapeutic measures (eg, physical therapy or rehabilitation), with the goal to provide symptom relief and functional improvement, explaining clinical improvement in conservatively treated patients.

The severity level of the SCS at baseline influences clinical outcome. A higher-grade SCS can be associated with irreversible structural

changes not rectifiable by spinal decompression, whereas in lower-grade stenosis, symptoms are more likely to be reversible.[38] In the surgically treated cohort, patients partaking in the 6-month follow-up had a more severe SCS at baseline level, putting patients in the surgically treated group at higher risk for irreversible symptoms. Missing clinical benefit of surgical intervention in late-stage SCS has been reported.[13–15] A more in-depth characterization of disease activity and symptom burden as well as a larger cohort of low-grade stenosis receiving a surgical intervention might elucidate this further. Contrasting the other clinical outcome measures, the Nurick scale revealed a nonsignificant trend toward clinical deterioration regarding walking abilities in both treatment cohorts after 6 months. Previous comparative studies have emphasized possible reasons for diverging outcomes between Nurick and mJOA scores in SCS patients receiving decompression surgery.[39] Moreover, the Nurick scale has been implicated to be less sensitive to improvement following surgery compared to multiple scoring systems,[40] especially due to its focus on employment consequences. Therefore, the Nurick scale might not be the optimal outcome measure to evaluate therapy success.

Study limitations

To the best of our knowledge, our study is the first trial evaluating the differences in T1 relaxation times of SCS between conservative and surgical treatment. However, some study limitations need to be acknowledged. First, a high drop out rate between baseline scan and follow-up examination was recorded, due to various reasons (eg, unwillingness to do a second scan, individual's declining or improving health). Moreover, the distribution of stenosis severity grade differs significantly between treatment groups, due to therapy being decided according to clinical standard independently from study participation, with surgical treatment being recommended more frequently to high-grade SCS patients with more severe clinical symptoms.

Second, the inclusion of an additional group of healthy participants would have been beneficial to account for other influencing variables. No harmonized treatment regimen was implemented in the conservative treatment group regarding physical therapy, rehabilitation, or medication. All therapies were coordinated by the treating clinicians and, therefore, dependent on their individual approach, without collection of data on treatment measures for study purposes. It remains unknown whether different conservative therapy approaches might influence T1 relaxation times long-term. Moreover, no information on structural causes for spinal cord narrowing was collected, possibly influencing the variability of imaging results as well as prompting alternative surgical approaches.[41] Another complicating factor is the strong variation in the clinical presentation of SCS, which not necessarily correlates with the severity grade observed in neuroimaging. Electrophysiological studies might provide beneficial information and should be included in future studies. Additionally, the duration of symptoms and stenosis development might vastly differ between patients reducing comparability. This could possibly explain missing correlations between imaging findings and functional assessments.

Clinical feasibility, artifact impact, and generalizability

The T1-mapping method used in the present study,[30,31] compared to previously described techniques, has the advantage of very fast image acquisition. It is, therefore, considered very robust with respect to motion artifacts, which frequently impair MR-imaging in patients with degenerative disease of the spinal collum associated with pain and impaired range of motion. We consider the used T1 mapping technique as feasible in clinical practice, as it does not rely on special requirements for MR-equipment or handling. Due to its very fast scan time, the technique provides economical and workload-related advantages as well. This technique has also been used in other neurological diseases by our working group, including patients with impaired motor functions susceptible for motion artifacts,[42] emphasizing the generalizability of the applied method in a broader spectrum of diseases.

Concluding remarks

The longitudinal assessment revealed significant changes in ΔT1-values of SCS patients undergoing decompressive spine surgery. This emphasizes the possible applicability of T1-mapping in the diagnosis of SCS and as a supportive measure for treatment recommendations and follow-up evaluation. However, additional studies with larger, more-streamlined cohorts as well as longitudinal analyses of healthy cohorts are warranted.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

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REFERENCES

1. Lenga P, Papakonstantinou V, Kiening K, et al. Outcomes of cervical spinal stenosis surgery in patients aged ≥ 65 years based on insurance status: a single-center cohort study from a tertiary center in Germany. Acta Neurochir (Wien). 2023;165:3089-96.
2. Kellgren JH, Lawrence JS. Osteo-arthrosis and disk degeneration in an urban population. Ann Rheum Dis. 1958;17:388-97.
3. Lawrence JS. Disc degeneration. Its frequency and relationship to symptoms. Ann Rheum Dis. 1969;28:121-38.

4. Matsumoto M, Fujimura Y, Suzuki N, et al. MRI of cervical intervertebral discs in asymptomatic subjects. J Bone Joint Surg Br. 1998;80:19-24.
5. McCormick WE, Steinmetz MP, Benzel EC. Cervical spondylotic myelopathy: make the difficult diagnosis, then refer for surgery. Cleve Clin J Med. 2003;70:899–904.
6. Kalsi-Ryan S, Karadimas SK, Fehlings MG. Cervical spondylotic myelopathy: the clinical phenomenon and the current pathobiology of an increasingly prevalent and devastating disorder. Neuroscientist. 2013;19:409-21.
7. St Clair S, Bell GR. Natural history of cervical spondylotic myelopathy. Semin Spine Surg. 2007;19:2-5.
8. Hug A, Hähnel S, Weidner N. Diagnostik und konservative Therapie zervikaler und lumbaler Spinalkanalstenosen. Nervenarzt. 2018;89:620-31.
9. Witiw CD, Mathieu F, Nouri A, Fehlings MG. Clinico-radiographic discordance: an evidence-based commentary on the management of degenerative cervical spinal cord compression in the absence of symptoms or with only mild symptoms of myelopathy. Glob Spine J. 2018;8:527-34.
10. Bakhsheshian J, Mehta VA, Liu JC. Current diagnosis and management of cervical spondylotic myelopathy. Glob Spine J. 2017;7:572-86.
11. Takahashi M, Sakamoto Y, Miyawaki M, Bussaka H. Increased MR signal intensity secondary to chronic cervical cord compression. Neuroradiology. 1087;29:550-56.
12. Harkins KD, Xu J, Dula AN, et al. The microstructural correlates of T1 in white matter. Magn Reson Med. 2016;75:1341-45.
13. Karpova A, Craciunas S, Chua SY, et al. Accuracy and reliability of MRI quantitative measurements to assess spinal cord compression in cervical spondylotic myelopathy: a prospective study. Evid Based Spine Care J. 2010;1:56-57.
14. Sampath P, Bendebba M, Davis JD, Ducker TB. Outcome of patients treated for cervical myelopathy. A prospective, multicenter study with independent clinical review. Spine (Phila Pa 1976). 2000;25:670-76.
15. Sun Y, Yu K, Wang H, et al. Diagnosis and treatment of hidden lesions in "mild" cervical spondylotic myelopathy patients with apparent symptoms. Medicine (Baltimore). 2017;96:e7623.
16. Pratali RR, Smith JS, Ancheschi BC, et al. A technique for dynamic cervical magnetic resonance imaging applied to cervical spondylotic myelopathy: a reliability study. Spine (Phila Pa 1976). 2019;44:E26-E32.
17. Schatlo B, Remonda L, Gruber P, et al. Cervical spine prospective feasibility study: dynamic flexion-extension diffusion-tensor weighted magnetic resonance imaging. Clin Neuroradiol. 2019;29:523-32.
18. Wright D, Martin S, Pereira EA, et al. High field structural MRI in the management of degenerative cervical myelopathy. Br J Neurosurg. 2018;32:595-98.
19. Battiston M, Schneider T, Prados F, et al. Fast and reproducible in vivo T1 mapping of the human cervical spinal cord. Magn Reson Med. 2018;79:2142-48.
20. Maier IL, Hofer S, Joseph AA, et al. Quantification of spinal cord compression using T1 mapping in patients with cervical spinal canal stenosis—preliminary experience. Neuroimage Clin. 2019;21:101639.
21. Gelman N, Ewing JR, Gorell JM, et al. Interregional variation of longitudinal relaxation rates in human brain at 3.0 T: relation to estimated iron and water contents. Magn Reson Med. 2001;45:71-79.
22. Hofer S, Wang X, Roeloffs V, Frahm J. Single-shot T1 mapping of the corpus callosum: a rapid characterization of fiber bundle anatomy. Front Neuroanat. 2015;9:57.
23. Koenig SH, Brown RD 3rd, Spiller M, Lundbom N. Relaxometry of brain: why white matter appears bright in MRI. Magn Reson Med. 1990;14:482-95.
24. Vymazal J, Righini A, Brooks RA, et al. T1 and T2 in the brain of healthy subjects, patients with Parkinson disease, and patients with multiple system atrophy: relation to iron content. Radiology. 1999;211:489-95.
25. Maier IL, Hofer S, Eggert E, et al. T1 mapping quantifies spinal cord compression in patients with various degrees of cervical spinal canal stenosis. Front Neurol. 2020;11:574604.
26. Rasoanandrianina H, Massire A, Taso M, et al. Regional T1 mapping of the whole cervical spinal cord using an optimized MP2RAGE sequence. NMR Biomed. 2019;32:e4142.
27. Smith SA, Edden RA, Farrell JA, et al. Measurement of T1 and T2 in the cervical spinal cord at 3 Tesla. Magn Reson Med. 2008;60:213-19.
28. Kang Y, Lee JW, Koh YH, et al. New MRI grading system for the cervical canal stenosis. AJR Am J Roentgenol. 2011;197:W134-40.
29. Wang X, Roeloffs V, Merboldt K, et al. Single-shot multi-slice T1 mapping at high spatial resolution—inversion-recovery FLASH with radial undersampling and iterative reconstruction. Open Med Imaging J. 2015;9:1-8.
30. Roeloffs V, Voit D, Frahm J. Spoiling without additional gradients: radial FLASH MRI with randomized radiofrequency phases. Magn Reson Med. 2016;75:2094-932.
31. Deichmann R, Haase A. Quantification of T1 values by SNAPSHOT-FLASH NMR imaging, J Magn Reson. 1992;96:608-12.
32. Schindelin J, Arganda-Carreras I, Frise E, et al. Fiji—an open source platform for biological image analysis. Nat Methods. 2012;9:676-82
33. Japanese Orthopaedic Association score for cervical spondylotic myelopathy. J Jpn Orthop Assoc. 1975;99: prefatory note (in Japanese).
34. Revised Japanese Orthopaedic Association scores for cervical myelopathy. J Jpn Orthop Assoc. 1994;68:490–503 (in Japanese).
35. Ono K, Ebara S, Fuji T, et al. Myelopathy hand. New clinical signs of cervical cord damage. J Bone Joint Surg Br. 1987;69:215-19.
36. Singh A, Crockard HA. Quantitative assessment of cervical spondylotic myelopathy by a simple walking test. Lancet. 1999;354:370-73.
37. Ikegami S, Takahashi J, Misawa H, et al. Spinal cord MRI signal changes at 1 year after cervical decompression surgery is useful for predicting midterm clinical outcome: an observational study using propensity scores. Spine J. 2018;18:755-61.
38. Schmitt-Sody M, Kirchhoff C, Buhmann S, et al. Timing of cervical spine stabilisation and outcome in patients with rheumatoid arthritis. Int Orthop. 2008;32:511-16.
39. Revanappa KK, Rajshekhar V. Comparison of Nurick grading system and modified Japanese orthopaedic association scoring system in evaluation of patients with cervical spondylotic myelopathy. Eur Spine J. 2011;20:1545-51.
40. Vitzthum HE, Dalitz K. Analysis of five specific scores for cervical spondylogenic myelopathy. Eur Spine J. 2007;16:2096-103.
41. Heller JG, Schimandle JH. Operative treatment of degenerative cervical disk disease. J South Orthop Assoc. 1996;5:188-206.
42. Maier IL, Heide M, Hofer S, et al. High periventricular T1 relaxation times predict gait improvement after spinal tap in patients with diopathic normal pressure hydrocephalus. Clin Neuroradiol. 2022;32:1067-76.

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