

The SIR values were evaluated by three observers twice for each patient. These observers were blinded to the surgical data. The average score of the three observers was used in this study.

Data analysis

Pearson correlation analysis was used to examine the relationship among neurologic scores, SIR, and duration of the disease. The signal intensity changes on T2-WI were classified as “cystic type” and “diffuse type” on the basis of MRI morphologic classification of cervical spondylotic myelopathy [6]. Variables that showed significant relationship ($p < .05$) on univariate analysis were entered into stepwise multivariate regression to determine the variance of the JOA improvement rate. $SIR < 1$ represents a more significant lower signal intensity change compared with the normal spinal cord. A p value $< .05$ denoted the presence of a significant difference. All statistical analyses were conducted using the SPSS software (version 15.0, SPSS, Chicago, IL).

Results

Figures 1 and 2 show representative cases. Figure 1 shows MRI scans of a 54-year-old woman with cervical spondylotic myelopathy who showed 66.7% (fairly good) neurologic improvement at the latest follow-up. The preoperative mid-sagittal T2-WI scan showed intramedullary increased SI at C4–C5 level. The SIR on T2-WI was 1.90, representing increased cord SI (0.05 cm^2 ; small round)/normal cord SI at C7–T1 disc level (0.3 cm^2 ; large round). SIR on T1-WI was 1.13, calculated by the aforementioned equation at the same lesion detected on T2-WI.

The MRIs in Fig. 2 are those of a 59-year-old woman with cervical spondylotic myelopathy who showed 28.6% neurologic deterioration at follow-up. The mid-sagittal T2-WI scan showed intramedullary increased SI at C5–C6 level. The calculated SIRs by the aforementioned equation were 2.07 on T2-WI and 0.93 on T1-WI.

Demographic data and clinical findings

Table 2 summarizes patient demographics and clinical outcome. The study subjects included 96 men and 52 women (mean age at surgery: 69.6 years, range, 44–88 years, Cervical Spondylotic Myelopathy: $n=103$, ossification of the posterior longitudinal ligament: $n=48$), with a mean duration of neurologic symptoms of 8.1 months (range, 3–36 months). The mean JOA improvement rate was 54.7 ± 16.3 (range, 11.1–100). The mean SIRs on T1-WIs and on T2-WIs were 1.13 ± 0.17 (range, 0.71–1.55) and 1.83 ± 0.37 (range, 1.07–3.24), respectively. In our study, SIR on T1-WIs was < 1 before surgery in 32

EVIDENCE & METHODS

Context

The authors assessed spinal cord signal intensity in patients with cervical compressive myelopathy to determine the correlation with postoperative recovery.

Contribution

They found that a low intensity signal on T1 imaging preoperatively was correlated with poor neurological outcome. They also found a similar correlation for decreased signal intensity on T1 and increased signal intensity on T2 (relative to preoperative findings).

Implications

Prognostic information, such as this, is helpful for informed consent and surgical decision-making. This study had a reasonable number of patients and used a 1.5T MRI machine. Further investigation with higher quality MRI and more patients will be helpful.

—The Editors

Table 1
Japanese Orthopedic Association scoring system for assessment of cervical myelopathy

Category	Score (points)
Motor function of the upper extremity	
Unable to eat with either chopsticks or a spoon	0
Able to eat with spoon but not with chopsticks	1
Able to eat with chopsticks but inadequately	2
Able to eat with chopsticks but awkwardly	3
Normal	4
Motor function of the lower extremity	
Unable to walk	0
Needs a cane or other walking aid on flat ground	1
Needs walking aid only on stairs	2
Able to walk unaided, but slowly	3
Normal	4
Sensory function	
Upper extremity	
Apparent sensory disturbance	0
Minimal sensory disturbance	1
Normal	2
Lower extremity	
Apparent sensory disturbance	0
Minimal sensory disturbance	1
Normal	2
Trunk	
Apparent sensory disturbance	0
Minimal sensory disturbance	1
Normal	2
Bladder function	
Urinary retention or incontinence	0
Severe dysuria (sense of retention)	1
Slight dysuria (pollakiuria, retardation)	2
Normal	3

Note: The score in a normal subject is the total of the best scores: (I+II+III+IV)=17.

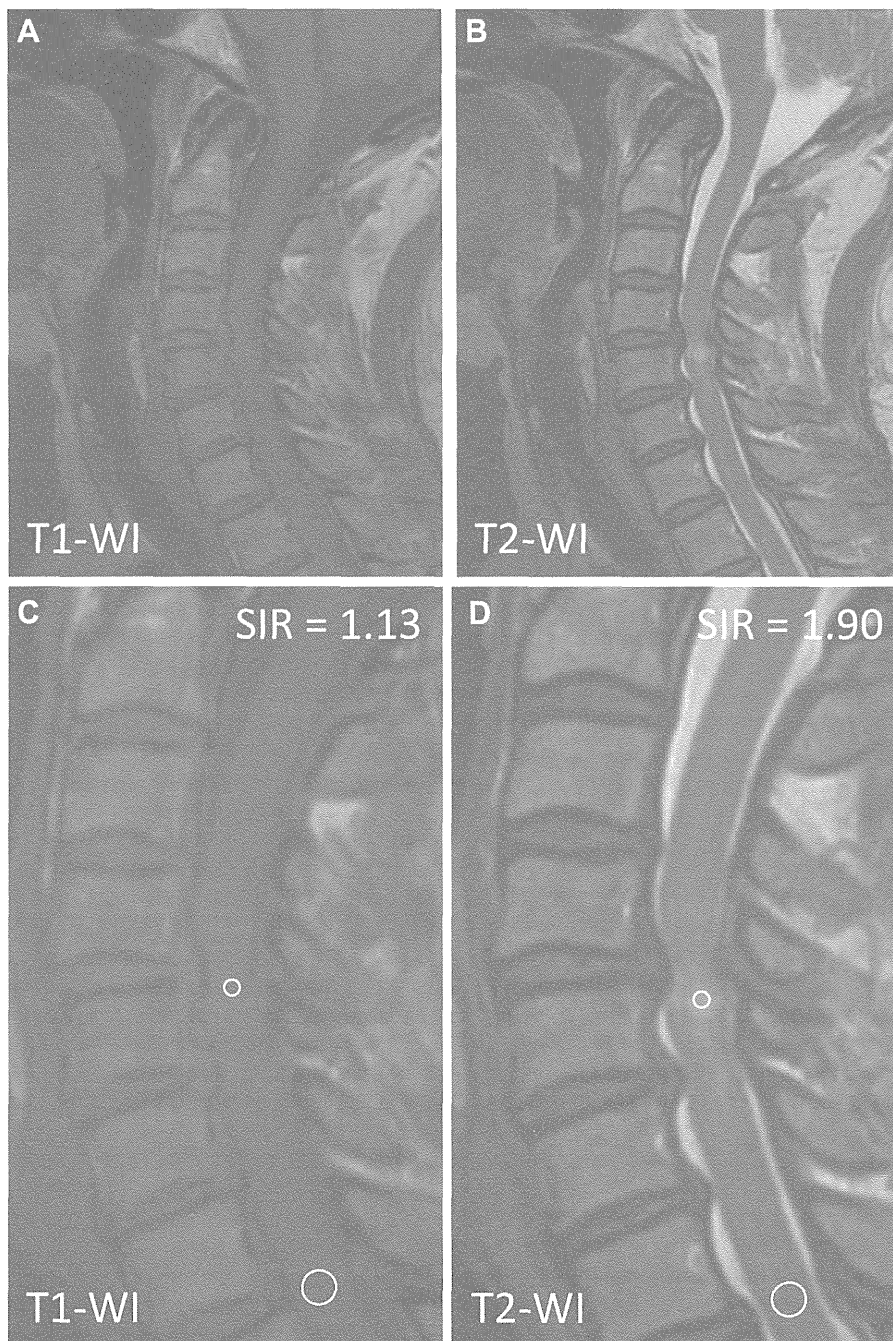


Fig. 1. A 54-year-old woman with cervical spondylotic myelopathy showed 66.7% (from 14 to 16) neurologic improvement at follow-up. (A) mid-sagittal T1-weighted MRI, (B) mid-sagittal T2-weighted MRI. Note the increased intramedullary signal intensity at C4–C5 level. (C) SIR is calculated by the mid-sagittal increased cord signal intensity (smaller round) / mid-sagittal normal cord signal intensity at the C7-T1 disc level (larger round) on T1-WI. (D) SIR on T2-WI is calculated using the same equation on the same lesion on T1-WI. MRI, magnetic resonance imaging; SIR, signal intensity ratio; WI, weighted image.

of 148 patients (21.6%). The preoperative neurologic score correlated with age ($R^2=0.126$, $p<.01$), postoperative neurologic improvement ($R^2=0.0404$, $p=.0148$) and disease duration ($R^2=0.0632$, $p<.01$). There were no significant intraobserver or interobserver differences in SIR on T1- and T2-WIs.

Relationship between SIR and preoperative neurologic scores

Figure 3 shows the relationship between SIRs for T1-WIs and T2-WIs and preoperative neurologic scores. A lower preoperative JOA score was associated with a

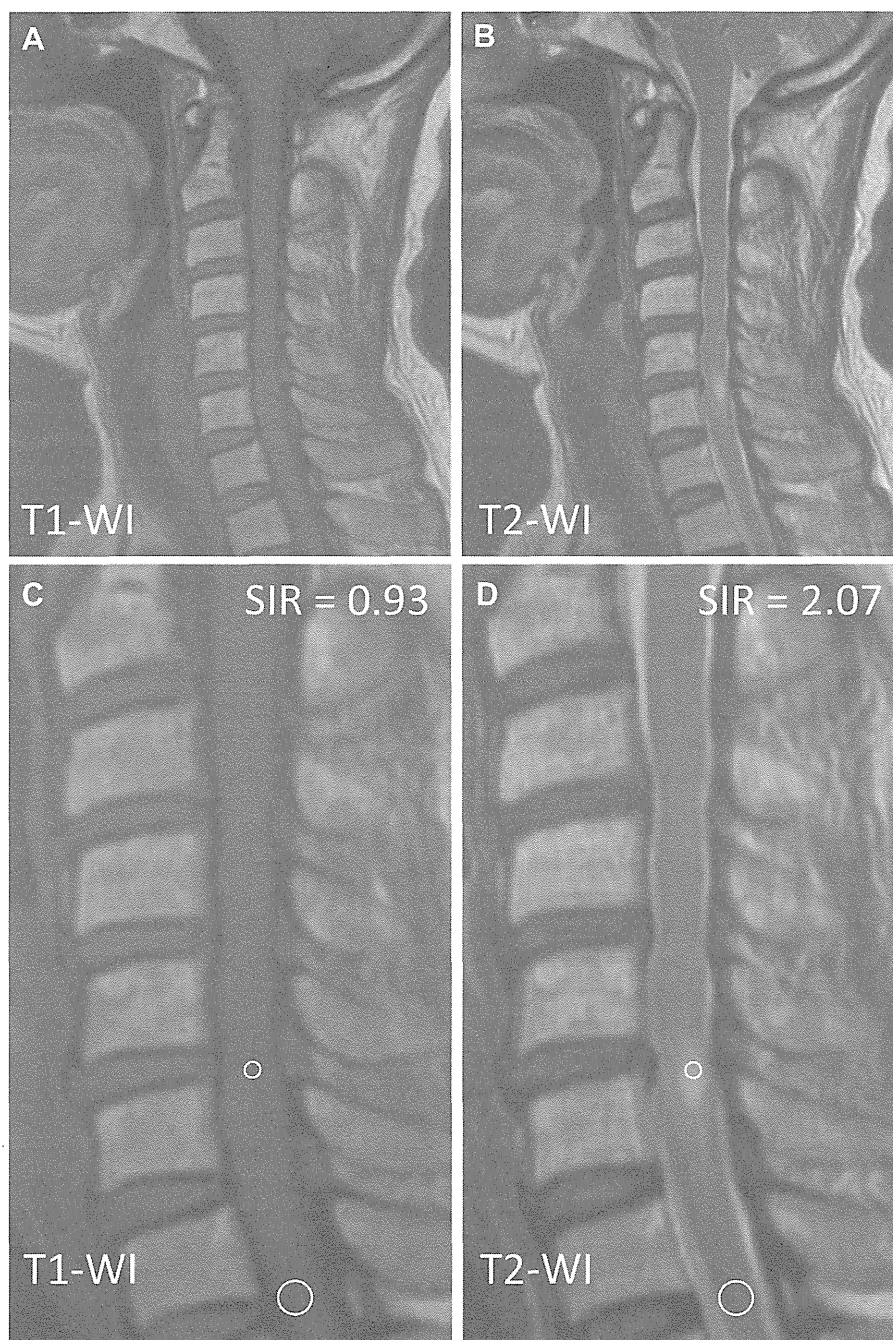


Fig. 2. A 59-year-old woman with cervical spondylotic myelopathy showed 28.6% (from 10 to 12) neurologic deterioration at follow-up. (A) mid-sagittal T1-weighted MRI, (B) mid-sagittal T2-weighted MRI, which shows intramedullary increased signal intensity at C5–C6 level. (C) SIR is calculated by the mid-sagittal increased cord signal intensity (smaller round) / mid-sagittal normal cord signal intensity at the C7–T1 disc level (larger round) on T1-WI. (D) SIR on T2-WI is calculated using the same equation on the same lesion on T1-WI. MRI, magnetic resonance imaging; SIR, signal intensity ratio; WI, weighted image.

lower SIR on T1-WIs ($R^2=0.102$, $p<.01$, Fig. 3, Left). On the other hand, there was no correlation between high intramedullary SI on T2-WIs and preoperative JOA score ($R^2=0.00040$, $p=.809$, Fig. 3, Right).

Relationship between SIR and neurologic outcome

A lower postoperative neurologic improvement was associated with a lower SIR on T1-WIs ($R^2=0.172$, $p<.01$,

Table 2

Demographic data	
Sex	96 men, 52 women
Age, years	69.6±9.8 (44–88)
Duration, months	8.1±5.4 (3–36)
Disease	103 CSM, 48 OPLL
Pre-JOA score (range)	11.0±2.2 (3–15.5)
Follow-up JOA score	14.2±1.8 (7–17)
JOA improvement rate	54.7±16.3 (11.1–100)
MRI findings (SIR)	
SIR on T1-WIs	1.13±0.17 (0.71–1.55)
SIR on T2-WIs	1.83±0.37 (1.07–3.24)

CSM, Cervical Spondylotic Myelopathy; JOA, Japanese Orthopedic Association; MRI, magnetic resonance imaging; OPLL, ossification of the posterior longitudinal ligament; SIR, signal intensity ratio.

Note: Data are mean±SD (range) or number of patients.

Fig. 4, Left). However, there was no correlation between high intramedullary SI on T2-WIs and postoperative neurologic improvement ($R^2=0.00624$, $p=.340$, Fig. 4, Middle). Preoperative JOA score correlated with postoperative neurologic improvement ($R^2=0.0912$, $p<.01$, Fig. 4, Right).

Relation between disease duration and SIR and neurologic improvement

A longer duration of symptoms was associated with a lower SIR on T1-WIs ($R^2=0.321$, $p<.01$, Fig. 5, Left). A similar relation was found between JOA neurologic improvement rate and disease duration ($R^2=0.177$, $p<.01$, Fig. 5, Right). However, there was no relation between disease duration and high intramedullary signal intensity on T2-WIs ($R^2=0.0022$, $p=.571$, Fig. 5, Middle).

Relationship between SIR and MRI classification on sagittal T2-WIs

On the basis of the morphologic classification on MRI of cervical spondylotic myelopathy [6], 28 patients were classified as “cystic type” and 120 patients were classified “diffuse type.” There was no difference in SIR on T1-WIs between the two groups (SIR cystic type:

1.16±0.22, SIR diffuse type: 1.14±0.18, Fig. 6, Left). On the other hand, the SIR on T2-WIs was significantly greater in the cystic type (2.11±0.36) compared with the diffuse type (1.75±0.31, $p<.01$, Fig. 6, Middle). There was no difference in JOA score between the two types (Fig. 6, Right).

Multivariate regression analysis for neurologic improvement rate

Univariate analysis identified significant relationships between the rate of neurologic improvement and each of age, SIR on T1-WIs, preoperative JOA score, and disease duration (Table 3). Multivariate analysis that included the aforementioned variables indicated that these four variables could explain 24.3% of the variance in neurologic improvement rate. SIR on T1-WIs and disease duration were the two main significant contributors; with SIR on T1-WIs being the strongest contributor (β -coefficient=0.256).

Relationship between changes in SIR on follow-up MRI and neurologic outcome

In this study, 25 patients underwent follow-up MRI within 6 months after surgery (mean 9.1±2.7 months, range 6–15 months). The SIR on follow-up T1-WIs correlated significantly with postoperative JOA improvement rate ($R^2=0.521$, $p<.01$, Fig. 7A). The high intramedullary signal intensity on follow-up T2-WIs also correlated with postoperative JOA improvement rate ($R^2=0.0317$, $p=.030$, Fig. 7B).

The Δ change in SIR (follow-up minus preoperative) on T1-WIs correlated significantly with the postoperative JOA improvement rate ($R^2=0.233$, $p<.01$, Fig. 7C). Five of the 25 patients (20.0%) whose SIR on T1-WIs changed from ≥ 1 before surgery to <1 after surgery showed a poor rate of neurologic improvement (33.3±9.7%). In none of the patients did T1-WIs-SIR change from <1 to ≥ 1 . The Δ change in SIR on T2-WIs correlated negatively with the rate of postoperative neurologic improvement ($R^2=0.121$, $p<.01$, Fig. 7D). Figure 8 shows a representative case with changes in SIR on T1-WI from >1 to <1 (1.12 to 0.98) and increased SIR on

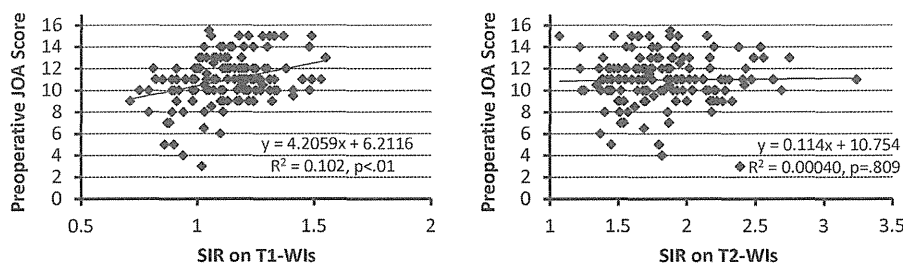


Fig. 3. Relationship between SIR and preoperative neurologic scores. (Left) SIR on T1-WIs correlated with preoperative JOA score. (Right) T2-WIs did not correlate with preoperative JOA score. JOA, Japanese Orthopedic Association; SIR, signal intensity ratio; WI, weighted image.

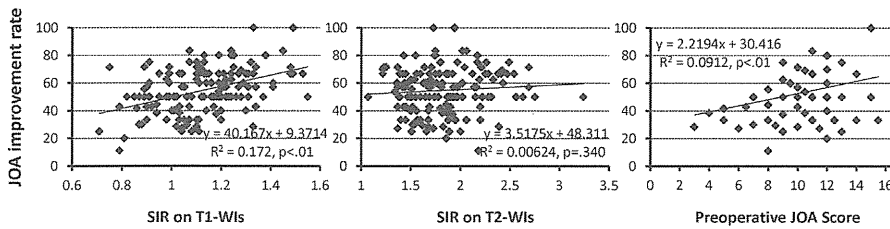


Fig. 4. Relationship between SIR and clinical outcome. JOA improvement rate correlated with SIR on T1-WIs (Left) but not on T2-WIs (Middle). Preoperative JOA score (Right) correlated with JOA improvement rate. JOA, Japanese Orthopedic Association; SIR, signal intensity ratio; WI, weighted image.

postoperative T2-WI (1.55–1.80). The patient with CSM underwent surgery (C4 subtotal spondylectomy) and showed poor neurologic rate of improvement of 28.6% at follow-up.

Discussion

The elucidation of factors that contribute to prognosis of patients with ossification of the posterior longitudinal ligament and CSM has been investigated by several groups [5,8,10–12]. Recognition of the functional capacity and functional normalization of the chronically damaged spinal cord are important clinical issues. It is also important to identify those factors that determine neurologic improvement after surgery. Regarding predictors of surgical outcome, age at the time of presentation [10], chronicity of myelopathic symptoms [5,10,11,13–15], signal changes on preoperative MRI, and their regression/persistence [2–4,16–18] have been considered key predictors.

The utility of MRI signal intensity has been widely studied, and various authors have speculated on its histopathologic significance and impact on recovery rate. High signal intensity on T2-weighted MRI indicates local pathologic changes in the spinal cord, and patients with compressive myelopathy and high signal intensity on T2-WI usually have a poor prognosis even after surgical intervention [4,16]. Despite such evidence, many studies could not show a significant relationship between high signal intensity on T2-WI and postoperative prognosis [5,7,17,19].

What is the reason for this observation? Although the exact reason is unknown, the following may explain this phenomenon. Although MRI provides high specificity in the assessment of morphologic changes and intramedullary state of the spinal cord, it is almost impossible to estimate potential recovery of the spinal cord on preoperative MRI without appropriate quantitative analysis. Furthermore, the signal intensity in each MRI is irregular because the sequence of parameters is individually selected for each patient. Although quantitative analysis in our study showed no statistical significance for SIR on T2-WIs, SIR on T1-WIs correlated significantly with preoperative neurologic scores and postoperative neurologic improvement. Theoretically, progressive changes should appear as high signal intensity lesions in the intramedullary region. High signal intensity is observed on T2-WI in patients with early-stage myelomalacia, whereas the intermediate stage includes variable degree of cystic necrosis of the central gray matter, which is better visualized on T2-weighted MRI; and the main features of late-stage myelomalacia are central cystic degeneration, formation of syrinx, and atrophy [20–22].

Some authors have proposed that increased intramedullary signal intensity of the spinal cord and cyst formation could represent signs of advanced spinal cord damage, as they represent diffuse neuronal cell loss and replacement with glial cells [19]. In our study, although the SIR on T2-WIs was significantly greater in the cystic type than the diffuse type, SIR on T1-WIs was not always lower in the cystic type, and there was no relationship between these qualitative MRI classification and postoperative neurologic improvement, which is in contrast to the findings of

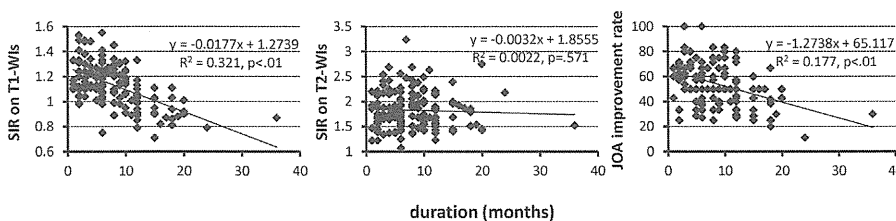


Fig. 5. Relationships between (Left) SIR on T1-WIs and disease duration, (Middle) SIR on T2-WIs and disease duration, and (Right) JOA improvement rate with disease duration. JOA, Japanese Orthopedic Association; SIR, signal intensity ratio; WI, weighted image.

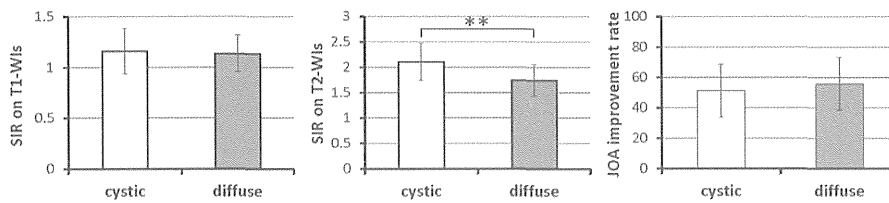


Fig. 6. Relationships between SIR and MRI classification. (Left) SIR on T1-WIs for “cystic” and “diffuse” lesions. (Middle) SIR on T2-WIs for “cystic” and “diffuse” lesions. (Right) JOA improvement rate according to the two types of lesions. JOA, Japanese Orthopedic Association; SIR, signal intensity ratio; WI, weighted image. ** $p < .01$.

qualitative MRI morphologic classification. The main limitation of the MRI classification used in previous studies is the poor agreement of the results among the studies because (1) the signal intensity on MRI is irregular in each scan, even when using the same MRI system, because the different sequence parameters are selected individually for each patient, (2) differences in the methods used for assessment, and (3) possible judgment errors by each investigator.

The significance of decreased signal intensity on T1-WI also has been studied. Many authors have confirmed that decreased signal intensity on preoperative T1-WI is a marker of poor prognosis [7,17,18,23]. On the basis of the results reported in the literature, a high intensity signal on T2-WIs in early-stage compressive myelopathy indicates edema and gliosis (which may be reversible), whereas a low intensity signal on T1-WIs represents myelomalacia and necrosis (which are considered irreversible). In our study, SIR on T1-WIs and postoperative neurologic outcome correlated negatively with disease duration. Surgical decompression of the spinal cord can restore blood circulation to the spinal cord, reduce swelling, and enhance regeneration of fibers, thus reducing or normalizing the high signal intensity in the intramedullary region. In the late stages, necrosis and syrinx become irreversible, limiting the capability of regaining neurologic function through surgery although it may still be warranted and effective to prevent further damage [18]. Our results also suggested that low intensity signal on preoperative T1-WIs was a significant predictor

of poor postoperative neurologic outcome. However, one of the main problems in assessing signal intensity on T1-WIs is that it is difficult to detect changes in signal intensity on T1-WIs compared with detecting changes in high signal intensity on T2-WIs. In our quantitative analysis of the signal, 21.6% of the patients had SIR on T1-WIs of <1 before surgery, which is a greater percentage compared with previous reports [6,7]. To obtain reliable results, quantitative analysis and uniformity of methods of analysis are necessary [24]. Quantitative analysis can potentially detect with high precision changes in low signal intensity on T1-WIs.

In the present study, the neurologic outcome was poor in patients who showed a decrease in signal intensity on postoperative T1-WIs, especially those in whom SIR on T1-WIs changed from ≥ 1 to <1 . A similar result may be expected for those patients with increase in signal intensity on postoperative T2-WIs. This finding indicates that pathological changes, such as necrosis, myelomalacia, and spongiform changes in the gray matter, are ongoing processes and cannot be ascertained by preoperative MRI alone [6]. Arvin et al. [25] showed that postoperative MRI findings at 6 months were predictive of outcome; the persistence and type of T2 signal change and lack of re-expansion of the cord correlated with poor recovery. These results highlight the importance of postoperative MRI in the prediction of neurologic recovery, because signal changes may evolve even after decompressive surgery.

Conclusion

Quantification of MRI signal changes in patients with cervical compressive myelopathy was used in the present study to define intramedullary signal changes in relation to clinical outcome and prognostic significance. Low signal intensity in the preoperative T1-WI, but not T2-WI, seems to correlate with poor postoperative neurologic outcome. Furthermore, decrease in signal intensity on postoperative T1-WIs and increase in signal intensity on postoperative T2-WIs can predict poor neurologic outcome and represent ongoing pathological changes in the compressed spinal cord. Preoperative and postoperative SIR on MRI could be potentially useful for prediction of postoperative neurologic outcome.

Table 3

Results of stepwise multivariate regression analysis

Variable= β_0	JOA improvement rate	
	β -coefficient	p Value
Age	-0.0884	.263
SIR on T1-WIs	0.256	.00468
Preoperative JOA score	0.0986	.246
Disease duration	-0.212	.0262

JOA, Japanese Orthopedic Association; SIR, signal intensity ratio; WI, weighted image.

Note: All independent variables were entered into the regression model.

Values denoted are β -coefficient values (95% confidence intervals).

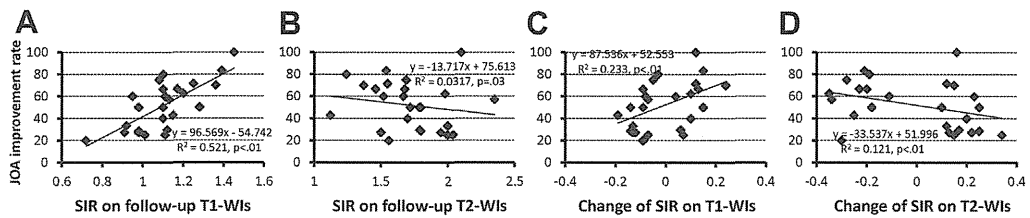


Fig. 7. Relationships between JOA improvement rate (clinical outcome) and (A) SIR on T1-WIs of follow-up MRI, (B) SIR on T2-WIs of follow-up MRI, (C) changes in SIR of T1-WIs (after–before surgery), and (D) changes in SIR of T2-WIs (after–before surgery). All values correlated with JOA improvement rate. JOA, Japanese Orthopedic Association; SIR, signal intensity ratio; WI, weighted image.

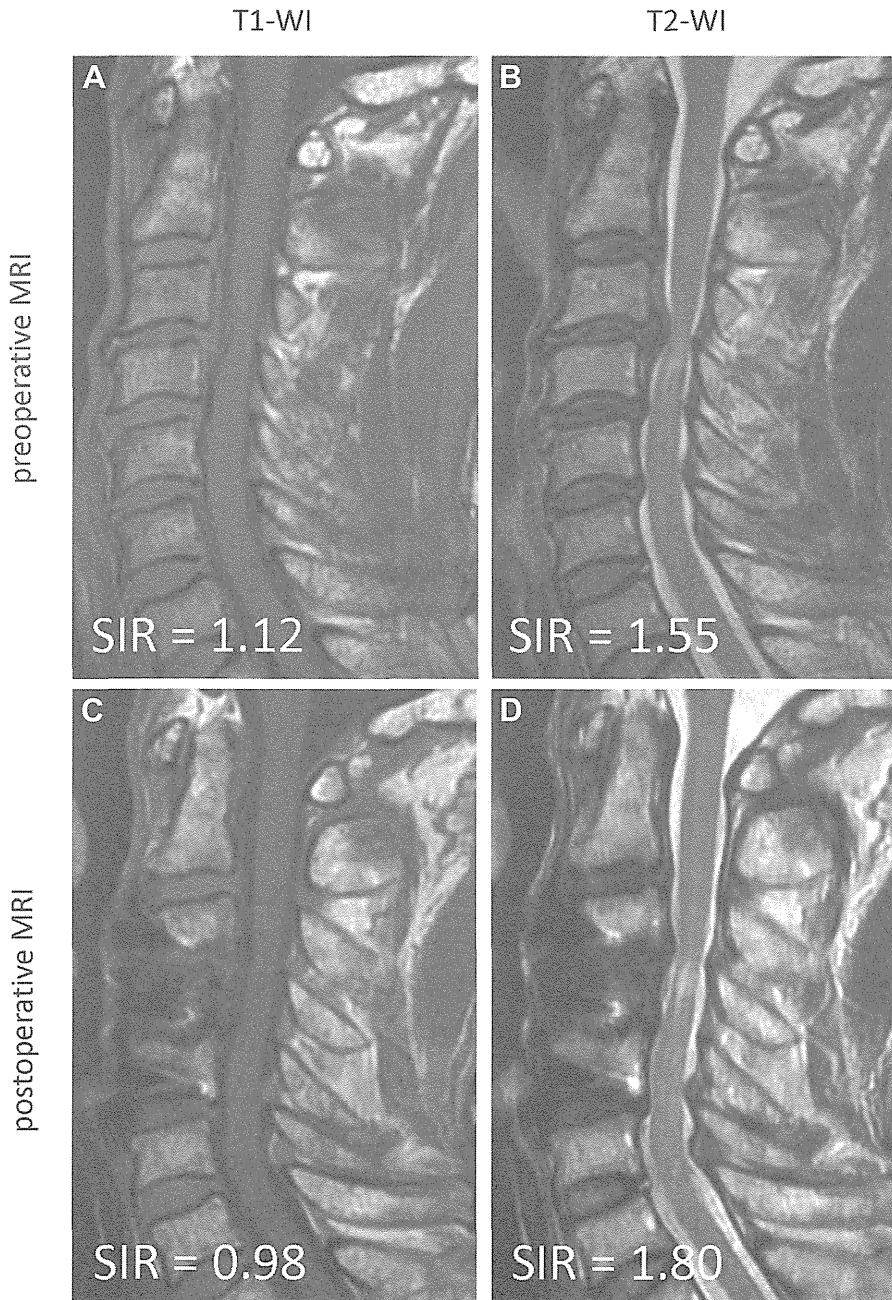


Fig. 8. A representative case with changes in SIR on T1-WI from >1 to <1. A 62-year-old woman with cervical spondylotic myelopathy showed 28.6% (from 10 to 12) neurologic deterioration at follow-up. (A) Preoperative mid-sagittal T1-weighted MRI, (B) preoperative mid-sagittal T2-weighted MRI shows intramedullary increased signal intensity at C3–C4 level, (C) postoperative mid-sagittal T1-weighted MRI, and (D) postoperative mid-sagittal T2-weighted MRI shows decrease of signal intensity on T1-WI and increase on T2-WI. MRI, magnetic resonance imaging. SIR, signal intensity ratio; WI, weighted image.

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60 脊髄障害性疼痛

Spinal cord related pain syndrome

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脊髄損傷を始めとする脊髄の障害は、しばしば多彩な痛みを引き起こす。その疼痛の分類は、Siddall らによる分類¹⁾が広く用いられている。中でも特徴的な症状である神経障害性の痛みは、一般的には損傷の髄節 (at level) と、損傷髄節以下の症状 (below level) の2つに分けられる。At level の症状としては、損傷早期から発現し、主に脊髄後角由来による痛みと考えられており、アロディニア、痛覚過敏を認める。Below level の場合には、主に脊髄視床路や脊髄網様体路由来の痛みと考えられており、脊髄腹側損傷に多い痛覚過敏や灼熱痛が認められる (表)。

脊髄障害性疼痛症候群は、後縦靭帯骨化症や脊髄空洞症などの難病・難治性疾患や脊髄損傷後、脊髄腫瘍術後などの脊髄障害に起因して引き起こ

される難治性の疼痛症候群と定義される。厚生労働省の難治性疾患克服研究事業として行った「脊髄障害性疼痛症候群の実態の把握と病態の解明に関する研究班」(<http://www.nanbyou.or.jp/entry/2440>) の調査ではその有病率はおよそ調査人口の0.15%とされている²⁾。その病態解明や治療に付いて、筆者らは同研究班の事業の一環として、全国3,206の整形外科および脳神経外科の認定施設を対象とした全国アンケート調査を行った。取り込み基準として、脊髄髄節レベルに痛みやしびれを伴う症例で、MRIでの脊髄圧迫病変、髄内輝度変化、脊髄膨大・萎縮などの器質的な変化が認められることや、非ステロイド性抗炎症薬 (NSAIDs) による疼痛軽減効果が低いことなどを設定した。この調査の結果では、原疾患の内訳は、圧迫性脊

表 脊髄障害性疼痛の分類 (文献1より引用改変)

型	系 統	特異的構造・病理
侵害受容性 (nociceptive)	筋骨格系	骨、関節、筋の外傷または炎症 機械的不安定症、筋スパズム 二次的過用症候群
	内臓系	腎臓結石、腸管、括約筋機能不全など 反射異常性頭痛
神経因性 (neuropathic)	損傷髄節より上位 (above level)	圧迫性単神経炎 複合性局所疼痛症候群 (CRPS)
	損傷髄節 (at level)	神経根圧迫 (馬尾を含む) 脊髄空洞症 脊髄外傷/虚血 二重のレベルでの脊髄および神経根損傷 (損傷早期から発現, アロディニア・痛覚過敏を認める)
	損傷髄節より下位 (below level)	脊髄外傷/虚血 (脊髄腹側損傷に多く、痛覚過敏・灼熱痛)

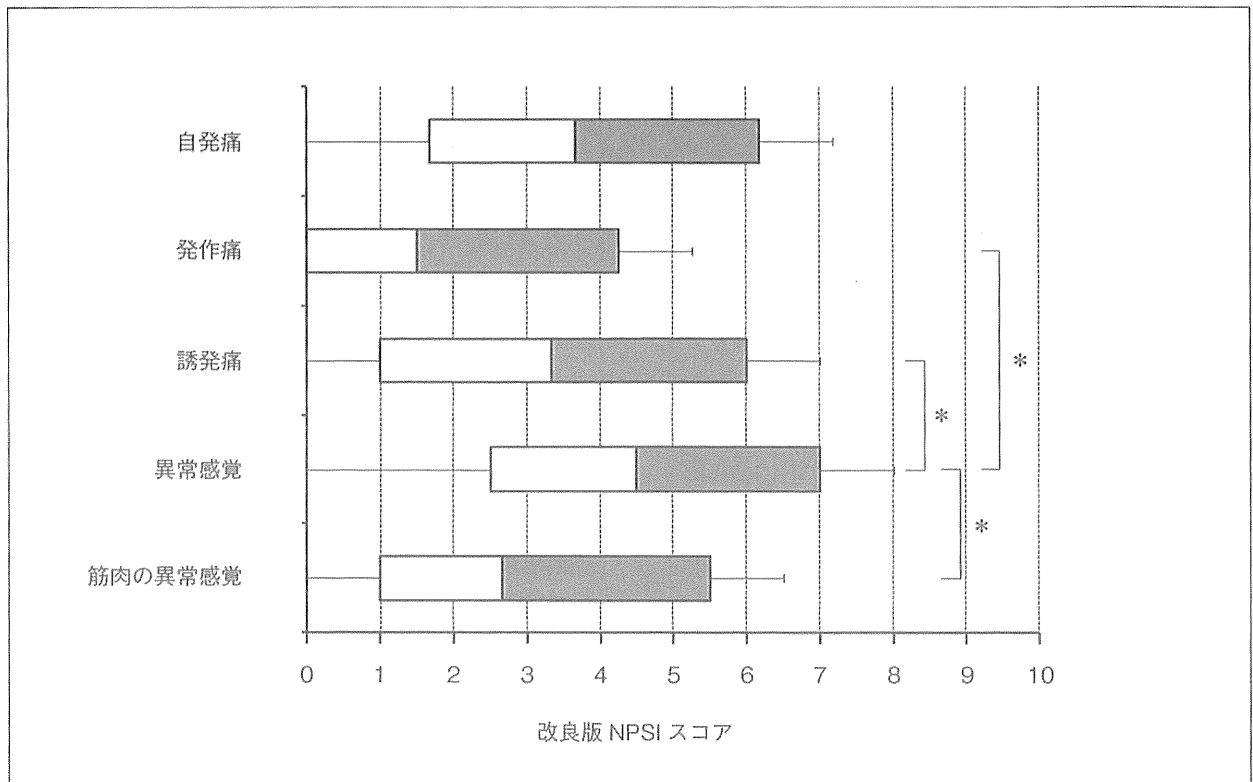


図 損傷髄節レベル (at level) における疼痛の種類

髄症（頸椎症性脊髄症や後縦靱帯骨化症）が46.3%と最も多く、脊髄損傷は17.4%であった。損傷髄節レベル (at level) の疼痛は62.5%の症例でみられ、疼痛の種類としては、異常感覚、自発痛が多く、上肢のピリピリとしたしびれや、灼けつくようなしびれの訴えが多かった（図）。一方、損傷髄節より下位レベル (below level) は38.7%の症例でみられ、疼痛の種類としては、筋肉の異常感覚の訴えが一番多く、発作痛の頻度は低かった。本症候群の痛みの発生機序としては、①脊髄後角を中心とした灰白質障害、②脊髄視床路などを含めた索路（白質）障害、③後根障害などによる求心路遮断性の痛みが考えられる³⁾。

脊髄損傷後疼痛は、最も治療が難しい問題の一つとされ、ADLやQOLを低下させ、さらに心理的・精神的ストレスとなる。脊髄損傷後の痛みは持続もしくは時間の経過と共に悪化し、受傷後の亜急性期（3～6カ月後）に神経障害性疼痛があると、痛みは3～5年続く傾向にあると示される。脊髄損傷後の慢性疼痛の有病率は、70～80%程度

とする報告が多い。脊髄損傷に伴う神経因性疼痛の発生機序について、明確に記載されている報告はないが、脊髄損傷後に起こる脊髄後角レベルおよび上位中枢神経レベルでの様々な可塑性変化を基盤に発生していることは間違いないと考えられる。痛みの特徴として、完全損傷、不全損傷では神経因性疼痛の出現頻度に違いはないという論文がある一方で、アロディニアは不全損傷に有意に多いとも言われている。

脊髄腫瘍術後の慢性疼痛については、手術症例85例を対象とした報告では、平均 neuropathic pain symptom inventory (NPSI) スコアが10点以上の中等度もしくは高度の疼痛を訴える症例は48例/85例(56%)であり、特にパレステジア (paresthesia)/ジセステジア (dysesthesia) の項目が高いとされている⁴⁾。

これらの病態に対する薬物療法としては、ガバペンチン、アミトリプチリンなどの三環系抗うつ薬、セロトニン・ノルアドレナリン再取り込み阻害薬 (SNRI)、オピオイドなどが用いられてきた