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CLINICAL AND IMMUNOBIOCHEMICAL MARKERS AND THEIR CORRELATIONS IN PATIENTS WITH DEGENERATIVE-DYSTROPHIC DISEASES OF THE LUMBAR SPINE

F. Z. Aripkhodjayev,
S. U. Asilova
Independent Researcher, the Head of the Spine Sergery and
Pain Management Department, Akfa Medline Hospital

Abstract
Degenerative-dystrophic diseases of the lumbar spine are associated with impaired immunobiochemical homeostasis, requiring a comprehensive clinical and laboratory assessment. Purpose: To investigate the correlations between immunobiochemical and coagulation parameters in patients with degenerative lumbar spine disorders. Materials and Methods: A total of 102 patients were examined; serum levels of osteocalcin, β-CrossLaps, CRP, VEGF-A, TGF-β1, TNF-α, tPA, and PAI were analyzed along with coagulation indices (PT, APTT, TT, fibrinogen). Results: Significant correlations were revealed between inflammatory, angiogenic, and bone remodeling markers. Elevated CRP, VEGF-A, and TNF-α levels were associated with shortened coagulation times and hypercoagulable tendencies. Conclusion: The imbalance between inflammatory and coagulation systems plays a crucial role in the progression of degenerative spinal disorders.

Keywords: Degenerative spinal diseases; immunobiochemical markers; coagulation; cytokines; VEGF-A; TNF-α; CRP; osteocalcin.

Introduction

Degenerative-dystrophic diseases of the lumbar spine (DDLDLS) are a leading cause of musculoskeletal disorders in military personnel, due to increased physical activity. The chronic course of these diseases is accompanied by severe pain, dysfunction of the spinal segment, and a decrease in quality of life [4, 6, 9, 12]. In recent years, researchers have focused not only on clinical manifestations but also on the study of immunobiochemical markers reflecting bone remodeling, inflammation, and tissue resorption. Identification and analysis of these indicators allows for a deeper understanding of the pathogenesis of the disease and individualized treatment approaches. This is especially important in the context of the use of minimally invasive technologies, including cellular correction methods [2, 5, 8, 10].

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Combining clinical characteristics with immunobiochemical data offers new opportunities for predicting the course of DDZPO. Analysis of correlations between clinical parameters and markers of bone and immune metabolism provides insight into systemic disorders in this patient population. Establishing significant relationships can serve as the basis for developing new diagnostic and therapeutic strategies. In military medicine, this is particularly important, as it not only improves treatment effectiveness but also accelerates the rehabilitation of military personnel, reducing the time it takes to restore their combat readiness [1, 3, 7, 11].

To conduct a correlation analysis between clinical and immunobiochemical parameters, we selected 30 patients with a history of repeated surgical procedures.

Purpose of the study: to study the correlations of immunobiochemical markers in patients with degenerative-dystrophic diseases of the lumbar spine.

Materials and methods of research:

To achieve this goal, a comprehensive clinical, laboratory, and instrumental examination of 102 patients aged 27 to 90 years with lumbar intervertebral disc herniations was conducted in 2023–2024. Following surgical treatment, the patients were divided into two groups depending on the PEEK cage filler used: the first group included 52 patients who received a βTCR/BMAC combination, while the second group included 50 patients who received βTCR alone. The diagnosis was based on clinical and functional criteria in accordance with the International Classification of Diseases (ICD-10) and confirmed by the results of a comprehensive examination, including anamnesis, clinical examination, laboratory (general and biochemical blood tests, urinalysis) and instrumental methods (X-ray, CT, MSCT, ECG, echocardiography). Particular attention was paid to the duration of the pathological process, as well as the presence of concomitant and previously suffered diseases.

Dynamic observation was carried out in a hospital and outpatient clinic setting at 3, 6, 12, and 24 months postoperatively. To assess bone remodeling processes, serum osteocalcin (OC) and type I collagen degradation products (β-CrossLaps) levels were determined using a HITACHI 911 automated analyzer (Roche Diagnostics, Germany) and reagents from Cormay (Poland). Concentrations of C-reactive protein (CRP), vascular endothelial growth factor (VEGF-A), transforming growth factor β1 (TGF-β1), tumor necrosis factor α (TNF-α), tissue plasminogen activator (tPA), and plasminogen activator inhibitor (PAI) were determined by enzyme-linked immunosorbent assay using the Protein Contour and Cytokine test kits (St. Petersburg, Russia). Statistical data processing was performed using IBM SPSS Statistics 23. Standard Shapiro–Wilk and Kolmogorov–Smirnov tests were used to assess the normality of distribution. In cases of normal distribution, differences between samples were assessed using the Student t-test; in cases of non-normal distribution, the Mann–Whitney U-test was used. Correlations between indicators were determined using the Pearson method, calculating the r coefficient and its statistical significance.

Research results:

Studying correlations between immunological parameters and bone resorption markers is of significant scientific and practical interest in degenerative diseases of the lumbar spine. Such data allows us to identify the pathogenetic mechanisms underlying the progression of destructive processes. The importance of this analysis lies in its ability to predict the course of the disease and evaluate the effectiveness of therapeutic interventions.

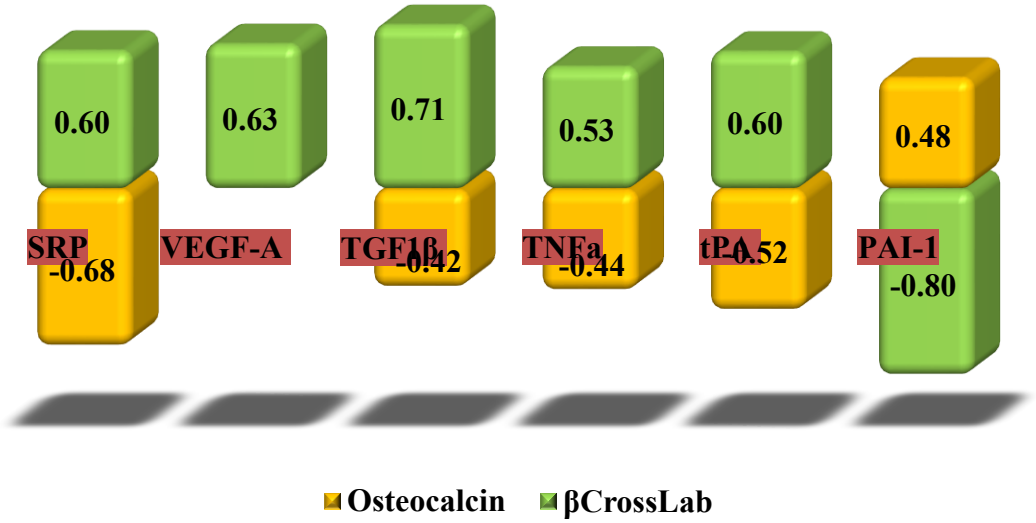

Fig. 1. Correlation links between bone resorption markers and immunological ones (P≤0.05)

A correlation analysis revealed significant associations between bone metabolism markers (osteocalcin, β-CrossLaps) and indicators of inflammation, angiogenesis, and fibrinolysis. The most significant correlations were found for C-reactive protein (CRP), VEGF-A, TGF-β1, TNF-α, tPA, and PAI-1. The presence of both positive and negative associations indicates a complex interaction between bone remodeling processes and immune-inflammatory mechanisms in patients with degenerative diseases of the lumbar spine.

The negative correlation between osteocalcin and CRP (r=–0.68) suggests that increased systemic inflammation is accompanied by a decrease in osteogenic activity. This can be explained by the suppressive effect of proinflammatory cytokines on osteoblast function, which slows bone formation. Conversely, β-CrossLaps correlates positively with CRP levels (r=0.60), reflecting increased bone resorption in the presence of inflammation. Thus, inflammation is a key factor shifting the balance of bone remodeling toward catabolism.

The relationship between bone turnover markers and VEGF-A, which reflects angiogenesis processes, is intriguing. A positive correlation was found between β-CrossLaps and VEGF-A (r = 0.63), indicating that active bone resorption is accompanied by stimulation of vascular growth. This may reflect a compensatory mechanism aimed at ensuring adequate blood supply to remodeling bone tissue. At the same time, elevated VEGF-A levels may enhance the inflammatory response, further exacerbating bone destruction.

The negative correlation of osteocalcin with TGF-β1 (r = –0.42) and TNF-α (r = –0.44) confirms the suppressive effect of inflammatory and fibrogenic factors on osteoblastic activity. Concurrently, β-CrossLaps demonstrates a strong positive correlation with TGF-β1 (r = 0.71) and a moderate positive correlation with TNF-α (r = 0.53). These data indicate that increased levels of these cytokines are accompanied by increased bone matrix degradation. Thus, inflammation and fibrotic remodeling are key components of pathological bone metabolism in DDD.

Fibrinolysis parameters are particularly important. Osteocalcin correlates negatively with tPA (r = –0.52), while β-CrossLaps is positively associated with this marker (r = 0.60). These data suggest that activation of the fibrinolytic system is associated primarily with increased bone resorption rather than bone formation. This may be due to the overall activation of catabolic processes, which simultaneously destroy both bone and extracellular matrix.

The strongest correlation between β-CrossLaps and PAI-1 was found (r = –0.80). This finding indicates that inhibition of fibrinolysis is associated with decreased bone resorption. Presumably, excessive inhibition of fibrinolysis prevents the breakdown of the extracellular matrix, limiting osteoclast activity. In contrast, osteocalcin correlates positively with PAI-1 (r = 0.48), which may reflect the association of bone formation processes with an increased susceptibility to thrombosis and fibrosis (Fig. 1).

Thus, the identified correlations confirm the complex interplay between inflammatory, angiogenic, and fibrinolytic mechanisms and bone remodeling processes in degenerative diseases of the spine. Inflammation and angiogenesis enhance bone resorption, while osteoblast activity is suppressed by cytokines. The fibrinolytic system plays a dual role, influencing both catabolic and anabolic processes. These data allow us to consider immunobiochemical markers as potential predictors of the disease course and the effectiveness of therapy.

We further studied the interactions between immune markers and coagulation system parameters, which is particularly important in lumbar disc herniations. Chronic inflammation and tissue destruction are accompanied by activation of coagulation and fibrinolytic mechanisms, reflecting the systemic nature of the pathological process. Correlation analysis allows us to identify which immunological factors have the greatest impact on the development of hypercoagulability or, conversely, on the activation of fibrinolysis. These data provide an important basis for prognosticating the disease course and optimizing combination therapy in this patient population.

The results of the correlation analysis demonstrate significant negative relationships between the coagulation hemostasis parameters (PT, APTT, TT) and key immunological markers. Thus, prothrombin time (PT) is inversely associated with the levels of C-reactive protein (r = –0.56), VEGF-A (r = –0.65), TGF-1β (r = –0.62), TNF-α (r = –0.31), and especially with tissue plasminogen activator (tPA, r = –0.75). A positive correlation was found with plasminogen activator inhibitor (PAI-1, r = 0.73), indicating an increase in prothrombotic tendencies with activation of the inflammatory cascade. These data suggest that inflammatory and angiogenic mediators directly affect the reduction of blood clotting time, forming a hypercoagulable background.

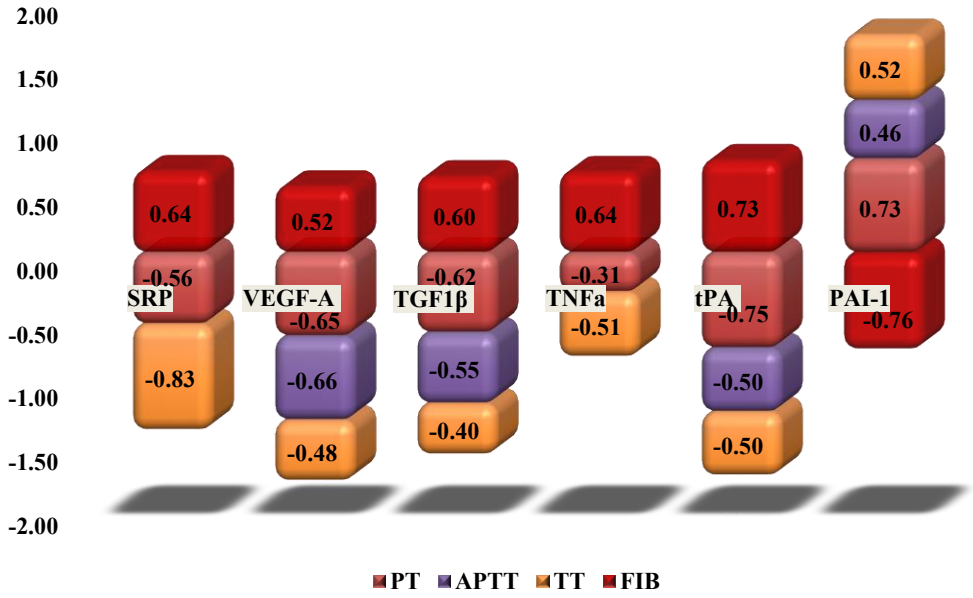

Fig. 2. Correlation links between immunological and blood coagulation markers, (P≤0.05)

Analysis of the activated partial thromboplastin time (APTT) relationship also revealed significant correlations with immune factors. Negative correlations were recorded with VEGF-A (r = –0.66), TGF-1β (r = –0.55), and tPA (r = –0.50), confirming activation of the coagulation system under conditions of increased expression of these mediators. Furthermore, the positive correlation of APTT with PAI-1 (r = 0.46) emphasizes the inhibitor's role in stabilizing the prothrombotic state. These data indicate that inflammatory and angiogenic signals lead to accelerated blood clotting and an imbalance between coagulation and fibrinolysis. This may explain the predisposition of patients with intervertebral disc herniations to microcirculatory disorders.

Thrombin time (TT) exhibits the most pronounced negative correlations among all coagulation parameters. Thus, a decrease in TT is associated with increased levels of CRP (r = –0.83), VEGF-A (r = –0.48), TGF-1β (r = –0.40), TNF-α (r = –0.51), and tPA (r = –0.50) (Fig. 2). A positive correlation with PAI-1 (r = 0.52) confirms its involvement in the suppression of fibrinolytic activity and the formation of a stable thrombotic state. Taken together, this demonstrates that with high activity of inflammatory and angiogenic markers, the coagulation cascade is activated at an accelerated rate. This pattern may reflect the pathogenetic role of chronic inflammation in the generation of hypercoagulability syndrome.

Fibrinogen (FN) deserves special attention, demonstrating opposite correlations with immune and coagulation parameters. It is positively associated with CRP (r = 0.64), VEGF-A (r = 0.52), TGF-1β (r = 0.60), TNF-α (r = 0.64), and tPA (r = 0.73), indicating its close dependence on the inflammatory and angiogenic status. A negative correlation with PAI-1 (r = –0.76) was

revealed, suggesting that fibrinolytic activity is more pronounced at high fibrinogen concentrations.

The overall pattern of identified associations suggests that patients with lumbar disc herniations exhibit a pronounced interaction between inflammatory-immune and coagulation mechanisms. Increased inflammation, characterized by increased CRP and TNF-α, is associated with the activation of angiogenic factors (VEGF-A, TGF-1β), leading to accelerated blood clotting. Furthermore, the activity of the fibrinolytic system (tPA) manifests itself in ambiguous ways: on the one hand, it accelerates fibrin degradation, but on the other, it is accompanied by a compensatory decrease in PAI-1, limiting this process. This combination of factors creates a state of chronic hypercoagulability with a risk of thrombotic complications (Fig. 5.4).

Conclusion:

The results of the correlation analysis support the hypothesis of a relationship between immune markers of inflammation and angiogenesis and impaired coagulation homeostasis. The combination of elevated levels of CRP, VEGF-A, TGF-1β, TNF-α, and tPA with shortened coagulation parameters (PT, APTT, TT) reflects the development of an unfavorable prothrombotic profile. Concurrently, decreased PAI-1 levels further perpetuate the hypercoagulable state. These changes have not only diagnostic but also prognostic value, allowing one to assess the risk of vascular complications in this patient population.

A correlation analysis revealed close relationships between immunological markers of inflammation, angiogenesis, and coagulation system parameters in patients with lumbar disc herniations. Increased levels of CRP, VEGF-A, TGF-1β, TNF-α, and tPA are associated with increased coagulation parameters (PT, APTT, and TT), indicating the development of a hypercoagulable state. Concurrently, a compensatory decrease in PAI-1 reflects a tendency toward limited fibrinolytic activity, which perpetuates a prothrombotic background.

In the context of surgical treatment, particularly in transforaminal lumbar interbody fixation (TLIF) procedures, these changes acquire particular clinical significance. Modern approaches utilize mesenchymal stem cells, which possess not only osteoinductive and osteoconductive potential. When used in combination with correction of immune and coagulation disorders, this opens new prospects for increasing the effectiveness of surgical treatment and improving long-term outcomes in this patient population.

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