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PREDICTORS OF EARLY RE-NECROSECTOMY IN DIABETIC PATIENTS WITH NECROTIZING SOFT TISSUE INFECTIONS

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Summary.

Necrotizing soft tissue infections in patients with diabetes mellitus are characterized by an aggressive clinical course and a high rate of repeat surgical intervention.

Objective of the study. *To identify predictors of early re-necrosectomy and assess their prognostic value.*

Materials and methods. *This single-centre cohort study enrolled 128 patients with necrotizing soft tissue infections and concurrent diabetes mellitus treated between 2016 and 2025, with re-necrosectomy within 72 hours defined as the primary endpoint. The study was conducted in accordance with the Declaration of Helsinki and applicable national regulations governing biomedical research involving human subjects. The study protocol received approval from the institutional review board of the treating facility. Prior to enrolment, all participants provided written informed consent for the use of de-identified clinical and laboratory data for research purposes. Statistical analysis was carried out with IBM SPSS Statistics 26.0 and MedCalc 20.0. The study was conducted at Bukhara State Medical Institute under the institutional research programme entitled «Early Detection, Diagnosis, and Novel Treatment and Prevention Strategies for Pathological Factors Affecting Population Health in the Bukhara Region During the Post-COVID-19 Pandemic Period (2022-2026).»*

Results. *Re-necrosectomy within the early postoperative period was carried out in 89 patients (69.5%); this group more frequently had a prolonged history of diabetes mellitus, higher HbA1c levels and admission glycaemia, and a more pronounced systemic inflammatory response. The most substantial intergroup differences were identified through analysis of local cytological and microbiological parameters: patients who required early re-necrosectomy demonstrated a significant elevation in the neutrophil destruction index, tissue destruction index, and microbial-cellular index. This group also exhibited greater microbial mass density, a higher proportion of polymicrobial associations, and a predominance of Gram-negative flora, reflecting a more aggressive infectious process and indicating the need for broader surgical debridement.*

Conclusions. *Comprehensive assessment of local cytological and microbiological parameters in conjunction with lactate levels enables prediction of the need for re-necrosectomy within the first 72 hours.*

Keywords: *Necrotizing Soft Tissue Infections; Diabetes Mellitus; Re-Necrosectomy; Predictive Model; Lactate.*

Introduction

Necrotizing soft tissue infections represent among the most severe forms of surgical infection, characterised by rapid involvement of fascial planes with subsequent extension to muscular structures. The clinical course is frequently aggressive, and outcome largely depends on the timing of initial surgical debridement [1,2]. Even brief delays in source control are associated with increased rates of multiple organ dysfunction and mortality [3].

In patients with diabetes mellitus, necrotizing soft tissue infections follow a distinct course, with metabolic instability and microangiopathy impairing tissue perfusion and complicating intraoperative delineation of viable tissue margins; clinical series have demonstrated that such patients more frequently require repeat surgical intervention and exhibit a more severe disease course [4-6].

The contemporary management concept for necrotizing soft tissue infections calls for aggressive initial surgical debridement with maximal radical resection of non-viable tissue; however, even strict adherence to these principles does not eliminate the risk of progressive necrobiotical process. During the first 24 hours after intervention, tissue viability margins may remain indeterminate, while ischaemic changes continue to develop in the setting of microvascular compromise and microbial expansion [7-9]. Data from large retrospective series indicate that a substantial proportion of patients require repeat surgical revision, with the decision to proceed to re-necrosectomy most commonly made within the first 48-72 hours after the index operation [10,11]. This interval is precisely when the subsequent clinical trajectory of the disease is determined.

Established prognostic scoring systems for necrotizing soft tissue infections are primarily oriented toward predicting mortality or severe septic complications [12,13]. Their utility in guiding decisions regarding re-necrosectomy is limited, as the parameters on which they are based reflect an already established systemic response. The need for repeat surgical revision, however, arises earlier, at a stage when local changes precede systemic manifestations [14].

Published evidence highlights the significance of local factors – including depth of involvement, microbial spectrum, and degree of tissue destruction – in determining an unfavourable disease course [15]. An increased proportion of anaerobic and Gram-negative microorganisms, together with the formation of polymicrobial associations, correlates with a more severe clinical course and the need for expanded surgical intervention. Clinical series emphasise that local changes

frequently precede systemic decompensation in their severity and may serve as an early indicator for repeat wound revision [16,17]. Nevertheless, systematised models integrating early local cytological and microbiological parameters for the purpose of predicting re-necrosectomy remain scarce in the literature.

During the first 24 hours after surgery, the margins of viable tissue may remain equivocal, and the clinical picture does not always reflect the true depth of involvement; the decision to proceed to repeat revision is therefore frequently made on the basis of incomplete information [18,19], underscoring the need for objective criteria enabling assessment of the risk of repeat intervention.

Objective of the study. To identify independent predictors of early re-necrosectomy in patients with diabetes mellitus and necrotizing soft tissue infections.

Материал и методы исследования

The study was conducted at a single surgical inpatient facility and had a cohort design. A total of 128 patients with necrotizing soft tissue infections and concurrent diabetes mellitus who received treatment between 2016 and 2025 were enrolled. Patients were recruited consecutively on the basis of clinical and intraoperative evidence of necrotising involvement.

The study was conducted in accordance with the Declaration of Helsinki and applicable national regulations governing biomedical research involving human subjects. The study protocol received approval from the institutional review board of the treating facility. Prior to enrolment, all participants provided written informed consent for the use of de-identified clinical and laboratory data for research purposes.

Inclusion criteria were: age older than 18 years, confirmed diagnosis of type 1 or type 2 diabetes mellitus, completion of initial surgical debridement, and availability for follow-up during the early postoperative period. Patients with terminal multiple organ failure, active systemic inflammatory diseases, and those transferred to another facility before 72 hours after surgery were excluded.

The primary endpoint was early re-necrosectomy, defined as repeat surgical intervention carried out within 72 hours of initial debridement for progression of the necrobiotical process, advancing local necrosis, or persistence of non-viable tissue. Patients were allocated to two groups according to whether the primary endpoint was reached.

Initial surgical debridement was carried out on an emergency basis and involved wide opening of fascial compartments with excision of non-viable tissue until adequate perfusion was established. The decision to proceed to repeat revision was made by the attending surgeon on the basis of clinical dynamics, local wound status, and laboratory findings, without reference to the predictive parameters under investigation, thereby precluding any influence on clinical management.

Laboratory and Cytological Methods. Material for cytological analysis was obtained by impression smear from the wound surface immediately after initial surgical debridement. Preparations were fixed and stained by the Romanowsky–Giemsa method; cell counts were performed at ×1000 magnification (immersion) using an AxioLab.A1 microscope (Carl Zeiss, Germany).

The neutrophil destruction index (NDI) was calculated as the percentage (%) of degenerative neutrophil forms relative to their total number in the field of view. The absolute neutrophil count was expressed as cells per field of view (cells/FOV)

The tissue destruction index (TDI) was defined as the ratio of fibre fragments and cellular debris to the total number of cells in the inflammatory infiltrate and was expressed in arbitrary units.

The microbial-cellular index (MCI) was calculated as the ratio of microbial mass density to the neutrophil count and was expressed in arbitrary units.

Microbial mass density was assessed semi-quantitatively using a three-point scale (1-3 points) based on the number of bacterial aggregates per field of view on Gram staining. Staining was carried out by the standard method using an AxioLab.A1 light microscope (Carl Zeiss, Germany).

The Gram-negative-to-Gram-positive flora ratio was calculated as the ratio of Gram-negative microorganisms to Gram-positive forms in the smear and expressed as a dimensionless coefficient. The proportion of polymicrobial complexes was defined as the percentage (%) of fields of view in which mixed bacterial associations were identified.

Routine Laboratory Parameters. Complete blood count was obtained using an XN-1000 automated haematology analyser (Sysmex, Japan). The following parameters were measured: haemoglobin concentration (g/L), leucocyte count ($\times 10^9$/L), neutrophil proportion (%), and platelet count ($\times 10^9$/L).

Biochemical blood analysis was carried out on a Cobas c501 automated biochemistry analyser (Roche Diagnostics, Germany). The measured parameters included glucose (mmol/L), creatinine (μmol/L), urea (mmol/L), total protein (g/L), albumin (g/L), and lactate (mmol/L).

Coagulation parameters were determined using a Sysmex CA-1500 coagulometer (Sysmex, Japan) and included prothrombin time (s), international normalised ratio (units), fibrinogen concentration (g/L), and D-dimer (mg/L FEU).

Microbiological culture was carried out on solid nutrient media – blood agar and MacConkey agar (HiMedia, India) – with incubation at 37 °C in a Binder BD 56 incubator (Binder GmbH, Germany). Colony-forming units were expressed as log CFU/g of tissue.

Statistical Analysis. Statistical analysis was carried out using IBM SPSS Statistics version 26.0 (IBM Corp., USA) and MedCalc version 20.0 (MedCalc Software Ltd., Belgium). Distribution normality was assessed by the Shapiro–Wilk test, with quantitative data subsequently presented as mean and standard deviation or median and interquartile range according to the distribution pattern.

Intergroup comparisons of quantitative parameters were conducted using Student's t-test or the Mann–Whitney U test, while categorical data were analysed by the chi-square test or Fisher's exact test

Independent predictors of early re-necrosectomy were identified through univariable analysis followed by

multivariable logistic regression modelling, with results expressed as odds ratios with 95% confidence intervals.

The discriminative capacity of the model was evaluated by receiver operating characteristic analysis with calculation of the area under the curve and corresponding 95% confidence interval; the optimal cut-off value was determined by the Youden index, and sensitivity, specificity, positive predictive value, and negative predictive value were additionally calculated. Internal stability of the model was verified by bootstrap validation with 1,000 resampling iterations, and the significance level was set at 0.05

The study was conducted in accordance with the ethical principles of biomedical research; the protocol received approval from the institutional review board, and all data were analysed in de-identified form.

Results and Discussion

Re-necrosectomy within the first 72 hours of the index procedure was carried out in 89 of 128 patients (69.5%), while the remaining 39 patients did not require repeat revision within this period.

Age and sex distribution did not differ significantly between the groups, and the proportion of diabetes mellitus types was likewise comparable. Patients who required re-necrosectomy, however, more frequently had a prolonged history of diabetes and higher HbA1c levels and admission glycaemia, with a greater prevalence of the neuroischaemic form of diabetic foot syndrome and a higher rate of insulin therapy requirement. Among laboratory parameters, statistically significant differences were identified with respect to lactate, leucocyte count, and D-dimer levels (Table 1)

Table 1

Baseline clinical and metabolic characteristics of patients according to early re-necrosectomy status.

Parameter	Entire cohort (n=128)	No re-necrosectomy (n=39)	Re-necrosectomy\ ≤72 ч (n=89)	p
Age, years	58.3 ± 11.4	56.7 ± 10.8	59.0 ± 11.6	0.21
Male sex, n (%)	79 (61.7%)	22 (56.4%)	57 (64.0%)	0.39
Type 2 DM, n (%)	115 (89.8%)	33 (84.6%)	82 (92.1%)	0.18
DM duration >10 years, n (%)	78 (60.9%)	19 (48.7%)	59 (66.3%)	0.048
HbA1c, %	9.4 ± 1.2	8.9 ± 1.1	9.6 ± 1.2	0.003
Admission glycaemia, mmol/L	11.8 ± 2.6	10.9 ± 2.1	12.2 ± 2.7	0.01
Neuroischaemic DFS, n (%)	68 (53.1%)	16 (41.0%)	52 (58.4%)	0.049
Insulin therapy, n (%)	73 (57.0%)	17 (43.6%)	56 (62.9%)	0.037
NSTI – NF, n (%)	63 (49.2%)	24 (61.5%)	39 (43.8%)	0.06
NSTI – NM, n (%)	65 (50.8%)	15 (38.5%)	50 (56.2%)	0.06
Leucocyte count, $\times 10^9$/L	17.2 ± 4.8	15.9 ± 4.1	17.8 ± 5.0	0.04
Lactate, mmol/L	2.6 ± 0.9	2.1 ± 0.6	2.9 ± 0.9	<0.001
D-dimer, mg/L FEU	1.34 ± 0.52	1.11 ± 0.39	1.44 ± 0.57	0.002

Note. Quantitative variables are presented as mean ± standard deviation, while categorical variables are expressed as absolute numbers with percentages. Intergroup comparisons of quantitative parameters were carried out using Student's t-test or the Mann–Whitney U test according to the distribution pattern, and categorical variables were analysed by the chi-square test or Fisher's exact test. DM – diabetes mellitus; HbA1c – glycated haemoglobin; neuroischaemic DFS – neuroischaemic form of diabetic foot syndrome; NSTI – necrotizing soft tissue infection; NF – necrotising fasciitis; NM – necrotising myositis; FEU – fibrinogen equivalent units.

Local parameters assessed within the first 24 hours after surgery differed more substantially between the groups: patients who required re-necrosectomy demonstrated higher NDI, TDI, and MCI values, with microbial mass density and the Gram-negative/Gram-positive ratio likewise shifted toward unfavourable values (Table 2).

Table 2

Early local parameters within the first 24 hours after initial surgical debridement.

Parameter	No re-necrosectomy (n=39)	Re-necrosectomy ≤72 ч (n=89)	P
NDI, %	38.4 ± 11.2	64.7 ± 13.5	<0.001
TDI, arbitrary units	0.96 ± 0.41	2.21 ± 0.73	<0.001
MCI, arbitrary units	0.011 ± 0.006	0.031 ± 0.012	<0.001
Microbial mass density, points	1.4 ± 0.5	2.6 ± 0.6	<0.001
Gram-negative/Gram-positive ratio, coefficient	0.82 ± 0.33	1.79 ± 0.54	<0.001
Proportion of polymicrobial complexes, %	34.6 ± 12.8	67.2 ± 15.4	<0.001

Note. All parameters were assessed within the first 24 hours after initial surgical debridement of the site. NDI – neutrophil destruction index; TDI – tissue destruction index; MCI – microbial-cellular index. Microbial mass density was evaluated semi-quantitatively using a three-point scale, and all data are presented as mean ± standard deviation; intergroup comparisons were carried out using Student's t-test or the Mann–Whitney U test according to the distribution pattern.

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In univariable analysis, each of the local parameters demonstrated an association with early re-necrosectomy. On transition to the multivariable model, the neutrophil destruction index, tissue destruction index, microbial-cellular index, microbial mass density, Gram-negative/Gram-positive flora ratio, and lactate level retained statistical significance, with the greatest contribution to the model attributable to parameters reflecting structural tissue disorganisation and the degree of microbial imbalance. Elevated lactate concentration was likewise associated with an increased probability of repeat intervention (Table 3).

Table 3

Multivariable logistic regression of early re-necrosectomy predictors

Parameter	β	SE	OR	95% CI	p
NDI, %	0.041	0.012	1.04	1.02-1.07	0.001
TDI	0.87	0.29	2.39	1.36-4.19	0.002
MCI	52.4	17.3	3.14	1.67-5.91	0.001
Microbial mass density	0.96	0.34	2.61	1.35-5.03	0.004
Gram-negative/Gram-positive ratio	0.73	0.28	2.07	1.19-3.60	0.009
Lactate, mmol/L	0.81	0.24	2.25	1.41-3.59	<0.001

Note. β – logarithmic regression coefficient; SE – standard error; OR – odds ratio; 95% CI – 95% confidence interval. The multivariable model was constructed by stepwise logistic regression incorporating variables that reached significance in univariable analysis, with statistical significance defined as p < 0.05.

Assessment of the model's discriminative capacity demonstrated high prognostic accuracy, with the area under the ROC curve of 0.924 indicating good separation between risk groups with respect to early re-necrosectomy. The selected cut-off value yielded a balanced combination of sensitivity and specificity, and bootstrap validation with 1,000 resampling iterations revealed no substantial reduction in AUC, thereby confirming the stability of the derived coefficients (Table 4)

Table 4

ROC analysis of the predictive model for early re-necrosectomy.

Parameter	Value
AUC	0.924
95% CI	0.879-0.961
Optimal cut-off (Youden index)	0.63
Sensitivity	88.8%
Specificity	82.1%
PPV	91.2%
NPV	76.7%
Overall accuracy	86.7%
Bootstrap AUC (1,000 iterations)	0.912

Note. AUC – area under the ROC curve; CI – confidence interval; PPV – positive predictive value; NPV – negative predictive value. The 95% CI for AUC was calculated by the DeLong non-parametric method, and internal model stability was assessed by bootstrap validation with 1,000 resampling iterations.

The findings indicate that combining early local cytological and microbiological parameters with a systemic marker of tissue hypoperfusion enables identification of patients at elevated probability of re-necrosectomy within the first 72 hours after the index operation.

The fact that a substantial proportion of patients required re-necrosectomy within three days underscores the difficulty of defining true tissue involvement margins at the time of the index procedure, particularly in patients with diabetic microangiopathy [19]. Even after wide excision, zones of impaired perfusion may persist.

In the present study, the local parameters obtained within the first 24 hours after surgery proved to be of decisive importance. Elevation of the neutrophil destruction index and tissue destruction index reflected both the activity of the inflammatory process and the depth of structural damage to the fascial and muscular framework [20]. Unlike systemic markers, these parameters characterise the immediate condition of the wound surface and permit assessment of the residual reparative potential of the tissues. Clinical series emphasise that it is the severity of local destruction, rather than indices of systemic toxicity alone, that determines the need for expanded surgical intervention [21], and the present data are consistent with this position, confirming that local morphocytological assessment carries independent prognostic value.

The observed differences in microbial spectrum merit closer examination. Patients who required re-necrosectomy more frequently exhibited a predominance of Gram-negative flora and an increased proportion of mixed associations, changes that the literature associates with a more aggressive course of necrotizing soft tissue infections [22,23]. In contrast to studies focusing on sepsis and mortality, the present data demonstrate the relevance of the microbial profile specifically to early surgical decision-making.

The association between local parameters and lactate level warrants specific consideration. Elevated lactate concentration was associated with a higher probability of re-necrosectomy, potentially reflecting the degree of tissue hypoperfusion and the depth of ischaemic injury. In

clinical investigations of necrotizing soft tissue infections, lactate elevation is regarded as a marker of disease severity and septic complication risk [24]; in the present series, however, this parameter retained an independent association specifically with the early surgical outcome, suggesting its role as an indicator of unfavourable local disease progression rather than systemic dysfunction alone.

The high area under the ROC curve indicates that combining several complementary parameters affords more precise risk stratification than assessment of individual markers in isolation. It should be noted that the majority of existing models for necrotizing soft tissue infections are directed toward predicting mortality or severe systemic complications [25,26], with the question of tactical decision-making regarding re-necrosectomy in the early postoperative period receiving virtually no attention in these scoring systems In this context, the proposed approach addresses the practical challenge faced by the surgeon confronting diagnostic uncertainty during the first 24 hours after the index operation.

The present findings carry certain limitations that merit acknowledgement. The single-centre design may affect the reproducibility of the data in other clinical settings, and no external validation of the model on an independent sample was carried out. Nevertheless, the consecutive patient enrolment and uniform algorithm for local parameter assessment reduce the risk of systematic bias, and internal validation demonstrated stability of the regression coefficients with preservation of discriminative capacity/

The findings support the value of early cytological and microbiological assessment of the wound surface, which, in conjunction with lactate level, may serve as a practical guide when deciding on repeat revision within the first 72 hours after the index operation.

Conclusions

The rate of early re-necrosectomy in patients with diabetes mellitus and necrotizing soft tissue infections remains high at 69.5%, reflecting the aggressive nature of the pathological process in this patient population. Independent predictors of early repeat surgical intervention include the neutrophil destruction index, tissue destruction index, microbial-cellular index, microbial mass density, Gram-negative/Gram-positive flora ratio, and blood lactate level.

The developed multivariable predictive model demonstrated high discriminative capacity (AUC = 0.924), indicating substantial diagnostic value. Comprehensive assessment of local cytological, microbiological, and systemic metabolic parameters enables early risk stratification and contributes to the optimisation of surgical management in patients with necrotizing soft tissue infections.

Directions for Future Research. Multicentre external validation of the model and development of a clinical decision-making algorithm for repeat revision represent priorities for subsequent investigation.

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All authors have reviewed the final version of the manuscript and consent to its publication.

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ПРЕДИКТОРИ РАННЬОЇ ПОВТОРНОЇ НЕКРЕКТОМІЇ У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ З НЕКРОТИЗУЮЧИМИ ІНФЕКЦІЯМИ М'ЯКИХ ТКАНИН

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Резюме.

Некротизуючі інфекції м'яких тканин у пацієнтів з цукровим діабетом характеризуються агресивним клінічним перебігом та високим рівнем повторних хірургічних втручань.

Мета дослідження. Визначити предиктори ранньої ренекросектомії та оцінити їх прогностичну цінність.

Матеріали та методи. У цьому одноцентровому когортному дослідженні взяли участь 128 пацієнтів з некротичними інфекціями м'яких тканин та супутнім цукровим діабетом, які лікувалися між 2016 і 2025 роками, при цьому ренекрозектомія протягом 72 годин була визначена як первинна кінцева точка. Дослідження проводилося відповідно до Гельсінської декларації та чинних національних норм, що регулюють біомедичні дослідження за участю людей. Протокол дослідження отримав схвалення інституційної етики лікувального закладу. Перед залученням усі учасники надали письмову інформовану згоду на використання анонімних клінічних та лабораторних даних для дослідницьких цілей. Статистичний аналіз проводився за допомогою IBM SPSS Statistics 26.0 та MedCalc 20.0. Дослідження проводилося в Бухарському державному медичному інституті в рамках інституційної дослідницької програми під назвою «Раннє виявлення, діагностика та новітні стратегії лікування та профілактики патологічних факторів, що впливають на здоров'я населення Бухарської області в період після пандемії COVID-19 (2022-2026)».

Результати. Ренекрозектомію в ранньому післяопераційному періоді було проведено 89 пацієнтам (69,5%); у цій групі частіше спостерігався тривалий анамнез цукрового діабету, вищі рівні HbA1c та глікемії при госпіталізації, а також більш виражена системна запальна реакція. Найбільш суттєві міжгрупові відмінності були виявлені шляхом аналізу локальних цитологічних та мікробіологічних параметрів: у пацієнтів, яким потрібна була рання ренекрозектомія, спостерігалося значне підвищення індексу руйнування нейтрофілів, індексу руйнування тканин та мікробно-клітинного індексу. У цій групі також спостерігалася більша щільність мікробної маси, вища частка полімікробних асоціацій та переважання грамнегативної флори, що відображає більш агресивний інфекційний процес та вказує на необхідність ширшого хірургічного очищення рани.

Висновки. Комплексна оцінка локальних цитологічних та мікробіологічних параметрів у поєднанні з рівнем лактату дозволяє прогнозувати необхідність ренекрозектомії протягом перших 72 годин.

Ключові слова: некротизуючі інфекції м'яких тканин; цукровий діабет; ренекрозектомія; прогностична модель; лактат.

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