Orthopaedic Surgery

Open Access

CLINICAL ARTICLE

Progression of Spinal Ligament Ossification in Patients with Thoracic Myelopathy

Jiliang Zhai, MD[1], Shigong Guo, MD[2], Jiahao Li, BM[1], Bingrong Chen, BM[1], Yu Zhao, MD[1]

[1]*Department of Orthopaedic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing, China and* [2]*Department of Rehabilitation Medicine, Southmead Hospital, Bristol, UK*

Objective: To evaluate the rate of increase in thickness and cross-section area (CSA) of the ossification in thoracic myelopathy with or without cervical and lumbar spinal ligament ossification.

Methods: A total of 24 patients with 170 segments (47 ligamentum flavum [OLF] and 123 cases of ossification of the posterior longitudinal ligament [OPLL]) of spinal ligament ossification between January 2012 and March 2019 at a single institution were retrospectively reviewed. Demographic data, classification of OPLL, Sato classification of OLF, pre- and postoperative neurological function and complications were recorded. The thickness and CSA at the segment of maximum compression were measured with Image J software on the axial CT image.

Results: Twelve female and 12 male patients with thoracic myelopathy and spinal ligament ossification were enrolled in the study. The mean age of the patients was 54.0 ± 11.9 years with an average follow-up of 22.2 ± 23.5 months. Overall, the mean rate of progression in thickness and CSA was 1.2 ± 1.6 and 18.4 ± 50.6 mm^2/year, respectively. Being female, aging (≥45 years), and lower BMI (<28 kg/m^2) predisposed patients to have faster ossification growth in thickness and CSA. The difference between the rate of OPLL and OLF progression in thickness and CSA was not significant. However, the rate of OPLL progression in the thoracic spine was significantly higher than that in the cervical spine regarding thickness (1.4 ± 1.9 vs. 0.6 ± 0.7 mm/year) and CSA (27.7 ± 72.0 vs. 7.3 ± 10.3 mm^2/year).

Conclusion: This is the first study to investigate ligament ossification progression in patients with thoracic myelopathy. The difference between the rate of OPLL and OLF progression in thickness and CSA was not significant. However, the rate of thoracic OPLL progression in thickness and CSA was significantly higher than that in the cervical spine.

Key words: ossification of the ligamentum flavum; ossification of posterior longitudinal ligament; spinal ligaments; ossification; cross-sectional area

Introduction

Ossification of spinal ligaments includes ossification of the posterior longitudinal ligament (OPLL), ligamentum flavum (OLF), anterior longitudinal ligament, and supra/interspinous ligament.[1] OPLL and OLF attracted greater attention from clinicians because they can cause spinal cord compression and neurological disability.

In Japan, the incidence of OPLL among patients with spinal diseases was between 1.9% and 4.3%, and the rate of cervical and thoracic OPLL was 3.2% and 0.8%, respectively.[2] Other Asian countries have a similar prevalence as Japan, which was reported to be up to 3.0%.[3] However, the prevalence was much lower in North American and European countries, which ranged from 0.1% to 1.7%.[4,5] The prevalence of OLF also varies depending on the diagnostic imaging method used. In Japan, the rate of OLF in the outpatient setting when using plain X-ray films was about 4.5%,[6] and the incidence in men and women was 6.2% and 4.8%, respectively.[7] However, when using computer tomography (CT), the prevalence of thoracic OLF was a high as 36% in a study

Address for correspondence Yu Zhao, MD, Department of Orthopaedic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shuaifuyuan 1#, Dongcheng District, Beijing 100730, China; Email: zhaoyupumch@163.com
Jiliang Zhai and Shigong Guo contributed equally to this manuscript.
Funding information This work was supported by a grant from the National Natural Science Foundation of China (NO. 82072508).
Received 3 December 2021; accepted 29 March 2022

of 3013 patients with respiratory diseases in Japan.[8] In southern China, a survey of 1736 healthy volunteers who underwent whole-spine magnetic resonance imaging (MRI) found OLF in 3.8% of all cases, and multilevel OLF in 31.8% of the OLF cases.[9] The prevalence of thoracic, lumbar, and cervical OLF was approximately 38.5%, 26.5%, and 0.9%, respectively.[10,11] Moreover, ossified ligament disease was often multifocal or coexisted with each other.[7,12,13] Cervical OPLL could coexist with OLF with a rate of up to 64.6%,[14] and combined with thoracic OPLL or OLF with a rate of 29.2%[15] and 34%,[16,17] respectively.

Multiple segments of spinal ligaments ossification are common in patients with myelopathy.[18] Generally, treatment for these patients is a resection of the symptomatic segment alone followed by careful observation of the remaining segments.[19,20] However, the surgical results were not always satisfactory if ossification coexisted in other segments,[18] and it was not uncommon for surgeons to have to resect the ossified lesions at multiple segments with additional surgeries.[19] In several studies, radiographic progression of cervical OPLL was observed in about 70% of patients after laminoplasty and adversely affected long-term outcomes.[21] Yu *et al.*[18] reported that late neurological function deficit was observed in four cases (5.1%), due to the occurrence of thoracic OLF and/or OPLL compression in nonoperative segments at more than 4 years of follow-up.

Progression of ossification or recurrence of compression of the spinal cord could induce neurological deterioration and reduce patient satisfaction following surgical decompresion.[22–24] Thus, prediction of the progression of ossification of spinal ligaments is necessary. Radiographic progression of cervical OPLL has been reported in previous studies. In regards to the effects of surgical intervention on the natural history of OPLL, several case series studies of laminoplasty with a follow-up of more than 10 years showed that axial progression of OPLL presented in as many as 50%–70% of patients.[25] However, the progression of spinal ligament ossification in patients with thoracic myelopathy has not been explored before. The aims of this study were: (i) to evaluate the rate of increase in thickness and cross-section area (CSA) of the ossification in thoracic myelopathy with or without cervical and lumbar spinal ligament ossification; (ii) to analyze the factors related with the rate of growth in thickness and CSA; (iii) to study the relation between the growth of ossified ligament and neurological function.

Methods

Patients

A total of 149 patients with thoracic spinal stenosis at a single institution between January 2012 and March 2019 were retrospectively reviewed. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethical Committee of Peking Union Medical College Hospital (NO.S-K1941). Patient consent was not needed as this was a retrospective review of patient notes with no identifiable information. The inclusion criteria were as follows: (i) diagnosis of thoracic myelopathy due to OLF or/and OPLL, and patient who underwent posterior thoracic decompression and fusion with instrumentation; (ii) initial and subsequent follow-up CT scans using the same imaging protocol; (iii) OPLL or OLF present in follow-up CT images.

The exclusion criteria were the presence of thoracic disc herniation, ankylosing spondylitis, thoracic spinal fracture, spinal deformity, infection and tumor.

Demographic data, classification of OPLL, Sato classification of OLF,[26] pre- and postoperative neurological function and complications were recorded. The Japanese Orthopaedic Association (JOA) scoring system (17-point scale) was used to evaluate pre- and postoperative neurological status.

Radiographic Measurement

Image J software (National Institutes of Health) was used for radiographic measurement. Two observers who were orthopaedic spinal surgeons independently interpreted the radiological findings and performed the measurements. All images were reviewed twice by each observer, and the mean findings were used in the analysis. The thickness of the ligament ossification was measured using anteroposterior diameter (APD) for OPLL and unilateral diameter (UD) for OLF, and CSA was defined as the area of ossification mass.

Measurement of Anteroposterior Diameter and Unilateral Diameter

First, we made a calibration for Image J software according to the scale on the axial CT image at the segment of maximum compression. Then, we drew a line from the anterior to the posterior margin of the ossification mass for OPLL, and the Image J software automatically calculated the thickness (a) of the mass (Figure 1A), which was defined as APD. The maximum thickness of the unilateral ossified mass from top to bottom (d) was measured as UD for OLF (Figure 1B).

Measurement of Cross-Section Area

After making a calibration for Image J software on the axial CT image, we drew a circle around the mass on the CT image and the Image J software automatically calculated the CSA of the mass (Figure 1C,D).

Statistical Analysis

The Statistical Package for Social Sciences (SPSS Inc.) software was used for data analysis. Interclass correlation coefficients (ICCs) were used to assess interobserver reliability. *t*-test and Mann–Whitney *U*-test were used for continuous variables. Pearson's and Spearman's correlation coefficients were used to analyze the association between the rate of growth in thickness of CSA and sex, age, body mass index (BMI), location of ossification, and other factors. A p value <0.05 was considered statistically significant.

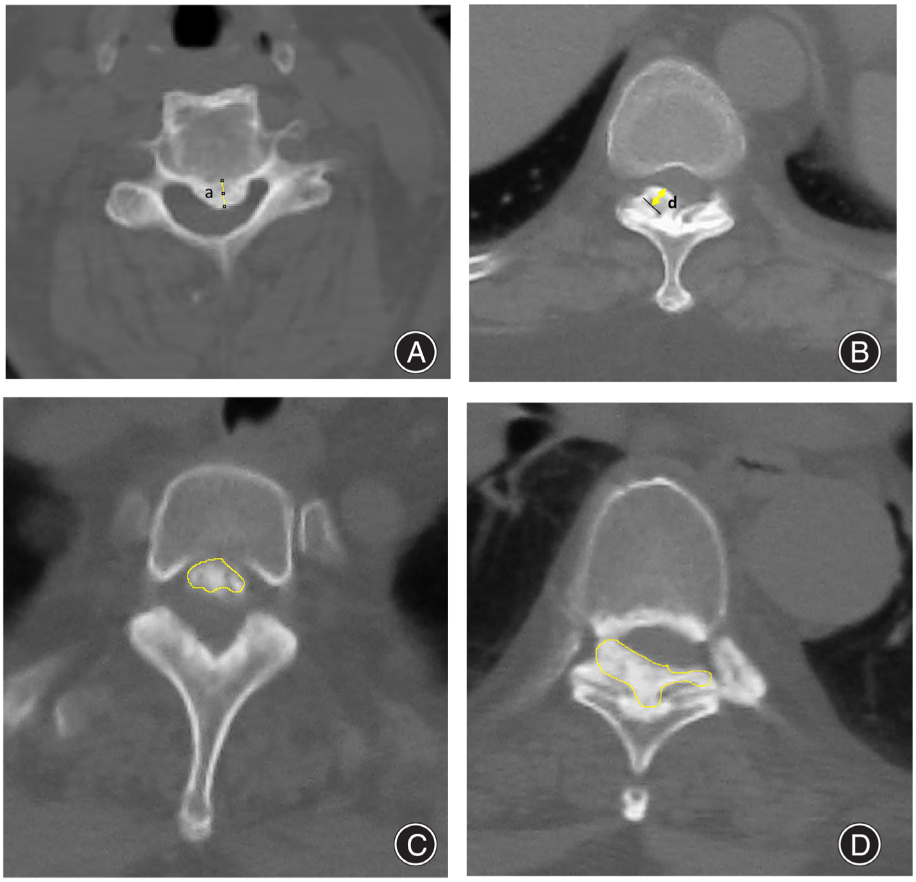

Fig. 1 Measurement of the thickness and CSA of ligament ossification. (A), APD of OPLL was the length from the anterior to the posterior margin of ossification mass (a). (B), UD of OLF was the thickness of unilateral ossified mass from top to bottom (d). (C) and (D), CSA of OPLL and OLF was the cross-section area of the ossified mass, which was automatic calculated by Image J software.

Results

Demographics

Twenty-four consecutive patients (12 female and 12 male) with 170 segments (47 OLF and 123 OPLL) of spinal ligament ossification were ultimately included in the analysis (Table 1). The mean age of the patients was 54.0 ± 11.9 years (range 30–70 years) with an average follow-up of 22.2 ± 23.5 months (range 3.0–79.7 months). The average value of BMI was 29.4 ± 5.0 kg/m^2 (range 20.4 ± 46.5 kg/m^2).

Clinical Results

According to Sato classification, 11 segments of OLF were classified as lateral type, 10 segments were extended type, one was enlarged type, 20 were fused type, and five were tuberous type. The type of OPLL was classified as focal in 14 segments, continuous in 18, segmented in 81, and mixed in 10. Twelve of the patients underwent a second thoracic spinal canal decompression and fusion due to either ossification progression and/or aggravation of neurological dysfunction following the initial surgery. One patient underwent revision surgery due to malposition of the screw and surgical site infection. One patient suffered from a urinary tract infection and recovered after completing a course of intravenous antibiotics. The JOA score improved from 13.3 ± 1.8 preoperatively to 14.2 ± 1.9 postoperatively. However, the mean score decreased to 12.6 ± 2.2 at the last follow-up and four patients suffered from neurological deficit during the follow-up period.

TABLE 1 Location of the ossified ligament

	Cervical	T1–4	T5–8	T9–12	Lumbar
OLF	/	10	19	15	3
OPLL	37	40	23	15	8

The Rate of Progression in Thickness and Cross-Section Area

The ICC value for inter-observers and intra-observers, who were responsible for the radiographic measurement, was 0.917 (95% confidence interval [CI], 0.909–0.969) and 0.965 (95% CI, 0.942–0.972), respectively. The mean rate of progression of all the segments in the thickness and CSA was 1.2 ± 1.6 and 18.4 ± 50.6 mm^2/year, respectively. The rate of ossification growth in patients with different gender, age, and BMI were shown in Table 2. The rate of growth in thickness were similar between males and females ($t = -1.774$, $p = 0.078$) while the rate of CSA increase was

TABLE 2 Subanalysis the rate of ossification growth in patients with different gender, age, and BMI

	Gender		Age (years)			BMI (kg/m^2)	
	Male	Female	<45	45–59	≥60	<28	≥28
Thickness (mm/year, mean ± SD)	0.9 ± 1.4	1.4 ± 1.7	0.5 ± 0.6	1.4 ± 2.0	1.2 ± 1.2	1.5 ± 1.9	0.8 ± 1.0
CSA (mm^2/year, mean ± SD)	8.5 ± 14.0	25.9 ± 65.0	5.1 ± 4.8	26.9 ± 70.6	14.0 ± 16.2	26.9 ± 67.3	8.6 ± 11.2

significantly higher in females than that in males ($t = -2.569$, $p = 0.012$). In age subgroup analysis, the middle aged and elderly patients had similar growth rates. Young patients (<45 years) had significantly lower rate of thickness growth and CSA growth as compared to the middle aged (45–59 years) ($p = 0.005$ and 0.032, respectively). Young patients also had significantly lower thickness growth rate as compared to the elderly patients while the difference did not reach significant level in the CSA growth rate ($p = 0.035$ and 0.416, respectively). The rate of ossification development was significant slower in patients with higher BMI (≥28 kg/m^2) than that in patients with BMI less than 28 kg/m^2 ($t = 2.705$ and 2.547, $p = 0.008$ and 0.012, respectively).

Comparison of Ossification Progression between Ossification of Posterior Longitudinal Ligament and Ossification of Ligamentum Flavum

During the follow-up period, the mean rate of increase of thickness was 1.1 ± 1.4 and 1.2 ± 1.7 mm/year and the rate of progression of CSA was 13.4 ± 18.0 and 20.3 ± 58.3 mm^2/year in the group of OLF and OPLL, respectively. There were no significant differences between the two groups referring to the rate of ossification progression in thickness and CSA ($t = -0.276$ and -0.796, $p = 0.783$ and 0.427, respectively). For thoracic OPLL and OLF, the rate of progression in thickness was 1.4 ± 1.9 and 1.0 ± 1.1 mm/year, and the rate of progression in CSA was 27.7 ± 72.0 and 13.4 ± 18.5 mm^2/year, respectively. The difference between the rate of thoracic OPLL and OLF progression in thickness and CSA was also not significant ($t = -1.413$ and -1.657, $p = 0.160$ and 0.101, respectively). However, the rate of OPLL progression in thickness (1.4 ± 1.9 *vs* 0.6 ± 0.7 mm/year, $t = -3.267$, $p = 0.001$) and CSA (27.7 ± 72.0 *vs* 7.3 ± 10.3 mm^2/year, $t = -2.453$, $p = 0.016$) in the thoracic spine were significantly higher than that in the cervical spine.

Discussion

The Rate of Ossification of Posterior Longitudinal Ligament Progression

Cervical OPLL progression was reported in patients who were treated conservatively[27–29] or surgicaly.[25,30–32] Ogawa *et al.*[30] retrospectively reviewed 72 patients with cervical OPLL who underwent laminoplasty and were followed up with a mean time of 9.5 years. A total of 63.9% of the patients had OPLL progression of more than 2 mm and the thickness increased by a mean of 3.9 mm, with a length increase of 26.3 mm. In a serial radiographic analysis of laminoplasty for more than 10 years, cervical OPLL longitudinal progression was seen with a mean of 12.8 mm, combined with a mean of 3.4 mm in thickness. The mean progression per year was 1 mm in length, and 0.3 mm in thickness.[31] Kato *et al.*[32] performed a serial radiographic analysis of 44 patients who underwent laminectomy with a mean follow-up of 14.1 years. A total of 70% of them had OPLL progression, and the mean longitudinal and transverse spread were 10.5 and 3.2 mm, respectively.[32] The mean rate of progression of cervical OPLL in thickness and length in these studies was approximately 0.3 mm/year (0.23 ~ 0.41 mm/year) and 1 mm/year (0.7 ~ 2.7 mm/year), respectively. Although many studies had been presented about cervical OPLL progression, no study had investigated the increase of ligament ossification in patients with thoracic OPLL in previous studies. The rate of OPLL progression in thickness in our study was significantly higher than that in cervical OPLL in previous studies, whether in cervical (0.6 mm/year) or thoracic spine (1.4 mm/year). Besides, our study showed that the rate of OPLL progression in thoracic spine was significantly higher than that in cervical spine regarding CSA (27.7 *vs* 7.3 mm^2/year). A plausible explanation for these different results could be that the cases enrolled in our study were different and most of the thoracic OPLL cases coexisted with OLF and had greater potential to ossify. However, the mechanism was not fully understood and may need further study.

The Rate of Ossification of Ligamentum Flavum Progression

The risk factors for presence of OLF including ageing, genetic predisposition, metabolic abnormalities, mechanical stress, and fusion of adjacent intervertebral levels.[23] However, the underlying etiology and pathogenesis of OLF progression after surgery are mostly unknown and may similar to OPLL,[33] which included (i) surgical stimulation, (ii) mechanical stress change, (iii) spontaneous growth of ossification, and (iv) postoperative instability.[34] Until now, there were no studies related to the growth rate of OLF. Our study is the first one to report the growth rate of OLF, which was 1.1 ± 1.4 and 13.4 ± 18.0 mm^2/year in thickness and CSA, respectively. And the rate of thoracic OLF progression in thickness and CSA was 1.0 and 13.4 mm^2/year, respectively. Besides, we found no significant differences between the two groups of OLF and OPLL in terms of the rate of ossification progression in thickness and CSA.

Risk Factors for the Growth of Ligament Ossification

Multiple regression modeling showed that age at operation and type of OPLL were significant predictors of postoperative longitudinal and transverse progression of OPLL. Younger age at operation and a mixed or continuous pattern of ossification were found to be highly predictive of progression of OPLL.[25,31] Katsumi *et al.*[28] evaluated 41 conservatively treated cervical OPLL patients with CT-based 3D analysis. The increase of ossification volume was 7.5% with a mean annual rate of 4.1%. Younger age is the most significant predictor of OPLL progress and the highest rate presented in the 30–49 years' age group. This study also demonstrated that there was no effect of gender, diabetes, family history, and OPLL type and location on the rate of lesion progression. In contrast, the risk factors of the increase of ossification in our study included age, gender, and BMI. Being female, aging (≥45 years), and lower BMI (<28 kg/m^2) predisposed to have faster ossification growth in thickness and CSA. We also found the rate of OPLL progression in the thoracic spine was significantly higher than that in the cervical spine regarding thickness (1.4 ± 1.9 vs. 0.6 ± 0.7 mm/year) and CSA (27.7 ± 72 vs. 7.3 ± 10.3 mm^2/year).

Relation between Ligament Ossification and Neurological Deficit

The relationship between the progression of ligament ossification and neurological decline is controversial and only correlation between cervical OPLL progression and neurological deficit was reported in the past. Although there have been reports of the low prevalence of symptomatic OPLL progression after laminoplasty, the frequency of OPLL progression has also been reported to be as high as 70%.[34] Some studies showed that pathological compression by the ossified ligament below a certain critical point may not induce myelopathy.[27,35] However, other investigators insisted that the progression of OPLL after laminoplasty should not be overlooked.[34,35] Until now, there have been no studies exploring the relationship between thoracic ossification progression and neurological deterioration. Twelve patients in this study underwent a second thoracic spinal decompression and fusion due to ossification progression and worsening neurological dysfunction. Pre- and postoperative JOA of these patients were significantly lower than that in the patients without a second surgery. However, it was not related to age, BMI, the thickness, and CSA of ossification lesion.

Limitations

There were several potential limitations to this study. Firstly, only 24 patients were enrolled in this study due to the strict inclusion criteria. However, 170 segments of ligament ossification were able to be analyzed. Secondly, due to technical limitations, it may not have always been possible for the radiological images to be cut at exactly the same cutting angles, which could theoretically lead to potential variability in the imaging assessment for ossification. However, as CT scans using the same protocol were included in this study and the ICC calculated in this study was noticeably high, this suggests that radiographic evaluation of ossification was accurate and valid. Thirdly, as the mean follow-up was less than 2 years, a longer follow-up period should be considered in future studies.

Conclusions

To our knowledge, this is the first study to investigate the progression of ligament ossification in patients with thoracic myelopathy. Overall, the mean rate of progression in thickness and CSA was 1.2 ± 1.6 and 18.4 ± 50.6 mm^2/year, respectively. Being female, aging (≥45 years), and lower BMI (<28 kg/m^2) predisposed to have faster ossification growth in thickness and CSA. As for OLF and OPLL, the mean rate of increase of thickness was 1.1 ± 1.4 and 1.2 ± 1.7 mm/year and the mean progress of CSA was 13.4 ± 18.0 and 20.3 ± 58.3 mm^2/year, respectively. The results showed that the difference between the rate of OPLL and OLF progression in thickness and CSA was not significant. However, the rate of OPLL progression in thickness and CSA in the thoracic spine was significantly higher than that in the cervical spine. Understanding the nature of ossification progression and its clinical sequelae may aid the physician in the diagnosis, treatment, rehabilitation, and prognostication of patients with thoracic myelopathy.

Authors' Contributions

Prof. Yu Zhao and Jiliang Zhai conceived, designed, and supervised the study; radiographic measurement was done by Jiliang Zhai and Jiahao Li; Bingrong Chen led the statistical analysis of the data; The first draft of the manuscript was written by Jiliang Zhai and edited by Shigong Guo. All authors read and approved the final manuscript before submission.

Conflicts of Interest

None.

Acknowledgements

None.

References

1. Ohara Y. Ossification of the ligaments in the cervical spine, including ossification of the anterior longitudinal ligament, ossification of the posterior longitudinal ligament, and ossification of the ligamentum flavum. Neurosurg Clin N Am. 2018;29:63–8.
2. Kurosa Y, Yamaura I, Nakai O, Shinomiya K. Selecting a surgical method for thoracic myelopathy caused by ossification of the posterior longitudinal ligament. Spine (Phila Pa 1976). 1996;21:1458–66.
3. Matsunaga S, Sakou T. Ossification of the posterior longitudinal ligament of the cervical spine: etiology and natural history. Spine (Phila Pa 1976). 2012;37:E309–14.
4. Belanger TA, Roh JS, Hanks SE, Kang JD, Emery SE, Bohlman HH. Ossification of the posterior longitudinal ligament. Results of anterior cervical decompression

and arthrodesis in sixty-one North American patients. J Bone Joint Surg Am. 2005;87:610–5.
5. Boody BS, Lendner M, Vaccaro AR. Ossification of the posterior longitudinal ligament in the cervical spine: a review. Int Orthop. 2019;43:797–805.
6. Hirabayashi S. Ossification of the ligamentum flavum. Spine Surg Relat Res. 2017;1:158–63.
7. Gao R, Yuan W, Yang L, Shi G, Jia L. Clinical features and surgical outcomes of patients with thoracic myelopathy caused by multilevel ossification of the ligamentum flavum. Spine J. 2013;13:1032–8.
8. Mori K, Kasahara T, Mimura T, et al. Prevalence, distribution, and morphology of thoracic ossification of the yellow ligament in Japanese: results of CT-based cross-sectional study. Spine (Phila Pa 1976). 2013;38:E1216–22.
9. Guo JJ, Luk KD, Karppinen J, Yang H, Cheung KM. Prevalence, distribution, and morphology of ossification of the ligamentum flavum: a population study of one thousand seven hundred thirty-six magnetic resonance imaging scans. Spine (Phila Pa 1976). 2010;35:51–6.
10. Hirabayashi H, Ebara S, Takahashi J, et al. Surgery for thoracic myelopathy caused by ossification of the ligamentum flavum. Surg Neurol, 2008,69:114–116, 116.
11. Chachan S, Kasat NS, Keng P. Cervical Myelopathy Secondary to Combined Ossification of Ligamentum Flavum and Posterior Longitudinal Ligament-A Case Report. Int J Spine Surg. 2018;12:121–5.
12. Yu L, Li B, Yu Y, Li W, Qiu G, Zhao Y. The Relationship Between Dural Ossification and Spinal Stenosis in Thoracic Ossification of the Ligamentum Flavum. J Bone Joint Surg Am. 2019;101:606–12.
13. Yu Y, Li W, Yu L, Qu H, Niu T, Zhao Y. Population-based design and 3D finite element analysis of transforaminal thoracic interbody fusion cages. J Orthop Translat. 2020;21:35–40.
14. Kawaguchi Y, Nakano M, Yasuda T, et al. Characteristics of ossification of the spinal ligament; incidence of ossification of the ligamentum flavum in patients with cervical ossification of the posterior longitudinal ligament - analysis of the whole spine using multidetector CT. J Orthop Sci. 2016;21:439–45.
15. Ono M, Russell WJ, Kudo S, et al. Ossification of the thoracic posterior longitudinal ligament in a fixed population. Radiological and neurological manifestations. Radiology. 1982;143:469–74.
16. Fujimori T, Watabe T, Iwamoto Y, Hamada S, Iwasaki M, Oda T. Prevalence, concomitance, and distribution of ossification of the spinal ligaments: results of whole spine CT scans in 1500 Japanese patients. Spine (Phila Pa 1976). 2016; 41:1668–76.
17. Park JY, Chin DK, Kim KS, Cho YE. Thoracic ligament ossification in patients with cervical ossification of the posterior longitudinal ligaments: tandem ossification in the cervical and thoracic spine. Spine (Phila Pa 1976). 2008;33:E407–10.
18. Yu S, Wu D, Li F, Hou T. Surgical results and prognostic factors for thoracic myelopathy caused by ossification of ligamentum flavum: posterior surgery by laminectomy. Acta Neurochir (Wien). 2013;155:1169–77.
19. Inamasu J, Guiot BH. A review of factors predictive of surgical outcome for ossification of the ligamentum flavum of the thoracic spine. J Neurosurg Spine. 2006;5:133–9.
20. Kuh SU, Kim YS, Cho YE, et al. Contributing factors affecting the prognosis surgical outcome for thoracic OLF. Eur Spine J. 2006;15:485–91.
21. Katsumi K, Izumi T, Ito T, Hirano T, Watanabe K, Ohashi M. Posterior instrumented fusion suppresses the progression of ossification of the posterior longitudinal ligament: a comparison of laminoplasty with and without instrumented fusion by three-dimensional analysis. Eur Spine J. 2016;25: 1634–40.
22. Chen Y, Chen DY, Wang XW, Lu XH, Yang HS, Miao JH. Single-stage combined decompression for patients with tandem ossification in the cervical and thoracic spine. Arch Orthop Trauma Surg. 2012;132:1219–26.
23. Kanno H, Takahashi T, Aizawa T, Hashimoto K, Itoi E, Ozawa H. Recurrence of ossification of ligamentum flavum at the same intervertebral level in the thoracic spine: a report of two cases and review of the literature. Eur Spine J, 2018,27-*Suppl* 3:359–367.
24. Kim JK, Ryu HS, Moon BJ, Lee JK. Clinical Outcomes and Prognostic Factors in Patients With Myelopathy Caused by Thoracic Ossification of the Ligamentum Flavum. Neurospine. 2018;15:269–76.
25. Inamasu J, Guiot BH, Sachs DC. Ossification of the posterior longitudinal ligament: an update on its biology, epidemiology, and natural history. Neurosurgery. 2006;58:1027–39.
26. Ahn DK, Lee S, Moon SH, Boo KH, Chang BK, Lee JI. Ossification of the ligamentum flavum. Asian Spine J. 2014;8:89–96.
27. Matsunaga S, Kukita M, Hayashi K, et al. Pathogenesis of myelopathy in patients with ossification of the posterior longitudinal ligament. J Neurosurg. 2002;96(2 Suppl):168–72.
28. Katsumi K, Watanabe K, Izumi T, et al. Natural history of the ossification of cervical posterior longitudinal ligament: a three dimensional analysis. Int Orthop. 2018;42:835–42.
29. Izumi T, Hirano T, Watanabe K, Sano A, Ito T, Endo N. Three-dimensional evaluation of volume change in ossification of the posterior longitudinal ligament of the cervical spine using computed tomography. Eur Spine J. 2013;22: 2569–74.
30. Ogawa Y, Toyama Y, Chiba K, et al. Long-term results of expansive open-door laminoplasty for ossification of the posterior longitudinal ligament of the cervical spine. J Neurosurg Spine. 2004;1:168–74.
31. Iwasaki M, Kawaguchi Y, Kimura T, Yonenobu K. Long-term results of expansive laminoplasty for ossification of the posterior longitudinal ligament of the cervical spine: more than 10 years follow up. J Neurosurg. 2002;96(2 Suppl): 180–9.
32. Kato Y, Iwasaki M, Fuji T, Yonenobu K, Ochi T. Long-term follow-up results of laminectomy for cervical myelopathy caused by ossification of the posterior longitudinal ligament. J Neurosurg. 1998;89:217–23.
33. Li KK, Chung OM, Chang YP, So YC. Myelopathy caused by ossification of ligamentum flavum. Spine (Phila Pa 1976). 2002;27:E308–12.
34. Lee CH, Sohn MJ, Lee CH, Choi CY, Han SR, Choi BW. Are There Differences in the Progression of Ossification of the Posterior Longitudinal Ligament Following Laminoplasty Versus Fusion?: A Meta-Analysis. Spine (Phila Pa 1976). 2017;42: 887–94.
35. Matsunaga S, Sakou T, Taketomi E, Komiya S. Clinical course of patients with ossification of the posterior longitudinal ligament: a minimum 10-year cohort study. J Neurosurg, 2004, 100(3 Suppl) Spine:245–248.