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MARKERS OF MICROCIRCULATORY INSUFFICIENCY AND IMMUNE DYSFUNCTION IN THE PROGNOSIS OF SEPSIS IN DIABETIC FOOT SYNDROME

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Boymurodov Khasan Abdurakhmonovich
Tashkent State Medical University

Abstract

Diabetic foot syndrome (DFS) is one of the most severe and socially significant complications of diabetes mellitus, characterized by a high frequency of infectious processes, prolonged wound healing, risk of amputation, and mortality. According to various studies, infectious complications in DFS occur in 40–60% of patients and are often complicated by systemic inflammatory response and sepsis, which significantly worsens prognosis and increases hospital mortality rates.

Microcirculatory disturbances and immune dysfunction play a key role in the pathogenesis of infectious complications in diabetic foot. Diabetic microangiopathy leads to reduced tissue perfusion, hypoxia, and impaired delivery of oxygen and nutrients, creating favorable conditions for infection progression and necrotic changes. At the same time, patients with diabetes mellitus exhibit significant defects in innate and adaptive immunity, including neutrophil and macrophage dysfunction, cytokine imbalance, and decreased phagocytic activity.

Modern concepts of sepsis pathogenesis in DFS consider it a result of the combined impact of local ischemic changes and systemic immune dysregulation. However, clinical diagnosis of early-stage sepsis in this patient population remains challenging because classical signs of systemic inflammatory response may be attenuated or atypical against the background of chronic hyperglycemia and comorbidities. Therefore, identifying objective laboratory and instrumental markers that reflect the degree of microcirculatory insufficiency and immune dysfunction, and allow early sepsis risk stratification, is particularly relevant.

The use of microcirculatory markers (tissue perfusion parameters, lactate levels, endothelial dysfunction indicators) combined with immunological and inflammatory markers can improve the accuracy of predicting septic complications and support timely adjustment of therapeutic strategies. Given the increasing prevalence of diabetes and the growing number of patients with complicated DFS, this research direction has significant clinical and practical importance.

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Thus, studying markers of microcirculatory insufficiency and immune dysfunction in predicting sepsis in patients with DFS is a current scientific and clinical task aimed at improving treatment outcomes and reducing the incidence of severe complications.

Keywords

diabetic foot syndrome; microcirculatory insufficiency; immune dysfunction; sepsis; risk stratification; infectious complications; diabetic microangiopathy; inflammatory response.

Introduction

Diabetic foot syndrome (DFS) remains one of the most severe and clinically significant forms of chronic diabetes complications, characterized by a high frequency of infectious and necrotic lesions, progressive course, and unfavorable outcomes. Epidemiological studies report that 15–25% of patients with diabetes develop trophic foot ulcers during their lifetime, and more than half of these cases are complicated by bacterial infection, significantly increasing the risk of systemic inflammatory response, sepsis, and multiple organ failure. Despite advances in surgical and medical treatments, mortality in complicated DFS, particularly in septic conditions, remains consistently high.

The leading role in the pathogenesis of infectious complications in DFS is played by significant microcirculatory disturbances caused by diabetic microangiopathy and endothelial dysfunction. Chronic hyperglycemia leads to structural and functional changes in the microvascular bed, including thickening of capillary basement membranes, decreased capillary density, increased vascular permeability, and impaired regulation of vascular tone. These changes are accompanied by tissue hypoxia, metabolic acidosis, and accumulation of anaerobic metabolism products, creating favorable conditions for colonization and invasion by pathogenic microorganisms and hindering effective wound healing.

Another significant factor in infection progression in DFS is immune dysfunction. Patients with diabetes exhibit impairments in both innate and adaptive immunity, manifested by decreased neutrophil chemotaxis and phagocytic activity, impaired macrophage function, imbalance between pro- and anti-inflammatory cytokines, and changes in humoral immunity. Against the background of microcirculatory insufficiency and tissue ischemia, these immune disturbances acquire a systemic character, promoting infection generalization and sepsis development.

Modern sepsis concepts describe it as a life-threatening condition caused by dysregulated immune response to infection, accompanied by tissue perfusion

impairment and organ dysfunction. Patients with DFS represent a high-risk group for sepsis development, requiring particular attention to early diagnosis and prediction of adverse outcomes. However, clinical manifestations of sepsis in this population are often subtle, and traditional clinical and laboratory criteria may be insufficiently sensitive and specific in the early stages.

Recently, there has been growing interest in studying markers of microcirculatory insufficiency and immune dysfunction as potential tools for early sepsis diagnosis and risk stratification. Tissue perfusion parameters, lactate levels, endothelial dysfunction markers, and immunological and inflammatory biomarkers may reflect the severity of pathophysiological changes and serve as prognostic indicators of infection severity. Comprehensive assessment of these parameters allows not only accurate risk evaluation but also optimization of intensive therapy, surgical interventions, and antibiotic treatment strategies.

Thus, investigating markers of microcirculatory insufficiency and immune dysfunction in predicting sepsis in DFS is a timely and clinically relevant task aimed at reducing severe complications, improving patient survival, and enhancing the effectiveness of comprehensive treatment.

Materials and Methods

The study was conducted at the 2nd Surgical Intensive Care Unit of Tashkent State Medical University and had a prospective observational design. Patients with type 2 diabetes mellitus hospitalized with clinically confirmed DFS complicated by infectious and inflammatory processes of varying severity were included.

A total of 22 patients were enrolled, hospitalized between 2024 and 2025. The mean age was 58 ± 1.2 years. DFS diagnosis was based on clinical evaluation, laboratory, and instrumental studies in accordance with national and international guidelines.

Inclusion and Exclusion Criteria

Inclusion: type 2 diabetes mellitus; clinical signs of DFS with infection; age over 18 years; informed consent.
Exclusion: oncological diseases; immunodeficiency; decompensated terminal chronic diseases; refusal to participate.

Clinical Examination

All patients underwent a comprehensive clinical evaluation, including assessment of general condition, hemodynamic parameters, local infection severity, and soft tissue/bone involvement of the foot. Severity was assessed using standard scales and criteria, including systemic inflammatory response and organ dysfunction. Sepsis was diagnosed according to Sepsis-3 criteria.

Microcirculation Assessment

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Microcirculatory insufficiency was assessed using clinical and laboratory markers of tissue perfusion: blood lactate levels, acid-base balance, and, where available, peripheral circulation parameters (Doppler ultrasonography, transcutaneous oxygen tension, capillaroscopy).

Immunological and Laboratory Studies

Immune status was evaluated via complete blood count, biochemical analysis, and measurement of inflammatory and immune biomarkers, including C-reactive protein (CRP), procalcitonin (PCT), interleukin-6, and tumor necrosis factor-alpha.

Microbiological Studies

All patients underwent microbiological examination of wound exudate, pathogen identification, and antibiotic sensitivity testing to guide therapy and assess the relationship with sepsis development.

Statistical Analysis

Data were expressed as mean ± SD. Parametric or non-parametric tests were applied depending on distribution. Correlation analyses were performed between microcirculatory and immune markers and sepsis risk. Differences were considered significant at $p < 0.05$.

Ethical Considerations

The study complied with the Helsinki Declaration. The protocol was approved by the local ethics committee. All patients provided informed consent.

Results

The study included 22 patients with type 2 diabetes and DFS complicated by infection. Mean age was 58 ± 1.2 years; males predominated.

Patient Characteristics

Table 1. Clinical and Demographic Characteristics (n = 22)

Parameter	Value
Age, years (M ± SD)	58 ± 1.2
Male, n (%)	14 (63.6%)
Female, n (%)	8 (36.4%)
Diabetes duration, years	11.3 ± 2.1
Coronary artery disease, n (%)	12 (54.5%)
Hypertension, n (%)	16 (72.7%)

Infection Severity

Table 2. Infection Severity in DFS

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Severity	Patients, n (%)
Mild	5 (22.7%)
Moderate	10 (45.5%)
Severe	7 (31.8%)

Microcirculatory Markers

Table 3. Microcirculation Parameters

Parameter	Mean Value
Blood lactate, mmol/L	2.8 ± 0.4
Metabolic acidosis, n (%)	9 (40.9%)
Clinical signs of hypoperfusion, n (%)	11 (50%)

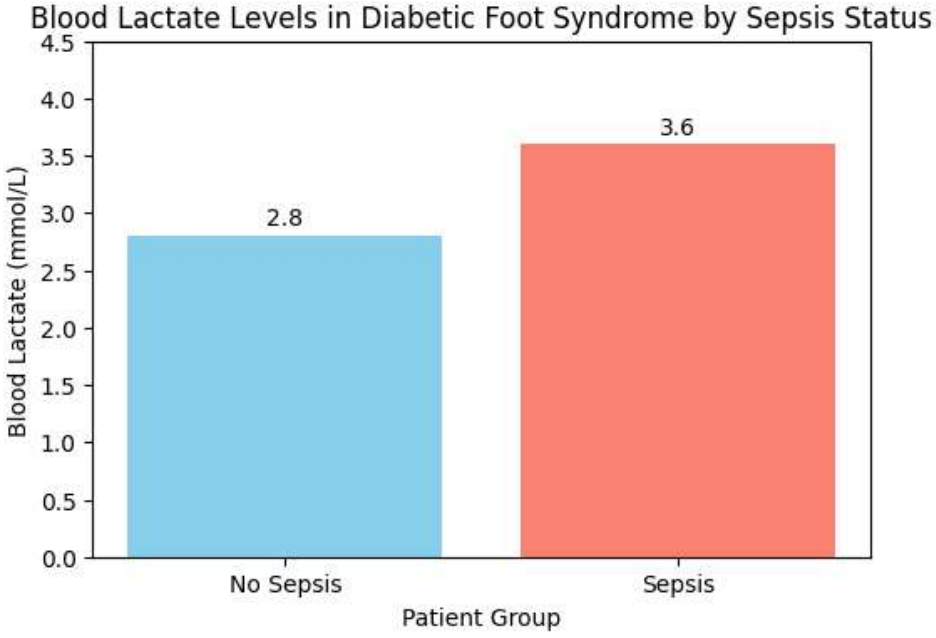

Figure 1. Blood Lactate Levels in Diabetic Foot Syndrome by Sepsis Status

Patients with sepsis had higher lactate levels, reflecting pronounced tissue hypoperfusion and microcirculatory insufficiency. Elevated lactate may serve as a prognostic marker for septic complications.

Immune and Inflammatory Markers

Table 4. Immune and Inflammatory Markers

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Parameter	Mean (M ± SD)
CRP, mg/L	96.4 ± 12.7
PCT, ng/mL	1.9 ± 0.5
Leukocytes, ×10⁹/L	13.6 ± 1.8

Sepsis Development

Sepsis was diagnosed in 6 patients (27.3%). This group demonstrated combined microcirculatory insufficiency and immune dysfunction, confirming their prognostic value.

Table 5. Sepsis Incidence

Parameter	n (%)
No sepsis	16 (72.7%)
Sepsis	6 (27.3%)

Correlation analysis revealed a significant positive relationship between lactate, PCT, and sepsis risk ($r > 0.5$, $p < 0.05$).

Conclusions

1. Patients with DFS and infection exhibit pronounced microcirculatory disturbances, manifested by tissue hypoperfusion and elevated blood lactate.
2. Immune and inflammatory dysfunction, including elevated CRP, PCT, and leukocytosis, correlates with infection severity and sepsis risk.
3. Sepsis occurred in 27.3% of patients, accompanied by combined microcirculatory and immune dysregulation.
4. Blood lactate and PCT levels have significant prognostic value for sepsis risk stratification in DFS.
5. Comprehensive assessment of microcirculatory and immune markers enables early identification of high-risk patients and informs intensive therapy and surgical management.

REFERENCES:

1. Armstrong D.G., Boulton A.J.M., Bus S.A. Diabetic foot ulcers and their recurrence. *N Engl J Med*. 2017;376(24):2367–2375.
2. Lipsky B.A., Senneville É., Abbas Z.G. et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes. *Diabetes Metab Res Rev*. 2020;36(S1):e3280.

3. Edmonds M., Manu C., Vas P. The current burden of diabetic foot disease. *J Clin Orthop Trauma*. 2021;17:88–93.

4. Singer M., Deutschman C.S., Seymour C.W. et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801–810.

5. Hotchkiss R.S., Moldawer L.L. Dysregulated host response to infection in sepsis. *Nat Rev Immunol*. 2014;14(3):193–206.

6. Ince C., Mayeux P.R., Nguyen T. et al. The endothelium in sepsis. *Shock*. 2016;45(3):259–270.

7. Schaper N.C., van Netten J.J., Apelqvist J. et al. IWGDF Guidelines on the prevention and management of diabetic foot disease. *Diabetes Metab Res Rev*. 2020;36(S1):e3269.

8. Frykberg R.G., Banks J. Challenges in the treatment of chronic wounds. *Adv Wound Care*. 2015;4(9):560–582.

9. Game F., Jeffcoate W. The role of neuropathy and ischemia in diabetic foot infection. *Diabetes Metab Res Rev*. 2016;32(S1):S84–S91.

10. Vincent J.L., Dubois M.J., Schmit X. et al. The value of blood lactate kinetics in critically ill patients. *Crit Care*. 2008;12(6):R163.

11. Pierrakos C., Vincent J.L. Sepsis biomarkers: a review. *Crit Care*. 2010;14(1):R15.

12. Delamaire M., Maugendre D., Moreno M. et al. Impaired leukocyte functions in diabetic patients. *Diabet Med*. 1997;14(1):29–34.

13. Falanga V. Wound healing and its impairment in the diabetic foot. *Lancet*. 2005;366(9498):1736–1743.

14. Kumar A., Roberts D., Wood K.E. et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in septic shock. *Crit Care Med*. 2006;34(6):1589–1596.

15. Blatun L.A., Paskhalova Yu.S. Infectious complications of diabetic foot syndrome. *Surgery*. 2019;7:45–52.