Email:

conference@houghtonstreetreview.com

Website:

www.houghtonstreetreview.com/index.php/conference

© 2026 International Online Conference on Multidisciplinary Academic Research. All Rights Reserved.

Editor-in-Chief:

Dr. Ewelum Johnson Nnadi

Managing Editors:

1.Harold Jan R. Terano

2.Dr. Mandakini Singla

3.Massoud Kaykhaii








# IMMUNOMORPHOLOGICAL PHENOTYPE OF THE LIGAMENTUM FLAVUM ASSOCIATED WITH PROGRESSIVE POSTOPERATIVE EPIDURAL FIBROSIS IN DEGENERATIVE LUMBAR SPINAL STENOSIS

**Khaydarov Farrukh Nuritdinovich**
doctor_farrukh@mail.ru
https://orcid.org/0009-0001-4402-6259
Bukhara State Medical Institute, Bukhara, Uzbekistan
**Umarov Numonjon Nasirovich**
numonjonumarov@gmail.com
https://orcid.org/0009-0006-5341-6327
National Medical Center, Tashkent, Uzbekistan
**Makhmanazarov Orifjon Mirzonazar ugli**
orif_9292@bk.ru
https://orcid.org/0009-0003-9231-7186
Bukhara State Medical Institute, Bukhara, Uzbekistan
https://doi.org/10.5281/zenodo.22897338

**Abstract.** The study evaluated the preoperative immunomorphological phenotype of the ligamentum flavum in relation to the subsequent course of postoperative epidural fibrosis. Tissue samples were assessed in 40 reference patients and 86 patients with degenerative lumbar spinal stenosis; the latter were retrospectively classified as having a favorable postoperative course (n=54) or progressive epidural fibrosis (n=32). Progressive fibrosis was associated with greater tissue fibrosis, collagen accumulation, loss of elastic fibers, macrophage infiltration, increased SPP1 and TGF-β1 expression, Smad3 activation, and expansion of the α-SMA-positive compartment. A combined high-fibrotic phenotype was present in 40.6% of patients who subsequently developed progressive epidural fibrosis, compared with 11.1% in the favorable-course group.

**Keywords:** ligamentum flavum, lumbar spinal stenosis, epidural fibrosis, SPP1, TGF-β1, CD68, α-SMA, immunohistochemistry.

# УМСТВЕННАЯ РАБОТОСПОСОБНОСТЬ И КАЧЕСТВО СНА КАК ГИГИЕНИЧЕСКИЕ ПОКАЗАТЕЛИ ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ ПОДРОСТКОВ ПРИ ГИБРИДНОМ ОБУЧЕНИИ

**Хайдаров Фаррух Нуритдинович**
doctor_farrukh@mail.ru
https://orcid.org/0009-0001-4402-6259
Бухарский государственный медицинский институт, Бухара, Узбекистан
**Умаров Нуъмонжон Насирович**
numonjonumarov@gmail.com
https://orcid.org/0009-0006-5341-6327
Национальный медицинский центр, Ташкент, Узбекистан
**Махманазаров Орифжон Мирзоназар ўғли**
orif_9292@bk.ru

Email:

conference@houghtonstreetreview.com

Website:

www.houghtonstreetreview.com/index.php/conference

© 2026 International Online Conference on Multidisciplinary Academic Research. All Rights Reserved.

Editor-in-Chief:

Dr. Ewelum Johnson Nnadi

Managing Editors:

1.Harold Jan R. Terano

2.Dr. Mandakini Singla

3.Massoud Kaykhaii








https://orcid.org/0009-0003-9231-7186

Бухарский государственный медицинский институт, Бухара, Узбекистан

**Аннотация.** В исследовании оценивали предоперационный иммуноморфологический фенотип желтой связки в связи с последующим течением послеоперационного эпидурального фиброза. Тканевые образцы были исследованы у 40 пациентов референсной группы и 86 больных с дегенеративным стенозом поясничного отдела позвоночного канала; последние ретроспективно были разделены на подгруппы с благоприятным послеоперационным течением (n=54) и прогрессирующим эпидуральным фиброзом (n=32). Прогрессирование фиброза сопровождалось более выраженным фиброзным ремоделированием ткани, накоплением коллагена, утратой эластических волокон, макрофагальной инфильтрацией, повышением экспрессии SPP1 и TGF-β1, активацией Smad3 и расширением α-SMA-положительного компартмента. Комбинированный высокофибротический фенотип выявлен у 40,6% пациентов, у которых впоследствии развился прогрессирующий эпидуральный фиброз, тогда как в группе с благоприятным течением его частота составила 11,1%.

**Ключевые слова:** желтая связка, стеноз поясничного отдела позвоночного канала, эпидуральный фиброз, SPP1, TGF-β1, CD68, α-SMA, иммуногистохимия.

**Relevance.** Postoperative epidural fibrosis varies considerably among patients undergoing comparable decompressive procedures. The biological state of the hypertrophic ligamentum flavum at the time of surgery may characterize an already established individual fibrotic response and therefore provide information on the risk of subsequent excessive scar formation.

**Objective.** To determine the immunomorphological characteristics of the ligamentum flavum associated with subsequent progression of postoperative epidural fibrosis.

**Materials and Methods.** The analysis included 40 reference patients and 86 patients with degenerative lumbar spinal stenosis. According to subsequent postoperative scar progression, the stenosis group was divided into a favorable-course subgroup (n=54) and a progressive epidural fibrosis subgroup (n=32). Histological morphometry included fibrosis area, collagen matrix, residual elastic-fiber area, elastic-fiber fragmentation, and cellular density. Immunohistochemical assessment included CD68, SPP1, TGF-β1, nuclear p-Smad3, α-SMA, and collagen types I and III.

**Discussion.** Fibrosis area increased from 21.24±1.35% in the reference group to 36.28±1.37% in the favorable-course subgroup and 47.90±1.73% in patients with subsequent progressive epidural fibrosis. Residual elastic-fiber area decreased in the same sequence from 57.66±1.57% to 48.99±1.40% and 40.39±1.58%, respectively. The collagen-to-elastin ratio reached 1.40±0.12 in the unfavorable subgroup.

CD68-positive cell density increased from 28.07±1.06 cells/mm² in reference tissue to 35.12±0.97 and 42.16±1.14 cells/mm². The SPP1 H-score increased from 59.80±3.10 to 83.74±2.39 and 105.35±3.12, whereas the TGF-β1 H-score increased

Email:

conference@houghtonstreetreview.com

Website:

www.houghtonstreetreview.com/index.php/conference

© 2026 International Online Conference on Multidisciplinary Academic Research. All Rights Reserved.

Editor-in-Chief:

Dr. Ewelum Johnson Nnadi

Managing Editors:

1.Harold Jan R. Terano

2.Dr. Mandakini Singla

3.Massoud Kaykhaii








from 69.23±2.68 to 95.14±2.70 and 109.24±2.60. Nuclear p-Smad3 demonstrated a similar gradient: 61.14±2.51, 80.87±2.43, and 95.70±2.69.

The α-SMA-positive interstitial area was greatest in the progressive fibrosis subgroup (15.02±0.69%), compared with 12.77±0.48% in favorable-course patients and 9.60±0.62% in reference tissue. Collagen type I-positive area increased to 47.39±1.34% in the unfavorable subgroup. In contrast, the collagen I/III ratio did not significantly distinguish the groups, indicating that the adverse phenotype was related mainly to the total extent of matrix accumulation rather than to a major shift between these two collagen types.

Preserved elastic architecture was detected in 65.0% of reference patients and 22.2% of patients with a favorable course, but in none of the patients with progressive fibrosis. The combined high-fibrotic phenotype was identified in 13/32 (40.6%) patients with progressive epidural fibrosis, 6/54 (11.1%) with favorable postoperative evolution, and no reference patients.

**Conclusion.** It was established that subsequent progressive epidural fibrosis was preceded by a more pronounced fibrotic and inflammatory remodeling of the ligamentum flavum. It was demonstrated that increased CD68, SPP1, TGF-β1/p-Smad3 activity and expansion of the α-SMA-positive compartment accompanied collagen accumulation and loss of the elastic framework. The combined immunofibrotic phenotype of the ligamentum flavum may be considered a tissue indicator of increased individual susceptibility to excessive postoperative scar formation.

## References

1. Azril A., Huang K.Y., Liu H.Y., et al. Clinical implications of linking microstructure, spatial biochemical, spatial biomechanical, and radiological features in ligamentum flavum degeneration // JOR Spine. 2024;7(3):1365.
2. Fei C., Chen Y., Tan R., et al. Single-cell multi-omics analysis identifies SPP1+ macrophages as key drivers of ferroptosis-mediated fibrosis in ligamentum flavum hypertrophy // Biomark Res. 2025;13(1):33.
3. Hayashi F., Morimoto M., Higashino K., et al. Myofibroblasts are increased in the dorsal layer of the hypertrophic ligamentum flavum in lumbar spinal canal stenosis // Spine J. 2022;22(4):697–704.
4. Jiang C., Wang W., Chen Y.L., et al. Macrophage polarization and macrophage-related factor expression in hypertrophy of the ligamentum flavum // Eur Spine J. 2024;33(12):4476–4487.
5. Lee C.Y., Wu M.H., Huang T.J., et al. Hypertrophic Ligamentum Flavum in Lumbar Spine Stenosis Is Associated With the Increased Expression of Secreted Protein Acidic and Rich in Cysteine // Global Spine J. 2024;14(4):1248–1256.