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НОВЫЙ ДЕНЬ В МЕДИЦИНЕ  
NEW DAY IN MEDICINE**

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## ИСХОДЫ ТЕЧЕНИЯ НЕКРОБИОТИЧЕСКОГО ПРОЦЕССА МЯГКИХ ТКАНЕЙ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ

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### ✓ Резюме

*Сочетание цитологических индексов и экспресс микробиологических признаков позволяет сформировать надежный набор критериев, которые отражают ключевые механизмы развития некробиотического процесса при некротизирующих инфекциях мягких тканей у больных сахарным диабетом.*

*Ключевые слова: некротизирующие инфекции мягких тканей, прогнозирование, сахарный диабет*

## QANDLI DIABET BILAN OG'RIGAN BEMORLARDA YUMSHOQ TO'QIMALARNING NEKROBIOTIK JARAYONINING KECHISHINI YAKUNLARI

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### ✓ Rezyume

*Sitologik indekslar va tezkor mikrobiologik belgilarning kombinatsiyasi bizga diabet bilan og'rigan bemorlarda nekrotik yumshoq to'qimalar infeksiyalarida nekrobiotik jarayonning rivojlanishining asosiy mexanizmlarini aks ettiruvchi ishonchli mezonlar to'plamini shakllantirish imkonini beradi..*

*Kalit so'zlar: Nekrotik yumshoq to'qimalar infeksiyalari, prognoz, diabet*

## OUTCOMES OF THE COURSE OF THE NECROBIOTIC PROCESS OF SOFT TISSUE IN PATIENTS WITH DIABETES MELLITUS

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### ✓ Resume

*The combination of cytological indices and rapid microbiological signs allows us to formulate a reliable set of criteria that reflect the key mechanisms of the development of the necrobiotic process in necrotizing soft tissue infections in patients with diabetes mellitus.*

*Keywords: necrotizing soft tissue infections, prognosis, diabetes mellitus*

### Актуальность

Large international studies highlight that the prevalence of necrotizing infections continues to rise, and mortality rates remain high even with the use of modern intensive care methods. According to the Surgical Infection Society of North America (SISNA), 30-day mortality from severe forms of NIST associated with significant comorbidities reaches approximately 18-22%, and 1-year mortality exceeds 30%, highlighting the severity of the pathology and the significant burden on healthcare systems. (1,3,5,8).

This issue is particularly significant because traditional treatment methods (wide and aggressive necrosectomy, multi-stage CGO, and extensive tissue excisions) do not always lead to the expected improvement in patients with diabetes. Removing large volumes of tissue in these patients often impairs microcirculation, provokes secondary ischemia, and promotes the further development of necrobiotic changes. This fact has been repeatedly confirmed by both international and domestic studies (2, 4, 6). It has been noted that the risk of amputation in patients with diabetes and NF increases almost twofold compared to patients without diabetes, and mortality in NM reaches the highest levels among all soft tissue infections. Under these conditions, the surgeon faces a dilemma: insufficient necrosectomy can lead to the preservation of an active soft tissue transition zone, while excessive excision can lead to critical tissue loss and the body's reserve capacity, not to mention the need for a prolonged postoperative recovery period due to impaired healing.

An additional challenge is the lack of universal tools that allow for an objective assessment of the intensity of the necrobiotic process early on and the monitoring of the transition zone (7, 9, 10).

In this regard, the implementation of integrated approaches combining early risk stratification, objective assessment of microcirculation, rapid cytology, and modern physical methods of local intervention is particularly important. Such technologies not only allow for a more accurate determination of the extent of primary necrosectomy but also provide differentiated subsequent management strategies, which is especially important in patients with diabetes, who have limited tissue reparative capacity. Thus, the issue of early diagnosis and comprehensive differentiated treatment of severe forms of NIST in patients with diabetes remains relevant at the global, regional, and national levels. The development of prognostic criteria, optimization of the extent of surgical intervention, and the integration of modern local intervention methods can significantly improve treatment outcomes, reduce the incidence of amputations and mortality, and ensure more efficient use of healthcare resources..

**Purpose of the study:** development of methods for predicting the course of the necrobiotic process of soft tissues in patients with diabetes mellitus.

### **Materials and methods**

The clinical material consisted of 128 patients with diabetes mellitus who were treated and examined for severe forms of NIST at a multidisciplinary medical center in the Bukhara region from 2016 to 2025. In accordance with the study's objectives and goals, all patients were divided into two groups. The control group included 63 patients treated between 2016 and 2020, when the traditional approach to treating necrotizing lesions was used. The study group included 65 patients observed between 2021 and 2025, when the comprehensive LDA approach we developed was used. This division allowed us to compare the disease course and clinical outcomes during different periods of organizational and technological development of the surgical service, as well as to objectively evaluate the impact of the proposed approach on the dynamics of the necrobiotic process.

The gender distribution of patients in the two groups was similar, although some differences were still observed (Table 2.1). Thus, the control group included 25 women (39.7%) and 38 men (60.3%), while in the study group the proportion of men was slightly higher, amounting to 41 (63.1%) and 24 women (36.9%).

Overall, the composition of patients included in the study reflected the typical clinical profile of patients with severe forms of NSTI associated with diabetes. The sample included individuals of various ages, with a predominance of older patients and a significant duration of the underlying disease. Concomitant disorders, metabolic status characteristics, and the distribution of etiologic factors formed a stable profile of clinical material, which allowed us to characterize both the initial conditions for the onset of the infection and the associated conditions influencing its course. This dataset provided sufficiently comprehensive initial clinical data for subsequent analysis and comparison of treatment outcomes..

### **Results and discussion**

The data obtained showed that increasing degrees of soft tissue necrobiosis are accompanied by significant changes in the cytological characteristics of the imprint smears. Taken together, this forms

a consistent transition from the intact periphery to the questionable zone and then to the formed necrotic lesion, as reflected in the Spearman rank coefficients.

In the group of primary indices, four indicators stood out as demonstrating the closest correlation with the progression of the necrobiotic process. The IDN had a strong positive correlation coefficient ( $r=0.919$  at  $p<0.001$ ), reflecting the sequential destruction of polymorphonuclear cells as tissue dies. The IGN also demonstrated a pronounced linear correlation ( $r=0.798$  at  $p<0.001$ ), consistent with the increase in the volume of detritus and lysis of cellular structures in more severe areas. Comparable behavior was demonstrated by the MCI ( $r=0.731$  at  $p<0.001$ ), indicating an increasing imbalance between the microbial mass and the number of protective cells. The last of the leading markers, the tissue destruction index, showed a stable positive correlation ( $r=0.835$  at  $p<0.001$ ), emphasizing the direct relationship between the volume of fibrous framework destruction and the severity of necrobiosis.

Other indicators demonstrated moderate correlations, with the total neutrophil count increasing toward the lesion center with a coefficient of  $r=0.467$  ( $p=0.004$ ). The amount of cellular debris showed a similar pattern ( $r=0.493$  at  $p=0.003$ ). The density of microbial masses showed a moderate direct relationship ( $r=0.416$  at  $p=0.010$ ). Individual cytological elements, on the other hand, decreased as necrobiosis worsened. These included macrophages ( $r=-0.357$  at  $p=0.018$ ) and IFO ( $r=-0.558$  at  $p=0.001$ ), highlighting a decrease in phagocytosis activity and depletion of the macrophage reserve in the zone where necrobiosis processes predominate.

As the degree of soft tissue necrobiosis intensified, the structure of the microbial flora changed consistently, reflecting a transition from a relatively preserved periphery to a zone of severe destruction. The weakest correlations were observed among Gram (+) forms. The proportion of Gram (+) cocci had a negative correlation coefficient ( $r=-0.412$  at  $p=0.011$ ), indicating a decrease in their role as they move toward zones of deeper destruction. Gram (+) rods demonstrated similar dynamics ( $r=-0.365$  at  $p=0.023$ ). All of these reflect a tendency for early aerobic colonizers to be displaced by growing gram-negative and anaerobic flora.

More pronounced changes were observed among gram-negative forms, with the proportion of gram-negative cocci increasing moderately, as evidenced by an  $r=0.458$  coefficient at  $p=0.005$ . Gram-negative rods showed significantly greater changes ( $r=0.784$  at  $p<0.001$ ), underscoring their key role in progressive necrobiosis. The proportion of these microorganisms clearly increased toward the zone of complete necrosis, consistent with the known ability of gram-negative rods to actively proliferate in ischemic and damaged tissue.

The strongest correlation was demonstrated by groups associated with the anaerobic component, with obligate anaerobes having a correlation coefficient of  $r=0.852$  ( $p<0.001$ ), the highest value among all parameters. The ratio of anaerobes to aerobes also increased toward severe soft tissue lesions ( $r=0.771$  at  $p<0.001$ ), reflecting a profound shift in the ecosystem toward anaerobic metabolism. Aerobic forms, on the other hand, decreased, as confirmed by a negative correlation of  $r=-0.531$  ( $p=0.002$ ). This creates a holistic picture in which the severity of necrobiosis is directly linked to the increased development of the anaerobic Gram-negative profile of the infection.

The characteristics of mixed microbial communities require special attention, especially when the proportion of polymicrobial complexes had one of the highest correlation coefficients at  $r=0.827$  at  $p<0.001$ . This indicator demonstrates that as necrobiosis intensifies, the microflora becomes not only more aggressive in composition but also more synergistic, which intensifies the destructive effect on tissue. Facultative anaerobes demonstrated a moderately pronounced positive dependence ( $r=0.497$  at  $p=0.003$ ), occupying an intermediate position between early and late participants in the infectious process.

The ratio of Gram (-) to Gram (+) forms also increased as tissue condition worsened ( $r=0.813$  at  $p<0.001$ ), forming a characteristic pattern consistent with the severity of necrobiosis. This value, along with the coefficients for Gram (-) rods, obligate anaerobes, and polymicrobial complexes, is among the strongest correlation markers.

The correlation coefficients for the IDN reflected the most pronounced association of this indicator with the express microbiological characteristics of the wound surface. High positive coefficients were found for Gram (-) rods ( $r=0.742$  at  $p<0.001$ ) and for the Gram (-) to Gram (+) ratio ( $r=0.771$  at  $p<0.001$ ), demonstrating a stable association between increased neutrophil destruction and a shift in

flora toward aggressive Gram (-) forms. An even more pronounced relationship was found between IDN and obligate anaerobes ( $r=0.904$  at  $p<0.001$ ), as well as with the proportion of polymicrobial complexes ( $r=0.789$  at  $p<0.001$ ) and the anaerobe/aerobe ratio ( $r=0.758$  at  $p<0.001$ ). IGN showed a similar profile, with coefficients of  $r=0.703$  for gram (-) rods,  $r=0.863$  for obligate anaerobes,  $r=0.941$  for gram (-) / gram (+),  $r=0.722$  for anaerobes/aerobes, and  $r=0.755$  for polymicrobial complexes at a significance level of  $p<0.001$  for all relationships.

This set of correlations indicates that IDN and IGN simultaneously respond to the deepening of the necrobiotic process and a shift in the microbial ecosystem toward an anaerobic-Gram(-) profile. An increase in the proportion of Gram(-) forms is accompanied by increased neutrophil cytolysis and the accumulation of purulent-necrotic debris, creating a vicious cycle of further tissue destruction. The prevalence of obligate anaerobes reflects the development of profound ischemic conditions, in which cell death accelerates and the severity of proteolysis increases. The increase in the proportion of polymicrobial complexes is consistent with the fact that mixed consortia have a higher damaging potential and more quickly deplete the protective resources of neutrophils and macrophages. In this configuration, IDN and IGN act as early indicators of the transition from an active inflammatory response to the phase of necrotic tissue breakdown.

The IGN demonstrated one of the most significant sets of correlation values among all cytological parameters. Associations with gram (-) rods were  $r=0.768$  at  $p<0.001$ , with obligate anaerobes  $r=0.923$  at  $p<0.001$ , with the gram (-)/gram (+) ratio  $r=0.791$  at  $p<0.001$  and with anaerobes/aerobes  $r=0.979$  at  $p<0.001$ . Correlation with polymicrobial complexes reached  $r=0.812$  at  $p<0.001$ . The ICT showed even more pronounced correlations, namely,  $r=0.881$  with Gram (-) rods,  $r=0.946$  with obligate anaerobes,  $r=0.804$  for Gram (-) / Gram (+),  $r=0.793$  for anaerobes/aerobes, and  $r=0.838$  for polymicrobial complexes, with a significance level of  $p <0.001$  for each combination. This profile demonstrates that the ICT and ICT are most sensitive to microbial shifts associated with severe necrobiosis.

The correlation structure of the ICT and ICT emphasizes that these indicators reflect the most profound pathobiological elements of the necrobiotic process. The increased Gram (-) / Gram (+) and anaerobes/aerobes ratios demonstrate that the active growth of anaerobic-Gram-negative flora is superimposed on a pronounced deficit in local perfusion. Against this background, MCI records an imbalance between the number of microbial masses and inflammatory infiltrate cells, which becomes critical as necrobiosis progresses. ITD, in contrast, reflects the "final" stage of the pathological cascade, where the destruction of the fibrous framework and intercellular structure intensifies simultaneously with microbial expansion. The increasing proportion of polymicrobial complexes creates conditions in which the synergistic interaction of different types of microorganisms accelerates tissue breakdown. This configuration underscores the importance of MCI and ITD as markers of deep destruction, closely linked to the microbial patterns of severe necrotizing infections.

Thus, comparing cytological characteristics with microbiological parameters allowed us to identify a stable system of relationships reflecting the progression of necrobiosis from early changes to the phase of severe tissue destruction. An increase in the proportion of gram-negative rods and obligate anaerobes was accompanied by a consistent shift in the cytological profile toward an increase in destructive forms of neutrophils, increased purulent-necrotic decay, increased microbial-cellular imbalance, and loss of tissue matrix structural integrity. This configuration emphasizes that the degree of necrobiosis is formed under the simultaneous influence of microbial aggression and the local cellular response, and each of the four identified indices reflects a separate element of this process. The combination of the identified patterns creates a sufficient basis for moving to the next stage, which requires formalizing the obtained characteristics in the form of an integrated scale capable of quantitatively assessing the degree of necrobiosis and serving as a tool for early.

### Conclusions

1. The PIN-SD-AI intelligent system demonstrated the highest diagnostic value, with an AUC of 0.96 and a CI of 0.93–0.99. Sensitivity was 92.3%, specificity 90.1%, positive predictive value 89.5%, and negative predictive value 93.7%. A threshold value of 0.65 provided an overall accuracy of 91.5%.

2. The combination of cytological indices and rapid microbiological tests allows for the development of a reliable set of criteria that reflect the key mechanisms underlying the development of necrobiotic processes in NIMT in patients with diabetes.

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