

Observational Study



Uncinate Process Area as a New Sensitive Morphological Parameter to Predict Cervical Neural Foraminal Stenosis

Jong-Uk Mun, MD¹, Hyung Rae Cho, MD², Seon Hwan Kim, MD², Jee In Yoo, MD³, Keum Nae Kang, MD⁴, Syn-Hae Yoon, MD⁴, and Young Uk Kim, MD, PhD³

From: ¹Department of Orthopaedic Surgery, Changwon Gyeongsang National University Hospital, Republic of Korea; ²Department of Anesthesiology and Pain Medicine, Myongji Hospital, Hanyang University College of Medicine, Goyang, Korea; ³Department of Anesthesiology and Pain Medicine, Catholic Kwandong University of Korea College of Medicine, International St. Mary's Hospital, Incheon, Korea; ⁴Department of Anesthesiology and Pain Medicine, National Police Hospital, Seoul, Korea

Address Correspondence:
Young Uk Kim MD, PhD
Department of Anesthesiology and Pain Medicine, Catholic Kwandong University of Korea College of Medicine, International St. Mary's Hospital, Incheon, Republic of Korea
E-mail: uk201@hanmail.net

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Background: Hypertrophy of the uncovertebral joint has been considered as a major cause of cervical neural foraminal stenosis (CNFS). The cross-sectional area of the uncinate process is a key morphologic parameter in the identification of uncovertebral joint hypertrophy. To evaluate the connection between CNFS and the uncinate process, we devised a new morphological parameter, the uncinate process area (UPA).

Objective: We hypothesized that the UPA is an important morphologic parameter in the diagnosis of CNFS.

Study Design: Retrospective observational study.

Setting: The single center study in Incheon, Republic of Korea.

Methods: UPA data were collected from 146 patients with CNFS and 197 control subjects who underwent neck computed tomography (CT) as part of a routine medical examination. Neck CT images were obtained from all subjects. The whole cross-sectional area of the bone margin of the uncinate process was measured at the C5-6 intervertebral disc level on CT scans using a picture archiving and communications system.

Results: The average UPA was 15.52 mm² in the control group and 29.97 mm² in the CNFS group. The CNFS group displayed significantly greater UPA levels ($P < 0.001$). Regarding the validity of the UPA as a predictor of CNFS, the receiver operating characteristic curve analysis revealed an optimal cut-off point for the UPA of 21.15 mm², with 91.8% sensitivity, 93.4% specificity, and an area under the curve of 0.972 (95% CI, 0.956-0.989) in the CNFS group.

Limitations: Anatomically, the UP is located on the superior lateral surfaces of the C3-7 cervical vertebral bodies. However, we focused on the C5-6 uncovertebral joint level, because many previous studies revealed C6 UP has the greatest height among UP and C5-6 uncovertebral joint hypertrophy is a primary cause of CNFS.

Conclusions: The newly devised UPA is a sensitive parameter for assessing CNFS. A hypertrophied UPA is associated with an increased risk of CNFS. We think that this result will be helpful for diagnostic radiology in evaluating patients with CNFS.

Institutional Review Board (IRB) approval number: IS16RISI0002

Key words: Uncinate process area, cervical neural foraminal stenosis, Uncovertebral joint hypertrophy, optimal cut-off point, cross-sectional area

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The uncovertebral joints are unique and clinically important anatomical features of the cervical spine. In the degenerative or aged cervical vertebrae, osteophytes arising from an uncinate process (UP) can cause cervical neural foraminal stenosis (CNFS) (1). CNFS is a common cause of pain in the neck and

upper extremity (2). Foraminal narrowing may present as a sharp arm or neck pain, paraesthesia, numbness or tingling sensation with symptom spreading to the distal portion of the arms. Motor symptoms such as weakness may sometimes accompany sensory symptoms in aggravated narrowing (3). Morphologic parameters such as ligamentum flavum, epidural space area, and disk herniation have been associated with disc degeneration, aging and CNFS (4,5). Hypertrophic change of the uncinat process has been considered a major cause of CNFS (6,7).

To evaluate the connection between CNFS and hypertrophy of the uncinat process, we devised a new morphological parameter, called the uncinat process area (UPA). The association of the UPA with CNFS is unclear. We hypothesized that the cross-sectional area of UPA is an important morphologic parameter in the diagnosis of CNFS. We compared the UPA between CNFS patients and control subjects using computed tomography (CT) scans. The aims of this retrospective study were to investigate the optimal cut-off value of UPA in patients with CNFS and evaluate the usefulness of UPA as an objective diagnostic hallmark in determining the CNFS.

METHODS

Patients

This study was registered at the Catholic Kwandong University College of Medicine, Republic of Korea (IS16RISI0002). The Institutional Review Board reviewed and approved the research protocol. We retrospectively reviewed patients who visited our Pain Clinic from March 2014 to October 2015, and who were diagnosed with CNFS. The UPA of cervical segment (C5-6) was measured using neck CT images in 2 groups of individuals: those diagnosed with CNFS and a control group. The CNFS group included 146 patients (84 males and 62

females) with a mean age of 60.43 ± 7.93 years (range, 50 to 79 years).

The inclusion criteria of the CNFS group were: 1) clinical symptoms compatible with CNFS, such as chronic neck stiffness, neck pain, headache, tingling sensation and numbness in the arm; 2) neuroforaminal stenosis at C5-6; 3) neck CT image taken within 12 months of the first diagnose and available for review; and 4) age > 50 years of age. Exclusion criteria were: 1) history of previous cervical spinal injury or cervical surgery; 2) any congenital spine defect or disorder that could affect pain intensity; and 3) history of spinal interventions, such as neuroplasty.

All patients were enrolled after the diagnosis of CNFS was confirmed by an experienced board-certified neuroradiologist. To compare the UPA between patients with and without CNFS, we also enrolled a control group of individuals who underwent neck CT as part of a routine medical examination. We only enrolled patients in the control group who had no CNFS-related symptoms. The control group included 197 individuals (88 men and 109 women) with a mean age of 60.40 ± 8.01 years (range, 50 to 79 years) (Table 1). The UPA in the control group were also examined at the C5-6 facet joint level.

CT Scanning Protocol

All CT scans were done at the Department of Spine Center, Catholic Kwandong International St Mary's Hospital, Incheon, Republic of Korea. In both groups, the CT images were obtained using the same technique and patient positioning using reconstructed 3-dimensional technique. The CT images were obtained with a SOMATOM Definition FLASH or AS (Siemens Medical Solutions, Forchheim, Germany) scanner. The CT parameters were 120 kVp and 100 effective mAs with dose modulation. Reconstruction was done using 140 f medium algorithm (3 mm increment without a gap), and 170 f very-sharp ASA algorithm (3 mm increments without a gap). All CT images were submitted for both the cervical spine (width 350 Hounsfield Units (HU); level 50 HU) and the neck (width 1500 HU; level -700 HU) window settings of axial and coronal planes on the picture archiving and communication system.

Image Analysis

We measured the UPA at the C5-6 level of CT scans using a picture archiving and communications system (Fig. 1). The UPA's cross-sectional area as indirect indicator of 3 dimensional surface area was measured by an

Table 1. Comparison of the characteristics of control and CNFS groups.

Parameter	Control Group (n = 197)	CNFS Group (n = 146)
Gender (male/female)	88 / 109	84/62 (NS)
Age (years)	60.40 \pm 8.01	60.43 \pm 7.93 (NS)
UPA (mm ²)	15.52 \pm 3.56	27.97 \pm 5.92 (P < 0.001)

Data represent the mean \pm standard deviation (SD) or the numbers of patients. CNFS, cervical neural foraminal stenosis; UPA, uncinat process area; NS, not statistically significant (P > 0.05)

outlining method with INFINITT system at the C5-6 level. We assessed one side of the UPA at the most stenotic neural foramen (Fig. 1A). In order to obtain accurate measurements, we magnified the CT images by 3 times using the INFINITT PACS system (INFINITT Healthcare, Seoul, Republic of Korea) (Fig. 1B). Coronal CT images were obtained through the lateral borders (side edges) of the superior surface of the vertebral bodies of the fifth and sixth cervical vertebrae for each individuals (Fig. 1C).

Statistical Analyses

Data are expressed as mean \pm standard deviation (SD). We compared the UPA between the control and CNFS groups using unpaired t-tests. The relationship between the UPA and age related changes were analyzed using a one-way ANOVA. The validity of the UPA for diagnosis of disease was estimated by Receiver Operator Characteristics (ROC) curves, optimal cut-off value, area under the curve (AUC), sensitivity, and specificity with 95% confidence intervals (CIs). *P*-values < 0.05 were considered statistically significant. SPSS for Windows version 22 (IBM SPSS Inc., Chicago, IL) was used for the statistical analyses.

RESULTS

Age and gender were not significantly different between the groups (Table 1). The mean UPA of the control group measured $15.78 \pm 3.69 \text{ mm}^2$ in subjects aged 50-59 years, $15.17 \pm 3.47 \text{ mm}^2$ in those 60-69 years of age, and $15.23 \pm 3.25 \text{ mm}^2$ in those 70-79 years of age (Table 2). In the control group, we found no statistically significant relationships between the UPA and age-related changes in the one-way ANOVA ($F = 0.009$; $df = 2$; $P = 0.991$). The mean UPA of the CNFS group measured $28.55 \pm 6.67 \text{ mm}^2$ in those aged 50-59 years, $27.01 \pm 5.03 \text{ mm}^2$ in those 60-69 years of age, and $28.18 \pm 5.05 \text{ mm}^2$ in those 70-79 years of age (Table 3). In the CNFS group, no statistically significant relationships were evident between the UPA and asymptomatic age-related changes ($F = 1.021$; $df = 2$; $P = 0.363$).

The average UPA was $15.52 \pm 3.56 \text{ mm}^2$ in the control group and was $27.97 \pm 5.92 \text{ mm}^2$ in the CNFS group. CNFS patients had significantly greater UPA ($P < 0.001$) than control subjects (Table 1). Regarding the validity of the UPA as predictors of CNFS, ROC curve analysis showed that the optimal cut-off point of the UPA was 21.15 mm^2 , with 91.8% sensitivity, 93.4% specificity (Table 4), and AUC of 0.97 (95% CI, 0.96-0.99) (Fig. 2).

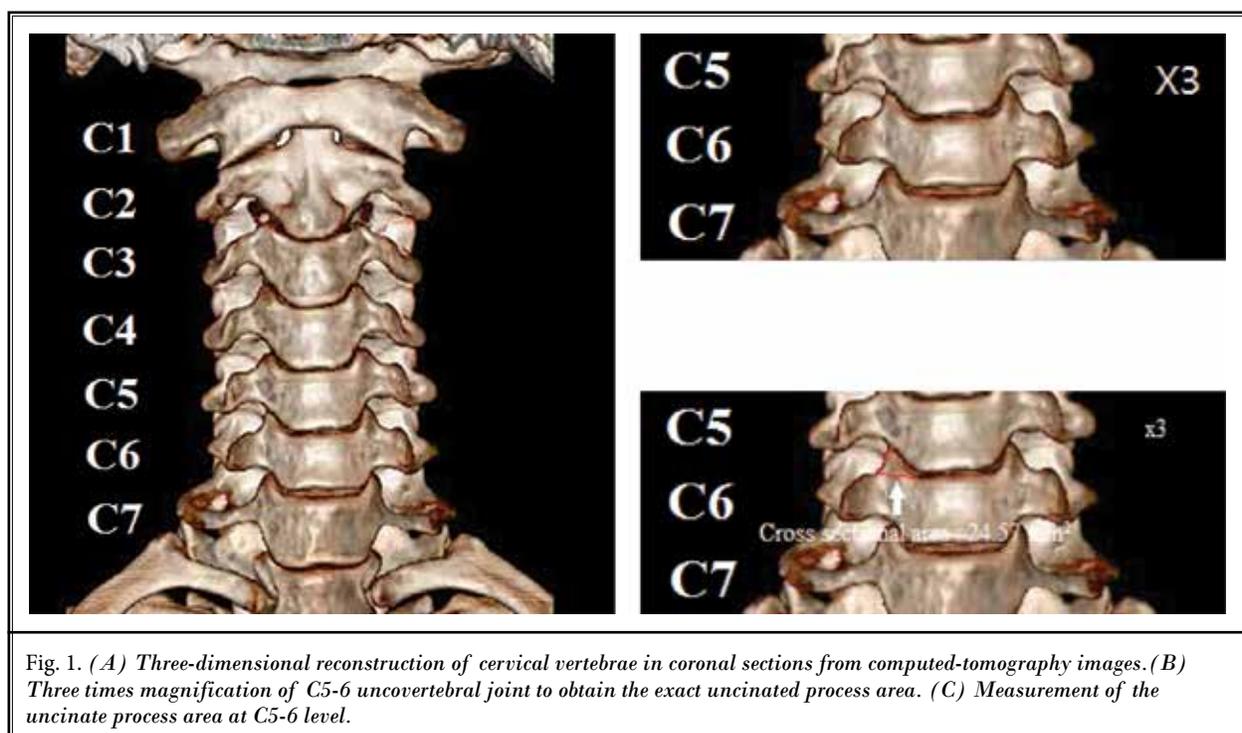


Fig. 1. (A) Three-dimensional reconstruction of cervical vertebrae in coronal sections from computed-tomography images. (B) Three times magnification of C5-6 uncoversal joint to obtain the exact uncinate process area. (C) Measurement of the uncinate process area at C5-6 level.

Table 2. Age distribution of patients with mean UPA of control group.

Age (years)	Male (N)	Female (N)	Total (N)
50-59	16.64 ± 4.07 mm ² (50)	15.08 ± 3.23 mm ² (62)	15.78 ± 3.69 mm ² (112)
60-69	14.90 ± 3.69 mm ² (24)	15.40 ± 3.33 mm ² (29)	15.17 ± 3.47 mm ² (53)
70-79	15.80 ± 3.57 mm ² (14)	14.78 ± 3.00 mm ² (18)	15.23 ± 3.25 mm ² (32)

UPA, uncinat process area

Table 3. Age distribution of patients with mean UPA of CNFS group.

Age (years)	Male (n)	Female (n)	Total (n)
50-59	30.06 ± 6.48 mm ² (48)	25.75 ± 6.20 mm ² (26)	28.55 ± 6.67 mm ² (74)
60-69	27.22 ± 5.81 mm ² (24)	26.82 ± 4.29 mm ² (26)	27.01 ± 5.03 mm ² (50)
70-79	30.32 ± 5.21 mm ² (12)	25.61 ± 3.61 mm ² (10)	28.18 ± 5.05 mm ² (22)

UPA, uncinat process area; CNFS, cervical neural foraminal stenosis

DISCUSSION

CNFS occurs as a result of neuroforaminal volume loss which is multifactorial and includes hypertrophy of the UP. Ultimately, if the foraminal narrowing distorts or compresses the exiting cervical nerve root, the patient will likely become symptomatic. Significant narrowing of the cervical foramen may present as a sharp arm or neck pain, paresthesia, numbness or tingling sensation with or without symptom spreading to the distal portion of the upper extremities. Motor symptoms such as weakness may accompany sensory symptoms in aggravated cases (8-17).

The uncovertebral joints consist of the lateral margins of the superior endplate of the vertebral body (the UP), which are found in the cervical spine from C3-C7 (and occasionally T1) along with their articulation with the adjacent inferior endplate of the superior vertebral body at its echancrue (18). The UP is an important bony landmark that becomes flatter and larger as individuals age, and loses its bony and sharp characteristics (7). The uncovertebral joint is thought to be responsible for the degree of mobility and stability of the cervical vertebrae by limiting side-to-side movement of the cervical vertebral bodies (18). Uncovertebral joints with hypertrophic changes can prevent motion and allow for the growth of osteophytes, leading to the formation of heterotopic ossification (19).

The uncovertebral joints permit lateral bending and axial rotation, while limiting vertebral side to side motion. The UP also reduces cervical motion in all loading modes (18,20). The UP functions in accomplishing greater motion without overstressing the intervertebral disk and provides stability during degeneration (18). Hartman demonstrated that osteophytes that arise from the posterior aspect of the UP project into the neural foramen. The cervical nerve roots are related to the uncovertebral articulations and become angulated and mechanically irritated by the intruding uncovertebral osteophyte (21). Yilmazlar et al (22) have reported that the location of the UP in a motion segment pre-

disposes to uncovertebral osteophyte formation, which produces intervertebral foraminal stenosis resulting in neural compression .

However, an association between CNFS and UP as a morphologic parameter on CT has not been reported previously. Moreover, there are no objective morphologic parameters based on 3-dimensional (3D) CT imaging to indicate uncovertebral joint hypertrophy. We thought that the cross-sectional area of UP could be an objective, precise, clear measurement parameter to evaluate uncovertebral joint hypertrophy. In our present study, the UPA was measured from 3D reconstruction of CT images. To our best knowledge, this measurement has not been reported previously.

The present results demonstrate the association of UPA and CNFS. CNFS patients had significantly greater UPA than control subjects. Our interpretation of these associations is that hypertrophy of the UPA might be related to continuous stress, which might increase the UPA. The process of facet joint hypertrophy begins with mechanical stress during rotation and flexion, which leads to increased force on the facet joints and extensive abrasion (23,24). This etiology could alter the morphologic features of UP. Degeneration of the disc may also increase stressful force on the facet joints (25). Therefore, osteophyte production and bony hypertrophy along with posterolateral inclination of the UP have been implicated as the main factors producing neural foraminal narrowing (21).

Hypertrophic change of the cervical facet joint was correlated with male gender and with neck pain (6). The authors also found that hypertrophic changes of the facet joint of the cervical spine occurred with greater frequency at C4-5 and C5-6, and was usually lateral (6). Choi et al (26) re-

ported the case of a cerebellar infarction that started from compression of the proximal vertebral artery by a hypertrophied uncovertebral joint at the C5-6 level. Nagamoto et al (1) reported that cervical radiculopathy is related to osteophyte formation around the UP. Cervical radiculopathy generally occurred in the lower cervical spine, particularly C5-6. Pait et al (27) reported that the height of the UP increased from C3 to C7, with the greatest height of the UP at the C6 level. In main axial rotation, C5-6 was the most mobile segment (1). Thus, we measured the UPA at the C5-6 level to obtain accurate measurements at the articulation with the highest frequency of symptomatic degenerative changes.

We strictly controlled for age (all participants were older than 50 years) because Wang et al (3,28,29) reported that CNFS can be identified in the majority of patients older than 50 years of age. Rudy et al (30) also reported that UP hypertrophy is associated with age. For every year increase in age, hypertrophy increases. However, unlike previous studies, our results show no significant variation from 50 to 79 years of age. Our interpretation of this result is that pathophysiology of CNFS is much more important than age. We also strictly controlled the age range to reduce age bias. The positive correlation between the UPA and the CNFS could be explained as such, an increase in UPA is associated with an increase in CNFS. The optimal cut-off value for the UPA was 21.15 mm² with an AUC of 0.97 (95% CI, 0.96-0.99). We suggest that UPA is a precise, objective, and clear morphological parameter that predict CNFS.

Limitations

There are several limitations to the present study. First, there might be errors associated with measuring the UPA on CT. Although we tried to measure this morphologic parameter in the coronal reconstructed image that best showed the UPA at the level of the C5-6 uncovertebral joint, the coronal images we analyzed to measure the cross-sectional area could be inhomogeneous because of differences in the cutting angle in CT resulting from individual anatomic variation and technical problems. Second, anatomically, the UP is located on the superior lateral surfaces of the C3-7 cervical vertebral bodies. We only focused on the C5-6 uncovertebral joint level, since many previous studies revealed that the C6 UP has the greatest height, and C5-6 uncovertebral joint hypertrophy is a primary cause of CNFS. If future research includes the UPA of other cervical levels, data comparing patients with CNFS to normal subjects could provide more accurate analyses

Table 4. Sensitivity and specificity of each cut-off point of the UPA for prediction of cervical neural foraminal stenosis.

UPA (mm ²)	Sensitivity (%)	Specificity (%)
7.82	100	0
18.78	96.6	80.7
21.15*	91.8	93.4
23.14	76.7	98
24.56	68.5	99
48.67	0	100

Best cut-off point on the receiver operating characteristic curve; UPA, uncinate process area

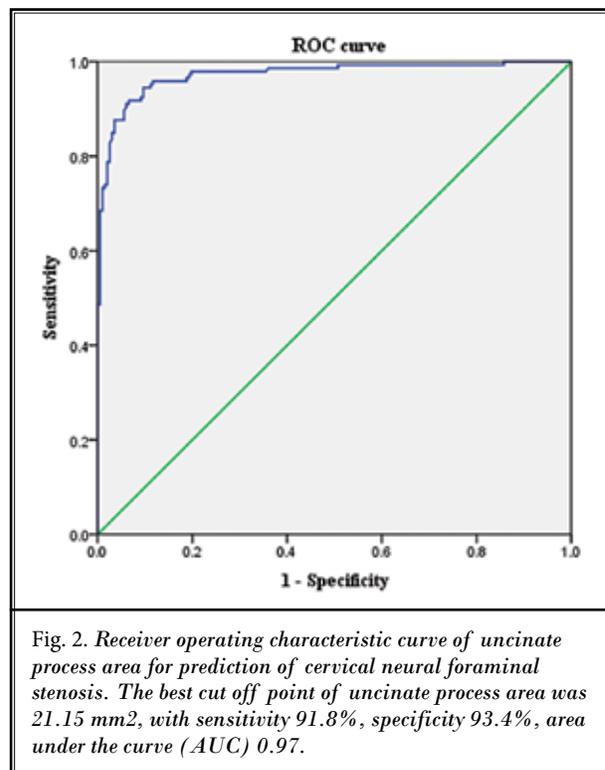


Fig. 2. Receiver operating characteristic curve of uncinate process area for prediction of cervical neural foraminal stenosis. The best cut off point of uncinate process area was 21.15 mm², with sensitivity 91.8%, specificity 93.4%, area under the curve (AUC) 0.97.

and a better understanding of the UP/UPA role in symptomatic CNFS. Third, CNFS represents a combination of multiple pathogenic causes, including intervertebral disks herniation, ligamentum flavum stiffness, and hypertrophic facet disease; however, we only focused on UP. Further studies should address the association between integral morphologic parameters of CNFS rather than the UPA alone.

In spite of these limitations, this is the first study to document that the UPA is associated with CNFS.

CONCLUSION

UPA is a new sensitive parameter for assessing CNFS. The optimal cut-off point for the UPA is 21.15 mm², with 91.8% sensitivity, 93.4% specificity, and AUC

of 0.97 in the CNFS. We hope that this result will be helpful to evaluate patients with CNFS.

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