Dural Ossification Associated with Ossification of Ligamentum Flavum in the Thoracic Spine

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Primary Subject Heading: Radiology and imaging
Secondary Subject Heading: Neurology
Keywords: Dural ossification, Ossification of ligamentum flavum, Thoracic spine, imaging signs
Dural Ossification Associated with Ossification of Ligamentum Flavum in the Thoracic Spine

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Investigation performed at the Department of Orthopaedic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

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Abstract

Objectives: To investigate the incidence, distribution, and radiological characteristics of dural ossification (DO) associated with ossification of ligamentum flavum (OLF) in the thoracic spine.

Design: A retrospective radiographical analysis.

Setting: This study was conducted at a single institution in China.

Participants: Fifty-three OLF patients who underwent posterior decompression surgery between January 2011 and July 2015 in a single institution were enrolled in this study.

Outcome measures: The demographic distribution, radiological data, and detailed surgical records were collected. Firstly, preoperative CT images of decompressed segments was evaluated to identify imaging signs of DO. The “tram tack sign” (TTS), “comma sign” (CS) and “bridge sign” (BS) were considered as characteristic imaging findings of DO in OLF. Four kinds of confusing signs (false TTS) were identified and excluded. Then, detailed surgical records were reviewed to finally identify segments with DO.

Results: The incidence of DO in OLF patients was 43.4%. The incidence of DO in OLF segments was 21.5%. OLF was more common in lower thoracic spine, and more than half (53.8%) of the DO located in T9-12. TTS was the most common signs, but it might be misdiagnosed. After excluding four kinds of false TTS, the sensitivity and specificity of imaging diagnosis were 94.23% and 94.21%, respectively.

Conclusions: DO was relatively common in thoracic OLF, especially in T9-12. TTS, CS, and BS could be used for preoperative imaging diagnosis of DO. However, TTS might be misdiagnosed. After excluding four kinds of false TTS, the accuracy of imaging diagnosis was relatively high.
Strengths and limitations of this study

- This study made up for the current lack of understanding of dural ossification (DO) associated with ossification of ligamentum flavum (OLF) in the thoracic spine.
- The incidence, distribution, and radiological characteristics of DO were described and analyzed in detail.
- The study increased the accuracy of identifying DO in OLF before surgery.
- The study population was limited to OLF patients who need surgical treatment.
**Introduction**

Ossification of ligamentum flavum (OLF) is the most common cause of thoracic spinal stenosis[1-3], especially in Asian populations. With the progression of OLF, the spinal cord will be subjected to severe compression and the patient may eventually be paralyzed. Surgical treatment is generally accepted as the best option[2-6]. When compressed, the dura mater may also ossify. Then the ossified ligamentum flavum and dura fuse to be one inseparable bony tissue. This will increase the difficulty of surgery and the risk of spinal cord injury and cerebrospinal fluid leakage[7 8]. Preoperative identification of DO can help surgeons to adopt appropriate surgical technique and get prepare to deal with the intraoperative dural laceration. In a preliminary study, the “tram track sign” (TTS) and “comma sign” (CS) were reported to be associated with DO[9]. However, due to the relatively small study population and lack of awareness of these specific image signs, accurate diagnosis of DO could not be obtained in previous studies[2 10]. Since the incidence of OLF and DO is relatively low, few studies have focused on this issue[2 9 10]. The incidence, distribution of DO were also unclear. The present study aimed to investigate the incidence, distribution, and radiological characteristics of DO in thoracic OLF.

**Methods**

**Study population**

OLF patients who underwent posterior thoracic decompression surgery between January 2011 and July 2015 in a single institution were enrolled in this retrospective cohort study. The exclusion criteria included trauma, infection, tumor, and deformity. Fifty-three cases were finally included in this study, with institutional review board approval. Clinical data, preoperative computed tomography (CT), and detailed surgical records were available for all the included patients.

**Imaging evaluation and identification of DO**

Preoperative axial CT scans of surgical decompression segments were the primary imaging to be assessed for every included patient. In our preliminary
screening study, the “tram tack sign” (TTS), “comma sign” (CS) and “bridge sign” (BS) were considered as characteristic imaging findings of DO in OLF (Fig.1). TTS and CS had been reported in previous studies[9 10]. Tram track sign was defined as a hyperdense bony excrescence, with a hypodense center[9] (Figs.1A/D). It consisted of three parts in the axial CT scan: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). These three parts together formed a tram-track-like shape. Comma sign was an imaging manifestation of ossification of one-half of the dura mater[9] (Figs.1B/E). Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura. Bridge sign was a hyperdense bony connection of bilateral OLF (Figs.1C/F). The dorsal ossified dura presented as a bridge between bilateral ossified ligamentum flavum. Segments with the above signs on axial CT images would be initially diagnosed with DO in OLF.

TTS might be misdiagnosed as found in previous studies[2 10] and our preliminary screening study. So we defined and excluded four kinds of confusing signs (false TTS) (Fig.2): false TTS consisted of facet joint (Fig.2-A); false TTS consisted of ossified ligamentum flavum and superior articular process (Fig.2-B); false TTS between ossified ligamentum flavum and lamina (Fig.2-C); and false TTS between inner and outer bone cortex of superior articular process (Fig.2-D). For atypical signs, reference to adjacent imaging of the same segment might be helpful (Fig.2-E).

To ensure reliability, imaging evaluation was performed before review of surgical records. Surgical decompression segments would then be divided into the following three categories (initial diagnosis): non-OLF segments, OLF segments without DO, and OLF segments with DO. After imaging evaluation, surgical records were reviewed to identify which segments were truly associated with DO. This would be regarded as the final diagnosis. The incidence and distribution of DO were recorded.
Statistical analyses

Initial diagnosis was compared with the final diagnosis for calculating the sensitivity and specificity of imaging diagnosis. The test accuracy, positive and negative predictive values were also calculated. Data were presented as mean ± standard deviation (SD). SPSS software (version 20.0, Chicago, Illinois, USA) was used for statistical analysis.

Results

Population

Fifty-three OLF patients (26 female; age: 53.87 ± 10.42, range: 30 - 74) were included in this retrospective study. 23 cases (13 female) had intraoperative evidence of DO. The mean age of DO group was 54.65±9.62, comparing to 53.27±11.12 in the Non-DO group (P>0.05) (Table I).

Incidence

Of the 53 included patients, 242 surgical decompression segments were diagnosed with OLF by axial CT scan. 52 segments from 23 OLF patients had DO related to OLF. The incidence of DO in OLF segments was 21.5% (52/242) and the incidence of DO in OLF patients was 43.4% (23/53) (Table I).

<table>
<thead>
<tr>
<th>Table I: Basic information of included OLF patients</th>
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<tbody>
<tr>
<td>OLF with DO</td>
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<tr>
<td>Cases</td>
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<td>Sex (Female/male)</td>
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<td>Segments</td>
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<td>Incidence of DO in OLF segments:</td>
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<td>Incidence of DO in OLF patients:</td>
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Distribution

The distribution of OLF and DO was shown in figure 3. OLF was more common in lower thoracic spine, and more than half (53.8%) of the DO located in T9-12. The
majority of DO patients (20/23, 87.0%) had only 1-3 segments involved (Fig.4).

**Accuracy of imaging diagnosis**

In the imaging evaluation, 60 segments were initially thought to have DO. Of them, 11 segments with TTS had no intraoperative evidence of DO (Table II). Nearly a half in these (5/11, 45.5%) were adjacent to segments with DO. Only four patients without DO were misdiagnosed with DO. Of the 52 segments with DO, three did not have any of the aforementioned special imaging signs. The remaining 49 segments had both intraoperative evidence of DO and imaging findings of TTS, CS or BS. 90.4% of the segments with DO had TTS. CS (13.4%) and BS (13.4%) could exist alone or accompanied by TTS in the images (Table II). The sensitivity and specificity of imaging diagnosis were 94.23% (49/52) and 94.21% (179/190), respectively (Table III). Positive predictive value was relatively low (81.67%, 49/60), due to the false positive of TTS.

<table>
<thead>
<tr>
<th>Table II. Correlation between imaging signs and DO in OLF</th>
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<tr>
<td>TTS</td>
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<td>CS</td>
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<tr>
<td>BS</td>
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<tr>
<td>No TTS, CS or BS</td>
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*TTS: Tram track sign       CS: Comma sign          BS: Bridge sign
*CS/BS existed alone for 1 segment and accompanied by TTS in 6 segments

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<th>Table III. Assessment of Accuracy of Imaging Diagnosis</th>
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<tr>
<td>Segments with T/C/B</td>
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<td>Segments without T/C/B</td>
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Sensitivity=94.23% (49/52)                  Specificity=94.21% (179/190)
Positive predictive values=81.67% (49/60)   Negative predictive values=98.35% (179/182)
Test accuracy=94.21% (49+179/242)             T: tram track sign
C: comma sign                                    B: bridge sign
Discussion

As the primary cause of thoracic myelopathy, OLF commonly affects the lower thoracic in adults between 40 and 60 years of age[2-4 11 12]. This was supported by the present study, which further indicated that more than half (53.8%) of the DO was also located in T9-12 (Fig.3). The relatively high frequency of motion in this section may be one cause of this phenomenon[13 14].

Since conservative treatment is ineffective, surgical decompression has become the best option for OLF patients[2-6]. When dura mater ossifies together with ligamentum flavum, the difficulty and risks of surgery will significantly increase. In this present study, the incidence of DO in OLF patients was as high as 43.4%, which was consistent with the study of Muthukumar[9]. It indicated the importance of diagnosis of DO. Preoperative identification of DO can help surgeons to adopt appropriate surgical technique and get prepare to deal with the intraoperative dural laceration[2 9].

It has been documented that the diagnostic value of MRI for DO associated with OLF or OPLL (ossification of posterior longitudinal ligament) was inferior to CT[8 9]. Therefore axial CT scan of surgical decompression segments was used as the primary image to be evaluated in this study. TTS, CS, and BS were considered as characteristic imaging signs of DO in OLF. TTS was the most common signs among them. However, it might be misdiagnosed. In the study by Sun XZ et al[10], the diagnostic specificity of TTS was only 59%. Misdiagnosis was also pointed out by Sun J et al[2], but no plausible solution was proposed. In our preliminary screening study, we found that the TTS in diagnosis of DO should be more precisely called “tram track sign between ossified ligamentum flavum and dura mater”. To improve the accuracy of diagnosis, we defined and excluded four kinds of confusing signs (false TTS) (Fig.2): false TTS consisted of facet joint (Fig.2-A); false TTS consisted of ossified ligamentum flavum and superior articular process (Fig.2-B); false TTS between ossified ligamentum flavum and lamina (Fig.2-C) and false TTS between inner and outer bone cortex of superior articular process (Fig.2-D). Among them, the
false TTS of ossified ligamentum flavum and superior articular process or lamina were easily misdiagnosed as DO[2]. For atypical signs, reference to adjacent imaging of the same segment sometimes could be helpful (Fig.2-E). After excluding these false TTS, the specificity of imaging diagnosis was 94.21% (179/190) and the sensitivity remained high at 94.23% (49/52).

However, there were still 11 segments without DO, while having false positives of TTS. It led that the positive predictive value of imaging diagnosis was relatively low (81.67%, 49/60). We further analyzed these misdiagnosed segments and found that five of them were adjacent to the segments with DO. This phenomenon was previously reported in literature[12]. False positive TTS of another 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior and dural side of ligamentum flavum) (Fig.5). This was uncommon but hard to distinguish from TTS of ossified ligamentum flavum and dura mater. The remaining 3 segments were misdiagnosed for irregular signal. All the segments with BS or CS had DO.

The exact pathogenesis of OLF is still unknown. Both intrinsic [15-21] and extrinsic[22-24] factors were reported to be associated with the ossification of spinal ligament. Currently, mechanical stress as an extrinsic factor is thought to be important in the process of OLF. When the spinal ligament is under tension stress, some fibroblastic cells can transform into chondrocytes and expression of BMP-2, TGFβ and Sox9 will increase[23 24]. Yayama et al postulated that ossification of dura mater is probably due to dilution of the above cytokines related to osteogenesis from ossified ligamentum flavum[23]. According to this, we further hypothesized that DO starts at the portion that is directly in contact with the ossified ligamentum flavum. Since there is no gap between ossified dura and ligamentum flavum, no special imaging signs will appear. This could explain why some segments with DO did not have any of the aforementioned special imaging signs in previous studies[9 10] and ours. Only when the ossification extended to the surrounding dura mater that was not in contact with ossified ligamentum flavum, these special imaging findings would appear. In the same segment CT scan of some patients, the most serious compression
level did not have these special imaging findings, while adjacent levels under less
compression did (Fig.6). This phenomenon was a supporting evidence of our
hypothesis.

This study made a comprehensive analysis of DO. Radiological characteristics of
DO were described and analyzed in detail. Limitations still exist in the present study.
The study population was OLF patients who need surgical treatment. So the incidence
and distribution of DO reported in the present study was restricted to this population.
The mechanism and progression of DO need further investigate in the future. Large
sample multi-center prospective studies are still needed to further assess the accuracy
of imaging diagnosis.

Conclusions

DO was relatively common in thoracic OLF. T9-12 were the most frequently
involved segments. TTS, CS and BS could be used for the preoperative imaging
diagnosis of DO. However, TTS might be misdiagnosed. After excluding four kinds of
false TTS, the accuracy of imaging diagnosis was relatively high.

Contributors Study design (Yu Zhao, MD, Bo Li, MD, Guixing Qiu, MD, Shigong
Guo, MRCS); Data acquisition (Yu Zhao, MD, Bo Li, MD, Wenjing Li, MD, Ye Li,
MD, Huiming Peng, MD, Chu Wang, MD); Analysis and interpretation of data (Yu
Zhao, MD, Bo Li, MD, Shigong Guo, MRCS, Wenjing Li, MD, Ye Li, MD)

Funding This work was supported by grant from the National Natural Science
Foundation of China (NO.81572093) and Beijing Natural Science Foundation
(7162153).

Competing interests None declared.

Ethics approval The Institutional Review Board (IRB) of Peking Union Medical
College Hospital (PUMCH).

Data sharing statement No additional data are available.
References


10. Sun XZ, Chen ZQ, Qi Q, et al. Diagnosis and treatment of ossification of the ligamentum flavum


Figure legends

Figure 1.

Figs.1 (A-F) special imaging findings of DO.
Figs.1-A/D Tram track sign (A: bilateral, D: unilateral): a hyperdense bony excrescence, with a hypodense center. TTS consisted of three parts: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). Figs.1-B/E Comma sign: ossification of one-half of the dura mater. Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura. Figs.1-C/F Bridge sign: a hyperdense bony connection of bilateral OLF. Dorsal ossified dura presented as a bridge between bilateral ossified ligamentum flavum.

Figure 2.

Figs.2 (A-E) four kinds of confusing signs (false TTS) and analysis of adjacent levels: Fig.2-A false TTS of facet joint; Fig.2-B false TTS of ossified ligamentum flavum and superior articular process; Fig.2-C false TTS between ossified ligamentum flavum and lamina; Fig.2-D false TTS between inner and outer bone cortex of superior articular process. Fig.2-E imaging E2 was adjacent level of the same segment with E1. Adjacent imaging (E2) could help to identify the imaging findings in E1 was false TTS of ossified ligamentum flavum and superior articular process.

Figure 3.

Fig.3 Distribution of OLF and DO: OLF was more common in lower thoracic spine. More than half (53.8%) of the DO located in T9-12.

Figure 4.
**Fig.4** Number of involved segments in patients with DO: The majority (87.0%) of DO patients had only 1-3 segments involved.

Figure 5.

**Figs.5 (A-C)** False positive TTS of 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior side and dural side).

Figure 6.

**Figs.6 (A-C)** CT scan of the same segment: the most serious compression level (A) had no TTS, while adjacent levels (B, C) under less compression did.
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34x28mm (600 x 600 DPI)
Figure 2. Figs.2 (A-E) four kinds of confusing signs (false TTS) and analysis of adjacent levels: Fig.2-A false TTS of facet joint; Fig.2-B false TTS of ossified ligamentum flavum and superior articular process; Fig.2-C false TTS between ossified ligamentum flavum and lamina; Fig.2-D false TTS between inner and outer bone cortex of superior articular process. Fig.2-E imaging E2 was adjacent level of the same segment with E1. Adjacent imaging (E2) could help to identify the imaging findings in E1 was false TTS of ossified ligamentum flavum and superior articular process.

20x18mm (600 x 600 DPI)
Figure 3. Fig.3 Distribution of OLF and DO: OLF was more common in lower thoracic spine. More than half (53.8%) of the DO located in T9-12.
Figure 4. Number of involved segments in patients with DO: The majority (87.0%) of DO patients had only 1-3 segments involved.

238x136mm (200 x 200 DPI)
Figure 5. Figs.5 (A-C) False positive TTS of 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior side and dural side).

227x111mm (200 x 200 DPI)
Figure 6. Figs. 6 (A-C) CT scan of the same segment: the most serious compression level (A) had no TTS, while adjacent levels (B, C) under less compression did.

203x107mm (300 x 300 DPI)
STROBE Statement—checklist of items that should be included in reports of observational studies

<table>
<thead>
<tr>
<th>Item No</th>
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<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
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<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract [1-2]</td>
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<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found [1-2]</td>
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<td><strong>Introduction</strong></td>
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<td>Explain the scientific background and rationale for the investigation being reported [4]</td>
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<td>State specific objectives, including any prespecified hypotheses [4]</td>
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<td><strong>Methods</strong></td>
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<td>Present key elements of study design early in the paper [4]</td>
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<td><strong>Setting</strong></td>
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<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [4-5]</td>
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<td><strong>Participants</strong></td>
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<td>(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up [N/A]</td>
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<td>Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls [4-5]</td>
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<td>Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants [N/A]</td>
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<td>(b) Cohort study—for matched studies, give matching criteria and number of exposed and unexposed [N/A]</td>
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<td>Case-control study—for matched studies, give matching criteria and the number of controls per case [N/A]</td>
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<td><strong>Variables</strong></td>
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<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [5]</td>
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<td><strong>Data sources/measurement</strong></td>
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<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [5]</td>
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<td>Describe any efforts to address potential sources of bias [5]</td>
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<td>Explain how the study size was arrived at [6]</td>
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<td><strong>Quantitative variables</strong></td>
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<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [5-6]</td>
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<td>(a) Describe all statistical methods, including those used to control for confounding [5-6]</td>
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<td>(d) Cohort study—if applicable, explain how loss to follow-up was addressed [N/A]</td>
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<td>Case-control study—if applicable, explain how matching of cases and controls was addressed [6]</td>
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<td>Cross-sectional study—if applicable, describe analytical methods taking account of sampling strategy [N/A]</td>
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<td>(g) Describe any sensitivity analyses [5-6]</td>
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Results

Participants 13* (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [6]
(b) Give reasons for non-participation at each stage [5-6]
(c) Consider use of a flow diagram [5-6]

Descriptive data 14* (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [6-7]
(b) Indicate number of participants with missing data for each variable of interest [6]
(c) Cohort study—Summarise follow-up time (eg, average and total amount) [N/A]

Outcome data 15* Cohort study—Report numbers of outcome events or summary measures over time [N/A]
Case-control study—Report numbers in each exposure category, or summary measures of exposure [6]
Cross-sectional study—Report numbers of outcome events or summary measures [N/A]

Main results 16 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [6-7]
(b) Report category boundaries when continuous variables were categorized [N/A]
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period [N/A]

Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [7]

Discussion

Key results 18 Summarise key results with reference to study objectives [7-8]

Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [9-10]

Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [7-9]

Generalisability 21 Discuss the generalisability (external validity) of the study results [7-10]

Other information

Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [10]

* Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Dural ossification associated with ossification of ligamentum flavum in the thoracic spine: a retrospective analysis

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| Complete List of Authors: | Li, Bo; Peking Union Medical College Hospital, Department of orthopaedics
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| Primary Subject Heading: | Radiology and imaging |
| Secondary Subject Heading: | Neurology |
| Keywords: | Dural ossification, Ossification of ligamentum flavum, Thoracic spine, imaging signs |
Dural ossification associated with ossification of ligamentum flavum in the thoracic spine: a retrospective analysis

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Abstract

Objectives: To investigate the incidence, distribution, and radiological characteristics of dural ossification (DO) associated with ossification of ligamentum flavum (OLF) in the thoracic spine.

Design: A retrospective radiographical analysis.

Setting: This study was conducted at a single institution in China.

Participants: Fifty-three OLF patients who underwent posterior decompression surgery between January 2011 and July 2015 in a single institution were enrolled in this study. The decompression segments were grouped according to imaging evaluation and intraoperative evidences.

Outcome measures: The demographic distribution, radiological data, and detailed surgical records were collected. Firstly, preoperative CT images of decompressed segments was evaluated to identify imaging signs of DO. The “tram tack sign” (TTS), “comma sign” (CS) and “bridge sign” (BS) were considered as characteristic imaging findings of DO in OLF. Four kinds of confusing signs (false TTS) were identified and excluded. Then, detailed surgical records were reviewed to finally identify segments with DO.

Results: The incidence of DO in OLF patients was 43.4%. The incidence of DO in OLF segments was 21.5%. OLF was more common in lower thoracic spine, and more than half (53.8%) of the DO located in T9-T12. TTS was the most common signs, but it might be misdiagnosed. After excluding four kinds of false TTS, the sensitivity and specificity of imaging diagnosis were 94.23% and 94.21%, respectively.

Conclusions: DO was relatively common in thoracic OLF, especially in T9-T12. TTS might be misdiagnosed. After excluding four kinds of false TTS, the accuracy of imaging diagnosis was relatively high.
Strengths and limitations of this study

- This study made up for the current lack of understanding of dural ossification (DO) associated with ossification of ligamentum flavum (OLF) in the thoracic spine.
- The incidence, distribution, and radiological characteristics of DO were described and analyzed in detail.
- The study increased the accuracy of identifying DO in OLF before surgery.
- The study population was limited to OLF patients who need surgical treatment.
Introduction

Ossification of ligamentum flavum (OLF) is the most common cause of thoracic spinal stenosis[1-3], especially in East Asian populations. With the progression of OLF, the spinal cord will be subjected to severe compression and the patient may eventually be paralyzed. Surgical treatment is generally accepted as the best option[2-6]. When compressed, the dura mater may also ossify. Then the ossified ligamentum flavum and dura fuse to be one inseparable bony tissue. This will increase the difficulty of surgery and the risk of spinal cord injury and cerebrospinal fluid leakage[7 8]. Preoperative identification of DO can help surgeons to adopt appropriate surgical technique and get prepare to deal with the intraoperative dural laceration. In a preliminary study, the “tram track sign” (TTS) and “comma sign” (CS) were reported to be associated with DO[9]. However, due to the relatively small study population and lack of awareness of these specific image signs, accurate diagnosis of DO could not be obtained in previous studies[2 10]. Since the incidence of OLF and DO is relatively low, few studies have focused on this issue[2 9 10]. The incidence, distribution of DO were also unclear. The present study aimed to investigate the incidence, distribution, and radiological characteristics of DO in thoracic OLF.

Methods

Study population

Thoracic OLF patients who underwent posterior decompression surgery between January 2011 and July 2015 in a single Chinese institution were enrolled in this retrospective cohort study. The exclusion criteria were OLF patients with thoracic trauma, infection, tumor, and deformity. Fifty-three cases were finally included in this study, with institutional review board approval. The main symptoms included numbness, zonesthesia, asthenia, gait disturbance, back pain, and bladder/bowel dysfunction. The indication of surgical treatment was neurological deterioration. All patients underwent open posterior decompression. Intraoperative, after resecting the lamina, the ossified ligamentum flavum was lifted and separated from the dura mater by gently dissection. If ossifying, the dura mater will fuse with the ossified
ligamentum flavum, which makes the separation impossible. In this condition, the ossified dura mater was also resected. Clinical data, preoperative computed tomography (CT), and detailed surgical records were available for all the included patients. The decompression levels were grouped according to imaging evaluation and intraoperative evidences described as blow.

**Imaging evaluation and identification of DO**

Preoperative axial CT scans of surgical decompression segments (involved vertebral levels) were the primary imaging to be assessed for every included patient. In our preliminary screening study, the “tram track sign” (TTS), “comma sign” (CS) and “bridge sign” (BS) were considered as characteristic imaging findings of DO in OLF (Fig.1). TTS and CS had been reported before. Tram track sign was defined as a hyperdense bony excrescence, with a hypodense center (Figs.1A/D). It consisted of three parts in the axial CT scan: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). These three parts together formed a tram-track-like shape. Comma sign was an imaging manifestation of ossification of one-half of the dura mater (Figs.1B/E). Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura. Bridge sign, which was firstly reported in this study, was a hyperdense bony connection of bilateral OLF (Figs.1C/F). The dorsal ossified dura presented as a bridge between bilateral ossified ligamentum flavum. Segments with the above signs on axial CT images would be initially diagnosed with DO in OLF.

TTS might be misdiagnosed as found in our preliminary screening study. So we defined and excluded four kinds of confusing signs (false TTS) (Fig.2): false TTS consisted of facet joint (Fig.2-A); false TTS consisted of ossified ligamentum flavum and superior articular process (Fig.2-B); false TTS between ossified ligamentum flavum and lamina (Fig.2-C); and false TTS between inner and outer bone cortex of superior articular process (Fig.2-D). For atypical signs, reference to adjacent imaging of the same segment might be helpful (Fig.2-E).
To ensure reliability, imaging evaluation was performed before review of surgical records. Two observers, blind to the groups, were responsible for the imaging evaluation. Surgical decompression segments would then be divided into the following three categories (initial diagnosis): non-OLF segments, OLF segments without DO, and OLF segments with DO. After imaging evaluation, surgical records were reviewed to identify which segments were truly associated with DO. This would be regarded as the final diagnosis. The incidence and distribution of DO were recorded.

Statistical analyses

Initial diagnosis was compared with the final diagnosis for calculating the sensitivity and specificity of imaging diagnosis. The test accuracy, positive and negative predictive values were also calculated. Data were presented as mean ± standard deviation (SD). SPSS software (version 20.0, Chicago, Illinois, USA) was used for statistical analysis.

Results

Population

Fifty-three OLF patients (26 female; age: 53.87 ± 10.42, range: 30 – 74) were included in this retrospective study. 23 cases (13 female) had intraoperative evidence of DO. The mean age of DO group was 54.65±9.62, comparing to 53.27±11.12 in the Non-DO group (P>0.05) (Table I).

Incidence

Of the 53 included patients, 242 surgical decompression segments were diagnosed with OLF by axial CT scan. 52 segments from 23 OLF patients had DO related to OLF. The incidence of DO in OLF segments was 21.5% (52/242) and the incidence of DO in OLF patients was 43.4% (23/53) (Table I).
Table I: Basic information of included OLF patients

<table>
<thead>
<tr>
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<th>OLF with DO</th>
<th>OLF without DO</th>
<th>Total</th>
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<tbody>
<tr>
<td>Cases</td>
<td>23</td>
<td>30</td>
<td>53</td>
</tr>
<tr>
<td>Sex (Female/ male)</td>
<td>13/10</td>
<td>13/17</td>
<td>26/27</td>
</tr>
<tr>
<td>Age (ys)</td>
<td>54.65±9.62</td>
<td>53.27±11.12</td>
<td>53.87 ± 10.42</td>
</tr>
<tr>
<td>Segments</td>
<td>52</td>
<td>190</td>
<td>242</td>
</tr>
</tbody>
</table>

Incidence of DO in OLF segments: 21.5% (52/242)
Incidence of DO in OLF patients: 43.4%(23/53)

Distribution

The distribution of OLF and DO was shown in figure 3. OLF was more common in lower thoracic spine, and more than half (53.8%) of the DO located in T9-T12. The majority of DO patients (20/23, 87.0%) had only 1-3 segments involved (Fig.4).

Accuracy of imaging diagnosis

In the imaging evaluation, 60 segments were initially thought to have DO. Of them, 11 segments with TTS had no intraoperative evidence of DO (Table II). Nearly a half in these (5/11, 45.5%) were adjacent to segments with DO. Only four patients without DO were misdiagnosed with DO. Of the 52 segments with DO, three did not have any of the aforementioned special imaging signs. The remaining 49 segments had both intraoperative evidence of DO and imaging findings of TTS, CS or BS. 90.4% of the segments with DO had TTS. CS (13.4%) and BS (13.4%) could exist alone or accompanied by TTS in the images (Table II). The sensitivity and specificity of imaging diagnosis were 94.23% (49/52) and 94.21% (179/190), respectively (Table III). Positive predictive value was relatively low (81.67%, 49/60), due to the false positive of TTS.
Table II. Correlation between imaging signs and DO in OLF

<table>
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<tr>
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<th>OLF with DO</th>
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<tr>
<td>TTS</td>
<td>47</td>
<td>11</td>
<td>58</td>
</tr>
<tr>
<td>CS 7 (CS=1, CS+TTS=6)*</td>
<td>0</td>
<td>7 (CS=1, CS+TTS=6)*</td>
<td></td>
</tr>
<tr>
<td>BS 7 (BS=1, BS+TTS=6)*</td>
<td>0</td>
<td>7 (BS=1, BS+TTS=6)*</td>
<td></td>
</tr>
<tr>
<td>No TTS, CS or BS</td>
<td>3</td>
<td>179</td>
<td>182</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>190</td>
<td>242</td>
</tr>
</tbody>
</table>

TTS: Tram track sign  
CS: Comma sign  
BS: Bridge sign

*CS/BS existed alone for 1 segment and accompanied by TTS in 6 segments

Table III. Assessment of Accuracy of Imaging Diagnosis

<table>
<thead>
<tr>
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<th>OLF with DO</th>
<th>OLF without DO</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segments with T/C/B</td>
<td>49</td>
<td>11</td>
<td>60</td>
</tr>
<tr>
<td>Segments without T/C/B</td>
<td>3</td>
<td>179</td>
<td>182</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>190</td>
<td>242</td>
</tr>
</tbody>
</table>

Sensitivity=94.23% (49/52)  
Specificity=94.21% (179/190)  
Positive predictive values=81.67% (49/60)  
Negative predictive values=98.35% (179/182)

Test accuracy=94.21% (49+179/242)  
T: tram track sign  
C: comma sign  
B: bridge sign

Discussion

As the primary cause of thoracic myelopathy, OLF commonly affects the lower thoracic in adults between 40 and 60 years of age[2-4 11 12]. This was supported by the present study, which further indicated that more than half (53.8%) of the DO was also located in T9-T12 (Fig.3). The relatively high frequency of motion in this section may be one cause of this phenomenon[13 14].

Since conservative treatment is ineffective, surgical decompression has become the best option for OLF patients[2-6]. When dura mater ossifies together with ligamentum flavum, the difficulty and risks of surgery will significantly increase. In this present study, the incidence of DO in OLF patients was as high as 43.4%, which was consistent with the study of Muthukumar[9]. It indicated the importance of
diagnosis of DO. Preoperative identification of DO can help surgeons to adopt appropriate surgical technique and get prepared to deal with the intraoperative dural laceration[2-9].

It has been documented that the diagnostic value of MRI for DO associated with OLF or OPLL (ossification of posterior longitudinal ligament) was inferior to CT[8-9]. Therefore, axial CT scan of surgical decompression segments was used as the primary image to be evaluated in this study. TTS, CS, and BS were considered as characteristic imaging signs of DO in OLF. TTS was the most common signs among them. However, it might be misdiagnosed. In the study by Sun XZ et al[10], the diagnostic specificity of TTS was only 59%. Misdiagnosis was also pointed out by Sun J et al[2], but no plausible solution was proposed. In our preliminary screening study, we found that the TTS in the diagnosis of DO should be more precisely called “tram track sign between ossified ligamentum flavum and dura mater”. To improve the accuracy of diagnosis, we defined and excluded four kinds of confusing signs (false TTS) (Fig.2): false TTS consisted of facet joint (Fig.2-A); false TTS consisted of ossified ligamentum flavum and superior articular process (Fig.2-B); false TTS between ossified ligamentum flavum and lamina (Fig.2-C) and false TTS between inner and outer bone cortex of superior articular process (Fig.2-D). Among them, the false TTS of ossified ligamentum flavum and superior articular process or lamina were easily misdiagnosed as DO[2]. For atypical signs, reference to adjacent imaging of the same segment sometimes could be helpful (Fig.2-E). After excluding these false TTS, the specificity of imaging diagnosis was 94.21% (179/190) and the sensitivity remained high at 94.23% (49/52).

However, there were still 11 segments without DO, while having false positives of TTS. It led that the positive predictive value of imaging diagnosis was relatively low (81.67%, 49/60). We further analyzed these misdiagnosed segments and found that five of them were adjacent to the segments with DO. This phenomenon was previously reported in literature[12]. False positive TTS of another 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior and dural side of ligamentum flavum) (Fig.5).
This was uncommon but hard to distinguish from TTS of ossified ligamentum flavum and dura mater. The remaining 3 segments were misdiagnosed for irregular signal. All the segments with BS or CS had DO.

The exact pathogenesis of OLF is still unknown. Both intrinsic [15-21] and extrinsic factors were reported to be associated with the ossification of spinal ligament. Currently, mechanical stress as an extrinsic factor is thought to be important in the process of OLF. When the spinal ligament is under tension stress, some fibroblastic cells can transform into chondrocytes and expression of BMP-2, TGFβ and SOX9 will increase[23 24]. Yayama et al postulated that ossification of dura mater is probably due to dilution of the above cytokines related to osteogenesis from ossified ligamentum flavum[23]. Based on literature, a potential mechanism of DO was proposed before[14]. The relative movement between OLF and compressed dura mater, due to the flexion and extension of spine, will cause local inflammation, leading to dural adhesion[14]. Then, the adhesion tissue can act as a tunnel to transport osteogenic cytokines mentioned above from OLF to compressed dura mater, which causes the dura mater directly adhered to OLF firstly ossifies [14]. According to this, DO may start at the portion that is directly in contact with the ossified ligamentum flavum. Since there is no gap between ossified dura and ligamentum flavum, no special imaging signs will appear. This could explain why some segments with DO did not have any of the aforementioned special imaging signs in previous studies[9 10] and ours. Only when the ossification extended to the surrounding dura mater that was not in contact with ossified ligamentum flavum, these special imaging findings would appear. In the same segment CT scan of some patients, the most serious compression level did not have these special imaging findings, while adjacent levels under less compression did (Fig.6). This phenomenon was a supporting evidence of our hypothesis.

This study made a comprehensive analysis of DO. Radiological characteristics of DO were described and analyzed in detail. Limitations still exist in the present study. The study population was OLF patients who need surgical treatment. So the incidence and distribution of DO reported in the present study was restricted to this population.
The mechanism and progression of DO need further investigate in the future. Large sample multi-center prospective studies are still needed to further assess the accuracy of imaging diagnosis.

Conclusions

DO was relatively common in thoracic OLF. T9-T12 were the most frequently involved segments. TTS might be misdiagnosed. After excluding four kinds of false TTS, the accuracy of imaging diagnosis was relatively high.

Contributors

Study design (Yu Zhao, MD, Bo Li, MD, Guixing Qiu, MD, Shigong Guo, MRCS); Data acquisition (Yu Zhao, MD, Bo Li, MD, Wenjing Li, MD, Ye Li, MD, Huiming Peng, MD, Chu Wang, MD); Analysis and interpretation of data (Yu Zhao, MD, Bo Li, MD, Shigong Guo, MRCS, Wenjing Li, MD, Ye Li, MD)

Funding

This work was supported by grant from the National Natural Science Foundation of China (NO.81572093) and Beijing Natural Science Foundation (7162153).

Competing interests

None declared.

Ethics approval

The Institutional Review Board (IRB) of Peking Union Medical College Hospital (PUMCH).

Data sharing statement

No additional data are available.


Figure legends

Figure 1.

Figs.1 (A-F) special imaging findings of DO.
Figs.1-A/D Tram track sign (A: bilateral, D: unilateral): a hyperdense bony excrescence, with a hypodense center. TTS consisted of three parts: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). Figs.1-B/E Comma sign: ossification of one-half of the dura mater. Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura. Figs.1-C/F Bridge sign: a hyperdense bony connection of bilateral OLF. Dorsal ossified dura presented as a bridge between bilateral ossified ligamentum flavum.

Figure 2.

Figs.2 (A-E) four kinds of confusing signs (false TTS) and analysis of adjacent levels: Figs.2-A false TTS of facet joint; Figs.2-B false TTS of ossified ligamentum flavum and superior articular process; Figs.2-C false TTS between ossified ligamentum flavum and lamina; Figs.2-D false TTS between inner and outer bone cortex of superior articular process. Figs.2-E imaging E2 was adjacent level of the same segment with E1. Adjacent imaging (E2) could help to identify the imaging findings in E1 was false TTS of ossified ligamentum flavum and superior articular process.

Figure 3.

Fig.3 Distribution of OLF and DO: OLF was more common in lower thoracic spine. More than half (53.8%) of the DO located in T9-T12.

Figure 4.

Fig.4 Number of involved segments in patients with DO: The majority (87.0%) of DO patients had only 1-3 segments involving DO.

Figure 5.

Figs.5 (A-C) False positive TTS of 3 segments were considered to be the imaging
manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior side and dural side).

Figure 6.

Figs.6 (A-C) CT scan of the same segment: the most serious compression level (A) had no TTS, while adjacent levels (B, C) under less compression did.
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99x92mm (300 x 300 DPI)
Figure 3.
Fig.3 Distribution of OLF and DO: OLF was more common in lower thoracic spine. More than half (53.8%) of the DO located in T9-T12.

191x109mm (300 x 300 DPI)
Figure 4.
Fig.4 Number of involved segments in patients with DO: The majority (87.0%) of DO patients had only 1-3 segments involving DO.

158x91mm (300 x 300 DPI)
Figure 5. Figs.5 (A-C) False positive TTS of 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior side and dural side).

185x91mm (300 x 300 DPI)
Figs. 6 (A-C) CT scan of the same segment: the most serious compression level (A) had no TTS, while adjacent levels (B, C) under less compression did.
STROBE Statement—checklist of items that should be included in reports of observational studies

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
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</table>
| **Title and abstract** | (a) Indicate the study’s design with a commonly used term in the title or the abstract [1-2]  
(b) Provide in the abstract an informative and balanced summary of what was done and what was found [1-2] |
| **Introduction** | |
| Background/rationale | Explain the scientific background and rationale for the investigation being reported [4] |
| **Objectives** | State specific objectives, including any prespecified hypotheses [4] |
| **Methods** | |
| Study design | Present key elements of study design early in the paper [4] |
| Setting | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [4-5] |
| Participants | (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up [N/A]  
Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls [4-5]  
Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants [N/A]  
(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed [N/A]  
Case-control study—For matched studies, give matching criteria and the number of controls per case [N/A] |
| Variables | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [5] |
| Data sources/measurement | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [5] |
| Bias | Describe any efforts to address potential sources of bias [5] |
| Study size | Explain how the study size was arrived at [6] |
| Quantitative variables | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [5-6] |
| Statistical methods | (a) Describe all statistical methods, including those used to control for confounding [5-6]  
(b) Describe any methods used to examine subgroups and interactions [5]  
(c) Explain how missing data were addressed [N/A]  
(d) Cohort study—If applicable, explain how loss to follow-up was addressed [N/A]  
Case-control study—If applicable, explain how matching of cases and controls was addressed [6]  
Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy [N/A]  
(g) Describe any sensitivity analyses [5-6] |

Continued on next page
### Results

#### Participants
- **13***
  - (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [6]
  - (b) Give reasons for non-participation at each stage [5-6]
  - (c) Consider use of a flow diagram [5-6]

#### Descriptive data
- **14***
  - (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [6-7]
  - (b) Indicate number of participants with missing data for each variable of interest [6]
  - (c) **Cohort study**—Summarise follow-up time (eg, average and total amount) [N/A]

#### Outcome data
- **15***
  - **Cohort study**—Report numbers of outcome events or summary measures over time [N/A]
  - **Case-control study**—Report numbers in each exposure category, or summary measures of exposure [6]
  - **Cross-sectional study**—Report numbers of outcome events or summary measures [N/A]

#### Main results
- **16***
  - (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [6-7]
  - (b) Report category boundaries when continuous variables were categorized [N/A]
  - (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period [N/A]

#### Other analyses
- **17***
  - Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [7]

### Discussion

#### Key results
- **18***
  - Summarise key results with reference to study objectives [7-8]

#### Limitations
- **19***
  - Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [9-10]

#### Interpretation
- **20***
  - Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [7-9]

#### Generalisability
- **21***
  - Discuss the generalisability (external validity) of the study results [7-10]

### Other information

#### Funding
- **22***
  - Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [10]

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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
### Dural ossification associated with ossification of ligamentum flavum in the thoracic spine: a retrospective analysis

<table>
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| Complete List of Authors: | Li, Bo; Peking Union Medical College Hospital, Department of orthopaedics  
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                          Zhao, Yu; Peking Union Medical College Hospital, Department of orthopaedics |
| Primary Subject Heading: | Radiology and imaging |
| Secondary Subject Heading: | Neurology |
| Keywords: | Dural ossification, Ossification of ligamentum flavum, Thoracic spine, imaging signs |
Dural ossification associated with ossification of ligamentum flavum in the thoracic spine: a retrospective analysis

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Investigation performed at the Department of Orthopaedic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

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Abstract

Objectives: To investigate the incidence, distribution, and radiological characteristics of dural ossification (DO) associated with ossification of ligamentum flavum (OLF) in the thoracic spine.

Design: A retrospective radiographical analysis.

Setting: This study was conducted at a single institution in China.

Participants: Fifty-three OLF patients who underwent posterior decompression surgery between January 2011 and July 2015 in a single institution were enrolled in this study. The decompression segments were grouped according to imaging evaluation and intraoperative evidences.

Outcome measures: The demographic distribution, radiological data, and detailed surgical records were collected. Firstly, preoperative CT images of decompressed segments was evaluated to identify imaging signs of DO. The “tram tack sign” (TTS), “comma sign” (CS) and “bridge sign” (BS) were considered as characteristic imaging findings of DO in OLF. Four kinds of confusing signs (false TTS) were identified and excluded. Then, detailed surgical records were reviewed to finally identify segments with DO.

Results: The incidence of DO in OLF patients was 43.4%. The incidence of DO in OLF segments was 21.5%. OLF was more common in lower thoracic spine, and more than half (53.8%) of the DO located in T9-T12. TTS was the most common signs, but it might be misdiagnosed. After excluding four kinds of false TTS, the sensitivity and specificity of imaging diagnosis were 94.23% and 94.21%, respectively.

Conclusions: DO was relatively common in thoracic OLF, especially in T9-T12. TTS might be misdiagnosed. After excluding four kinds of false TTS, the accuracy of imaging diagnosis was relatively high.
Strengths and limitations of this study

- This study made up for the current lack of understanding of dural ossification (DO) associated with ossification of ligamentum flavum (OLF) in the thoracic spine.
- The incidence, distribution, and radiological characteristics of DO were described and analyzed in detail.
- The study increased the accuracy of identifying DO in OLF before surgery.
- The study population was limited to OLF patients who need surgical treatment.
Introduction

Ossification of ligamentum flavum (OLF) is the most common cause of thoracic spinal stenosis[1-3], especially in East Asian populations. With the progression of OLF, the spinal cord will be subjected to severe compression and the patient may eventually be paralyzed. Surgical treatment is generally accepted as the best option[2-6]. When compressed, the dura mater may also ossify. Then the ossified ligamentum flavum and dura mater fuse to be one inseparable bony tissue. This will increase the difficulty of surgery and the risk of spinal cord injury and cerebrospinal fluid leakage[7 8]. Preoperative identification of DO can help surgeons to adopt appropriate surgical technique and get prepare to deal with the intraoperative dural laceration. In a preliminary study, the “tram track sign” (TTS) and “comma sign” (CS) were reported to be associated with DO[9]. However, due to the relatively small study population and lack of awareness of these specific image signs, accurate diagnosis of DO could not be obtained in previous studies[2 10]. Since the incidence of OLF and DO is relatively low, few studies have focused on this issue[2 9 10]. The incidence, distribution of DO were also unclear. The present study aimed to investigate the incidence, distribution, and radiological characteristics of DO in thoracic OLF.

Methods

Study population

Thoracic OLF patients who underwent posterior decompression surgery between January 2011 and July 2015 in a single Chinese institution were enrolled in this retrospective cohort study. The exclusion criteria were OLF patients with thoracic trauma, infection, tumor, and deformity. Fifty-three cases were finally included in this study, with institutional review board approval. The main symptoms included numbness, zonesthesia, asthenia, gait disturbance, back pain, and bladder/bowel dysfunction. The indication of surgical treatment was neurological deterioration. All patients underwent open posterior decompression. Intraoperative, after resecting the lamina, the ossified ligamentum flavum was lifted and separated from the dura mater by gently dissection. If ossifying, the dura mater will fuse with the ossified
ligamentum flavum, which makes the separation impossible. In this condition, the ossified dura mater was also resected. Clinical data, preoperative computed tomography (CT), and detailed surgical records were available for all the included patients. The decompression levels were grouped according to imaging evaluation and intraoperative evidences described as blow.

Imaging evaluation and identification of DO

Preoperative axial CT scans of surgical decompression segments (involved vertebral levels) were the primary imaging to be assessed for every included patient. In our preliminary screening study, the “tram tack sign” (TTS), “comma sign” (CS) and “bridge sign” (BS) were considered as characteristic imaging findings of DO in OLF (Fig.1). TTS and CS had been reported before. Tram track sign was defined as a hyperdense bony excrescence, with a hypodense center (Figs.1A/D). It consisted of three parts in the axial CT scan: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). These three parts together formed a tram-track-like shape. Comma sign was an imaging manifestation of ossification of one-half of the dura mater (Figs.1B/E). Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura mater. Bridge sign, which was firstly reported in this study, was a hyperdense bony connection of bilateral OLF (Figs.1C/F). The dorsal ossified dura mater presented as a bridge between bilateral ossified ligamentum flavum. Segments with the above signs on axial CT images would be initially diagnosed with DO in OLF.

TTS might be misdiagnosed as found in our preliminary screening study. So we defined and excluded four kinds of confusing signs (false TTS) (Fig.2): false TTS consisted of facet joint (Fig.2-A); false TTS consisted of ossified ligamentum flavum and superior articular process (Fig.2-B); false TTS between ossified ligamentum flavum and lamina (Fig.2-C); and false TTS between inner and outer bone cortex of superior articular process (Fig.2-D). For atypical signs, reference to adjacent imaging of the same segment might be helpful (Fig.2-E).
To ensure reliability, imaging evaluation was performed before review of surgical records. Two observers, blind to the groups, were responsible for the imaging evaluation. One was responsible for our preliminary screening study, who defined the “tram tack sign” (TTS), “comma sign” (CS), “bridge sign” (BS) and four kinds of confusing signs (false TTS). The other one was responsible for our diagnosis study using the defined criteria of different kinds of imaging signs. Surgical decompression segments would then be divided into the following three categories (initial diagnosis): non-OLF segments, OLF segments without DO, and OLF segments with DO. After imaging evaluation, surgical records were reviewed to identify which segments were truly associated with DO. This would be regarded as the final diagnosis. The incidence and distribution of DO were recorded.

Statistical analyses

Initial diagnosis was compared with the final diagnosis for calculating the sensitivity and specificity of imaging diagnosis. The test accuracy, positive and negative predictive values were also calculated. Data were presented as mean ± standard deviation (SD). SPSS software (version 20.0, Chicago, Illinois, USA) was used for statistical analysis.

Results

Population

Fifty-three OLF patients (26 female; age: 53.87 ± 10.42, range: 30 - 74) were included in this retrospective study. 23 cases (13 female) had intraoperative evidence of DO. The mean age of DO group was 54.65±9.62, comparing to 53.27±11.12 in the Non-DO group (P>0.05) (Table I).

Incidence

Of the 53 included patients, 242 surgical decompression segments were diagnosed with OLF by axial CT scan. 52 segments from 23 OLF patients had DO related to OLF. The incidence of DO in OLF segments was 21.5% (52/242) and the incidence of DO in OLF patients was 43.4% (23/53) (Table I).
Table I: Basic information of included OLF patients

<table>
<thead>
<tr>
<th></th>
<th>OLF with DO</th>
<th>OLF without DO</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Cases</td>
<td>23</td>
<td>30</td>
<td>53</td>
</tr>
<tr>
<td>Sex (Female/ male)</td>
<td>13/10</td>
<td>13/17</td>
<td>26/27</td>
</tr>
<tr>
<td>Age (ys)</td>
<td>54.65±9.62</td>
<td>53.27±11.12</td>
<td>53.87 ± 10.42</td>
</tr>
<tr>
<td>Segments</td>
<td>52</td>
<td>190</td>
<td>242</td>
</tr>
</tbody>
</table>

Incidence of DO in OLF segments: 21.5% (52/242)
Incidence of DO in OLF patients: 43.4% (23/53)

Distribution

The distribution of OLF and DO was shown in figure 3. OLF was more common in lower thoracic spine, and more than half (53.8%) of the DO located in T9-T12. The majority of DO patients (20/23, 87.0%) had only 1-3 segments involved (Fig.4).

Accuracy of imaging diagnosis

In the imaging evaluation, 60 segments were initially thought to have DO. Of them, 11 segments with TTS had no intraoperative evidence of DO (Table II). Nearly a half in these (5/11, 45.5%) were adjacent to segments with DO. Only four patients without DO were misdiagnosed with DO. Of the 52 segments with DO, three did not have any of the aforementioned special imaging signs. The remaining 49 segments had both intraoperative evidence of DO and imaging findings of TTS, CS or BS. 90.4% of the segments with DO had TTS. CS (13.4%) and BS (13.4%) could exist alone or accompanied by TTS in the images (Table II). The sensitivity and specificity of imaging diagnosis were 94.23% (49/52) and 94.21% (179/190), respectively (Table III). Positive predictive value was relatively low (81.67%, 49/60), due to the false positive of TTS.
Table II. Correlation between imaging signs and DO in OLF

<table>
<thead>
<tr>
<th></th>
<th>OLF with DO</th>
<th>OLF without DO</th>
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<tbody>
<tr>
<td>TTS</td>
<td>47</td>
<td>11</td>
<td>58</td>
</tr>
<tr>
<td>CS</td>
<td>7 (CS=1, CS+TTS=6)*</td>
<td>0</td>
<td>7 (CS=1, CS+TTS=6)*</td>
</tr>
<tr>
<td>BS</td>
<td>7 (BS=1, BS+TTS=6)*</td>
<td>0</td>
<td>7 (BS=1, BS+TTS=6)*</td>
</tr>
<tr>
<td>No TTS, CS or BS</td>
<td>3</td>
<td>179</td>
<td>182</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>190</td>
<td>242</td>
</tr>
</tbody>
</table>

TTS: Tram track sign  CS: Comma sign  BS: Bridge sign
*CS/BS existed alone for 1 segment and accompanied by TTS in 6 segments

Table III. Assessment of Accuracy of Imaging Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>OLF with DO</th>
<th>OLF without DO</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segments with T/C/B</td>
<td>49</td>
<td>11</td>
<td>60</td>
</tr>
<tr>
<td>Segments without T/C/B</td>
<td>3</td>
<td>179</td>
<td>182</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>190</td>
<td>242</td>
</tr>
</tbody>
</table>

Sensitivity=94.23% (49/52)  Specificity=94.21% (179/190)
Positive predictive values=81.67% (49/60)  Negative predictive values=98.35% (179/182)
Test accuracy=94.21% (49+179/242)
T: tram track sign  C: comma sign  B: bridge sign

Discussion

As the primary cause of thoracic myelopathy, OLF commonly affects the lower thoracic in adults between 40 and 60 years of age[2-4 11 12]. This was supported by the present study, which further indicated that more than half (53.8%) of the DO was also located in T9-T12 (Fig.3). The relatively high frequency of motion in this section may be one cause of this phenomenon[13 14].

Since conservative treatment is ineffective, surgical decompression has become the best option for OLF patients[2-6]. When dura mater ossifies together with
ligamentum flavum, the difficulty and risks of surgery will significantly increase. In this present study, the incidence of DO in OLF patients was as high as 43.4%, which was consistent with the study of Muthukumar[9]. It indicated the importance of diagnosis of DO. Preoperative identification of DO can help surgeons to adopt appropriate surgical technique and get prepare to deal with the intraoperative dural laceration[2 9].

It has been documented that the diagnostic value of MRI for DO associated with OLF or OPLL (ossification of posterior longitudinal ligament) was inferior to CT[8 9]. Therefore axial CT scan of surgical decompression segments was used as the primary image to be evaluated in this study. TTS, CS, and BS were considered as characteristic imaging signs of DO in OLF. TTS was the most common signs among them. However, it might be misdiagnosed. In the study by Sun XZ et al[10], the diagnostic specificity of TTS was only 59%. Misdiagnosis was also pointed out by Sun J et al[2], but no plausible solution was proposed. In our preliminary screening study, we found that the TTS in diagnosis of DO should be more precisely called “tram track sign between ossified ligamentum flavum and dura mater”. To improve the accuracy of diagnosis, we defined and excluded four kinds of confusing signs (false TTS) (Fig.2): false TTS consisted of facet joint (Fig.2-A); false TTS consisted of ossified ligamentum flavum and superior articular process (Fig.2-B); false TTS between ossified ligamentum flavum and lamina (Fig.2-C) and false TTS between inner and outer bone cortex of superior articular process (Fig.2-D). Among them, the false TTS of ossified ligamentum flavum and superior articular process or lamina were easily misdiagnosed as DO[2]. For atypical signs, reference to adjacent imaging of the same segment sometimes could be helpful (Fig.2-E). After excluding these false TTS, the specificity of imaging diagnosis was 94.21% (179/190) and the sensitivity remained high at 94.23% (49/52).

However, there were still 11 segments without DO, while having false positives of TTS. It led that the positive predictive value of imaging diagnosis was relatively low (81.67%, 49/60). We further analyzed these misdiagnosed segments and found that five of them were adjacent to the segments with DO. This phenomenon was
previously reported in literature[12]. False positive TTS of another 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior and dural side of ligamentum flavum) (Fig.5). This was uncommon but hard to distinguish from TTS of ossified ligamentum flavum and dura mater. The remaining 3 segments were misdiagnosed for irregular signal. All the segments with BS or CS had DO.

The exact pathogenesis of OLF is still unknown. Both intrinsic [15-21] and extrinsic[22-24] factors were reported to be associated with the ossification of spinal ligament. Currently, mechanical stress as an extrinsic factor is thought to be important in the process of OLF. When the spinal ligament is under tension stress, some fibroblastic cells can transform into chondrocytes and expression of BMP-2, TGFβ and SOX9 will increase[23 24]. Yayama et al postulated that ossification of dura mater is probably due to dilution of the above cytokines related to osteogenesis from ossified ligamentum flavum[23]. Based on literature, a potential mechanism of DO was proposed before[14]. The relative movement between OLF and compressed dura mater, due to the flexion and extension of spine, will cause local inflammation, leading to dural adhesion[14]. Then, the adhesion tissue can act as a tunnel to transport osteogenic cytokines mentioned above from OLF to compressed dura mater, which causes the dura mater directly adhered to OLF firstly ossifies [14]. According to this, DO may start at the portion that is directly in contact with the ossified ligamentum flavum. Since there is no gap between ossified dura mater and ligamentum flavum, no special imaging signs will appear. This could explain why some segments with DO did not have any of the aforementioned special imaging signs in previous studies[9 10] and ours. Only when the ossification extended to the surrounding dura mater that was not in contact with ossified ligamentum flavum, these special imaging findings would appear. In the same segment CT scan of some patients, the most serious compression level did not have these special imaging findings, while adjacent levels under less compression did (Fig.6). This phenomenon was a supporting evidence of our hypothesis.

This study made a comprehensive analysis of DO. Radiological characteristics of
DO were described and analyzed in detail. Limitations still exist in the present study. The study population was OLF patients who need surgical treatment. So the incidence and distribution of DO reported in the present study was restricted to this population. The mechanism and progression of DO need further investigate in the future. Large sample multi-center prospective studies are still needed to further assess the accuracy of imaging diagnosis.

Conclusions

DO was relatively common in thoracic OLF. T9-T12 were the most frequently involved segments. TTS might be misdiagnosed. After excluding four kinds of false TTS, the accuracy of imaging diagnosis was relatively high.

Contributors Study design (Yu Zhao, MD, Bo Li, MD, Guixing Qiu, MD, Shigong Guo, MRCS); Data acquisition (Yu Zhao, MD, Bo Li, MD, Wenjing Li, MD, Ye Li, MD, Huiming Peng, MD, Chu Wang, MD); Analysis and interpretation of data (Yu Zhao, MD, Bo Li, MD, Shigong Guo, MRCS, Wenjing Li, MD, Ye Li, MD)

Funding This work was supported by grant from the National Natural Science Foundation of China (NO.81572093) and Beijing Natural Science Foundation (7162153).

Competing interests None declared.

Ethics approval The Institutional Review Board (IRB) of Peking Union Medical College Hospital (PUMCH).

Data sharing statement No additional data are available.
References


Figure legends

Figure 1.

Figs.1 (A-F) special imaging findings of DO.

Figs.1-A/D Tram track sign (A: bilateral, D: unilateral): a hyperdense bony excrescence, with a hypodense center. TTS consisted of three parts: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). Figs.1-B/E Comma sign: ossification of one-half of the dura mater. Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura mater. Figs.1-C/F Bridge sign: a hyperdense bony connection of bilateral OLF. Dorsal ossified dura mater presented as a bridge between bilateral ossified ligamentum flavum.

Figure 2.

Figs.2 (A-E) four kinds of confusing signs (false TTS) and analysis of adjacent levels: Fig.2-A false TTS of facet joint; Fig.2-B false TTS of ossified ligamentum flavum and superior articular process; Fig.2-C false TTS between ossified ligamentum flavum and lamina; Fig.2-D false TTS between inner and outer bone cortex of superior articular process. Fig.2-E imaging E2 was adjacent level of the same segment with E1. Adjacent imaging (E2) could help to identify the imaging findings in E1 was false TTS of ossified ligamentum flavum and superior articular process.

Figure 3.

Fig.3 Distribution of OLF and DO: OLF was more common in lower thoracic spine. More than half (53.8%) of the DO located in T9-T12.

Figure 4.
Fig. 4 Number of involved segments in patients with DO: The majority (87.0%) of DO patients had only 1-3 segments involving DO.

Figure 5.

Figs. 5 (A-C) False positive TTS of 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior side and dural side).

Figure 6.

Figs. 6 (A-C) CT scan of the same segment: the most serious compression level (A) had no TTS, while adjacent levels (B, C) under less compression did.
Figs. 1 (A-F) special imaging findings of DO. Figs. 1-A/D Tram track sign (A: bilateral, D: unilateral): a hyperdense bony excrescence, with a hypodense center. TTS consisted of three parts: ossified dura mater (hyperdense), ossified ligamentum flavum (hyperdense), and the space between them (hypodense). Figs. 1-B/E Comma sign: ossification of one-half of the dura mater. Ossified dura mater and ligamentum flavum fused to be the head of the “comma”. The tail of the “comma” indicated that ossification extended to lateral or ventral dura. Figs. 1-C/F Bridge sign: a hyperdense bony connection of bilateral OLF. Dorsal ossified dura presented as a bridge between bilateral ossified ligamentum flavum.

140x115mm (300 x 300 DPI)
Figure 2. Figs. 2 (A-E) four kinds of confusing signs (false TTS) and analysis of adjacent levels: Fig. 2-A false TTS of facet joint; Fig. 2-B false TTS of ossified ligamentum flavum and superior articular process; Fig. 2-C false TTS between ossified ligamentum flavum and lamina; Fig. 2-D false TTS between inner and outer bone cortex of superior articular process. Fig. 2-E imaging E2 was adjacent level of the same segment with E1. Adjacent imaging (E2) could help to identify the imaging findings in E1 was false TTS of ossified ligamentum flavum and superior articular process.

99x92mm (300 x 300 DPI)
Distribution of OLF and DO

Fig. 3 Distribution of OLF and DO: OLF was more common in lower thoracic spine. More than half (53.8%) of the DO located in T9-T12.

191x109mm (300 x 300 DPI)
Figure 4.
Fig.4 Number of involved segments in patients with DO: The majority (87.0%) of DO patients had only 1-3 segments involving DO.

158x91mm (300 x 300 DPI)
Figure 5.
Figs. 5 (A-C) False positive TTS of 3 segments were considered to be the imaging manifestation of incomplete ossification of ligamentum flavum (ossification of the posterior side and dural side).
Figure 6.

Figs.6 (A-C) CT scan of the same segment: the most serious compression level (A) had no TTS, while adjacent levels (B, C) under less compression did.
STROBE Statement—checklist of items that should be included in reports of observational studies

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<th>Title and abstract</th>
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<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract [1-2]</td>
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<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found [1-2]</td>
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**Introduction**

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<td>Explain the scientific background and rationale for the investigation being reported [4]</td>
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**Objectives**

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<td>State specific objectives, including any prespecified hypotheses [4]</td>
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**Methods**

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<td>Present key elements of study design early in the paper [4]</td>
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<table>
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<tbody>
<tr>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [4-5]</td>
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**Participants**

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<td>(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up [N/A]</td>
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<td>Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls [4-5]</td>
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<tr>
<td></td>
<td>Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants [N/A]</td>
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<td>(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed [N/A]</td>
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<td>Case-control study—For matched studies, give matching criteria and the number of controls per case [N/A]</td>
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**Variables**

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<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable [5]</td>
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**Data sources/measurement**

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<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [5]</td>
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**Bias**

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<td>Describe any efforts to address potential sources of bias [5]</td>
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**Study size**

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<td>Explain how the study size was arrived at [6]</td>
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**Quantitative variables**

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<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [5-6]</td>
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**Statistical methods**

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<td>(a) Describe all statistical methods, including those used to control for confounding [5-6]</td>
</tr>
<tr>
<td></td>
<td>(b) Describe any methods used to examine subgroups and interactions [5]</td>
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<td></td>
<td>(c) Explain how missing data were addressed [N/A]</td>
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<td></td>
<td>(d) Cohort study—If applicable, explain how loss to follow-up was addressed [N/A]</td>
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<td>Case-control study—If applicable, explain how matching of cases and controls was addressed [6]</td>
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<td>Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy [N/A]</td>
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<td>(g) Describe any sensitivity analyses [5-6]</td>
</tr>
</tbody>
</table>

Continued on next page
### Results

**Participants** 13*

- (a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [6]
- (b) Give reasons for non-participation at each stage [5-6]
- (c) Consider use of a flow diagram [5-6]

**Descriptive data** 14*

- (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders [6-7]
- (b) Indicate number of participants with missing data for each variable of interest [6]
- (c) **Cohort study**—Summarise follow-up time (e.g., average and total amount) [N/A]

**Outcome data** 15*

- **Cohort study**—Report numbers of outcome events or summary measures over time [N/A]
- **Case-control study**—Report numbers in each exposure category, or summary measures of exposure [6]
- **Cross-sectional study**—Report numbers of outcome events or summary measures [N/A]

**Main results** 16

- (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included [6-7]
- (b) Report category boundaries when continuous variables were categorized [N/A]
- (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period [N/A]

**Other analyses** 17

- Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses [7]

### Discussion

**Key results** 18

- Summarise key results with reference to study objectives [7-8]

**Limitations** 19

- Discuss limitations of the study, taking into account sources of potential bias or imprecision.
- Discuss both direction and magnitude of any potential bias [9-10]

**Interpretation** 20

- Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [7-9]

**Generalisability** 21

- Discuss the generalisability (external validity) of the study results [7-10]

### Other information

**Funding** 22

- Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [10]

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
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Bo Li, Guixing Qiu, Shigong Guo, Wenjing Li, Ye Li, Huiming Peng, Chu Wang and Yu Zhao

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