

UC Davis

UC Davis Previously Published Works

Title

Degenerative Thoracic Myelopathy: A Scoping Review of Epidemiology, Genetics, and Pathogenesis.

Permalink

<https://escholarship.org/uc/item/50r9n97p>

Journal

Global Spine Journal, 14(5)

ISSN

2192-5682

Authors

Rujeedawa, Tanzil
Mowforth, Oliver
Davies, Benjamin
[et al.](#)

Publication Date

2024-06-01

DOI

10.1177/21925682231224768

Peer reviewed

Degenerative Thoracic Myelopathy: A Scoping Review of Epidemiology, Genetics, and Pathogenesis

Global Spine Journal
2024, Vol. 14(5) 1664–1677
© The Author(s) 2023
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/21925682231224768
journals.sagepub.com/home/gsj


Tanzil Rujedawa, BA¹ , Oliver D. Mowforth, MA, MB BChir MSt, MRCS¹ , Benjamin M. Davies, BSc, MPhil MRCS¹ , Cylene Yang, BSc, MBBS¹, Aria Nouri, MD, MSc^{1,2} , Jibin J. Francis, MBBCh, FCNeurosur, FRCS¹, Bizhan Aarabi, MD³, Brian K. Kwon, MD, PhD, FRCSC⁴, James Harrop, MD⁵, Jefferson R. Wilson, MD, PhD⁶ , Allan R. Martin, MD, PhD⁷, Vafa Rahimi-Movaghar, MD⁸, James D. Guest, MD, PhD⁹, Michael G. Fehlings, MD, PhD, FRCSC¹⁰ , and Mark R. Kotter, MD, MPhil, PhD¹

Abstract

Study Design: Literature Review.

Objective: Myelopathy affecting the thoracic spinal cord can arise secondary to several aetiologies which have similar presentation and management. Consequently, there are many uncertainties in this area, including optimal terminology and definitions. Recent collaborative cervical spinal research has led to the proposal and subsequent community adoption of the name *degenerative cervical myelopathy* (DCM), which has facilitated the establishment of internationally-agreed research priorities for DCM. We put forward the case for the introduction of the term *degenerative thoracic myelopathy* (DTM) and *degenerative spinal myelopathy* (DSM) as an umbrella term for both DCM and DTM.

Methods: Following PRISMA guidelines, a systematic literature search was performed to identify degenerative thoracic myelopathy literature in Embase and MEDLINE.

Results: Conditions encompassed within DTM include thoracic spondylotic myelopathy, ossification of the posterior longitudinal ligament, ossification of the ligamentum flavum, calcification of ligaments, hypertrophy of ligaments, degenerative disc disease, thoracic osteoarthritis, intervertebral disc herniation, and posterior osteophytosis. The classic presentation includes girdle pain, gait disturbance, leg weakness, sensory disturbance, and bladder or bowel dysfunction, often with associated back

¹ Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK

² Department of Clinical Neurosciences, Geneva University Hospitals, Geneva, Switzerland

³ University of Maryland, Baltimore, MD, USA

⁴ Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada

⁵ Thomas Jefferson University Hospital, Philadelphia, PA, USA

⁶ University of Toronto, Toronto, ON, Canada

⁷ Department of Neurosurgery, University of California Davis, Sacramento, CA, USA

⁸ Department of Neurosurgery, Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences, Tehran, Iran

⁹ Department of Neurosurgery and The Miami Project to Cure Paralysis, The Miller School of Medicine, University of Miami, Miami, FL, USA

¹⁰ Toronto Western Hospital, University Health Network, University of Toronto, Toronto, ON, Canada

Corresponding Author:

Oliver D. Mowforth, MA, MB BChir MSt, MRCS, Division of Academic Neurosurgery, Department of Clinical Neurosciences, Addenbrooke's Hospital, University of Cambridge, The Old Schools, Trinity Ln, Cambridge CB2 1TN, UK.

Email: om283@cam.ac.uk



Creative Commons Non Commercial No Derivs CC BY-NC-ND: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>) which permits non-commercial use, reproduction and distribution of the work as published without adaptation or alteration, without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

pain. Surgical management is typically favoured with post-surgical outcomes dependent on many factors, including the causative pathology, and presence of additional stenosis.

Conclusion: The clinical entities encompassed by the term DTM are interrelated, can manifest concurrently, and present similarly. Building on the consensus adoption of DCM in the cervical spine and the recent proposal of *degenerative cervical radiculopathy* (DCR), extending this common nomenclature framework to the terms *degenerative spinal myelopathy* and *degenerative thoracic myelopathy* will help improve recognition and communication.

Keywords

thoracic, myelopathy, ossification of the posterior longitudinal ligament, spondylosis, disc herniation, stenosis

Introduction

Myelopathy refers to a symptomatic spinal cord injury resulting from multiple causes, including degeneration, tumours, inflammation, infection, and vascular anomalies. It may occur at any spinal cord level, albeit most commonly at the cervical level. Myelopathies arise secondary to a range of aetiologies, however those resulting from degenerative spinal conditions are the most common. This review focuses on thoracic myelopathy and, in particular, myelopathy caused by degenerative conditions of the spine, which precipitate mechanical stress on the spinal cord.

The thoracic spine consists of 12 vertebrae from T1 to T12. Important distinguishing factors of the thoracic vertebrae include a body size that is larger than the cervical vertebrae but smaller than the lumbar vertebrae, pointed and downward-angled spinous processes, and articulation with the ribs. The latter is responsible for the reduced mobility of the thoracic spine compared to the cervical spine, which is thought to contribute to the lower prevalence of degenerative spinal myelopathy at the thoracic compared to the cervical level.^{1,2}

Myelopathy from thoracic spondylotic myelopathy, and other forms of thoracic spine degeneration, including ossification of the posterior longitudinal ligament (OPLL),³ ossification of the ligamentum flavum (OLF),⁴⁻⁶ calcification of ligaments,^{5,7} hypertrophy of ligaments,⁵ degenerative disc disease (DDD), thoracic osteoarthritis, intervertebral disc herniation (with the exception of acute herniation)^{8,9} and posterior osteophytes^{10,11} (Figure 1) share similarities in presentation and management. They trigger an uncommon, but disabling form of ‘slow motion’ spinal cord injury.

Many uncertainties challenge clinical care and research in this area, including significant heterogeneity in the use of terminology and definitions. Recent work in the cervical spine has resolved classification uncertainties with the proposal and subsequent community adoption of the term *degenerative cervical myelopathy* (DCM). DCM recognises that multiple degenerative spine pathologies converge on a common neurological phenotype, which is diagnosed and managed with similar approaches. This improvement in classification has also facilitated the establishment of common data elements and the definition of National Institute for Health Research (NIHR) James Lind Alliance (JLA) research priorities.^{12,13}

In this review we put forward the case for the introduction of the term *degenerative thoracic myelopathy* (DTM) to depict degenerative spinal pathologies affecting the thoracic spinal cord. A list of conditions that can be considered as constituents of DTM is provided in Table 1. We draw upon a structured search of the evidence and expert opinion to consolidate current knowledge and propose critical knowledge gaps. The choice of DTM is based on the framework used in the cervical spine (DCM and *degenerative cervical radiculopathy* (DCR)). We also propose a broader nomenclature of *degenerative spinal myelopathy* to capture all degenerative conditions of the spine associated with myelopathy, including DCM and DTM. Adopting this standardized terminology throughout the spine will help augment understanding, raise awareness and promote research efficiency.

Methods

A systematic literature search was performed in Embase and MEDLINE using the Ovid platform (Ovid Technologies, New York, USA), using an adapted version of a published search strategy for degenerative cervical myelopathy^{14,15} and following PRISMA guidelines¹⁶ from inception to 27th July 2022. Tables 2 and 3 outline the search strategy. The results of this search underwent title and abstract screening. Exclusion criteria included letters, editorials, opinion articles, corrections, and papers not relevant to DTM or the scope of the review. Neither informed consent nor institutional review board approval were required due to the nature of the study.

The majority of the screened papers had information irrelevant to DTM with a focus on topics such as cervical myelopathy, non-degenerative causes of myelopathy, and other spinal pathologies, such as osteomyelitis. Additionally, many papers focused on specific surgical procedures, which was outside the scope of this review. Papers meeting the inclusion criteria of a focus on degenerative pathology of the thoracic spinal column published in the English language were sought for retrieval. Retrieved papers were assessed for eligibility using a full-text review, and those that contained relevant information were included. The reference lists of included papers were also hand-searched to identify additional relevant studies. The search methodology is summarised in Figure 2. MEDLINE was searched first, with duplicate results

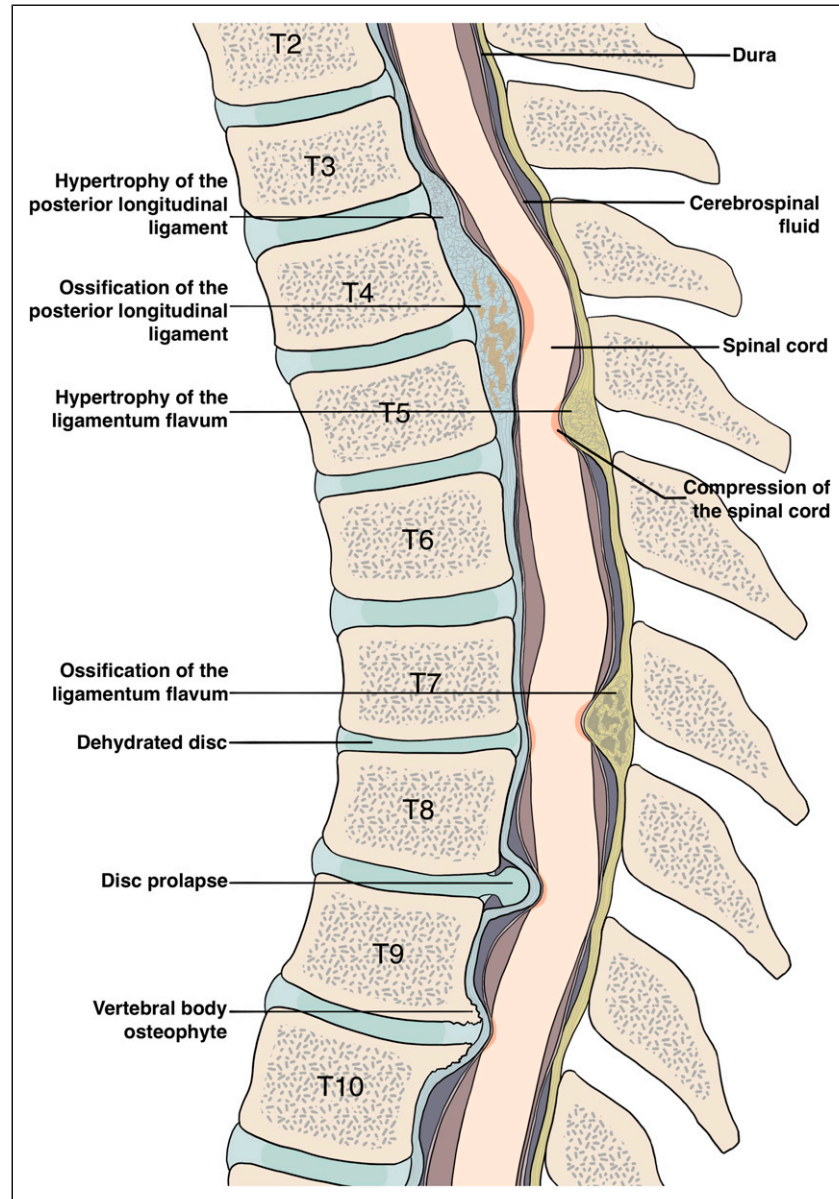


Figure 1. A sagittal view of the thoracic spine demonstrates several pathologies that can cause DTM, including spondylosis, degenerative disc disease, and ossification of the posterior longitudinal ligament.

from Embase automatically excluded from the search results. Included papers are listed in [Supplementary Table 1](#). Most papers were published after 2010; 11 papers were published in 2021 and 8 in the first 6 months of 2022. A narrative synthesis of the identified literature is presented; no statistical analysis was performed.

Discussion

Aetiology of DTM

Degenerative pathology in the thoracic spine that causes DTM can be divided into spondylotic (or osteoarthritic) and

non-osteoarthritic ([Figure 3](#)). Both subcategories can compromise the spinal cord via exerting mechanical stress. In addition, certain congenital disorders can predispose to DTM. For example, Ehler-Danlos syndrome predisposes to thoracic instability and subsequent myelopathy¹⁷; Scheuermann's disease is associated with thoracic disc herniation and OLF and is thus associated with an increased risk of DTM in affected individuals.^{18,19} Additionally, there may be a link between DTM and scoliosis, with a reported case of a patient with Klippel-Trenaunay-Weber syndrome having spinal stenosis and suffering from myelopathy.²⁰ However, due in part to the low incidence of thoracic myelopathy, research on predisposing factors is sparse.

Table 1. List of conditions From the International Classification of Diseases 11th Revision (ICD-11) That may be Considered Under the Umbrella Term DTM.

Classification Group	Specific Category
8B42 myelopathy	
FA37 certain joint disorders, not elsewhere classified	FA37.0 osteophyte FA37.Y other specified certain joint disorders, not elsewhere classified
FA80 intervertebral disc degeneration	FA80.4 intervertebral disc degeneration of thoracic spine without prolapsed disc FA80.5 intervertebral disc degeneration of thoracic spine with prolapsed disc FA80.6 intervertebral disc degeneration of thoracic spine with bony spur at the vertebra FA80.7 intervertebral disc degeneration of thoracic spine with nervous system involvement FA80.Y other specified intervertebral disc degeneration FA80.Z intervertebral disc degeneration, unspecified
FA81 Spondylolysis	FA81.0 Spondylolysis with slippage FA81.1 Spondylolysis without slippage FA81.Z Spondylolysis, unspecified
FA82 spinal stenosis	
FA83 ossification of spinal ligaments	
FA84 spondylolisthesis	FA84.0 spondylolisthesis with pars defect FA84.1 spondylolisthesis without pars defect FA84.Z spondylolisthesis, unspecified
FA8Y other specified degenerative condition of spine	
FA8Z degenerative condition of spine, unspecified	
FBIY other specified conditions associated with the spine	
FBIZ conditions associated with the spine, unspecified	

Table 2. Search Strategy for MEDLINE.

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions	
# Searches	Number of Results
1 myelopath*.mp. or exp spinal cord diseases/or (spinal cord adj3 (diseas* or disorder*)).mp. or myeloradiculopath*.mp. or spondylomyelopath*.mp. or spondylomyeloradiculopath*.mp. or (spinal cord adj3 Compress*).mp. or exp spinal cord compression/or exp ossification of posterior longitudinal ligament/or exp ligamentum flavum/or (("Japanese Orthop?edic association" adj2 score*) or (joa adj2 score*)).mp.	160243
2 exp Thoracic Vertebrae/or exp Thoracic cord/or thoracic.tw.	273334
3 1 and 2	28558
4 exp Atlanto-Occipital Joint/or exp Arteriovenous Fistula/or exp Radiotherapy/or exp Vitamin B 12/or exp Radiation/or exp Radiation Injuries/or exp Re-Irradiation/or exp Craniospinal Irradiation/or exp Whole-body Irradiation/or exp motor Neuron disease/or exp Amyotrophic lateral Sclerosis/or exp neoplasm/or exp metastasis/or exp Nervous system Malformations/or exp "autoimmune diseases of the nervous system"/or exp "congenital, hereditary, and neonatal diseases and abnormalities"/or exp virus diseases/or exp tuberculosis/or exp cyst/or exp hematoma/or exp infection/or hemangioma.mp. or cancer.mp. or meningioma.mp. or tumor*.mp. or cyst.mp. or h*ematoma.mp. or exp trauma/or exp vascular diseases/or web.ti. or acute.ti. or exp Myelin Sheath/or plexus.ti. or tuberculosis.mp. or myelitis.mp. or exp dog/or exp cat/or glioma.mp. or deficiency.ti. or exp multiple sclerosis/	12067042
5 3 not 4	2641
6 Limit 5 to english language	2248

As recently outlined for DCM,²² the pathophysiology of degenerative spinal myelopathy can be considered a function of mechanical stress, vulnerability and time, wherein mechanical stress consists of multiple mechanisms

of loading, not just compression. Spinal cord vulnerability is influenced by cellular processes, and systemic factors, such as genetic and adaptive protective mechanisms, including autoregulation of spinal cord perfusion and

Table 3. Search Strategy for Embase.

Embase	
# Searches	Number of Results
1 Myelopath*.mp. or exp myelopathy/or exp spondylosis/or spondylotic thoracic myelopathy.mp. or exp *spinal cord disease/ or thoracic spinal cord injury.ti.ab. or exp *myelography/or exp *myeloradiculopathy/or myeloradiculopath*.ti.ab. or (spinal cord adj3 (diseas* or disorder*).ti.ab. or spondylomyelopath*.ti.ab. or (spinal cord adj3 Compress*).ti.ab. or exp *spinal cord compression/or exp *Japanese Orthopaedic association score/or Japanese Orthop?edic Association.mp. or (Japanese Orthop?edic association adj2 scor*).mp. or (joa adj2 scor*).mp. or exp ligamentum flavum/or ossification of posterior longitudinal ligament.ti.ab. or exp *ligament calcinosis/or (exp posterior longitudinal ligament/and (exp *ossification/or ossifi*.ti.ab.))	308383
2 exp *thoracic vertebra/or exp *thoracic spinal cord/or thoracic.tw. or exp *thoracic spine/	230149
3 1 and 2	16449
4 exp atlantooccipital joint/or exp arteriovenous fistula/or exp radiotherapy/or exp cyanocobalamin/or exp radiation injury repair/or exp radiation injury/or exp *radiation/or exp re-irradiation/or exp irradiation/or exp craniospinal irradiation/or exp whole body radiation/or exp *motor neuron disease/or exp *amyotrophic lateral sclerosis/or neoplasm metastasis.mp. or exp metastasis/or exp *neoplasm/or exp malignant neoplasm/or exp radiation induced neoplasm/or exp myeloproliferative neoplasm/or exp vertebra hemangioma/or exp hemangioma/or exp nervous system malformation/or autoimmune diseases of the nervous system.mp. or autoimmune nervous system.mp. or (congenital, hereditary, and neonatal diseases and abnormalities).mp. or congenital disorder.mp. or exp genetic disorder/or newborn disease.mp. or exp virus infection/or exp tuberculosis/or exp cyst/or exp hematoma/or exp infection/or hemangioma.mp. or cancer.mp. or meningioma.mp. or tumor*.mp. or cyst.mp. or h*ematoma.mp. or exp trauma/or exp vascular diseases/or web.ti. or acute.ti. or exp Myelin Sheath/or plexus.ti. or tuberculosis.mp. or myelitis.mp. or exp dog/or exp cat/or glioma.mp. or deficiency.ti. or exp multiple sclerosis/	15244318
5 3 not 4	1607
6 Limit 5 to medline	228
7 5 not 6	1379
8 Limit 7 to english language	1232

nutritional status.²² The association between obesity and smoking and both DCM and DTM, suggests similar pathogenesis may exist for both DCM and DTM.²³ Moreover, the co-existence of DCM and DTM, such as by cervical and thoracic OLF and/or OPLL occurring concurrently, reinforces this hypothesis.²⁴

The aetiology of the mechanical stress that triggers DSM, i.e., whether it is due to static or dynamic mechanisms, can be used to subcategorise DTM.²⁵ Static spinal cord compression or spinal canal stenosis is the result of degenerative changes indenting the spinal cord, including osteophyte formation and ligament hypertrophy, calcification, and ossification.²⁵ Dynamic compression refers to compression as a result of movement, whether physiological or pathological. Due to the relatively reduced mobility of the thoracic spine, dynamic mechanisms are likely to be less important than in the cervical spine. Nevertheless, dynamic mechanisms may explain the increased rate of DTM in individuals with increased mobility and laxity of the thoracic spine.¹⁷ Importantly, static and dynamic mechanisms of spinal cord stress may occur concomitantly.²² Since dynamic mechanisms likely play a smaller role in DTM, a greater degree of static compression may well be needed compared to DCM to precipitate myelopathy.^{22,26} However, comparative analysis of the

MRIs of patients with DCM and DTM and correlation with their presentations are needed to evaluate this hypothesis.

DTM Conditions

The most common aetiology of DTM is dependent on the population. In Japanese populations, in which most of the included studies were conducted, OLF and OPLL are the commonest causes, followed by disc herniation, with rare causes including calcification of the ligamentum flavum and degenerative spondylolisthesis.^{11,27-31} A recent systematic review found that in Japan, 45% of cases were OPLL, 36.4% OLF, 16.5% OPLL with OLF and 2.1% disc herniation,³¹ whilst in China, 75.8% of cases were OLF, 13.8% disc herniation, 6.6% OPLL and 3.8% OPLL with OLF.³¹ That same study found that in the US, disc herniation is the commonest aetiology with 95.7% of cases, with OLF making up 3.6% and OPLL .5%.³¹ Overall, 41.5% of cases were OLF, 18.7% OPLL, 7.4% OPLL with OLF and 32.4% disc herniation.³¹ Another systematic review of surgical procedures on thoracic myelopathy found that of 2183 patients, 69.8% had OLF, 20.0% OPLL and 9.3% disc herniation.³⁰ Table 4 provides a summary of the prevalence of the different causes of DTM. Equivalent conditions affect the cervical spine, with the prevalence of each being similarly population-dependent.²¹

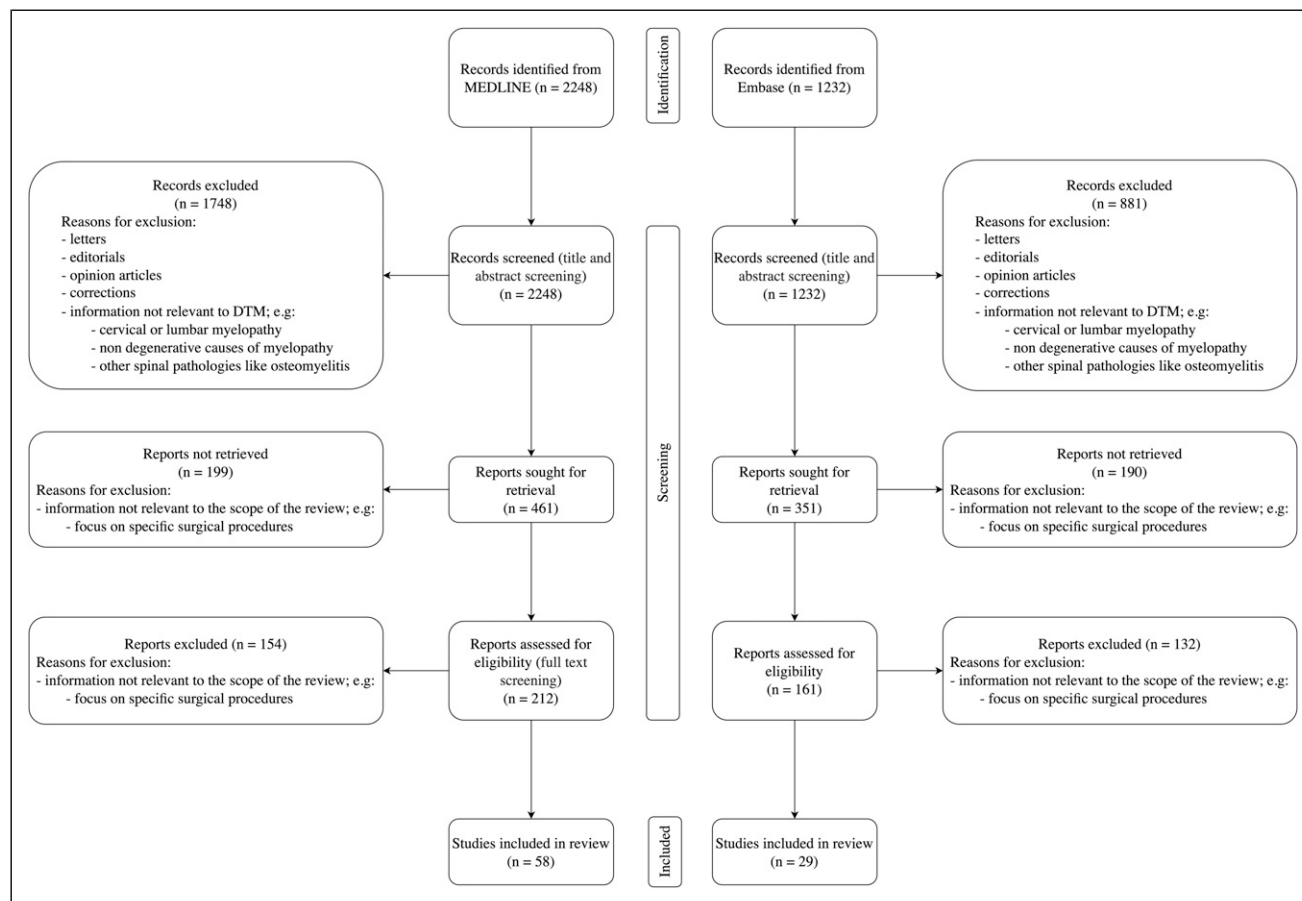


Figure 2. Search methodology flowchart based on PRISMA 2020 statement.¹⁶

Furthermore, multiple degenerative changes often occur simultaneously.³² For example, OLF and OPLL may present concomitantly,³¹ and coexistent OPLL, OLF, and thoracic disc herniation have also been reported.^{29,31}

Osteoarthritic Degenerative Conditions

Due to repetitive use, ageing, and environmental factors such as smoking, the proteoglycan composition of the nucleus pulposus changes, altering hydrostatic pressure, disc height, and subsequently force distribution.³³⁻³⁵ This can lead to a cascade of degenerative changes, which lead to osteophyte formation and intervertebral disc failure, such as disc bulging and herniation.^{25,36} Polymorphisms in several genes, such as those associated with cartilage and collagen formation like *AGC1* and *COL9A*, have been associated with this degenerative process,³⁷ indicating a possible genetic vulnerability.

Thoracic disc herniation is a cause of myelopathy with an estimated frequency between 1 per 1000 and 1 per million.³⁸⁻⁴⁰ It is less common than cervical disc herniation,⁴¹ which has an annual incidence of 18.6 per 100,000.⁴² In fact, thoracic disc herniation accounts for only .15-4% of all disc

operations.^{43,44} In approximately 40% of cases, the herniated disc is calcified. Typically, thoracic disc herniation occurs in middle-aged or older men and at levels below T8.^{9,41,45} The levels affected are classically at mechanical inflection points; increased mobility at these spinal levels is postulated to explain the increased prevalence of herniations.⁴¹

Spondylosis is another osteoarthritic degenerative condition that can cause myelopathy. Here, protruding osteophytes, formed by the degenerative processes outlined above, compress the spinal cord.⁴⁶ This condition is infrequent in the thoracic spine compared to the cervical and lumbar regions⁴⁶; the low prevalence is partly explained by the high rate of misdiagnosis due to its co-occurrence with cervical and lumbar spondylosis.⁴⁶

In addition, another cause of thoracic myelopathy secondary to osteoarthritic pathology is degenerative spondylolisthesis. In this condition, an increased pedicle-facet joint angle and facet joint disruption has been observed.⁴⁷ Whilst far more common in the cervical and lumbar regions,⁴⁸ it can also occur in the thoracic region, often secondary to intervertebral disc degeneration.⁴⁸ Thoracic degenerative spondylolisthesis tends to occur in combination with lumbar spondylosis, which can lead to misdiagnosis and subsequently

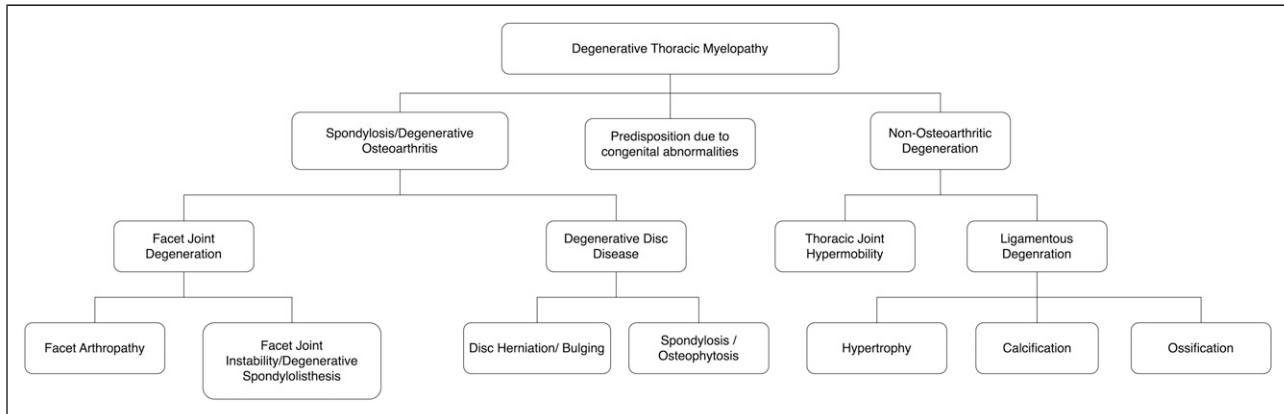


Figure 3. A conceptual differentiation of the constituents of degenerative thoracic myelopathy. DTM can be due to either osteoarthritic or non-osteoarthritic degeneration. In addition, certain congenital abnormalities can predispose individuals to DTM. Figure drawn with reference to Nouri et al 2015.²¹

Table 4. Comparison of Prevalence of Difference Causes of DTM

Study	Population	Size	OLF(%)	OPLL(%)	OPLL with OLF	Disc Herniation(%)
Shiqi et al 2020 ³⁰	All	2183	69.8	20.0	—	9.3
Chen et al 2020 ³¹	All	1935	41.5	18.7	7.4%	32.4
	Japan	662	36.4	45.0	16.5%	2.1
	China	625	75.8	6.6	3.8%	13.8
	USA	391	3.6	0.5	.2%	95.7

under-reporting.⁴⁸ Furthermore, it has also been associated with degenerative scoliosis.⁴⁹

Non-Osteoarthritic Degenerative Conditions

Changes in the spinal ligaments, notably the ligamentum flavum and the posterior longitudinal ligament, can lead to DTM. Although genetics may play a role in calcification, hypertrophy, and ossification of these ligaments, the fact that these phenomena usually manifest in older age implies a link with ageing and a likely degenerative aetiology.⁵⁰⁻⁵³

OLF is a condition whereby the ligamentum flavum undergoes progressive endochondral ossification.^{54,55} Ossification at multiple different spinal levels, i.e., tandem ossification, is a frequently recognised occurrence.^{3,25,31} OLF is more common in the thoracic spine compared to the cervical or lumbar spine, which may be due to the reduced mobility of this segment.⁵⁶⁻⁵⁸ The lower thoracic spine (T10-T12) is typically most affected.^{56,59-62} Thoracic OLF typically presents before 60 years of age⁵⁹ and is thought to be more prevalent in men,^{59-61,63,64} although this is inconsistent across studies.^{6,65,66} Genetic factors are believed to play a role in the development of OLF; an altered genome-wide DNA methylation profile has been reported in individuals with thoracic OLF.⁶⁷ Furthermore, overexpression of genes and transcription factors associated with the Notch and Wnt signaling

pathways such as *LGR5*, *ANGPT2*, *CX48*, *Runx2*, and *Osterix* have also been associated with OLF in overexpression and knockdown experiments.^{54,68-71} Polymorphisms in the *COL6A1* gene, which plays an important role in forming collagen, also appear to be associated with OLF.⁷² Nonetheless, environmental factors are likely to play a role; mechanical stress has been shown to promote OLF by inducing the Notch and Wnt pathways.⁷³ Diet appears to be another important factor,⁷⁴ and fluoride intake is associated with risk of OLF.⁷⁵ There is also an association with obesity.⁷⁶

OPLL is another non-osteoarthritic degenerative precipitant of DTM. This is a condition whereby the posterior longitudinal ligament undergoes progressive thickening and endochondral ossification.⁷⁷ Similar to OLF, tandem ossification is frequent.^{3,25,31} OPLL is more common in the cervical spine.⁷⁸ In the thoracic spine, the mid-levels are typically affected.^{29,31} Thoracic OPLL is less common than OLF and is most commonly seen in Asian populations,^{31,79,80} with most studies conducted in Japan.^{80,81} The prevalence is much lower in North America and Europe.⁸⁰ Moreover, thoracic OPLL seems to be more often reported in males,^{31,82} although reports are inconsistent.⁸³ Similar to OLF, both genetic and environmental factors play a role in the development of the condition. Increased expression of *IL17RC* and *COL6A1*, two osteogenic genes, have been associated with OPLL.⁸⁴⁻⁸⁷ IGF-1 has been associated with ligament ossification,⁸⁸ which may

explain the association between acromegaly and OPLL.⁸⁹ Hyperleptinemia and hyperinsulinemia are other factors involved in the development of OPLL,⁹⁰ as is obesity.^{78,90}

Prevalence

DTM is less common than DCM. This may be due to the reduced range of motion in the thoracic spinal segment.²⁷ Nonetheless, accurate estimation of DTM prevalence is currently a challenge due to the heterogeneity in the classification of DTM as separate clinical entities, the paucity of literature on the topic, and the fact that studies have been mainly performed in Asian populations. Underdiagnosis is another challenge.¹¹ The incidence of surgical interventions is an important estimate of the prevalence of thoracic myelopathy. However, this is likely to be a substantial underestimate. Surgical intervention for thoracic myelopathy has a reported prevalence of approximately .9 per 100,000 population, which is less 10% of that of cervical myelopathy, according to a retrospective study in Japan.⁹¹ These values were reported in studies of highly specific populations and are thus are not likely to be representative of the wider global epidemiology.

Presentation and Management

DTM may present with back or girdle pain, gait difficulty, leg weakness, sensory disturbance, and bladder or bowel dysfunction.^{27,92} Symptom burden usually increases over time. Initial symptoms typically include leg numbness, leg weakness, gait difficulty, and bladder or bowel disturbance.²⁷ Gait disturbance is particularly common in OPLL,^{27,93} and back pain at initial diagnosis is particularly associated with myelopathy at the upper or middle thoracic levels.²⁷ Neurological signs may include hyperreflexic patellar and ankle tendon reflexes, ankle clonus, and positive Babinski sign,

although with lower frequency if spinal cord compression is at lower levels of the thoracic spine.^{27,92} The severity of the disease can be scored using an adapted version of the modified Japanese Orthopedic Association (mJOA) score, assessing lower limb motor function, sensory dysfunction, and bladder and bowel issues.^{21,27,94} Table 5 provides a summary of the adapted mJOA score that can be used for DTM.

Furthermore, there are some rarer presentations of DTM. For example, high thoracic OLF may present with Horner's syndrome,⁹⁶ whilst foot drop can be a symptom of calcified thoracic disc herniation at T11–L1 level.⁹⁷

The symptoms described are also often present when cervical or lumbar spinal disorders compress neural elements, which can result in misdiagnosis and delayed treatment.^{27,98} False localising levels, whereby the symptoms appear to emanate from a different anatomical location than their true origin,^{99,100} are another challenge that complicates diagnosis. For instance, cervical cord compression may present with a thoracic sensory level, and thoracic cord compression may present with a lumbar sensory level.^{92,99} Furthermore, it is relatively common for other neurological problems, such as peripheral neuropathy or lumbar and cervical spine disease, to occur concurrently with thoracic myelopathy, adding further diagnostic challenge.^{92,101} Radiculopathy and myelopathy also often occur simultaneously.¹⁰² Finally, it is important always to consider the many non-degenerative conditions that can cause myelopathy, including autoimmune, inflammatory, and idiopathic causes.

Thoracic myelopathy tends to respond poorly to conservative management.^{103,104} Consequently, surgery is often required. Posterior decompressive laminectomy or laminoplasty and circumferential decompression via a posterior approach are the favoured approaches for posterior pathologies.³⁰ Posterior decompression is the most common operation for thoracic disc herniation, OLF, and OPLL,³⁰ whilst

Table 5. mJOA for DTM. Adapted From Hilton et al, 2019.⁹⁵

	Score	mJOA
Lower limb motor dysfunction	0	Complete loss of motor and sensory function
	1	Sensory preservation without ability to move legs
	2	Able to move legs but unable to walk
	3	Able to walk on flat floor with a walking aid
	4	Able to walk up and/or down stairs with a handrail
	5	Moderate to significant lack of stability but able to walk up and/or downstairs without handrail
	6	Mild lack of stability but walk unaided with smooth reciprocation
Sensory dysfunction	7	No dysfunction
	0	Complete loss of sensation
	1	Severe sensory loss or pain
	2	Mild sensory loss
Sphincter dysfunction	3	No sensory loss
	0	Inability to urinate voluntarily
	1	Marked difficulty with micturition
	2	Mild to moderate difficulty with micturition
	3	Normal micturition

Table 6. Summary of the Current Understanding of DTM and Uncertainties.

	Current Understanding	Uncertainty
Classification of DTM	Conditions causing DTM can be divided into spondylotic, non-spondylotic, and predisposition due to congenital conditions. Another classification is via pathophysiology whereby spinal cord stress can be due to static and dynamic mechanisms.	<ul style="list-style-type: none"> - Both classifications are based mainly on DCM research. Research is needed to assess the validity of the classifications for DTM. - Which congenital conditions predispose to DTM?
DTM conditions	The most common cause of DTM is OLF, followed by posterior osteophytosis, OPLL and disc herniation with rare causes being calcification of the ligamentum flavum and degenerative spondylolisthesis.	<ul style="list-style-type: none"> - The most is known about OLF and disc herniation. Research on the other conditions is lacking. - What are the genetic and environmental associations for each of the conditions?
Prevalence	Surgical intervention is the most accurate source of prevalence estimates. Approximately .9 per 100,000 population are affected by DTM.	<ul style="list-style-type: none"> - Studies investigating prevalence have been mainly carried out in specific Asian populations. Exploring prevalence in other populations is an important topic for future research.
Presentation	DTM may present with back or girdle pain, gait difficulty, leg weakness, sensory disturbance and bladder or bowel dysfunction. The burden of symptoms usually increases over time. Neurological signs may include hyperreflexic patellar and ankle tendon reflexes; ankle clonus and positive Babinski sign may also be present.	<ul style="list-style-type: none"> - The frequency, sensitivity, specificity and positive predictive value of the symptoms and signs are current uncertainties. - What are the differences in how each of the DTM pathologies present? - What is the best scoring system for grading the severity of DTM?
Management	Surgery is the first line of management and involves decompression of the spinal cord, with posterior decompression typically the favoured approach. Post-surgical outcome depends on many factors such as the specific causative pathology, symptom duration and presence of additional stenosis.	<ul style="list-style-type: none"> - How important is the timing of intervention for outcomes? - What is the role of novel therapies in DTM? - Which surgical technique works best for each pathology?

circumferential decompression is rarer and most commonly used in OPLL.³⁰ The preference for posterior decompression over circumferential decompression is related to factors such as reduced blood loss, lower complication rates, post-operation recovery rate, and less immediate neurologic deterioration.³⁰ Similar to the surgical approach for DCM,¹⁰⁵ there does not appear to be a clear difference between approaches with regard to long-term outcomes,³⁰ however conclusions are limited by a paucity of high quality comparative studies. Instrumented fusion may also be utilised alongside posterior decompression in OPLL, which has been associated with overall favourable outcomes.¹⁰⁶ Moreover, there appears to be a trend towards posterior instrumented fusion surgery for OLF, with 48.9% of cases in one prospective multicentre study being posterior decompression with instrumented fusion.¹⁰⁷

Anterior or lateral surgical approaches are performed less commonly but may be required for anterior compressive pathology; these come with the additional risks of damage to structures such as the aorta and oesophagus.¹⁰⁸ Nonetheless, anterior decompression for calcified discs may be associated with improved neurological outcomes.¹⁰⁹ Minimally invasive surgery has become increasingly common, particularly for disc herniations affecting a single thoracic level^{110,111}; however, data on minimally invasive surgery is sparse.

Post-surgical outcomes in DTM depend on many factors, such as the operative approach, causative pathology, symptom duration, and presence of additional stenosis.^{30,104} For OLF, statistically significant improvements of JOA scores are reported, although recovery is typically incomplete.^{57,59,112,113} Recovery is dependent on several factors, such as preoperative neurological status, duration of symptoms, imaging findings, age, sex, number of levels involved, and type of OLF.^{52,57,66,113,114} However, the preoperative severity of myelopathy appears to be the most important factor.^{57,66,113} Outcomes for surgical management of thoracic disc herniations are generally poorer than those for cervical disc herniation.¹¹⁵

Conclusion

Myelopathy of the thoracic spinal cord can be triggered by several interrelated, degenerative conditions that affect the thoracic spine, such as disc herniation, OLF, and OPLL. The paucity of published literature in this area is partly due to the relatively low prevalence of these conditions. The heterogeneity and inconsistency in the classification of DTM conditions as separate clinical entities further hinders synthesis of published data. Similar to the recent consensus process for DCM, we propose the introduction of the term *degenerative thoracic myelopathy* as an umbrella term for thoracic

myelopathies triggered by degenerative conditions of the thoracic spine. Whilst there may be early hurdles in adoption, this terminology will improve recognition and communication as well as promote research efficiency and accelerate understanding of DTM. The present proposal represents current evidence-based expert consensus; future wider consultation may be necessary to refine it further.

To further standardise the classification of myelopathies triggered by spinal degenerative pathologies, we propose the term *degenerative spinal myelopathy* (DSM) as overarching nomenclature for all degenerative spinal pathology triggering myelopathy. DSM as the umbrella term for DCM and DTM, will further aid communication and enable synergies, such as for studies investigating molecular and cellular changes underpinning myelopathies triggered by spine conditions, as well as their risk factors. Nevertheless, further research is needed both on DTM itself and on better defining how it compares to DCM. Table 6 provides a summary of the current understanding of DTM and current uncertainties.

Author Contributions

TR – conceptualization, manuscript drafting, and preparation, ODM – conceptualization, manuscript drafting, and preparation, BMD – conceptualization and manuscript review, CY – illustration and manuscript review, JF, BA, BKK, JH, MGF, JRW, ARM, VRM, JDG – manuscript review, MRK – conceptualization and manuscript preparation and review

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

Research in the MRK's laboratory is supported by a core support grant from the Wellcome Trust and MRC to the Wellcome Trust-Medical Research Council Cambridge Stem Cell Institute. MRNK is supported by a NIHR Clinician Scientist Award, CS-2015-15-023. BMD is supported by an NIHR Clinical Doctoral Fellowship. ODM is supported by an Academic Clinical Fellowship at the University of Cambridge.

Disclaimer

The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health.

ORCID iDs

Tanzil Rujeedawa  <https://orcid.org/0000-0002-7089-1684>
 Oliver D. Mowforth  <https://orcid.org/0000-0001-6788-745X>
 Benjamin M. Davies  <https://orcid.org/0000-0003-0591-5069>
 Aria Nouri  <https://orcid.org/0000-0002-4965-3059>
 Jefferson R. Wilson  <https://orcid.org/0000-0001-5965-0305>
 Michael G. Fehlings  <https://orcid.org/0000-0002-5722-6364>

Supplemental Material

Supplemental material for this article is available online.

References

1. El-Khoury GY, Whitten CG. Trauma to the upper thoracic spine: Anatomy, biomechanics, and unique imaging features. *Am J Roentgenol.* 1993;160(1):95-102. doi:10.2214/ajr.160.1.8416656.
2. Andriacchi T, Schultz A, Belytschko T, Galante J. A model for studies of mechanical interactions between the human spine and rib cage. *J Biomech.* 1974;7(6):497-507. doi:10.1016/0021-9290(74)90084-0.
3. Yamazaki M, Mochizuki M, Ikeda Y, et al. Clinical results of surgery for thoracic myelopathy caused by ossification of the posterior longitudinal ligament: Operative indication of posterior decompression with instrumented fusion. *Spine.* 2006;31(13):1452-1460. doi:10.1097/01.brs.0000220834.22131.fb
4. Akhaddar A, Mansouri A, Zrara I, et al. Thoracic spinal cord compression by ligamentum flavum ossifications. *Jt Bone Spine.* 2002;69(3):319-323. doi:10.1016/S1297-319X(02)00400-1.
5. Barnett GH, Hardy RW, Little J, Bay J. Thoracic spinal canal stenosis. *J Neurosurg.* 1988;68(1):160-161. doi:10.3171/jns.1988.68.1.0160.
6. Mo L, Wang Z, Du J. Thoracic myelopathy caused by ossification of the ligamentum flavum. *J Korean Neurosurg Soc.* 2013;46(3):189-194. doi:10.3340/jkns.2009.46.3.189.
7. Shiguematsu FY, de Souza ECC, Zimmermann AF, Castro GRW, Pereira IA, Neves FS. Thoracic myelopathy due to calcification of the ligamentum flavum with hyperproteinorachia and responsive to steroid therapy: Case report. *Rev Bras Reumatol.* 2012;52(3):438-446.
8. Teufack S, Campbell P, Sharma P, et al. Thoracic myelopathy due to an intramedullary herniated nucleus pulposus: First case report and review of the literature. *Neurosurgery.* 2012;71(1):199-202. doi:10.1227/NEU.0b013e3182582cfl.
9. Cornips EMJ, Janssen MLF, Beuls EAM. Thoracic disc herniation and acute myelopathy: Clinical presentation, neuroimaging findings, surgical considerations, and outcome: Clinical article. *J Neurosurg Spine.* 2011;14(4):520-528. doi:10.3171/2010.12.SPINE10273.
10. Seidenwurm DJ, Wippold FJ, Cornelius RS, et al. ACR appropriateness criteria® myelopathy. *J Am Coll Radiol.* 2012;9(5):315-324. doi:10.1016/j.jacr.2012.01.010.
11. Girardi FP, Sax OC, Salzmann S, Shue J. JSM neurosurgery and spine literature review of thoracic myelopathy: Causes of acute worsening. *JSM Neurosurg Spine.* 2016;4(4):4-7.
12. Davies B, Mowforth O, Sadler I, et al. Recovery priorities in degenerative cervical myelopathy: A cross-sectional survey of an international, online community of patients. *BMJ Open.* 2019;9(10):e031486. doi:10.1136/bmjopen-2019-031486.
13. Davies BM, Khan DZ, Mowforth OD, et al. RE-CODE DCM (REsearch objectives and Common data elements for degenerative Cervical myelopathy): A Consensus process to improve

- research efficiency in DCM, through establishment of a standardized dataset for Clinical research and the definition of the Re. *Glob spine J*. 2019;9(1 Suppl):65S-76S. doi:10.1177/2192568219832855.
14. Khan MA, Mowforth OM, Kuhn I, Kotter MRN, Davies BM. Development of a validated search filter for Ovid Embase for degenerative cervical myelopathy. *Health Info Libr J*. 2021;1:1-9. doi:10.1111/hir.12373
 15. Davies BM, Goh S, Yi K, Kuhn I, Kotter MRN. Development and validation of a MEDLINE search filter/hedge for degenerative cervical myelopathy. *BMC Med Res Methodol*. 2018;18(1):1-8. doi:10.1186/s12874-018-0529-3.
 16. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*. 2021;372. doi:10.1136/bmj.n71.
 17. Henderson FC, Austin C, Benzel E, et al. Neurological and spinal manifestations of the Ehlers–Danlos syndromes. *Am J Med Genet Part C Semin Med Genet*. 2017;175(1):195-211. doi:10.1002/ajmg.c.31549.
 18. Ding Y, Lv S, Dong S, Cui J, Cao Z, Chen Y. Relationship between scheuermann disease and symptomatic thoracic spinal stenosis: A retrospective study. *Acta Orthop Traumatol Turc*. 2021;55(3):253-257. doi:10.5152/j.aott.2021.20022.
 19. Kapetanios GA, Hantziadis PT, Anagnostidis KS, Kirkos JM. Thoracic cord compression caused by disk herniation in Scheuermann's disease: A case report and review of the literature. *Eur Spine J*. 2006;15(SUPPL. 5):553-558. doi:10.1007/s00586-005-0053-0.
 20. Arai Y, Takagi T, Matsuda T, Kurosawa H. Myelopathy due to scoliosis with vertebral hypertrophy in Klippel-Trenaunay-Weber syndrome. *Arch Orthop Trauma Surg*. 2002;122(2):120-122. doi:10.1007/s004020100334.
 21. Nouri A, Tetreault L, Singh A, Karadimas SK, Fehlings MG. Degenerative cervical myelopathy: Epidemiology, genetics, and pathogenesis. *Spine*. 2015;40(12):E675-E693. doi:10.1097/BRS.0000000000000913
 22. Davies BM, Mowforth O, Gharooni AA, et al. A new Framework for investigating the biological basis of degenerative Cervical myelopathy [AO spine RECODE-DCM research priority number 5]: mechanical stress, vulnerability and time. *Glob Spine J*. 2022;12(1_suppl):78S-96S. doi:10.1177/219256822111057546.
 23. Rujeedawa T, Mowforth OD, Brannigan J, et al. A single centre service evaluation of degenerative cervical and thoracic myelopathy. *J Clin Neurosci*. 2023;117(August):168-172. doi:10.1016/j.jocn.2023.10.002.
 24. Park JY, Chin DK, Kim KS, Cho YE. Thoracic ligament ossification in patients with cervical ossification of the posterior longitudinal ligaments: tandem ossification in the cervical and thoracic spine. *Spine*. 2008;33(13):E407-E410. doi:10.1097/BRS.0b013e318175c276
 25. Badhiwala JH, Ahuja CS, Akbar MA, et al. Degenerative cervical myelopathy — update and future directions. *Nat Rev Neurol*. 2020;16(2):108-124. doi:10.1038/s41582-019-0303-0.
 26. Davies BM, Mowforth OD, Smith EK, Kotter MRN. Degenerative cervical myelopathy. *BMJ*. 2018;360(February):8-11. doi:10.1136/bmj.k186.
 27. Ando K, Imagama S, Kobayashi K, et al. Clinical Features of thoracic myelopathy: A single-Center study. *JAAOS Glob Res Rev*. 2019;3(11):e18. doi:10.5435/jaaosglobal-d-18-00090.
 28. Sato T, Kokubun S, Tanaka Y, Ishii Y. Thoracic myelopathy in the Japanese: Epidemiological and clinical observations on the cases in Miyagi Prefecture. *Published online*. 1998;184(1):1-11.
 29. Hou X, Sun C, Liu X, et al. Clinical features of thoracic spinal stenosis-associated myelopathy. *J Spinal Disord Tech*. 2016;29(2):86-89. doi:10.1097/BSD.0000000000000081.
 30. Zhu S, Wang Y, Yin P, Su Q. A systematic review of surgical procedures on thoracic myelopathy. *J Orthop Surg Res*. 2020;15(1):1-10. doi:10.1186/s13018-020-02081-y.
 31. Chen G, Fan T, Yang X, Sun C, Fan D, Chen Z. The prevalence and clinical characteristics of thoracic spinal stenosis: A systematic review. *Eur Spine J*. 2020;29(9):2164-2172. doi:10.1007/s00586-020-06520-6.
 32. Yan C, Tan HY, Ji CL, et al. The clinical value of three-dimensional measurement in the diagnosis of thoracic myelopathy caused by ossification of the ligamentum flavum. *Quant Imaging Med Surg*. 2021;11(5):2040-2051. doi:10.21037/qims-20-713.
 33. Nixon J. Intervertebral disc mechanics: A review. *JR Soc Med*. 1986;79(2):100-104. doi:10.1177/014107688607900211.
 34. Ferguson SJ, Steffen T. Biomechanics of the aging spine. *Eur Spine J*. 2003;12(SUPPL. 2):97-103. doi:10.1007/s00586-003-0621-0.
 35. Palepu V, Kodigudla M, Goel VK. Biomechanics of disc degeneration. *Adv Orthop*. 2012;2012:1-17. doi:10.1155/2012/726210.
 36. Galbusera F, Van Rijsbergen M, Ito K, Huyghe JM, Brayda-Bruno M, Wilke HJ. Ageing and degenerative changes of the intervertebral disc and their impact on spinal flexibility. *Eur Spine J*. 2014;23(SUPPL. 3):31. doi:10.1007/s00586-014-3203-4.
 37. Chan D, Song Y, Sham P, Cheung KMC. Genetics of disc degeneration. *Eur Spine J*. 2006;15(SUPPL. 3):317-325. doi:10.1007/s00586-006-0171-3.
 38. Yoshihara H. Surgical treatment for thoracic disc herniation: An update. *Spine*. 2014;39(6):315. doi:10.1097/BRS.000000000000171.
 39. Court C, Mansour E, Bouthors C. Thoracic disc herniation: Surgical treatment. *Orthop Traumatol Surg Res*. 2018;104(1):S31-S40. doi:10.1016/j.otsr.2017.04.022.
 40. Quint U, Bordon G, Preissl I, Sanner C, Rosenthal D. Thoracoscopic treatment for single level symptomatic thoracic disc herniation: a prospective followed cohort study in a group of 167 consecutive cases. *Eur Spine J*. 2012;21(4):637-645. doi:10.1007/s00586-011-2103-0.
 41. Stino AM, Lorusso SJ. Myelopathies due to structural Cervical and thoracic disease. *Contin Lifelong Learn Neurol*. 2018;

- 24(2):567-583. doi:10.1212/CON.0000000000000594. Spinal Cord Disorders).
42. Radhakrishnan K, Litchy WJ, O'Fallon WM, Kurland LT. Epidemiology of cervical radiculopathy: a population-based study from Rochester, Minnesota, 1976 through 1990. *Brain*. 1994;117(2):325-335. doi:10.1093/brain/117.2.325.
 43. Schimel S, Deeb ZL. Herniated thoracic intervertebral disks. *J Comput Tomogr*. 1985;9(2):141-143. doi:10.1016/0149-936X(85)90009-8.
 44. Hott JS, Feiz-Erfan I, Kenny K, Dickman CA. Surgical management of giant herniated thoracic discs: analysis of 20 cases. *J Neurosurg Spine*. 2005;3(3):191-197. doi:10.3171/spi.2005.3.3.0191.
 45. Gay CW, Bishop MD, Beres JL. Clinical presentation of a patient with thoracic myelopathy at a chiropractic clinic. *J Chiropr Med*. 2012;11(2):115-120. doi:10.1016/j.jcm.2011.10.007.
 46. Marzluff JM, Hungerford GD, Kempe LG, Rawe SE, Trevor R, Perot PL. Thoracic myelopathy caused by osteophytes of the articular processes. Thoracic spondylosis. *J Neurosurg*. 1979;50(6):779-783. doi:10.3171/jns.1979.50.6.0779.
 47. Shimada Y, Kasukawa Y, Miyakoshi N, Hongo M, Ando S, Itoi E. Spondylolisthesis of the thoracic spine. Case report. *J Neurosurg Spine*. 2006;4(5):415-418. doi:10.3171/spi.2006.4.5.415.
 48. Hsieh PC, Lee ST, Chen JF. Lower thoracic degenerative spondylolisthesis with concomitant lumbar spondylosis. *Clin Neurol Neurosurg*. 2014;118:21-25. doi:10.1016/j.clineuro.2013.11.019.
 49. Ploumis A, Transfeldt EE, Denis F. Degenerative lumbar scoliosis associated with spinal stenosis. 2007;7:428-436. doi:10.1016/j.spinee.2006.07.015
 50. Stapleton CJ, Pham MH, Attenello FJ, Hsieh PC. Ossification of the posterior longitudinal ligament: genetics and pathophysiology. *Neurosurg Focus*. 2011;30(3):22-25. doi:10.3171/2010.12.FOCUS10271.
 51. Stetler WR, La Marca F, Park P. The genetics of ossification of the posterior longitudinal ligament. *Neurosurg Focus*. 2011;30(3):40-42. doi:10.3171/2010.12.FOCUS10275.
 52. Inamasu J, Guiot BH, Sachs DC. Ossification of the posterior longitudinal ligament: An update on its biology, epidemiology, and natural history. *Neurosurgery*. 2006;58(6):1027-1038. doi:10.1227/01.NEU.0000215867.87770.73.
 53. Ning S, Chen Z, Fan D, et al. Genetic differences in osteogenic differentiation potency in the thoracic ossification of the ligamentum flavum under cyclic mechanical stress. *Int J Mol Med*. 2017;39(1):135-143. doi:10.3892/ijmm.2016.2803.
 54. Daniels AH, McDonald CL, Basques BA, Kuris EO. Ossified ligamentum Flavum: epidemiology, treatment, and Outcomes. *J Am Acad Orthop Surg*. 2022;30(12):E842-E851. doi:10.5435/JAAOS-D-21-01253.
 55. Yayama T, Mori K, Okumura N, et al. Wnt signaling pathway correlates with ossification of the spinal ligament: A micro-RNA array and immunohistochemical study. *J Orthop Sci*. 2018;23(1):26-31. doi:10.1016/j.jos.2017.09.024.
 56. Maigne JY, Ayrat X, Guérin-Surville H. Frequency and size of ossifications in the caudal attachments of the ligamentum flavum of the thoracic spine. Role of rotatory strains in their development - an anatomic study of 121 spines. *Surg Radiol Anat*. 1992;14(2):119-124. doi:10.1007/BF01794886.
 57. Miyakoshi N, Shimada Y, Suzuki T, et al. Factors related to long-term outcome after decompressive surgery for ossification of the ligamentum flavum of the thoracic spine. *J Neurosurg*. 2003;99(3 Suppl):251-256. doi:10.3171/spi.2003.99.3.0251.
 58. Liao CC, Chen TY, Jung SM, Chen LR. Surgical experience with symptomatic thoracic ossification of the ligamentum flavum. *J Neurosurg Spine*. 2005;2(1):34-39. doi:10.3171/spi.2005.2.1.0034.
 59. Li Z, Ren D, Zhao Y, et al. Clinical characteristics and surgical outcome of thoracic myelopathy caused by ossification of the ligamentum flavum: a retrospective analysis of 85 cases. *Spinal Cord*. 2016;54(3):188-196. doi:10.1038/sc.2015.139.
 60. Yu S, Wu D, Li F, Hou T. Surgical results and prognostic factors for thoracic myelopathy caused by ossification of ligamentum flavum: posterior surgery by laminectomy. *Acta Neurochir (Wien)*. 2013;155(7):1169-1177. doi:10.1007/s00701-013-1694-0.
 61. Lang N, Yuan HS, Wang HL, et al. Epidemiological survey of ossification of the ligamentum flavum in thoracic spine: CT imaging observation of 993 cases. *Eur Spine J*. 2013;22(4):857-862. doi:10.1007/s00586-012-2492-8.
 62. Ando K, Imagama S, Ito Z, et al. Predictive factors for a poor surgical outcome with thoracic ossification of the ligamentum flavum by multivariate analysis: A multicenter study. *Spine*. 2013;38(12). doi:10.1097/BRS.0b013e31828ff736.
 63. Miyasaka K, Kaneda K, Sato S, et al. Myelopathy due to ossification or calcification of the ligamentum flavum: Radiologic and histologic evaluations. *Am J Neuroradiol*. 1983;4(3):629-632.
 64. Mori K, Kasahara T, Mimura T, et al. Prevalence, distribution, and morphology of thoracic ossification of the yellow ligament in Japanese; results of ct-based cross-sectional study. *Spine*. 2013;38(19). doi:10.1097/BRS.0b013e31829e018b
 65. Guo JJ, Luk KDK, Karppinen J, Yang H, Cheung KMC. Prevalence, distribution, and morphology of ossification of the ligamentum flavum: A population study of one thousand seven hundred thirty-six magnetic resonance imaging scans. *Spine*. 2010;35(1):51-56. doi:10.1097/BRS.0b013e3181b3f779
 66. Kang KC, Lee CS, Shin SK, Park SJ, Chung CH, Chung SS. Ossification of the ligamentum flavum of the thoracic spine in the Korean population: Clinical article. *J Neurosurg Spine*. 2011;14(4):513-519. doi:10.3171/2010.11.SPINE10405.
 67. Fan T, Meng X, Sun C, et al. Genome-wide DNA methylation profile analysis in thoracic ossification of the ligamentum flavum. *J Cell Mol Med*. 2020;24(15):8753-8762. doi:10.1111/jcmm.15509.
 68. Qu X, Chen Z, Fan D, et al. Notch signaling pathways in human thoracic ossification of the ligamentum flavum. *J Orthop Res*. 2016;34(8):1481-1491. doi:10.1002/jor.23303.

69. Chen Q, Wanghan J, Wang Y, et al. Connexin 43 affects thoracic ossification of ligamentum flavum by regulating the p38 MAPK-RUNX2 signaling pathway. *Tissue Cell*. 2022; 76(January):101760. doi:10.1016/j.tice.2022.101760.
70. Yang X, Chen Z, Meng X, et al. Angiopoietin-2 promotes osteogenic differentiation of thoracic ligamentum flavum cells via modulating the Notch signaling pathway. *PLoS One*. 2018; 13(12):1-11. doi:10.1371/journal.pone.0209300.
71. Yang X, Sun C, Meng X, et al. LGR5 regulates osteogenic differentiation of human thoracic ligamentum flavum cells by Wnt signalling pathway. *J Cell Mol Med*. 2022(February 2021):3862-3872. doi:10.1111/jcmm.17420.
72. Qu X, Hou X, Chen Z, Chen G, Fan T, Yang X. Association analysis and functional study of COL6A1 single nucleotide polymorphisms in thoracic ossification of the ligamentum flavum in the Chinese Han population. *Eur Spine J*. 2021; 30(10):2782-2790. doi:10.1007/s00586-021-06932-y.
73. Fan D, Chen Z, Wang D, Guo Z, Qiang Q, Shang Y. Osterix is a key target for mechanical signals in human thoracic ligament Flavum Cells. *J Cell Physiol*. 2007;211:577-584.
74. Mobbs RJ, Dvorak M. Ossification of the ligamentum flavum: Diet and genetics. *J Clin Neurosci*. Published online 2007: 703-705.
75. Wang W, Kong L, Zhao H, et al. Thoracic ossification of ligamentum flavum caused by skeletal fluorosis. *Eur Spine J*. 2007;16(8):1119-1128. doi:10.1007/s00586-006-0242-5.
76. Zhang H, Deng N, Zhang L, Zhang L, Wang C. Clinical risk Factors for thoracic Ossification of the ligamentum Flavum: A Cross-sectional study based on spinal thoracic three-dimensional computerized tomography. *Risk Manag Health Policy*. 2022;15(May):1065-1072. doi:10.2147/rmhp.s361730.
77. Boody BS, Lendner M, Vaccaro AR. Ossification of the posterior longitudinal ligament in the cervical spine: A review. *Int Orthop*. 2019;43(4):797-805. doi:10.1007/s00264-018-4106-5.
78. Endo T, Takahata M, Koike Y, Iwasaki N. Clinical characteristics of patients with thoracic myelopathy caused by ossification of the posterior longitudinal ligament. *J Bone Miner Metab*. 2020;38(1):63-69. doi:10.1007/s00774-019-01026-8.
79. Matsunaga S, Sakou T. Ossification of the posterior longitudinal ligament of the cervical spine: Etiology and natural history. *Spine*. 2012;37(5):309-314. doi:10.1097/BRS.0b013e318241ad33
80. Zhai J, Guo S, Li J, Chen B. Progression of spinal ligament Ossification in patients with thoracic myelopathy. 2022; 3(82072508):1-6. doi:10.1111/os.13291
81. Baaj AA, Smith DA, Vale FL, Uribe JS. Surgical approaches to thoracic ossification of the posterior longitudinal ligament. *J Clin Neurosci*. 2012;19(3):349-351. doi:10.1016/j.jocn.2011.05.025.
82. Ono M, Russell WJ, Kudo S, et al. Ossification of the thoracic posterior longitudinal ligament in a fixed population. Radiological and neurological manifestations. *Radiology*. 1982; 143(2):469-474. doi:10.1148/radiology.143.2.7071349.
83. Liang H, Liu G, Lu S, et al. Epidemiology of ossification of the spinal ligaments and associated factors in the Chinese population: a cross-sectional study of 2000 consecutive individuals. *BMC Musculoskelet Disord*. 2019;20(1):1-12. doi:10.1186/s12891-019-2569-1.
84. Wang P, Liu X, Zhu B, et al. Association of IL17RC and COL6A1 genetic polymorphisms with susceptibility to ossification of the thoracic posterior longitudinal ligament in Chinese patients. *J Orthop Surg Res*. 2018;13(1):1-6. doi:10.1186/s13018-018-0817-y.
85. Wang P, Teng Z, Liu X, Liu X, Kong C, Lu S. A new single nucleotide polymorphism affects the predisposition to thoracic ossification of the posterior longitudinal ligament. *J Orthop Surg Res*. 2019;14(1):1-8. doi:10.1186/s13018-019-1481-6.
86. Wang P, Teng Z, Liu X, Liu X, Kong C, Lu S. The COL6A1 rs201153092 single nucleotide polymorphism, associates with thoracic ossification of the posterior longitudinal ligament. *Mol Med Rep*. 2020;21(1):191-200. doi:10.3892/mmr.2019.10846.
87. Wang P, Liu X, Zhu B, et al. Identification of susceptibility loci for thoracic ossification of the posterior longitudinal ligament by whole-genome sequencing. *Mol Med Rep*. 2018;17(2): 2557-2564. doi:10.3892/mmr.2017.8171.
88. Goto K, Yamazaki M, Tagawa M, et al. Involvement of insulin-like growth factor I in development of ossification of the posterior longitudinal ligament of the spine. *Calcif Tissue Int*. 1998;62(2):158-165. doi:10.1007/s002239900410.
89. Kamakura D, Fukutake K, Nakamura K, et al. Acromegaly presenting with myelopathy due to ossification of posterior longitudinal ligament: a case report. *BMC Musculoskelet Disord*. 2021;22(1):1-7. doi:10.1186/s12891-021-04232-6.
90. Ikeda Y, Nakajima A, Aiba A, et al. Association between serum leptin and bone metabolic markers, and the development of heterotopic ossification of the spinal ligament in female patients with ossification of the posterior longitudinal ligament. *Eur Spine J*. 2011;20(9):1450-1458. doi:10.1007/s00586-011-1688-7.
91. Aizawa T, Sato T, Tanaka Y, et al. Thoracic myelopathy in Japan: epidemiological retrospective study in Miyagi Prefecture during 15 years. *Tohoku J Exp Med*. 2006;210(3):199-208. doi:10.1620/tjem.210.199.
92. Filatov A, Hammond TC, Swerdloff MA. Compressive thoracic myelopathy. *Compressive Thorac Myelopathy Neurol Neurol Sci Open Access*. 2021;4(2):1023. <https://meddocsonline.org/>
93. Imagama S, Ando K, Kobayashi K, et al. Factors for a good surgical outcome in posterior decompression and dekyphotic corrective fusion with instrumentation for thoracic ossification of the posterior longitudinal ligament: prospective single-center study. *Oper Neurosurg*. 2017;13(6):661-669. doi:10.1093/ons/oxp043.
94. Hirabayashi K, Miyakawa J, Satomi K, Maruyama T, Wakano K. Operative results and postoperative progression of ossification among patients with ossification of cervical posterior longitudinal ligament. *Spine*. 1981;6(4):354-364. doi:10.1097/00007632-198107000-00005

95. Hilton B, Tempest-Mitchell J, Davies B, Kotter M. Route to diagnosis of degenerative cervical myelopathy in a UK healthcare system: a retrospective cohort study. *BMJ Open*. 2019;9(5):1-9. doi:10.1136/bmjopen-2018-027000.
96. Kim DH, Lee SH, Lee JS, Song GS, Son DW. High thoracic ossification of ligamentum flavum causing partial Horner syndrome. *Br J Neurosurg*. 2021;35(2):231-232. doi:10.1080/02688697.2018.1441976.
97. Cong M, Si M, Hou Y, Ma H, Nie L. Foot drop as the initial symptom caused by thoracic disc herniation. *Eur Spine J*. 2022;31(7):1795-1801. doi:10.1007/s00586-022-07254-3.
98. Toribatake Y, Baba H, Kawahara N, Mizuno K, Tomita K. The epiconus syndrome presenting with radicular-type neurological features. *Spinal Cord*. 1997;35(3):163-170. doi:10.1038/sj.sc.3100369.
99. Rousseff RT, Tzvetanov P. False localising levels in spinal cord compression. *NeuroRehabilitation*. 2006;21(3):219-222. doi:10.3233/nre-2006-21304.
100. Lamer AJ. False localising signs. *J Neurol Neurosurg Psychiatry*. 2003;74(4):415-418. doi:10.1136/jnnp.74.4.415.
101. Martinez-Del-Campo E, Moon K, Kalb S, Soriano-Baron H, Theodore N. Surgical management of a patient with thoracic spinal cord herniation: technical case report and review. *Neurosurgery*. 2015;77(3):E492-E498. doi:10.1227/NEU.0000000000000860.
102. Oyinkan Marquis B, Capone PM. *Myelopathy*. *Handb Clin Neurol*. 2016;136:1015-1026. doi:10.1016/B978-0-444-53486-6.00052-1.
103. Matsuyama Y, Yoshihara H, Tsuji T, et al. Surgical outcome of ossification of the posterior longitudinal ligament (OPLL) of the thoracic spine: Implication of the type of ossification and surgical options. *J Spinal Disord Tech*. 2005;18(6):492-497. doi:10.1097/01.bsd.0000155033.63557.9c.
104. Chang UK, Choe WG, Chung CK, Kim HJ. Surgical treatment for thoracic spinal stenosis. *Spinal Cord*. 2001;39(7):362-369. doi:10.1038/sj.sc.3101174.
105. Fehlings MG, Barry S, Kopjar B, et al. Anterior versus posterior surgical approaches to treat cervical spondylotic myelopathy: Outcomes of the prospective multicenter AOSpine North America CSM study in 264 patients. *Spine*. 2013;38(26):2247-2252. doi:10.1097/BRS.0000000000000047.
106. Maruyama J, Furuya T, Maki S, et al. Posterior decompression and fixation for thoracic spine Ossification: A 10-year follow-up study. *J Clin Med*. 2023;12(17):9-16. doi:10.3390/jcm12175701.
107. Ando K, Imagama S, Kaito T, et al. Outcomes of surgery for thoracic myelopathy owing to thoracic Ossification of the ligamentum Flavum in a nationwide multicenter prospectively collected study in 223 patients: Is instrumented Fusion necessary? *Spine*. 2020;45(3):E170-E178. doi:10.1097/BRS.0000000000003208
108. Min JH, Jang JS, Lee SH. Clinical results of ossification of the posterior longitudinal ligament (OPLL) of the thoracic spine treated by anterior decompression. *J Spinal Disord Tech*. 2008; 21(2):116-119. doi:10.1097/BSD.0b013e318060091a.
109. Quraishi NA, Khurana A, Tsegaye MM, Boszczyk BM, Mehdian SMH. Calcified giant thoracic disc herniations: Considerations and treatment strategies. *Eur Spine J*. 2014; 23(SUPPL. 1):76-83. doi:10.1007/s00586-014-3210-5.
110. Khoo LT, Smith ZA, Asgarzadie F, et al. Minimally invasive extracavitary approach for thoracic discectomy and interbody fusion: 1-Year clinical and radiographic outcomes in 13 patients compared with a cohort of traditional anterior trans-thoracic approaches - Clinical article. *J Neurosurg Spine*. 2011; 14(2):250-260. doi:10.3171/2010.10.SPINE09456.
111. Zhao W, Shen C, Cai R, et al. Minimally invasive surgery for resection of ossification of the ligamentum flavum in the thoracic spine. *Wideochirurgia I Inne Tech Maloinwazyjne*. 2017;12(1):96-105. doi:10.5114/wiitm.2017.66473.
112. Okada K, Oka S, Tohge K, Ono K, Yonenobu K, Hosoya T. Thoracic myelopathy caused by ossification of the ligamentum flavum: Clinicopathologic study and surgical treatment. *Transplantation*. 1973;16(3):280-287. doi:10.1097/00007632-199103000-00005.
113. He S, Hussain N, Li S, Hou T. Clinical and prognostic analysis of ossified ligamentum flavum in a Chinese population. *J Neurosurg Spine*. 2005;3(5):348-354. doi:10.3171/spi.2005.3.5.0348.
114. Sung UK, Young SK, Yong EC, et al. Contributing factors affecting the prognosis surgical outcome for thoracic OLF. *Eur Spine J*. 2006;15(4):485-491. doi:10.1007/s00586-005-0903-9.
115. Patel N. Surgical disorders of the thoracic and lumbar spine: Guide for neurologists. *Neurol Pract*. 2002;73(1):48.