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ORIGINAL ARTICLE

Glycosaminoglycans Composition Associated with Ligamentum Flavum Hypertrophy in Degenerative Lumbar Spine Diseases

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Abstract

Introduction: hypertrophy of the ligamentum flavum, also called yellow ligament, is a major contributor to lumbar spinal canal stenosis in degenerative spine diseases. Elastic fibers, collagen, proteoglycans and glycosaminoglycans are key components of the extracellular matrix of the ligamentum flavum, playing essential roles in maintaining its structural integrity and function. However, the molecular mechanisms underlying ligamentum flavum hypertrophy, particularly those involving alterations in glycosaminoglycans composition, remain poorly understood.

Objective: to analyze the composition of glycosaminoglycans in the ligamentum flavum of patients with degenerative lumbar spine diseases, with the aim of identifying molecular alterations associated with ligamentum flavum hypertrophy.

Methods: thirty Ligamentum flavum samples were surgically obtained from patients diagnosed with either lumbar disc herniation or spinal canal stenosis. Sulfated glycosaminoglycans were extracted, identified, and quantified using agarose gel electrophoresis and specific glycosidases digestion. Ligamentum flavum thickness was measured using magnetic resonance imaging, and statistical analyses were performed to assess correlations between ligamentum flavum thickness and glycosaminoglycans composition.

Results: a significant increase in chondroitin sulfate level was detected and found to be positively correlated with the degree of ligamentum flavum thickening. In contrast, dermatan sulfate levels did not show significant variation across different degrees of ligamentum flavum hypertrophy.

Conclusion: ligamentum flavum hypertrophy in degenerative lumbar spine conditions is associated with specific alterations in glycosaminoglycans composition, particularly an increase in chondroitin sulfate content. These findings suggest that chondroitin sulfate, a highly anionic constituent of the extracellular matrix, may play a pivotal role in the pathophysiology of ligamentum flavum thickening observed in degenerative lumbar spine disease.

Keywords: lumbar stenosis, extracellular matrix, chondroitin sulfate, dermatan sulfate, chondroitin ABC lyase.

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Authors summary

Why was this study done?
This study was conducted to better understand the molecular mechanisms involved in the hypertrophy of the ligamentum flavum (LF), particularly focusing on changes in the composition of sulfated glycosaminoglycans (GAG), an important component of extracellular matrix that maintains structural integrity and function of LF.

What did the researchers do and find?
The researchers collected thirty ligamentum flavum (LF) samples from patients with lumbar disc herniation or spinal canal stenosis. They extracted, identified, and quantified sulfated glycosaminoglycans (GAGs) from these samples. They also measured LF thickness using magnetic resonance imaging (MRI) and performed statistical analyses to evaluate correlations between LF thickness and GAG composition. They found a significant increase in chondroitin sulfate levels, which was positively correlated with LF thickening.

What do these findings mean?
These results suggest that chondroitin sulfate may play a key role in the pathophysiology of ligamentum flavum hypertrophy in degenerative lumbar spine disease.

How do the research results change people's lives, and how can these findings be applied in decision-making?
IIntervertebral disc degeneration is highly prevalent worldwide and contributes to ligamentum flavum thickening. The thickening of the ligamentum flavum in the intervertebral spine leads to spinal canal narrowing and nerve compression which causes chronic pain that leads to limitations and reduces quality of life. The direct correlation between increased chondroitin sulfate and LF thickness highlights that this highly anionic molecule may potentially alter its interaction with cationic components of the extracellular matrix (ECM), which could consequently lead to structural modifications of the ECM, affecting the function of LF. The elucidation of the molecular mechanisms involved in LF thickening might contribute to new therapeutic alternatives using immunobiologicals, such as local injection of anti-chondroitin sulfate antibodies or chondroitin sulfate-binding inhibitory peptides.

Highlights
• The ligamentum flavum (LF) plays a fundamental role in the biomechanics and stability of the vertebral column.
• Intervertebral disc degeneration is highly prevalent worldwide and contributes to ligamentum flavum thickening causing chronic pain that leads to patients´s limitations and reduces quality of life.
• The present study shows a direct correlation between increased chondroitin sulfate and LF thickness.
• The increase in chondroitin sulfate suggests structural alterations of the extracellular matrix in LF hypertrophy.
• The data indicate potential molecular mechanisms underlying LF thickening.

INTRODUCTION

Population aging has become increasingly prominent in recent decades. The global population aged over 60 years increased from 12% in 2015 to 16% in 2022 and is projected to reach 23% by 2050, according to the ONU report[1]. In Brazil, recent data from the Brazilian Institute of Geography and Statistics (IBGE) indicate that in 2022, the population over 60 years exceeded 30 million people, representing a significant increase compared to previous decades[2]. Alongside this growth, there is a parallel rise in the incidence of degenerative musculoskeletal diseases, particularly those related to the spine, resulting in greater demand for medical care and considerable socioeconomic impact. In the past decade, the burden of low back pain has increased by 17%, leading to higher direct and indirect healthcare costs[1-4].

Among spinal pathologies, lumbar spinal canal stenosis is one of the most prevalent degenerative conditions associated with aging, commonly manifesting after the fifth decade of life. Affected patients may experience symptoms such as low back pain radiating to the lower limbs (sciatica) and neurogenic claudication, significantly compromising their quality of life. This condition is characterized by narrowing of the lumbar canal, primarily caused by facet joint osteoarthritis, intervertebral disc bulging, and notably, hypertrophy of the ligamentum flavum (LF)[5].

The LF is a fibroelastic structure extending from the second cervical vertebra to the first sacral vertebra, connecting adjacent laminae and contributing to spinal stability during movement[6]. Composed of approximately 70% elastic fibers and 30% collagen fibers within its extracellular matrix (ECM), the LF undergoes significant structural remodeling during aging, including a reduction in elastic fibers, an increase in collagen fibers, and changes in glycosaminoglycan (GAG) composition[7]. During this process, LF hypertrophy and intervertebral disc bulging occur, leading to a reduced vertebral canal diameter and compression of the spinal cord and nerve roots[8,9]. Despite its structural importance, the molecular mechanisms involved in LF thickening and specific alterations in components such as GAGs remain incompletely understood.

Recent studies have shown that ECM alterations, including changes in proteoglycan and GAG composition, play a central role in LF hypertrophy, contributing to vertebral canal narrowing[10-13].

LF hypertrophy involves complex interactions among mechanical stress, inflammatory processes, and molecular signaling pathways, notably the activation of TGF-β1/Smad, IL-6, and TNF-α pathways, which promote fibroblast proliferation, ECM remodeling, and fibrotic changes[10,14,15]. These alterations are accompanied by increased deposition of proteoglycans and GAGs, particularly chondroitin sulfate (CS), while the role of dermatan sulfate (DS) remains less clear[12,16,17]. Additionally, studies indicate that increased LF thickness may not always be associated with true hypertrophy but may result from the formation of ligamentum folds, especially in the upright position, further contributing to neural compression[18-20].

Recently, studies have identified decorin (DCN) as a potential mediator in preventing LF hypertrophy. Decorin is a small leucine-rich proteoglycan that acts as a natural inhibitor of TGF-β1, blocking its biological activity and consequently Smad2/3 signaling. Experimental studies have shown that decorin administration reduces the expression of fibrogenic markers such as type I collagen, fibronectin, and α-SMA, suggesting a significant antifibrotic role. Additionally, gene expression analyses have revealed that decorin modulates metabolic and immune pathways associated with fibrosis and inflammatory responses, making it a promising candidate for both understanding molecular mechanisms and developing therapeutic strategies[17].

These findings open perspectives for the use of molecules such as decorin as adjuvant therapeutic agents in the treatment of degenerative spinal conditions. By intervening at the onset of the fibrogenic process, it may be possible to delay or even reverse LF thickening, preventing progression to symptomatic stenosis and reducing the need for invasive surgical interventions.

Chondroitin sulfate, the main GAG present in the LF, contributes to the biomechanical properties of the ligament by influencing tissue hydration, elasticity, and resistance. Recent studies have shown that CS accumulation in the LF may correlate with the severity of hypertrophy and stenosis, suggesting its potential role as a molecular marker and therapeutic target for degenerative lumbar spine conditions[21].

Despite these advances, the molecular mechanisms leading to LF hypertrophy remain unclear. It is essential to understand whether this process results from chronic biomechanical stress due to repetitive spinal movements and/or is triggered by inflammatory changes in intervertebral discs and adjacent tissues. Identifying molecular markers associated with these transformations may have important implications for early diagnosis and the development of targeted therapies aimed at preventing or mitigating lumbar spinal canal stenosis and its associated neurological symptoms, such as neurogenic claudication and radiculopathy.

Thus, the objective is to correlate the glycosaminoglycan profile with LF thickening in patients with degenerative lumbar spine diseases, seeking to elucidate potential molecular alterations associated with this pathological process while highlighting potential biomarkers for early diagnosis and targeted intervention.

METHODS

Patients and Samples

Samples of the Ligamentum flavum (LF), also named yellow ligament, were collected from 30 patients submitted to surgical treatment in the lumbar spine segment, who presented spinal disc herniation or canal stenosis, for the period between August 2013 and August 2014, carried out in the hospitals Abreu Sodré in São Paulo (AACD) and Hospital Assunção, São Luiz Rede Dor, São Bernardo do Campo. The collection was performed by the same surgeon during the surgical act for radicular decompression of the spinal column. The study was approved by the Research Ethics Committee at the ABC School of Medicine under the number 12564313.2.0000.0082. All of the patients of this study agreed to participate and signed the free informed consent form. Patients were included who presented lumbar herniated disc, protrusion or extrusion, located in the central or lateral region of the vertebral canal, with more than three months of refractory symptoms to conservative treatment (clinical and rehabilitation), without previous surgery in the segment affected in the lumbar spine, in addition to patients who presented stenosis of the lumbar canal, suffering from neurological lameness, resulting from compression of the vertebral canal and hypertrophy of the yellow ligament in the lumbar spine segment. Among the exclusion criteria we highlight patients who presented pathologies of the spinal column associated with spinal disc herniation and stenosis of the lumbar canal, such as previous surgeries, fractures, tumors, inflammatory disease, as well as patients who refused to sign the free informed consent form.

Magnetic Resonance Imaging (MRI)

All of the patients were examined using an MRI, with axial sections in the T1 sequence, for the segments affected: L3L4, L4L5 and L5S1. The same examiner determined the degree of thickening of the yellow ligament in all of the cases and used the same RadiAnt DICOM viewer. The thickness of the yellow ligament was measured with a digital ruler with a resolution of 0.1 mm, based on line drawn transversally on the facet segment, through the middle portion of the yellow ligament. In cases of bilaterally asymmetric thickness, the higher value was used.

Extraction of sulfated glycosaminoglycans from tissues

The tissue samples were homogenized and kept in acetone for 24 hours, during which time the acetone was replaced several times. The resulting powdered tissue sample was submitted to proteolysis in the presence of 2mg of Maxatase (Biocon a Brasil Ind. Ltda., Rio de Janeiro, Brazil) / 100mg of dried tissue, in 0.05 M Tris-HCl buffer, pH 8.0, containing 0.15 M NaCl. Proteolysis was carried out for 24 h, at 55°C. Trichloroacetic acid (10% of final concentration) was added to the mixture, which was kept at 4°C for 15 minutes. The supernatant containing GAG was obtained after centrifugation (10min, 3,500 x g, 4°C). The sulfated glycosaminoglycans were precipitated by adding two volumes of methanol (24h, -20°C) overnight. The precipitate was collected by centrifugation for 20min, 3,500 x g, 4°C, dissolved in water and maintained at -80°C.

Quantification and identification of sulfated glycosaminoglycans

The sulfated glycosaminoglycans heparan sulfate (HS), dermatan sulfate (DS) and chondroitin sulfate (CS), were identified and quantified by agarose gel eletrophoresis in 0.05 M 1,3-diaminopropane (PDA) buffer, pH 9.0. After electrophoresis, at 100 V for 1 h, the GAGs were precipitated in 0.1% agarose gel, using a cationic detergent Cetavlon (cetyltrimethylammonium bromide, Sigma-Aldrich, St. Louis, MO), for 2 hours at room temperature. The gel was dried and dyed with toluidine blue 0.1% in acetic acid: ethanol: water (0.1: 5.0: 4.9). The quantification of the GAGs was performed by densitometry at 530nm. The standards used were chondroitin-4-sulfate from whale cartilage (Seikagaku Kogyo Co., Tóquio, Japão), dermatan sulfate from pigskin and heparam sulfato from bovine pancreas. The error of method for the electrophoresis was around 5%. The identity of the different sulfated galactosaminoglycans (chondroitin sulfate and dermatan sulfate) was confirmed by degradation with specific lyases, chondroitinases AC and ABC (Seikagaku Kogyo Co., Tóquio, Japão). Chondroitinase AC degrades only chondroitin sulfate, whilst chondroitinase ABC degrades both chondroitin sulfate and dermatan sulfate.

Statistical Analysis

The values obtained for each quantitative variable were organized and described using means and standard deviations. For the qualitative variables absolute and relative frequencies were used. The distributions were confirmed as parametric by the Kolmogorov-Smirnov test. The comparison between the means of the two groups, the Student t test was used (Mann Whitney test). For the comparison for more than two groups the ANOVA test was used in conjunction with the Kruscal-Wallis test. To verify the existence of correlation between two quantitative variables the Pearson correlation test was used. In all of the analyses, the statistical program SPSS® version 17.0 (SPSS® Inc; Illinois, USA) was used and a significance level of 5% ($p \leq 0.05$) was used for all the comparisons.

RESULTS

The region used for determining the thickness of the ligamentum flavum (LF) was defined by Magnetic Resonance Imaging (MRI), as shown in figure 1.

Based on MRI analysis, the samples were subdivided into three groups according to ligamentum flavum thickness, as shown in table 1.

Figure 2 shows that there is homogeneity within each analyzed group, with no statistically significant differences in age or gender among the groups, classified according to ligamentum flavum thickness. The mean age was 45.5 years in the group with LF thickness ≤ 2.9mm, while the groups with thickness between 3.0–3.9mm and ≥ 4.0mm had mean ages of 43.4 and 40.2 years, respectively ($p = 0.5877$), as shown in figure 2A. Additionally, the gender distribution did not differ significantly among the groups (figure 2B).

Enzymatic digestion with specific enzymes, chondroitinase AC and chondroitinase ABC, confirmed the presence of chondroitin sulfate (CS) and dermatan sulfate (DS) in the LF samples (figure 3A). Figure 3B illustrates the differences in the profiles of CS and DS according to the thickness of the intervertebral LF. Ligamentum flavum samples were found to contain chondroitin sulfate and dermatan sulfate, while heparan sulfate was not detected by agarose gel electrophoresis technique.

The chondroitin sulfate concentration was lower (0.03523 ± 0.10138µg/mg of tissue) in patients with ligamentum flavum thickness ≤2.9mm, compared to higher levels observed in ligaments measuring 3.0–3.9mm (0.8800 ± 0.1700µg/mg) and ≥4.0mm (1.826 ± 0.1390µg/mg), respectively.

A significantly higher expression of chondroitin sulfate was observed in samples with thicker LF (figure 4A), suggesting that this glycosaminoglycan is associated with the hypertrophic process of the LF in patients with intervertebral disc degeneration.

Statistical analysis revealed a strong positive correlation between ligamentum flavum thickness and chondroitin sulfate concentration, as evidenced by the high correlation coefficient shown in figure 4B.

Figure 4 shows that there was no difference between the concentration of dermatan sulfate and variation of LF thickness (figure 5A). Furthermore, there was no correlation between LF thickness and dermatan sulfate expression, as shown in figure 4B).

It is important to highlight that no statistically significant differences in chondroitim sulfate or dermatan sulfate concentrations were observed between females and males within each group defined by LF thickness, as shown in table 2 (Mann Whitney test).

Table 1: Number of samples in each group according to ligamentum flavum thickness

Number of Samples	Thickness of Ligamentum flavum (mm)
13	≤ 2,9
8	3,0 – 3,9
9	≥ 4,0

Table 2: Statistical differences in chondroitim sulfate and dermatan sulfate concentrations between females and males within each ligamentum falvum groups

Tickness of Ligamentum flavum (mm)	Chondroitim sulfate (p value)	Dermatan sulfate (p value)
≤ 2.9 (Female vesus Male)	0.7857	0.1156
3.0-3.9 (Female vesus Male)	0.1797	0.4762
≥ 4.0 (Female vesus Male)	0.1905	0.5556

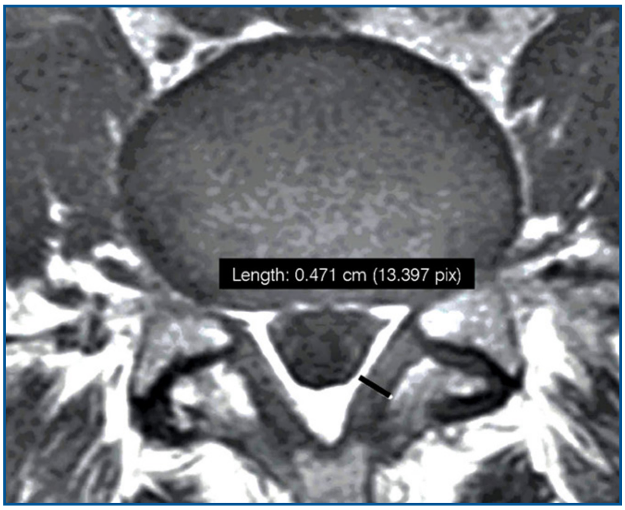

Figure 1: Magnetic Resonance Imaging of the intervertebral disc. The thickness of the ligamentum flavum was measured as indicated in the MRI image.

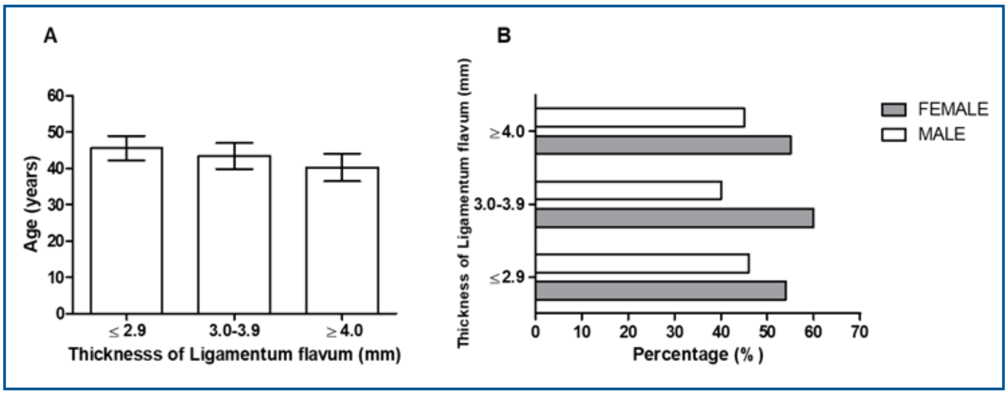

Figure 2: Analysis of age and gender variables in each study group. A. Average age of patients with intervertebral disc degeneration according to the thickness of Ligamentum flavum in each group ≤ 2.9 mm, 3.0–3.9 mm; ≥ 4.0 mm. ANOVA test using Kruscal-Wallis test, p = 0,5877. B. Percentage of females (FEMALE) and males (MALE) according to the thickness of ligament in each group. ANOVA test using Kruscal-Wallis test, p = 0,0762.

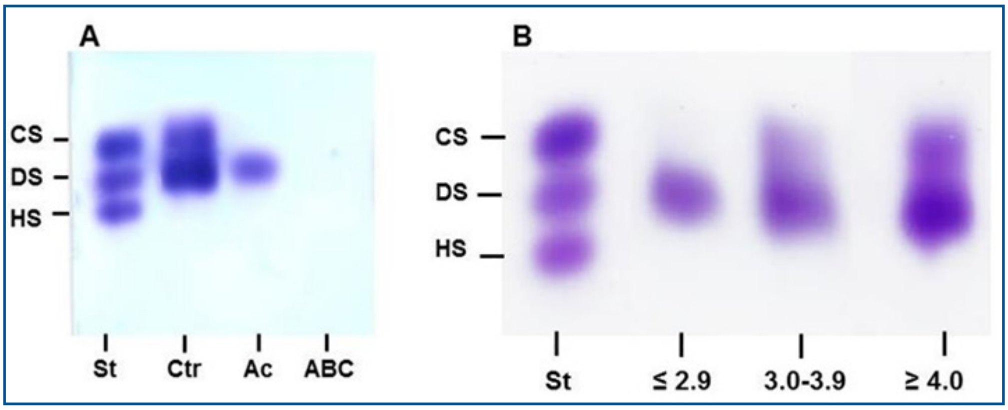

Figure 3: Sulfated glycosaminoglycan profile. A. Agarose gel electrophoresis to identify sulfated glycosaminoglycans using specific enzymes. St. 5 µg/mL of standard of chondroitin sulfate (CS), dermatan sulfate (DS), and heparan sulfate (HS); Ctr Sample of ligamentum flavum without enzymatic disgestion. AC. Sample of ligamentum flavum after digestion with chondroitinase AC, that cleaves chondroitin sulfate; ABC. Sample of ligamentum flavum after digestion with chondroitinase ABC that cleaves both chondroitin sulfate and dermatan sulfate. B. Profile of sulfated glycosaminoglycans in agarose gel electrophoresis. St. 5 µg/mL of standard of chondroitin sulfate (CS), dermatan sulfate (DS), and heparan sulfate (HS); ≤ 2.9, 3.0–3.9; ≥ 4.0 represents the thickness (mm) of ligamentum flavum of each sample from three patients with intervertebral disc degeneration.

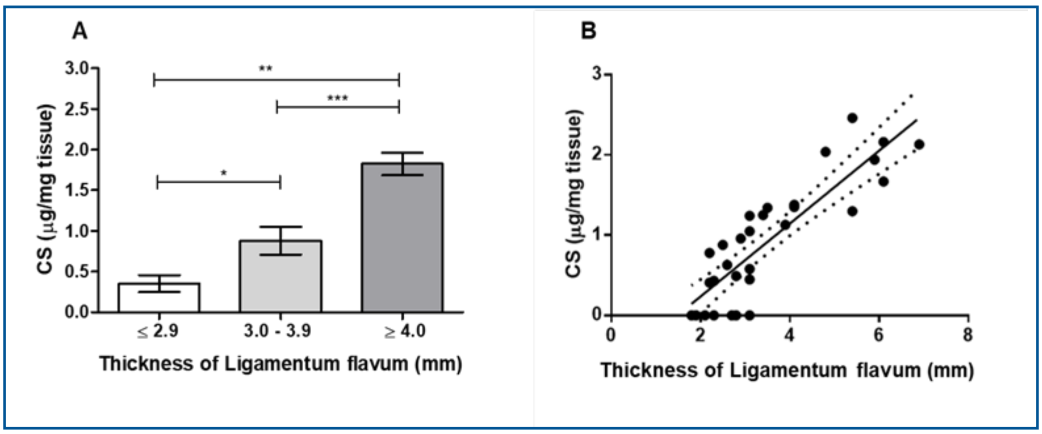

Figure 4. Expression of chondroitin sulfate in accordance with thickness of the ligamentum flavum. The values represent the amount of chondroitin sulfate expressed as mean and standard error representing triplicate assays. The quantification was obtained after agarose gel electrophoresis, as described. ANOVA and Kruscal-Wallis test */**/***p < 0.0001. The quantification of chondroitin sulfate was expressed in µg/mL of tissue sample according to ligament thickness in each group ≤ 2.9 mm, 3.0-3.9 mm and ≥ 4.0 mm. The correlation between chondroitin sulfate and thickness was determined by Pearson correlation test, r = +0.865 and p < 0.0001.

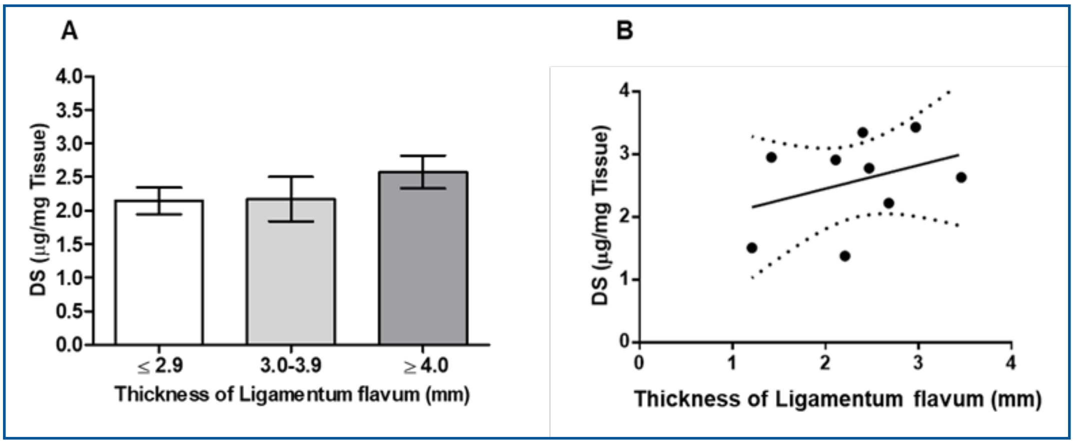

Figure 5. Expression of dermatan sulfate in accordance with thickness of the Ligamentum flavum. The values represent the amount of dermatan sulfate expressed as mean and standard error representing triplicate assays. The quantification was obtained after agarose gel electrophoresis, as described in Methods. ANOVA test, $p = 0.549$. The quantification of dermatan sulfate was expressed in µg/mL of tissue sample according to ligament thickness in each group ≤ 2.9 mm, 3.0-3.9 mm and ≥ 4.0 mm. The correlation between dermatan sulfate and thickness was determined by Pearson correlation Pearson correlation test, $r = +0.277$, $p = 0.139$.

DISCUSSION

The ligamentum flavum is an essential structure for the stability of the vertebral column. It connects the laminae of adjacent vertebrae along the entire spine, from the cervical to the lumbar region, forming part of the posterior wall of the spinal canal. The ligamentum flavum (LF) is a connective tissue extending from the second cervical vertebra to the first sacral vertebra, functioning to stabilize the spine during movement while maintaining a smooth surface over the dural sac, preventing adhesions and compressions. Degenerative changes, such as LF hypertrophy, are associated with lumbar spinal canal stenosis and represent one of the main factors contributing to neural compression in elderly individuals.

Although segmental instability is considered a key factor, understanding the underlying mechanisms connecting mechanical stress to LF hypertrophy has advanced. Chronic mechanical stress can induce fibroblast proliferation, the secretion of growth factors such as Transforming Growth Factor Beta (TGF-β1), and the deposition of extracellular matrix (ECM) components, including collagen and proteoglycans15. Additionally, hypoxia and inflammation, frequently present in degenerated discs, also contribute to this process by activating signaling pathways mediated by Interleukine-6 (IL-6) and Tumor Necrosis Factor Alpha (TNF-α), leading to ECM changes[6,16].

Nakatani et al. observed an increase in TGF-β mRNA expression during the initial phase of LF hypertrophy. However, despite TGF-β being present in all analyzed samples, no correlation was found between LF thickness and the expression of this growth factor[15].

In this study, a direct correlation was observed between the increase in chondroitin sulfate (CS) and LF thickening in patients with degenerative lumbar spine diseases, suggesting that CS accumulation may be related to the hypertrophic process. Chondroitin sulfate, an abundant glycosaminoglycan in the ECM, is known for its hydrophilic properties, contributing to tissue hydration and turgor. Its accumulation in hypertrophic LF may lead to increased tissue volume, exacerbating vertebral canal narrowing. Additionally, CS can influence the organization and structural integrity of the ECM, and its predominance may indicate an imbalance in GAG composition during the degenerative process, favoring matrix accumulation at the expense of elasticity. These findings are consistent with Yabe et al., who demonstrated an increase in CS and DS rich proteoglycans in thickened LF, present as linear polysacharides linked to a core protein forming the proteoglycans decorin and versican, respectively. This reinforces the importance of GAG in ECM remodeling during hypertrophy[12].

Morover, the present study showed no significant quantitative differences in DS content between groups, which could initially suggest a lack of DS involvement in the hypertrophic process. Nonetheless, recent studies indicate that even without expressive quantitative alterations, DS plays fundamental roles in regulating fibrillogenesis and ECM organization by modulating collagen fibril formation and alignment[22,23]. Additionally, proteoglycans such as decorin, which contain DS chains, are essential for modulating TGF-β1 activity, regulating fibrogenic processes, and limiting excessive collagen deposition in tissues[17].

The proteoglycan decorin has been identified as a potential antifibrotic agent in the context of LF hypertrophy, acting as a natural TGF-β1 inhibitor and reducing the expression of fibrogenic markers such as type I collagen, fibronectin, and α-SMA, while also modulating pathways related to fibrosis and inflammatory responses[16].

It is well established that glycosaminoglycan chains can determine specificity and function[21]. The organization of LF elastic fibers and the arrangement of the ECM during hypertrophy appear to be associated with different proteoglycan expression profiles[12].

It has been demonstrated that chondroitin sulfate and glucosamine supplementation may attenuate symptomatic disc degeneration symptoms[24]. Possibly, CS exerts structural modulation effects on cartilage, promoting ECM organization, suggesting therapeutic efficacy, as already observed in osteoarthritis[25]. The therapeutic efficacy of CS in osteoarthritis suggests that GAG expression in extracellular matrix may significantly impact degenerative pathologies. A detailed understanding of changes in GAG chain composition during LF hypertrophy, with a predominance of CS chains, is fundamental for better understand the molecular mechanisms involved in hypertrophy of ligament flavum and provides knowledge that might be useful to targeted intervention to prevent or mitigate lumbar spinal canal stenosis and its associated neurological symptoms.

The data suggests that the molecular processes involved in the degenerative progression of LF hypertrophy may be dependent on chondroitin sulfate.

CONCLUSION

Intervertebral disc degeneration is highly prevalent worldwide and contributes to ligamentum flavum thickening. The thickening of the ligamentum flavum in the intervertebral spine leads to spinal canal narrowing and nerve compression which causes chronic pain that leads to limitations and reduces quality of life. The direct correlation between increased chondroitin sulfate and LF thickness highlights that this highly anionic molecule may potentially alter its interaction with cationic components of the extracellular matrix (ECM), which could consequently lead to structural modifications of the ECM, affecting the function of LF. The elucidation of the molecular mechanisms involved in LF thickening might contribute to new therapeutic alternatives using immunobiologicals, such as local injection of anti-chondroitin sulfate antibodies or chondroitin sulfate-binding inhibitory peptides.

The findings of this study reinforce the importance of glycosaminoglycans in the pathophysiology of LF hypertrophy.

Author Contributions

MAS Pinhal and RP cavalheiro developed the concept of the study and participated in its design. MF Campos, LR Monteiro, LF Ondiciati and T Saleti participated in data acquisition, MAS Pinhal, MF Campos contributed to the analysis of the data and critically revised the manuscript. All authors have read and approved the final version of the manuscript.

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Conflicts of Interest

Nothing to declare.

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Resumo

Introdução: a hipertrofia do ligamentum flavum, também denominado ligamento amarelo, é um dos principais fatores que contribuem para a estenose do canal vertebral lombar em doenças degenerativas da coluna. Fibras elásticas, colágeno, proteoglicanos e glicosaminoglicanos são componentes-chave da matriz extracelular do LF, desempenhando papéis essenciais na manutenção de sua integridade estrutural e funcional. No entanto, os mecanismos moleculares envolvidos na hipertrofia do ligamentum flavum, especialmente aqueles relacionados a alterações na composição dos glicosaminoglicanos, ainda são pouco compreendidos.

Objetivo: analisar a composição dos glicosaminoglicanos no ligamentum flavum de pacientes com doenças degenerativas da coluna lombar, visando identificar alterações moleculares associadas à hipertrofia do ligamento.

Método: trinta amostras de ligamentum flavum foram obtidas cirurgicamente de pacientes diagnosticados com hérnia de disco lombar ou estenose do canal vertebral. Os glicosaminoglicanos sulfatados foram extraídos, identificados e quantificados por eletroforese em gel de agarose e digestão com glicosidases específicas. A espessura do ligamentum flavum foi medida por meio de imagens de ressonância magnética e análises estatísticas foram realizadas para avaliar as correlações entre a espessura do ligamentum flavum e a composição dos glicosaminoglicanos.

Resultados: foi detectado um aumento significativo nos níveis de condroitim sulfato, correlacionado positivamente com o grau de espessamento do ligamentum flavum. Em contraste, os níveis de dermatam sulfato não apresentaram variações significativas entre os diferentes graus de hipertrofia do ligamentum flavum.

Conclusão: a hipertrofia do ligamentum flavum em condições de degeneração da coluna lombar está associada a alterações específicas na composição dos glicosaminoglicanos, em especial ao aumento do conteúdo de condroitim sulfato. Esses achados sugerem que o condroitim sulfato, um componente altamente aniônico da matriz extracelular, pode desempenhar um papel fundamental na fisiopatologia do espessamento do ligamentum flavum observado nas doenças degenerativas da coluna lombar.

Palavras-chave: estenose lombar, matriz extracelular, chondroitim sulfato, dermatam sulfato, condroitinase ABC.