

Figure 2. Receiver operating characteristic curves to determine the cutoff transcranial motor-evoked potentials amplitude expressed in % of baseline (**A**) and in μ V (**B**) at the intraoperative point of deterioration.

motor deficits, even comparing similarly deteriorated muscles by excluding any muscles whose amplitudes remained above the cutoff amplitude (12.3% of the baseline) at the intraoperative point of deterioration (Figure 4).

DISCUSSIONS

Spine

Although the use of TcMEP has proven to be a successful and reliable neuromonitoring technique during spine surgery, the alarm point of the TcMEP response remains controversial. Quinones-Hinojosa *et al*⁸ advocated the "waveform criterion" that was based on changes in waveform complexity. Calancie and Molano⁹ introduced the "threshold criterion," which was based on an increase in stimulation threshold voltage. Recently, our group also reported another waveform criterion.¹⁰ The main category of criteria, however, looks at the muscle response amplitude. Some have used the same criteria as is used for SSEP, that is, a 50% or greater decrease in amplitude and 10% or greater delayed latency.^{6,11} Langeloo *et al*¹² introduced the standard of 80% or greater decrease

in amplitude. Sala et al¹³ adopted binary presence-or-absence criteria in which a complete loss of amplitude is the alarm point. These differences may be partly due to the variability of settings between the studies, including different patient populations having different etiologies and different operative procedures in different level of spine. But most importantly, the lack of adequate data on the cutoff amplitude of TcMEP for predicting postoperative motor deficits has led to endless controversy over the alarm criteria. The reason not having adequate data is that most studies include none or only a few cases with postoperative motor deficits. 6,11,14-16 And, only a few reports have an adequate number of patients with postoperative motor deficits together with intraoperative neurophysiological data.^{1,12} In this prospective study, we had 12 cases with postoperative motor deficits and performed corticospinal tract (CST) monitoring on 12 major lower extremity muscles in each patient to draw the assessable ROC curves and to identify a cutoff point for predicting postoperative motor deficits in thoracic spine surgery for the first time.

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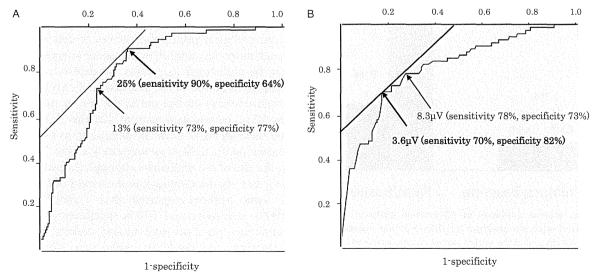


Figure 3. Receiver operating characteristic curves to determine the cutoff transcranial motor-evoked potentials amplitude expressed in % of baseline (A) and in μV (B) at the end of surgery.

Minimum Amplitude				Final Amplitude			
Cutoff Value	Sensitivity (%)	Specificity (%)	AUROC (%)	Cutoff Value	Sensitivity (%)	Specificity (%)	AUROC (%)
12.3%	87.7	64.0	78.2	25.2%	90.4	64.0	80.7
1.9 μV	68.5	82.7	80.6	3.6 μV	69.9	82.2	80.4

To our knowledge, there is only 1 report determining the cutoff amplitude of TcMEP from an ROC curve. Lieberman *et al*¹⁷ reported on 35 cases who received corrective surgery in the lumbar spine for a fixed sagittal imbalance deformity of whom 25 patients had TcMEP deterioration of greater than 80% reduction in MEP amplitude at 1 or more muscles, and 10 cases had postoperative motor weakness. They precisely evaluated TcMEP amplitude and resultant postoperative motor deficits and identified the optimal threshold to be -67% of baseline. As would be expected, the optimal threshold for thoracic surgery in our study was 12.3% (-77.7%) of baseline, which is much lower than their threshold for lumbar surgery.

This is the first report describing a cutoff amplitude in absolute microvolts rather than just as a percent of baseline amplitude. The ROC curves suggest that absolute value is as appropriate as relative value for expressing the cutoff value for postoperative motor deficits. The difference is only that the absolute cutoff points have higher specificity and the relative cutoff points have higher sensitivity. The area under the curve is equivalent. There are 2 evident advantages of employing the absolute amplitude. First, there is no need to determine a

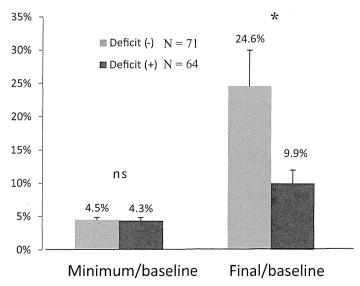


Figure 4. Mean relative amplitude of transcranial motor-evoked potentials compared with the baseline amplitude at the intraoperative point of deterioration and at the end of surgery was compared between muscle groups with or without postoperative motor deficits. One hundred thirty-five muscles whose minimum amplitudes were below the cutoff amplitude (12.3% of baseline) were included. Results are shown as mean \pm SEM (error bars). *P < 0.05.

baseline amplitude, which is sometimes difficult to accurately assess in the early, unstable stage of anesthesia. Second, extra time is not needed to compare the intraoperative amplitude measurements with the baseline amplitude; each amplitude value can be assessed by itself. But there is an evident limitation on this absolute value method. Baseline amplitude can be variable depending on the anesthesia regimens and monitoring conditions, and there is no evidence that the absolute cutoff amplitude that suggests the postoperative motor deficit is not affected by the baseline amplitude. Absolute cutoff amplitude may vary from institute to institute depending on the anesthesia regimens and monitoring conditions.

Clinical significance of the TcMEP amplitude at the end of surgery has not been clarified. The TcMEP amplitude is supposed to reflect the functional integrity of the spinal cord, which can change dramatically during the operation. Therefore, it is important to monitor TcMEP amplitudes throughout the operative procedure. Although many studies lack data on the final waves, some clearly describe the final wave status. Although some report that the wave recovery at the end of surgery did not help predict postoperative motor deficits,6 most authors reported the positive association between the recovery of TcMEP wave and the postoperative motor status. 5,14,16 In this study, the muscles without postoperative motor deficits had a 2.5-fold greater final amplitude than the muscles with postoperative motor deficits, even among patients with an equally decreased amplitude at deterioration point (Figure 4). This result suggests that recovery of TcMEP amplitude does reflect postoperative motor status. However, from a clinical standpoint, waves at deterioration point are much more meaningful, in that some interventional procedure can be performed to reverse the deterioration of functional integrity reflected in the decrease in TcMEP amplitude at the deteriorated point but not at the end of surgery. In addition, the ROC curves demonstrate that the TcMEP amplitude at the intraoperative point of deterioration can predict postoperative motor deficits as accurately as the TcMEP amplitude at the end of the procedure although the intraoperative amplitude has big disadvantage in the aspect of time course.

Some authors reported that TcMEP monitoring had 100% sensitivity and 100% specificity or close to that for predicting postoperative motor deficits, 5,6 but this seems unrealistic and could be misleading. The ROC curves in this study clearly show the true profile of TcMEP monitoring as not having a single cutoff point which can perfectly distinguish cases with postoperative motor deficit from cases

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without them, and setting the alarm criteria with a safety margin will inevitably produce some false positives. Considering these limitations of TcMEP, we recommend multimodality monitoring including spinal cord-evoked potential or SSEP in thoracic spine surgery.

Our study had several limitations. First, we included surgical procedures for spinal conditions with multiple etiologies, and the cutoff amplitude of TcMEP may vary depending on etiology and operative procedure. Second, although distal muscles are more appropriate for CST monitoring, 18,19 we included many major muscles including proximal muscle groups. But the cutoff value may differ between muscles. Further studies should clarify these topics. To prevent postoperative motor deficits, the cutoff amplitude derived in this study should not be directly used as the actual alarm criteria. Rather, in an attempt to prevent any postoperative motor deficits, the amplitude for an alarm point should be considerably higher than the cutoff amplitude identified in this study, allowing a safety margin with an acceptable number of false positives.

In conclusion, our study identified the cutoff amplitude for TcMEP monitoring both at the intraoperative point of deterioration and at the end of thoracic spine surgery. We expressed the amplitude in both microvolts and as a percentage of baseline amplitude and found that both values are equally useful. The amplitude at the intraoperative point of deterioration could predict postoperative motor deficits as well as the amplitude at the end of surgery.

Key Points

- ☐ Of 76 patients who underwent thoracic spine surgery under electrophysiological monitoring using TcMEP, 73 monitored muscles in 12 patients showed postoperative motor deficits.
- ☐ Muscles with postoperative motor deficits demonstrated significantly low (P < 0.001) TcMEP amplitude compared with muscles without postoperative motor deficits, both at the deteriorated point and at the end of surgery, although baseline amplitude did not differ significantly.
- ☐ The mean TcMEP amplitude was significantly (2.5fold) greater at the end of surgery in the muscles with postoperative motor deficits than that in the muscles without postoperative motor deficits, even selecting only muscles that demonstrated deterioration at the deteriorated point below the cutoff amplitude (12% of baseline amplitude).
- Cutoff amplitudes for postoperative motor deficit at the deteriorated point and at the end of surgery were 12% and 25% of baseline amplitude, with sensitivity/ specificity being 90%/64%, 88%/64%, respectively.

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SURGERY

Predictive Factors for a Poor Surgical Outcome With Thoracic Ossification of the Ligamentum Flavum by Multivariate Analysis

A Multicenter Study

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Study Design. Retrospective multi-institutional study.

Objective. The purpose of this study was to describe the surgical outcomes in patients with ossification of the ligamentum flavum (OLF) and determine the influence of an ossified anterior longitudinal ligament (OALL) on the clinical features and surgical outcomes in thoracic OLF.

Summary of Background Data. Detailed analyses of surgical outcomes of thoracic OLF have been difficult because of rarity of this disease

Methods. We identified 96 patients (77 males and 19 females with a mean age at surgery of 63.4 ± 10.3 yr) who underwent surgery for thoracic OLF and investigated their preoperative symptoms, severity of symptoms and myelopathy, disease duration, magnetic resonance imaging and computed tomographic findings, surgical procedure, intraoperative findings, and postoperative recoveries. The presence of OALL found at or near the most severely affected OLF level on sagittal computed tomographic images was classified into 1 of the following 4 types: (1) "no discernible type" (type N); (2) "one-sided type" (type O); (3) "discontinuous type" (type D); and (4) "continuous type" (type C). Multivariate logistic regression analysis

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was used to compute odds ratios and 95% confidence intervals to identify the risk factors associated with surgical outcomes.

Results. The mean Japanese Orthopaedic Association score was 5.6 points preoperatively and 7.8 points 2 years postoperatively, yielding a mean recovery rate of 44.6%. Disease duration, presence of ossified dura mater, and type D OALL were the important factors for predicting surgical outcomes.

Conclusion. After evaluating surgical outcomes on the largest sample size of OLF surgical procedures thus far, our results show that disease duration, ossification of the dura mater, and the presence of type D OALL were risk factors related to surgical outcomes.

Key words: thoracic ossification of the ligamentum flavum, ossified anterior longitudinal ligament, predictive factors for a poor surgical outcome.

Level of Evidence: 3 Spine 2013;38:E748–E754

horacic ossification of the ligamentum flavum (T-OLF) is a relatively rare spinal disorder that generally requires surgical intervention due to its progressive nature and its poor response to conservative therapy. The prevalence of OLF has been reported at 3.8% to 26%, 1-3 which is very similar to the prevalence of cervical ossification of the posterior longitudinal ligament (OPLL).4 However, predictive factors for OLF are unclear because of the paucity of reports on this condition, unlike cervical OPLL.^{1,5-15} Because obtaining detailed data and analysis from a single center study on this topic have been insufficient and difficult, we investigated clinical features, radiological findings, and surgical outcomes of OLF in a multicenter study of the Nagova Study Group. We reported surgical results of 63 patients who underwent single level surgery for thoracic OLF-induced myelopathy in a multi-institutional retrospective survey. 16 That study classified any ossified anterior longitudinal ligament (OALL) that was adjacent to or at the same vertebral level as a patient's OLF using sagittal computed tomographic (CT) images. We identified patients with "discontinuous" type OALL when it existed either immediately rostral or caudal to the OLF but

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TABLE 1. Summary of Demographic Data in 96 Patients With T-OLF					
Sex					
Male	77				
Female	19				
Mean age	63.4 yr (range, 36–83)				
Mean follow-up	44.9 mo (range, 24–118)				
Mean disease duration	16.6 mo (range, 0.5–120)				
Preoperative JOA score	5.6 (range, 1.0–9.0)				
Postoperative JOA score	7.8 (range, 2.0–11.0)				
JOA recovery rate 44.6 (range, -20.0 to 100.0)					
T-OLF indicates thoracic ossification of the ligamentum flavum; JOA,					

not at the OLF intervertebral level. Discontinuous type OALL had more preoperative severe symptoms and poorer surgical outcomes. Therefore, we conducted a study on a large number of patients, which included both the previous, single-level patients with T-OLF and those with multilevel T-OLF who had undergone surgery; we analyzed their pre- and postoperative symptoms, radiological findings, and intraoperative findings. The aim of this multicenter study is to determine factors related to the surgical outcomes including any type of OALL that may have been present in the patients with OLF by multivariate logistic regression analysis. This study had the largest sample size describing surgical outcomes of thoracic OLF.

MATERIALS AND METHODS

Japanese Orthopaedic Association.

Patient Population

Between 2000 and 2008, 19,364 patients who underwent spinal surgery were registered in the database of the research group, a study group for spinal diseases. We excluded patients who underwent surgery for cervical and thoracic ossified posterior longitudinal ligament (OPLL) or cervical spondylosis myelopathy (CSM) before their OLF surgery or during

follow-up. We identified 107 patients who underwent surgery for thoracic OLF-induced myelopathy and who were then observed for a minimum of 2 years postoperatively. Preoperative symptoms, severity of symptoms and myelopathy, disease duration, magnetic resonance imaging (MRI) and CT findings, surgical procedure, intraoperative findings, and postoperative recovery were investigated in these patients. Ninety-six patients were ultimately included in this study, because 11 patients were excluded from analysis due to a lack of detailed follow-up data. There were 77 males and 19 females with a mean age at surgery of 63.4 ± 10.3 years (range, 36–83 yr). The mean disease duration from onset to surgery was 16.6 ± 22.1 months (range, 0.5–120 mo) (Table 1).

We evaluated the severity of a patient's myelopathy before and after surgery using the Japanese Orthopaedic Association (JOA) scoring system for thoracic myelopathy (total of 11 points), which was derived from the JOA scoring system for cervical myelopathy by eliminating the motor and sensory scores for the upper extremities. ^{16,17} We evaluated postoperative improvement of symptoms using the recovery ratio of the JOA score and the Hirabayashi method ([postoperative JOA score] × 100%), with a recovery ratio of 100% indicating the best postoperative improvement. This study was approved by the ethics committee of each institution, and all patients were informed that the data from their cases would be used for the study.

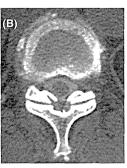
Axial CT Classification of OLF

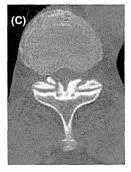
We used Sato classification that evaluates CT images¹⁸ and found the following 4 types of OLF in our subjects: lateral, extended and enlarged, fused, and tuberous (Figure 1).

Sagittal CT Image Classification of OALL Relative to the OLF

We classified any OALL that was adjacent to or at the same vertebral level as the patient's most severe OLF level using sagittal CT images. ¹⁶ We found 4 types according to where the OALL was located relative to the most severe OLF level (Figure 2): (1) type N, "no discernible," OALL immediately







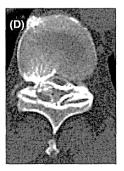


Figure 1. The CT axial classification of OLF with scans obtained at the middle of the facet joint. (A) Lateral type. The ossified ligamentum flavum is located only in the capsular portion of the ligamentum flavum, which can be detected at the lateral edge of the spinal canal. (B) Extended and enlarged type. The ossified ligamentum flavum is located at the surface of the ligamentum flavum and protrudes into the spinal canal. (C) Fused type. Bilateral ossified ligament flavum fused at the middle of the ossified ligamentum flavum. (D) Tuberous type. Fused ossified ligament flavum formed a tuberous mass at the middle of the spinal canal. OLF indicates ossification of the ligamentum flavum; CT, computed tomographic.

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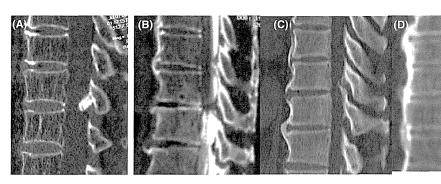


Figure 2. The CT sagittal classification of OALL at the OLF level. (**A**) No discernible OALL immediately rostral or caudal to the most severe OLF level (type N); (**B**) one-sided (type O), in which the OALL exists either immediately rostral or caudal to the most severe OLF level but not at the most severe OLF intervertebral level; (**C**) discontinuous (type D), in which the OALL is present both rostrally and caudally to the most severe OLF level but not at the most severe OLF level; and (**D**) continuous (type C), in which the OALL extends from the rostral to the caudal levels, including the most severe OLF level. CT indicates computed tomographic; OALL, ossified anterior longitudinal ligament; OLF, ossification of the ligamentum flavum.

rostral or caudal to the most severe OLF level; (2) type O, "one-sided," in which the OALL exists either immediately rostral or caudal to the most severe OLF level but not at the most severe level; (3) type D, discontinuous, in which the OALL is present both rostrally and caudally to the most severe OLF level but not at the most severe OLF level; and (4) type C, "continuous," in which the OALL extends from the rostral to the caudal levels including the most severe OLF level. Two board-certified orthopedic spine surgeons reviewed all images twice. These orthopedic surgeons have primarily performed spine surgical procedures, and they interpret spine CT and MR images daily in their clinical and research practices. The 2 reviewers identified and characterized the abnormalities by consensus. Neither orthopedic spine surgeon had received information pertaining to age, sex, clinical history, symptoms, and/or surgical outcomes at the time of the interpretation. They identified each thoracic OLF in the 96 patients and assessed its axial and sagittal CT classification.

Statistical Analysis

Data were analyzed using the SPSS version 19 software package (IBM SPSS Statistics 19.0, IBM Corporation, Armonk, NY). The mean values are presented as mean ± SD. Statistical analysis was performed by Tukey multiple comparison tests and 1-way analysis of variance. The multivariate logistic regression analyses were used to compute odds ratios and a 95% confidence interval to identify the risk factors associated with surgical outcomes. A recovery rate in the JOA scale score of 50% or higher was considered a good outcome as reported previously. A P value less than 0.05 was considered statistically significant. Intra- and interobserver reliabilities on axial CT classification of OLF and sagittal CT image classification of OALL relative to the OLF were assessed using weighted kappa statistics. ²⁰

RESULTS

Radiographical Findings

MRI and CT were performed on all patients. There were only 3 patients (3.1%) decompressed at the middle thoracic spine

(T5-T9) and 9 patients (9.4%) decompressed at the upper thoracic spine (T1-T5). The majority of the affected levels (84 patients [87.5%]) were in the lower thoracic region (T9– T12). The numbers of decompressed levels were single level in 63 patients (65.6%), 2 levels in 26 (27.1%), and more than 2 levels in 7 (7.3%). Intramedullary signal intensity change on MR images was observed in 81 patients (84.4%). Morphological classifications, as determined by axial CT images, were lateral in 14 patients (14.6%), extended and enlarged in 31 (32.3%), fused in 41 (42.7%), and tuberous in 10 (10.4%). We classified the morphology of the OALLs as seen in sagittal CT images as type N in 38 patients (39.6%), type O in 32 (33.3%), type D in 15 (15.6%), and type C in 11 (11.5%) (Table 2). The intraobserver and interobserver reliabilities were 0.939 (observer 1), 0.924 (observer 2), and 0.942 (interobserver) for axial CT classification of OLF; they were 0.970, 0.985, and 0.964, respectively, for sagittal CT image classification.

Surgical Methods and Outcomes

The mean IOA score was 5.6 points preoperatively, and 7.8 points at 2 years postoperatively, yielding a mean recovery rate of 44.6%. Thus, a statistically significant improvement in the JOA score was obtained at the 2-year follow-up examination (P < 0.01, paired t test) (Table 1). Laminectomy was performed in 32 patients (33.3%), laminoplasty in 55 (57.3%), and posterior decompression and fusion with instrumentation in 9 (9.4%). Patients with OLF in whom bilateral OLF was not fused in the middle of the spinal canal were basically treated with laminoplasty whereby a high-speed drill and punch were used to cut the laminae bilaterally located over the level of the OLF. The laminar flap was lifted up with a clamp and the interspinous and supraspinous ligaments in the rostral and caudal portions of the laminar flap were cut with a knife and punch. After removing the OLF, the laminar flap was repositioned over the original site with suture. Laminectomies were performed at a single level above and below the area of the OLF. The extent of facet joint resection was less than half a joint for both procedures. Surgical procedures with instrumentation had facet resection of more than half

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TABLE 2. Type of Ossification and Surgical Method							
OLF	No. (%)	Lateral	Extended and Enlarged	Fused	Tuberous		
·	96 (100%)	14	31	41	10		
Laminectomy	32 (33.3%)	1	11	18	2		
Laminoplasty	55 (57.3%)	13	19	21	2		
Posterior decompression and fusion with instrumentation	9 (9.4%)	0	1	2	6		
OALL		Type N	Туре О	Type D	Туре С		
	96 (100%)	38	32	15	11		
Laminectomy	32 (33.3%)	9	12	7	4		
Laminoplasty	55 (57.3%)	25	16	7	7		
Posterior decompression and fusion with instrumentation	9 (9.4%)	4	4	1	0		
OALL indicates ossified anterior longitudinal ligamen	t; OLF, ossification of th	e ligamentum flavu	ım.				

a joint. The lateral type of OLF was most frequently treated with laminoplasty, the extended and enlarged type and fused type with laminectomy and laminoplasty, and the tuberous type was most frequently treated with fusion. There was no tendency for a particular type of surgery to be performed relative to the type of OALL (Table 2). Intraoperatively, we found adhesions to the dura mater (ossification of the dura mater) in 43 patients (44.8%). Of these 43 patients with ossified dura mater, 7 (16.3%) experienced a dural tear during surgery, which was repaired with 5-0 silk sutures, fibrin glue sprayed directly onto the dura mater, and a gelatin sponge placed over the repaired site. Most patients with dural adhesions or ossification received laminectomy or fusion surgery. Only 5 patients received laminoplasty, and in these patients, dural adhesion was in the center. After cutting laminae bilaterally, we dissected between the laminae and dura. Fortunately, there were no neurological complications associated with the dural tears.

Relationship of Recovery Rate to Various Factors

There were no statistically significant differences between the recovery rate and sex, diabetes mellitus, OLF level, OLF number CT axial classification, and surgical methods. The statistically significant factors were age, disease duration, CT sagittal classification, signal intensity on T2WI, and ossification of dura mater. In particular, the recovery rate of type D in CT sagittal classification was significantly lower than the recovery rate of the 3 other groups (Table 3).

Factors Related to Surgical Outcomes

The recovery rate was 50% or higher in 47 patients (50.0%). We assessed preoperative factors related to surgical outcome (recovery rate of \geq 50%) including age, disease duration, CT axial classification, CT sagittal classification, signal intensity on T2WI, and ossification of dura mater, which had a statistically significant relationship with recovery rate. We used

a cutoff value of 50% because a recovery rate of more than 50% has been considered good to excellent in previous literature. As a result, disease duration (odds ratio; 1 for <6 mo vs. 2.53 [95% confidence interval; 4.84–13.2, P=0.001] for 6 to 12 mo and 3.02 [3.99–22.9, P=0.001] for 12 mo or longer), type D CT sagittal classification (odds ratio; 1 for type N vs. 0.068 [0.005–0.852, P=0.037] for type D), and presence of ossified dura mater (odds ratio; 1 for presence of ossified dura mater vs. 0.104 (0.018–0.602, P=0.011) for absence of ossified dura mater) were significantly associated with the surgical outcome (Table 4).

DISCUSSION

OLF has been recognized as a cause of myeloradiculopathy since Polgar²² first reported it in 1920. It is possible to diagnose thoracic OLF by MRI and CT.1,15 The incidence of thoracic OLF has been reported at 3.8% to 25% including asymptomatic cases.^{1,2} However, these are limited reports without sufficient numbers of patients, that is, at least 20 or more. 1,5,6,8-15 Reported cases of thoracic OLF occurred most commonly in the lower thoracic spine followed by upper thoracic spine. 1,2,10,23 Similar to previous studies, we had 9 patients with upper level, 3 patients with middle level, and 84 patients with lower level lesions. The reasons for the high frequency of OLF at lower thoracic levels include increased mechanical stress where the thoracic vertebrae form the junction between the rigid rib cage and the elastic lumbar spine,24 a direct correlation between increased mobility of the spine and repetitive mild trauma,25 and high tensile force present in the posterior column.²⁶

Although duration of symptoms, age, and signal intensity change of the spinal cord have been studied as important factors of cervical myelopathy,²⁷ there have been only a few reports on predictive factors for poor surgical outcome in OLF surgery including older age, midthoracic OLF, more than 2 segments of OLF, coexisting OPLL or other spinal

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Sex Recovery Rate (%) P Male 77 (80.0) 46.1 ————————————————————————————————————	TABLE 3. Relationship of Recovery Rate to Various Patient Factors						
Male 77 (80.0) 46.1 Female 19 (20.0) 38.7 0.232 Mean age* 32 (33.3) 51.6 60 60-70 40 (41.7) 45.3 0.031 >70 24 (25.0) 34.1 0.009 Diabetes mellitus 88 (91.7) 45.3 0.465 Absent 88 (91.7) 45.3 0.465 Disease duration (mo)* 45.3 0.465 26 36 (37.5) 62.2 6-12 6-12 15 (15.6) 47.8 0.001 >12 45 (46.9) 29.5 0.001 OLF level 71-T5 9 (9.4) 53.4 53.4 T5-T9 3 (3.1) 49.4 0.317 T9-T12 84 (87.5) 43.5 0.604 Number of OLF levels 46 2 26 (27.1) 42.3 0.634 >2 7 (7.3) 40.3 0.876 62.2 6.64 6.2 6.64 6.2 6.64 6.2 6.64 6.64 6.2 6.64 6.2 6.64 6.64 6.2 6.		No. (%)		P			
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<60	Female	19 (20.0)	38.7	0.232			
60-70 40 (41.7) 45.3 0.031 >70 24 (25.0) 34.1 0.009 Diabetes mellitus Present 8 (8.3) 36.8	Mean age*						
>70 24 (25.0) 34.1 0.009 Diabetes mellitus 8 (8.3) 36.8 36.8 Absent 88 (91.7) 45.3 0.465 Disease duration (mo)* 45.3 0.465 6 36 (37.5) 62.2 66.12 66.12 15 (15.6) 47.8 0.001 >12 45 (46.9) 29.5 0.001 OLF level 71-T5 9 (9.4) 53.4 53.5 0.604 64.4 64.4 63.65.6) 46 64.2 26.(27.1) 42.3 0.634 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53.4 53	<60	32 (33.3)	51.6				
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<6	Absent	88 (91.7)	45.3	0.465			
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OLF level T1-T5 9 (9.4) 53.4 T5-T9 3 (3.1) 49.4 0.317 T9-T12 84 (87.5) 43.5 0.604 Number of OLF levels 1 63 (65.6) 46 42.3 0.634 2 26 (27.1) 42.3 0.634 >2 7(7.3) 40.3 0.876 CT axial classification Lateral 14 (14.6) 54.4 54.4 Extended and enlarged 31 (32.3) 48.9 0.733 Fused 41 (42.7) 38.7 0.342 Tuberous 10 (10.4) 42.1 0.067 CT sagittal classification* Type N 38 (39.6) 48.9 48.9 Type O 32 (33.3) 43.2 2.048 Type D 15 (15.6) 30.4 0.008 Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001	6–12	15 (15.6)	47.8	0.001			
T1-T5 9 (9.4) 53.4 T5-T9 3 (3.1) 49.4 0.317 T9-T12 84 (87.5) 43.5 0.604 Number of OLF levels 1 63 (65.6) 46 46 2 26 (27.1) 42.3 0.634 ≥2 7(7.3) 40.3 0.876 CT axial classification Lateral 14 (14.6) 54.4 54.4 Extended and enlarged 31 (32.3) 48.9 0.733 Fused 41 (42.7) 38.7 0.342 Tuberous 10 (10.4) 42.1 0.067 CT sagittal classification* Type N 38 (39.6) 48.9 48.9 Type O 32 (33.3) 43.2 2.048 Type D 15 (15.6) 30.4 0.008 Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001 Surgical methods <t< td=""><td>>12</td><td>45 (46.9)</td><td>29.5</td><td>0.001</td></t<>	>12	45 (46.9)	29.5	0.001			
T5-T9 3 (3.1) 49.4 0.317 T9-T12 84 (87.5) 43.5 0.604 Number of OLF levels 0.63 (65.6) 46 0.634 2 26 (27.1) 42.3 0.634 >2 7(7.3) 40.3 0.876 CT axial classification 0.876 0.876 Extended and enlarged 31 (32.3) 48.9 0.733 Fused 41 (42.7) 38.7 0.342 Tuberous 10 (10.4) 42.1 0.067 CT sagittal classification* 38 (39.6) 48.9 0.067 CT sagittal classification 0.067 0.007 0.008 0.008 Type N 38 (39.6) 48.9 0.008 0.008 Type D 15 (15.6) 30.4 0.008 Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* 0.001 0.001 Surgical methods 0.001 0.001 Laminectomy 32 (33.3) 39.6 0.001	OLF level						
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Number of OLF levels 1 63 (65.6) 46 2 26 (27.1) 42.3 0.634 >2 7(7.3) 40.3 0.876 CT axial classification Lateral 14 (14.6) 54.4	T5-T9	3 (3.1)	49.4	0.317			
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CT axial classification Lateral 14 (14.6) 54.4 Extended and enlarged 31 (32.3) 48.9 0.733 Fused 41 (42.7) 38.7 0.342 Tuberous 10 (10.4) 42.1 0.067 CT sagittal classification* Type N 38 (39.6) 48.9 48.9 Type O 32 (33.3) 43.2 2.048 Type D 15 (15.6) 30.4 0.008 Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001 Surgical methods Laminectomy 32 (33.3) 39.6 -	2	26 (27.1)	42.3	0.634			
Lateral 14 (14.6) 54.4 Extended and enlarged 31 (32.3) 48.9 0.733 Fused 41 (42.7) 38.7 0.342 Tuberous 10 (10.4) 42.1 0.067 CT sagittal classification* Type N 38 (39.6) 48.9 Type O 32 (33.3) 43.2 2.048 Type D 15 (15.6) 30.4 0.008 Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001 Surgical methods Laminectomy 32 (33.3) 39.6 ————————————————————————————————————	>2	7(7.3)	40.3	0.876			
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CT sagittal classification* Type N 38 (39.6) 48.9 Type O 32 (33.3) 43.2 2.048 Type D 15 (15.6) 30.4 0.008 Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001 Surgical methods Laminectomy 32 (33.3) 39.6	Fused	41 (42.7)	38.7	0.342			
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Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001 Surgical methods Laminectomy 32 (33.3) 39.6		32 (33.3)	43.2	2.048			
Type C 11 (11.5) 53.5 0.238 Signal intensity of spinal cord on T2WI* Present 81 (84.4) 40.6 40.6 Absent 15 (15.6) 66.1 0.001 Surgical methods Laminectomy 32 (33.3) 39.6	Type D	15 (15.6)	30.4	0.008			
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Surgical methods Laminectomy 32 (33.3) 39.6				0.001			
Laminectomy 32 (33.3) 39.6		· · · · · · · · · · · · · · · · · · ·	de la constanta				
		32 (33.3)	39.6				
				0.337			

TABLE 3. (Continued)						
	No. (%)	Recovery Rate (%)	P			
Posterior decompression and fusion with instru- mentation	9 (9.4)	42.1	0.964			
Ossification of dura mate	er*					
Present	43 (44.8)	34.3				
Absent	53 (55.2	53.0	0.001			
*Statistically significant difference ($P < 0.05$).						
OLF indicates ossification of the ligamentum flavum; CT, computed tomography.						

disorders, a lower preoperative JOA score, intramedullary high signal intensity on MR imaging, 10 and a longer duration of symptoms before surgical intervention.8 There has been only 1 report discussing OALL around OLF segments.¹⁶ In this study, duration of symptoms, ossification of dura mater, and discontinuous type of OALL on sagittal CT images were significantly important factors. A long duration of symptoms and compression to the spinal cord with OLF may cause irreversible injury to the spinal cord similar to what is seen in cervical myelopathy. There have been reports of the tuberous type of OLF frequently adhering to the dura mater, and the tuberous type tended to have a poor outcome in this study. Moreover, the ossification of dura mater may be related to multiple factors: duration of symptoms, difficulty in surgical technique, and postoperative instability because laminectomy is usually chosen to treat this type of OLF.8

Resnick et al²⁸ have used the term OALL interchangeably with diffuse idiopathic skeletal hypertrophy, which is characterized by flowing calcification/ossification of ligaments, particularly along the anterolateral aspect of the axial skeleton across contiguous vertebral bodies with preservation of intervertebral disc height. Although the rate of progression of OALL may be related to increased cervical motion,^{29,30} there is still a high incidence in the thoracic spine which is a relatively immobile region.³¹ We found a correlation between the presence of OALL around vertebral levels affected by OLF in our past study,16 suggesting an effect from mechanical stress arising from the OALL as well as the OLF.16 In this study, CT sagittal classification type D was a significantly important factor for a poorer outcome after OLF surgery, although multivariate analysis included both multilevel and single level OLF because there was only 1 single level subject that could be easily classified. This increased symptom severity and the poorer outcome may be due to the focusing of mechanical stress when the OALL is present both rostrally and caudally to the OLF intervertebral level (type D) and the addition of micromotion on the vulnerable spinal cord, even within the relatively stiff thoracic spine segments. In contrast, patients with type C had a good postoperative recovery, possibly because the continuous segment of the OALL still present

(Continued)

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table 4. Factors Related to Surgical Outcomes by Multivariate Logistic Regression Analysis						
	Odds Ratio (95% Confidence Interval)	P				
Mean age						
<60	1					
60–70	4.21 (0.68–26.18)	0.123				
>70	1.54 (0.30–7.97)	0.610				
Disease duration (mo)*						
<6	1					
6–12	2.53 (4.84–13.2)	0.001				
>12	3.02 (3.99–22.9)	0.001				
CT axial classification						
Lateral	1					
Extended and enlarged	2.74 (0.157–47.963)	0.490				
Fused	0.459 (0.047–4.468)	0.502				
Tuberous	1.358 (0.177–10.398)	0.768				
CT sagittal classification*						
Туре N	1					
Туре О	0.223 (0.02–2.471)	0.221				
Type D	0.068 (0.005–0.852)	0.037				
Туре С	0.091 (0.006–1.435)	0.088				
Signal intensity on T2WI						
Present	1					
Absent	0.497 (0.068–3.616)	0.490				
Ossification of dura mater*						
		1				

after decompression may have prevented additional micromotion about the spinal cord.

*Statistically significant difference (P < 0.05). CT indicates computed

0.104 (0.018-0.602)

There was no significant difference in the surgical outcomes among the 3 methods in this study. Unlike thoracic OPLL, it is possible to decompress the spinal cord directly by removing OLF from the posterior side. However, we thought that the area would need stability from instrumentation if the facets had not been preserved because of this approach. Furthermore, we speculate that better surgical outcomes are possible for patients with OALL type D using instrumentation that provides a more stable environment for the vulnerable spinal cord. Unfortunately, there was only 1 patient with OALL type D who underwent posterior fusion in this study. Further prospective studies on a greater number of patients

are needed for a better determination of the effects of surgical procedures on surgical outcomes for OLF and to compare fusion and nonfusion surgery. However, we think that OALL occurring around the OLF level is an important factor for predicting surgical outcome when there are myelopathic symptoms because OALL and OLF can be asymptomatic.

CONCLUSION

Ninety-six patients with thoracic OLF were evaluated in a multicenter study. Symptoms of thoracic OLF improved with surgery, but patients with longer duration of symptoms, ossified dura mater, and type D OALL had poorer surgical outcomes. A prospective study on the predictive factors for poor surgical outcome in thoracic OLF surgery will be necessary in the future.

Key Points

- Multi-institutional retrospective study of surgically treated patients with OLF in the thoracic spine was conducted.
- ☐ The mean JOA score was 5.6 points preoperatively and 7.8 points 2 years postoperatively, yielding a mean recovery rate of 44.6%.
- ☐ The presence of OALL found at or near the most severely affected OLF level on sagittal CT images was classified into 1 of 4 types: no discernible type (type N); one-sided type (type O); discontinuous (type D); and continuous type (type C).
- ☐ Disease duration, presence of ossified dura mater and type D OALL were the important factors for predicting surgical outcomes.

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DIAGNOSTICS

Prevalence, Distribution, and Morphology of Thoracic Ossification of the Yellow Ligament in Japanese

Results of CT-Based Cross-Sectional Study

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Study Design. A cross-sectional study.

Objective. To gain an insight for the prevalence, morphology, and distribution of thoracic ossification of the yellow ligament (OYL) by computed tomography (CT) and review of the literature.

Summary of Background Data. The epidemiology and etiology of OYL remains obscure. To date, to the best of our knowledge, there is no study that comprehensively evaluated thoracic spine by CT to assess the prevalence, distribution, and morphology of OYL in a large enough sample size with wide age distribution.

Methods. The participants of this study were the patients who have undergone chest CT for the examination of pulmonary diseases in our institute. The patients with previous thoracic spine surgery and younger than 15 years were excluded. Prevalence, distribution, and morphology of thoracic OYL were reviewed.

Results. A total of 3013 patients (1261 females and 1752 males) with the mean age of 65 years were recruited. The CT-based evidence of OYL was noted in 1094 (428 females and 666 males) individuals (36%). Single-level involvement was noted in 532 cases, whereas 562 individuals presented multilevel involvement.

Statistical analyses revealed that OYL was noted at a significantly higher rate among the males (P = 0.022). Of a total of 2051 OYLs, 779 central type OYLs, a mushroom-shaped ossification localized at the center of laminae, and 1272 noncentral type OYLs were noted. Distribution of the thoracic OYL formed 2 peaks with the highest and second highest peak found at T10–T11 and T4–T5, respectively.

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Interestingly, OYL is noted at consistent rates after the age of 30; however, its size increased in age-dependent manners.

Conclusion. The prevalence of thoracic OYL in Japanese was 36%. A further study disclosing the association between clinical manifestations and size and/or morphology of OYL is warranted.

Key words: ossification, yellow ligament, ligamentum flavum, thoracic spine, prevalence, epidemiology, morphology, classification, OYL, OLF.

Level of Evidence: N/A Spine 2013;38:E1216-E1222

ssification of the yellow ligament (OYL), synonymous with ossification of the ligamentum flavum (OLF), is characterized by the replacement of the yellow ligament with mature, lamellar bone. It was first described by Polgar in 1920² and can result in neurological compromises through compression of spinal cord. 1

OYL has been documented to occur predominantly in the East Asian population, particularly in Japanese.³ It has been reported that OYL is commonly associated with the lower thoracic spine and can affect both younger and elder individuals independent of sex.⁴

The recent genetic analyses have lead to increasing interests in understanding the underlying mechanism of ossifying plaques in OYL.⁵ However, much less attention has been paid for epidemiological aspects of this entity. Indeed, in the past 3 decades, there have been only 4 reports that described the prevalence of OYL in English literature.⁶⁻⁹ However, these studies impose several limitations such as sample size and/or the modality of diagnosis. Thus, the epidemiology and etiology of OYL remains obscure.

The thoracic spine is the most frequently involved area of OYL. However, standard plain radiograph is not an adequate modality of diagnosis of thoracic OYL due to complex anatomy of thoracic region. The radiographical evidence of OYL can be masked by superimposed bony structures such as ribs. ¹⁰ In contrast, computed tomography (CT), probably the most suitable modality to identify the ossification, allows us precise localization of thoracic OYL no matter what

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superimposition of the thoracic complexities.¹¹ To date, to the best of our knowledge, this study encompasses the largest sample of thoracic spine studied by CT scan with wide age distribution. In this study, we carefully evaluated prevalence, morphology, and distribution of OYL by CT and reviewed previously published literature.

MATERIALS AND METHODS

Participants

The participants of this study were the patients who have undergone chest CT scanning for the examination of pulmonary diseases in our institute from January 2010 to September 2010. A total of 3013 consecutive patients were recruited for the analysis. Of the total of 3013 patients, there were 1261 females and 1752 males, with the mean age of 65 years (range, 16–97 yr). The patients with previous thoracic spine surgery and younger than 15 years were excluded from the study. The presences of OYL as well as clinical parameters such as age, sex, and body mass index were retrospectively reviewed. The local ethics committee approved this study.

Radiological Examination

All chest CT scans were axial, 0.5-mm thick, sequential, and obtained in supine position without gantry tilt (120 kV, 160 mA, 0.5 s) using a Toshiba Aquilion CX (Toshiba Medical Systems Corporation, Japan). These data were reconstructed in the condition suitable for bone evaluation by the software

application (AquariusNet Viewer, TeraRecon, Inc., CA). This software application allows us to reconstruct optimal sagittal, coronal and axial views to identify OYL. On CT scans, lesions of OYL are seen as ossified masses arising from the lamina. Definitive OYL was determined according to the previous report with slight modifications. Briefly, a positive case of OYL was defined as a distinctive ossified plaque within the yellow ligament, but calcifications of the yellow ligament and facet osteophytes were excluded. Consistent with previous reports, ^{9,12,13} a differential diagnosis of these lesions could be made on CT. All CT scans were evaluated by 2 of the authors (K.M. and T.K.); differences were settled by consensus to minimize intra- and interobserver bias and errors.

To the best of our knowledge, there is no universally approved classification of OYL on CT. We therefore classified OYL into the following 5 subtypes: small, medium, large, extralarge, and central type according to previous reports with some modifications^{7,14,15} (Figure 1). An ossification that is distinctly identified on CT scan despite being smaller than 3 mm in its thickness was designated as "small." We designated an ossification that is larger than 3 mm in thickness but smaller than one-fourth of the anteroposterior diameter of the spinal canal as "medium." We designated those larger than one-fourth of the anteroposterior diameter of the spinal canal as "large," and those larger than half of the anteroposterior diameter as "extralarge." We designated central type, though not previously addressed, a mushroom-shaped ossification localized at the center of laminae where the



Figure 1. Classification of the ossification of yellow ligament on computed tomography. (A) *Small*: a clear ossification but smaller than 3 mm in thickness. (B) *Medium*: an ossification that is larger than 3 mm in thickness but smaller than one-fourth of the anteroposterior diameter of the spinal canal. (C) *Large*: an ossification larger than one-fourth of the anteroposterior diameter of the spinal canal. (D) *Extra large*: an ossification larger than half of the anteroposterior diameter. (E) *Central*: a mushroom-shaped ossification localized at the center of laminae.

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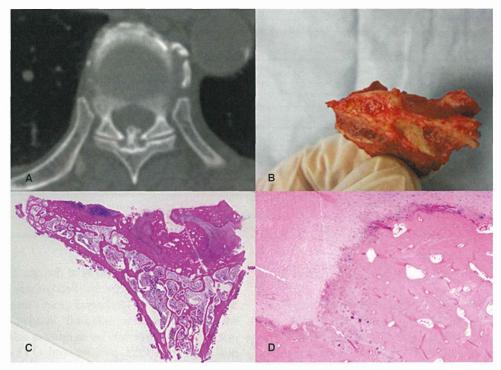


Figure 2. Radiological, macroscopical, and histological description of central type ossification of the yellow ligament. (**A**) Axial image of CT. (**B**) Macroscopic image of resected specimen. (**C**) Panoramic view of the resected specimen, (**D**) Histopathological examination of the resected specimen. The degenerated yellow ligament was gradually replaced by endochondral ossification. Cartilage cap as in osteochondroma was absent (original magnification ×100). CT indicates computed tomography.

Table 1).

ligamentum flavum is the thinnest. Because of its localization, we simply designated it as "central" type. The size of central type OYL was determined following the same criteria to that of the noncentral type OYL. We also evaluated the level and involvement pattern, either unilateral or bilateral involvements, of OYL.

Histological Evaluation

We have experienced the cases with thoracic myelopathy due to central type OYL, a mushroom-shaped ossification localized at the center of laminae where the ligamentum flavum is the thinnest (Figure 2A). We performed *en bloc* laminectomy to maintain the morphology of this central type OYLs (Figure 2B). The obtained samples were immediately fixed in 10% formaldehyde solution, decalcified and embedded in paraffin as a routine manner and proceeded to the histological evaluation.

Statistical Analysis

Student t test, Welch test, and χ^2 test were used when appropriate. P < 0.05 was considered as statistically significant. The software application used for the analysis was Stata/MP 12.0 (StataCorp LP, TX).

RESULTS

Distribution and Prevalence of OYLs

During this investigation, we often encountered a mushroomshaped ossification localized at the center of laminae where In total of OYL-positive individuals, single-level involvement was noted in 532 cases (49%), whereas 562 individuals (51%) presented multilevel involvement. Among those with multilevel involvements, OYL was noted at 2 levels in 326

Statistical analyses revealed that OYL was noted at a significantly higher rate among the males (P = 0.022). In addition, they also revealed that mean age of the OYL-positive individuals was significantly higher than that of the OYL-negative individuals (Table 1). This was due to the higher age of the OYL-positive males. The mean age of OYL-positive males was significantly higher than that of OYL-negative males, 68 and 65 for the OYL-positive and OYL-negative males, respectively, (P < 0.0001, Table 1).

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by endochondral ossification. Cartilage cap as in osteochon-

droma was not encountered. Accordingly, these finding are

were noted in 1094 (428 females and 666 males) individuals

(36%), and their mean age was 66 years (range, 16–93 yr,

The CT-based evidences of OYL including the central type

compatible with OYL (Figure 2C, D).

In turn, there was no difference in the age between the OYL-positive and OYL-negative females, 64 *versus* 64, respectively (P = 0.84, Table 1).

cases, at 3 levels in 137 cases, at 4 levels in 63 cases, 5 levels

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			0	YL		
	М	ale	Female		Total	
Physics 1	+		+		+	<u> </u>
Number	666	1086	428	833	1094	1919
Age (mean ± SD) (yr)	68 ± 12	65 ± 15	64 ± 14	64 ± 15	66 ± 13	64 ± 15
Р	<0.	0001	0.	84	0.0	013
BMI (mean ± SD) (kg/m²)	22 ± 3.4	22 ± 3.4	22 ± 3.4	22 ± 3.8	22 ± 3.4	22 ± 3.6
Р	0.	16	0.	 21	0.0)83

in 19 cases, 6 levels in 13 cases, 7 levels in 1 case, and 8 levels in 3 cases.

Of the total of 2051 levels of the spine involved with OYL, 779 central type OYLs and 1272 noncentral type OYLs were noted in the total 1094 OYL-positive individuals. Distribution of the OYLs in the thoracic segments formed 2 peaks with the highest and second highest peak found at T10-T11 and T4-T5, respectively (Figure 3). The highest peak consisted of noncentral type OYLs, but the second highest peak consisted mostly of the central type OYLs (Figure 3). We then compared the prevalence of OYL among each 10-year age group, that is, 10s, 20s, 30s and so on. OYL was noted at a consistent rate after the age of 30 with the noncentral type noted at around 25% and central type OYL at around 7.5%.

The total 1272 noncentral type OYLs consist of 468 (37%) small, 516 (40%) medium, 200 (16%) large, and 88 (6.9%) extralarge. In turn, the total 779 central type OYLs consist of 201 (26%) small, 356 (46%) medium, 150 (19%) large, and 72 (9.2%) extralarge types. Interestingly, percentages of larger OYL increased consistently in age-dependent manners in both noncentral and central type OYLs. Percentage of the large and extralarge in noncentral OYL increased from 0% and 0% of the age 20s to 23% and 9% of the age 80s, respectively. Percentage of the large and extralarge central OYL

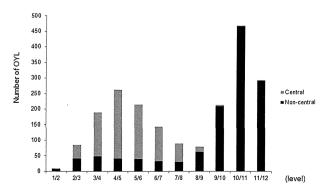


Figure 3. The distribution of 2051 OYLs. Distribution of the OYLs in the thoracic segments formed 2 peaks with the highest and second highest peak found at T10-T11 and T4-T5, respectively. OYL indicates ossification of the yellow ligament.

increased from 0% and 0% of the age 20s to 26% and 10% of the age 80s, respectively. (Percentages of other age groups: data not shown.) Unilateral involvement was observed in 443 cases, whereas bilateral involvement was observed in 829 cases. There was no significant difference of body mass index between OYL-positive and OYL-negative individuals (Table 1).

DISCUSSION

This study disclosed the precise prevalence of thoracic OYL in Japanese population. According to our review of the literature, this study covers the largest number of participants with wide range of age.

One must acknowledge that previous epidemiological studies with insufficient number of participants have hampered our knowledge. High prevalence of OYL has been reported among Asian, especially the Japanese. 1,4,6,8 Using conventional analysis of the radiographs of 1058 participants, Ohtsuka et al8 reported prevalence of OYL as 4.5%. In contrast, Al-Orainy and Kolawole¹² reported a much higher lumbar OYL prevalence of 35.4% by studying lumbar CT examination of 82 Saudis.

There have been few previous studies reporting the OYL prevalence among Caucasians with limited number of case reports of OYL. 16-18 Although OYL has been considered uncommon among Caucasians, Williams et all reported a prevalence of 26% among 100 American individuals using thoracic and abdominal CT scan. The increased prevalence reported by Williams et al7 might result from a higher detection rate enabled by CT scan. Al-Orainy and Kolawole¹² also assumed that higher detection rate by CT scan might have contributed to the higher prevalence of OYL in their study. These results suggest that the diagnostic modality has an important impact on the evaluation of the spinal ossification.

Through a review of English literature, we encountered 4 studies reporting the prevalence of thoracic OYL⁶⁻⁹ (Table 2). Three out of these 4 studies have reported the prevalence of OYL based on the general population^{6,8,9} Kudo et al⁶ reported a prevalence of 5.3% among 1744 general population using standard lateral "chest" radiographs. Ohtsuka et al8 reported a prevalence of 5.9% in males and 3.6% in females among

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TABLE 2. Previously Reported Prevalence of Ossification of the Yellow Ligament							
Reference	Country	Sample Size	Target	Mean Age (Range), yr	Modality	Prevalence (%)	
Kudo et al ⁶	Japan	1744	GP	NA (30-80<)	Lateral chest radiographs	Males: 6.2, Females: 4.8	
	United States	100	Р	Males: 47 (18–74)		26	
Williams <i>et al</i> ⁷				Females: 42 (5–89)	Chest and abdominal CT		
Ohtsuka <i>et al</i> ⁸	Japan	1058	GP	62.8 (50–80<)	Lateral thoracic spine radiographs	Males: 5.9, Females: 3.6	
Guo et al ⁹	China	1736	GP	38 (8–88)	MRI of whole spine, CT	3.8	
Mori et al (present study)	Japan	3013	Р	65 (16–97)	Chest CT*	36	

^{*}The data were reconstructed in the condition suitable for bone evaluation by the software application.

1058 general population using standard lateral thoracic spine radiographs. In turn, using whole spine magnetic resonance imaging analysis, Guo *et al*⁹ reported that the overall prevalence of 3.8% among 1736 Southern Chinese population. However, one must note that the participants' mean age of their study was much younger, that is, 38 years. Thus, all of the earlier listed 4 studies impose important limitations of diagnostic modality and/or age of participants.

The ligamentum flavum is a connective tissue that attached to the posterior side of the caudal lamina and the anterior side of the rostrally adjacent lamina. The ligamentum flavum extends laterally from the midline to the intervertebral foramen forming the superior-posterior boundary of the foramen. It then turns dorsally outside the foramen to fuse with the capsule of the articular facets.¹⁹ Histologically, the tissue consists of elastin and collagen. Functionally, the ligamentum flavum provides a static, elastic force to support the spinal column in its return to a neutral position after flexion and extension movements. Thus, when the ligamentum flavum is replaced by mature bone in OYL, its osseous morphology should be V shaped or a part of V shape on axial CT images (Figure 1A–D).

During this investigation, we often encountered a mush-room-shaped ossification localized at the center of laminae where the ligamentum flavum is the thinnest. Because of its localization, we simply designated it as a central type (Figure 1E). To the best of our knowledge, there have been 2 previous case reports, which addressed briefly the similar ossification^{7,15}; however, they did not establish an exact criterion of such ossification. In the image-based differential diagnoses of the OYL, conditions like calcifications of the yellow ligament, meningioma, and osteochondroma of the spine must be included. Morphologically speaking, the central type OYL mimics osteochondroma of the spine; however, spinal osteochondromas are uncommon etiology with the prevalence of only 1.3% to 4.1% of solitary osteochondromas.²⁰

Careful histological evaluation of surgically resected specimens of our central type OYLs revealed the absence of cartilage cap as in osteochondroma. In turn, the degenerated

ligamentum flavum was gradually replaced by endochondral ossification (Figure 2C, D). Accordingly, these finding are compatible with OYL, and its differential diagnoses were clearly ruled out. These findings were consistent with those of the previous report by Yanagi *et al*¹⁵ using fresh cadaver study.

Although it has been 90 years since the first description of OYL,² very little is known about the pathophysiology of OYL. Currently, hypotheses about the contribution of mechanical/ traumatic,^{11,21-23} metabolic,^{24,25} environmental,^{26,27} chronic degenerative,^{28,29} biological/hereditary,^{30,31} and genetic^{5,32} factors have been proposed. In turn, it still remains unknown how the central type OYL arises at the center of laminae where the ligamentum flavum becomes the thinnest; however, the likely explanation is the difference of mechanical stress.

Noncentral type OYLs predominantly occur in lower thoracic region where the spinal alignment is straight, whereas central type OYLs predominantly occur in high to midthoracic regions where the spinal alignment is kyphosis (Figure 3). Thus, distribution of different OYL types may have resulted from altered mechanical environments. Further examination to elucidate pathogenesis of the lesions is warranted.

Interestingly, OYL is noted at consistent rates after the age of 30 with the noncentral type noted at around 25% and the central type at around 7.5%. However, the size of OYL, particularly of the noncentral type OYL, increased in age-dependent manners. These findings suggest that inherent factors such as genetic background might also play an important role in susceptibility of OYL. In turn, the degenerative or mechanical process might contribute their growth; however, inter- and intrarelation of mechanical, degenerative and possibly genetic factors in the pathogenesis of OYL should be elucidated. Perhaps, longitudinal follow-up of general population study may contribute to this.

Prevalence of OYL among the general population may be much higher than once expected in general. Guo *et al*⁹ reported that 32% of cases in their series displayed multilevel involvements of OYL. Indeed, multilevel involvements of OYL were found in 51% in this study. Furthermore, OYL may occur in combination with ossification of posterior longitudinal

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GP indicates general population; P, patients; NA, not available; CT, computed tomography; MRI, magnetic resonance imaging

ligament of the spine (OPLL), which aggravates myelopathy if concomitantly present.³³ Takeuchi et al³⁴ reported case series of thoracic paraplegia due to neglected thoracic compressive lesions developing after lumbar decompression surgery. Taking these all findings into consideration; we advocate that the evaluation of whole spine not to overlook latent risk of concomitant OPLL and OYL when treating patients with ossification of the spinal ligaments.

This study is a patient-based study, but not a populationbased study. We used the data of chest CT examination for pulmonary diseases but not for general population. This is the inescapable limitation of this study. However, the favorable aspect of this study protocol is that it does not impose further radiological exposure on the participants.

CONCLUSION

Despite a thorough review of literature, there have been no previous studies addressing the relationship between OYL and pulmonary diseases. Nonetheless, it does not totally cancel the possibility that pulmonary diseases have no impact on the prevalence of OYL. Possible association between OYL and pulmonary diseases remains to be elucidated, perhaps by other studies. In addition, the patients with severe OYL with neurological compromise would have visited hospital for gait disturbance not for pulmonary diseases. Thus, it is possible that the prevalence of severe OYL may be underestimated. Another limitation of this study is that we cannot evaluate clinical manifestations and OYL observed in this study.

OYL are now widely recognized as a primary cause of radiculomyelopathy^{1,3}; however, they are usually asymptomatic when the lesions are small. Indeed, it has been reported that 25% of thoracic OYL are asymptomatic.³⁵ A further study that will make it possible to disclose the association between clinical manifestations and size and/or morphology of OYL is warranted.

➤ Key Points

- ☐ To date, this study covers the largest number of participants, which elucidate CT-based prevalence of OYL.
- ☐ The prevalence of thoracic OYL in Japanese was 36% and it is more frequent in males.
- ☐ This study designates a novel subtype of mushroom-shaped ossification localized at the center of laminae.
- ☐ We suggest that inherent and degenerative factors might play an important role in susceptibility

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Biomechanical analysis of the spinal cord in Brown-Séquard syndrome

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Abstract. Complete Brown-Séquard syndrome (BSS) resulting from chronic compression is rare and the majority of patients present with incomplete BSS. In the present study, we investigated why the number of cases of complete BSS due to chronic compression is limited. A 3-dimensional finite element method (3D-FEM) spinal cord model was used in this study. Anterior compression was applied to 25, 37.5, 50, 62.5 and 75% of the length of the transverse diameter of the spinal cord. The degrees of static compression were 10, 20 and 30% of the anteroposterior (AP) diameter of the spinal cord. When compression was applied to >62.5 or <37.5% of the length of the transverse diameter of the spinal cord, no increases in stress indicative of complete BSS were observed. Compression of 50% of the length of the transverse diameter of the spinal cord resulted in a stress distribution that may correspond to that in complete BSS cases, when the degree of compression was 30% of the AP diameter of the spinal cord. However, compression within such a limited range rarely occurs in clinical situations and, thus, this may explain why the number of cases with complete BSS is low.

Introduction

Brown-Séquard syndrome (BSS) is a syndrome consisting of ipsilateral upper motor neuron paralysis (hemiplegia) and loss of proprioception with contralateral pain and temperature sensation deficit. BSS is usually observed in association with traumatic spinal cord injuries, extramedullary spinal cord tumors, spinal hemorrhages, degenerative disease and infectious and inflammatory causes, including multiple scle-

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rosis (1). There have also been a few reports of BSS associated with intradural spinal cord herniation or disc herniation (2,3). Furthermore, complete BSS due to chronic compression is rare and most patients present with an incomplete form of this condition (4).

In the present study, a 3-dimensional finite element method (3D-FEM) was used to analyze the stress distribution of the spinal cord under various compression levels corresponding to five different lengths of the transverse diameter. Three levels of static compression corresponding to 10, 20 and 30% of the anteroposterior (AP) diameter were used for each of these five conditions. This model was used to investigate why the number of cases of complete BSS resulting from chronic compression is limited.

Materials and methods

Construction of the 3D-FEM spinal cord model. The Abaqus 6.11 (Dassault Systèmes Simulia Corp., Providence, RI, USA) standard finite element package was used for FEM simulation. The 3D-FEM spinal cord model used in this study consisted of gray and white matter and pia mater. In order to simplify calculation in the model, the denticulate ligament, dura and nerve root sheaths were not included. Pia mater was included since it has been demonstrated that spinal cord with and without this component shows significantly different mechanical behaviors (5). The spinal cord was assumed to be symmetrical about the mid-sagittal plane, so that only half the spinal cord required reconstruction and the whole model could be integrated by mirror image. This model simulated chronic compression of the cervical spinal cord. The vertebral canal model consisting of lamina was established by measuring 13 cervical computed tomographic myelographs (Fig. 1). A rigid flat plate was used as a compression factor from the anterior surface of the spinal cord and its width was 25, 37.5, 50, 62.5 and 75% of the length of the transverse diameter of the spinal cord (Fig. 2). The rigid flat plate was located at the longitudinal center of the spinal cord. The spinal cord consists of three distinct materials: the white and gray matter and the pia mater. The mechanical properties (Young's modulus and Poisson's ratio) of the gray and white matter were determined using data obtained from the tensile stress strain curve and stress relaxation tests under various strain rates (6,7). The

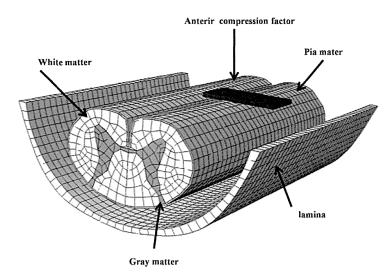
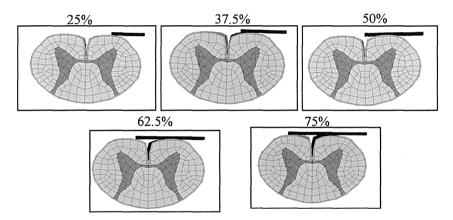


Figure 1. Three-dimensional finite element method (3D-FEM) model of the spinal cord and the vertebral canal model consisting of lamina.



 $Figure\ 2.\ The\ rigid\ flat\ plate\ applied\ compression\ to\ 25,37.5,50,62.5\ and\ 75\%\ of\ the\ length\ of\ the\ transverse\ diameter\ of\ the\ spinal\ cord.$

mechanical properties of the pia mater were obtained from a previous study (8). The mechanical properties of the lamina and flat plate were stiff enough to enable the spinal cord to be pressed. Based on the assumption that no slippage occurs at the interfaces of white and gray matter and pia mater, these interfaces were glued together. Data concerning the friction coefficient between the bone and spinal cord were not available. The coefficient of friction between lamina and the spinal cord was 'glue' at the contact line and 'frictionless' next to the part in contact. Similarly, the coefficient of friction between the rigid flat plate and spinal cord was 'glue' at the contact interfaces and 'frictionless' next to the part in contact. To simulate the axial injury model of the spinal cord, nodes at the bottom and top of the spinal cord model were constrained in all directions. The spinal cord and the rigid flat plate were symmetrically meshed with 20-node elements. With a FEM model of 50% of the length of the transverse diameter of the spinal cord, the total number of isoparametric 20-node elements was 12,535 and the total number of nodes was 76,993.

Static compression model. For the simulation of BSS, anterior static compression was applied to the spinal cord by the rigid flat plate at 25, 37.5, 50, 62.5 and 75% of the length of

the transverse diameter of the spinal cord. The degrees of compression were 10, 20 and 30% of the AP diameter of the spinal cord. A 10% compression was first applied to the spinal cord, followed by compressions of 20 and 30%. In total, 15 different compression combinations were evaluated.

Results

Under compression of 25% of the length of the transverse diameter of the spinal cord with a rigid flat plate, the stresses were extremely low when the degree of compression was 10% of the AP diameter of the spinal cord. The stress was confined to part of the gray matter and to the anterior funiculus. At 20% compression, the stress on the anterior horn and part of the anterior funiculus was slightly increased. At 30% compression, high stresses were observed in the gray matter, anterior funiculus and part of the lateral funiculus, but not the posterior funiculus (Fig. 3A).

Compression of 37.5% of the length of the transverse diameter of the spinal cord with a rigid flat plate resulted in stresses that were very low when the compression of the AP diameter of the spinal cord was 10%. The stresses on the gray matter and anterior funiculus were slightly increased when 20% compression was applied. At 30% compression, high stresses

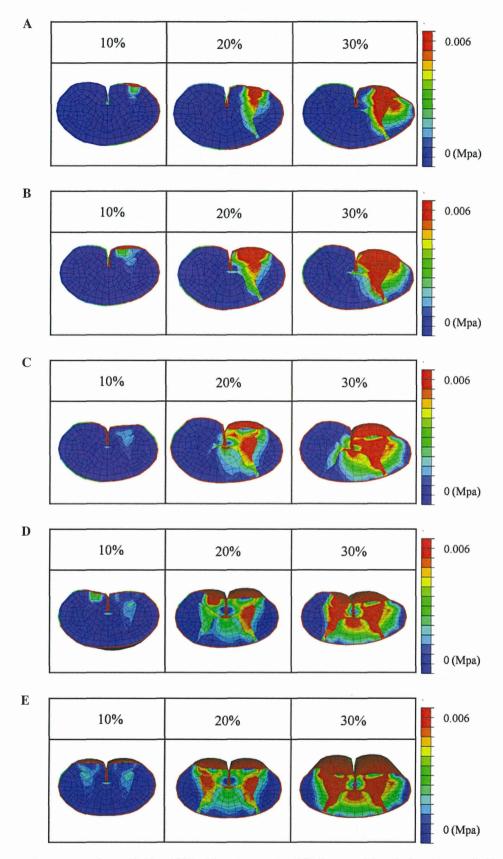


Figure 3. Static compression corresponding to 10, 20 and 30% of the anteropostrior (AP) diameter of the spinal cord was applied by compression of (A) 25, (B) 37.5, (C) 50, (D) 62.5 and (E) 75% of the length of the transverse diameter of the spinal cord with a rigid flat plate.

were observed in the gray matter, anterior funiculus and lateral funiculus, while the stress was moderately increased in part of the posterior funiculus (Fig. 3B).

When 50% of the length of the transverse diameter of the spinal cord was compressed with a rigid flat plate, the stress was very low when the degree of compression was 10% of