The Postoperative Prognosis of Thoracic Ossification of the Ligamentum Flavum can be Described by a Novel Method: The Thoracic Ossification of the Ligamentum Flavum Score

Deluo Wu[1,2], Hongwei Wang[1], Pan Hu[3], Weijie Xu[4], Jun Liu[1]

■ OBJECTIVE: **To create an available thoracic ossification of the ligamentum flavum (TOLF) score as a rudimentary predictor for the postoperative prognosis of TOLF.**

■ METHODS: **A retrospective review was conducted for all patients with TOLF who received surgical decompression from April 2012 to February 2019. The TOLF score consists of 5 components, namely, the age at surgery (1–3 points), diabetes mellitus (1 point), preoperative duration of symptoms (1–2 points), spinal canal axial remnant area ratio (0–2 points), and intramedullary signal change on magnetic resonance imaging (1 point). The scores of all patients were calculated and analyzed for their correlation with the postoperative recovery ratio. In addition, intraoperative blood loss, urinary catheter indwelling time, cerebrospinal fluid leakage, and postoperative neurologic deterioration were also measured.**

■ RESULTS: **A total of 64 patients were included. The mean TOLF score at the final follow-up was 4.6 points in the excellent group (20 patients), 5.0 points in the good group (29 patients), and 7.3 points in the poor group (15 patients). A higher TOLF score predicts lower postoperative recovery ratio ($P = 0.000$), longer urinary catheter indwelling time ($P = 0.023$), and higher incidence of postoperative neurologic deterioration ($P = 0.000$). However, no correlation was identified between the TOLF score and intraoperative blood loss ($P = 0.755$) or cerebrospinal fluid leakage ($P = 0.911$).**

■ CONCLUSIONS: **The TOLF score is a novel and rudimentary scoring system that describes the predictive factors that indicate the postoperative prognosis of TOLF.**

INTRODUCTION

Thoracic myelopathy caused by thoracic ossification of the ligamentum flavum (TOLF) is a rare and unexplained ligament ossification disease, which is the main cause of thoracic spinal stenosis. TOLF results in a reduction in the volume of the thoracic spinal canal and physical compression of the spinal cord and (or) nerve roots, followed by a variety of clinical symptoms and signs.[1-3] TOLF has been reported more frequently in eastern Asian countries, with a prevalence of 3.8% in southern China,[4] and a prevalence of 6.2% for men and 4.8% for women in Japan.[5] Progression of TOLF is slow and difficult to visualize; conservative treatment is usually ineffective, and it has to be surgically treated when symptoms appear.

Several surgical procedures have been developed for the treatment of TOLF, the most common and classic one is the posterior decompression by laminectomy. However, surgical outcomes vary with this approach.[6-12] In a systematic review of postoperative complications of TOLF, cerebrospinal fluid leakage was the most frequently reported with a rate of 19% of 475 patients, and postoperative neurologic deterioration was reported in 5% of 475 patients.[13] Insufficient judgment regarding surgical prognosis may give rise to inappropriate surgical strategy and cause great inconvenience to patients. Thus, the appropriate surgical strategy

Key words
- Ligamentum flavum
- Ossification
- Postoperative prognosis
- Score
- Thoracic

Abbreviations and Acronyms
mJOA: Modified Japanese Orthopaedic Association
MRI: Magnetic resonance imaging
RR: Recovery ratio
TOLF: Thoracic ossification of the ligamentum flavum

From the [1]Department of Orthopedics, General Hospital of Shenyang Military Area Command of Chinese PLA, Shenyang, Liaoning; [2]Graduate School, Dalian Medical University, Dalian, Liaoning; [3]Department of Orthopedics, Chinese Medicine Hospital of Dianjiang County, Dianjiang, Chongqing; and [4]Graduate School, Jinzhou Medical University, Jinzhou, Liaoning, China

To whom correspondence should be addressed: Jun Liu, Ph.D. [E-mail: junliu_gh@163.com]

Deluo Wu and Hongwei Wang contributed equally to this work.

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Table 1. Correlations Between the Postoperative Recovery Ratio and Influencing Factors According to Logistic Regression Analysis

		Classification of RR (%)			
Factors	**Total**	**Excellent**	**Good**	**Poor**	***P***
Sex					0.946
Male	36	10	17	9	
Female	28	10	12	6	
Age at surgery (years)					0.002
<50	13	7	6	0	
50–60	23	6	13	4	
>60	28	7	10	11	
BMI					0.884
≤27	19	6	8	5	
>27	45	14	21	10	
Hypertension					0.451
Yes	17	6	7	4	
No	47	14	22	11	
Diabetes mellitus					0.006
Yes	6	0	2	4	
No	58	20	27	11	
Smoking history					0.528
Yes	21	6	10	5	
No	43	14	19	10	
Drinking history					0.867
Yes	13	4	7	2	
No	51	16	22	13	
Preoperative duration of symptoms (months)					0.012
≤24	44	15	26	3	
>24	20	5	3	12	
Urination disorder					0.542
Yes	21	8	9	4	
No	43	12	20	11	
Preoperative mJOA score					0.181
Average		4.9	4.7	5.4	
Range		1–8	2–7	4–9	
Ossified ligamentum flavum segment					0.078
Upper thoracic	9	1	7	1	
Middle thoracic	2	0	2	0	
Lower thoracic	53	19	20	14	
Intramedullary signal change on MRI					0.016
Yes	26	4	10	12	
No	38	16	19	3	

Continues

Table 1. Continued

Factors	Total	Classification of RR (%)			*P*
		Excellent	Good	Poor	
Dural ossification					0.124
Yes	21	8	8	5	
No	43	12	21	10	
Spinal canal axial remnant area ratio					0.009
<0.30	26	4	11	11	
0.30–0.60	38	16	18	4	
>0.60	0	0	0	0	
Developmental spinal stenosis					0.159
Yes	17	7	6	4	
No	47	13	23	11	

A *P* value of <0.05 was considered statistically significant.
RR, recovery ratio; BMI, body mass index; mJOA, modified Japanese Orthopaedic Association; MRI, magnetic resonance imaging.

is based on preoperative evaluation of the disease, postoperative prediction of surgical outcomes, and effective communication with the patient. To our knowledge, there is presently no definitive scoring system that predicts the postoperative prognosis of TOLF in a reproducible, quantifiable way. The establishment and development of a standardized scoring system for TOLF would be important for patients' perioperative counseling regarding treatment strategies and surgical outcomes. Our aim is to validate whether the TOLF score is a predictor of surgical prognosis, and to determine if the TOLF score is associated with postoperative complications such as cerebrospinal fluid leakage and postoperative neurologic deterioration.

METHODS

After approval by the local institutional review board, a retrospective review was conducted for all patients with a diagnosis of TOLF and who received surgical decompression from April 2012 to February 2019 at a single institution in China. The surgical approach of all patients is en bloc unroof laminectomy for the posterolateral wall of the thoracic canal. The same surgeon performed surgeries of all patients. All patients were followed up by telephone or outpatient review. Patients with incomplete clinical and imaging data; those who presented with other thoracic myelopathies, such as ossification of the posterior longitudinal ligament or thoracic disc herniation; those who suffered from other spinal diseases, including cervical or lumbar spinal problems, infection, fracture, tumor, spinal deformity, or history of spinal surgery were excluded.

Patient data were recorded and analyzed by 1 researcher who has been working in spinal specialty for 5 years. Magnetic resonance imaging (MRI) and 3-dimensional computed tomography scanning was performed in all patients. The modified Japanese Orthopaedic Association (mJOA) scoring system was used to evaluate preoperative and postoperative neurologic function. Postoperative recovery was evaluated by the recovery ratio (RR): RR = (postoperative-preoperative mJOA)/(11 preoperative mJOA) × 100%.[14,15] According to the postoperative RR, all patients were divided into an excellent

Table 2. Determination of the Thoracic Ossification of the Ligamentum Flavum Score for Surgical Outcome Prognosis

Variables	Points
Age at surgery (years)	
<50	1
50–60	2
>60	3
Diabetes mellitus	
No	0
Yes	1
Preoperative duration of symptoms (months)	
≤24	1
>24	2
Spinal canal axial remnant area ratio	
>0.60	0
0.30–0.60	1
<0.30	2
Intramedullary signal change on MRI	
No	0
Yes	1

MRI, magnetic resonance imaging.

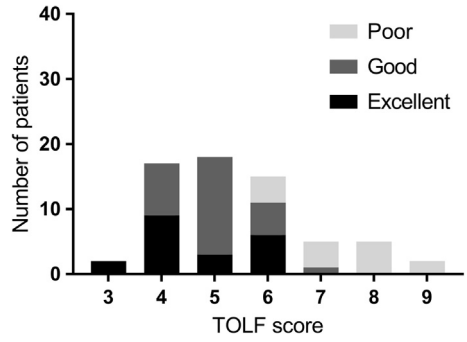

Figure 1. Distribution of thoracic ossification of the ligamentum flavum scores in terms of postoperative recovery among the excellent group, good group, and poor group ($P = 0.000$). TOLF, thoracic ossification of the ligamentum flavum.

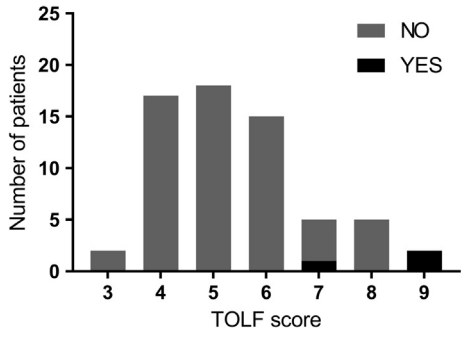

Figure 3. Distribution of thoracic ossification of the ligamentum flavum score in terms of postoperative neurologic deterioration ($P = 0.000$). TOLF, thoracic ossification of the ligamentum flavum.

group (75% ≤ RR ≤100%), a good group (50% ≤ RR <75%), and a poor group (RR <50%). Clinical and imaging parameters that could affect surgical outcome were assessed: sex, age at surgery, body mass index, the presence of hypertension or diabetes mellitus, smoking history, drinking history, preoperative duration of symptoms, urination disorder, preoperative mJOA score, ossified ligamentum flavum segment, intramedullary signal change on MRI, dual ossification, spinal canal axial remnant area ratio,[15,16] and developmental spinal stenosis. Correlations between these possible influencing factors and postoperative recovery were analyzed by logistic regression (Table 1).

According to results of logistic regression analysis, there are 5 factors that are correlated with postoperative recovery. Thus, the TOLF score consists of 5 components, namely, age at surgery (1–3 points), the presence of diabetes mellitus (1 point), preoperative duration of symptoms (1–2 points), spinal canal axial remnant area ratio (0–2 points), and intramedullary signal change on MRI (1 point), and it provides a novel and rudimentary scoring system with a score of 2–9 points (Table 2). The TOLF scores of all patients were calculated and analyzed for their correlation with the postoperative RR, intraoperative blood loss, urinary catheter indwelling time, cerebrospinal fluid leakage, and postoperative neurologic deterioration.

Statistical Analyses

SSPS for Windows Version 17.0 (SPSS Inc., Chicago, Illinois, USA) was used for the data analysis. The indicators for the TOLF scoring system were analyzed and determined by logistic regression. One-way analysis of variance was used to assess the differences of TOLF scores in the postoperative RR and in intraoperative blood loss and urinary catheter indwelling time. The Pearson rank correlation was used to evaluate the statistical correlation between the TOLF scores and cerebrospinal fluid leakage and postoperative neurologic deterioration. We use the receiver operating characteristic curves to calculate the sensitivity and specificity of the scoring system. The results are presented as the mean ± standard deviation. A P value of <0.05 was considered statistically significant.

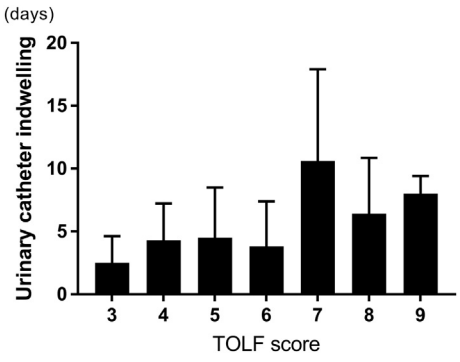

Figure 2. The correlation between thoracic ossification of the ligamentum flavum score and urinary catheter indwelling ($P = 0.023$). TOLF, thoracic ossification of the ligamentum flavum.

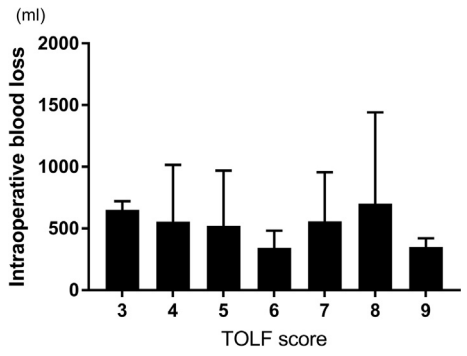

Figure 4. The correlation between thoracic ossification of the ligamentum flavum score and intraoperative blood loss ($P = 0.755$). TOLF, thoracic ossification of the ligamentum flavum.

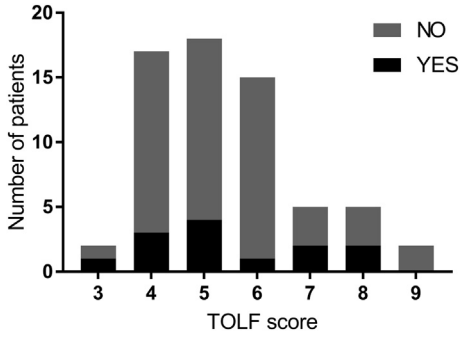

Figure 5. Distribution of thoracic ossification of the ligamentum flavum score in terms of postoperative cerebrospinal fluid leakage ($P = 0.911$). TOLF, thoracic ossification of the ligamentum flavum.

RESULTS

A total of 64 patients were included, with an average follow-up time of 33.8 months (12–65 months). The mean age of all patients was 57.4 years (range, 36–76 years). The distribution of the TOLF scores is shown in Table 2. The scores of 64 patients were distributed between 3 and 9 points. The mean score at the final follow-up was 4.6 points in the excellent group (20 patients), 5.0 points in the good group (29 patients), and 7.3 points in the poor group (15 patients). The results showed that a higher TOLF score was significantly indicative of a lower postoperative RR and a poorer surgical outcome ($P = 0.000$; Figure 1).

The average days of urinary catheter indwelling, which was recorded from the beginning of surgery to the recovery of urinary function, was 4.95 days (range, 1–22 days). A higher TOLF score was correlated with a longer urinary catheter indwelling time ($P = 0.023$; Figure 2). There was a strong statistical difference between the TOLF score and postoperative neurologic deterioration ($P = 0.000$; Figure 3). However, no correlation was found between the TOLF score and intraoperative blood loss ($P = 0.755$; Figure 4) or postoperative cerebrospinal fluid leakage ($P = 0.911$; Figure 5).

DISCUSSION

It is known that the TOLF score is the first scoring system to predict the postoperative prognosis of thoracic myelopathy caused by TOLF. Although the progression of TOLF is slow and difficult to visualize, TOLF must be surgically treated once symptoms appear. With regard to TOLF surgery, many surgical complications are well known, including cerebrospinal fluid leakage, postoperative neurologic deterioration, intraoperative hemorrhage, and surgical site infection, as reported in many studies.[8,13-15,17] However, the predictive factors of TOLF are variable and uncertain, and the establishment of the TOLF score is necessary. We screened 5 significant preoperative factors by logistic regression analysis. The TOLF score assesses postoperative prognosis using these components, including age at surgery, the presence of diabetes mellitus, preoperative duration of symptoms, spinal canal axial remnant area ratio, and intramedullary signal change on MRI. A higher score indicates poorer postoperative recovery and a higher incidence of postoperative complications according to our data analysis.

At present, few articles have reported a significant correlation between age and postoperative recovery in patients with thoracic myelopathy caused by TOLF.[18-20] Kojima et al.[21] reported that 2 young patients aged 22 years with extensive ossification of the thoracic ligamentum flavum demonstrated good surgical outcomes and postoperative recoveries. The prevalence of ossification of the ligamentum flavum was highest in the 50–59 year age group and increased with age in China, as described by Lang et al.[22] Our study showed that the mean ratio of postoperative recovery was 68.6% for patients aged <50 years, 57.6% for patients aged 50–60 years, and 34.1% for those aged >60 years. The surgical outcome of patients aged <60 years was significantly better than that of patients aged >60 years. The difference of postoperative RR in the 3 age groups is significant ($P = 0.026$). Thus, we awarded 1 point to patients aged <50 years, 2 points to patients aged 50–60 years, and 3 points to patients aged >60 years in the distribution of the TOLF score. The spinal cord of young patients has good plasticity, young patients have more active metabolism of organs and systems, stronger cognitive abilities, and shorter rehabilitation times; thus, young patients may get better effects during surgical recovery than older patients.

There was a significant correlation between the preoperative duration of symptoms and the surgical recovery rate; the shorter the duration predicts the better the recovery after surgery.[23-26] However, some studies have reported conflicting results.[18] The reason for this contradiction may be that the latent period of the compressed spinal cord is so long that it is irreversibly damaged when clinical symptoms appear, so the preoperative duration does not significantly affect the surgical recovery. Furthermore, the statistical type 2 error may be significant because of the small sample size. Chang et al.[23] considered that a symptom duration of >24 months significantly affected the surgical

Table 3. Sensitivity and Specificity of the Thoracic Ossification of the Ligamentum Flavum Score

				95% CI			
Variables	Area	Standard Error	Asymptotic Sign	Lower Bound	Upper Bound	Sensitivity (%)	Specificity (%)
TOLF score	0.719	0.069	0.005	0.584	0.853	81.8	54.0

CI, confidence interval; TOLF, thoracic ossification of the ligamentum flavum.

recovery. In our study, the symptom duration of 64 patients ranged from 1 month to 72 months, with an average of 20.1 months. Based on the reasons described earlier, we chose 24 months as the cutoff point for the preoperative duration of symptoms in the TOLF scoring system.

The spinal canal axial remnant area ratio is a direct imaging observation index for the degree of spinal cord compression. It is clearly correlated with postoperative recovery. The increased volume of the ossified ligamentum flavum results in spinal stenosis and physical compression of the spinal cord, leading to severe damage of the blood supply to the spinal cord.[15,25] When ossification is removed, ischemia-reperfusion injury may emerge and cause postoperative neurologic deterioration and poor surgical outcomes. Sanghvi et al.[15] showed that the spinal canal axial remnant area ratio was correlated with preoperative neurologic status. Lee et al.[27] considered that the cross-sectional area of ossification of the ligamentum flavum >33% on axial computed tomography scan could be used as an index for the diagnosis of thoracic myelopathy caused by TOLF. The spinal canal axial remnant area ratios of our patients were all below 60%. The mean ratio of postoperative recovery was 69.8% for the group defined below 30%, and 48.6% for the group defined between 30% and 60% in our study.

Diabetes mellitus is a metabolic disease and an organ autoimmune disease that affects the normal activities of various types of connective tissues and organs, such as bone and cartilage.[28] Many studies have reported that diabetes mellitus is associated with abnormal metabolism of the ligamentum flavum, but the mechanism for this association is unknown. Luo et al.[29] showed that hyperglycemia-driven sorbitol pathway activation may increase the susceptibility of patients with diabetes mellitus to ligamentum flavum hypertrophy. Braddock et al.[30] used a mouse model of diabetes and found that elevated blood glucose may lead to an increase in insulin-like growth factor; eventually, the incidence of TOLF increased in these diabetic mice. However, there have been few reports of the association between diabetes mellitus and postoperative recovery in TOLF. This study showed that the incidence of diabetes mellitus was 9.4% in 64 patients. The mean postoperative RR was 34.5%, which was significantly lower than that of the patients without diabetes mellitus. The reason for this result may be that diabetes causes microvascular disorders, which may directly or indirectly affect the blood supply of the spinal cord, resulting in poor postoperative recovery.

The pathological manifestations of intramedullary signal change on MRI are edema in gray or white matter, loss of nerve cells, Wallerian degeneration, gliosis, and demyelination.[18,31,32] In our study, preoperative MRI of 26 patients showed intramedullary signal changes, with a mean postoperative RR of 49.7%. The ratio of patients without intramedullary signal changes on MRI was 70.2%, indicating better surgical recovery than patients with signal changes. This result shows that the patients with intramedullary signal changes had severe spinal cord damage resulting from ossification of the ligamentum flavum. Unfortunately, we failed to collect postoperative signal changes on MRI, which could reveal whether spinal cord injury is reversible.

The scores of all patients were calculated. The distribution of all patient scores ranged from 3 points to 9 points, and no patient had the lowest score of 2 points. The results showed that a higher TOLF score predicts a lower postoperative RR ($P = 0.000$), longer urinary catheter indwelling time ($P = 0.023$), and higher incidence of postoperative neurologic deterioration ($P = 0.000$). However, no correlation was identified between the TOLF score and intraoperative blood loss ($P = 0.755$) or cerebrospinal fluid leakage ($P = 0.911$). The urinary catheter indwelling time recorded from the beginning of the operation to the normal recovery of urinary function seriously affected patients' quality of life. A recent study showed that the predictive factors of postoperative neurologic deterioration in TOLF surgery were the presence of dural tears, spinal cord injury, and extra-dural hematoma.[33] There was no correlation between the TOLF score and intraoperative blood loss or cerebrospinal fluid leakage. The reason for this result may be that these complications are not only affected by the clinical and imaging characteristics of patients but also by intraoperative factors, such as the approach chosen by the surgeon. As shown in **Table 3**, we know that the sensitivity is 81.8% and specificity is 54.0%. Probably because of the small sample size, the specificity of TOLF score is not high. We will enlarge the sample size in subsequent research to improve the sensitivity and specificity and perfect this scoring system.

The retrospective design is the main limitation of our study, and the predictive factors require further validation in a prospective manner. Compared with face-to-face follow-up, telephone follow-up is somewhat an unreliable method. The sample size is small, which may affect the scientificity and feasibility of the article. The TOLF score does not include all variables, such as proprioception in the big toe or conservative treatment, which may affect the prognosis and complications.[18] The incidence of postoperative neurologic deterioration was not high, which may influence the rationale of the TOLF score design. We acknowledge that the prognosis of TOLF is affected by a variety of factors and cannot be fully represented by the TOLF score. Therefore, we expect more studies to continue developing the TOLF score or to create a new scoring system to assess the postoperative prognosis of TOLF. Prospective studies of multicenter cooperation are necessary to test and update the TOLF scoring system in terms of predicting the postoperative prognosis of TOLF.

CONCLUSIONS

The TOLF score is a novel and rudimentary scoring system that describes the relational factors that can indicate the postoperative prognosis of TOLF, although there are some flaws and potential limitations. This scoring system will not only help doctors create a suitable treatment plan but also help patients better understand the prognosis of their disease.

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