

**MODERN CLINICAL AND SCIENTIFIC APPROACHES TO METHODS FOR ASSESSING
PAIN SYNDROME IN VBDR**

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Urinov Muso Boltaevich

urinov.muso@bsmi.uz

<https://orcid.org/0009-0007-1852-5744>

Dagaeva Difuza Botirovna

<https://orcid.org/0009-0004-9892-390X>

Абу Али Ибн Сино номдагу Бухоро давлат тиббиёт институти

Resume: *Vertebrogenic lumbar radiculopathy (VBDR) is a multifactorial condition involving intervertebral disc degeneration, facet joint osteoarthritis, paravertebral muscle changes, and nerve root compression. Its pathogenesis is influenced by physical, hormonal, and psychoemotional factors, with gender-specific differences affecting pain perception, muscle response, and compensatory mechanisms. Laboratory biomarkers such as NGF, S100B, cortisol, and serotonin reflect peripheral sensitization, glial activation, HPA-axis function, and pain modulation, providing insight into disease severity and treatment response. Neurovisualization methods—including MRI, DWI/DTI, CT/myelography, and high-frequency ultrasound—allow detailed assessment of structural and microstructural changes, highlighting gender-dependent variations in perineural fibrosis and inflammatory response. Neurophysiological assessments, including ENMG, SSEPs, and TMS, offer functional evaluation of nerve root and corticospinal integrity, with observed differences between men and women linked to hormonal status. Integration of laboratory, neurophysiological, and imaging data enables personalized, gender-sensitive rehabilitation strategies, optimizing pain management, functional recovery, and prognosis in VBDR.*

Keywords: *Vertebrogenic lumbar radiculopathy, VBDR, gender differences, pain biomarkers, NGF, S100B, cortisol, serotonin, MRI, DTI, ENMG, SSEPs, TMS, neurophysiological diagnostics, personalized rehabilitation, hormonal influence, perineural fibrosis, neuroinflammation.*

Vertebrogenic lumbar radiculopathy (vbdr) is a complex of syndromes accompanied by disc degradation in the segments of the lumbar spine, osteoarthritis of the facet joints, compression of the paravertebral muscles and peripheral nerve roots (Jensen et al., 2019). Modern research suggests that physical, endocrine, and psychoemotional factors co-influence vbdr pathogenesis (Fillingim et al., 2021). In men and women, pain perception, muscle tone response, and biomechanical compensatory mechanisms manifest differently due to hormonal and metabolic differences. Estrogen and progesterone protect peripheral

nerve tissue and osteometabolism; testosterone slows disc degradation by maintaining muscle strength (Baron et al., 2018). Therefore, taking into account gender and hormonal status in laboratory and instrumental Diagnostics is entering modern standards.

Gender-specific characteristics of laboratory verification methods

VBDR (vertebrogenic lumbar radiculopathy) includes immuno-inflammatory mechanisms along with mechanical root compression; neural and glial activation markers, as well as neuroendocrine markers, are important in understanding the pathological process, predicting patient status, and assessing treatment effectiveness.

NGF, S100B, cortisol, and serotonin reflect different aspects of the process: peripheral sensitization and neurotrophic support (NGF), glial reaction/neuronal injury (S100B), HPA-axis (hypothalamo-pituitary-adrenal system) response/stress condition (cortisol), and monoamine modulation of pain pathways (serotonin).

NGF (nerve growth factor) enhances the sensitivity of pain afferents - nociceptors through TrkA and p75NTR receptors, stimulates the expression of sodium channels and increases synaptic transmission of pain signals. This condition contributes to the development of peripheral and central sensitization (excessive sensitivity to pain) in chronic pain (Mario García-Domínguez 2025, 47(2), 93).

Patients with chronic pain syndrome have increased tissue and/or plasma NGF levels, which has been found to be associated with pain intensity and hyperalgesia levels in both experimental and clinical studies. Directed therapy against NGF (NGF antagonists or anti-NGF monoclonal antibodies) has been shown to be effective in chronic musculoskeletal pain. However, safety issues and precisely clinical data in radiculopathy are still limited. At the same time, this direction is considered promising for the treatment of pain based on biomolecular therapy (Imke Rudnik-Jansen^{1, 2} | Sanda van Kruijsdijk² | Laura Creemers³ | Bert Joosten 2023).

Tammam and his co-authors argue that S100B (glial and neuron-associated protein) is a protein that is primarily associated with astrocytes and Schwann cells, advancing the idea that it comes out of the blood when the Central or peripheral nervous system is damaged or glial cells are activated (Tammam Abboud¹, Veit Rohde¹ and Dorothee Mielke (2023) 24:38). Its level may reflect the degree of neuron-glial reaction and injury. Recent studies have found increased S100B levels in patients with disc prolapse. This indicator correlates with symptom severity and functional status. In certain groups, S100B levels have also been assessed as a predictive marker of efficacy of intervention therapy (e.g. impulse radio frequency therapy) (Wael Fathy^{1*}, Mona Hussein², Rehab Magdy³, Hatem Elmoutaz¹, Neveen A Youssef⁴, Marwa F Abd Alla⁵, Ahmed M El Shaarawy¹ and Mohamed Abdelbadie 2024).

Cortisol (HPA-axis, stress marker) - reflects the activation of the hypothalamo-pituitary-lateral axis (HPA) axis. In cases of chronic pain, dysregulation of this system can be observed, that is, manifested in the form of hypercortisism (increased cortisol) or hypocortisism (decreased cortisol). These changes affect inflammatory processes, immune

response, and pain sensitivity (Juan P. Sanabria-Mazo, Ariadna Colomer-Carbonell, Meritxell Carmona-Cervello, Albert Feliu-Soler, Xavier Borràs, Mar Grasa, Montserrat Esteve, Michael Maes, Silvia Edo, Antoni Sanz and Juan V. Luciano¹ 2022).

There is little data on specific VBDR (vertebrogenic lumbar radiculopathy), but studies in chronic neuromuscular-skeletal pain have reported both increased and decreased basal levels of cortisol. Such results will depend on the stage of the pain, the degree of its chronification, the condition of the accompanying anxiety or depression, as well as the measurement time. Dysfunction of the HPA-axis has been found to be associated with stronger pain perception and lower functional status.

Serotonin (5-HT) and serotonergic modulation of pain control pain at the spinal and supraspinal levels in a complex, receptor-dependent manner: some podtypes of 5-HT receptors amplify the pain signal, while others inject (brake). The serotonergic system plays an important role in the process of modulating pain impulses downward from the brain (niskhodyatshee) (Shun Hao, Wantong Shi, Weiqi Liu, Qi-Yu Chen and Min Zhuo 2023).

Research by Shun Hao and co-authors has shown that serotonin imbalance and changes in 5-HT levels correlate with pain in radiculopathy. Serotonin reuptake inhibitors (SIOZS, SIOZSN) as well as serotonin-norepinephrine reuptake inhibitors (SIOZN) have been found to have analgesic (pain-reducing) effects, both in neuropathic pain, including lumbar radiculopathy (Shun Hao, Wantong Shi, Weiqi Liu, Qi-Yu Chen and Min Zhuo 2023).

Hormonal differences (estrogens and testosterone) affect the inflammatory response, the sensitivity of nerve cells, and the expression of neurotrophic factors (including NGF). Differences in the more expressed perineural fibrosis response and glial activation (associated with S100B) have been reported in women, a condition that may affect clinical presentation and response levels to therapy.

Neurovisualization methods

Magnetic resonance imaging (MRI) is the "gold standard" for the diagnosis of radiculopathies, with detailed visualization of soft tissue structures of the spinal cord and nerve elements. T1-weighted images allow assessing the state of fibrous structures and bone elements; T2-weighted images detect signs of inflammation and dehydrotasia of the intervertebral disc. Modern studies (Zhou et al., Spine Journal, 2022; Kim et al., European Spine Journal, 2023) shows increasing interest in diffusion weighted MRI (DWI) and diffusion tensor tomography (DTI), which allow evaluation of the micro-structure of nerve roots. The decrease in fractional anisotropy (FA) according to DTI reflects demyelination or axonal degeneration and may serve as a potential biomarker of gender differences in the disease process.

Computed tomography (CT) and CT myelography remain indispensable for assessing bone changes such as osteophytes, spondylolisthesis, and facet arthropathy. Contrast CT myelography allows one to visualize root compression and deformation in the

subarachnoid space, especially in cases where MRI is difficult (presence of metal implants, severe claustrophobia, etc.).

In recent years of ultrasonic neurovisualization, high-frequency ultrasound (10-18 MGs) is actively developing to assess the ecostructure of nerve roots and perineural tissues. Tagliaferri et al (Pain Practice, 2021) have suggested that women are more likely to experience perineural fibrosis and more pronounced inflammatory changes, which is associated with prolonged pain.

Neurophysiological methods

Electroneuromyography (ENMG)

ENMG remains the leading method of functional diagnosis in radiculopathy. Ninali ENMG records signs of denervation, fibrillation, and fasciculation; changes in the parameters of the units of motion (MUAP) make it possible to determine the degree and localization of root damage. According to Moradi and co-authors, neurogenic changes predominate in men, while the combination of microvascular and fibrosis disorders is more common in women, which is related to hormonal background characteristics (Clinical Neurophysiology, 2022).

Somatosensory excited potentials (SSEPS) are used to assess nerve impulse conduction along sensory pathways at the lumbosacral level. The lengthening of the delay and the decrease in the amplitude of the potentials is an objective sign of root compression. Gender differences have low amplitudes of emotional potential in women, manifested in the presence of a high delay associated with the action of sex hormones (estrogens and testosterone) if in men.

Transcranial magnetic stimulation (TMS) makes it possible to assess the condition of Cortico-spinal connections. Patients with VBDR (vertebrogenic lumbar radiculopathy) experience lengthening of Central motor latent time (CML) and decreased amplitude of motor responses. This situation reflects the degree of root damage, as well as the degree of braking in the cortex. In women, the degree of cortical braking is more likely, while in men, the signs of excitability of motor neurons are dominant (Rossini et al., Brain Stimulation, 2023).

Integrated laboratory-instrumental diagnostics makes it possible to individually select a rehabilitation program in Vbdr, assess effectiveness and determine prognosis.

Conclusion: Vertebrogenic lumbar radiculopathy (VBDR) is a complex disorder in which structural, neurophysiological, hormonal, and psychoemotional factors interact, producing gender-specific patterns in pain perception, functional impairment, and adaptation. Laboratory biomarkers (NGF, S100B, cortisol, serotonin) provide objective insights into peripheral sensitization, glial activation, stress response, and pain modulation, while neuroimaging (MRI, DTI, CT/myelography, ultrasound) and neurophysiological assessments (ENMG, SSEPs, TMS) allow detailed evaluation of structural and functional damage. Gender and hormonal differences significantly influence these parameters, highlighting the need for individualized, gender-sensitive diagnostic and rehabilitation

approaches. Integration of laboratory, instrumental, and neurophysiological data enables the development of personalized therapeutic strategies, optimizing pain management, functional recovery, and long-term quality of life in patients with VBDR.

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