Risk Factors for Poor Outcomes of Thoracic Ossification of Ligamentum Flavum After Laminectomy

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Background:  
Thoracic ossification of ligamentum flavum (TOLF) is a common pathological change of the thoracic ligamentum flavum. Identifying the risk factors for poor prognosis is critical for choosing suitable surgical methods.

Material/Methods:  
A total of 64 patients with TOLF after laminectomy were reviewed between January 2010 and April 2018 at the Department of Spine Surgery of the Third Hospital of Hebei Medical University. The Japanese Orthopaedic Association (JOA) scale was used to evaluate the neurological function of patients. According to the average JOA improvement rate, the patients were divided into the good prognosis group (Group GP) and the poor prognosis group (Group PP). Multivariate logistic regression analysis was used to identify the risk factors for poor outcomes.

Results:  
The average JOA improvement rate was 53.04±24.29%. Group GP comprised 33 patients, while Group PP comprised 31 patients. Duration of preoperative symptoms (P=0.005), intramedullary high signal intensity (P=0.001), dural ossification rate (P=0.002), and sagittal configuration of ossification (P=0.012) were significantly higher in Group PP than in Group GP. Multivariate logistic analysis showed that duration of preoperative symptoms (P=0.022), intramedullary high signal intensity (P=0.010), dural ossification (P=0.007) and sagittal configuration of ossification (P=0.029) were risk factors for poor outcomes of TOLF after laminectomy.

Conclusions:  
After surgical treatment of TOLF, the symptoms of some patients either recovered slowly or did not recover. Longer than 17 months of preoperative symptoms, intramedullary high signal intensity, dural ossification, and sagittal configuration of ossification were the risk factors for poor outcomes of TOLF after laminectomy.

Keywords:  
Ligamentum Flavum • Osteogenesis • Spinal Cord Injuries

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Background

Thoracic ossification of the ligamentum flavum (TOLF) is a pathological change of the thoracic ligamentum flavum in which the ligament tissue is replaced by new heterotopic bone tissue, and often appears in the lower thoracic vertebra, especially T9-T12. Ossification compresses the spinal cord, causing spinal cord compression symptoms [1-5]. In addition to the above symptoms, some patients also have root compression. However, separate nerve root stimulation is rarely observed [6]. Once the spinal cord is compressed by TOLF, the conservative treatment effect is poor, and surgery is the only effective method. Miyakoshi [7] found that the duration of symptoms before surgery was closely related to surgical prognosis. Hence, early detection, diagnosis, and treatment play an important role in prognosis of the disease. Traditional open surgery includes posterior laminectomy, laminectomy and internal fixation, and laminoplasty, of which laminectomy has become one of the classic operations [8-12]. In recent years, various minimally invasive techniques have been gradually applied for the treatment of TOLF [12,13]. Although various decompression operations have been applied for the treatment of TOLF, the postoperative efficacy is occasionally unsatisfactory, and the degree of postoperative recovery is also difficult to predict. Several studies have discussed the risk factors of TOLF, but no consensus has been reached [14]. Identifying the risk factors for poor prognosis is critical for choosing suitable surgical methods. In this study, we aimed to identify the risk factors for poor prognosis of laminectomy for TOLF to provide a theoretical basis for the selection and improvement of surgery.

Material and Methods

Patients

We retrospectively selected the patients diagnosed with TOLF who were treated by laminectomy at the Spine Surgery Department of the Third Hospital of Hebei Medical University between January 2010 and April 2018. Inclusion criteria were: 1. Patients diagnosed as TOLF and treated by laminectomy; 2. Complete clinical data available; 3. The last follow-up was ≥2 years. Exclusion criteria were: 1. Combined with anterior herniated disc that significantly compressed the spinal cord or nerve roots; 2. Combined with other spinal cord-related diseases; 3. Trauma, inflammation, infection, and tumor involvement of the spine; 4. Combined with severe cervical or lumbar nerve compression. A total of 64 patients were included in the study; the mean age was 59.31±6.79 years, with 39 males and 25 females. Among these, 44 patients underwent open laminectomy and 20 underwent open laminectomy with internal fixation. Patients with higher-than-average JOA improvement rate were assigned to the good prognosis group (Group GP), while patients with lower-than-average JOA improvement rate were assigned to the poor prognosis group (Group PP).

Imaging and Clinical Evaluation

Patients underwent 1.5-T thoracic I (SIEMENS MAGNETOM Symphony), 1-mm CT plain scan, and thoracic vertebrae X-rays in positive and lateral positions before the operation. During the follow-up, the patients underwent thoracic vertebrae X-rays in positive and lateral positions. The nerve function of the patients was evaluated by the Japanese Orthopaedic Association (JOA) score before the operation, at 2 weeks after operation, and at the final follow-up (Figure 1). The JOA score of thoracic nerve function (full score 11) was modified based on the JOA score of cervical spine [15] (full score 17) [16]. A score of 4 for ambidextrous dexterity and a score of 2 for both upper limbs were removed from the CERVICAL JOA score (Table 1). Evaluation of neurological function improvement rate at the last follow-up was calculated using the equation: JOA score improvement rate=(JOA score at the last follow-up-preoperative JOA score)/[11-preoperative JOA score]×100%. We recorded data on patients’ age, sex, duration of preoperative symptoms (months), follow-up duration (months), ossification segments, number of ossification segments, presence or absence of intramedullary high signal intensity in T2WI, presence or absence of dural ossification, previous basic medical history (hypertension, diabetes, heart disease, cerebrovascular disease), surgical method, and configurations of OLF in sagittal (beak or round) plane.

Statistical Analysis

SPSS 22.0 (IBM, Armonk, NY, USA) statistical software was used for analysis, and the test level was α=0.05. The measurement data were compared between the 2 groups and analyzed by
Table 1. Modified thoracic JOA scoring scale.

| Functional score         |          |
|--------------------------|----------|
| **Lower-extremity function** |          |
| 0                        | Impossible to walk |
| 1                        | Need cane or aid on flat ground |
| 2                        | Need cane or aid only on stairs |
| 3                        | Possible to walk without cane or aid but slowly |
| 4                        | Normal |
| **Lower-extremity sensory function** |          |
| 0                        | Apparent sensory loss |
| 16                       | Minimal sensory loss |
| 2                        | Normal |
| **Trunk sensory function** |          |
| 0                        | Apparent sensory loss |
| 1                        | Minimal sensory loss |
| 2                        | Normal |
| **Bladder function**     |          |
| 0                        | Complete retention |
| 1                        | Sense of retention or dribbling or straining |
| 2                        | Urination frequency or hesitancy |
| 3                        | Normal |

In 1 patient, postoperative lower limb muscle strength was reduced from preoperative level IV to level II, which was treated with hormones and dehydration drugs. At the 24-month follow-up, the patient’s muscle strength returned to the preoperative level. The average preoperative JOA score was 5.03±1.49, and the JOA score at the last follow-up was 8.11±1.66, which was significantly higher than that before surgery (P<0.001). The average improvement rate was 53.04±24.29%. Among them, 33 patients had a higher-than-average improvement rate and were included in Group GP, while the other 31 patients had a lower-than-average improvement rate and were included in Group PP.

There were no statistically significant differences in age, sex, follow-up duration, ossification segments, number of ossification segments, previous history, or surgical method between Group GP and Group PP (Table 2). Two patients in Group GP had ossification in 3 vertebral bodies, 2 patients in Group PP had ossification in 3 vertebral bodies, and 2 patients had ossification in 4 vertebral bodies. The preoperative symptom duration of Group GP was 18.12±10.05 months, which was significantly lower than that of Group PP. Preoperative MRI of 29 patients in Group PP accompanied by intramedullary high signal intensity (93.55%) in T2WI was significantly higher than that of 19 patients in Group GP (57.58%) (Table 2). In the preoperative CT scan, 12 patients in Group PP were found to have dural ossification, while only 2 patients in Group GP were found to have dural ossification, and the difference between the 2 groups was statistically significant (Table 2). Sagittal configuration of ossification was also identified as a risk factor in this study, 8 (24.2%) patients had beak-type ossification in Group GP and 17 (54.8%) in Group PP, and the difference was also statistically significant.

In the univariate logistic regression analysis, 4 factors were included in the multivariate logistic model: preoperative symptom duration, intramedullary high signal intensity in T2WI, epidural ossification, and sagittal configuration of ossification. Multivariate logistic analysis found that preoperative duration of symptoms, intramedullary high signal intensity in T2WI, epidural ossification, and sagittal configuration of ossification were risk factors for poor prognosis of laminectomy for TOLF, and their OR and 95% CI were 1.078 (1.011-1.151), 16.016 (1.949-131.586), 13.999 (2.067-94.825), and 4.722 (1.168-19.088), respectively (Table 3). We also measured the sensitivity, specificity, and cutoff value of preoperative symptom duration for poor postoperative symptom recovery.

The mean preoperative symptom duration of the patients was 22.14±12.05 months, and the mean follow-up time was 31.85±7.66 months. All operations were successfully performed.

**Results**

The mean preoperative symptom duration of the patients was 22.14±12.05 months, and the mean follow-up time was 31.85±7.66 months. All operations were successfully performed.
|                                | Group GP (33 cases) | Group PP (31 cases) | t/z  | P value |
|--------------------------------|---------------------|---------------------|------|---------|
| Age                            | 58.42±5.87          | 60.26±7.63          | 0.815| 0.415   |
| Sex (Male/Female)              | 21/12               | 18/13               | 0.208| 0.648   |
| Duration of symptoms before surgery (months) | 18.12±10.05        | 26.42±12.67         | 2.787| 0.005   |
| Follow-up duration (months)    | 32.07±7.85          | 30.83±7.22          | 1.249| 0.212   |
| Ossification of segments       |                     |                     | 4.002| 0.135   |
| T1-4                           | 3                   | 7                   |      |         |
| T5-86                          | 11                  | 19                  |      |         |
| T9-12                          | 32                  | 26                  |      |         |
| Number of ossified segments    |                     |                     | 1.753| 0.416   |
| 1                              | 22                  | 16                  |      |         |
| 2                              | 9                   | 11                  |      |         |
| >2                             | 2                   | 4                   |      |         |
| Accompanied by hypersignal of thoracic cord | 19            | 29                  | 11.032| 0.001  |
| Configurations of OLF in sagittal plane | 6.286           |                     |      | 0.012   |
| Beak-type                      | 8                   | 17                  |      |         |
| Round-type                     | 25                  | 14                  |      |         |
| Accompanied by epidural ossification | 2              | 12                  | 9.970| 0.002   |
| Past history                   |                     |                     |      |         |
| Diabetes                       | 8                   | 11                  | 0.968| 0.325   |
| Hypertension                   | 12                  | 14                  | 0.531| 0.747   |
| Coronary heart disease         | 5                   | 5                   | 0.638| 0.425   |
| Cerebrovascular disease        | 4                   | 7                   | 1.229| 0.268   |
| Operation method               |                     |                     | 0.207| 0.249   |
| Open laminectomy               | 21                  | 22                  |      |         |
| Open laminectomy and internal fixation | 11               | 9                   |      |         |
| JOA score                      |                     |                     |      |         |
| Preoperative                   | 5.33±1.53           | 4.71±1.40           | 1.650| 0.099   |
| Follow-up                      | 9.30±0.81           | 6.84±1.37           | 6.427| <0.001  |
| t/z                            | 5.078               | 4.645               |      |         |
| P value                        | <0.001              | <0.001              |      |         |
| JOA improvement rate (%)       | 33.60±18.67         | 71.31±11.16         | 6.902| <0.001  |
Our study found no significant difference in preoperative JOA score. These patients have poor postoperative neurological function, preoperative incontinence, and lower grade, TOLF segment number, coexisting OPLL, CT classification, and intramedullary high signal intensity were not related to surgical prognosis, while the duration of symptoms or neurological score before surgery could not be used to predict prognosis due to inconsistent results. Ando [23] conducted a multi-center study and found that duration of preoperative symptoms, dural ossification, and type D ossification were associated with prognosis of surgery. He [24] showed that preoperative symptom duration and JOA score were important predictors of postoperative JOA score and recovery rate. Patients with gaitism, patella and/or ankle clonus positive, and MRI high intramedullary signal had poor prognosis. Zhang [14] found that preoperative signal strength of thoracic spinal cord was highly predictive of poor prognosis.

Studies [25] have pointed out that long-term compression of the spinal cord leads to damage of the anterior horn of the spinal cord, interruption of the conduction pathway of the lumbar-sacral reflex center, preoperative incontinence, and lower JOA score. These patients have poor postoperative neurological recovery.

Our study found no significant difference in preoperative JOA score between the 2 groups, so the influence of preoperative JOA score on prognosis could not be evaluated. After laminectomy, the JOA score of the patients was significantly improved during follow-up compared with that before surgery, with an average improvement rate of 53.04±24.29%, indicating that laminectomy is an effective treatment for TOLF.

Different studies have drawn different conclusions about the effect of duration of symptoms before surgery. He et al [24] reported that early surgical intervention had a positive effect on prognosis, which was refuted by Hur Hyuk [26]. In this study, preoperative symptom duration was found to have a significant effect on prognosis, which was same as He et al. Moreover, our study found that the threshold for preoperative duration of symptoms was 17 months, which was similar to Chang et al [27]. This suggests that preoperative symptoms lasting longer than 17 months lead to poor postoperative prognosis, so early surgical intervention is the key to improve the prognosis of patients.

MRI is the most commonly used method for spinal cord evaluation, and it can clearly display the anatomical conditions of thoracic cord, compression, and signal changes. Studies [28] have shown that the incidence of intramedullary high signal intensity of patients with thoracic stenosis due to TOLF is 41-79%. In terms of the effect of T2-weighted intramedullary signal on surgical prognosis, it is generally believed that when the spinal cord at the affected segment is subjected to long-term compression and ischemia, it can show high signals in the MRI T2WI. Inamasu [1] believed that the degree of spinal cord compression was significantly correlated with the intramedullary signal in T2WI. Our study also found a significant difference between the good and poor outcome groups (P=0.001).

Dural ossification is a common complication of TOLF. The ossified dura and ligamentum flavum form an integral whole, which significantly increases the risk of dural tear, cerebrospinal fluid leakage, and nerve root injury [12,29], and is one of the risk factors for poor prognosis. Wang et al [11] found that the volume of the thoracic spinal canal was smaller than that of cervical and lumbar canals, and the thoracic cord blood supply was less due to its fewer anastomosis branches, and the ability of collateral circulation to supply blood was poor, so the tolerance to ossification compression was poor. Even if

| Table 3. Multivariate logistic regression analysis results. |
|---------------------------------------------------------|
| **Duration of symptoms**                                |
| **P value**                                             |
| 0.022                                                   |
| **OR**                                                  |
| 1.078                                                   |
| **95% CI**                                              |
| 1.011-1.151                                             |
| **Thoracal cord hypersignal**                            |
| **P value**                                             |
| 0.010                                                   |
| **OR**                                                  |
| 16.016                                                  |
| **95% CI**                                              |
| 1.949-131.586                                          |
| **Dural ossification**                                  |
| **P value**                                             |
| 0.007                                                   |
| **OR**                                                  |
| 13.999                                                  |
| **95% CI**                                              |
| 2.067-94.825                                           |
| **Configuration of OLF**                                |
| **P value**                                             |
| 0.029                                                   |
| **OR**                                                  |
| 4.722                                                   |
| **95% CI**                                              |
| 1.168-19.088                                           |
there is no dural ossification, the dura is often associated with ossification and should be carefully explored while removing ossification. If adhesion occurs, the dura should be carefully and gently separated to reduce the incidence of epidural tear.

We also found that the sagittal configuration of ossification had a significant effect on the operative prognosis, and the beak-type patients had poor postoperative neurological recovery. We hypothesized that this may be because beak-type ossification acts like an awl on the spinal cord, which increases the difficulty of surgery and generally puts more pressure on the spinal cord, which is the same as Sung Uk Kuh’s view [30]. However, Li et al [31] found that the sagittal configuration of patients’ ossification had no effect on postoperative prognosis, and Kang et al [10] suggested that patients with beaks have a better prognosis. These differences may be due to the insufficient sample size and the difference among surgeons, which leads to different results. Hence, further study is needed.

This study had some limitations. 1. This was a retrospective and single-center study with a small sample size, especially in the minimally invasive group. Hence, a multi-center study with a large sample size is needed to confirm our findings. 2. The longest duration of neurological function recovery after TOLF is unclear, so the minimum follow-up time of 2 years in our study may be insufficient.

Conclusions

In conclusion, some of the patients did not experience the expected effect, and our study found that longer than 17 months of preoperative symptoms, intramedullary high signal intensity, dural ossification, and sagittal configuration of ossification were the risk factors for poor outcomes of TOLF after laminectomy. According to the results, we need more complete evaluation of patients’ preoperative status and radiologic features to predict the surgical outcome for TOLF.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.
25. Sanghvi AV, Chhabra HS, Mascarenhas AA, et al. Thoracic myelopathy due to ossification of ligamentum flavum: A retrospective analysis of predictors of surgical outcome and factors affecting preoperative neurological status. Eur Spine J. 2011;20(2):205-15

26. Hur H, Lee JK, Lee JH, et al. Thoracic myelopathy caused by ossification of the ligamentum flavum. J Korean Neurosurg Soc. 2009;46(3):189-94

27. Chang UK, Choe WJ, Chung CK, et al. Surgical treatment for thoracic spinal stenosis. Spinal Cord. 2001;39(7):362-69

28. Kägi S, Ciurea A, Micheroli R. Ossification of the ligamentum flavum. Rheumatology (Oxford, England). 2020;59(7):1616

29. Sun XZ, Chen ZQ, Qi Q, et al. Diagnosis and treatment of ossification of the ligamentum flavum associated with dural ossification. Clinical article. J Neurosurg Spine. 2011;15(4):386-92

30. Kuh SU, Kim YS, Cho YE, et al. Contributing factors affecting the prognosis surgical outcome for thoracic OLF. Eur Spine J. 2006;15(4):485-91

31. Li Z, Ren D, Zhao Y, et al. Clinical characteristics and surgical outcome of thoracic myelopathy caused by ossification of the ligamentum flavum: A retrospective analysis of 85 cases. Spinal Cord. 2016;54(3):188-96