Materials and methods

This study was approved by the ethics committee of the University Hospital. All patients gave their consent for participation. Twenty OPLL patients (12 male and 8 female; mean age 63.6 years; range 53–80 years) who had been followed conservatively at the University Hospital were included in the analysis. CT examinations were performed using a 16-row CT system (Light Speed QX/I; GE Healthcare Japan, Tokyo, Japan) until 2006, and thereafter using a 64-row multislice CT system (Aquilion; Toshiba Medical System Corporation, Tochigi, Japan). The imaging conditions with the former system were as follows: slice thickness, 1.25 mm; field of view, 14 mm; voltage, 120 kV; current, 178 mA. The conditions with the latter were as follows: slice thickness, 1.0 or 0.5 mm; field of view, 14 mm; voltage, 120 kV; current, 75 mA. The examinations were performed twice in each patient, with an interval of at least 1 year between the two scans; the mean interval was 22 months (range 12–45 months). All ossifications of the vertebrae were identified semi-automatically by a single examiner based on DICOM data for CT images using the MIMICS® software (Materialise Japan Co. Ltd., Yokohama, Japan), and a 3D model for volume calculation was created automatically. The first step was to identify the affected vertebra and ossification using a threshold of 226–3,071 HU, as defined by MIMICS®, for the detection of bone. In the second step, the ossification was detached from the posterior aspect of the vertebral body between the bases of both pedicles, using both axial and sagittal slice images. In the third step, the region of ossification was isolated using the same threshold, and a 3D model was created. In the last step, the ossification volume was determined using the MIMICS® software, based on the 3D model. The types of OPLL based on the 3D form were classified as continuous, segmental, mixed, or circumscribed according to the criteria proposed by the Investigation Committee on Ossification of Spinal Ligaments of the Japanese Ministry of Public Health and Welfare (Fig. 1) [16]. To ensure the precision of volume calculation based on differences in slice thickness, images of a phantom (KYOTO KAGAKU Co., LTD.), 300 mm in length and 7.5 mm in diameter, were taken at slice thicknesses of 0.5 and 1.0 mm, and the errors in 10 measurements of individual data were estimated.

The ossification volume was calculated twice for each measurement to determine the mean volume, and to evaluate intraobserver error. Since ossification size varies widely, evaluation of change in ossification volume is affected by the original size. Therefore, the change in ossification volume between the first and second CT examinations was calculated as the rate of increase. The annual rate of increase was also calculated. The measurement error was defined as the difference from the average value, and the percentage error was also calculated and evaluated.

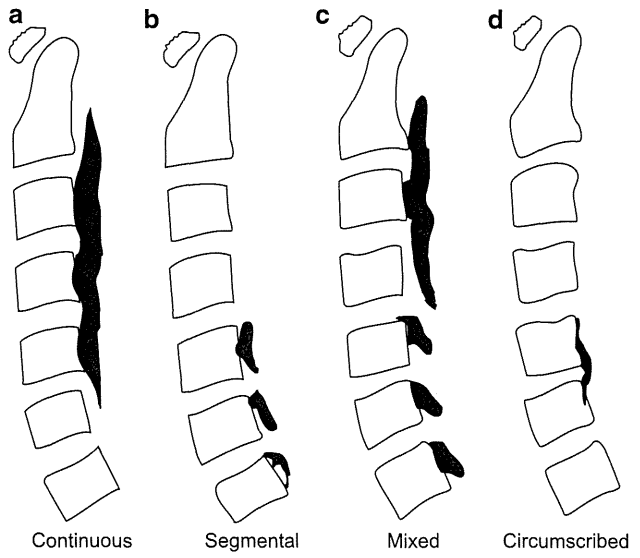

Fig. 1 Classification of the types of OPLL. OPLL was classified into four types according to the classification established by the Investigation Committee on Ossification of Spinal Ligaments of the Japanese Ministry of Public Health and Welfare. **a** Continuous, **b** segmental, **c** mixed, **d** circumscribed

Classification of OPLL and range of ossification were evaluated with an X-ray and compared with those obtained during the CT. The length of the ossification lesion, maximum thickness and a spinal canal occupation rate of OPLL were measured in the lateral view of X-ray radiographs. The spinal canal occupation rate of OPLL was also measured using the axial view of a CT. The spinal canal occupation rate was expressed as the percentage ratio of the maximum thickness of ossification to the midsagittal diameter of cervical canal [2]. Correlation analysis was performed using the length, thickness of OPLL, spinal canal occupation rate (measured using X-ray and CT) and the rate of increase in the volume of OPLL.

Statistical analysis

The SPSS software package for Windows 2005 (Version 14.0; SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. The slice thickness measurement error for the phantom and the two ossification volume measurements were analyzed using intra-class correlation coefficients (ICCs). Because ossification volume in the first and second measurements had similar variance, Student's t test was applied to evaluate it, at a significance level of 0.05.

Results

All patients were eligible for disease classification and measurement of ossification volume. The 3D model showed a change in the vertebral form associated with growth of the distal part of the lesion and increase in the volume of the lesion on the left (Fig. 2), and allowed detailed classification. The type of OPLL was classified as continuous in 3 patients, segmented in 3, and mixed in 14 (Table 1). There were no changes in disease classification in any of the 20 patients during the study period. OPLL was identified in the cervical vertebrae C2–7 in 15 cases and were evaluated using X-rays. In nine cases, the classification done using X-rays corresponded with classification done using a CT, and the range of ossification lesions corresponded with CT findings in three cases. Thus, a CT was able to confirm the range of the ossification lesion more finely.

The 10 measurements of the phantom at slice thicknesses of 0.5 and 1.0 mm showed a coefficient of variation of 0.16 and 0.13 %, respectively, an inter-slice error of 0.12 %, and an ICC of 0.856 ($p < 0.01$). The mean error in the two measurements for each patient was 1.16 %, and the ICC was 0.999 ($p < 0.01$). The mean ossification volume was 1,831.68 ± 1,302.12 mm^3 at the first examination and 1,928.31 ± 1,363.15 mm^3 at the second, showing a significant mean increase in ossification volume (96.63 mm^3; $p = 0.0002$) over 22 months. The mean rate of increase in volume between the first and second CT examinations was 5.95 % (range 0.08–15.09 %). The mean annual rate of lesion increase was 3.33 % (range 0.08–7.79 %). The location and direction of the increased ossification were confirmed three-dimensionally in some patients with a larger increase in volume. In these patients, longitudinal progression of the ossification in the C2-3 intervertebral space was observed. However, the progression could not be evaluated in detail in patients with a smaller increase in volume.

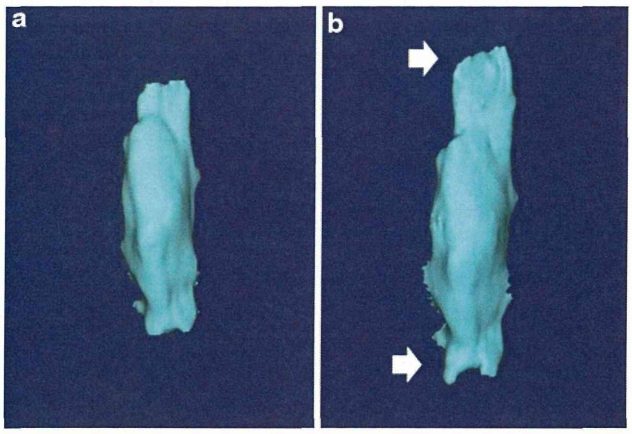

Fig. 2 Image of the 3D model. **a** Length 54.72 mm, Volume 3,654.09 mm^3. **b** Length 66.75 mm, Volume 4,283.70 mm^3, Increase 629.61 mm^3. The rate of increase was 17.23 %, and the annual rate of increase was 3.09 %

The measurement of the length of OPLL using X-rays was possible in 10 cases. The maximum thickness was recorded in 19 cases. OPLL could not be identified clearly in X-rays because of overlap with shoulder in the lateral view. Therefore, the measurement of the length and the thickness were possible in all cases. The mean progression of length was 1.22 mm (0.07–3.22), thickness was 0.30 mm (0.01–0.65), and spinal canal occupation rate was 1.78 % (0.08–7.79) (Table 2). Measurement of spinal canal occupation rate using CT was possible in all cases. The mean progression of the spinal canal occupation rate was 1.84 % (0.02–5.40) (Table 2). There was no correlation between the rate of increase in volume of OPLL progression of length, thickness, spinal canal occupation rate using either X-ray or CT.

Discussion

Our method of using CT imaging is novel and can precisely evaluate the volume of OPLL at one point and provide information about the progression of OPLL during a given period with minimal analytical error. Chiba et al. [6, 7] reported the incidence of ossification progression based on computer analysis of X-ray images in patients who had undergone laminoplasty. Measurements of ossification length and thickness using 2D X-ray images are possible to a certain extent [17, 18]. However, its accuracy is reduced due to errors associated with the imaging procedure. For example, ossification width and volume are not measurable. Other disadvantages of X-ray analysis include inability to identify small-area ossifications and to accurately locate the ossification. When evaluating a pulmonary nodule, 3D measurement is more reliable in determining changes in growth [12–15].

Ossification not identifiable by X-ray examination can be evaluated on CT images, and therefore, the classification discrimination may differ from that obtained by X-ray imaging. Multidimensional evaluation of ossification can be achieved with CT images, but it is difficult to evaluate continuity on 2D X-ray images. On 3D images, however, evaluation of continuity and classification of ossification are comparatively simple [19]. With CT images, changes in ossification form and thickness on the caudal side can be evaluated in detail in patients with ossifications growing toward the cranial side. Slight graininess of the images associated with slice thickness is seen at ossification boundaries. In this study, a thinner slice produced clearer boundaries on 3D images.

Table 1 Patient demographic data and measurement value

	Age	Sex	Type	Area	Interval (M)	Volume at first examination (mm^3)	Volume at second examination (mm^3)	Rate of increase (%)	Annual rate of increase (%)	Increase part
Case 1	62	M	Co	C2–4	36	3,654.09	4,092.72	12.00	4.00	Local
Case 2	68	F	Mi	C3–7	25	2,248.55	2,469.90	9.84	4.73	Diffuse
Case 3	65	F	Ci	C5	12	478.09	483.22	1.07	1.07	Diffuse
Case 4	62	M	Co	C2–4	24	809.81	828.29	2.28	1.14	Diffuse
Case 5	69	M	Mi	C3–6	24	1,130.69	1,203.90	6.47	3.24	Diffuse
Case 6	57	F	Mi	C3–6	45	1,908.68	2,171.56	13.77	3.67	Diffuse
Case 7	73	M	Mi	C2–7	24	4,967.98	5,087.29	2.40	1.20	Intervertebral
Case 8	74	M	Mi	C3–7	12	2,580.11	2,667.31	3.38	3.38	Intervertebral
Case 9	53	F	Co	C2–3	39	1,749.72	1,935.91	10.64	4.73	Diffuse
Case 10	68	M	S	C5–6	36	151.85	174.76	15.09	5.03	Local
Case 11	62	M	Mi	C2–6	12	1,387.09	1,461.49	5.36	5.36	Intervertebral
Case 12	57	F	Mi	C2–4	24	410.35	438.16	6.78	3.39	Local
Case 13	63	M	Mi	C2–7	12	2,510.77	2,512.88	0.08	0.08	Diffuse
Case 14	67	M	Mi	C2–7	12	3,673.29	3,836.25	4.44	4.44	Local
Case 15	58	M	Mi	C2–6	12	2,653.84	2,690.66	1.39	1.39	Diffuse
Case 16	58	M	Mi	C3–7	17	1,751.41	1,777.10	1.47	1.04	Local
Case 17	58	F	Mi	C3–7	18	431.60	482.05	11.69	7.79	Local
Case 18	60	F	Ci	C6	12	25.81	27.14	5.15	5.15	Diffuse
Case 19	58	F	Mi	C3–7	12	2,208.59	2,265.15	2.56	2.56	Local
Case 20	80	M	Mi	C4–7	12	1,901.31	1,960.41	3.11	3.11	Diffuse
Mean	63.6				22.0	1,831.68	1,928.31	5.95	3.33	

Co continuous, *S* segmented, *Mi* mixed, *Ci* circumscribed

By calculating exact volumes, it was possible to derive an accurate numerical estimate of both overall absolute value of the volume of ossification and its rate of progression over time, and to compare these volumes with those derived from subsequent scans. Considering that the error of volume calculation associated with slice thickness was minimal (0.12 %), the precision of the measurements was obviously high and only a slight degree of intra-examiner error was evident. The ossification volume increased annually to some extent in all the studied patients. Since ossification size varies markedly among individuals, the absolute value of the increase in ossification volume can differ considerably depending on the original size. Therefore, we used the rate of increase in volume, since comparable evaluation of increased ossification among all the patients based on the absolute volume would have been difficult. The evaluation based on the rate of increase in volume was not affected by the original size of the ossification, and, therefore, was useful for comparative study. The mean annual rate of increase in volume was 3.33 %, implying that the spinal canal narrows gradually with time. In this study, there was no correlation between the canal stenosis ratio of maximum thickness and annual progression rate. Ossification volume did not increase, but the maximum thickness did which increased lesions. A high rate of progression is a potential risk factor for myelopathy due to spinal canal stenosis. Further analyses of the location and the direction of increased ossification are necessary to elucidate the detailed history of progression and to establish the preventive methods and the effective treatment. This method may be useful to examine the risk factors for progression of OPLL, to determine the timing for initiating the drug therapy for prevention of OPLL that may be available in the near future, and to identify the progression of OPLL in different surgical procedures. The authors believe that their novel method allows detailed evaluation of ossification progression, which cannot be achieved using X-ray evaluation.

There were several potential limitations to this study. First, a threshold of 226–3,071 HU was set as an appropriate value for detection. As this threshold setting was defined by MIMICS for the detection of bone, and was not specific for ossification, the volume of the ossification might have been over- or underestimated in some cases. However, identification of ossification and volume calculation were done at the same CT examination with the same threshold setting, and thus evaluation based on comparison of volumes would have been valid. Second, the

Table 2 Measurement value of X-rays and CT

	Length at first examination (mm)	Length at second examination (mm)	Length at increase (mm)	Thickness at first examination (mm)	Thickness at second examination (mm)	Thickness of increase (mm)	Canal stenosis ratio at first examination (%) (X-ray)	Canal stenosis ratio at second examination (%) (X-ray)	Canal stenosis ratio of increase (%) (X-ray)	Canal stenosis ratio at first examination (%) (CT)	Canal stenosis ratio at second examination (%) (CT)	Canal stenosis ratio of increase (%) (CT)
Case 1	63.50	66.37	2.87	10.11	10.22	0.11	77.06	77.42	0.37	71.81	74.41	2.60
Case 2	82.75	86.63	3.88	6.36	6.40	0.04	53.63	53.83	0.20	56.69	62.09	5.40
Case 3	–	–	–	5.58	5.59	0.01	44.29	45.12	0.83	51.41	51.50	0.09
Case 4	42.70	43.95	1.25	4.93	5.50	0.57	39.69	43.17	3.48	38.01	41.18	3.17
Case 5	–	–	–	6.57	6.81	0.24	41.29	41.42	0.13	38.85	41.77	2.92
Case 6	–	–	–	6.70	7.32	0.62	61.87	62.09	0.22	54.81	58.01	3.20
Case 7	108.87	109.32	0.45	5.81	6.04	0.23	42.60	43.77	1.17	31.74	34.77	3.02
Case 8	61.58	61.95	0.37	5.93	6.57	0.64	55.21	61.52	6.30	66.70	69.26	2.55
Case 9	50.99	52.05	1.06	5.74	6.08	0.34	40.94	43.37	2.43	40.89	40.91	0.02
Case 10	5.56	5.74	0.18	3.56	3.87	0.31	25.56	27.98	2.43	19.45	20.78	1.33
Case 11	–	–	–	5.18	5.34	0.16	38.54	39.38	0.84	40.57	41.68	1.11
Case 12	–	–	–	2.55	3.20	0.65	20.95	26.40	5.45	26.32	26.37	0.05
Case 13	–	–	–	8.65	8.85	0.20	51.03	52.06	1.03	47.24	50.10	2.87
Case 14	51.79	53.51	1.72	7.43	7.50	0.07	57.64	57.69	0.05	57.15	57.87	0.72
Case 15	77.42	77.80	0.38	6.57	6.87	0.30	49.55	50.85	1.30	46.52	47.44	0.92
Case 16	–	–	–	–	–	–	–	–	–	51.29	54.05	2.75
Case 17	–	–	–	4.79	5.10	0.31	38.72	41.06	2.34	36.39	39.38	2.99
Case 18	5.42	5.49	0.07	3.18	3.20	0.02	24.96	25.00	0.04	25.13	25.66	0.53
Case 19	–	–	–	5.32	5.86	0.54	34.52	37.78	3.26	30.29	30.37	0.07
Case 20	–	–	–	8.97	9.27	0.30	71.70	73.57	1.87	62.81	63.36	0.54
Mean	55.06	56.28	1.22	5.83	6.13	0.30	44.34	46.11	1.77	44.70	46.55	1.84

method used for identification of ossification was not completely automatic, and thus accidental errors might have occurred. However, the ICC calculated in this study was obviously high, suggesting that the evaluation of ossification volume was accurate and valid.

The next step is to analyze the risk factors for OPLL progression using our novel method, to verify those that have been described in previous studies [6, 17].

Conclusion

We measured ossification volume based on a novel method involving creation of a 3D model from DICOM data obtained from CT images. The novel method described here appears to be very useful for quantitative evaluation of OPLL with only minimal measurement error. It is also expected to be useful for identifying the risk factors associated with progression of OPLL, to determine the timing for preventive therapy, and to identify progression during surgical procedures.

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Conflict of interest None.

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Spine

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DIAGNOSTICS

Ossification of the Posterior Longitudinal Ligament in Not Only the Cervical Spine, but Also Other Spinal Regions

Analysis Using Multidetector Computed Tomography of the Whole Spine

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Study Design. A prospective cohort study.

Objective. To evaluate ossification of the posterior longitudinal ligament (OPLL) of the whole spine in patients with cervical OPLL and to analyze which types of cervical OPLL were associated with the other lesions in the thoracic and/or lumbar spine.

Summary of Background Data. OPLL is most frequently seen in the cervical spine. The coexisting ossified lesions are sometimes observed in other spinal regions. However, coexisting OPLL in other spinal regions have not yet been precisely evaluated in patients with cervical OPLL.

Methods. One hundred seventy-eight patients with a diagnosis of cervical OPLL whose plain radiographs were obtained were included. Computed tomographic images of the whole spine were obtained. The ossification index (OS index) was newly determined according to the sum of the levels of vertebral bodies and intervertebral discs with OPLL. The patients were divided into 2 groups, the group that had OPLL only in the cervical spine (C group) and the group that had OPLL in multilevel spinal regions other than the cervical spine (M group).

Results. Ninety-five (53.4%) had OPLL not only in the cervical spine, but also in other spinal regions. The M group had more females than the C group. The incidence of bridge formation in the cervical spine was higher in M group than in C group. More females had a high OS index. A positive correlation was found between the OS index of the cervical spine and the OS index of the thoracic and lumbar spine; however, the *r* value was small.

Conclusion. This study demonstrated that more than half of the patients with cervical OPLL had coexisting OPLL in the thoracic and/or lumbar spine. We strongly recommend computed tomographic analysis of the whole spine for patients with radiographical evidence of OPLL in the cervical spine for the early detection of additional sites of ossification.

Key words: OPLL, whole spine, cervical spine, thoracic spine, lumbar spine, CT.

Level of Evidence: 4

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Ossification of the posterior longitudinal ligament (OPLL) is characterized by replacement of the ligamentous tissue by ectopic new bone formation. OPLL often causes narrowing of the spinal canal and has been recognized as a cause of cervical myelopathy and/or radiculopathy.[1,2] The cause of OPLL is still unknown, but recent studies have suggested that there is a strong genetic background for OPLL.[3] Morbidity associated with OPLL in Japan is estimated to range from 1.9% to 3.2%. In other Asian and Eastern countries, such morbidity is equivalent or lower. It is 0.12% in the United States and 0.1% in Germany.[4] OPLL is most frequently seen in the cervical spine. Cervical OPLL is divided into 4 types, continuous type, segmental type, mixed type, and other type.[5] Coexisting ossified lesions are sometimes observed in other spinal regions. OPLL in the thoracic spine occurs at the upper and middle levels, and it is very difficult to treat some cases with thoracic OPLL.[6–9] OPLL is also known to occur in the lumbar spine with reportedly severe symptoms.[10] However, few studies have assessed the incidence of the coexisting OPLL in other spinal regions in patients with cervical OPLL. A radiological population study using 1058 people in Japan revealed that 3.2% had cervical OPLL and 0.8% had thoracic OPLL. The percentage of the estimated coexisting OPLL in the patients with cervical OPLL was 9% in that study.[11] Wada *et al*[12] reported that 17.5% of

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patients with cervical OPLL had coexisting OPLL in the thoracic spine and 12.6% had OPLL in the lumbar spine. These studies were based on plain radiographs. Because it is very difficult to thoroughly evaluate OPLL by only plain radiographs, particularly in the upper thoracic spine, the coexisting OPLLs in other spinal regions have not been precisely evaluated to date. The purpose of this study was to evaluate OPLL of the whole spine in patients with cervical OPLL and analyze which types of cervical OPLL were associated with other lesions in the thoracic and/or lumbar spine by using multidetector computed tomography (CT) of the whole spine.

MATERIALS AND METHODS

This study included 178 patients with a diagnosis of cervical OPLL by plain radiographs. All of the patients were treated in our university hospital. There were 108 males and 70 females, with an average age of 67.0 years (range, 36–86 yr). Informed consent was obtained from each patient before enrollment in the study, and the study was approved by the institutional review board of our university hospital. Regarding medical history, seventy-nine patients had a history of cervical laminoplasty, which is a posterior decompression surgery in the cervical spine. This posterior procedure does not directly approach OPLL. Fifteen patients underwent posterior decompression surgery in the thoracic spine, and 17 patients underwent posterior decompression surgery in the lumbar spine. The patients who underwent anterior decompression surgery for the treatment of OPLL were excluded in this study, because anterior decompression surgery might affect the configuration of OPLL. Lateral radiographs of the cervical spine were obtained in all patients. Ossification types of the cervical OPLL were classified as continuous type, segmental type, mixed type, and other type according to the criteria proposed by the Investigation Committee on the Ossification of Spinal Ligaments of the Japanese Ministry of Public Health and Welfare.[5] CT images of the whole spine, including the cervical, thoracic, and lumbar spine from the occipital bone to sacrum, were also obtained in all patients on the same day when lateral radiographs of the cervical spine were obtained. We used a multidetector CT (SOMATOME Sensation 64 Cardiac, SIEMENS Co., Erlangen, Germany) for the evaluation of OPLL of the whole spine. To obtain CT images, specific parameters were applied: 1 tube rotation per second, 17.28 mm/s table feed speed, 160 mA, and 120 kV. Image reconstructions were performed using a CT console (Wizard, SIEMENS Co., Erlangen, Germany) at a 0.5-mm interval from the 0.75-mm scan slice data. A technique was used for threshold to determine bone density. The images were constructed using the bone window images. Then, the incidence of OPLL in the cervical spine from the Clivus to C7 and in other spinal regions from T1 to S1 was evaluated by the CT images. The analysis was independently performed by 3 senior spine surgeons (M.N., T.Y., and S.S.). When there was disagreement among observers, they re-evaluated and discussed the images to decide on the levels and the types of OPLL. Ossified lesions were checked at each vertebral body and intervertebral disc level because OPLLs were found at the levels of both vertebral bodies and intervertebral discs. The ossification index (OS index) was newly determined by the sum of the levels of vertebral bodies and intervertebral discs where OPLL existed. When the ossification area extended from the vertebral body level to the intervertebral disc level, we counted the ossified lesions of each vertebral body level and intervertebral disc level. Theoretically, the maximum OS index is 14 in the cervical spine. The OS index in the thoracic spine was in the range from 0 to 24, and the index in the lumbar spine was from 0 to 11. OPLL at a certain level was judged to be present when at least 2 out of 3 observers were in agreement.

Inter-rater and intrarater reliability measures were determined by calculating the Fleiss Kappa coefficient using a dedicated MATLAB (MathWorks, Paris, France) program. Kappa values of 0.00 to 0.20 were considered to indicate slight agreement, 0.21 to 0.40 fair agreement, 0.41 to 0.60 moderate agreement, 0.61 to 0.80 substantial agreement, and 0.81 to 1.00 almost perfect agreement.[13,14] Inter-rater and intrarater percentage of agreement was calculated as well.

The patients were divided into the following 4 groups: OPLL only in the cervical spine (C group), OPLL in the cervical spine and thoracic spine (CT group), OPLL in the cervical spine and lumbar spine (CL group), and OPLL in the cervical, thoracic, and lumbar spine (CTL group). For the analysis, we combined 3 groups (CT, CL, and CTL groups) to represent the group having OPLL in multilevel spinal regions in addition to the cervical spine (M group). The age and sex were compared between the C group and the M group. To determine the detailed characteristics of OPLL in the cervical spine, we examined the existence of bridge formation of OPLL in the cervical spine. When the ossified lesions formed a bridge with the posterior border of the adjacent vertebral body, it was judged as "bridge formation" in cervical OPLL. The OS index of the cervical spine was assessed. The incidence of "bridge formation" in cervical OPLL and the OS index of the cervical spine were also compared between the C group and the M group. Furthermore, we analyzed the relationship between the OS index of the cervical spine and the OS index of the thoracic and lumbar spine.

STATISTICAL ANALYSIS

Data are presented as the mean value ± standard deviation. The Student unpaired t test was used for the statistical analysis of the difference in age and the OS index of the cervical spine between the C group and the M group. The χ^2 test was used for the statistical analysis of the difference in sex, the type of cervical OPLL, and the existence of bridge formation of cervical OPLL between the 2 groups. The Pearson simple linear regression and correlation was used for analysis of the relationship between the OS index of the cervical spine and the OS index of the thoracic and lumbar spine. JMP version 9 software (SAS Institute Inc., Cary, NC) was used for the analysis and $P < 0.05$ was considered as statistically significant.

RESULTS

Inter-rater and Intrarater Reliability and Agreement

The averaged Fleiss Kappa coefficient of inter-rater agreement was 0.83 ± 0.008, according to 3 observers. The intrarater reliability for the existence of OPLL was 81.5% (95% confidence interval, 77.7–84.7), 98.1% (95% confidence interval, 96.5–99.0), and 92.7% (95% confidence interval, 90.0–94.7).

Incidence of Coexisting Ossified Lesions of OPLL and OS Index

Ninety-five patients (53.4%) had OPLL not only in the cervical spine, but also in other spinal regions. In 33 patients (18.5%), ossified lesions of OPLL were spread in the thoracic and lumbar spine (CTL group) (Figure 1). No significant difference was found in the average age between the C group and the M group. The M group had more females than the C group. Regarding the cervical OPLL type, 40 patients had continuous type, 57 had segmental type, 78 had mixed type, and 3 had other type. Among these types, there was no statistical difference in the distribution of the cervical OPLL type between the 2 groups (Table 1). Bridge formation of cervical OPLL was found in 20 patients (24.1%) in the C group and in as many as 36 patients (37.9%) in the M group. The incidence of bridge formation in the cervical spine was statistically higher in the M group than in the C group (Table 1).

The OS index of the total spine in these patients was in the range from 1 to 36 and that of the cervical spine was in the range from 1 to 13. There were more female patients with a high OS index of the whole spine (Figure 2). In particular, the 10 patients with an OS index of more than 20 were all females. The OS index of the cervical spine in the M group was significantly greater than in the C group (Table 1). A significant positive correlation was found between the OS index of the cervical spine and the OS index of the thoracic and lumbar spine; however, the r value was small ($r = 0.258$) (Figure 3). Some patients had a low OS index in the cervical spine, whereas their OS index of the thoracic and lumbar spine was high.

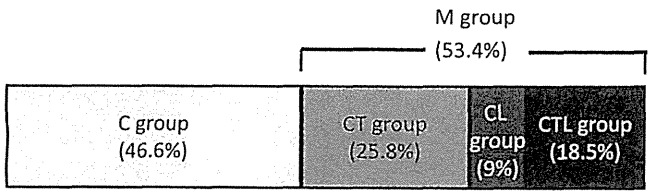

Figure 1. The incidence of OPLL considering the whole spine. Of the 178 patients, 83 (46.6%) had OPLL only at the cervical spine (C group), 46 (25.8%) had OPLL at the cervical and thoracic spine (CT group), 16 (9%) had OPLL at the cervical and lumbar spine (CL group), and 33 (18.5%) had OPLL at the cervical, thoracic, and lumbar spine (CTL group). The patients with OPLL in multilevel spinal regions other than the cervical spine were 95 (53.4%) (M group). CT indicates computed tomography; OPLL, ossification of the posterior longitudinal ligament.

TABLE 1. Comparison of Age, Sex, and OPLL Characteristics Between C Group and M Group

	C Group	M Group	*P*
Age (yr)	68.3 ± 10.0	65.9 ± 10.2	0.4
Sex: male/female	57/26	51/44	0.041
Cervical OPLL type			0.87
Continuous type	14	36	
Segmental type	34	23	
Mixed type	34	44	
Other type	1	2	
Bridge formation at the cervical spine: ±	20/63	36/59	0.047
OS index of the cervical spine	4.9 ± 2.4	6.9 ± 3.3	0.0015

OPLL indicates ossification of the posterior longitudinal ligament; OS index, ossification index.

Representative Cases

Case 1

A 73-year-old female had multilevel OPLL of the whole spine (Figure 4). She had OPLL at vertebral levels C2, C3, C4, C5, T1, T2, T3, T4, T12, L1, and L2 and intervertebral levels C2–C3, C4–C5, C5–C6, T1–T2, T2–T3, T3–T4, T12–L1, L1–L2, and L2–L3. Her OPLL in the cervical spine was mixed type. She also had ossification of ligamentum flavum at T8–T9 level. Her OS index of the whole spine was 20.

Case 2

A 68-year-old female had multilevel OPLL of the whole spine (Figure 5). Her OPLL in the cervical spine was mixed type.

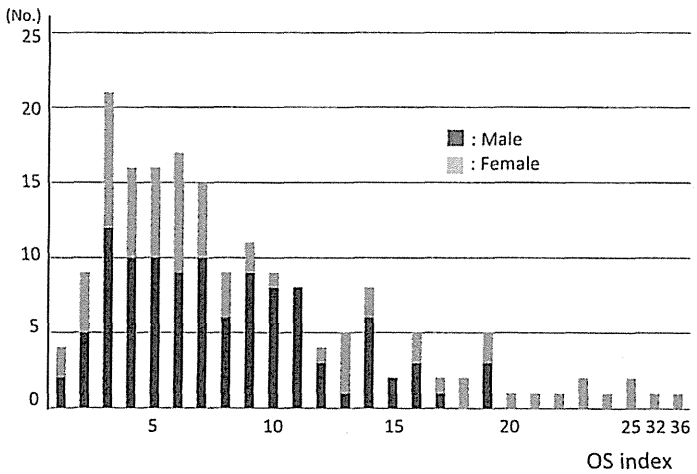

Figure 2. The OS index of all of the patients according to sex. The patients who had a high-OS index were predominantly females. OS indicates ossification.

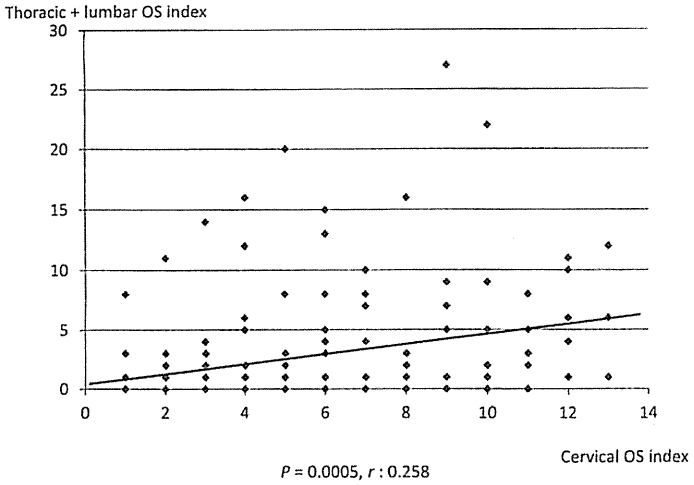

Figure 3. The relationship between the OS index of the cervical spine and the OS index of the thoracic and lumbar spine. A positive correlation was found between the 2 indexes; however, the r value was small (r = 0.258). OS index indicates ossification index.

She had previously undergone 6 spinal operations; including cervical laminoplasty, thoracic laminectomy, and fusion with instrumentation, and lumbar laminectomy. She had OPLL bridge formation from C4 to C6. Her OS index was 32.

Case 3

A 51-year-old female had multilevel OPLL in the cervical, thoracic, and lumbar spine (Figure 6). She had a small OPLL in the cervical spine, and this ossified lesion was classified as "other type" of OPLL. However, she had massive OPLL in the thoracic and lumbar spine. Her OS index was 13.

DISCUSSION

The cause of OPLL remains uncertain, however, it is well known that OPLL has a strong genetic component.[15–17] Epidemiological studies in the Japanese population have shown that genetic background is a contributory factor in OPLL.[5,17] Recent articles reviewed the genetic background and pathophysiology in patients with OPLL.[18,19] In contrast, several environmental factors, such as diet,[20] obesity, and glucose metabolism[21] might be related to the disease. The age of onset of OPLL is usually in the 50s. The segregation rate in siblings corresponds neither with the hypothesis of autosomal dominant inheritance nor with that of autosomal recessive inheritance.[16,17] Therefore, multiple factors, including several genetic components and environmental risks, are related to the development of OPLL.

This study demonstrated that more than half of the patients with cervical OPLL had coexistent OPLL in the thoracic and lumbar spine. Because the inter- and intraobserver agreement ratio was quite high, the data should be reliable. A previous article reported that less than 20% of the patients with cervical OPLL had coexistent OPLL.[11] That was based on lateral radiographs of the cervical, thoracic, and lumbar spine. However, it is impossible to evaluate ossified lesions precisely in the spinal canal on radiographs. High-quality CT is a useful imaging tool for more detailed evaluation. Here, we used multidetector CT with a very thin slice of less than 1 mm. Because more than half of the patients with cervical OPLL had coexistent OPLL in other spinal regions, we recommend CT analysis of the whole spine, when OPLL in the cervical spine is seen on radiographs. Thoracic OPLL and lumbar OPLL can cause very severe clinical symptoms.[8,11] It has been reported that severe symptoms and a lengthy preoperative period are related to surgical outcome in spine surgical procedures.[7] Furthermore, the surgical results for patients with tandem ossification in the cervical and thoracic spine have been reported.[22,23] A Japanese multi-institutional retrospective study regarding surgical results and related factors for OPLL of the thoracic spine revealed that one of the factors was marked ossification at the upper thoracic spine.[8] It is very difficult to detect ossified lesions at the upper thoracic spine on plain radiographs, because the shoulders obscure the findings of the upper thoracic spine. The study also found that the outcome tended to be favorable in patients with a morbidity period of less than 1 year.[8] Therefore, usage of whole spine CT images for early detection of thoracic and lumbar OPLL is important for diagnostic and therapeutic management in patients with cervical OPLL.

We have newly developed the OS index as a marker of the severity of OPLL. OPLL can occur not only at the vertebral level, but also at the intervertebral level. The total number of the levels of OPLL should be reasonable for evaluating the severity of OPLL. This study indicated that severe OPLL in the cervical spine is related to severe OPLL in the thoracic and lumbar spine. However, the *r* value was not so high. Furthermore, some patients with a small OPLL in the cervical spine showed severe OPLL in the thoracic and lumbar spine. Therefore, OPLL of the whole spine cannot be predicted by only viewing OPLL in the cervical spine. On the basis of this

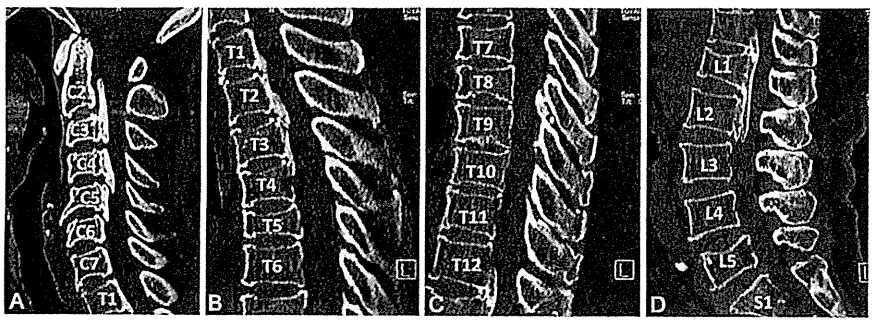

Figure 4. A 73-year-old female had multilevel OPLL of the whole spine. Her OS index of the whole spine was 20. (A) cervical spine, (B) upper thoracic spine from T1-6, (C) lower thoracic spine from T7-12, and (D) lumbar spine.

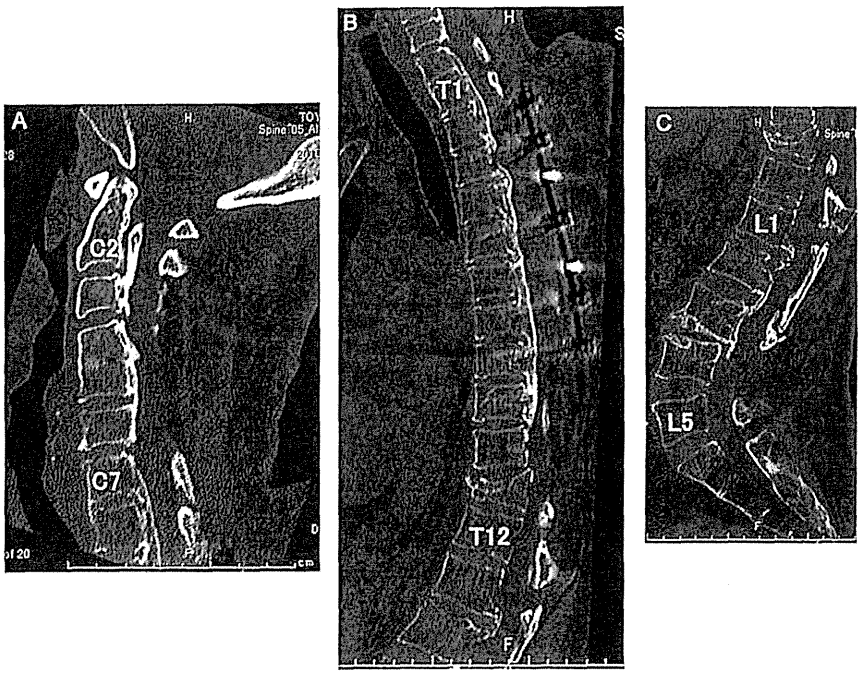

Figure 5. A 68-year-old female had multilevel OPLL of the whole spine. Her OS index was 32. (**A**) cervical spine, (**B**) thoracic spine, and (**C**) lumbar spine.

fact, CT images of the whole spine are necessary to evaluate OPLL thoroughly in patients with cervical OPLL.

The previous study indicated that OPLL has a male predominance of 2:1 to 3:1.[24] However, patients with severe OPLL, meaning the patients with a high OS index of the whole spine, were predominantly females. Thus, hormonal factors might have an effect on the extension of OPLL of the whole spine. Wada *et al*[12] and Okada *et al*[25] found that the serum total estrogen level is positively correlated with the extent of ossification.[26] Osteoblast-like cells have an estrogen receptor.[27] Previous reports have suggested that estrogen acts directly on human bone cells and modulates the extracellular matrix and other proteins involved in the maintenance of skeletal mineralization and remodeling.[27,28] Estrogen has bone formation activity with the aid of TGF-beta and BMP.[12] Previous data showed that TGF-beta 1 polymorphism is not a factor associated with the occurrence of OPLL, but rather it is a factor related to the area of the ossified lesion.[29] These reactions by estrogen and TGF-beta might affect the extent of OPLL. The detailed explanation of why patients with a high OS index are predominantly females is still unclear. This is an important research theme for the future.

This study has several limitations. First, the number of patients was small, compared to the previous radiological study. A multicenter study should be carried out to collect many patients with OPLL. Second, we did not check the relationship between the clinical symptoms and OPLL lesions. Third, the effect of the surgical procedure was not assessed. More than 40% of the patients had a history of posterior decompression of the whole spine. Although posterior

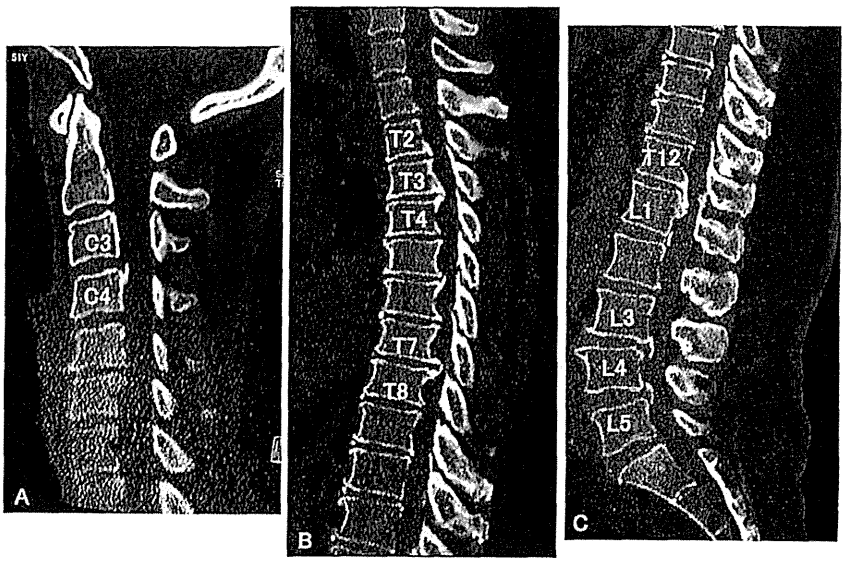

Figure 6. A 51-year-old female had multilevel OPLL in the cervical, thoracic, and lumbar spine. She had massive OPLL in the thoracic and lumbar spine, although her OPLL in the cervical spine was rather small. Her OS index was 13. (**A**) cervical spine, (**B**) thoracic spine, and (**C**) thoraco-lumbar spine.

decompression does not directly approach OPLL, one might think that surgical intervention affects the ossified lesions of OPLL. The anterior approach to OPLL directly affects the ossified lesion of OPLL, thus patients with a history of anterior approach were excluded in this study. Lastly, we must consider the potential risk of radiation by CT. The total amount of radiation for the whole spinal CT is estimated to be 15.8 mSv in each patient. Thus, in general unnecessary CT examinations for patients should be avoided.

CONCLUSION

This study using multidetector CT demonstrated that more than half of the patients with cervical OPLL had coexistent OPLL in the thoracic and/or lumbar spine. We strongly recommend CT analysis of the whole spine for the early detection of OPLL of the whole spine in patients whose radiographs show OPLL in the cervical spine.

➢ Key Points

- ❑ Ninety-five (53.4%) had OPLL not only in the cervical spine, but also in other spinal regions.
- ❑ Females were more likely to have multiple areas of OPLL.
- ❑ CT analysis of the whole spine for patients with radiographical evidence of OPLL in the cervical spine is strongly recommended for the early detection of additional sites of ossification.

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Clinical Study

Variables affecting postsurgical prognosis of thoracic myelopathy caused by ossification of the ligamentum flavum

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Abstract

BACKGROUND CONTEXT: Ossification of the ligamentum flavum (OLF) may result in thoracic myelopathy (TM) because of narrowing of the spinal canal. Because symptoms vary and are subjective, diagnosis of TM caused by OLF is sometimes difficult when based on symptoms and physical examination. Posterior decompression is indicated in patients with TM caused by OLF because it is believed that surgery is the most effective treatment. However, surgical outcomes vary. We are unaware of reports of objective presurgical diagnostic parameters, such as neurologic and radiologic findings, relating to the postsurgical prognosis in patients with TM caused by OLF.
PURPOSE: To determine which presurgical and surgical variables were most closely related to postsurgical prognosis of TM caused by OLF.
STUDY DESIGN: Retrospective review of the records of the cohort of patients who had undergone surgery from 1988 through 2008 at the University of Toyama Hospital for TM caused by OLF.
PATIENT SAMPLE: Forty-one patients who had surgery for TM caused by OLF that was progressive, severe, or both and for which the diagnosis was based on clinical, radiologic, and pathologic evaluations.
OUTCOME MEASURES: Relationship between the highest follow-up Japanese Orthopaedic Association (JOA) score for neurologic evaluation and of Hirabayashi's formula to indicate the extent of normalization after surgery with respect to the following 10 variables: age at surgery; sex; duration of presurgical symptoms; complications of diabetes mellitus; complications of hypertension; presence of presurgical hyperreflexia in either or both of the patellar tendon reflex and the Achilles tendon reflex; presurgical impairment of joint position sense in the big toes; number of levels affected by OLF; concurrent spinal lesions including ossification of the posterior longitudinal ligament; and intramedullary change of the spinal cord seen on magnetic resonance imaging (MRI).
METHODS: Multiple linear analyses were used to evaluate the variables related to postsurgical recovery.
RESULTS: Presurgical impairment of joint position sense in the big toe was the most important predictor of the highest postsurgical JOA score and of the highest percentage recovery rate. The number of affected OLF levels also predicted the postsurgical highest JOA score, but not statistically significantly so. Age at surgery, sex, and duration of symptoms presurgically did not affect postsurgical recovery. Complications of diabetes mellitus or of hypertension did not affect percentage recovery rate. The difference between recovery rate in patients with or without concurrent spinal lesions was not significant. Presurgical hyperreflexia was not correlated with recovery.

FDA device/drug status: Not applicable.

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Postsurgical JOA scores and percentage recovery rates of scores in patients whose presurgical MRIs had shown intramedullary signal change were not statistically significantly different from those whose MRIs had not shown signal change.

CONCLUSIONS: An excellent postoperative prognosis is not always possible in patients with TM caused by OLF. It may be important to check for impairment of joint position sense in the big toe, the number of levels affected by OLF, and presurgical intramedullary signal change on MRI before continuing to surgery.

Keywords: Ossification of the ligamentum flavum; Prognostic factor; Joint position sense; JOA score; Thoracic myelopathy

Introduction

Ossified lesions in the spinal canal, such as ossification of the posterior longitudinal ligament (OPLL) and ossification of the ligamentum flavum (OLF), can lead to spinal cord compression. Ossification of the posterior longitudinal ligament and OLF are characterized by replacement of ligamentous tissue by ectopic new bone formation [1–3]. Ossification of the posterior longitudinal ligament mainly affects the cervical spine, often resulting in cervical myelopathy [4]. In contrast, OLF is mainly observed at the middle third of the thoracic spine, and it may cause thoracic myelopathy (TM) because of narrowing of the spinal canal [5,6]. Ossification of the ligamentum flavum is less frequently seen than OPLL [7], although there are numerous reports regarding the clinical characteristics and surgical treatment of TM caused by OLF from Japan [7–14] and other Asian countries [15–20]. Thoracic myelopathy caused by OLF has also been reported in white people [21–26] and in North Africans [27].

Because symptoms vary, diagnosis of TM caused by OLF is sometimes difficult when based on symptoms and physical examination [7]. Motor palsy in the lower extremities is fairly frequent. Hyperreflexia, sustained clonus, and Babinski reflex, the long-tract signs in the spinal cord, indicate spinal cord dysfunction. Symptoms of TM caused by OLF, such as motor weakness, hyperesthesia and hypalgesia, and impaired deep sense in the lower extremities, sometimes mimic those of lumbar disorders [7,28], although TM usually causes hyperreflexia in the patellar tendon reflex (PTR) and Achilles tendon reflex (ATR). Lumbar disorders usually do not cause hyperreflexia in these two reflexes, and in contrast, a lesion near the conus medullaris causes a hyporeflexia in both reflexes [12]. Sensory disturbance below the lesion, which is determined by examining the patient's senses of light touch, pain, temperature, vibration, and joint position sense, accords with the extent of damage of the spinal cord tract. It has been speculated that decrease in deep sense, such as decrease in joint position sense, is important because disturbance of joint position sense causes unsteadiness of gait [29,30]. In fact, patients with cervical myelopathy have impaired joint position sense in the lower extremities [30–33].

Posterior decompression is indicated in patients with TM caused by OLF because it is believed that surgery management is the most effective treatment [12]. However, surgical outcomes vary [12,13]. Shiokawa et al. [12] and Miyakoshi et al. [13] found that the duration of presurgical symptoms affects surgical outcome. Lengthy duration of presurgical symptoms is associated with a poor prognosis. Based on their findings, Shiokawa et al. [12] and Miyakoshi et al. [13] recommended early decompression in the course of TM caused by OLF. However, symptoms are only subjective parameters of diagnosis. For example, some patients might not be able to accurately report when symptoms started. Thus, we are unaware of reports of objective presurgical diagnostic parameters, such as neurologic and radiologic findings, in relation to postsurgical prognosis in patients with TM caused by OLF. To determine which presurgical and surgical variables were most closely related to postsurgical prognosis of TM caused by OLF, we retrospectively reviewed the records of cases of TM caused by OLF and treated surgically.

Materials and methods

Records of patients who had undergone spinal surgery at the University of Toyama Hospital from 1988 through 2008 were reviewed. Cases meeting criteria supporting a diagnosis of TM caused by OLF were reviewed. Duration of symptoms before surgery was noted. Records of neurologic findings were carefully reviewed.

Criteria supporting a diagnosis of TM caused by OLF were based on findings of clinical, radiologic, and pathologic evaluations. Clinical evaluation was based on history and physical examination. In the physical examination, responses to tests for deep tendon reflexes (PTR or ATR) were classified into six categories: 0, none; 1, diminished; 2, normal; 3, exaggerated; 4, transient clonus; and 5, sustained clonus. Transient or sustained clonus on either PTR or ATR was deemed as hyperreflexia in the lower extremity.

Sensory disturbances in light touch, pinprick, and joint position sense were evaluated. In evaluating joint position sense, the examiner separately held each of the patient's big toes, moved it up and down, and asked the patient about the position of the big toe. When the patient could not correctly tell the position of a big toe, disturbance of joint position sense was determined to be present.

Presurgical neurologic evaluation was graded using the score devised by the Japanese Orthopaedic Association (JOA). The maximum JOA score [34] is 17 points, but we excluded the sections regarding upper extremity function. Therefore, the maximum score was 11 (Table 1). Presurgical general complications, such as diabetes mellitus and hypertension, were also noted. Exclusion criteria were other neuromuscular disorders, other spine surgery, vitamin B deficiency, or alcoholism, before or after surgery for TM caused by OLF.

Presurgical radiologic examination consisted of evaluating the entire spine by ordinary radiography, computed tomography, myelography, and in some cases, magnetic resonance imaging (MRI). The extent of ossified spinal lesions, including OLF and OPLL, was evaluated. Cases in which a high-intensity signal was demonstrated on T2-weighted MRI of the spinal cord were determined to have had "intramedullary change." Pathologic evaluation of surgical specimens was used to confirm the diagnosis of OLF based on radiologic examination.

Surgical indication and methods

Indication for surgery was TM caused by OLF that was progressive, severe, or both.

En bloc decompressive laminectomy and complete removal of OLF was carried out in all patients. A midline incision was made at the site of the lesion. The paravertebral muscles were dissected and the laminae were exposed. Spinous processes were removed using a rongeur, and a laminectomy was performed with a high-speed drill. The ossified lesions were carefully resected microscopically by use of a diamond drill or a small-angled punch rongeur. After the spinal cord was decompressed, the paravertebral muscle and the supraspinous ligament were sutured. Patients were required to stay in bed for 2 days after surgery, and they were allowed to walk assisted by a brace thereafter. An orthotic was used for as long as 2 months after surgery. Posterior fusion and instrumentation surgery was not undertaken in cases in which radiologic instability had not been noted.

When coexisting lesions were present at other spinal levels, neurologic findings and imaging studies were carefully considered. Coexisting lesions at other spinal levels that were considered to be likely causes of symptoms were surgically treated either at the same time as thoracic laminectomy or later. Anterior surgical decompression was also done in cases with insufficient posterior decompression of the spinal cord caused by OPLL.

Postsurgical evaluation

Postsurgical evaluation was based on surgical time, blood loss during surgery, blood transfusion during and after surgery, and JOA score.

EVIDENCE & METHODS

Context
Ossification of the ligamentum flavum in the thoracic spine is uncommon. The authors delineate prognostic factors for outcomes following decompressive surgery.

Contribution
They found that loss of great toe proprioception, multilevel involvement, cord signal changes, and severe baseline neurological involvement negatively impacted outcomes.

Implications
The information is quite helpful in surgical decision making and for informed consent of patients.

—The Editors

The extent of recovery, which indicated the extent of normalization after surgery, was calculated by modifying Hirabayashi's formula [35] so as to use 11 (the maximum JOA score in our study) instead of 17 (the maximum JOA score including the sections regarding upper extremity function) in the denominator: (postsurgical score−presurgical score)×100/(11−presurgical score). The highest percentage recovery during follow-up was taken as the highest extent of normalization as measured by Hirabayashi's formula. Follow-up was attempted at 6-month intervals. Reasons for neurologic deterioration were assessed.

For patients who died, age and cause of death were noted. The relationship between the cause of death and the spinal cord lesion was analyzed.

To determine the variables affecting the surgical outcome, we evaluated the relationship between the highest follow-up JOA score and the greatest extent of recovery

Table 1
Japanese Orthopaedic Association score [34] modified to exclude the sections regarding upper extremity function

Element	Finding	Points
Walking	Unable to walk	0
	Need walking aid on flat ground	1
	Need handrail on stairs	2
	Can walk without aid but slight spasticity	3
	Normal	4
Sensory		
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	0
	Severe dysuria	1
	Slight dysuria	2
	Normal	3

with respect to the following 10 variables: age at surgery; sex; duration of presurgical symptoms; complications of diabetes mellitus; complications of hypertension; presence of presurgical hyperreflexia in either or both of PTR and ATR; presurgical impairment of joint position sense in the big toes; number of levels affected by OLF; concurrent spinal lesions including OPLL; and intramedullary change of the spinal cord shown on MRI.

Statistical analysis

Data were presented as the mean value (standard deviation [SD]). Student *t* test and Fisher exact test were used for statistical analysis of the difference in the mean values and proportions between the group with the variable and the control group without it. Fisher's Z transformation was used to calculate 95% confidence intervals (CIs) of correlation coefficients. Multiple linear analyses were used to evaluate the variables related to postsurgical recovery. Angular transformation was used to normalize data with skewed distribution (recovery rate [%] at max) before statistical analysis. Statistical analyses were performed with the use of SAS software, version 9.1 (SAS Institute, Cary, NC, USA). Alpha was set at 0.05.

Study approval and informed consent and funding

The study was approved by the institutional review board of the University of Toyama Hospital. Informed consent was obtained from each patient after surgery. The study did not receive any external funding.

Results

Demographics

The 31 men and 10 women who underwent surgery for TM caused by OLF had a median (range) age of 61 (32–75) years (Table 2).

Clinical features of OLF

Ossification of the ligamentum flavum was predominant at lower thoracic levels, such as T9–T10, T10–T11, and T11–T12, rarely occurring at midthoracic levels (Table 2). Presurgically, all patients exhibited TM characterized by exaggerated tendon jerk of the patellar reflex, Achilles reflex, or both, and spasticity in their lower extremities, except for three patients (32, 40, and 41), who had peripheral neuropathy caused by concurrent lumbar lesions. Ossification of the posterior longitudinal ligament in the cervical or thoracic levels, or both, was observed in eight patients. Although three (16, 20, and 31) of these eight patients had concurrent cervical OPLL, TM was predominant.

Other concurrent surgery

Eight patients (16, 25, 27, 31, 32, 36, 38, and 41) also underwent decompressive surgery at other spinal regions at the same time as thoracic laminectomy because coexisting cervical or lumbar lesions could not be excluded from causing the symptoms in their lower extremities. Two of these patients (16 and 31) underwent en bloc cervical laminoplasty. The other six underwent lumbar laminectomy.

A patient (8) who had OLF and thoracic disc herniation underwent simultaneous posterior decompression and anterior interbody fusion. Another patient (3) who had both thoracic OLF and thoracic OPLL first underwent posterior decompression and then 3 weeks later anterior decompression and interbody fusion.

Surgical events

Median (range) time for thoracic posterior surgery was 230 (100–489) minutes. Median (range) surgical time for OLF at each level was 59 (20–165) minutes. Median (range) total bleeding during surgery was 570 (70–2,080) mL. Median (range) bleeding per OLF level was 111 (28–500) mL. Fourteen (34%) patients received transfusions, including two patients who received autologous transfusion. Dural tear was observed in 10 (24%) patients. No major complications occurred during surgery. Postsurgical surgical site infection did not occur in any patient.

Clinical outcome after surgery

All patients could be contacted longer than 1 year after surgery. In two patients, neurologic findings deteriorated during follow-up period. The cause of deterioration in Patient 16 was vertebral fracture caused by trauma 16 years after surgery, and in Patient 31, dementia 3 years after surgery.

No patient died from complications that were related to their surgery. During follow-up, two patients, 18 and 24, died from malignant tumors at ages 67 and 65 years, respectively, which were 12 and 3 years from the time of surgery. Another two patients, 5 and 35, died from ischemic heart disease at ages 51 and 73 years, respectively, which were 8 and 2 years from the time of surgery.

Variables affecting postsurgical outcome

Multiple linear regression analyses (Table 3) showed that presurgical impairment of joint position sense in the big toe was the most important predictor of the highest postsurgical JOA score and of the highest percentage recovery rate. The number of affected OLF levels also predicted of postsurgical highest JOA score, but not statistically significantly so (Table 3).

Age at surgery, sex, and duration of symptoms presurgically, which ranged from 1 to 84 months (Table 2), were not predictors of postsurgical outcomes (Table 3). Although

Table 2
Demographic characteristics and presurgical and postsurgical findings

No.	Age (y)*	Sex	Duration (mo): presurg symptoms	DM	HT	Presurg PTR†		Presurg ATR†		Presurg JOA‡
						R	L	R	L	
1	32	M	6	No	No	4	3	5	4	4
2	37	M	6	No	No	3	3	2	2	7
3	39	M	3	No	No	5	5	5	5	5
4	41	M	48	No	No	3	3	4	5	2
5	43	M	6	Yes	No	3	3	5	5	7
6	47	M	3	Yes	No	3	4	4	5	6
7	49	M	6	No	No	4	4	4	4	2
8	50	M	2	No	No	4	4	4	4	4
9	51	F	1	Yes	Yes	3	3	4	4	2.5
10	52	F	6	No	No	2	3	0	2	2
11	52	M	60	No	No	4	4	4	4	5
12	53	F	24	No	No	4	3	1	2	7
13	53	M	1	Yes	No	2	3	2	3	2
14	54	M	48	No	No	4	3	4	4	3.5
15	54	M	9	No	No	3	3	2	2	6.5
16	56	M	2	No	No	4	4	5	5	1.5
17	56	F	12	No	No	3	3	3	3	6
18	59	M	2	No	No	4	4	5	5	3
19	59	M	6	No	No	3	3	4	4	7.5
20	60	M	12	No	No	3	2	4	3	3
21	61	M	12	No	No	3	3	1	1	5
22	62	M	4	Yes	Yes	4	4	4	4	2
23	62	F	1	No	No	4	4	3	3	2
24	62	M	84	No	No	5	5	5	5	1
25	63	F	12	No	No	3	3	1	1	2.5
26	65	M	4	No	No	3	3	4	4	5
27	65	M	3	No	No	3	3	2	2	6
28	67	M	6	Yes	Yes	3	3	2	3	4
29	68	M	12	No	No	3	2	1	1	2
30	69	M	12	No	No	3	3	4	4	7
31	69	F	6	No	No	4	4	3	3	6
32	70	M	36	Yes	No	1	1	1	1	7
33	70	F	2	Yes	No	3	2	1	1	4
34	71	M	1	No	No	3	3	2	2	9
35	71	M	4	No	Yes	3	3	4	4	2
36	73	F	60	Yes	No	3	3	2	2	5
37	73	F	6	No	No	3	3	2	2	5
38	73	M	12	Yes	No	3	3	4	4	3
39	74	M	3	No	No	4	4	4	4	4
40	74	M	NR	Yes	No	0	0	0	0	5
41	75	M	6	No	No	1	1	1	1	3

No.	Impaired joint position sense	No. of OLF levels	OLF level(s)	Other spinal lesions	Intramedullary change on MRI
1	No	3	T9–T12	None	Yes
2	Yes	3	T9–T12	None	Yes
3	No	4	T4–T8	T4–T8 OPLL	ND
4	No	1	T6–T7	None	ND
5	No	1	T11–T12	T12–L1 OPLL	ND
6	Yes	1	T3–T4	T2–T3 OPLL	ND
7	Yes	3	T10–L1	None	No
8	No	5	T7–T12	T9–T10 disc herniation	Yes
9	Yes	6	T7–L1	None	Yes
10	No	2	T9–T11	None	ND
11	No	3	T4–T5; T9–T11	None	ND
12	No	3	T11–L2	None	ND
13	No	1	T10–T11	T8–T9 OPLL	ND
14	No	3	T3–T5; T9–T10	None	Yes
15	No	2	T10–T12	None	Yes
16	No	1	T3–T4	C2–T1; T3–T5 OPLL	ND
17	No	3	T9–T12	T8–T9 disc herniation	No

(*Continued*)

Table 2
(*Continued*)

No.	Impaired joint position sense	No. of OLF levels	OLF level(s)	Other spinal lesions	Intramedullary change on MRI
18	Yes	2	T2–T4	None	ND
19	Yes	2	T9–T11	None	ND
20	No	5	T7–T12	C3–T1 OPLL	ND
21	Yes	5	T8–L1	None	Yes
22	Yes	5	T8–L1	None	ND
23	Yes	2	T10–T12	None	Yes
24	Yes	4	T2–T6	None	ND
25	No	1	T11–T12	L2–L5 spinal stenosis	No
26	No	3	T2–T3; T10–T12	None	No
27	NR	2	T9–T11	L3–L4 spinal stenosis	Yes
28	Yes	1	T10–T11	None	ND
29	NR	5	T1–T6	None	Yes
30	Yes	1	T10–T11	None	ND
31	No	1	T11–T12	C3–C7; T3–T6 OPLL	No
32	No	2	T10–T12	L3–L5 spinal stenosis	ND
33	Yes	1	T10–T11	None	Yes
34	No	1	T11–T12	None	No
35	Yes	5	T5–T6; T8–T12	T2–T3 OPLL	ND
36	Yes	3	T10–L1	L2–L4 spinal stenosis	ND
37	No	2	T10–T12	None	No
38	Yes	1	T10–T11	L2–L5 spinal stenosis	ND
39	Yes	1	T12–L1	None	No
40	Yes	3	T9–T12	None	Yes
41	No	3	T9–T12	L1–L3 spinal stenosis	No

No.	Surgical procedure(s)
1	T9–T12 laminectomy
2	T10–T11 laminectomy
3	T4–T8 laminectomy; T4–T9 AIF
4	T5–T8 laminectomy
5	T9–L1 laminectomy
6	T1–T4 laminectomy
7	T9–L1 laminectomy
8	T7–T12 laminectomy; T9–T10 AIF
9	T7–L1 laminectomy
10	T10–T11 laminectomy
11	T4–T5 and T9–T10 laminectomy
12	T12–L1 laminectomy
13	T7–T11 laminectomy
14	T2–T5 and T8–T11 laminectomy
15	T10–T12 laminectomy
16	C3–T1 laminoplasty; T2–T5 laminectomy
17	T9–T12 laminectomy
18	T2–T4 laminectomy
19	T9–T11 laminectomy
20	T8–T12 laminectomy
21	T8–L1 laminectomy
22	T10–T12 laminectomy
23	T10–T12 laminectomy
24	T2–T5 laminectomy
25	T11–T12 laminectomy; L2–L5 PLF; L4–L5 TLIF
26	T10–T12 laminectomy
27	T9–T11 and L3–T4 laminectomy
28	T10–T12 laminectomy
29	T1–T6 laminectomy
30	T10–T11 laminectomy
31	C3–C7 laminoplasty; T1–T6 and T11–T12 laminectomy
32	T10–T12 and L3–L5 laminectomy
33	T10–T11 laminectomy
34	T11–T12 laminectomy
35	T8–L1 laminectomy
36	T9–L4 laminectomy

(*Continued*)

Table 2
(*Continued*)

No.	Surgical procedure(s)
37	T10–T12 laminectomy
38	T10–T11 and L2–L5 laminectomy
39	T12–L1 laminectomy
40	T9–T12 laminectomy
41	T9–L3 laminectomy

No.	Duration (y): follow-up[§]	JOA (1 mo)[¶]	JOA (final follow-up)[‖]	Highest follow-up JOA[#]	% RR (1 mo)**	Highest % RR[††]
1	3	6.5	8	8	35.7	57.1
2	3	8.5	8.5	8.5	37.5	37.5
3	13	6	7	7	16.7	33.3
4	9	7.5	10	10	61.1	88.9
5	5	9	10	10	50	75
6	6	9	9	9	60	60
7	8	3.5	5	5	16.7	33.3
8	1	6.5	9	9	35.7	71.4
9	3	3.5	3.5	3.5	11.8	11.8
10	18	4	6	6	22.2	44.4
11	9	8.5	8	8	58.3	50
12	6	9	10	10	50	75
13	5	7	7	7	55.6	55.6
14	7	4.5	5	5	13.3	20
15	1	8	8	8	33.3	33.3
16	16	7	2	10.5	58	94.7
17	4	6	7.5	7.5	0	30
18	5	6	6	6	37.5	37.5
19	1	8	9	9	14.3	42.9
20	8	8	9.5	9.5	62.5	81.3
21	5	5	5	5	0	0
22	6	2	3	3	0	11.1
23	3	5.5	6.5	6.5	38.9	50
24	1	3	3	3	20	20
25	2	7.5	10	10	58.8	88.2
26	7	8	10	10	50	83.3
27	6	6	6	6	0	0
28	9	5	6	6	14.3	28.6
29	4	4	5.5	5.5	22.2	38.9
30	4	7	7	7	0	0
31	3	7.5	0	9	30	60
32	10	8	11	11	25	100
33	5	5.5	7.5	7.5	21.4	50
34	2	10	11	11	50	100
35	1	3	4	4	11.1	22.2
36	15	5	5	5	0	0
37	2	6.5	7	7	25	33.3
38	1	4	6	6	12.5	37.5
39	3	6	6	6	28.6	28.6
40	1	6	6	6	16.7	16.7
41	4	5	6	6	25	37.5

Presurg, presurgical; DM, complications of diabetes mellitus; HT, complications of hypertension; PTR, patellar tendon reflex; ATR, Achilles tendon reflex; JOA, Japanese Orthopaedic Association score; R, right side; L, left side; M, male; F, female; NR, not recorded; OLF, ossification of the ligamentum flavum; MRI, magnetic resonance imaging; OPLL, ossification of the posterior longitudinal ligament; ND, not done; AIF, anterior interbody fusion; PLF, posterior lumbar fusion; TLIF, transforaminal lumbar interbody fusion; RR, recovery rate.

* Mean (standard deviation), 59.4 (11.3) y; median (range), 61 (32–75) y.

† Scores: 0, none; 1, diminished; 2, normal; 3, exaggerated; 4, transient clonus; 5, sustained clonus.

‡ Mean (standard deviation), 4.2 (2.0).

§ Mean (standard deviation), 5.5 (4.2) y.

¶ Mean (standard deviation), 6.2 (1.9) y.

‖ Mean (standard deviation), 6.8 (2.5); $p<.001$ presurgical JOA score (paired t test).

Mean (standard deviation), 7.2 (2.2); $p<.001$ presurgical JOA score (paired t test).

** Mean (standard deviation), 28.8 (19.9)%.

†† Mean (standard deviation), 44.9 (28.7)%.

Table 3
Multiple linear analyses of surgical outcome

Variables	JOA (1 mo)		JOA (highest follow-up)		JOA (final follow-up)	
	β Coefficient	p Value	β Coefficient	p Value	β Coefficient	p Value
Intercept	10.011	<.001	10.235	<.001	11.350	.001
Age at surgery	−0.028	.301	−0.011	.690	−0.048	.241
Sex	0.451	.473	0.350	.594	1.025	.286
Duration (y): presurg symptoms	−0.095	.588	−0.236	.205	−0.052	.846
Complications of DM	0.284	.694	0.410	.588	1.144	.302
Complications of HT	−1.816	.130	−1.823	.146	−2.509	.167
Hyperreflexia*	−0.045	.942	0.360	.573	−1.105	.239
Impaired presurg joint position†	−1.406	.029	−2.245	.002	−1.416	.137
No. of OLF levels	−0.412	.072	−0.466	.053	−0.089	.793
Duration (y): follow-up	−0.081	.224	−0.024	.726	−0.140	.171

Variables	% RR (1 mo)		% RR (highest follow-up)	
	β Coefficient	p Value	β Coefficient	p Value
Intercept	64.959	.006	63.345	.034
Age at surgery	−0.361	.214	0.056	.881
Sex	3.253	.627	4.508	.607
Duration (y): presurg symptoms	−0.595	.751	−2.724	.271
Complications of DM	1.949	.800	9.438	.353
Complications of HT	−5.469	.663	−10.693	.517
Hyperreflexia*	8.471	.200	11.891	.170
Impaired presurg joint position†	−17.587	.012	−35.504	<.001
No. of levels affected by OLF	−4.329	.076	−4.784	.131
Duration (y): follow-up	−0.332	.638	−0.071	.939

JOA, Japanese Orthopaedic Association score; presurg, presurgical; DM, diabetes mellitus; HT, hypertension; OLF, ossification of the ligamentum flavum; RR, recovery rate.

* Hyperreflexia in the lower extremity was deemed as present when a response to tests for the patellar tendon reflex or for the Achilles tendon reflex scored as 4 (transient clonus) or 5 (sustained clonus) on either side (see Table 2).

† Presurgical joint position sense was not recorded in two male patients, 27 and 29.

diabetes mellitus was a complication in 11 patients (Table 2), diabetic neuropathy was not severe in any. Complications of diabetes or of hypertension were not predictors of surgical outcomes (Table 3). Presurgical hyperreflexia was not a predictor of surgical outcome (Table 3) and was not correlated with recovery (Table 4).

Presurgical impairment of joint position sense in the big toe had been observed in 18 (46%) of the 39 patients in whom it was recorded (Table 2). Presurgical JOA scores were not significantly different between patients with unimpaired or impaired joint position sense (Table 5). However, presurgical impairment of joint position sense was significantly related to postsurgical outcome. In patients who had presurgical impairment of joint position sense, JOA scores and percentage recovery rates at 1 month postsurgically and at final follow-up were significantly lower than those in patients without impairment (Table 5).

The extent of severity of postsurgical neurologic status, determined by the highest JOA score, was highly positively correlated with the extent of severity of presurgical neurologic status (Fig. 1).

Thirteen patients had OLF at one intervertebral level, eight patients at two levels, and 20 at three or more levels. The number of levels having OLF was moderately negatively correlated ($r=-0.34$; 95% CI, $-12.43<r<-0.64$; $p=.031$) with the highest percentage recovery rate (Fig. 2).

Table 4
Hyperreflexia and surgical outcome

Variables	Hyperreflexia*		p Value
	Absent	Present	
Male; female	11; 6	20; 4	.270
Age (y) at surgery (mean [SD])	63.6 (10.3)	56.3 (11.2)	.039
JOA score (mean [SD])			
Presurg	4.8 (2.0)	4.0 (2.0)	.213
1-Mo postsurg	6.3 (1.7)	6.2 (2.1)	.864
Final follow-up	7.2 (1.9)	7.3 (2.4)	.984
% Recovery rate			
1-Mo postsurg	23.9 (18.7)	32.2 (20.4)	.195
Final follow-up	40.8 (31.2)	47.7 (27.1)	.456

SD, standard deviation; JOA, Japanese Orthopaedic Association score; presurg, presurgical; postsurg, postsurgical.

* Hyperreflexia in the lower extremity was deemed as present when a response to tests for the patellar tendon reflex or for the Achilles tendon reflex scored as 4 (transient clonus) or 5 (sustained clonus) on either side (see Table 2).

Table 5
Presurgical joint position sense and surgical outcome

Variables	Presurgical joint position sense		p Value
	Unimpaired	Impaired	
Male*; female	15; 6	14; 4	.726
Age (y) at surgery (mean [SD])	56.2 (11.7)	62.2 (10.6)	.105
JOA score (mean [SD])			
Presurg	4.6 (2.1)	4.0 (2.0)	.369
1-Mo postsurg	7.1 (1.5)	5.3 (2.0)	.002
Final follow-up	7.6 (2.8)	6.2 (1.8)	.043
% Recovery rate			
1-Mo postsurg	38.9 (18.2)	19.0 (16.3)	.001
Final follow-up	62.5 (25.5)	27.1 (18.2)	<.001

SD, standard deviation; JOA, Japanese Orthopaedic Association score; presurg, presurgical; postsurg, postsurgical.

* Presurgical joint position sense was not recorded in two male patients, 27 and 29.

Maximum recovery rate in the 16 patients with concurrent lesions was mean (SD), 53% (32%) and that in the 25 patients without lesions was mean (SD), 40 (26%), a difference that was not significant (p=.198).

Of the 21 patients who had undergone presurgical MRI, intramedullary signal change was seen in 12 (57%) (Table 2). This change was observed at the level of the most severe spinal cord compression. Presurgical JOA scores were not significantly different whether intramedullary signal change was seen (Table 6). Postsurgical JOA scores and percentage recovery rates of scores in patients whose presurgical MRIs had shown intramedullary signal change were not statistically significantly different from those whose MRIs had not shown signal change.

Of the 21 patients who had undergone presurgical MRIs, 12 (1, 2, 8, 9, 14, 15, 21, 23, 27, 29, 33, and 40) also underwent postsurgical MRIs. Of these 12, nine (1, 2, 9, 14, 15, 21, 23, 29, and 40) had presurgical MRIs showing intramedullary signal change, and the other three (26, 31, and 34) did not.

Of the nine patients whose presurgical MRIs showed intramedullary signal change, seven (1, 2, 9, 14, 21, 29, and 40) still had intramedullary signal change observed on postsurgical MRI (Fig. 3). These seven patients complained of postsurgical symptoms, such as gait disturbance, sensory disturbance, and vesicoureteral reflex. In the other two patients (15 and 23), postsurgical MRIs did not show intramedullary signal change. Postsurgical neurologic findings showed improvement in each. The highest percentage recovery rate in these two patients was 33.3% and 50%, respectively.

Of the three patients (26, 31, and 34) whose presurgical MRIs did not show intramedullary signal change, postsurgical MRIs also did not show intramedullary signal change.

Discussion

In investigating objective variables affecting surgical outcome, we found that presurgical impairment of joint position sense in the big toe was the most important predictor of postsurgical prognosis. Also, patients with more affected levels of OLF had a poorer prognosis. Presurgical signal change in the spinal cord shown on MRI might unfavorably affect postsurgical recovery.

The mean percentage recovery rate as evaluated by JOA score reached a highest value of 45% during follow-up in this study. This finding was comparable with those of two previous reports [12,13] of outcomes of surgery for OLF, in which postsurgical percentage recovery rates as calculated by using JOA scores were 44% and 47%, respectively. Using the Nurick functional score [36], a six-grade score (0–5) in which 0 is the highest, Shiokawa et al. [12] reported that 13 (42%) of the 31 patients who underwent surgery of OLF of the thoracic spine had a postsurgical score of only 2 or 3, indicating fair results.

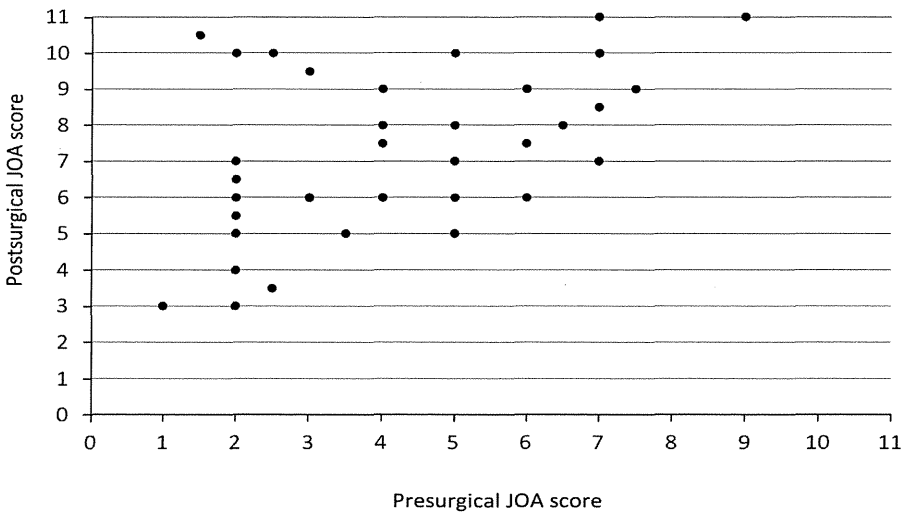

Fig. 1. Correlation between the highest postsurgical JOA score and the presurgical JOA score with the extent of severity of presurgical neurologic status; r=0.51; 0.25<95% confidence interval<0.86; p<.001. JOA, Japanese Orthopaedic Association.