At the impact site, DHA-containing PCs exhibited irreversible reductions in an impact site-specific manner. This abnormal reduction began from 1 d post-SCI and evolved up to 8 weeks after SCI. The IMS results for DHA-containing PCs, i.e., PC (diacyl-16:0/22:6) and PC(diacyl-18:0/22:6), are shown in Fig. 3. In the control samples, four proximal/distal spinal cord sections showed the aforementioned selective gray matter distribution, which remained unaltered 12 h post-SCI. However, a primary reduction was observed at 1 d after SCI, which was severe around the central canal and gray commissure. While the decreased levels at the anterior and posterior horns were initially moderate (arrowheads),the DHA-PCs were even absent from these regions at 1 week after SCI. This DHA-PC reduction is unique due to its irreversible nature; indeed, DHA-PC reductions continued to evolve at 2 and 8 weeks post-SCI. These observations are summarized in the upper panel of Fig. 5a, in which averaged ion intensities of DHA-PCs from each whole section have been calculated and represented as 3D bar charts. The semi-quantified data also support the gradual decrease in DHA-PCs from 1 week after SCI (Fig. 5, orange arrows). The bottom panel in Fig. 5a shows extracted bar charts for the impacted site from the 3D chart, and we confirmed that the reduction in DHA-PCs—both PC(diacyl-16:0/22:6) and PC (diacyl-18:0/22:6)—between normal and 8 weeks post-injury was statistically significant ($p<0.0001$: normal (approx. 1300 data points) vs. 8 w (approx. 1200 data points): Welch t-test, for all three distinct animals). Given that other studies have reported the disappearance of motor neurons during the progression of SCI damage observed from 1 d after SCI , the irreversible reduction in DHA-PCs observed in the present study may result from an irreversible deficit of the neurons and could lead to motor dysfunction. Thus, DHA-PC reduction may represent a potential clinical indicator to evaluate the pathology of SCI.

Temporary elevations of AA-containing PCs after SCI

We also found that AA-containing PCs showed stage- and tissue location-specific patterns of increase. Interestingly, such elevations were temporary events that were resolved by 8 weeks post-SCI. The IMS results for two AA-PCs, i.e., PC (diacyl-16:0/20:4) and PC(diacyl-18:0/20:4), are shown in Fig. 4. As shown in the red square, both AA-PCs showed intense increases at the impact site at 1 week post-SCI, whereas alterations at other tissue locations were minimal. These observations are summarized in the lower panel of Fig. 5b, in which averaged ion intensities of the AA-PCs from each whole section are shown. The data also demonstrate that, for both AA-PCs, the impact site exhibited the largest AA-PC signal values at 1 week after treatment, which were approximately 2.5-fold greater than in other sections at the same SCI stage. Moreover, the values gradually decreased with time after SCI. We also confirmed that the increases in the AA-PCs—both PC(diacyl-16:0/20:4) and PC(diacyl-18:0/20:4)—between normal and 1 week post-injury were statistically significant ($p>0.001$: normal (approx. 1300 data points) vs. 1w (2000 data points / Welch t-test, for all three distinct animals).

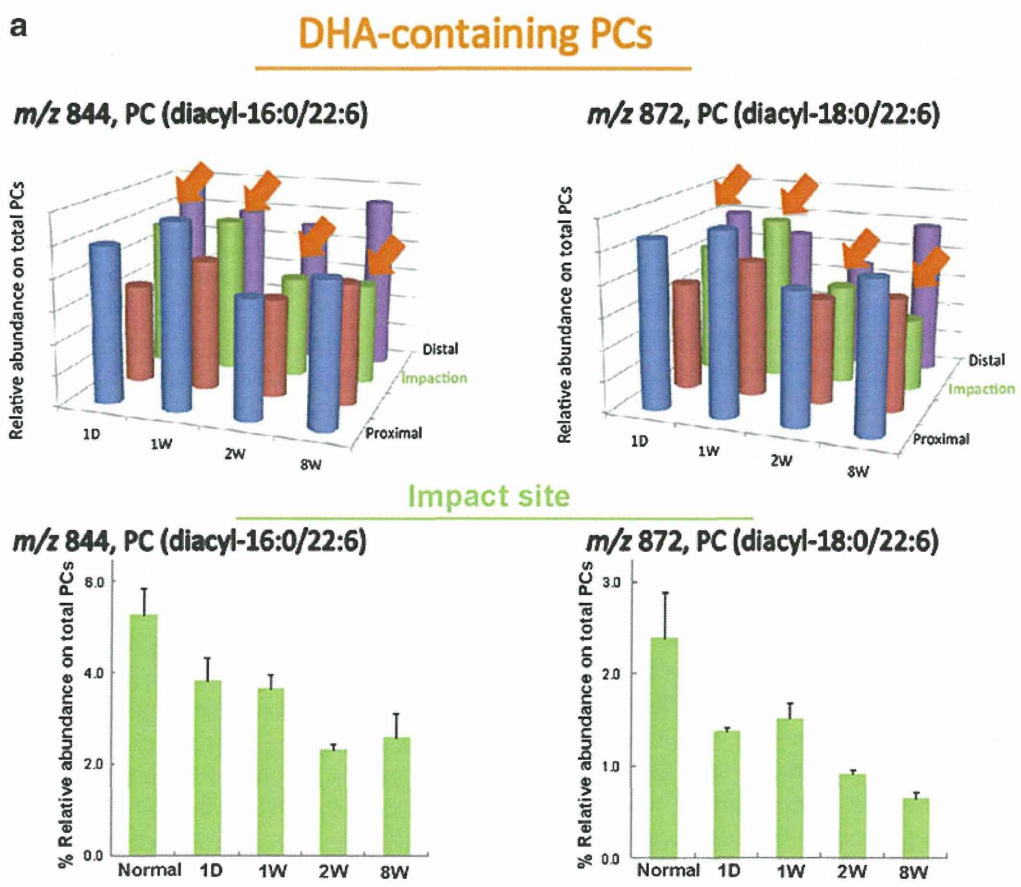
Fig. 5a–b Semi-quantified IMS data for DHA- and AA-PCs. The 3D bar charts represent averaged ion intensities for DHA-PCs (**a**) and AA-PCs (**b**) calculated from the IMS data for each whole section. These semi-quantified data support the gradual decrease of DHA-PCs at 1 week post-SCI (*orange arrows*). In addition, the data demonstrate that, for two AA-PCs, the impact site tissue at 1 week after treatment exhibited the largest AA-PC signal values, which were approximately 2.5-fold greater than the other sections at the same time point (*red arrows*). The *lower panels* in **a** and **b** show extracted bar charts for the impacted site from the 3D charts. (n=3, error bars, S.E.)

Both the timing and location of the elevated AA-PCs suggest that they may be derived from invasive immune cells that penetrate into the spinal cord body thorough the impaired blood–brain barrier (BBB), which may occur as a series of spatiotemporal events following SCI. Such immune cells are known to produce several kinds of bioactive lipids, including PGs derived from AA. Indeed, there may be a greater molecular flux through the AA cascade in immune cells compared with other cells, resulting in increased AA storage in the form of AA-containing PCs in the cell membrane. Clinically, PGs produced by invasive immune cells are closely associated with inflammation [31–33]. Thus, we proceeded to conduct a detailed analysis of elevated AA-PCs as well as PG profiling.

Invasive immune cells may represent a source of elevated AA-PCs and LPCs

If invasive immune cells represent the source of elevated AA-PCs, the spatial distribution of AA-PCs should reveal co-localization with invasive cells that accumulate in areas of tissue. Therefore, we performed a detailed analysis of the AA-PC distribution in the slice containing the site of impact at 1 week after SCI (Fig. 6). Accurate interpretation of the lipid distribution data obtained by IMS also requires histological data and lipid ion distribution images. Therefore, we stained tissue sections with H&E after performing IMS and subsequently superimposed ion and microscopic images obtained from the same section (lower panels of Fig. 6). As can be seen from the upper panels in Fig. 6, a large number of invading cell nuclei were found in tissue from the impact site (hematoxylin-positive dots), which were not seen in the proximal section. Moreover, close examination of the area indicated by arrows (also see the inset)—where immune cells were invading the spinal cord body—revealed a strong signal for the AA-PC distribution in the expected area of tissue.

We subsequently analyzed LPC molecular species, which are hydrolysates of PCs produced as by-products following the


a
DHA-containing PCs
m/z 844, PC (diacyl-16:0/22:6)
m/z 872, PC (diacyl-18:0/22:6)
Relative abundance on total PCs
1D
1W
2W
8W
Distal
Impaction
Proximal
Impact site
% Relative abundance on total PCs
Normal
b
AA-containing PCs
m/z 820, PC (diacyl-16:0/20:4)
m/z 848, PC (diacyl-18:0/20:4)

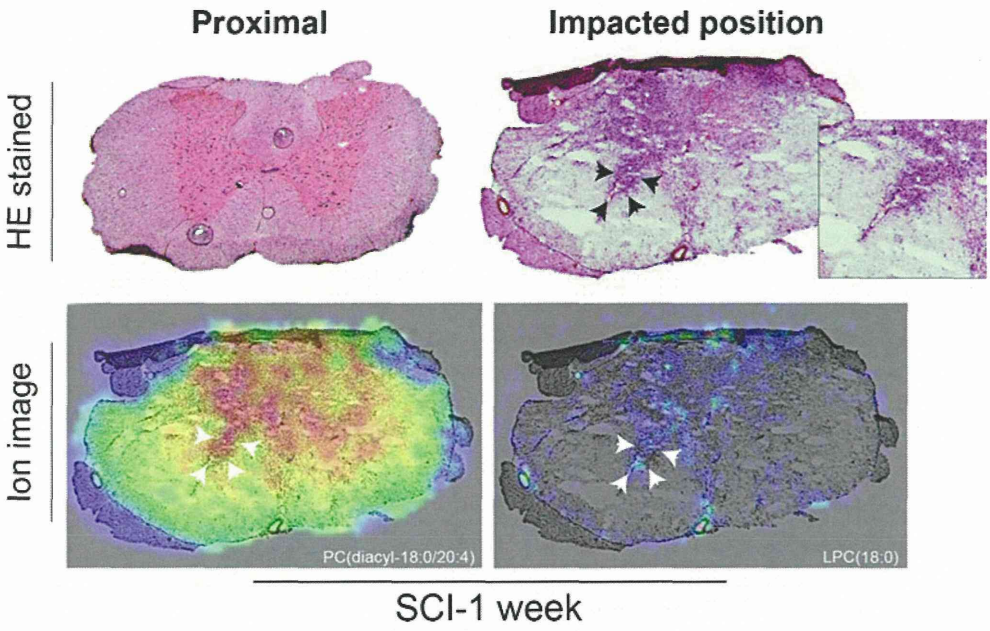


Fig. 6 Invasive immune cells may represent sources of elevated AA-PCs and LPCs. Microscopic images of H&E-stained tissue sections at 1 week post-SCI after IMS measurement of the proximal and impact site regions (*upper panel*). Ion images for PC (diacyl-18:0/20:4) and a potential hydrolysate, LPC (18:0), were superimposed on the H&E image (*lower panel*). The area indicated by *arrows* represents the region in which immune cells were invading into the spinal cord body (see also the *inset* of the H&E-stained image of the impact site)

catalysis of the release of fatty acid at the *sn*-2 position of glycerol by phospholipase A2 (PLA2). In particular, enrichment of the corresponding LPC [LPC(18:0)], produced from the elevated AA-PC [PC(diacyl-18:0/20:4)] in the immune-cell-rich region, would provide further evidence that invasive immune cells hydrolyze AA-PC and release AA, resulting in the production of PGs in the area of invasion. In general, LPC (18:0) level was elevated at the impact site between one and two weeks after SCI (see also Fig. S2 of the ESM). Furthermore, we found that LPC(18:0) was elevated in an area that corresponded to PC(diacyl-18:0/20:4) accumulated area, while LPC was localized in a more region-specific manner (Fig. 6, lower-right panel; arrows). LPC localized on the border area—where the invasive cells were in contact with cells of the spinal cord body—as well as on major blood vessels. Therefore, elevated region-specific production of PGs may result in increased inflammation. Taken together, these results suggest that invasive immune cells accumulate in an area that contains both elevated AA-PC and LPC, supporting the hypothesis that AA-PC-rich immune cells produce PGs in the area of invasion—presumably at the border area where the immune cells are in contact with spinal cord cells.

PGE2 displayed an elevation pattern similar to AA-PCs and LPC

Finally, we profiled PGs in the spinal cord tissue blocks in order to confirm our hypothesis that invasive immune cells—originating from the impaired BBB at 1–2 weeks after SCI—specifically produced PGs in the tissue area where elevated AA-PCs and LPC were co-localized. Accordingly, there may be a PG species that exhibits increases in the impact-site tissue blocks that show a similar elevation/descent pattern to the immune cell invasion event and the pattern of AA-PC/LPC elevation. Thus, we employed LC-ESI-MS/MS in MRM mode for simultaneous quantification of trace amounts of PGs. In general, PGs are produced under normal conditions and maintained at very low concentrations (on the order of pg/mg tissue) [34], as the production, diffusion, and degradation of PGs must be regulated due to their strong bioreactivity. We found that all analyzed five PGs were increased after SCI. In particular, PGE2 showed a very similar elevation/descent pattern to that of AA-PC and LPC described above.

A 3D bar chart representing the results of PG quantification in the impact-site tissue blocks at four time points as well as the sham-operated sample is shown in Fig. 7. All of the

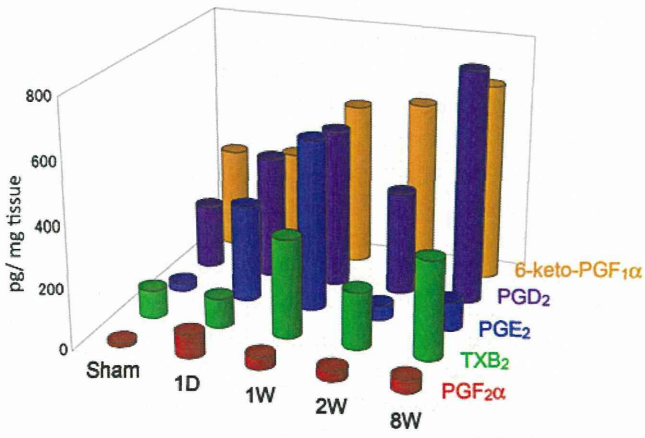


Fig. 7 Spatiotemporal peak in PG production in spinal cord blocks following SCI. We employed LC-ESI-MS/MS in the MRM mode for the simultaneous quantification of trace amounts of PGs. The 3D bar chart represents the results of PG quantification in tissue blocks corresponding to the impact site at four different time points and the sham sample

analyzed PGs increased following SCI, and each PG displayed characteristic elevation/descent patterns. In particular, TXB2, PGE2, and PGD2 produced the first elevation peak at 1 week post-SCI. However, while the PGE2 peak was temporary and had almost completely resolved by 2–8 weeks post-SCI, PGD2 and TXB2 exhibited a bimodal pattern, producing a second elevation at 8 weeks after SCI. In addition, PGF2a produced a single-peak elevation at 1 d after SCI, and 6-keto-PGF1a displayed a gradual increase. Since the first elevation peak for most PGs was observed at 1 week after SCI, it is likely that the invasive immune cells produce these types of PGs. Among the PGs, the dynamics of PGE2 may result from invasion and subsequent resolution, though further evidence is required to prove this concept.

PGE2 has been implicated in the induction of central sensitization of spinal neurons; therefore, information on the spatial production pattern of PGE2 in the injured spinal cord is important to determine the type and location of the neurons affected. Our data demonstrated that the maximum elevation of PGE2 occurred 1 week after SCI. However, while we were unable to directly identify where PGE2 is produced, imaging data on the more abundant AA-PCs and LPC indirectly implied that PGE2 may be produced at the edge of the area of invasive immune cells. Further improvements in IMS methodology enabling the imaging of PGs at high spatial resolution will be required to test this hypothesis.

In addition, it is possible that microglial cells contribute to PG elevation, particularly that of PGE2, since microglial cells are activated in response to primary SCI [33] and proliferate during the subacute phase. For example, obvious PGE2 elevation was observed 1 day post-injury. As microscopy did not indicate clear immune-cell invasion at this time point, we should consider the contribution of microglia to PGE2 production at this time point. Moreover, in vitro studies indicate that microglia are indeed able to synthesize and release PGE2 [35–38]. Therefore, microglial PGE2 may also play an important role in the generation of central sensitization after SCI .

One method to directly determine whether invaded immune cells and activated microglia are responsible for PG elevation is to analyze the specific lipid profile of purified immune cells (including microglia) separated from SCI tissue samples. This could be achieved by combining cell sorting and quantitative mass spectrometry, which we are now implementing. Such additional in vitro experiments in which microglial cells are separately cultured and stimulated are required to evaluate the capacity of these cells for PG production.

A degree of PG elevation was maintained and had evolved at 8 weeks post-SCI. Since the invasion of immune cells was almost resolved by 8 weeks post-SCI, it is possible that SCI induced reorganization of the spinal cord body, thereby altering cellular populations and properties [33] and resulting in continuous PG production. Such tissue reorganization is likely to be caused by the subacute and severe inflammation mediated by the invasive immune cells; therefore, the profile of the five PGs analyzed in this study may be used to evaluate the stage of SCI-induced inflammation, i.e., acute vs. chronic inflammation.

Conclusion

IMS and LC-ESI MS/MS analyses revealed both quantitative and qualitative changes in lipids with respect to the amount of PCs, the LPC distribution, and the amount of PGs generated. Thus, invasive immune cells that penetrated from the impaired BBB at 1–2 weeks after SCI may have specifically produced PGs in areas of tissue where elevated AA-PCs and LPC were commonly found. Although our data demonstrated that PGE2 elevation was maximal 1 week after SCI, we were unable to directly identify where PGE2 is produced. Thus, further improvements in IMS methodology to enable the imaging of PGs are required.

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References

1. Piomelli D, Astarita G, Rapaka R (2007) A neuroscientist's guide to lipidomics. Nat Rev Neurosci 8:743–754
2. Takamori S, Holt M, Stenius K, Lemke EA, Grønborg M, Riedel D, Urlaub H, Schenck S, Brügger B, Ringler P, Müller SA, Rammner B, Gräter F, Hub JS, De Groot BL, Mieskes G, Moriyama Y, Klingauf J, Grubmüller H, Heuser J, Wieland F, Jahn R (2006) Molecular anatomy of a trafficking organelle. Cell 127:831–846
3. Rohrbough J, Broadie K (2005) Lipid regulation of the synaptic vesicle cycle. Nat Rev Neurosci 6:139–150
4. Jacobson K, Mouritsen OG, Anderson RG (2007) Lipid rafts: at a crossroad between cell biology and physics. Nat Cell Biol 9:7–14
5. Allen JA, Halverson-Tamboli RA, Rasenick MM (2007) Lipid raft microdomains and neurotransmitter signalling. Nat Rev Neurosci 8:128–140
6. Williams JH, Errington ML, Lynch MA, Bliss TV (1989) Arachidonic acid induces a long-term activity-dependent enhancement of synaptic transmission in the hippocampus. Nature 341:739–742
7. Dinh TP, Carpenter D, Leslie FM, Freund TF, Katona I, Sensi SL, Kathuria S, Piomelli D (2002) Brain monoglyceride lipase participating in endocannabinoid inactivation. Proc Natl Acad Sci USA 99:10819–10824
8. Hermann GE, Rogers RC, Bresnahan JC, Beattie MS (2001) Tumor necrosis factor-alpha induces cFOS and strongly potentiates glutamate-mediated cell death in the rat spinal cord. Neurobiol Dis 8 (4):590–599
9. Buczynski MW, Svensson CI, Dumlao DS, Fitzsimmons BL, Shim JH, Scherbart TJ, Jacobsen FE, Hua XY, Yaksh TL, Dennis EA (2010) Inflammatory hyperalgesia induces essential bioactive lipid production in the spinal cord. J Neurochem 114(4):981–993
10. Ma L, Nagai J, Ueda H (2010) Microglial activation mediates de novo lysophosphatidic acid production in a model of neuropathic pain. J Neurochem 115(3):643–653

11. Nagai J, Ueda H (2011) Pre-emptive morphine treatment abolishes nerve injury-induced lysophospholipid synthesis in mass spectrometrical analysis. J Neurochem 118(2):256–265
12. Buczynski MW, Svensson CI, Dumlao DS, Fitzsimmons BL, Shim JH, Scherbart TJ, Jacobsen FE, Hua XY, Yaksh TL, Dennis EA (2010) Inflammatory hyperalgesia induces essential bioactive lipid production in the spinal cord. J Neurochem 114(4):981–993
13. Girod M, Shi Y, Cheng JX, Cooks RG (2011) Mapping lipid alterations in traumatically injured rat spinal cord by desorption electrospray ionization imaging mass spectrometry. Anal Chem 83:207–215
14. Sugiura Y, Setou M (2010) Imaging mass spectrometry for visualization of drug and endogenous metabolite distribution: toward in situ pharmacometabolomes. J Neuroimmune Pharmacol 5:31–43
15. Garrett TJ, Yost RA (2006) Analysis of intact tissue by intermediate-pressure MALDI on a linear ion trap mass spectrometer. Anal Chem 78:2465–2469
16. Jackson SN, Woods AS (2009) Direct profiling of tissue lipids by MALDI-TOFMS. J Chromatogr B 877:2822–2829
17. Cornett DS, Reyzer ML, Chaurand P, Caprioli RM (2007) MALDI imaging mass spectrometry: molecular snapshots of biochemical systems. Nat Methods 4:828–833
18. Sugiura Y, Konishi Y, Zaima N, Kajihara S, Nakanishi H, Taguchi R, Setou M (2009) Visualization of the cell-selective distribution of PUFA-containing phosphatidylcholines in mouse brain by imaging mass spectrometry. J Lipid Res 50:1776–1788
19. Murphy RC, Hankin JA, Barkley RM (2009) Imaging of lipid species by MALDI mass spectrometry. J Lipid Res 50(Suppl): S317–S322
20. Touboul D, Brunelle A, Halgand F, De La Porte S, Laprévote O (2005) Lipid imaging by gold cluster time-of-flight secondary ion mass spectrometry: application to Duchenne muscular dystrophy. J Lipid Res 46:1388–1395
21. Sugiura Y, Taguchi R, Setou M (2011) Visualization of spatiotemporal energy dynamics of hippocampal neurons by mass spectrometry during a kainate-induced seizure. PLoS One 6(3):e17952
22. Sugiura Y, Shimma S, Konishi Y, Yamada MK, Setou M (2008) Imaging mass spectrometry technology and application on ganglioside study; visualization of age-dependent accumulation of C20-ganglioside molecular species in the mouse hippocampus. PLoS One 3:e3232
23. Delvolve AM, Colsch B, Woods AS (2011) Highlighting anatomical sub-structures in rat brain tissue using lipid imaging. Anal Meth 3:1729–1736
24. Setou M (ed)(2010) Imaging mass spectrometry (Protocols for Mass Microscopy). Springer, Berlin
25. Burnum KE, Cornett DS, Puolitaival SM, Milne SB, Myers DS, Tranguch S, Brown HA, Dey SK, Caprioli RM (2009) Spatial and temporal alterations of phospholipids determined by mass spectrometry during mouse embryo implantation. J Lipid Res 50:2290–2298
26. Matsumoto J, Sugiura Y, Yuki D, Hayasaka T, Goto-Inoue N, Zaima N, Kunii Y, Wada A, Yang Q, Nishiura K, Akatsu H, Hori A, Hashizume Y, Yamamoto T, Ikemoto K, Setou M, Niwa S (2011) Abnormal phospholipids distribution in the prefrontal cortex from a patient with schizophrenia revealed by matrix-assisted laser desorption/ionization imaging mass spectrometry. Anal Bioanal Chem 400:1933–1943
27. Beck G, Sugiura Y, Shinzawa K, Kato S, Setou M, Tsujimoto Y, Sakoda S, Sumi-Akamaru H (2011) Neuroaxonal dystrophy in calcium-independent phospholipase A2beta deficiency results from insufficient remodeling and degeneration of mitochondrial and presynaptic membranes. J Neurosci 31:11411–11420
28. Kita Y, Takahashi T, Uozumi N, Shimizu T (2005) A multiplex quantitation method for eicosanoids and platelet-activating factor using column-switching reversed-phase liquid chromatography-tandem mass spectrometry. Anal Biochem 342:134–143
29. Puolitaival SM, Burnum KE, Cornett DS, Caprioli RM (2008) Solvent-free matrix dry-coating for MALDI imaging of phospholipids. J Am Soc Mass Spectrom 19:882–886
30. Hankin JA, Barkley RM, Murphy RC (2007) Sublimation as a method of matrix application for mass spectrometric imaging. J Am Soc Mass Spectrom 18:1646–1652
31. Zhao P, Waxman SG, Hains BC (2007) Extracellular signal-regulated kinase-regulated microglia-neuron signaling by prostaglandin E2 contributes to pain after spinal cord injury. J Neurosci 27(9):2357–2368
32. Redensek A, Rathore KI, Berard JL, López-Vales R, Swayne LA, Bennett SA, Mohri I, Taniike M, Urade Y, David S (2011) Expression and detrimental role of hematopoietic prostaglandin D synthase in spinal cord contusion injury. Glia 59(4):603–614
33. Zhang J, Fujii S, Wu Z, Hashioka S, Tanaka Y, Shiratsuchi A, Nakanishi Y, Nakanishi H (2006) Involvement of COX-1 and up-regulated prostaglandin E synthases in phosphatidylserine liposome-induced prostaglandin E2 production by microglia. J Neuroimmunol 172:112–120
34. Yoshikawa K, Kita Y, Kishimoto K, Shimizu T (2006) Profiling of eicosanoid production in the rat hippocampus during kainic acid-induced seizure: dual phase regulation and differential involvement of COX-1 and COX-2. J Biol Chem 281:14663–14669
35. Minghetti L, Polazzi E, Nicolini A, Levi G (1998) Opposite regulation of prostaglandin E2 synthesis by transforming growth factor-beta1 and interleukin 10 in activated microglial cultures. J Neuroimmunol 82:31–39
36. Hoozemans JJ, Veerhuis R, Janssen I, van Elk EJ, Rozemuller AJ, Eikelenboom P (2002) The role of cyclo-oxygenase 1 and 2 activity in prostaglandin E(2) secretion by cultured human adult microglia: implications for Alzheimer's disease. Brain Res 951:218–226
37. Ajmone-Cat MA, Nicolini A, Minghetti L (2003) Prolonged exposure of microglia to lipopolysaccharide modifies the intracellular signaling pathways and selectively promotes prostaglandin E2 synthesis. J Neurochem 87:1193–1203
38. Ikeda-Matsuo Y, Ikegaya Y, Matsuki N, Uematsu S, Akira S, Sasaki Y (2005) Microglia-specific expression of microsomal prostaglandin E2 synthase-1 contributes to lipopolysaccharide-induced prostaglandin E2 production. J Neurochem 94:1546–1558

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Examination of the influence of ossification of the anterior longitudinal ligament on symptom progression and surgical outcome of ossification of the thoracic ligamentum flavum: a multicenter study

Clinical article

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Object. The purpose of this study was to provide the first evidence for the influence of an ossified anterior longitudinal ligament (OALL) on the clinical features and surgical outcomes in an ossified ligamentum flavum (OLF) in the thoracic region.

Methods. Sixty-three patients who underwent surgery for a 1-level thoracic OLF were identified, and preoperative symptoms, severity of symptoms and myelopathy, disease duration, MR imaging and CT findings, surgical procedure, intraoperative findings, complications, and postoperative recovery were investigated in these patients. Entities of OALLs were found on sagittal CT images to be adjacent to or at the same vertebral level as the OLF were classified into 4 types: no discernible type (Type N), one-sided (Type O), discontinuous (Type D), and continuous (Type C).

Results. The duration of symptoms was especially long for Types D and C OALLs. Patients with Type D OALLs had a significantly worse percentage of recovery, as well as worse preoperative JOA scores.

Conclusions. The authors' results showed that a Type D OALL had strong associations with preoperative severity of symptoms and surgical outcomes. These findings may allow surgeons to determine the severity of preoperative symptoms and the probable surgical outcomes from the OALL classifications. Moreover, surgery with instrumentation for Type D OALLs may produce better surgical outcomes. *(DOI: 10.3171/2011.10.SPINE11296)*

Key Words • thoracic ossification of the ligamentum flavum • ossified anterior longitudinal ligament • surgical outcome • multicenter study

Ossification of the thoracic ligamentum flavum, first described in 1920 by Polgár,[20] causes thoracic myelopathy. Thoracic myelopathy due to an OLF generally requires surgical intervention because of its progressive nature and its poor response to conservative therapy. The prevalence of OLF has been reported to be 3.8%–26%,[2,6,28] which is very similar to the prevalence of cervical ossification of the posterior longitudinal ligament.[17] However, predictive factors for an OLF are unclear because of the paucity of reports on this condition.[1–3,5,8,9,14,15,23,26,27,30] Given that obtaining detailed data and analysis from a single-center study on this topic has been insufficient and difficult, we investigated clinical features, radiological findings, and surgical outcomes of OLFs in a multicenter study.

Although the classification of OLF of Sato et al.[22] using axial CT images has been used in several studies,[1,3,14,30] the surgical outcomes in these reports did not correlate significantly to the classifications. Unlike an OPLL, a thoracic OLF occurs most frequently in the lower thoracic

Abbreviations used in this paper: ALL = anterior longitudinal ligament; CSM = cervical spondylosis myelopathy; DISH = diffuse idiopathic skeletal hypertrophy; JOA = Japanese Orthopaedic Association; OALL = ossified ALL; OLF = ossified ligamentum flavum; OPLL = ossified posterior longitudinal ligament.

region.[2] This may be due to the anatomical character of this spinal region, that is, the thoracolumbar spine, which receives most of the mechanical and dynamic stresses. Ossification of the ALL may also be seen in patients with an OLF. The rate of progression of an OALL also may be related to increased motion as with an OLF.[16,25] We surmised that having an OALL may contribute to the clinical features and surgical outcomes in thoracic OLF. In this multicenter study, we analyzed pre- and postoperative symptoms, radiological findings, intraoperative findings, and surgical outcomes as they related to any type of OALL that may have been present in patients with an OLF. This is the first study in which symptom severity and surgical outcome of thoracic OLFs have been evaluated relative to concurrent OALL.

Methods

Patient Population

Between 2000 and 2008, 19,364 patients who underwent spinal surgery were registered in the database of the Nagoya Spine Group, a study group for spinal diseases at Nagoya University and related institutions. We identified 63 patients who underwent single-level surgery for thoracic OLF-induced myelopathy and observation for a minimum of 2 years postoperatively. Preoperative symptoms, severity of symptoms and myelopathy, disease duration, MR imaging and CT findings, surgical procedures, intraoperative findings, complications, and postoperative recovery were evaluated in these patients. We excluded patients who had undergone surgery for cervical and thoracic OPLLs or cervical spondylosis myelopathy before surgery for their OLF or during follow-up. We evaluated the severity of a patient's myelopathy before and after surgery using the JOA scoring system (Table 1). We evaluated postoperative improvement of symptoms using the recovery ratio of the JOA score and the Hirabayashi method[4] ([postoperative JOA score − preoperative JOA score]/[17 − preoperative JOA score] × 100%), with a recovery ratio of 100% indicating the best postoperative improvement.

Axial CT Classification of OLF

We used the classification for OLFs of Sato et al.,[22] which evaluates CT images and found the following 4 types of OLFs in our patients: lateral, extended and enlarged, fused, and tuberous (Fig. 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 a patient's OLF using sagittal CT images. We found the following 4 types according to where the OALL was located relative to the OLF (Fig. 2): no discernible OALL immediately rostral or caudal to the OLF (Type N); one-sided (Type O), in which the OALL exists either immediately rostral or caudal to the OLF but not at the OLF intervertebral level; discontinuous (Type D), in which the OALL is present both rostrally and caudally to the OLF but not at the same level as the OLF; and continuous (Type C), in which the OALL extends from the rostral to the caudal levels, including the OLF level.

TABLE 1: Scoring system for the treatment of thoracic myelopathy according to the JOA*

Score	Description
LE motor function	
0	unable to stand or walk by any means
1	unable to walk w/o a support on level ground
2	walks independently on level ground but needs support on stairs
3	capable of fast walking but clumsily
4	normal
sensory function	
LE	
0	complete loss of touch & pain sensation
1	>50% of normal sensation &/or moderate pain or numbness
2	normal
trunk	
0	complete loss of touch & pain sensation
1	>50% of normal sensation &/or moderate pain or numbness
2	normal
bladder function	
0	urinary retention &/or incontinence
1	sense of retention &/or dribbling &/or thin stream &/or incomplete continence
2	urinary retardation &/or pollakiuria
3	normal

* The total score for a healthy individual is 11. Abbreviation: LE = lower extremity.

Statistical Analysis

Data were analyzed using SPSS software (version 19, IBM SPSS). The mean values are presented as the mean ± SD. We used the Mann-Whitney U-test to analyze differences between 2 groups and the Tukey test to analyze differences among 4 groups, with $p < 0.05$ as the points of statistical significance.

Results

Clinical Data

Sixty-three patients underwent surgery for a thoracic OLF, comprising 49 men and 14 women, with a mean age at surgery of 63.9 ± 10.0 years (range 36–83 years). In these patients, there were 94 levels of involvement. The mean disease duration from symptom onset to surgery was 17.4 ± 21.4 months (range 1–120 months). The initial symptoms were numbness of the lower extremities in 51 patients (80.9%), gait disturbance in 28 (44.4%), weakness of the lower extremities in 11 (16.7%), strangulating sensation of the trunk in 8 (12.7%), and urinary distur-

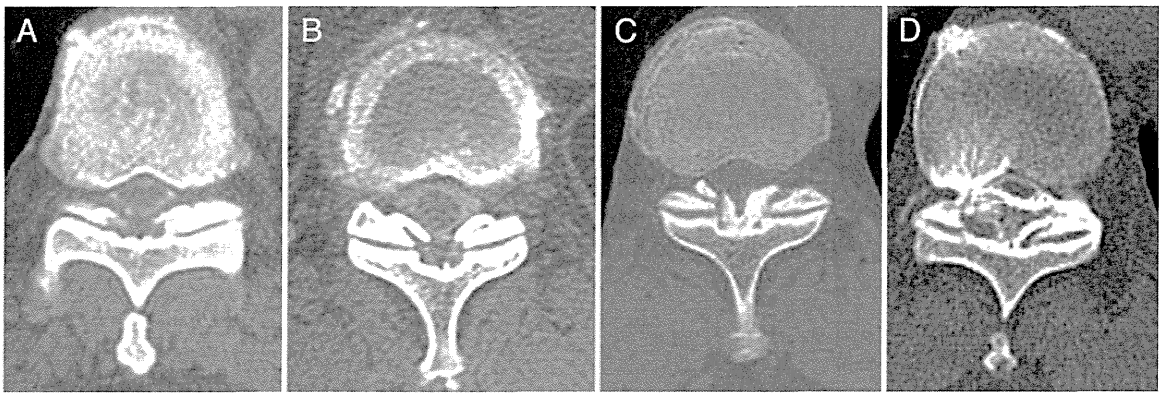

FIG. 1. Axial CT classification of OLFs, with scans obtained at the middle of the facet joint. **A:** Lateral type. The OLF is located only in the capsular portion of the ligamentum flavum, which can be detected at the lateral edge of the spinal canal. **B:** Extended and enlarged type. The OLF is located at the surface of the ligamentum flavum and protrudes into the spinal canal. **C:** Fused type. Bilateral OLFs fuse at the middle of the OLF. **D:** Tuberous type. Fused OLFs make a tuberous mass at the middle of the spinal canal.

bance in 3 (4.8%) (some patients presented with multiple symptoms) (Table 2).

Radiographic Findings

The levels decompressed for the OLF-induced myelopathy are shown in Fig. 3. No decompressions were performed between T-5 and T-9, and the majority of the affected levels (in 57 patients [90.5%]) were in the lower thoracic region. Intramedullary signal intensity change on MR images was observed in 55 patients (87.3%). Morphological classifications, as determined by axial CT images, were lateral in 9 patients, extended and enlarged in 17 patients, fused in 32 patients, and tuberous in 5 patients (15, 31, 37, and 11 cases, respectively, accounting for multilevel involvement). We classified the morphology of the OALLs as seen on sagittal CT images as Type N in 28 patients, Type O in 22 patients, Type D in 7 patients, and Type C in 6 patients (Table 3). The OLF and the OALL tended to progress at a similar rate (Fig. 4).

Duration of Symptoms in Relation to Ossification Type

The types of OALL and OLF associated with longer symptom durations also tended to be more greatly (but not significantly) ossified. Interestingly, the duration of symptoms was especially long in patients with Type D and C OALLs (Table 3).

Surgical Methods and Intraoperative Findings

Laminectomy was performed in 24 patients, laminoplasty in 32 patients, and posterior decompression and fusion with instrumentation in 7 patients (Table 4). Patients with an OLF in which bilateral ossification of the ligamentum flavum was not fused in the middle of the spinal canal were treated with laminoplasty, whereby the laminae were removed en bloc and then returned after decompression. 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 of the joint for both procedures. Surgeries with instrumentation had facet resection of more than half a joint. Evaluation of the surgical procedures performed with the various morphological OLF types showed that the lateral type was most frequently treated with laminoplasty; the extended and enlarged, and fused types were treated with laminectomy

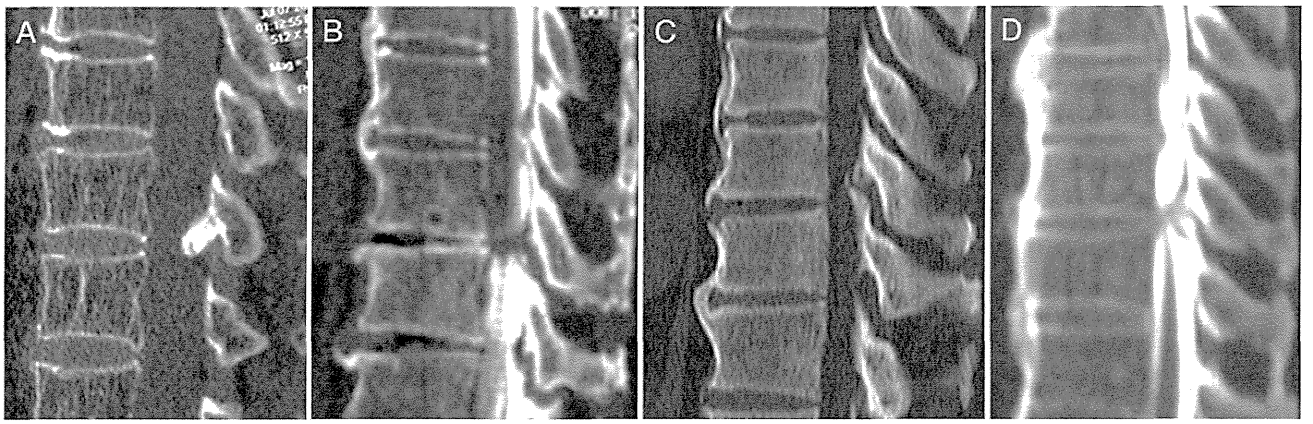

FIG. 2. Sagittal CT classification of OALLs at the OLF level. **A:** Type N, showing no OALL around the OLF level. **B:** Type O, in which the OALL exists at the rostral or caudal end of the OLF level but not at the OLF level. **C:** Type D, in which OALL exists at both the rostral and caudal ends of the OLF level but none at the OLF level. **D:** Type C, in which an OALL exists from the rostral to caudal level including the OLF level.

TABLE 2: Demographics and clinical data of patients

Parameter	Value*
sex	
male	49
female	14
age in yrs	
mean	63.9
range	36–83
follow-up in mos	
mean	42.3
range	24–118
disease duration in mos	
mean	17.4
range	1–120
initial symptoms	
LE numbness	51 (80.9)
gait disturbance	28 (44.4)
LE weakness	11 (16.7)
urinary disturbance	3 (4.8)

* Except for mean values, the values indicate the number of patients with percentages in parentheses.

and laminoplasty; and the tuberous type was treated with fusion. There was no tendency for a particular type of surgery to be performed relative to the type of the OALL. This held true whether the procedure was performed in upper or lower thoracic lesions (Table 5).

Intraoperatively, we found adhesions of the OLF to the dura mater in 23 patients (36.5%). When adhesions were present and an OALL was also present, the OLF tended to adhere to the dura mater (Table 6).

Preoperative Severity and Surgical Outcome by Ossification Type

The mean preoperative JOA score was 5.8 ± 2.2 (range 1–9). Patients with Type D OALL had a significantly lower JOA score among the OALL types, although there was no significant difference in JOA scores among the OLF types (Table 7).

The mean recovery rate was 46.1% ± 29.0% (range 2%–11%) at the 2-year follow-up. The surgical outcome

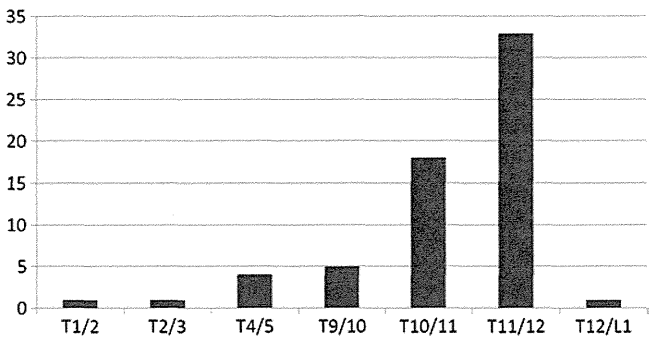

FIG. 3. Bar graph showing the number of OLF levels at each joint.

TABLE 3: Summary of patient data and symptom duration classified by type of OLF and OALL

Variable	No. of Patients (%)	Mean Duration (mos)
signal intensity change	55 (87.3)	
axial CT classification		
lat	9 (14.3)	7.44 ± 7.1
extended & enlarged	17 (27.0)	13.5 ± 18.5
fused	32 (50.8)	22.9 ± 25.2
tuberous	5 (7.9)	13.2 ± 21.4
sagittal CT classification		
Type N	28 (44.4)	17.0 ± 20.0
Type O	22 (34.9)	10.7 ± 8.8
Type D	7 (11.1)	32.4 ± 41.6
Type C	6 (9.5)	26.5 ± 22.5

did not differ among our classifications of OLF, and the lateral, and extended and enlarged types had correlatively better outcomes. Based on our OALL classifications, patients with a Type D OALL had a significantly worse percentage of recovery, as well as worse preoperative JOA scores (Table 7). We also calculated the mean recovery rate excluding patients who received posterior decompression and fusion, in case the recovery rate was affected by the use of surgical instrumentation. Patients with a Type D OALL also had a significantly worse percentage of recovery (Table 8).

Complications

There were some perioperative complications. One patient with a fused-type OLF and a Type D OALL received a laminectomy, but the thoracic myelopathy continued to progress immediately after surgery and then recovered to the preoperative condition during follow-up. Three patients (4.8%) sustained a dural tear intraoperatively, but there was no exacerbation of paralysis. Of 36 patients (57.1%) in whom intraoperative spinal cord (motor evoked potential) monitoring was performed, only 1 showed a decrease in amplitude. After temporary suspension of the surgical procedure, the amplitude recovered and aggravated paralysis did not occur after surgery. One

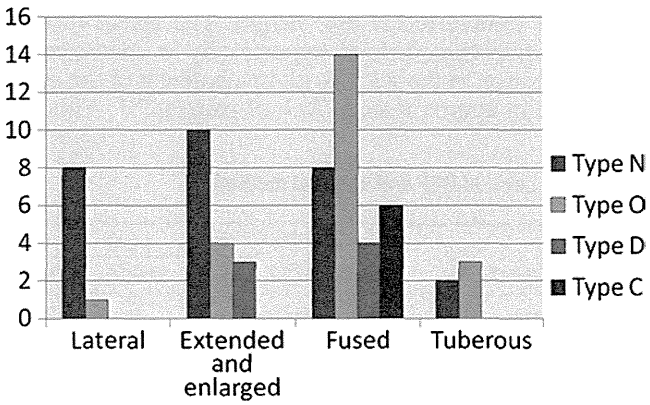

FIG. 4. Bar graph showing the relationship between OLFs and OALLs. The OLFs and OALLs tend to progress at a similar rate.

TABLE 4: Type of ossification and surgical methods

Type of Op	No. of Patients (%)									
	OLF					OALL				
	Lat	Extended & Enlarged	Fused	Tuberous	Total	Type N	Type O	Type D	Type C	Total
laminectomy	1	7	15	1	24 (38.1)	7	10	5	2	24 (38.1)
laminoplasty	8	9	15	0	32 (50.8)	18	8	2	4	32 (50.8)
posterior decompression & fusion w/ instrumentation	0	1	2		7 (11.1)	3	4	0	0	7 (11.1)

patient who received a laminectomy had a fused-type OLF, as well as a Type D OALL, and underwent further fusion surgery because of exacerbation of paralysis due to progressive kyphosis at the decompression level.

Discussion

Since 1920, when Polgár[20] first reported on a thoracic OLF, the number of reports of thoracic OLFs has increased. However, these are limited reports without sufficient numbers of patients (that is, at least 20).[1–3,5,8,9,14,15,23,26,30] It is possible to diagnose thoracic OLF by using MR imaging and CT scanning.[2,15] The incidence of ossification of the thoracic ligamentum flavum has been reported to be 3.8%–25%, including asymptomatic cases.[2] Reported cases of thoracic OLF occurred most often in the lower thoracic spine, followed by the upper thoracic spine.[2,5,6,19] Similar to previous studies, 6 of our patients had upper-level lesions and 57 patients had lower-level lesions; there were no middle-level lesions. The reasons for the high frequency of OLFs 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,[18] a direct correlation between increased mobility of the spine and repetitive mild trauma,[11] and high tensile force present in the posterior column.[24]

Resnick et al.[21] used the term "ossification of the anterior longitudinal ligament" 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. The spinal form of diffuse idiopathic skeletal hypertrophy is characterized by ossification of the ALL, with involvement of the cervical spine in approximately 76% of patients.[10,13] Although the rate of progression of ossification of the ALL may be related to increased cervical motion,[16,25] there is still a high incidence in the thoracic spine, which is a relatively immobile segment.[12] The relationship between a thoracic OLF and an OALL has not been reported previously. In this study, we found that OALLs present around vertebral levels were affected by OLFs. This correlation may be due to the mechanical stress arising from the OALL, as well as the OLF, as mentioned earlier.

Symptom Severity and Surgical Outcome in Relation to Classification of OALLs

Morphological classification of an OLF based on sagittal plane features has been attempted using MR images, but it was not predictive of outcome.[7] In the current study, patients with an OLF who also had a Type D OALL had more severe symptoms preoperatively and poorer outcomes after surgery for their OLF, although there were no obvious differences in symptoms or outcomes when we considered only OLF classifications. This increased symptom severity and the worse outcome may be due to the focusing of mechanical stress when the OALL is present both rostrally and caudally to the OLF (Type D), as well as the addition of micromotion on the vulnerable spinal cord, even within the essentially immobile thoracic spine segments. In contrast, patients with a Type C OALL had a good postoperative recovery, possibly because the continuous segment of the OALL was produced before the myelopathy became severe. It is interesting that Type D and Type C OALLs had different outcomes after the OLF surgeries, despite similarly long disease durations.

TABLE 5: Level of OLF and surgical method

Type of Op	No. of Patients (%)	Level		
		Upper	Middle	Lower
laminectomy	24 (38.1)	3	0	21
laminoplasty	32 (50.8)	2	0	30
posterior decompression & fusion w/ instrumentation	7 (11.1)	1	0	6
total (%)	63	6 (9.5)	0	57 (90.5)

TABLE 6: Summary of patients with adhesions of the OLF to the dura mater

Type of Ossification	No. of Patients (%)
OLF	
lat	2 (22.2)
extended & enlarged	2 (11.8)
fused	17 (53.1)
tuberous	2 (40)
OALL	
Type N	9 (32)
Type O	6 (27.3)
Type D	3 (42.9)
Type C	5 (71.4)

TABLE 7: Preoperative JOA score and postoperative improvement by type of ossification*

Type of Ossification	Mean JOA Score	Mean % Recovery in JOA Score	p Value
OLF			
lat	5.8 ± 1.6	58.6 ± 19.1	
extended & enlarged	5.4 ± 2.8	52.8 ± 29.2	
fused	5.7 ± 2.0	39.8 ± 30.1	
tuberous	7.6 ± 1.1	40.7 ± 29.7	
OALL			
Type N	5.8 ± 2.0	49.4 ± 27.0	
Type O	6.1 ± 2.0	45.3 ± 31.9	
Type D	2.9 ± 0.9	19.9 ± 14.7	<0.05
Type C	7.8 ± 1.5	63.9 ± 22.2	
overall	5.8 ± 2.2	46.1 ± 29.0	

* Only significant p values are recorded.

TABLE 8: Postoperative improvement by ossification, with the exception of patients who underwent fusion*

Type of Ossification	Mean % Recovery in JOA Score	p Value
OLF		
lat	58.6 ± 19.1	
extended & enlarged	53.6 ± 30.0	
fused	39.1 ± 31.0	
tuberous	50	
OALL		
Type N	49.8 ± 27.8	
Type O	46.7 ± 33.2	
Type D	19.9 ± 14.7	<0.05
Type C	63.9 ± 22.2	

* Only significant p values are listed.

We originally calculated and compared surgical outcomes for patients who did not undergo posterior fusions, since instrumentation and stabilization may have directly affected the outcome; however, the surgical outcomes were similar whether fusion surgery was included or not. This suggests that the location of OALL segments around OLF segments affects surgical outcome.

There have been reports on predictive factors for poor surgical outcome in OLF surgery, including older age, a midthoracic OLF, involvement of more than 2 segments with the OLF, a coexisting OPLL or other spinal disorders, a lower preoperative JOA score, an intramedullary high signal intensity on MR imaging,[5] and a longer duration of symptoms before surgical intervention.[1] However, there have not been reports regarding OALLs around OLF segments. We believe that an OALL occurring around the OLF level is also an important factor for predicting surgical outcome.

Surgical Methods for Thoracic OLFs Based on the Classification of OALLs

There have been no reports on surgical outcomes of a thoracic OLF when using instrumentation. In thoracic OPLL surgery, instrumentation can correct or prevent the progression of kyphosis, thereby enhancing and maintaining decompression.[29] In this study, patients with a Type N, O, or C OALL had a relatively good OLF surgical outcome with laminectomies or laminoplasties. On the other hand, patients with a Type D OALL had restricted recovery of the spinal cord due to the focusing of mechanical stress and micromotion explained previously. Unfortunately, there were not enough patients in the Type D classification to allow subgroup analysis between decompression and instrumented fusion. Therefore, this is a biomechanical presumption due to the mechanical stresses present at the affected level. The increased stability achieved with instrumentation may have influenced the surgical outcome of the OLF. Although further studies on a greater number of patients are necessary to better determine the effects of surgical procedures on surgical outcomes for OLFs, surgery with instrumentation for Type D OALLs may have better surgical outcome.

Study Limitations

Limitations in the present study include its retrospective nature. However, because the yearly incidence of thoracic OLFs is relatively low, prospective studies have been difficult. The Nagoya Spine Group comprises spinal specialists at Nagoya University and related institutions who use similar imaging tests and treatment strategies. Although this study evaluated patients with a thoracic OLF who underwent single-level decompression, more than 1 spinal segment is frequently involved. Moreover, this is the first report that examines surgical outcomes for a thoracic OLF as it relates to the concurrent presence of an OALL. These results may also serve as basic data for prospective studies that are planned in the near future. Another limitation is that the stability achieved using instrumentation may have influenced the surgical outcome.

Conclusions

Sixty-three patients with thoracic OLFs were evaluated in a multicenter study. Symptoms of thoracic OLFs improved with surgery, but patients with Type D OALLs had more severe symptoms preoperatively and poorer surgical outcomes. Surgery with instrumentation for Type D OALLs may produce a better surgical outcome.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Ando. Acquisition of data: Ando, Kato, Yukawa, Kawakami, Sato, Matsubara, Kanemura, Matsuyama, Ishiguro. Analysis and interpretation of data: Ando. Drafting the article: Ando. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ando. Statistical analysis: Ando, Wakao, Hirano, Tauchi, Muramoto.

Administrative/technical/material support: Ando, Ishiguro. Study supervision: Ando, Imagama.

References

1. Aizawa T, Sato T, Sasaki H, Kusakabe T, Morozumi N, Kokubun S: Thoracic myelopathy caused by ossification of the ligamentum flavum: clinical features and surgical results in the Japanese population. **J Neurosurg Spine 5:**514–519, 2006
2. 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) 35:**51–56, 2010
3. He S, Hussain N, Li S, Hou T: Clinical and prognostic analysis of ossified ligamentum flavum in a Chinese population. **J Neurosurg Spine 3:**348–354, 2005
4. Hirabayashi K, Miyakawa J, Satomi K, Maruyama T, Wakano K: Operative results and postoperative progression of ossification among patients with ossification of cervical posterior longitudinal ligament. **Spine (Phila Pa 1976) 6:**354–364, 1981
4. 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 5:**133–139, 2006
6. Kudo S, Ono M, Russell WJ: Ossification of thoracic ligamenta flava. **AJR Am J Roentgenol 141:**117–121, 1983
7. Kuh SU, Kim YS, Cho YE, Jin BH, Kim KS, Yoon YS, et al: Contributing factors affecting the prognosis surgical outcome for thoracic OLF. **Eur Spine J 15:**485–491, 2006
8. Li F, Chen Q, Xu K: Surgical treatment of 40 patients with thoracic ossification of the ligamentum flavum. **J Neurosurg Spine 4:**191–197, 2006
9. Liao CC, Chen TY, Jung SM, Chen LR: Surgical experience with symptomatic thoracic ossification of the ligamentum flavum. **J Neurosurg Spine 2:**34–39, 2005
10. Mader R: Clinical manifestations of diffuse idiopathic skeletal hyperostosis of the cervical spine. **Semin Arthritis Rheum 32:**130–135, 2002
11. Maigne JY, Ayral X, Guérin-Surville H: Frequency and size of ossifications in the caudal attachments of the ligamentum flavum of the thoracic spine. Role of rotatory strains in their development. An anatomic study of 121 spines. **Surg Radiol Anat 14:**119–124, 1992
12. McCafferty RR, Harrison MJ, Tamas LB, Larkins MV: Ossification of the anterior longitudinal ligament and Forestier's disease: an analysis of seven cases. **J Neurosurg 83:**13–17, 1995
13. Meyer PR Jr: Diffuse idiopathic skeletal hyperostosis in the cervical spine. **Clin Orthop Relat Res (359):**49–57, 1999
14. Miyakoshi N, Shimada Y, Suzuki T, Hongo M, Kasukawa Y, Okada K, et al: Factors related to long-term outcome after decompressive surgery for ossification of the ligamentum flavum of the thoracic spine. **J Neurosurg 99 (3 Suppl):**251–256, 2003
15. Nishiura I, Isozumi T, Nishihara K, Handa H, Koyama T: Surgical approach to ossification of the thoracic yellow ligament. **Surg Neurol 51:**368–372, 1999
16. Oga M, Mashima T, Iwakuma T, Sugioka Y: Dysphagia complications in ankylosing spinal hyperostosis and ossification of the posterior longitudinal ligament. Roentgenographic findings of the developmental process of cervical osteophytes causing dysphagia. **Spine (Phila Pa 1976) 18:**391–394, 1993
17. Ohtsuka K, Terayama K, Yanagihara M, Wada K, Kasuga K, Machida T, et al: A radiological population study on the ossification of the posterior longitudinal ligament in the spine. **Arch Orthop Trauma Surg 106:**89–93, 1987
18. Okada K, Oka S, Tohge K, Ono K, Yonenobu K, Hosoya T: Thoracic myelopathy caused by ossification of the ligamentum flavum. Clinicopathologic study and surgical treatment. **Spine (Phila Pa 1976) 16:**280–287, 1991
19. Park BC, Min WK, Oh CW, Jeon IH, Kim SY, Kyung HS, et al: Surgical outcome of thoracic myelopathy secondary to ossification of ligamentum flavum. **Joint Bone Spine 74:**600–605, 2007
20. Polgár F: Über interarkuelle Wirbelverkalkung. **Fortschr Geb Röntgen 40:**292–298, 1929
21. Resnick D, Shaul SR, Robins JM: Diffuse idiopathic skeletal hyperostosis (DISH): Forestier's disease with extraspinal manifestations. **Radiology 115:**513–524, 1975
22. Sato T, Kokubun S, Tanaka Y, Ishii Y: Thoracic myelopathy in the Japanese: epidemiological and clinical observations on the cases in Miyagi Prefecture. **Tohoku J Exp Med 184:**1–11, 1998
23. Shiokawa K, Hanakita J, Suwa H, Saiki M, Oda M, Kajiwara M: Clinical analysis and prognostic study of ossified ligamentum flavum of the thoracic spine. **J Neurosurg 94 (2 Suppl):** 221–226, 2001
24. Smith DE, Godersky JC: Thoracic spondylosis: an unusual cause of myelopathy. **Neurosurgery 20:**589–593, 1987
25. Suzuki K, Ishida Y, Ohmori K: Long term follow-up of diffuse idiopathic skeletal hyperostosis in the cervical spine. Analysis of progression of ossification. **Neuroradiology 33:**427–431, 1991
26. Wang W, Kong L, Zhao H, Dong R, Li J, Jia Z, et al: Thoracic ossification of ligamentum flavum caused by skeletal fluorosis. **Eur Spine J 16:**1119–1128, 2007
27. Wang W, Kong L, Zhao H, Dong R, Zhou J, Lu Y: Thoracic myelopathy caused by ossification of ligamentum flavum of which fluorosis as an etiology factor. **J Orthop Surg Res 2:**6, 2007
28. Williams DM, Gabrielsen TO, Latack JT, Martel W, Knake JE: Ossification in the cephalic attachment of the ligamentum flavum. An anatomical and CT study. **Radiology 150:**423–426, 1984
29. Yamazaki M, Mochizuki M, Ikeda Y, Sodeyama T, Okawa A, Koda M, et al: Clinical results of surgery for thoracic myelopathy caused by ossification of the posterior longitudinal ligament: operative indication of posterior decompression with instrumented fusion. **Spine (Phila Pa 1976) 31:**1452–1460, 2006
30. Yayama T, Uchida K, Kobayashi S, Kokubo Y, Sato R, Nakajima H, et al: Thoracic ossification of the human ligamentum flavum: histopathological and immunohistochemical findings around the ossified lesion. **J Neurosurg Spine 7:**184–193, 2007

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ORIGINAL ARTICLE

Clinical results of and patient satisfaction with cervical laminoplasty for considerable cord compression with only slight myelopathy

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Abstract
Purpose There is no established consensus on the indications for surgery in patients with considerable cord compression but only slight myelopathy. The purpose of this study is to stimulate discussion about the indications for surgery in these patients.
Methods The records of consecutive patients who underwent cervical laminoplasty (CLP) during 3.5 years were reviewed. Those patients whose pre-operative Japanese Orthopaedic Association score (JOA score, maximum 17) for cervical myelopathy was 16 points or more, indicating that they had very slight myelopathy, were selected. The postoperative JOA scores of these patients were checked via a chart review, and they were sent a survey asking about their degree of satisfaction with the results of surgery.
Results Of 143 patients who underwent CLP, 14 presented with a preoperative JOA score of 16 or more. No patients showed a postoperative deterioration in JOA score. Nine patients complained of pre-operative hand numbness and this symptom disappeared postoperatively in seven cases. Most patients were satisfied with the results of the surgery: "very satisfied" in 11 cases and none selected "slightly dissatisfied" or "very dissatisfied".
Conclusions We believe that surgery can rescue well-informed and deliberately selected patients with only slight myelopathy, because their symptoms improve and they are freed from persistent anxiety.

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Keywords Cervical spondylotic myelopathy · Ossification of posterior longitudinal ligament · Cervical laminoplasty · Surgical indication · Patient satisfaction

Introduction

There is no established consensus on the indications for surgery in patients with considerable cord compression but only slight myelopathy. The myelopathy may progress with time and become irreversible, and the surgical results and satisfaction of patients with late-stage myelopathy are usually poor [1, 2]. However, surgery is always accompanied by the risk of major and minor complications, which should not be ignored. Furthermore, some patients may do well with conservative treatment [3]. We should weigh the former against the latter, taking into consideration many factors such as age, activity, general condition, understanding, psychological status and social background of the patients, dynamic factors, the severity of cord compression, and the intramedullary high signal intensity on T2 weighted MR images, and our own surgical skill and experience. However, we often waver between conservative treatment and surgery. Two recent review papers on cervical spondylotic myelopathy (CSM) [1, 2] and the Japanese Orthopaedic Association (JOA) guidelines for cervical ossification of posterior longitudinal ligament (OPLL) recommend conservative treatment for patients with mild myelopathy. In contrast, some neurosurgeons aggressively perform prophylactic surgery for those with cord compression and few symptoms.

Cervical laminoplasty (CLP) is a very popular technique for treating cervical myelopathy in our country, which has a higher incidence than Western countries of patients with developmental canal stenosis necessitating a wide range of

decompression. This technique is well established and the reported complication rates are acceptable, but some problems such as axial symptoms or C5 palsy have not been fully resolved [4–6]. The long term results of this technique is satisfactory, with the preservation of the enlarged cervical canal area and the maintenance of JOA scores for cervical myelopathy (JOA score, Table 1, maximum score 17 points) [7].

Table 1 Criteria for evaluation of the severity of cervical myelopathy (JOA[a] score)

I. Motor function
A. Upper limbs, hands and fingers
0 = Unable to feed oneself with any cutlery
1 = Able to feed oneself with a spoon but not with chopsticks; writing is impossible
2 = Able to feed oneself with chopsticks, though awkwardly; writing is possible but not practical
3 = Slightly clumsy use of chopsticks; writing is clumsy but practical
4 = Normal
B. Upper limbs, shoulder and elbow joints
−2 = Manual muscle testing of deltoid or biceps muscles ≤ 2
−1 = Manual muscle testing of deltoid or biceps muscles = 3
−0.5 = Manual muscle testing of deltoid or biceps muscles = 4
0 = Manual muscle testing of deltoid or biceps muscles = 5
C. Lower limbs
0 = Chairbound or bedridden
0.5 = Able to stand but unable to walk
1 = Requires walking aids
1.5 = Walks unaided but with difficulty
2 = Needs support when going up and down stairs
2.5 = Needs support when going down stairs
3 = Capable of fast walking but with some difficulty
4 = Normal
II. Sensory function
A. Upper limbs
0 = Complete sensory loss
0.5 = Severe sensory loss
1 = Mild sensory loss
1.5 = Subjective numbness without sensory loss
2 = Normal
B. Trunk, same as A
C. Lower limbs, same as A
III. Bladder function
0 = Retention and/or incontinence
1 = Sense of retention and/or incomplete continence
2 = Retardation and/or pollakiuria
3 = Normal

[a] The Japanese Orthopaedic Association

In the present study, we retrospectively investigated through a chart review and survey the clinical results and satisfaction of the patients who underwent CLP despite having only slight myelopathy. We focused on CLP because it is the one of the most popular and established technique, by which we have treated many patients. The purpose of this study is to stimulate discussion about the indications for surgery rather than to draw a conclusion.

Materials and methods

The records of consecutive patients who underwent CLP to treat myelopathy between April 2006 and September 2009 were reviewed. CLP was generally performed for patients with cervical spinal canal stenosis ranging across three or more intervertebral discs and with lordotic or straight alignment. In all cases, one of the spinal surgeons in our hospital decided on and performed the surgery. Exclusion criteria were CLP shortly after spinal cord injury, previous cervical surgery and concomitant foraminotomy or fusion. The patients' pre-operative JOA scores were reviewed. The patients whose pre-operative JOA score was 16 points or more were selected. A JOA score of 16 or more indicates very slight if any myelopathy, and was selected as the threshold because considering only extreme cases makes the purpose of the present study clearer. Further, the complaints of most of these patients were only numbness or sensory disturbance of the hands. This made the group homogenous and made the interpretation of the results simpler. The postoperative JOA scores of these patients were checked through a chart review and they were sent a survey asking about pre-operative symptoms, symptoms at the time of response, why they underwent surgery, and their degree of satisfaction with the result (Table 2).

Before surgery, all patients were well informed about the possibility of worsening of their symptoms with ageing, their irreversibility, the effects and limitations of the conservative treatments, the risks of the operation including very rare major complications such as mortality or permanent quadriplegia and more popular complications such as axial symptoms or C5 palsy, and the limitations of the surgery. The merits and demerits of both conservative and surgical treatment were thoroughly explained. We sometimes took a lot of time if the patients and their family had many questions. Only patients, who and whose family essentially understood the above explanation, became candidates for operation. After discussion, the final decision was made by the patients and their families.

The precise technique for CLP and its postoperative care has been described elsewhere [8]. Briefly, the technique was conventional double-door laminoplasty, except that suture anchors instead of interlaminar spacers were used to

Table 2 Survey sheet

Question 1: Select your pre-operative symptoms (multiple selections are allowed)
0: None
1: Nuchal and shoulder pain or stiffness
2: Numbness in the hand
3: Clumsiness of the hand
4: Numbness in the lower limbs
5: Difficulty in walking
6: Disturbance of urination
7: Others
Question 2: Select your postoperative symptoms (multiple selections are allowed)
0: None
1: Nuchal and shoulder pain or stiffness
2: Numbness in the hand
3: Clumsiness of the hand
4: Numbness in the lower limbs
5: Difficulty in walking
6: Disturbance of urination
7: Others
Question 3: Why did you decide to undergo the operation (multiple selections are allowed)?
1: Because my activities of daily living were disturbed by the symptoms, although they were slight, and I wanted to improve them by undergoing the operation
2: Because the doctors (including those at previous hospitals) recommended the operation
3: Because I wanted to avoid being disabled in the future
4: Because I hated to live with anxiety about the future
5: Others
Question 4: Are you satisfied with the results of the surgery (one selection)?
1: Very satisfied
2: Slightly satisfied
3: Neither satisfied nor dissatisfied
4: Slightly dissatisfied
5: Very dissatisfied
Free comments

keep the split laminae open. The bilateral muscles attached to the C2 and/or C7 spinous processes were preserved as far as possible. Patients wore a soft collar for about two weeks after surgery.

Results

The total number of patients who fulfilled the selection criteria was 146. However, the pre-operative JOA scores of three patients were not available, resulting in 143 patients (89 males and 54 females) being selected. Their mean age

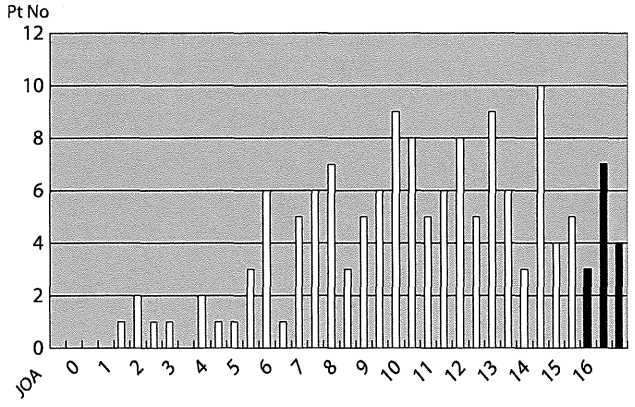

Fig. 1 Distribution of pre-operative JOA scores of the patients who underwent CLP. *Black bars* indicate the patients whose pre-operative JOA score was 16 or more

was 66.6 years (33–92 years). The diagnosis was CSM in 120 patients and OPLL in 23 patients. The mean pre-operative JOA score was 10.9 points and its distribution in these patients is shown in Fig. 1.

Fourteen patients had a pre-operative JOA score of 16 or more (9.7%, 11 males and three females) (Fig. 1, Table 3). Four patients had the maximum JOA score of 17. Seven patients complained of numbness in the hands without sensory disturbance, resulting in a JOA score of 16.5. The JOA score of the remaining three patients was 16: two patients complained of mild sensory loss in the hands and one patient complained only of being unable to fully extend the fingers of the left hand. Although some patients complained of clumsiness of the hand or numbness pre- and/or postoperatively, they were allocated the maximum score when the clumsiness was not objectively detectable or the subjective numbness was occasional. The mean age of patients with a JOA score of 16 or more was 51.9 years (35–67 years), while that of the remainder was 68.2 years. The mean age of the patients with a JOA score of 12 or less (a widely accepted indication for CLP) was 70.9 years. Of the 14 patients with a JOA score of 16 or more, nine were diagnosed with CSM and five with OPLL. Eleven were referred patients. Two of the non-referred patients came to us asking for a second opinion because in a previous hospital they were strongly recommended to undergo surgery in spite of their mild symptoms.

Plain radiograms and MRI of all the patients demonstrated considerable cervical spinal canal stenosis without remarkable instability. Dural tube compression at three or more levels and spinal cord deformity were observed on MRI in all cases. Disappearance of the cerebrospinal fluid signal on T2 weighted MRI was observed in all but one patient (case 11, Fig. 2). Three patients demonstrated the intramedullary high signal intensity on T2 weighted MR images.

Table 3 Details of the patients undergoing CLP with pre-operative JOA score of 16 or more

Case	Age (years)	Pre-operative JOA score	Postoperative JOA score (at final FU)	Postoperative term of survey (months)	Pre-operative symptoms (Q1)	Present symptoms (Q2)	Decision (Q3)	Satisfaction (Q4)	Range of CLP
1	56	16.5	17	38	2	None	4	1	C2–6, T3, 4
2	58	16.5	16.5	26	2	2	1, 3	1	C2–6
3	54	16.5	17	25	1, 2, 3, 5	None	1	1	C2–7
4	61	17	17	14	1	None	3, 4	1	C3–7
5	64	16.5	17	12	2	1	2, 3	1	C3–7
6	35	16	17	12	1, 2, 3	1, 3	4	1	C3–T2
7	35	16	16	12	2	1, 2	1	1	C3–6
8	56	16	16.5	12	1, 2	1, 2	1, 2	3	C3–7
9	40	16.5	17	12	2	1	2, 4	1	C2–7
10	40	17	17	12	7	1, 7	5	3	C1–T1
11	40	16.5	17	12	1, 2, 5	1, 4	3, 4	1	C3–7
12	61	17	17	12	1	1	2, 4	2	C2–7
13	67	17	17	12	None	1	2, 4	1	C3–7
14	60	16.5	17	10	1, 2	None	3, 4, 5	1	C1–7

Numbers in the columns from Q1 to Q4 correspond to the selection numbers in the survey (Table 2)

CLP cervical laminoplasty, *JOA* Japanese Orthopaedic Association, *FU* follow up, *Q1–Q4* question number in the survey

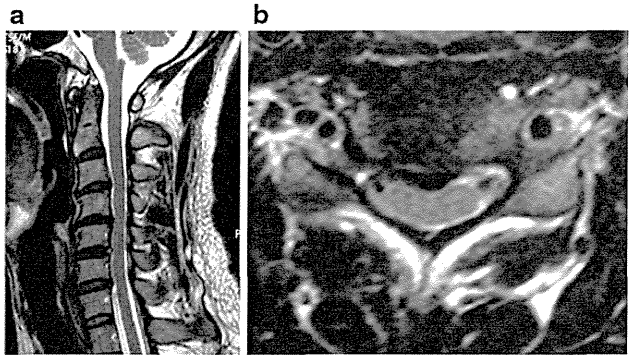

Fig. 2 Pre-operative T2 weighted sagittal MRI (**a**) and axial MRI at C4/5 (**b**) of case 11. Dural tube compression and spinal cord deformity are apparent, but the cerebrospinal fluid signal was barely detectable on both sagittal and axial images. No intramedullary high signal intensity was observed on T2 weighted MR images

The final JOA score was obtained at least 10 months postoperatively in all cases. The survey was retrieved from all patients (response rate 100%), and the mean postoperative follow-up at response was 15.8 months (10–38 months). The demographic data and the survey results for these 14 patients are shown in Table 3. The final JOA scores of these patients were all 16 or more, and none showed deterioration in the JOA score after surgery. Four patients pre-operatively and 11 postoperatively had the maximum score. Nine patients complained of numbness in the hand pre-operatively, which was the most common symptom. This symptom disappeared postoperatively in seven cases. Seven patients pre-operatively and nine postoperatively complained of axial symptoms such as nuchal or shoulder pain or stiffness. Five patients complained postoperatively of de novo axial symptoms. In four of them, the symptom was mild and the activity of daily living was not disturbed. Only one patient complained of moderate shoulder stiffness, which affected his activity. However, none required sick leave or analgesics for the axial symptoms. On the other hand, axial symptoms disappeared postoperatively in three patients.

The reason why the patients underwent the operation showed no particular trends. The most common reason was "because I hated living with anxiety about the future", selected by eight of the 14 patients, followed by "because the doctors recommended surgery" and "because I wanted to avoid being disabled in the future" (five votes each), then "because I wanted to improve my slight symptoms" (four votes). Four of five patients who selected "because the doctors recommended surgery" had been recommended to undergo surgery by their previous doctors.

Most of the patients were satisfied with the results of the surgery, that is, "very satisfied" in 11 cases, "slightly satisfied" in one, and "neither satisfied nor dissatisfied" in two. There were no patients who selected "slightly dissatisfied" or "very dissatisfied". The main reasons for their satisfaction, which were identified from patients' free comments made in the survey, were "my symptoms were improved" and "I can live without anxiety about palsy". One patient who selected "neither satisfied nor dissatisfied" (case 10) commented "I recommend the operation to patients in the same situation as me to prevent worsening of

their symptoms". One patient (case 3) was very satisfied because after surgery he was able to play the violin as he used to. Before the operation, he was sometimes unable to move his fingers dexterously while playing the violin, although he had no difficulty in daily living and his preoperative upper extremity motor function score was the maximum (four points).

Case presentation (case 11)

A 40-year-old man was referred to us to treat an osteoid osteoma in the left L2 superior articular process. His only complaint was low back pain and he was classified as a non-referred patient. However, he had a history of transient quadriplegia after jumping from a height, at which time the cervical spinal canal stenosis was identified. At that time, the quadriplegia disappeared completely after several days of emergency admission in another hospital. Plain lateral radiograms of his cervical spine demonstrated a straight alignment with an anterior–posterior distance of the spinal canal of 10–12 mm, and MRI demonstrated spinal canal stenosis with considerable cord compression from C3/4 to C6/7 (Fig. 2). Although he had slight numbness on the ulnar side of both hands, no sensory disturbance was observed. The reflexes of his upper extremities were within normal limits, but bilateral patellar tendon reflexes were exaggerated. No pathological reflex was observed. Manual muscle testing of the four extremities demonstrated no muscle weakness. His JOA score was 16.5 points. We did not recommend surgery, although we presented it as one of the options. We advised him to give up his hobby of driving in car races to prevent possible irreversible quadriplegia caused by a car accident.

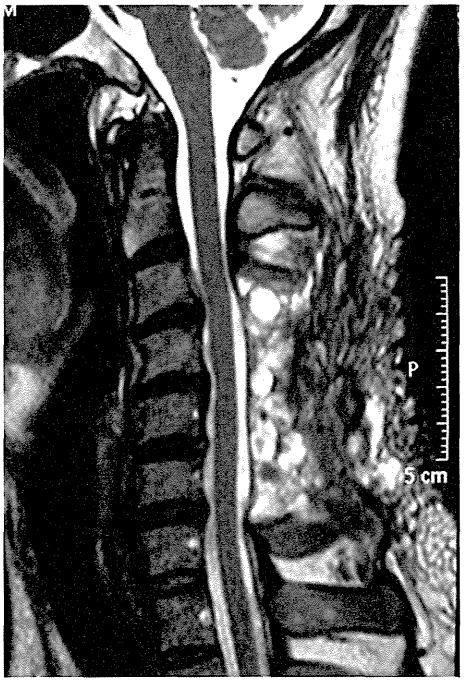

Fig. 3 Postoperative T2 weighted sagittal MRI of case 11 two weeks after surgery. The dural tube was successfully decompressed from C3/4 to C6/7

After the successful resection of the lumbar osteoid osteoma, he decided to undergo CLP. He did not want to give up car racing, partly because it was closely related to his job of running a tyre shop. He underwent CLP from C3 to C7 (double-door laminoplasty from C4 to C6 with concomitant resection of distal lamina of C3 and proximal lamina of C7) (Fig. 3). His postoperative course was uneventful.

At 1 year after operation, the numbness in his hands had disappeared. Although he complained of occasional nuchal pain and stiffness (which he had also complained of preoperatively), he returned to his work and car racing with peace of mind. He chose "very satisfied" in the survey, and commented that he was happy, without anxiety about the future.

Discussion

The natural history of CSM or OPLL is not well known. Symptoms are often stable, at least in the short term, and only a modest number of patients improve while a significant minority eventually deteriorates. Worsening can occur in a gradual and stepwise progressive fashion. However, there are patients who present with sudden irreversible quadriplegia caused by minor trauma, although this is rare. However, the clinical course of an individual patient is difficult to predict [1]. Even MRI cannot reliably predict who will benefit from surgery and who will not. It is generally believed that the predictive factors for a good surgical outcome may include shorter duration of disease and milder neuroimaging [1, 2], suggesting that early or prophylactic surgery for myelopathy may be effective. However, we should remember that surgery is always accompanied by the possibility of major and minor complications [4], which makes the indications for surgery in patients with considerable cord compression but slight myelopathy controversial.

In two recent review papers on CSM, the authors recommended a careful observation for asymptomatic or mildly myelopathic patients [1, 2]. These recommendations, however, were drawn from statistical analysis of mostly middle-term follow-up of such patients. In the present study, some of the patients who underwent surgery focused on the possible irreversible worsening of their symptoms rather than the risks of the operation. The mean age of the patients who underwent surgery was 16 years

younger than those patients whose pre-operative JOA score was less than 16 points. This may reflect the patients' concern about the remainder of their life: we should remember that it is very important for some patients, particularly young patients, to live without anxiety about the future. Another reason may be that the JOA score would be higher in younger patients than in older patients with the same grade of myelopathy because of a better ability to compensate in younger patients.

Another point to note in the present study is that some people were happy after surgery because their slight symptoms (numbness in the hands in most cases) were relieved. Conservative treatment is usually recommended for patients with mild myelopathy, not because the symptoms improve with conservative treatment but because in most cases the symptoms do not deteriorate for a long time. Some patients, however, want to completely remove their slight symptoms even at the risk of surgery. For patients with apparent myelopathy, we usually explain that numbness is one of the symptoms least likely to disappear after surgery. However, in spite of repeated pre-operative explanations, some patients, in particular those with the intramedullary high signal intensity on T2 weighted MR images, complained of residual numbness after surgery even though other symptoms improved. In general, only a small percentage of patients experience complete recovery of numbness, so it was surprising that numbness disappeared in seven of nine patients in the present study. Further, one patient was pleased because he was again able to play the violin as he used to. In this series, we can recall another patient of 56 years old with a pre-operative JOA score of 15 who was very satisfied with his surgery for the same reason. One patient (case 6) was also satisfied because his finger extension improved postoperatively. We should note that a slight symptom, even if of little importance from our standpoint, might be a major problem for patients, in particular younger patients.

These results may raise questions about the surgeon's refusal to operate on patients simply because the patients do not present with apparent myelopathy. However, we should note with caution that the number of patients who complained of axial symptoms increased postoperatively, although the symptoms did not markedly disturb the patients' daily lives. We have used a conventional technique for CLP although several less invasive techniques have been recommended to reduce axial symptoms [9]. Although this is not the focus of the present paper, refined techniques may reduce the number of patients with de novo axial symptoms. However, four of five patients who presented with de novo axial symptoms after operation were very satisfied. This may demonstrate that freedom from anxiety and improvement of slight neurological symptoms are much more important for them than the presence of mild axial symptoms.

We want to stress that we are by no means radical surgeons. We believe that thoughtless expansion of the indications for CLP should be strictly avoided. The proportion of patients in our series who were operated on in spite of their high JOA score may be felt to be too high. However, our hospital is a university hospital, and many of the patients were referred to us asking for a final decision when their previous surgeons hesitated to operate. If these surgeons did not have doubts, they would not have recommended their patients to come to us, because CLP is one of the most popular surgical techniques in our country. In addition, we should stress that many of the referred patients chose to be treated conservatively after our explanations of their myelopathy and the risks/benefits of CLP, although to present the exact number of these is impossible.

In the present study, we show the clinical results and the satisfaction of the patients who underwent CLP despite their slight symptoms. Their clinical results were good and their satisfaction was high. It would be impossible to draw a scientific conclusion based on the results of the present study because the number of the patients is small, the follow-up was short, conservatively treated patients were not followed or compared, and the patients' satisfaction was closely related to not only clinical results but also their understanding and philosophy. However, our results may stimulate discussion concerning the indications for CLP in such patients, in particular for young, active, intelligent patients, against the prevailing opinion. We should keep several points in mind as a basis for the discussion. First, all the information about the natural course of the disease, the effects and limitations of conservative treatments and in particular about major and minor complications of surgery that may result in permanent sequelae, should be given to the patients, although some of these are not well known. Second, we should understand that patients' high satisfaction does not always justify surgery. Usually advanced age and better postoperative health status were significantly associated with higher satisfaction [10, 11]. Although our patients were young, their postoperative health status was high with few sequelae, probably as a result of the early surgery, and this may have heightened their satisfaction. However, patient satisfaction is subjective and is easily affected by the surgeons' pre-operative explanation. We should try to keep a scientifically neutral position and always be careful not to mislead the patient.

Nevertheless, we believe that some selected patients are actually rescued by undergoing surgery, because their symptoms, although slight, improve and they are freed from persistent anxiety. Our endeavours to reduce the complication rate of surgery may widen the indications of CLP for these patients. However, we should be careful and

modest in draw a conclusion, because long-term results of cervical laminoplasty more than 20 or 30 years are not fully known. Further, we should attempt to scientifically determine the natural course of cervical myelopathy, the long-term prognosis of conservative treatment and the probability of irreversible palsy caused by minor trauma, to provide more precise information to these patients. Lastly, we should always caution ourselves not to expand thoughtlessly the indications for surgery.

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Conflict of interest The authors certify that no actual or potential conflict of interest in relation to this article exists.

References

1. Tracy JA, Bartleson JD (2010) Cervical spondylotic myelopathy. Neurologist 16:176–187
2. Klineberg E (2010) Cervical spondylotic myelopathy: a review of the evidence. Orthop Clin N Am 41:193–202
3. Shimomura T, Sumi M, Nishida K, Maeno K, Tadokoro K, Miyamoto H, Kurosaka M, Doita M (2007) Prognostic factors for deterioration of patients with cervical spondylotic myelopathy after nonsurgical treatment. Spine 32:2474–2479
4. Ratliff JK, Cooper PR (2003) Cervical laminoplasty: a critical review. J Neurosurg 98(suppl 3):230–238
5. Hosono N, Yonenobu K, Ono K (1996) Neck and shoulder pain after laminoplasty A noticeable complication. Spine 21: 1969–1973
6. Sakaura H, Hosono N, Mukai Y, Ishii T, Yoshikawa H (2003) C5 palsy after decompression surgery for survical myelopathy: review of the literature. Spine 28:2447–2451
7. Kimura A, Seichi A, Inoue H, Hoshino Y (2011) Long-term results of double-door laminoplasty using hydroxyapatite spacers in patients with compressive cervical myelopathy. Eur Spine J 20(9):1560–1566
8. Miyata M, Neo M, Fujibayashi S, Takemoto M, Nakamura T (2008) Double-door cervical laminoplasty with the use of suture anchors, technical note. J Spinal Disord Tech 21:575–578
9. Shiraishi T (2002) A new technique for exposure of the cervical spine laminae. Technical note. J Neurosurg 96(suppl 1):122–126
10. Young GJ, Meterko M, Desai KR (2000) Patient satisfaction with hospital care: effects of demographic and institutional characteristics. Med Care 38:325–334
11. Hekkert KD, Cihangir S, Kleefstra SM, van den Berg B, Kool RB (2009) Patient satisfaction revisited: a multilevel approach. Soc Sci Med 69:68–75

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Three-dimensional measurement of growth of ossification of the posterior longitudinal ligament

Clinical article

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Object. Ossification of the posterior longitudinal ligament (OPLL) is a progressive disease that causes cervical myelopathy. Because 2D evaluation of ossification growth with plain lateral radiographs has limitations, the authors developed a unique technique to measure ossification progression and volume increase by using multidetector CT scanning.

Methods. The authors used serial thin-slice volume data obtained by multidetector CT scanning in 5 patients. The mean patient age was 63 years, and the mean follow-up duration was 3.1 years. First, a 3D model of OPLL was semiautomatically segmented at a specific threshold. Then, a preoperative model of OPLL was superimposed on a postoperative model using voxel-based registration of the vertebral bodies. Progression and volume increase were measured using a digital viewer that was developed by the authors. Progression was visualized using a color-coded contour on the surface of the OPLL model.

Results. All patients had progression of 0.5 mm or greater. The mean values concerning OPLL growth were as follows: maximum progression length, 4.7 mm; progression rate, 1.5 mm/year; volume increase, 1622 mm^3; volume expansion rate, 37%; and volume increase rate, 484 mm^3/year. The accuracy of superimposition by voxel-based registration, defined as closeness to the true value, was less than 0.31 mm. For intraobserver reproducibility of the volume measurement, the mean intraclass correlation coefficient, root mean square error, and coefficient of variation were 0.987, 16.0 mm^3, and 1.7%, respectively.

Conclusions. Ossification of the posterior longitudinal ligament progresses even after surgery. Three-dimensional evaluation with the aid of CT scans is a useful and reliable method for assessing that growth.
(DOI: 10.3171/2011.11.SPINE11502)

Key Words • **ossification** • **posterior longitudinal ligament** • **three-dimensional** • **volume increase** • **progression** • **voxel-based registration** • **growth**

Ossification of the posterior longitudinal ligament is a progressive disease with ectopic bone formation in the spinal canal.[4,7,17] Surgical invasion, young age, and type of OPLL have been reported to be risk factors for progression.[2,10] However, the course of natural progression is still unclear, because OPLL grows slowly, by the millimeter. Previous studies have reported documentation of the progression of OPLL by plain radiography.[1,2,5,6] To the best of our knowledge, however, there have been no reports of 3D evaluation of OPLL growth. We developed a unique technique to evaluate growth three-dimensionally using multidetector CT scanning. We then conducted a study to determine the validity of our technique.

Abbreviations used in this paper: CV = coefficient of variation; ICC = intraclass correlation coefficient; OPLL = ossification of the posterior longitudinal ligament; RMSE = root mean square error.

Methods

Data Source

We evaluated thin-slice CT volume data, available at more than 2-year intervals, that had been obtained in 5 patients. All patients had a history of surgery for cervical OPLL; we had access to CT volume data for OPLL before