Table 3
Prevalence of MRI measures and cervical myelopathy among different diameter of cervical spinal canal

Factors	Diameter of cervical spinal canal (mm) <13	13–15	≥15	p value
Men				
N	21	162	136	
Age, y	69.5±12.0	69.1±12.8	64.9±14.9	.027
Height, cm	163.7±5.6	163.6±6.8	165.8±7.7	.025
Weight, kg	67.6±10.5	61.7±10.6	67.0±12.3	.0002
Body mass index, kg/m^2	25.2±3.3	23.0±3.2	24.2±3.4	.0006
MRI measures				
Cervical cord compression, N (%)	13 (61.9)	58 (35.8)	22 (16.2)	<.0001
Increased signal intensity, N (%)	5 (23.8)	9 (5.6)	1 (0.7)	<.0001
Diameter of spinal cord (mm)	6.2±0.5	6.8±0.8	7.2±0.8	<.0001
Cervical myelopathy, N (%)	1 (4.8)	2 (1.2)	0 (0)	.09
Women				
N	108	383	149	
Age, y	68.7±13.3	67.2±12.8	60.4±13.4	<.0001
Height, cm	149.1±7.2	151.4±7.1	153.9±6.7	<.0001
Weight, kg	49.8±8.1	53.2±9.6	54.8±9.4	.0001
Body mass index, kg/m^2	22.4±3.2	23.2±3.7	23.2±3.8	.12
MRI measures				
Cervical cord compression, N (%)	36 (33.3)	92 (24.0)	11 (7.4)	<.0001
Increased signal intensity, N (%)	2 (1.9)	8 (2.1)	0 (0)	.21
Diameter of spinal cord (mm)	6.5±0.9	6.9±0.8	7.0±0.8	<.0001
Cervical myelopathy, N (%)	12 (11.1)	12 (3.1)	0 (0)	<.0001

MRI, magnetic resonance imaging.

Note: For categorical data, the chi-square test was used to assess the presence of significant differences among different diameters of the cervical spinal canal.

For continuous outcomes, comparison was made by the analysis of variance test differences among different diameters of the cervical spinal canal.

Regarding MRI measurements, the prevalence of cervical cord compression and ISI among persons with a CSC diameter less than 13 mm, which was considered to be developmental canal stenosis [14], was 61.9% and 23.8% in men and 33.3% and 1.9% in women, respectively. Above all, a CSC diameter less than 13 mm was observed in more than 10% of the participants. Of those with a CSC diameter less than 13 mm, cervical cord compression (ie, the preliminary step in the development of CM) was also observed in 61.9% of men and 33.3% of women. From these results, the number of people who have a risk for CM was considered quite high in the general population. Countee and Vijayanathan [15] reported that congenital stenosis in men with a cervical canal diameter of 14 mm or less was associated with quadriplegia after trauma. In the present study, we noted that the narrower the diameter of the CSC, the higher the prevalence of ISI. Of note, the distribution of prevalence between men and women was different. Increased signal intensity was seen in approximately 10% of men younger than 60 years, whereas it was seen in only 1% of women younger than 60 years, and was relatively higher in older people. In the present study, the prevalence of the clinical CM was significantly higher in the narrower CSC group. The result may show that patients with a narrowed spinal canal are more likely to develop CM. Further longitudinal studies are needed to clarify the causal

Table 4
The odds ratio and 95% confidence interval of increased signal intensity, diameter of spinal cord, diameter of cervical spinal canal, and canal-to-body ratio for cervical myelopathy

Variables	Cervical cord compression OR* (95% CI)	p value	Cervical myelopathy OR (95% CI)	p value
Age, y (+10 y)	23.6 (9.62–60.0)	<.0001	11.0 (1.15–133.9)	.047
Women (vs. men)	1.41 (1.03–1.92)	.032	4.33 (1.50–18.4)	.018
Body mass index, kg/m^2 (+1 SD)	2.12 (0.87–5.16)	.095	1.04 (0.94–1.15)	.41
Increased signal intensity positive	18.8 (6.87–66.4)	<.0001	6.32 (1.36–21.8)	.007
Diameter of spinal cord, mm (−1 mm)	1.40 (1.17–1.68)	.0002	1.46 (0.93–2.31)	.11
Diameter of cervical spinal canal, mm (−1 mm)	1.67 (1.45–1.93)	<.0001	2.73 (1.83–4.23)	<.001
Canal-to-body ratio (−10%)	1.85 (1.60–2.16)	<.0001	2.12 (1.47–3.16)	.0001

OR, odds ratio; CI, confidence interval; SD, standard deviation.

* OR was calculated by multiple logistic regression analysis after adjustment for age, gender, and body mass index.

relationship between narrowed spinal canal and CM. In addition, we clarified the positive association between cervical cord compression and spinal cord diameter, whereas the diameter of the spinal cord itself was not a significant predictive factor for CM. This may indicate that the spinal cord can become atrophied in individuals with cervical cord compression or in those who have a congenitally narrow spinal cord.

The present study also clarified the difference in age- and sex-related changes in the CSC diameter and CBR. The CSC has been the focus as a risk factor for CM [14,16]. However, in recent years, the CBR rather than CSC diameter has been reported to be a useful predictor for CM because of a magnification error resulting from the focus-to-film distance and the object-film distance on MRI [17]. However, Blackley et al. [18] showed that there is currently a poor correlation between the CBR and the true sagittal diameter of the spinal canal on computed tomography scans because of the wide normal variations in the diameter of the vertebral body. Therefore, the characteristics of the variations between the CSC diameter and the CBR should be considered. Of note, the present study found the CSC diameter to be higher in men than in women. However, the CBR was higher in women than in men, which is the reason for the increased diameter of the vertebral body in men. Therefore, the differences between the sexes should be taken into account when considering the CBR as a risk factor for CM.

Study limitations

The present study had several limitations. First, although more than 1,000 participants were included in the present study, these participants may not represent the general population because they were recruited from only two areas of Japan. However, anthropometric measurements were compared between the participants of the present study and the general Japanese population [19], and no significant differences in BMI were found between the participants in the present study and the Japanese population at large in both sexes (BMI [standard deviation] in men: 23.71 kg/m^2 [3.41 kg/m^2] and 23.95 kg/m^2 [2.64 kg/m^2], p=.33, respectively; BMI [standard deviation] in women: 23.06 kg/m^2 [3.42 kg/m^2] and 23.50 kg/m^2 [3.69 kg/m^2], p=.07, respectively). Second, the distribution of the CSC diameter applies to only a small portion of the Japanese population and cannot be extrapolated to other populations.

Conclusions

This study confirmed the significant association of the narrow CSC diameter with CM in a population-based cohort. The results prompt future studies to look into the various factors affecting the dimensions of the CSC, apart from aging.

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References

[1] Murone I. The importance of the sagittal diameters of the cervical spinal canal in relation to spondylosis and myelopathy. J Bone Joint Surg Br 1974;56:30–6.

[2] Eismont FJ, Clifford S, Goldberg M, et al. Cervical sagittal spinal canal size in spine injury. Spine 1984;9:663–6.

[3] Goto S, Umehara J, Aizawa T, et al. Comparison of cervical spinal canal diameter between younger and elder generations of Japanese. J Jap Orthop Ass 2010;15:97–103.

[4] Kato F, Yukawa Y, Suda K, et al. Normal morphology, age-related changes and abnormal findings of the cervical spine. Part II: magnetic resonance imaging of over 1,200 asymptomatic subjects. Eur Spine J 2012;21:1499–507.

[5] Ishimoto Y, Yoshimura N, Muraki S, et al. Prevalence of symptomatic lumbar spinal stenosis and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study. Osteoarthritis Cartilage 2012;20:1103–8.

[6] Nagata K, Yoshimura N, Muraki S, et al. Prevalence of cervical cord compression and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study. Spine 2012;37:1892–8.

[7] Houten JK, Noce LA. Clinical correlations of cervical myelopathy and the Hoffmann sign. J Neurosurg Spine 2008;9:237–42.

[8] Sung RD, Wang JC. Correlation between a positive Hoffmann's reflex and cervical pathology in asymptomatic individuals. Spine 2001;26:67–70.

[9] Rhee JM, Heflin JA, Hamasaki T, et al. Prevalence of physical signs in cervical myelopathy: a prospective, controlled study. Spine 2009;34:890–5.

[10] Harrop JS, Hanna A, Silva MT, et al. Neurological manifestations of cervical spondylosis: an overview of signs, symptoms, and pathophysiology. Neurosurgery 2007;60(1 Suppl 1):S14–20.

[11] Matsumoto M, Toyama Y, Ishikawa M, et al. Increased signal intensity of the spinal cord on magnetic resonance images in cervical compressive myelopathy. Does it predict the outcome of conservative treatment? Spine 2000;25:677–82.

[12] Porter RW, Hibbert C, Wellman P. Backache and the lumbar spinal canal. Spine 1980;5:99–105.

[13] Hukuda S, Kojima Y. Sex discrepancy in the canal/body ratio of the cervical spine implicating the prevalence of cervical myelopathy in men. Spine 2002;27:250–3.

[14] Arnold JG Jr. The clinical manifestations of spondylochondrosis (spondylosis) of the cervical spine. Ann Surg 1955;141:872–89.
[15] Countee RW. Vijayanathan T. Congenital stenosis of the cervical spine: diagnosis and management. J Natl Med Assoc 1979;71: 257–64.
[16] Wolf BS. Khilnani M. Malis L. The sagittal diameter of the bony cervical spinal canal and its significance in cervical spondylosis. J Mt Sinai Hosp NY 1956;23:283–92.
[17] Pavlov H. Torg JS, Robie B. et al. Cervical spinal stenosis: determination with vertebral body ratio method. Radiology 1987;164:771–5.
[18] Blackley HR. Plank LD. Robertson PA. Determining the sagittal dimensions of the canal of the cervical spine. The reliability of ratios of anatomical measurements. J Bone Joint Surg Br 1999;81:110–2.
[19] Ministry of Health, Labour and Welfare. The report of National Health and Nutrition Survey 2005. Available at: www.mhlw.go.jp/bunya/kenkou/eiyou/dl/h20-houkoku-04.pdf. Accessed May 30, 2013.

Original Research

Contrast Enrichment of Spinal Cord MR Imaging Using a Ratio of T1-Weighted and T2-Weighted Signals

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Purpose: We aimed to assess if the T1-weighted (T1w)/T2-weighted (T2w) signal ratio could be used to improve image contrast in MR spinal cord imaging.

Materials and Methods: T1w and T2w cervical spinal cord MR images were acquired from 23 normal subjects using 3 Tesla (T) MR scanner. In addition, a multiple sclerosis patient, and a cervical spondylotic myelopathy patient were evaluated. White matter (WM) and gray matter (GM) signal intensities were measured for each image (T1w, T2w, and T1w/T2w) for seven cervical segments in each subject to calculate the contrast. Age-related changes in signal intensity were assessed at each location (lateral column, anterior column, dorsal column, and GM) for each image. Additionally, the imaging results of two subjects with spinal diseases and the controls were numerically compared.

Results: The contrast between the WM and GM in the T1w/T2w ratio image was approximately twice as much as that in the T1w and T2w images (mean ± SD = 1.8 ± 0.4). The signal intensity ratio was related to age. For both clinical patients, the signal intensities were significantly lower in the lesion areas in the ratio images.

Conclusion: The T1w/T2w ratio images demonstrated increased image contrast compared with T1w and T2w images alone and, reduced inter-individual signal intensity differences.

Key Words: contrast; magnetic resonance imaging; ratio; spinal cord; T1 weighted image; T2 weighted image
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MRI HAS BEEN used successfully for the diagnosis of various spinal cord diseases since the early 1980s. Fast spin echo (FSE) and gradient recalled echo (GRE) are the most commonly used sequences because they provide relatively good lesion contrast and anatomical resolution of spinal cord structures (1). However, it is still difficult to clearly discriminate gray matter (GM) from white matter (WM) in the spinal cord on routine spinal images acquired in clinical practice, despite distinct histological differences between the tissues (2,3). In addition, some intradural-extramedullary lesions cannot be differentiated from intramedullary lesions (4). Moreover, because the signal intensity of MRI varies with body size and its position relative to the coil (5–7), the changes are not always related to specific pathologic processes (8,9). Previously, several MRI-based approaches to improve the detection of pathological changes in the spinal cord have been investigated using the motion properties (diffusion) of water molecules (10–12) or relaxation times to measure the myelin water fraction (13–17).

Recently, Glasser and Van Essen showed that the ratio of the signal intensity in T1-weighted (T1w) MRI to the signal intensity in T2-weighted (T2w) MRI was sensitive to subtle differences in myelin content within the gray matter of the cerebral cortex (18). Although it is not certain to what extent the signal intensity of the T1w/T2w ratio image is related to the myelin content, the T1w/T2w ratio eliminates the signal intensity bias related to receiver coil sensitivity. Additionally, it increases the image contrast if the ratio is calculated using a pair of voxels at exactly the same anatomical location for both T1w and T2w MRI.

MATERIALS AND METHODS

Participants

Twenty-three healthy volunteers (15 men and 8 women; ages, 22–86 years; mean ± standard deviation (SD) = 44.5 ± 22.5) were recruited for this study. Additionally, two subjects with spinal myelopathies were enrolled to compare their spinal images with those of

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the control: One was a 39-year-old man who was diagnosed with multiple sclerosis (MS) 7 years prior. At the time of the experiment, he had muscle weakness and spasticity predominantly in both lower extremities (right side dominant). The Romberg sign was positive. We did not detect any brain lesions in this subject, except for transient bilateral low visual acuity. The other subject was a 77-year-old man who underwent a laminoplasty for cervical spondylotic (CS) myelopathy 5 years prior. His gait was spastic and the Romberg sign was positive. He had some paresthesia in both hands and a right-side dominant diminished tendon reflex. This study was approved by the Clinical Research Ethics Board of our institution, and all subjects gave written informed consent before the study began.

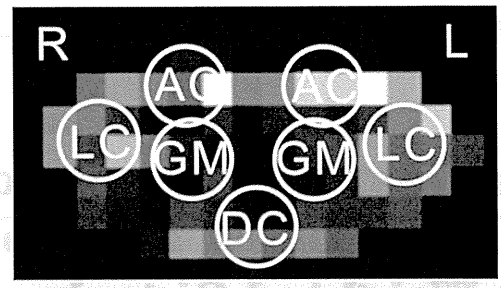

Figure 1. Signal intensity measurements. Using the original spatial resolution (1 × 1 mm) axial image of the T1w/T2w ratio, mean signal intensities were determined at seven locations (within a radius of 2 mm) that were determined visually for each segment.

MRI Data Acquisition

Two different MR images (see below) were acquired for each subject's cervical spinal cord on a 3 Tesla (T) MRI (Philips Medical Systems, Best, The Netherlands) using a 16-channel coil (SENSE Neurovascular coil 16). Each subject wore a Sternal Occipital Mandibular Immobilizer (SOMI) brace modified for MRI acquisition to minimize spontaneous movements of the head and neck. Three-dimensional (3D) T1w fast field gradient echo MR images were acquired with the following parameters: repetition time (TR) = 6.5 ms, echo time (TE) = 3.1 ms, 10° flip angle, field of view (FOV) 256 mm, matrix 256 mm × 256 mm, number of slices = 100, slice thickness = 2 mm, and axial (transverse) slice orientation. The resulting voxel size was 1 × 1 × 2 mm, and the acquisition time was 6 min 47 s. Next, 3D T2w turbo spin echo MR images were acquired with the following parameters: TR = 3200 ms, TE = 93 ms, 90° flip angle, FOV 256 mm, matrix 256 mm × 256 mm, number of slices = 100, slice thickness = 2 mm, and axial slice orientation. The resulting voxel size was 1 × 1 × 2 mm, and the acquisition time was 6 min 14 s. For both acquisitions, the SENSE algorithm (19) was used with a reduction factor of 1.8 and 1.5 for T1w and T2w, respectively.

Data Analysis

T1w/T2w ratio images were created from the magnitude images of the T1w and T2w acquisitions of each subject using in-house software developed in MATLAB (MathWorks, Natick, MA). In this study, the signal intensity of the T1w images was simply divided by the signal intensity of the T2w images at the same location, as determined from the original image coordinates. The T1w/T2w ratio erases the effect of the reception bias field (b) and increases the signal intensity related to pathological changes (x) as described by the following equation (18):

$$\mathrm{T1w/T2w} = x * b/((1/x) * b) = x^2$$

The segmental cervical spinal cord level was determined by its relative location to the cervical vertebrae in each subject. Thirty-three axial segmental images were chosen out of 100 images for each subject, which included all of the images from the cervical segments with a 2-mm separation between adjacent images. For each axial image, the signal intensities were measured at seven locations that were related to the left and right lateral columns (LC), anterior columns (AC), single dorsal column (DC), and the left and right GM from 1 × 1 mm image slices (Fig. 1). For illustrative purposes, the images were resampled to 0.25 × 0.25 mm voxels using bicubic interpolation and 2D Gaussian spatial filtering. Each location was visually determined using the T1w/T2w ratio images at a high resolution (0.25 × 0.25 mm), which clearly delineated the GM and LC, AC, and DC, illustrating the so-called 'butterfly' shape, and the mean signal intensity of the voxels within a 2-mm radius were calculated. Additionally, the mean signal intensities for the T1w and T2w images were automatically calculated using voxels at the same location.

Axial images of the cervical spinal cord at the C4 level for each image type (T1w, T2w, and T1w/T2w) were made in the original 1 × 1 mm horizontal resolution images. These axial images were resampled at a high resolution (0.25 × 0.25 mm) using MATLAB. Additionally, to compare the T1w/T2w ratio image with stained spinal cord tissue, the spinal cord tissue at the C3, C5, and C7 levels was extirpated at autopsy. The tissues were obtained from the cervical cord at autopsy from an 83-year-old Japanese woman who died of pontine hemorrhage. They were fixed for several weeks in 10% neutral formalin, then the C3, C5, and C7 spinal cord levels were confirmed by counting nerve roots by two neuropathologists, resected and embedded in paraffin. Procedures involving use of human material were performed in accordance with ethical guidelines set by Kyoto University. The sample was stained with Kluver-Barrera stain. They were first resampled at a resolution of 1 ×1mm and then resampled at 0.25 × 0.25 mm and Gaussian filtered using MATLAB.

The mean contrast between the WM locations (LC, AC, and DC) and GM (mean value across bilateral GM) was calculated using the following equation:

$$\mathrm{Contrast}\quad (\%) = 100 \times |I_w - I_g|/(I_w + I_g)$$

where I_w is the signal intensity of the WM (LC, AC, and DC) and I_g is the mean signal intensity of the bilateral GM.

The mean contrast was also assessed between each WM (LC, AC, and DC) location and mean GM value for

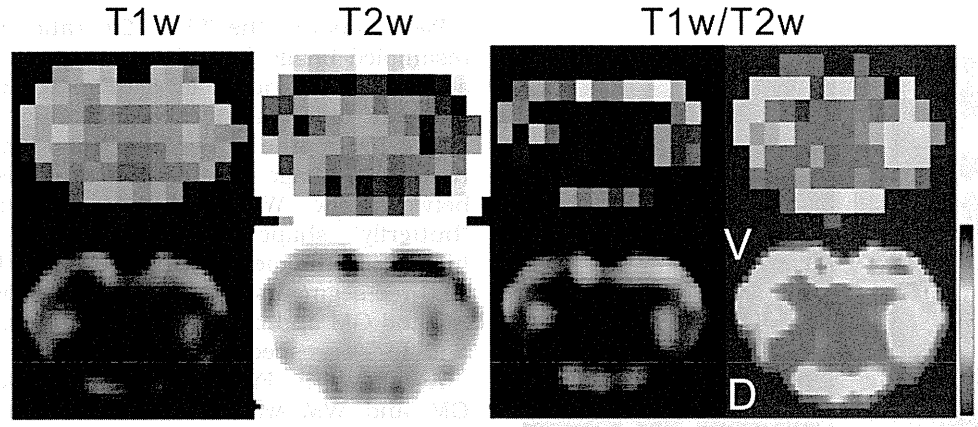

Figure 2. Comparison of the ratio images with the original MR images. The original resolution (1 × 1 mm) image (top) and the high resolution (0.25 × 0.25 mm) images for the T1w, T2w, and T1w/T2w ratio MRIs (bottom) are shown for the same cervical segment (C4) in one representative healthy subject. Contrast between the GM and WM is the highest for the T1w/T2w ratio images. The scale for each image is 10–90%.

all locations in the seven segments of the control subjects and for each image type (T1w, T2w, and T1w/T2w). Furthermore, the significance of the differences in mean contrast between the T1w/T2w ratio image and the T1w or T2w images were assessed for all locations by using a paired t-test with a Bonferroni correction.

Furthermore, using Pearson's correlation coefficient, we assessed the changes in signal intensity with age at each location (LC, AC, DC, and GM) at the C4 level for each image type (T1w, T2w, and T1w/T2w).

To check the reproducibility of the signal intensity measurement, the scan was acquired twice from nine healthy subjects (three women, aged 22–86 years). Six locations (signal intensity of the bilateral AC, LC, single DC, and the mean signal intensity of the bilateral GM) in seven segments from nine subjects were determined visually within a radius of 2 mm by using the T1w/T2w ratio images and using both measurements. Forty-two values from one subject were used to check the reproducibility of the measurement of each subject. The first signal intensity measurement at six locations in seven segments was performed by MT, and the second measurement of the same six locations in seven segments was performed by H.Y. Kendall's coefficient of concordance was used to assess the significance of the reproducibility.

Finally, we verified that signal intensity changes were due to pathological changes by using the signal intensities in the T1w/T2w ratio images from the 39-year-old MS patient and the 77-year-old CS myelopathy patient. The T1w/T2w ratio intensities were plotted as a graph with the normal range between the broken lines (± 2 SD), which was estimated using the values from the controls (22–45 years of age). Because the signal intensity was inversely related to the age, each subject's normal range was adjusted using linear interpolation.

RESULTS

Contrast Increase Using the T1w/T2w Ratio

The axial images of the cervical spinal cord at the C4 level for one subject are shown in Figure 2. Even in the original 1 × 1 mm horizontal resolution image, it

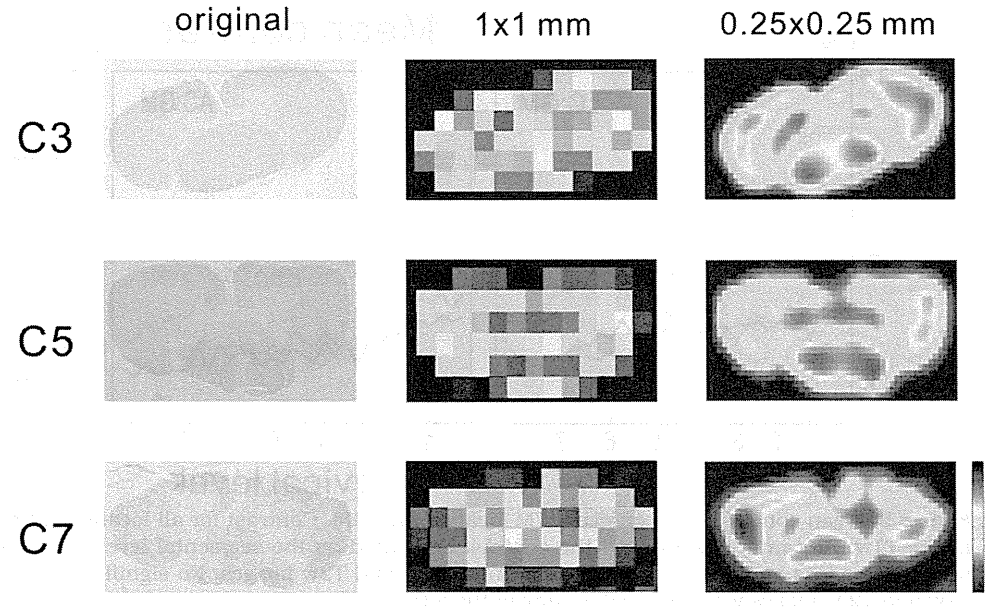

Figure 3. Spinal cord tissue at the C3, C5, and C7 levels. The spinal cord tissues at the C3, C5, and C7 levels were stained with Kluver-Barrera stain. They were first resampled at a resolution of 1 × 1 mm and then resampled at 0.25 × 0.25 mm and Gaussian filtered using MATLAB. (right side image).

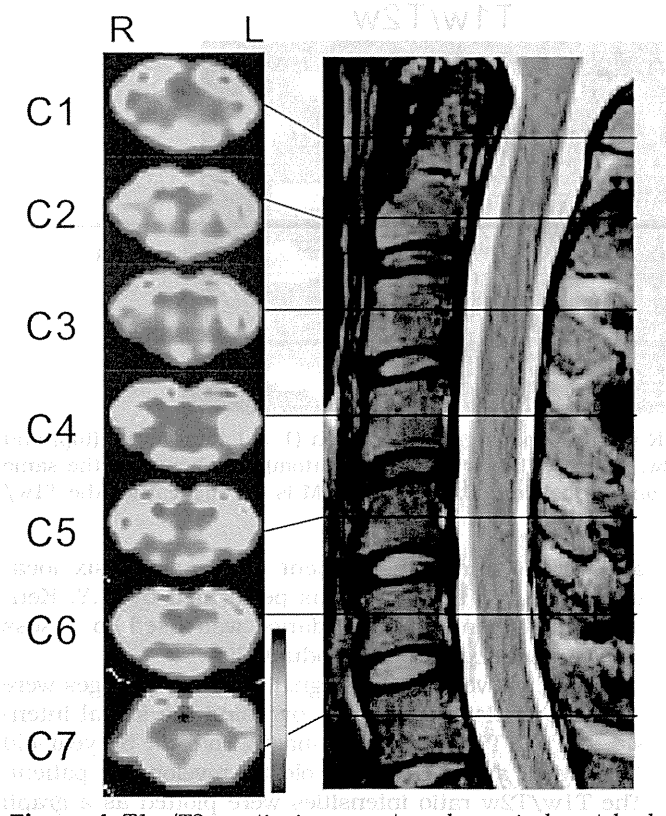

Figure 4. T1w/T2w ratio images at each cervical vertebral level. The right side of the figure shows the sagittal cervical T2w MR images. Axial T1w/T2w ratio images at each vertebral level (C1–C7) are shown on the left side of the figure (ventral at the top). High contrast between the GM and WM is seen at all cervical segments, but the so-called "butterfly" shape is the clearest at C4. The scale is 10–90% for each image.

is apparent that the contrast between the central GM and the peripheral WM is the highest for the T1w/T2w ratio image. The color T1w/T2w ratio image with high resolution (0.25 × 0.25 mm) clearly delineates the GM, illustrating the so-called "butterfly" shape.

We compared the T1w/T2w ratio image with the resampled image from the spinal cord tissue visually at the C3, C5, and C7 levels (Fig. 3). The signal intensity was different in each individual, but the color image from the T1w/T2w ratio image and the resampled image were similar in terms of distinction between the WM and GM, presenting a clear "butterfly" shape. In addition, the percentage in increase of the mean contrast between the LC and GM at three segments was 2.83%, and those between the AC and GM and between the DC and GM were 3.78% and 2.99%, respectively.

As shown in Figure 4, high contrast between the GM and WM was seen for all cervical segments, although the contrast was apparently related to the segmental level, with higher contrast observed in higher segments.

Figure 5 shows the mean contrast between the WM locations (LC, AC, and DC) and the GM (the mean value across the bilateral GM). Because no significant difference was observed between the right and left AC and LC contrast values, the averaged values are shown. Contrast was the highest at all locations and segmental levels in the T1w/T2w ratio images at approximately twice that of the T1w and T2w images. In addition, the contrast appeared to decrease as the segmental level increased.

Figure 6 shows that the mean contrast between the LC and GM for the T1w/T2w ratio images was 1.9 times larger than the mean contrast for the T1w images, and the values between the AC and GM and between the DC and GM were similar (2.2 and 1.9 times, respectively). The contrast increases in the T2w images were also similar, except for between the DC and GM values, which was 1.5 times. Additionally, the percentage in increase of the mean contrast between the LC and GM at seven segments was 6.38%, and those between the AC and GM and between the DC and GM were 6.01% and 3.51%, respectively.

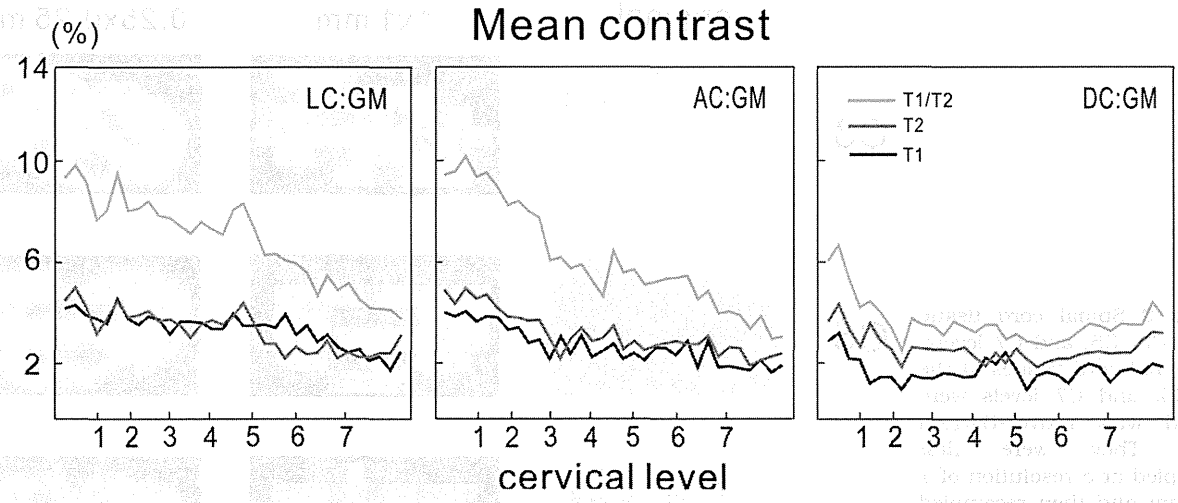

Figure 5. Mean contrast between each WM location and GM. Contrast for all locations at each segment level was the highest in the T1w/T2w ratio images, and the contrast decreased as the segmental level increased. The contrast for the T1w/T2w ratio images was approximately twice that of the T1w and T2w images. No significant difference in the contrast between the T1w and T2w images was observed for any of the locations.

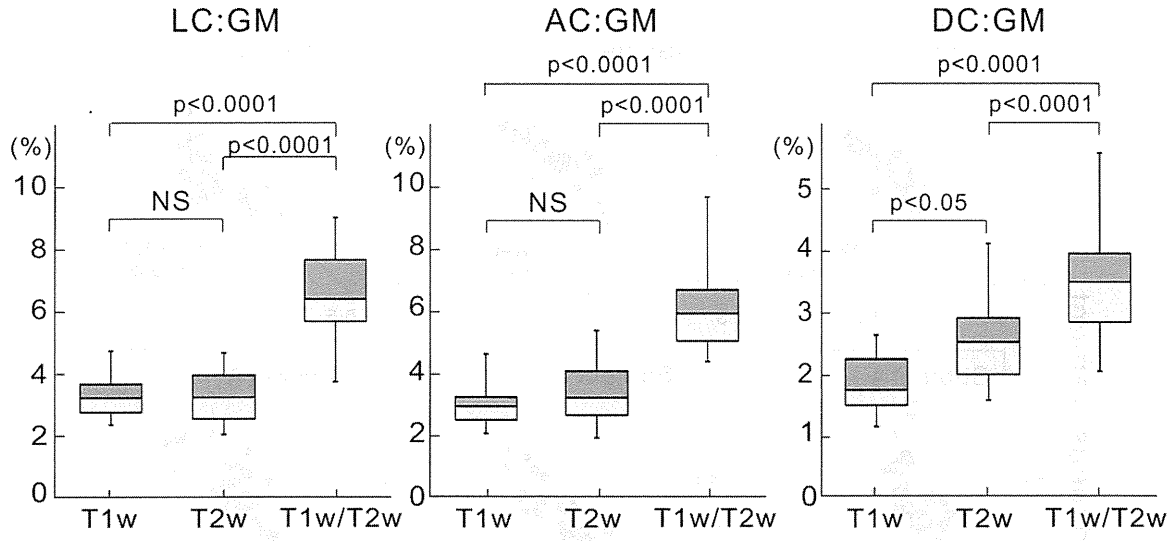

Figure 6. Mean contrast among all segments at each location for each subject. A paired t-test revealed a significant difference in contrast between the ratio (T1w/T2w) and the T1w or T2w image for all locations ($P < 0.0001$ with Bonferroni correction).

Effect of Age on the Signal Intensity

Figure 7 shows that the signal intensity of the T1w/T2w ratio images was inversely related to age at all locations (r: −0.60 ($P < 0.005$) to −0.42 ($P < 0.05$)). In contrast, no significant relationship was found between the signal intensity and age for the T1w or T2w images, except the GM signal in the T1w images.

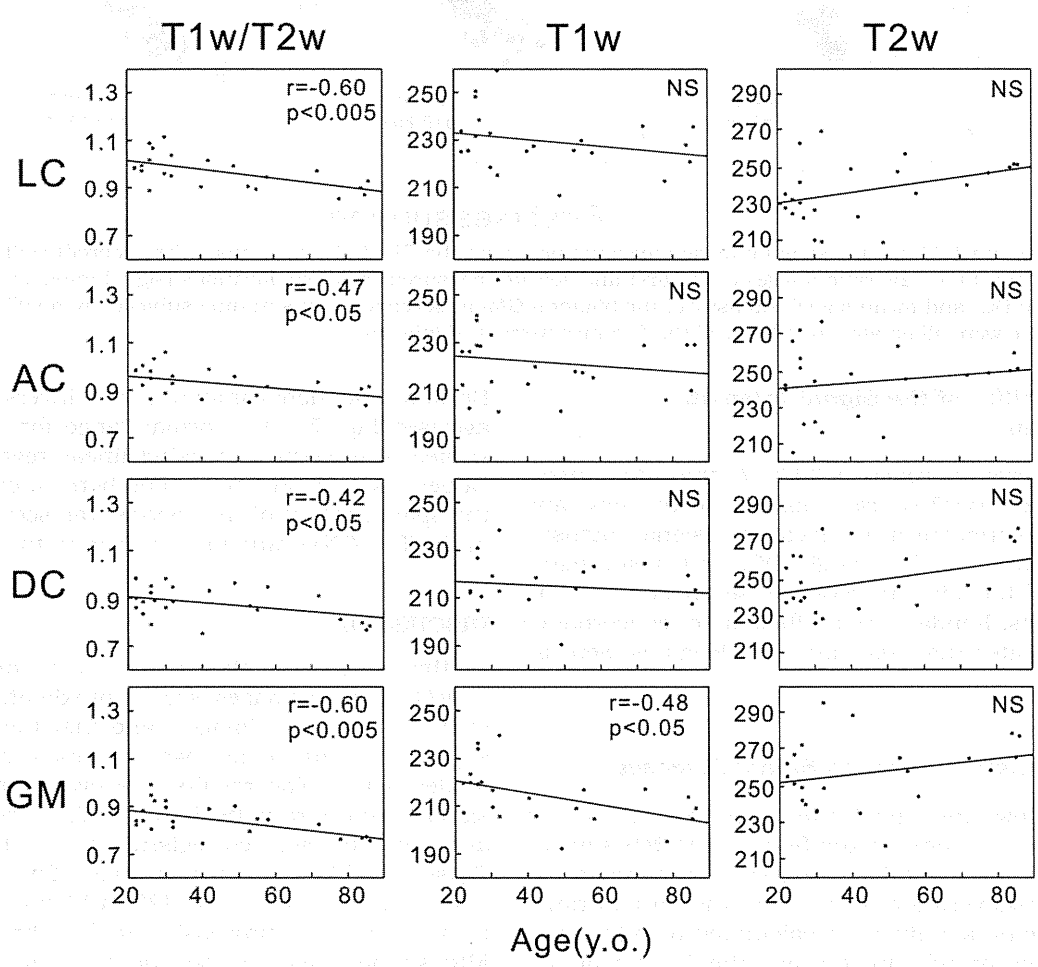

Figure 7. Signal intensity change with age at each location. For all locations, the signal intensity for the T1w/T2w ratio images at the C4 level inversely correlated with age. Note that the inter-individual variance for the same age range is substantially reduced in the T1w/T2w ratio images compared with the T1w or T2w signal intensity.

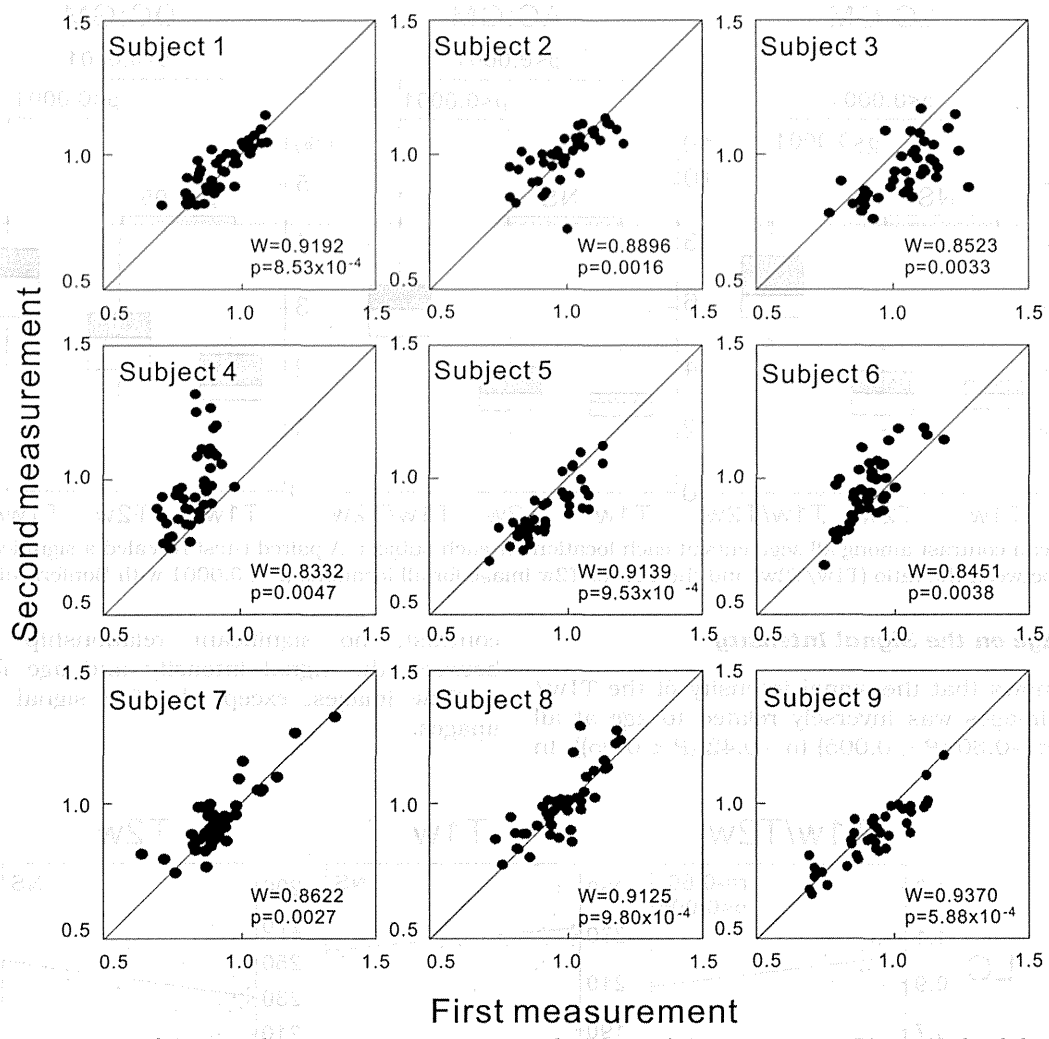

Figure 8. Reproducibility of the signal intensity measurement with the T1w/T2w ratio image. The reproducibility of the signal intensities in the T1w/T2w ratio images of the first and second measurement at six locations (signal intensity of the bilateral AC, LC, single DC, and mean signal intensity of the bilateral GM) at seven segments in nine subjects. Kendall's W coefficients of concordance were all greater than 0.8 and the *P*-values were all significant.

Reproducibility of the Signal Intensity Measurement

Figure 8 shows the reproducibility of the signal intensities in the T1w/T2w ratio images of the first and second measurement at six locations (signal intensity of the bilateral AC, LC, single DC, and mean signal intensity of the bilateral GM) at seven segments in nine subjects. Kendall's W coefficients of concordance were all greater than 0.8, and the *P*-values were all significant.

Signal Intensity Change in Spinal Diseases

Figure 9 shows the signal intensities (red line) in the T1w/T2w ratio image for the 39-year-old MS subject. Significantly low intensities were seen continuously in the one to two vertebral levels from the normal range between the broken lines, as calculated using the values from the controls. In contrast, the 77-year-old CS myelopathy subject showed a rather sharp decrease in signal intensity within a localized segmental level at several different segmental locations (Fig. 10). Because the signal intensity was inversely related to age (see Fig. 7), the normal range for a 77-year-old subject was estimated using linear regression of the values used in Figure 9. For both subjects' images, the spatial extent of the lesions was seen more clearly in the T1w/T2w ratio images than in the T2w images.

DISCUSSION

In this study, we showed that the contrast in the T1w/T2w ratio images was approximately twice that of the T1w or T2w images, and that the signal intensity of the ratio image was inversely related to the subject's age. The results, however, depends on the signal-to-noise ratio (SNR) of the T1w and T2w images and the precise co-registration of both images. Glasser and Van Essen registered T2w images to T1w images using FSL's FLIRT (20), which is considered to be the standard processing tool in brain functional MRI studies. Here, we set the voxel size at $1 \times 1 \times 2$ mm to optimize the SNR and spatial resolution considering a longitudinal orientation of the spinal cord. Because no standard acquisition software or MR

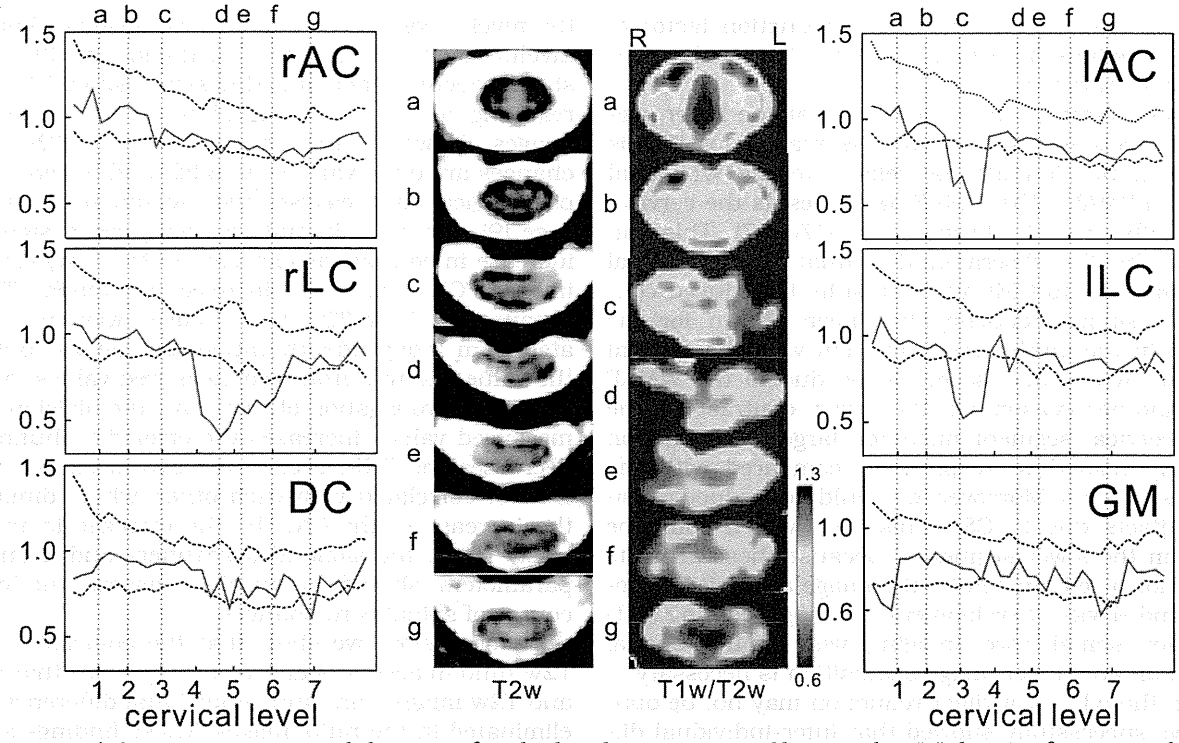

Figure 9. T1w/T2w ratio image at each location of multiple sclerosis patient. Slice number "c" deviates from control data at left AC and LC. Slice number "d,e" deviates from control data at right LC, however, DC falls in the range of control data.

pulse sequences for spinal cord imaging were used for spinal cord image registration, we used a SOMI brace (modified for MRI) to reduce body motion during the image acquisition, and the reproducibility of the signal intensity measurement was confirmed. Although we measured the contrast between WM and GM, the contrast increase does not rely on the exact localization of the WM and GM, meaning that the same discussion can also be made with two locations within the same tissue. Thus, the lower spatial resolution of the image to discriminate GM and WM is not a critical issue in the argument for the contrast increase with

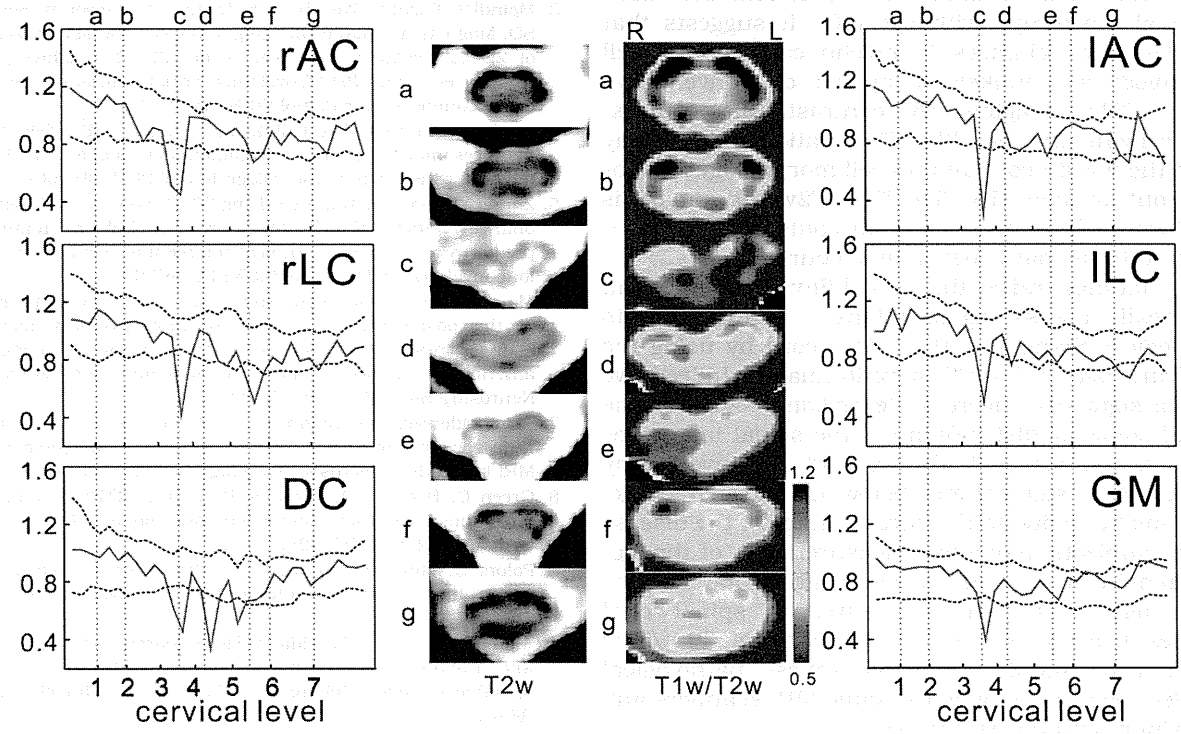

Figure 10. T1w/T2w ratio image at each location of cervical spondylotic myelopathy patient. Slice number "c" deviates from control data at every location, which is required for establishing accurate correlations with MRI parameters.

the T1w/T2w ratio; however, the reduction factor of SENSE was important to increase the SNR with a limited acquisition time.

The measured contrast decreased at the lower segmental levels for all images. The reason for this is unknown, but it might be related to the WM areal fraction (WMAF). The WMAF decreases as the cervical level shifts caudally (from C2 to C7) (17). This can worsen the GM discrimination (that is, WM signal contamination to GM), which results in reduced contrast. A similar tendency has been shown for the change in the myelin water fraction with the cervical segment, which also seems to be due to the WMAF (15). Another reason for the lower contrast in the lower cervical segment might be larger body motion (possibly related to respiration) compared with the upper segments. Moreover, we could not reduce possible artifacts due to CSF pulsation, which could be larger in the lower segments. Because these artifacts could not be eliminated by the image acquisition protocol and device, development of postprocessing software for spinal cord imaging with higher spatial resolution and faster image acquisition is necessary.

Even though our artifact reduction may not be optimal, we successfully showed that inter-individual differences in the signal intensity were eliminated by using the T1w/T2w ratio, and a clear relationship was seen between the signal intensity and age. One possible reason for the correlation with age is that the variance in signal intensity was reduced by cancelling the effect of body size and spinal cord location relative to the receiver coil. In the aging spinal cord, the density of nerve fibers decreases; consequently, the T1w/T2w ratio intensity might be reduced. Previous anatomical and morphological studies indicated a drop in the number of myelinated fibers (21) and decreased fractional anisotropy with age (10). It suggests that the age-related changes in myelin content and cell morphology are unlikely to appear on conventional T1w or T2w imaging. By contrast, the contrast enhancement in the T1w/T2w ratio images may reflect the myelin content and cell morphology by canceling out artifacts (18). The T1w/T2w ratio image is not always related to the myelin content; however, it is related to the pathological time course.

Our findings raise the possibility that one can numerically assess signal intensity change due to pathological changes in the spinal cord by using the signal intensity in T1w/T2w ratio images. Indeed, we found a significant decrease (exceeding −2 SD of the normal subjects' distribution) of the signal intensities in the lesion areas; both MS and CS myelopathy changes were significantly below the normal range, which might be due to the chronic stage of the disease in both subjects. Repetitive measurements of the signal intensity at the same lesion location may be useful to assess the clinical course of spinal cord diseases because the signal intensity of T1w/T2w ratio images should be stable unless pathological changes occur, as long as the same MRI scanners and acquisition parameters are used.

We acknowledge several limitations. First, the signal intensity in the ratio images is not always related to the myelin content in pathological lesions. When the myelin content decreases in a lesion, the T1w signal should decrease and the T2w signal should increase, resulting in decreased signal intensity in the ratio images. However, the actual T1w and T2w signal changes are quite variable (4,8,22) and depend on the pathological time course, even within the same disease (9). Second, although we observed a significant increase in contrast as expected in the T1w/T2w ratio images, CNR may not increase as much. This is because the T1w/T2w ratio images were not generated from independently measured signals, but from the values derived from two measured values. According to the propagation of error law, the division of two measured values increases the error distribution and decreases the SNR, even if the two measured values are not correlated with each other, which diminishes the increase in the CNR by the increase in the contrast. Third, the same MRI scanners and acquisition parameters should be used to assess the clinical course of spinal cord changes.

In conclusion, we show that the contrast of T1w/T2w ratio images was approximately twice that of T1w and T2w images, and inter-individual differences were eliminated in the ratio images. These findings suggest that the T1w/T2w ratio image represents a useful clinical protocol to numerically assess spinal cord image signal intensity.

REFERENCES

1. Ross JS. Newer sequences for spinal MR imaging: smorgasbord or succotash of acronyms? AJNR Am J Neuroradiol 1999;20:361–373.
2. Maier SE. Examination of spinal cord tissue architecture with magnetic resonance diffusion tensor imaging. Neurotherapeutics 2007;4:453–459.
3. Meindl T, Wirth S, Weckbach S, Dietrich O, Reiser M, Schoenberg SO. Magnetic resonance imaging of the cervical spine: comparison of 2D T2-weighted turbo spin echo, 2D T2*weighted gradient-recalled echo and 3D T2-weighted variable flip-angle turbo spin echo sequences. Eur Radiol 2009;19:713–721.
4. Do-Dai DD, Brooks MK, Goldkamp A, Erbay S, Bhadelia RA. Magnetic resonance imaging of intramedullary spinal cord lesions: a pictorial review. Curr Probl Diagn Radiol 2010;39:160–185.
5. Zhang YZ, Shen Y, Wang LF, Ding WY, Xu JX, He J. Magnetic resonance T2 image signal intensity ratio and clinical manifestation predict prognosis after surgical intervention for cervical spondylotic myelopathy. Spine 2010;35:E396–E399.
6. Mastronardi L, Elsawaf A, Roperto R, et al. Prognostic relevance of the postoperative evolution of intramedullary spinal cord changes in signal intensity on magnetic resonance imaging after anterior decompression for cervical spondylotic myelopathy. J Neurosurg Spine 2007;7:615–622.
7. van Walderveen MA, Kamphorst W, Scheltens P, et al. Histopathologic correlate of hypointense lesions on T1-weighted spin-echo MRI in multiple sclerosis. Neurology 1998;50:1282–1288.
8. Green C, Butler J, Eustace S, Poynton A, O'Byrne JM. Imaging modalities for cervical spondylotic stenosis and myelopathy. Adv Orthop 2012;2012:908324.
9. Poloni G, Minagar A, Haacke EM, Zivadinov R. Recent developments in imaging of multiple sclerosis. Neurologist 2011;17:185–204.
10. Mamata H, Jolesz FA, Maier SE. Apparent diffusion coefficient and fractional anisotropy in spinal cord: age and cervical spondylosis-related changes. J Magn Reson Imaging 2005;22:38–43.
11. Biton IE, Duncan ID, Cohen Y. High b-value q-space diffusion MRI in myelin-deficient rat spinal cords. Magn Reson Imaging 2006;24:161–166.

12. Cohen-Adad J, El Mendili MM, Lehericy S, et al. Demyelination and degeneration in the injured human spinal cord detected with diffusion and magnetization transfer MRI. Neuroimage 2011;55: 1024–1033.
13. MacMillan EL, Madler B, Fichtner N, et al. Myelin water and T(2) relaxation measurements in the healthy cervical spinal cord at 3.0T: repeatability and changes with age. Neuroimage 2011;54: 1083–1090.
14. Kozlowski P, Liu J, Yumg AC, Tetzlaff W. High-resolution myelin water measurements in rat spinal cord. Magn Reson Med 2008; 59:796–802.
15. Kolind SH, Deoni SC. Rapid three-dimensional multicomponent relaxation imaging of the cervical spinal cord. Magn Reson Med 2011;65:551–556.
16. Kaneoke Y, Furuse M, Inao S, et al. Spin-lattice relaxation times of bound water—its determination and implications for tissue discrimination. Magn Reson Imaging 1987;5:415–420.
17. Minty EP, Bjarnason TA, Laule C, MacKay AL. Myelin water measurement in the spinal cord. Magn Reson Med 2009;61:883–892.
18. Glasser MF, Van Essen DC. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2- weighted MRI. J Neurosci 2011;31:11597–11616.
19. Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P. SENSE: sensitivity encoding for fast MRI. Magn Reson Med 1999;42:952–962.
20. Jenkinson M, Bannister P, Brady M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. Neuroimage 2002;17; 825–841.
21. Terao S, Sobue G, Hashizume Y, Shimada N, Mitsuma T. Age-related changes of the myelinated fibers in the human corticospinal tract: a quantitative analysis. Acta Neuropathol 1994;88:137–142.
22. Ohshio I, Hatayama A, Kaneda K, Takahara M, Nagashima K. Correlation between histopathologic features and magnetic resonance images of spinal cord lesions. Spine 1993;18:1140–1149.

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Clinical Study

The association of combination of disc degeneration, end plate signal change, and Schmorl node with low back pain in a large population study: the Wakayama Spine Study

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Abstract

BACKGROUND CONTEXT: Disc degeneration (DD) reportedly causes low back pain (LBP) and is often observed concomitantly with end plate signal change (ESC) and/or Schmorl node (SN) on magnetic resonance imaging.

PURPOSE: The purpose of this study was to examine the association between DD and LBP, considering ESC and/or SN presence, in a large population study.

STUDY DESIGN/SETTING: Cross-sectional population-based study in two regions of Japan.

PATIENT SAMPLE: Of 1,011 possible participants, data from 975 participants (324 men, 651 women; mean age, 66.4 years; range, 21–97 years) were included.

OUTCOME MEASURES: Prevalence of DD, ESC, and SN alone and in combination in the lumbar region and the association of these prevalence levels with LBP.

METHODS: Sagittal T2-weighted images were used to assess the intervertebral spaces between L1–L2 and L5–S1. Disc degeneration was classified using the Pfirrmann classification system (grades 4 and 5 indicated degeneration); ESC was defined as a diffuse high signal change along

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either area of the end plate, and SN was defined as a small well-defined herniation pit with a surrounding wall of hypointense signal. Logistic regression analysis was used to determine the odds ratios (ORs) and confidence intervals (CIs) for LBP in the presence of radiographic changes in the lumbar region and at each lumbar intervertebral level, compared with patients without radiographic change, after adjusting for age, body mass index, and sex.

RESULTS: The prevalence of lumbar structural findings was as follows: DD alone, 30.4%; ESC alone, 0.8%; SN alone, 1.5%; DD and ESC, 26.6%; DD and SN, 12.3%; and DD, ESC, and SN, 19.1%. These lumbar structural findings were significantly associated with LBP in the lumbar region overall, as follows: DD, ESC, and SN, OR 2.17, 95% CI 1.2–3.9; L1–L2, OR 6.00, 95% CI 1.9–26.6; L4–L5, OR 2.56, 95% CI 1.4–4.9; and L5–S1, OR 2.81, 95% CI 1.1–2.3. The combination of DD and ESC was significantly associated with LBP as follows: L3–L4, OR 2.43, 95% CI 1.5–4.0; L4–L5, OR 1.82, 95% CI 1.2–2.8; and L5–S1, OR 1.60, 95% CI 1.1–2.3.

CONCLUSIONS: Our data suggest that DD alone is not associated with LBP. By contrast, the combination of DD and ESC was highly associated with LBP.

Keywords: Disc degeneration; End plate signal change; Schmorl node; Low back pain; Large population study; ROAD study

Introduction

Low back pain (LBP) causes functional impairment, diminished quality of life, loss of working ability, potential psychological distress, and increased health-care costs [1–3]. Magnetic resonance imaging (MRI) has become widely used in LBP diagnosis [4–15].

From the perspective of discogenic pain, the association between disc degeneration (DD) and symptoms remains controversial. Several reports have found that DD was a source of LBP [4–7], but others reported no association between DD and LBP [8,9]. This discrepancy is partly explained by the fact that DD often occurs concomitantly with various radiographic changes such as end plate signal change (ESC) and Schmorl node (SN). However, few studies have reported on the association of ESC and SN with LBP [10–14], and furthermore, to the best of our knowledge, no population-based study has examined the association of the combination of DD, ESC, and SN with LBP.

The purposes of this study were to examine the prevalence of combinations of DD, ESC, and SN in the lumbar region overall and to clarify the associations between LBP and combinations of DD, ESC, and SN in a large population.

Methods

Participants

The Wakayama Spine Study is a population-based study of degenerative spinal disease [15–17] performed in a subcohort of the large-scale population-based cohort study Research on Osteoarthritis/Osteoporosis against Disability (ROAD) [18,19]. Research on Osteoarthritis/Osteoporosis against Disability is a nationwide prospective study of bone and joint diseases consisting of population-based cohorts established in three communities in Japan. The participants were recruited from listings of resident registrations in three communities that have different characteristics: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama. The inclusion criteria, apart from residence in the communities mentioned previously, were the ability to walk to the survey site, report data, and understand and sign an informed consent form. The age of the participants recruited from the urban region was 60 years or older and that of the participants from the other two regions was 40 years or older [18]. A second visit of the ROAD study to the mountainous region of Hidakagawa and the coastal region of Taiji was performed between 2008 and 2010. From the inhabitants participating in the second visit of the ROAD study, 1,063 volunteers were recruited to MRI examinations. Among these volunteers, 52 declined to attend the examination and 1,011 provided an additional written informed consent for the mobile MRI examination and were recruited for registration in the Wakayama Spine Study. Among the 1,011 participants, those who had an MRI-sensitive implanted device (e.g., pacemaker) or other disqualifier were excluded. Ultimately, 980 individuals underwent whole-spine MRI. One participant who had undergone a previous cervical operation and four participants who had undergone previous posterior lumbar fusion were excluded from the analysis. Thus, whole-spine MRI results were available for 975 participants (324 men and 651 women) with an age range of 21 to 97 years (mean, 67.2 years for men and 66.0 years for women). Experienced board-certified orthopedic surgeons also asked all participants the following question regarding LBP: "Have you experienced LBP on most days during the past month, in addition to now?" Those who answered "yes" were defined as having LBP based on the previous studies [20–24]. All study participants provided informed consent, and the study design was approved by the appropriate ethics review boards.

Magnetic resonance imaging

A mobile MRI unit (Excelart 1.5 T; Toshiba, Tokyo, Japan) was used, and whole-spine MRI was performed for all participants on the same day as the examination. The participants were supine during the MRI, and those with rounded backs used triangular pillows under their head and knees. The imaging protocol included sagittal T2-weighted fast spin echo (repetition time, 4,000 ms/echo; echo time, 120 ms; and field of view, 300×320 mm) and axial T2-weighted fast spin echo (repetition time, 4,000 ms/echo; echo time, 120 ms; and field of view, 180×180 mm). Sagittal T1-weighted images were omitted owing to cost and time limitations; only T2-weighted images were obtained.

Radiographic assessment

Sagittal T2-weighted images were used to assess DD, ESC, and SN at all intervertebral levels from C2–C3 to L5–S1. The present study assessed L1–L2 to L5–S1 in the lumbar region.

Disc degeneration

Disc degeneration grading was performed by a board-certified orthopedic surgeon who was blinded to the background of the participants. The degree of DD on MRI was classified into five grades based on the Pfirrmann classification system [25], with grades 4 and 5 indicating DD. To evaluate intraobserver variability, 100 randomly selected MR images of the entire spine were rescored by the same observer more than 1 month after the first reading. Furthermore, to evaluate interobserver variability, 100 other MR images were scored by 2 orthopedic surgeons using the same classification. The intraobserver and interobserver variabilities of DD, as evaluated by kappa analysis, were 0.94 and 0.94, respectively.

End plate signal change

End plate signal change was defined as diffuse areas of high signal change along the end plates, tending to be linear and always parallel to the vertebral end plates on sagittal T2-weighted images. However, discerning the type of Modic changes [26,27] was not possible because of cost and time limitations of this large-scale study. Because the T1 sequence was not obtained, we considered Modic Type I/II (T2 high signal intensity end plate change) to reflect the presence of ESC and T2 isosignal intensity and Modic Type III (T2 low signal intensity end plate change) to reflect the absence of ESC. To evaluate the intraobserver and interobserver variabilities, two orthopedic surgeons scored MR images in the same manner. The intraobserver and interobserver variabilities of ESC evaluated by kappa analysis were 0.86 and 0.82, respectively.

Schmorl node

Schmorl node was characterized by a localized defect at the rostral, caudal, or both end plates, with a well-defined herniation pit in the vertebral body with or without a surrounding sclerotic rim (low signal on T2-weighted image) [14,28]. Erosive defects in the end plate in degenerate segments were not considered as SN [14,28]. To evaluate intraobserver and interobserver variabilities, two orthopedic surgeons scored MR images in the same manner. The intraobserver and interobserver variabilities for SN evaluated by kappa analysis were 0.92 and 0.84, respectively.

Statistical analyses

Radiographic changes were compared between sexes using the chi-square test. Multivariate logistic regression analysis was used to estimate the radiographic changes of DD, ESC, and SN presence in the lumbar region as dependent variables, with LBP as the independent variable, after adjustment for age, body mass index (BMI), and sex. Multivariate logistic regression analysis was used to estimate the respective associations of eight combinations of radiographic changes (none; DD alone; SN alone; ESC alone; DD and SN; DD and ESC; SN and ESC; and DD, ESC, and SN) in the lumbar region as dependent variables, with LBP as the independent variable, after adjustment for age, BMI, and sex. Multivariate logistic regression analysis was also used to estimate the association of 8 combinations of radiographic changes at each intervertebral level (L1–L2 to L5–S1) in the lumbar region after adjustment for age, BMI, and sex. All statistical analyses were performed using JMP, version 8 (SAS Institute Japan, Tokyo, Japan).

Prevalence of DD, ESC, and/or SN, defined as the proportion of the number of participants who demonstrated the presence of DD, ESC, and/or SN in the lumbar region divided by the total number of participants, was used to describe the frequency of DD, ESC, and/or SN. In this analysis, to clarify the associated factors using multivariate logistic regression analysis, we entered a variable reflecting the observation of DD, ESC, and/or SN (1, presence; 0, absence) as a dependent variable.

Table 1
Characteristics of the 975 participants in the present study

	Overall	Men	Women
No. of participants	975	324	651
Demographic characteristics			
Age, y	66.4±13.5	67.2±13.9	66.0±13.4
Height, cm	156.4±9.4	164.6±7.2	151.5±7.2
Weight, kg	56.8±11.5	64.5±11.6	53.0±9.4
BMI, kg/m^2	23.3±3.6	23.6±3.4	23.1±3.7
Symptom			
LBP (%)	393 (40.3)	119 (36.7)	274 (42.1)

BMI, body mass index; LBP, low back pain.
Note: Values are the mean±standard deviation.

Table 2
Prevalence of combination of radiographic change in the lumbar region according to sex

	Overall (%)	Men (%)	Women (%)
Total	975	324	651
None	85 (8.7)	35 (10.8)	50 (7.7)
DD alone	296 (30.4)	104 (32.1)	192 (29.5)
ESC alone	8 (0.8)	3 (0.9)	5 (0.8)
SN alone	15 (1.5)	6 (1.9)	9 (1.4)
DD and ESC	259 (26.6)	85 (26.2)	174 (26.7)
DD and SN	120 (12.3)	37 (11.4)	83 (12.8)
SN and ESC	6 (0.6)	0 (0)	6 (0.9)
DD, ESC, and SN	186 (19.1)	54 (16.7)	132 (20.3)

DD, disc degeneration; ESC, end plate signal change; SN, Schmorl node.

Note: Chi-square test was used to determine differences in radiographic change between men and women.

Table 3
Association between LBP and radiographic changes in the lumbar region

	Proportion of participants with LBP (%)	OR (95% CI)
None	25/85 (29.4)	1
DD alone	112/296 (37.8)	1.35 (0.8–2.3)
ESC alone	0/8 (0)	—
SN alone	5/15 (33.3)	1.14 (0.3–3.6)
DD and ESC	107/259 (41.3)	1.51 (0.9–2.6)
DD and SN	45/120 (37.5)	1.26 (0.7–2.3)
SN and ESC	3/6 (50.0)	2.06 (0.4–11.9)
DD, ESC, and SN	96/186 (51.6)	2.17 (1.2–3.9)*

CI, confidence interval; DD, disc degeneration; ESC, end plate signal change; LBP, low back pain; OR, odds ratio; SN, Schmorl node.

Note: Proportion of participants with LBP means the number of participants with LBP/the number of participants with each radiographic change. ORs were calculated by multivariate logistic regression analysis after adjustment for age, body mass index, and sex.

* $p<.01$.

Results

Table 1 shows the characteristics of the 975 participants in the present study including age and demographic measurements. Two-thirds of the participants were women.

The prevalence of DD, ESC, and SN in the lumbar region overall, without considering other radiographic changes, was 86.7%, 44.1%, and 29.6% in men and 89.6%, 48.7%, and 35.2% in women, respectively. Table 2 shows the prevalence of combinations of radiographic changes according to sex. DD alone demonstrated the highest prevalence, followed by DD and ESC and DD, ESC, and SN in both sexes. The prevalence of SN alone, ESC alone, or the combination of SN and ESC was small. The prevalence of combinations of radiographic changes in the lumbar region did not significantly differ between men and women.

When we evaluated DD, ESC, and SN in the lumbar region overall without considering other radiographic change, DD presence and ESC presence in the lumbar region were each significantly associated with LBP (DD: odds ratio [OR] 1.58, 95% confidence interval [CI] 1.02–2.49; ESC: OR 1.36, 95% CI 1.04–1.76). On the other hand, SN presence in the lumbar region was not significantly associated with LBP (OR 1.27, 95% CI 0.96–1.68). Next, to determine the effect of the combination of DD, ESC, and SN on LBP, we classified participants into eight groups: none; DD alone; ESC alone; SN alone; DD and ESC; DD and SN; SN and ESC; and DD, ESC, and SN. As shown in Table 3, the combination of DD, ESC, and SN in the lumbar region was significantly associated with LBP. Disc degeneration alone was not an associated factor for LBP.

Furthermore, as shown in Table 4, the effect of combinations of radiographic change at each intervertebral level from L1–L2 to L5–S1 on LBP was evaluated: the combination of DD, ESC, and SN was significantly associated with LBP at L1–L2, L4–L5, and L5–S1. Furthermore, the combination of DD and ESC was significantly associated with LBP at L3–L4, L4–L5, and L5–S1.

Discussion

The prevalence of DD, ESC, or SN in the lumbar region has been examined in some previous studies [11–15,26–32], but, to the authors' knowledge, no population-based studies have assessed the prevalence of the combination of DD, ESC, and SN in a large population using MRI. First, we found that prevalence of combinations of DD, ESC, and SN in the lumbar region was approximately 20%. By contrast, the prevalence of ESC alone, SN alone, and combination of SN and ESC was quite small, which is partly explained by the fact that DD was reported to have a strong positive linear relationship with ESC and/or SN in the previous studies [14,28,33].

The association of DD with LBP remains controversial. An association between DD in the lumbar region and LBP was previously demonstrated in a twin study and other previous studies [15,30,31]. However, some reports have observed a high prevalence of DD among asymptomatic volunteers, with no association between DD and LBP [8,9]. These studies may have been limited in that they did not account for interactions between radiographic changes including DD, ESC, and SN. The present study found that the combination of DD, ESC, and SN was significantly associated with LBP, whereas DD alone was not.

The association of Modic changes, which are the gold standard to diagnose ESC, with clinical symptoms, has been controversial in the clinical studies based on patient series and a population-based cohort [10–12,29,32]. The present study found that the combination of DD and ESC at L3–L4, L4–L5, and L5–S1 was significantly associated with LBP. Degenerative change of end plates becomes a source of LBP and affects DD. Because the lumbar vertebral end plate contains immunoreactive nerves, as shown in the studies of sheep and humans [33,34], it has been reported that an increased number of tumor necrosis factor–immunoreactive spinal nerve cells and fibers are present in end plates

Table 4
Association between LBP and radiographic changes at each level in the lumbar region

	L1–L2		L2–L3		L3–L4		L4–L5		L5–S1	
	Proportion of participants with LBP (%)	OR (95% CI)	Proportion of participants with LBP (%)	OR (95% CI)	Proportion of participants with LBP (%)	OR (95% CI)	Proportion of participants with LBP (%)	OR (95% CI)	Proportion of participants with LBP (%)	OR (95% CI)
None	225/593 (37.9)	1	153/416 (36.8)	1	121/347 (34.9)	1	74/228 (32.5)	1	99/284 (34.9)	1
DD alone	76/193 (39.4)	1.0 (0.7–1.4)	138/322 (42.9)	1.19 (0.9–1.6)	161/400 (40.3)	1.17 (0.9–1.6)	184/449 (41.0)	1.36 (0.9–1.9)	176/440 (40.0)	1.14 (0.8–1.6)
ESC alone	11/27 (40.7)	1.06 (0.5–2.3)	9/23 (39.1)	0.96 (0.4–2.3)	3/10 (30.0)	0.74 (0.2–2.7)	3/16 (18.8)	0.50 (0.1–1.6)	6/15 (40.0)	1.24 (0.4–3.6)
SN alone	19/46 (41.3)	1.07 (0.6–2.0)	15/40 (37.5)	1.03 (0.5–2.0)	10/22 (45.5)	1.58 (0.6–3.8)	5/14 (35.7)	1.18 (0.3–3.5)	1/1 (100)	—
DD and ESC	16/36 (44.4)	1.20 (0.6–2.4)	33/69 (47.8)	1.37 (0.8–2.3)	55/93 (59.1)	2.43 (1.5–4.0)*	81/164 (49.4)	1.82 (1.2–2.8)†	96/201 (47.8)	1.60 (1.1–2.3)*
DD and SN	31/61 (50.8)	1.47 (0.8–2.6)	32/73 (43.8)	1.14 (0.7–1.9)	24/70 (34.3)	0.84 (0.5–1.5)	16/52 (30.8)	0.84 (0.4–1.6)	3/15 (20.0)	0.45 (0.1–1.5)
SN and ESC	2/3 (66.7)	2.48 (0.2–53.8)	0/6 (0)	—	2/2 (100)	—	1/2 (50.0)	2.04 (0.08–52.5)	0/0 (0)	—
DD, ESC, and SN	13/16 (81.3)	6.00 (1.9–26.6)‡	13/26 (50.0)	1.49 (0.7–3.4)	17/31 (54.8)	2.07 (0.9–4.5)	29/50 (58.0)	2.56 (1.4–4.9)*	12/19 (63.2)	2.85 (1.1–2.3)*

CI, confidential interval; DD, disc degeneration; ESC, end plate signal change; LBP, low back pain; OR, odds ratio; SN, Schmorl node.
Note: Proportion of participants with LBP means the number of participants with LBP/the number of participants with each radiographic change. Multivariate logistic regression analysis of radiographic change was associated with LBP after adjustment for age, body mass index, and sex.
* $p<.05$.
† $p<.01$.
‡ $p<.005$.

demonstrating ESC [35]. Therefore, pain may originate from damaged end plates in patients with ESC.

Another possibility is that ESC is a proxy for discogenic pain, as ESC is most often seen in association with DD [12,36] and tumor necrosis factor–immunoreactive nerves have also been reported in DD [37]. Both the present results and a previous study indicate that the association between ESC and LBP appears to be stronger than that between DD and LBP [29]. Regarding the association between the level of ESC and LBP, Kuisma et al. [32] reported that both Modic type I and II lesions at L5–S1, but not at upper levels, are associated with LBP. However, the present study showed that the OR of LBP with Modic type I and II lesions at L3–L4 was higher than that at L5–S1. We speculate that the association of LBP symptoms with the L3–L4 level might be because of mechanical factors and alignment of the whole spine, but the pathophysiology of this phenomenon needs further investigation.

In the present study, SN alone was not significantly associated with LBP. In addition, most SNs were combined with DD. In fact, SN was not itself a risk factor for back pain but was an indicator of DD in the previous reports [13,14,28]. Furthermore, SN occurs when the cartilaginous end plate of the vertebral body has been disrupted [38]. Such a disruption can be produced by an intrinsic abnormality of the end plate itself or by alterations in the subchondral bone of the vertebral body [39]. Therefore, LBP might be a multifactorial condition arising from a combination of DD, ESC, and SN in the lumbar region.

Study limitations

The present study has several limitations. First, it is a cross-sectional study, so the transition from DD, ESC, and SN cannot be clarified. Second, more than 1,000 participants included in the present study may not represent the general population, as they were recruited from only 2 areas. To confirm whether the participants of the Wakayama Spine Study are representatives of the Japanese population, we compared anthropometric measurements and frequencies of smoking and alcohol drinking between the study participants and the general Japanese population. No significant differences in BMI were observed (men: 23.7 and 24.0, p=.33 and women: 23.1 and 23.5, p=.07). Furthermore, the proportions of current smokers and drinkers (those who regularly smoked or drank more than one drink per month) among men and that of current drinkers among women were significantly higher in the general Japanese population than in the study population, and no significant difference in current smokers was observed among women (men smokers, 32.6% in the Japanese population and 25.2% among study participants, p=.015; women smokers, 4.9% in the Japanese population and 4.1% among study participants, p=.50; men drinkers, 73.9% in the Japanese population and 56.8% among study participants, p<.0001; and women drinkers, 28.1% in the Japanese population and 18.8% among study participants,

p<.0001). These results suggest the likelihood that participants in this study had healthier lifestyles than the general Japanese population [40]. This "healthy" selection bias should be taken into consideration when generalizing the results obtained from the Wakayama Spine Study. Third, distinction of the type of Modic changes was not possible because owing to cost and time limitations, only T2-weighted images were obtained. However, Ohtori et al. [35] reported that both Modic type I and II changes were significantly associated with inflammation induced by tumor necrosis factor. Furthermore, the prevalence of Modic Type I was lower than that of Type II in a systematic review [41]. Therefore, we propose that high-intensity ESC on T2-weighted images is informative in the assessment of LBP. Fourth, the definition of LBP is different among many studies [24,32], and the result of association between LBP and radiographic change might be changed depending on the definition. We decided that the definition of LBP was "LBP on most days during the past month, in addition to now" from the previous reports [20–24].

Finally, the radiographic changes of DD, ESC, and SN in the lumbar region might not be strongly correlated with LBP. Low back pain can be caused by multiple factors including osteoporosis, back muscle strain, and psychosocial problems; thus, we can explain only a portion of the associated factors of LBP from MRI findings. Future investigations should include continued follow-up surveys of psychosocial and other factors.

Conclusions

We first investigated combinations of the radiographic changes DD, ESC, and SN in the lumbar region and at each intervertebral level and their association with LBP in a large population of individuals ranging in age from 21 to 97 years old. Our data suggest that DD alone is not an associated factor for LBP. By contrast, the combination of DD, ESC, and SN at L1–L2, L4–L5, and L5–S1 was significantly associated with LBP. Furthermore, the combination of DD and ESC at L3–L4, L4–L5, and L5–S1 was also significantly associated with LBP. Low back pain is caused by multiple factors beyond the scope of MRI findings. However, this study clarified that DD alone was not associated with LBP, whereas, by contrast, the combination of DD, ESC, and/or SN was associated with LBP. Although they may not be immediately applicable to clinical practice, these findings contribute to the progress of LBP research. Further investigations along with continued follow-up surveys will continue to elucidate the causes of LBP.

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References

[1] Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. Spine J 2008;8:8–20.

[2] Deyo RA, Tsui-Wu YJ. Descriptive epidemiology of low-back pain and its related medical care in the United States. Spine 1987;12:264–8.

[3] Andersson GB. Epidemiological features of chronic low-back pain. Lancet 1999;354:581–5.

[4] Luoma K, Riihimaki H, Luukkonen R, Raininko R, Viikari-Juntura E, Lamminen A. Low back pain in relation to lumbar disc degeneration. Spine 2000;25:487–92.

[5] Chou D, Samartzis D, Bellabarba C, Patel A, Luk KD, Kisser JM, et al. Degenerative magnetic resonance imaging changes in patients with chronic low back pain: a systematic review. Spine 2011;36:S43–53.

[6] Takatalo J, Karppinen J, Niinimaki J, Taimela S, Nayha S, Mutanen P, et al. Does lumbar disc degeneration on magnetic resonance imaging associate with low back symptom severity in young Finnish adults? Spine 2011;36:2180–9.

[7] Carragee E, Alamin T, Cheng I, Franklin T, van den Haak E, Hurwitz E. Are first-time episodes of serious LBP associated with new MRI findings? Spine J 2006;6:624–35.

[8] Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects: a prospective investigation. J Bone Joint Surg Am 1990;72:403e8.

[9] Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331:69–73.

[10] Weishaupt D, Zanetti M, Hodler J, Min K, Fuchs B, Pfirrmann CW, et al. Painful lumbar disc derangement: relevance of endplate abnormalities at MR imaging. Radiology 2001;218:420–7.

[11] Mitra D, Cassar-Pullicino VN, McCall IW. Longitudinal study of vertebral type-1 end-plate changes on MR of the lumbar spine. Eur Radiol 2004;24:1574–81.

[12] Toyone T, Takahashi K, Kitahara H, Yamagata M, Murakami M, Moriya H. Vertebral bone-marrow changes in degenerative lumbar disc disease. An MRI study of 74 patients with low back pain. J Bone Joint Surg Br 1994;76:757–64.

[13] Kjaer P, Leboeuf-Yde C, Korsholm L, Sorensen JS, Bendix T. Magnetic resonance imaging and low back pain in adults: a diagnostic imaging study of 40-year-old men and women. Spine 2005;30:1173–80.

[14] Williams FMK, Manek NJ, Sambrook PN, Spector TD, Macgregor AJ. Schmorl's nodes: common, highly heritable, and related to lumbar disc disease. Arthritis Rheum 2007;57:855–60.

[15] Teraguchi M, Yoshimura N, Hashizume H, Muraki S, Yamada H, Minamide A, et al. Prevalence and distribution of intervertebral disc degeneration over the entire spine in a population-based cohort: the Wakayama Spine Study. Osteoarthritis Cartilage 2014;22:104–10.

[16] Ishimoto Y, Yoshimura N, Muraki S, Yamada H, Nagata K, Hashizume H, et al. Prevalence of symptomatic lumbar spinal stenosis and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study. Osteoarthritis Cartilage 2012;20:1103–8.

[17] Nagata K, Yoshimura N, Muraki S, Hashizume H, Ishimoto Y, Yamada H, et al. Prevalence of cervical cord compression and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study. Spine 2012;37:1892–8.

[18] Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K, Akune T. Cohort profile: research on osteoarthritis/osteoporosis against disability (ROAD) study. Int J Epidemiol 2010;39:988–95.

[19] Yoshimura N, Muraki S, Oka H, Mabuchi A, En-Yo Y, Yoshida M, et al. Prevalence of knee osteoarthritis, lumbar spondylosis, and osteoporosis in Japanese men and women: the research on osteoarthritis/osteoporosis against disability study. J Bone Miner Metab 2009;27:620–8.

[20] Muraki S, Oka H, Akune T, Mabuchi A, En-Yo Y, Yoshida M, et al. Prevalence of radiographic lumbar spondylosis and its association with low back pain in elderly subjects of population-based cohorts: the ROAD study. Ann Rheum Dis 2009;68:1401–6.

[21] Muraki S, Akune T, Oka H, En-Yo Y, Yoshida M, Saika A, et al. Impact of knee and low back pain on health-related quality of life in Japanese women: the Research on Osteoarthritis against Disability (ROAD). Mod Rheumatol 2010;20:444–51.

[22] Muraki S, Akune T, Oka H, En-Yo Y, Yoshida M, Saika A, et al. Health-related quality of life in subjects with low back pain and knee pain in a population-based cohort study of Japanese men: the ROAD study. Spine 2011;36:1312–9.

[23] Muraki S, Akune T, Oka H, Ishimoto Y, Nagata K, Yoshida M, et al. Incidence and risk factors for radiographic lumbar spondylosis and lower back pain in Japanese men and women: the ROAD study. Osteoarthritis Cartilage 2012;20:712–8.

[24] Dionne CE, Dunn KM, Croft PR, Nachemson AL, Buchbinder R, Walker BF, et al. A consensus approach toward the standardization of back pain definitions for use in prevalence studies. Spine 2008;33:95–103.

[25] Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. Spine 2001;26:1873–8.

[26] Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disc disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 1988;166:193–9.

[27] Modic MT, Masaryk TJ, Ross JS, Carter JR. Imaging of degenerative disc disease. Radiology 1988;168:177–86.

[28] Mok FP, Samartzis D, Karppinen J, Luk KD, Fong DY, Cheung KM. ISSLS prize winner: prevalence, determinants, and association of Schmorl's nodes of the lumbar spine with disc degeneration: a population-based study of 2449 individuals. Spine 2010;35:1944–52.

[29] Kjaer P, Korsholm L, Bendix T, Sorensen JS, Leboeuf-Yde C. Modic changes and their associations with clinical finding. Eur Spine J 2006;15:1312–9.

[30] Battié MC, Videman T, Kaprio J, Gibbons LE, Gill K, Manninen H, et al. The Twin Spine Study: contributions to a changing view of disc degeneration. Spine J 2009;9:47–59.

[31] Cheung KM, Karppinen J, Chan D, Ho DW, Song YQ, Sham P, et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. Spine 2009;34:934–40.

[32] Kuisma M, Karppinen J, Niinimaki J, Ojala R, Haapea M, Heliovaara M, et al. Modic changes in endplates of lumbar vertebral bodies: prevalence and association with low back and sciatic pain among middle-aged male workers. Spine 2007;32:1116–22.

[33] Rajasekaran S, Babu JN, Arun R, Armstrong BR, Shetty AP, Murugan S. ISSLS prize winner: a study of diffusion in human lumbar discs: a serial magnetic resonance imaging study documenting the influence of the endplate on diffusion in normal and degenerate discs. Spine 2004;29:2654–67.

[34] Brown MF, Hukkanen MV, McCarthy ID, Redfern DR, Batten JJ, Crock HV, et al. Sensory and sympathetic innervation of the vertebral endplate in patients with degenerative disc disease. J Bone Joint Surg Br 1997;79:147–53.

[35] Ohtori S, Inoue G, Ito T, Koshi T, Ozawa T, Doya H, et al. Tumor necrosis factor-immunoreactive cells and PGP 9.5-immunoreactive nerve fibers in vertebral endplates of patients with discogenic low back pain and Modic type 1 or type 2 changes on MRI. Spine 2006;31:1026–31.

[36] Albert HB, Manniche C. Modic changes following lumbar disc herniation. Eur Spine J 2007;16:977–82.

[37] Freemont AJ, Peacock TE, Goupille P, Hoyland JA, O'Brien J, Jayson MI. Nerve ingrowth into diseased intervertebral disc in chronic back pain. Lancet 1997;350:178–81.

[38] Schmorl G. Uber Knorpelknotchen an den Wirbelbandscheiben (About cartilaginous node of the intervertebral disc). Fortschr Rontgenstr 1928;38:265–79.

[39] Wagner AL, Murtagh FR, Arrington JA, Stallworth D. Relationship of Schmorl's nodes to vertebral body endplate fractures and acute endplate disc extrusions. AJNR Am J Neuroradiol 2000;21:276–81.

[40] Ministry of Health, Labour and Welfare. The outline of the results of National Livelihood Survey 2007. Available at: http://www.mhlw.go.jp/toukei/list/20-19-1.html. Accessed December 24, 2014.

[41] Jensen TS, Karppinen J, Sorensen JS, Niinimaki J, Leboeuf-Yde C. Vertebral endplate signal changes (Modic change): a systematic literature review of prevalence and association with non-specific low back pain. Eur Spine J 2008;17:1407–22.

Research Report

Physical Performance Measures Associated With Locomotive Syndrome in Middle-Aged and Older Japanese Women

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ABSTRACT

Background: The Japanese Orthopaedic Association proposed a concept called locomotive syndrome (LS) to identify middle-aged and older adults at high risk of requiring health care services because of problems with locomotion. It is important to identify factors associated with the development of LS. Physical performance measures such as walking speed and standing balance are highly predictive of subsequent disability and mortality in older adults. However, there is little evidence about the relationship between physical performance measures and LS.

Purpose: To determine the physical performance measures associated with LS, the threshold values for discriminating individuals with and without LS, and the odds ratio of LS according to performance greater than or less than these thresholds in middle-aged and older Japanese women.

Methods: Participants were 126 Japanese women (mean age = 61.8 years). Locomotive syndrome was defined as a score of 16 or more on the 25-question Geriatric Locomotive Function Scale. Physical performance was evaluated using grip strength, unipedal stance time with eyes open, seated toe-touch, and normal and fast 6-m walk time (6MWT). Variables were compared between LS and non-LS groups.

Results: Fourteen participants (11.1%) were classed as having LS. Unipedal stance time, normal 6MWT, and fast 6MWT were significantly different between the 2 groups. The LS group had a shorter unipedal stance time and a longer normal and fast 6MWT than the non-LS group. For these 3 variables, the area under the receiver operating characteristic curve was greater than 0.7, and the threshold for discriminating the non-LS and LS groups was 15 s for unipedal stance time, 4.8 s for normal 6MWT and 3.6 s for fast 6MWT. These variables were entered into a multiple logistic regression analysis, which indicated that unipedal stance time less than 15 s was significantly related to LS (odds ratio = 8.46; $P < .01$).

Conclusion: Unipedal stance time was the physical performance measure that was most strongly associated with LS. This measure may be useful for early detection of LS.

Key Words: GLFS-25, locomotive syndrome, physical performance, unipedal stance time

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INTRODUCTION

Japan is facing the advent of a super-aged society. The Japanese Statistics Bureau reported that, in 2013, people aged 65 years or older accounted for 24% of the Japanese population.[1] The number of individuals who require nursing care is increasing because of the increasing incidence of stroke, senility, falls or fractures, dementia, joint disorders, and other health issues.[2]

The Japanese Orthopaedic Association has proposed a concept called locomotive syndrome (LS) to identify middle-aged and older adults at high risk of requiring health care services because of problems with locomotion.[2] This syndrome is caused by reductions in muscular strength and balance that occur with aging and locomotive pathologies such as osteoporosis, osteoarthritis, and lumbar spinal stenosis.[2] In women, the syndrome may also be caused by reductions in physical activity and bone density that occur after menopause. To prevent LS, Nakamura[3] recommended that individuals avoid deterioration of the locomotive organs and the development of orthopedic problems and maintain or improve walking ability.

Recently, a quantitative and evidence-based screening tool called the 25-question Geriatric Locomotive Function Scale (GLFS-25) was developed to identify individuals with LS.[4] The GLFS-25 is a self-completed questionnaire that

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There are no potential conflicts of interest.

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