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Research Progress on the Correlation Between Lumbar Paraspinal Muscle Fat Infiltration and Degenerative Lumbar Spondylolisthesis

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Abstract: ***Degenerative Lumbar Spondylolisthesis (DLS) is a common spinal degenerative disease that leads to low back pain and leg dysfunction in middle-aged and elderly people. In recent years, more and more attention has been paid to the functional status and morphological changes of lumbar paraspinal muscles, especially multifidus muscles, in the occurrence and development of DLS. As the core pathological feature of paraspinal muscle degeneration, fat infiltration is closely related to the severity, clinical symptoms and prognosis of DLS. This article aims to systematically review the imaging evaluation methods of fat infiltration, its correlation with DLS clinical and imaging parameters, potential interaction mechanisms (including the vicious cycle of inflammation, abnormal innervation, biomechanical imbalance and fat metabolism disorders), and new clinical treatment strategies based on muscle evaluation. Current evidence shows that paraspinal muscle fat infiltration is not only the result of DLS, but also actively participates in the progression of the disease. Therefore, in clinical diagnosis and treatment, it is of great significance to include the status of paraspinal muscles in the evaluation system and explore targeted muscle rehabilitation and protection strategies for improving the prognosis of DLS patients.***

Keywords: Degenerative lumbar spondylolisthesis, Paraspinal muscles, Multifidus muscle, Fatty infiltration, Muscle degeneration, Biomechanics, Magnetic resonance imaging.

1. Introduction

Degenerative lumbar spondylolisthesis (DLS) is a spinal disease that mainly occurs in L4/5 segment and is more common in middle-aged and elderly women. It is characterized by the forward [1]. The pathological basis of degenerative lumbar spondylolisthesis (DLS) is the extensive degeneration of the tri-joint complex such as intervertebral disc and facet joints, leading to segmental instability of the spine. Low back pain is the leading cause of disability worldwide, and DLS is one of the important causes. Although lumbar decompression and fusion surgery is an effective method for the treatment of severe DLS, the high cost and potential complications and sequelae have led researchers to explore earlier intervention [2].

In the past, researchers mostly focused on bony structures (such as spinal stenosis, facet joint hyperplasia) and intervertebral discs. However, as an important support for the dynamic stabilization system of the spine, the health of the paraspinal muscles is very important. Among them, the multifidus muscle is the most critical muscle to maintain the stability of lumbar spine segments due to its single-segment innervation characteristics and the deep position of the short moment arm. The degeneration of paraspinal muscles is mainly characterized by fat infiltration and muscle atrophy, which is called the decline of "muscle mass". A large number of studies have confirmed that the degree of fat infiltration of paraspinal muscles in DLS patients is significantly higher than that in controls without spondylolisthesis. A large sample retrospective study in 2022 further quantified this relationship and found that a larger percentage of spondylolisthesis was significantly associated [3].

Further studies revealed that the relationship between paraspinal muscle fat infiltration and DLS is not a simple causal relationship, but a complex, two-way promoting vicious cycle. Understanding the mechanism of this cycle is of key significance for breaking the cycle and developing new treatment strategies (such as precision rehabilitation and biotherapy). Therefore, this article aims to systematically review the research progress on the correlation between paraspinal muscle fat infiltration and DLS in recent years, from evaluation methods, clinical relevance, internal mechanisms to clinical enlightenment, so as to provide reference for clinical work and follow-up research.

2. Progress in Imaging Evaluation Methods of Lumbar Paraspinal Muscle Fat Infiltration

Accurate and reproducible quantification of the extent of paraspinal muscle fat infiltration is the basis for relevant clinical and mechanism research. The assessment methods have evolved from visual semi-quantitative grading in the early stage to accurate quantitative and functional assessment based on various imaging techniques.

2.1 Visual and Semi-quantitative Assessment Methods This is the Most Convenient Method in Clinical Practice

"Commonly used are modified Goutallier grades (0-4) or similar grades for percentage of fat infiltration area (e.g., grade 0: <10%; grade 1: 10-25%; grade 2: 26-50%; grade 3: >50%) [4]." The method is based on T1-or T2-weighted images of conventional MRI, and the range of fat signal replacing muscle signal is judged by visual inspection. The advantages of this method are that it is fast and intuitive, but it is strong subjectivity, poor repeatability, and difficult to detect subtle changes. It is mainly used for rapid screening and rough stratification of large samples.

2.2 Quantitative Assessment Based on Morphology.

This is the mainstream method of current research, mainly by calculating Fatty Cross-Sectional Area (FCSA) and Total Cross-Sectional Area (TCSA) of muscle infiltration. The ratio of FCSA/TCSA (fat fraction) was calculated.

Measurement technique: Target muscles (e.g., multifidus, erector spinae) were manually or semi-automatically delineated at the mid-disc level on axial T2-weighted images of lumbar spine MRI. By setting the signal intensity threshold, the muscle and fat area were distinguished, and then the fat fraction was calculated. In recent years, the introduction of artificial intelligence (AI) segmentation technology has greatly improved the efficiency and consistency of measurement [5].

Related parameters: In addition to fat fraction, the relative cross-sectional area of muscle (rCSA, usually normalized with reference to the area of the vertebral body at the same level) is a commonly used measure of muscle atrophy. It has been shown that in patients with two-segment DLS, the rCSA of the multifidus and erector spinae muscles from L1/2 to L5/S1 were significantly reduced compared with those in patients with single-segment DLS, suggesting more extensive atrophy [6].

2.3 Advanced Quantitative Imaging Techniques Based on Tissue Properties

This type of technology can go beyond morphology to provide biochemical information of muscle composition and function, which is the current research frontier.

Chemical shift encoded magnetic resonance imaging, such as IDEAL-IQ technology, can noninvasively and accurately quantify the fat fraction and R2* value of tissue, and its accuracy is comparable to magnetic resonance spectroscopy (MRS), which is known as the "gold standard" imaging method for fat quantification. It can also distinguish between intracellular and extracellular lip ids [7].

T2-mapping and diffusion tensor imaging: T2-mapping is sensitive to changes in water molecules in tissues and can indirectly reflect the inflammatory or edema status of muscles. Diffusion tensor imaging can evaluate the microstructure and [8] orientation of muscle fibers.

Blood oxygen level-dependent imaging: BOLD-fMRI can be used to assess the level of oxygenation metabolism during muscle activity and reflect the functional status [9]. (Table 1)

Table 1: Comparison of different imaging assessment methods

Methods of Assessment	Visual/semi-quantitative grading	CT measurement	Conventional MRI morphometry	Advanced quantitative MRI
Main Assessment parameters	Goutallier scale (0-4)	Muscle density (Hounsfield units, HU)	Fat cross-sectional area, totalcross-sectional area, fat fraction, relative cross-sectio nal area	Fat fraction, T2 value, ADC value, BOLD signal
Advantages	Fast, simple, no special post-processing software	The inspection is popular, fast, and has high spatial resolution	No radiation, good soft tissue contrast, accurate quantification	Noninvasive, quantifiable composition and function, and provide biochemical information
Limitations	Highly subjective, poorly repeatable and imprecise	There is radiation, and the resolution of soft tissue is lower than MRI	The processing time and the selection of measurement level affect the results	It requires special sequences, complex post-processing, and long scanning time
Clinical and research Applicability	Rapid clinical screening, large sample epidemiological study	Retrospective study based on CT images	Mainstream methods of clinical research, correlation analysis	Frontier mechanism research and accurate evaluation of therapeutic effect

3. Clinical and Imaging Correlation Between Paraspinal Muscle Fat Infiltration and DLS

A large number of cross-sectional and retrospective studies have confirmed that there is a clear correlation between paraspinal muscle fat infiltration and the presence, severity and clinical symptoms of DLS.

3.1 Correlation with the Presence and Severity of Spondylolisthesis

Compared with the control group without spondylolisthesis, the degree of multifidus muscle fat infiltration in the lesion segment (mostly L4/5) in DLS patients was significantly increased, while the muscle cross-sectional area was significantly decreased. This difference was statistically significant. More importantly, the degree of fat infiltration was positively correlated with the severity of slippage, commonly measured as Meyerding grade or slippage percentage. A 2023 quantitative analysis of 221 patients with L4/5 DLS in the journal Spine showed that percentage of spondylolisthesis was positively correlated with paraspinal muscle fat infiltration and negatively correlated with muscle volume. Multiple linear regression analysis showed that fat infiltration of multifidus muscle was one of the independent factors affecting the degree of spondylolisthesis [10].

3.2 Differences in Muscle Degeneration Patterns Between Single-segment and Two-segment DLS

A study in 2024 conducted an in-depth comparison of the paraspinal muscle degeneration patterns in patients with single-segment and two-segment DLS, revealing that more severe muscle degeneration may be associated with the expansion of the disease range. It was found that the degree of fat infiltration in the multifidus and erector spinae muscles from L1/2 to L5/S1 was higher in patients with two-segment DLS than in patients with single-segment DLS, and the muscle atrophy was also more extensive. This suggests that severe and extensive paraspinal muscle degeneration may lead to the overall mechanical imbalance of the spine, which may promote the disease progression from single segment to double segment [11].

3.3 Relationship with Sagittal Spino-pelvic Alignment

Sagittal spino-pelvic balance is the basis for maintaining normal posture and mechanical conduction. It has been found that the degeneration of paraspinal muscles is closely related to the abnormal sagittal parameters. The lumbar lordosis Angle and sacral slope Angle in DLS patients are usually larger than those without spondylolisthesis. Some studies have shown that the coexistence of reduced lumbar lordosis and herniated disc is more common in patients with more severe fat infiltration of the multifidus muscle. Another study found that fat infiltration of the multifidus and erector spinae muscles at the L5/S1 level was positively correlated with lumbar lordosis in patients with two-level DLS. These seemingly inconsistent results may reflect differences in compensatory mechanisms at different stages or subtypes of the disease, but collectively point to a tight interaction between muscle function and spine morphology [12].

3.4 Correlation with Clinical Symptoms

Paraspinal muscle fat infiltration was correlated with patient pain and dysfunction scores. Although the strength of the association varies across studies, a 2022 systematic review suggested an association between paraspinal muscle morphology and pain and dysfunction in patients with lumbar spinal stenosis. Muscle with severe fat infiltration, whose contraction efficiency and endurance are decreased, cannot effectively stabilize the spine, which may aggravate mechanical pain and affect the onset threshold and recovery of neurological claudication symptoms [13].

4. Discussion on the Mechanism of Interaction Between Paraspinal Muscle Fat Infiltration and DLS: A Vicious Circle

The latest view suggests that the causal relationship between IVDD and paraspinal muscle fat infiltration is not unidirectional, but a complex process that promotes each other and forms a vicious circle. This cycle is mainly driven by the following mechanisms:

4.1 Mechanisms of Paraspinal Muscle Fat Infiltration Promoted by DLS

4.1.1 Mechanisms of inflammatory response

Degenerated intervertebral disc tissue becomes an “inflammatory factor pool”, continuously releasing proinflammatory factors such as tumor necrosis factor-α and interleukin-1β. These factors act on adjacent paraspinal muscles through diffusion or vascular pathways, and activate signaling pathways such as nuclear factor-κB in muscles. On the one hand, they promote muscle protein degradation and lead to atrophy, on the other hand, they induce fibroadipose progenitor cells in muscles to differentiate into adipocytes, resulting in fat infiltration [14]. Animal experiments have confirmed that fatty infiltration of multifidus muscle occurs after intervertebral disc injury, even in the absence of direct nerve compression, and it is synchronous [15] with macrophage infiltration and increased TNF-α expression.

4.1.2 Denervation and abnormal neural control

DLS is often accompanied by stenosis of the spinal canal or lateral recess, which may compress the medial branch of the posterior branch of the spinal nerve innervating the multifidus muscle. Due to the single-level innervation of the multifidus muscle, the compression of the multifidus muscle can easily lead to the dysfunction of the innervation of this segment of the muscle. Denervation rapidly leads to muscle atrophy and eventual replacement by fat and fibrous tissue. Clinical MRI studies have observed signs of fat infiltration in the multifidus muscles innervated by a herniated disc compressing the nerve root within a few weeks.

4.1.3 Apraxia atrophy due to pain

Chronic low back pain is the main symptom of DLS. The pain causes the patient to move less and form a protective posture, which keeps the paraspinal muscles, especially the stabilizing muscles, in a state of “unloading” for a long time. Lacking effective contraction stimulation, muscles will follow the principle of “use in, lose out”, and atrophy and fat infiltration will occur. Long-term bed rest studies have confirmed that lipid accumulation [16] in skeletal muscle occurs rapidly.

4.1.4 Biomechanical imbalance

The loss of disc height, degeneration of facet joints and spondylolisthesis itself change the instantaneous center of rotation of the spinal segments, which reduces the moment arms and force generation efficiency of paraspinal muscles, especially the multifidus muscles. Muscles need to consume more energy to maintain stability, which can easily lead to fatigue and microscopic damage, and accelerate the degeneration process in an inflammatory environment.

4.2 Mechanisms of Paraspinal Muscle Fat Infiltration Exacerbating DLS

4.2.1 Endocrine and paracrine effects of adipose tissue

The infiltrated adipose tissue is not an inert filler, but an active endocrine organ. It secretes large amounts of pro-inflammatory factors and adipokines, such as leptin and adiponectin. These factors can spread to adjacent intervertebral discs, aggravating the inflammatory response of intervertebral disc cells and promoting the degradation of extracellular matrix, thereby accelerating intervertebral degeneration and further weakening spinal stability [17].

4.2.2 Loss of muscle stability

Fat infiltration causes muscle contraction, endurance, and reaction speed to decrease. The failure of the multifidus muscle, which is the core stabilizing muscle, causes the spinal segments to experience abnormal stress during daily activities, which aggravates the facet joint loading and the shear force of the intervertebral disc, thereby promoting the progression of spondylolisthesis.

4.2.3 Abnormal mechanical loading

The failure of hypofunctional paraspinal muscles to provide uniform and coordinated support leads to local stress concentration, which may accelerate endplate degeneration and disc herniation, forming a mechanical vicious cycle [18].

4.3 Vicious Cycle Mechanism of Intervertebral Disc Degeneration (IVDD) and Paraspinal Muscle Fat Infiltration

4.3.1 IVDD/DLS leads to muscle fat infiltration: 1) Inflammatory response: the degenerative intervertebral disc releases TNF-α, IL-1β, etc., activates the NF-κB pathway in the muscle, and induces adipose differentiation [19]. 2) Abnormal innervation: spinal stenosis compresses the posterior ramus of the nerve, leading to denervated atrophy and fatty degeneration of the multifidus muscle [20]. 3) Apraxia atrophy: chronic pain leads to decreased activity, disuse of muscles, and increased lipid deposition. 4) Biomechanical imbalance: spinal instability changes muscle moment arm, reduces work efficiency, and is prone to fatigue and injury [21].

4.3.2 Muscle fat infiltration aggravates IVDD/DLS: 1) The role of adipokines: adipose tissue secrees proinflammatory factors and leptin, which spread to the intervertebral disc and aggravates matrix degradation [22]. 2) Loss of stability: muscle contraction decreased, spinal segmental stability was further reduced, and abnormal stress increased [23]. 3) Abnormal mechanical load: the uneven muscle support leads to local stress concentration and accelerates the degeneration of intervertebral disc and facet joints.

5. The In-depth Understanding of the Relationship Between Paraspinal Muscle Fat Infiltration and DLS is Changing the Traditional Concept of Diagnosis and Treatment, and Giving Rise to New Strategies

5.1 Clinical Evaluation and Prognosis Prediction in the Evaluation of DLS Patients, in Addition to the Conventional Skeletal Structure Imaging, Paraspinal Muscles, Especially the Multifidus Muscles, should be Included in the Evaluation System

1) Comprehensive assessment of the condition: a deeper understanding of the source of the patient's pain and dysfunction (neurological, mechanical, and myogenic).

2) Predicting risk of disease progression: Severe paraspinal muscle degeneration may predict more rapid progression of spondylolisthesis or worse outcome of conservative treatment.

3) To guide surgical decision-making: For patients who are going to undergo surgery, severe fatty infiltration of the multifidus muscle may be associated with postoperative residual back pain and risk of adjacent segment degeneration, suggesting that more aggressive intraoperative muscle protection and postoperative rehabilitation programs may be needed [24].

5.2 New Targets for Treatment Strategies Breaking the Above Vicious Cycle Provides New Ideas for Treatment

1) Precision rehabilitation therapy: traditional lumbar and back muscle training may have limited effect on muscles with severe fat infiltration. In the future, rehabilitation should emphasize early intervention and individualized and targeted neuromuscular control training guided by imaging (such as BOLD-fMRI) to maximize the activation and training of deep stable muscles such as multifidus. Some studies have suggested that swimming training has the potential to reverse fat infiltration and improve function in animal models [24].

2) Anti-inflammatory and metabolic interventions: Drugs targeting inflammatory pathways (such as TNF-α inhibitors) or drugs regulating fat metabolism may theoretically become new options for delaying the co-degeneration of muscle and intervertebral disc, but this needs to be verified by further clinical studies [25].

3) Muscle protection techniques in surgery: In posterior surgery, minimally invasive techniques such as using muscle space approach, reducing electrocoagulation damage to muscle, and fine suture of fascia are very important for protecting the innervation and blood supply of the multifidus muscle and reducing postoperative muscle scarring and atrophy [26].

4) Exploration of new therapeutic techniques: physiotherapy, such as electrical stimulation with interfering currents, has been proposed as a potential approach to improve symptoms and prognosis. Muscle regeneration therapy based on stem cells is also one of the future exploration directions [27] [28].

5.3 Future Research Directions There are Still Many Problems to be Solved in This Field

1) Large-scale, prospective cohort studies are needed to clarify the efficacy of paraspinal muscle degeneration as a predictor of DLS;

2) There is a need to develop more intelligent and automated imaging analysis tools for routine application of muscle assessment in clinical work;

3) There is an urgent need for well-designed randomized controlled trials to verify the effectiveness of different rehabilitation methods and drugs on reversing or delaying paraspinal muscle fat infiltration;

4) To further clarify the specific pathways of signal transmission between muscle and intervertebral disc at the molecular biological level, and to find the key targets for intervention [29,30].

6. Conclusion In Conclusion, Fat Infiltration of Lumbar Paraspinal Muscles, Especially Multifidus Muscles, is a Key Link in the Process of Degenerative Lumbar Spondylolisthesis

A large number of imaging evidence has confirmed that there is a significant correlation between them in severity. The underlying mechanism is a vicious circle composed of inflammatory, neurological, mechanical and metabolic factors interweaving. DLS promotes fat infiltration and atrophy of paraspinal muscles through a variety of ways, and

degenerative muscles in turn aggravate disc degeneration and spinal instability by losing stable function and secreting harmful factors [31].

Therefore, the concept of diagnosis and treatment of modern DLS should be expanded from the simple perspective of “bone-intervertebral disc” to the holistic view of “bone-intervertebral disc-muscle”. Incorporating the assessment of paraspinal muscle status into routine clinical practice and based on this, developing early intervention, precise rehabilitation and muscle protective surgery strategies has important theoretical and practical significance for breaking this vicious cycle and improving the long-term prognosis of patients. Future research should be devoted to treating muscle mass as a modifiable therapeutic target, so as to open up a new path for the prevention and treatment of DLS.

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