

Prognostic value of cervical ligamentum flavum thickness as a morphological parameter to predict cervical stenosis

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Abstract

One of major causes of cervical central stenosis (CCS) is thickened change of cervical ligamentum flavum (CLF). The association of a morphological parameter called cervical ligamentum flavum thickness (CLFT) with CCS has not been reported yet. Thus, the purpose of this research was to investigate the relationship between CCS and CLFT.

Data were obtained from 88 patients with CCS. A total of 87 normal controls also underwent cervical spine magnetic resonance imaging (CSMRI). All subjects underwent axial T2-weighted CSMRI. Using our picture archiving and communications system, thickness of ligamentum flavum of the cervical spine at C6/7 level was analyzed.

The mean CLFT was 1.41 ± 0.24 mm in normal subjects and 2.09 ± 0.39 mm in patients with CCS. The CCS group was found to have significantly ($P < .001$) higher rate of CLFT than normal subjects. ROC curves were used to assess the usefulness of CLFT as a predictor of CCS. In the CCS group, the best practical cut-off-point of CLFT was 1.71 mm (sensitivity = 90.9%; specificity = 90.8%), with AUC of 0.94 (95% confidence interval: 0.90–0.98).

Greater CLFT values were associated with greater possibility of CCS. Thus, treating physician should carefully examine CLFT, as it can help diagnose CCS.

Abbreviations: AUC = area under the curve, CCS = cervical central stenosis, CLF = cervical ligamentum flavum, CLFT = cervical ligamentum flavum thickness, CSMRI = cervical spine magnetic resonance imaging, ROC curve = receiver operating characteristic curve.

Keywords: cervical central stenosis, cervical ligamentum flavum, cervical ligamentum flavum thickness

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1. Introduction

Cervical central stenosis (CCS) results from degeneration of cervical disc space, uncovertebral joint degradation, and hypertrophy of cervical facet, which dehydrate and collapse, thus increasing mechanical friction at the edge of the vertebral bodies at cartilaginous end plates.^[1–3] This repeated mechanical stress results in osteophyte formation and subperiosteal bone formation. Stenotic symptoms gradually arise during repeated cervical nerve root or spinal cord compression. They can manifest as myelopathy, radiculopathy, or neck pain syndromes.^[4–6] Cervical spine magnetic resonance imaging (CSMRI) is the most effective image modality for analyzing the cervical vertebrae such as cervical facet, ligamentum flavum, and intervertebral disk.^[7] An accurate CSMRI diagnosis of CCS is important to determine appropriate management.^[8] Previous researches have indicated that morphologic parameters such as cervical pedicles, cervical dural sac-thickness, and cervical lateral masses are associated with aging, disc degeneration, and CCS.^[9]

Anatomical research of cervical ligamentum flavum (CLF) is also critical to understand CCS. CLF height progressively increases from C2/3 to C6/7. It steadily decreases from medial to lateral within each cervical vertebra. CLF in cervical spine does not enter the cervical neural foramen.^[10] Both thickness and width are comparatively constant from caudal to cranial. The laminar surface area covered by CLF progressively increases from 33.0% in para midline at C2 level to 70.0% in para midline at C6 level.^[11]

However, previous studies did not assess the role of the thickness of CLF as a morphological determinant of CCS. To

Table 1
Comparison of characteristics of control and CCS groups.

Variable	Control Group n=87	CCS Group n=88	Statistical significance
Gender (male/female)	38/49	51/37	NS
Age, yrs	57.09±6.52	59.09±7.37	NS
CLFT, mm	1.41±0.24	2.09±0.39	<i>P</i> <.001

Data represent the mean±standard deviation (SD) or the numbers of patients. CCS = central cervical stenosis; CLFT = cervical ligament flavum thickness; NS = not statistically significant (*P*>.05).

analyze the relationship between CCS and thickness of the CLF, we made a new morphological determinant called CLF thickness (CLFT). We hypothesize that CLFT is an important morphologic determinant in the diagnosis of CCS. Therefore, the objective of this study was to use axial T2-weighted CSMRI to analyze CLFT in CCS patients and controls.

2. Methods

2.1. Patients

The Independent Ethics Committee of Catholic Kwandong University approved the current study (IRB protocol number: IS18RISI0016). We investigated patients who underwent CSMRI between May 2017 and July 2019 and who were diagnosed with CCS. We included patients over age 50 years if patients had clinical symptoms compatible with CCS (weakness of fingers or hand and loss of sensation or tingling in the upper extremities, cervicgia), the most stenotic level at C6/7, and CSMRI performed within 1 year of CCS diagnosis that was available for retrospective chart review. Our exclusion criteria were a history of previous cervical spinal cord damage or cervical spine surgery, congenital cervical spine defects, or cervical space occupying disease such as cysts or tumors, stroke, and syringomyelia.

We recruited 88 CCS patients who were diagnosed by 2 experienced neuroradiologists. In the CCS group, there were 51 (57.9%) males and 37 (42.1%) females with an average age of

59.09±7.37 years (range: 50–81 years) (Table 1). To investigate CLFT in CCS patients and normal subjects, we recruited normal subjects who underwent CSMRI as part of medical check-up. These normal subjects consisted of 87 participants [38 males (43.7%) and 49 females (56.3%)] with an average age of 57.09±6.52 years (range: 50–79 years) (Table 1). We analyzed CLFT in these normal subjects at C6/7 facet joint level.

2.2. Imaging parameters

CSMRI examinations were performed with 3T Avanto (Siemens, Erlangen, Germany) with 3T scanners (Philips Healthcare, The Netherlands). Cervical spine axial T2-W images with 4.00mm thick slices were obtained using the following parameters: zoom of 100.42%, 0.4mm intersection gap, 512ms/18ms repetition time/echo time, 458×318cm field of view, 815×253 matrix, and 15 echo train length.

2.3. Image analysis

T2-weighted axial CSMR images were obtained at the cervical facet joint location for all subjects. To measure CLFT at cervical facet joint on CSMRI, we used multimodality PACS network (INFINITT med-health Co., South Korea). CLFT was measured by drawing a linear line along the side of the cervical ligament facing the cervical spinal canal and along the cervical facet side. The thickest level at C6/7 point was recorded (Fig. 1).

2.4. Statistical analysis

Differences in demographic data between the normal and CCS groups were calculated using independent *t* tests. The ROC curve analysis was performed to calculate sensitivity, specificity, and the AUC for the validity of the CLFT. *P*-values<.05 were considered statistically significant. The relationship between age-related changes and CLFT was analyzed using 1-way analysis of variance (ANOVA). Data were entered and analyzed using Statistical Package for Social Science for Windows version 22 (SPSS Inc, Chicago, IL).

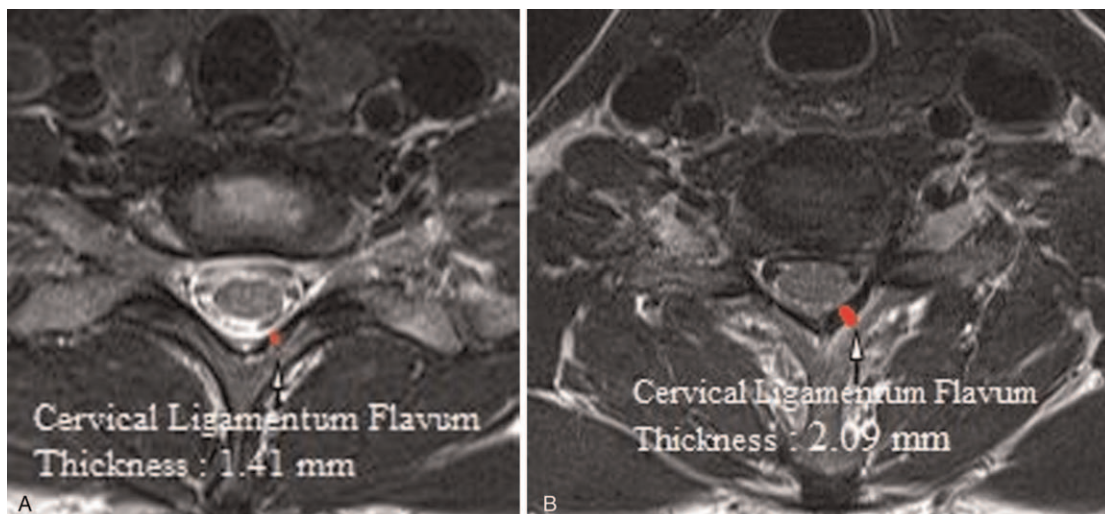


Figure 1. Measurement of the cervical ligament flavum thickness on cervical spine MRI. (A) Control group. (B) Central cervical stenosis group.

Table 2
Age distribution and mean CLFT of the control group.

Age distribution, yrs	Total (N) (87)
50–59	1.41 ± 0.24 mm (63)
60–69	1.39 ± 0.21 mm (20)
70–79	1.56 ± 0.39 mm (4)

CLFT = cervical ligament flavum thickness.

3. Results

Demographic factors were not significantly different between CCS and normal groups (Table 1). The mean CLFT was 1.41 ± 0.24 mm in the normal group and 2.09 ± 0.39 mm in the CCS group. The CCS group was found to have significantly (*P* < .001) higher rate of CLFT than the control group (Table 1). The mean CLFT of the normal group was 1.41 ± 0.24 mm in subjects aged 50 to 59 years, 1.39 ± 0.21 mm in subjects aged 60 to 69 years, and 1.56 ± 0.39 mm in subjected aged 70 to 79 years (Table 2). In the normal group, there was no significant correlation between age-related changes and CLFT in 1-way ANOVA (*F* = 0.861; *df* = 2; *P* = .426). The mean CLFT of the CCS group was measured to be 2.09 ± 0.45 mm in patients aged 50 to 59 years, 2.10 ± 0.29 mm in patients aged 60 to 69 years, and 2.10 ± 0.23 mm in patients aged 70 to 81 years (Table 3). In the CCS group, we did not find any statistically significant correlation between CLFT and age-related changes either (*F* = 0.006; *df* = 2; *P* = .994). ROC curves were prepared to assess the usefulness of CLFT as a predictor of CCS. In the CCS group, the best practical cut off-point was 1.71 mm (sensitivity = 90.9%; specificity = 90.8%), with AUC of 0.94 [95% confidence interval (95% CI): 0.90–0.98] (Table 4, Fig. 2).

4. Discussion

CCS is a multifactorial degenerative disease that can lead to neck pain and eventually spinal cord compression.^[12–16] It is the result of a reactive hypertrophy of osteophytes in the endplate and ligament, uncovertebral structures in conjunction with degeneration and bulging of the disk area. The consequence is a compression of the cervical spinal cord and restriction of the anterior-posterior diameter of the spinal canal.^[17–19] This process can lead to further nerve root or spinal cord injury and impingement.^[7]

Previous studies have analyzed associations between cervical canal’s medial–lateral diameter, cervical dural sac-thickness, cervical pedicles, and cervical lateral masses are associated with disc degeneration, aging, and CCS.^[20,21] Freedman et al^[21] have demonstrated that the lateral-medial diameter at the pedicle level of cervical canal is the most accurate and highly predictive. They also insisted that geometric characters of the cervical spinal canal were dangerous factors for a spinal cord injury.^[21] Kwon et al^[22] have announced anatomical differences in the thickness of dura

Table 3
Age distribution and mean CLFT of the CCS group.

Age distribution, yrs	Total (N) (88)
50–59	2.09 ± 0.45 mm (56)
60–69	2.10 ± 0.29 mm (22)
70–81	2.10 ± 0.23 mm (10)

CLFT = cervical ligament flavum thickness; CS = cervical central stenosis.

Table 4
Sensitivity and specificity of each cut-off point of CLFT.

CLFT, mm	Sensitivity (%)	Specificity (%)
0.95	100	2.3
1.41	95.5	48.3
1.54	94.3	73.6
1.71*	90.9	90.8
1.77	85.2	92.0
2.02	52.3	97.7

CLFT = cervical ligament flavum thickness.

* The best cut-off point on the receiver operating characteristic (ROC) curve.

mater with respect to cervical vertebral age and level. Prasad et al^[23] have reported that the diameter of the cervical spinal canal is a threshold indicator or AP straight line distance for CCS. Chaput et al^[24] have examined the lateral-medial diameter at the facet joint level of the cervical spinal canal in traumatic injury and found that the ratio of AP diameters is predictive of an acute spinal cord injury.

However, we frequently encounter discrepancies in CCS diagnosis according to previous reference imaging protocol. Previous grading system might have overlooked hypertrophy of CLF. Coughlin et al^[25] have reported that calcified hypertrophic CLF is a known entity that causes myelopathy of the cervical spine. They also insisted that noncalcified hypertrophic CLF could cause progressive cervical myelopathy. Hartman et al^[26] have shown mechanical play of posterior column segments in human cervical spine components. After analyzing interspinous/supraspinous ligaments, CLF, facet, and facets capsule using a robot-analysis system, they have concluded that CLF is very important mechanically in the cervical vertebrae. CLF contrib-

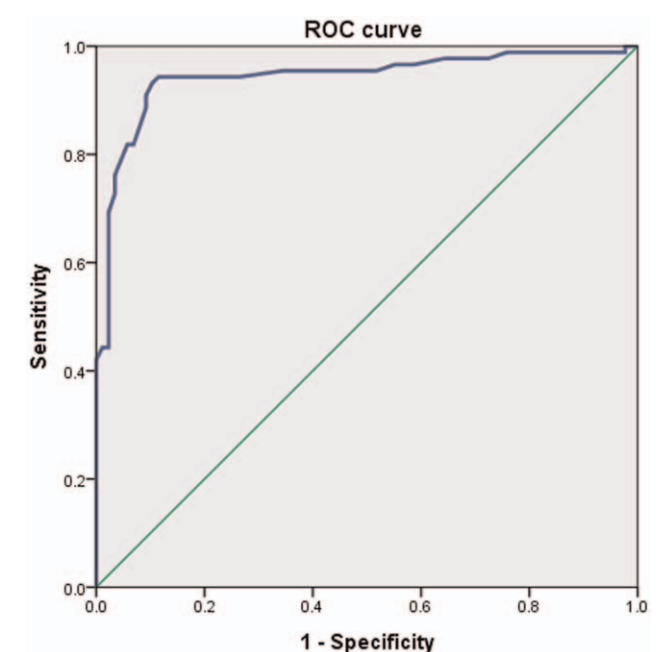


Figure 2. Receiver operating characteristic curve of cervical ligament flavum thickness for prediction of central cervical stenosis. The best cut off point of cervical ligament flavum thickness was 1.71 mm, with sensitivity of 90.9%, specificity of 90.8%, and AUC of 0.94. AUC = area under the curve.

utes to moment resistance in flexion.^[26] There are many previous researches of ligamentum flavum hypertrophy at thoracolumbar spine level. We thought that the same histopathologic and biomechanical changes could occur in the cervical vertebrae as well. Although the specific mechanism of hypertrophy of CLF is uncertain, Hur et al^[27] have reported that the presence of angiogenic factors and alterations in mechanical stress might offer critical link. They insist that the pathophysiology of hypertrophy of CLF involves a significant change of angiogenic factors, including angiopoietin-1, vascular endothelial growth factor (VEGF), fibroblast growth factor, and vascular endothelial-cadherin. They concluded that elderly patients with thicker CLF and increased segmental movement had higher concentrations of CD34⁺ capillaries and VEGF than their normal subjects, suggesting that these factors might play an important role in the pathogenesis of hypertrophy of CLF.^[27] However, no study has reported the optimal cut off point of CLFT to diagnose CCS clinically.

To analyze the relationship between CCS and hypertrophy of the CLF, we made a simple morphological diagnostic tool called CLFT. To the best of our knowledge, association CLFT with CCS has not been evaluated yet. We hypothesize that CLFT is a critical morphological diagnostic parameter in the diagnosis of CCS. We demonstrated a positive correlation between CCS and CLFT. In the current research, we found that cut off-point of CLFT at 1.71 mm had sensitivity of 90.9%, specificity of 90.8%, and AUC of 0.94 (95% CI: 0.90–0.98) to predict CCS. Our results suggest that CLFT is an objective and accurate morphological diagnostic parameter for CCS prediction. The current research included individuals aged above 50 years.

The cause of thickened CLF is that when CLF becomes harder and thicker, it loses its elasticity, and becomes longer in CSS.^[27,28] Thus, during repetitive motion of the cervical spine, harder and longer CLF may protrude into the cervical spinal canal, causing mechanical compression of the cervical spinal cord, which can be assessed on CSMRI as an increased diameter of CLFT. Thus, in patients with CSS, movement from extension to flexion causes significant spinal cord compression. In this study, we analyzed CLFT from CSMRI images. CSMRI studies are very important in the diagnosis of degenerative disorders of CCS and in highly detectable hypertrophy of CLF.^[29,30]

This study has some limitations. First, although we measured CLFT in T2-weighted axial images at the most stenotic facet joint level, there might be some measurement errors on CSMRI because axial cervical images might be inhomogeneous due to differences in the cutting angle of CSMRI resulting from posture in patients and individual anatomic variations. Second, the diameter and volume of the spinal canal are irregular. In addition, the shape of the cervical spinal canal can also change from flexion to extension, as the diameter of the osseous canal widens during flexion and narrows during extension. Moreover, vertebral disks and CLF may change during motion of cervical vertebrae.^[26] However, this study only investigated CLFT in conventional CSMRI. Finally, this research was retrospective in nature. In spite of these all limitations, this is the first research to report the association of CLFT with CCS.

5. Conclusion

We demonstrated that higher CLFT values were associated with higher possibility of CCS. Thus, treating physician should carefully examine CLFT, as it can help diagnose CCS.

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Author contributions

Conceptualization: Young Uk Kim.

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Methodology: Young Uk Kim.

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