Medical Journal of Bakırköy

Med J Bakirkoy 2026;22(Suppl 1):71-78

DOI: 10.4274/BMJ.galenos.2026.2026.6-7

Research

Association Between Nutritional Status and Proximal Re-Amputation in Patients Undergoing Amputation for Diabetic Foot Ulcers: The Role of GNRI and CONUT Scores

Diyabetik Ayak Ülseri Nedeniyle Ampütasyon Uygulanan Hastalarda Beslenme Durumu ile Proksimal Reampütasyon İlişkisinin Değerlendirilmesi: GNRI ve CONUT Skorlarının Rolü

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ABSTRACT

Objective: Diabetic foot ulcers (DFUs) are a major cause of lower extremity amputation; identifying patients at risk for progression to more proximal amputation levels remains a significant clinical challenge. This study aimed to evaluate the association between nutritional status and amputation level progression in patients undergoing surgical treatment for DFUs.

Methods: In this retrospective cohort study, 151 patients who underwent surgical amputation for DFUs between 2020 and 2025 were included. Nutritional status was assessed using the Geriatric Nutritional Risk Index (GNRI) and the Controlling Nutritional Status score. The primary outcome was amputation level progression, defined as the transition from minor to major amputation or to a more proximal level. Clinical, laboratory, and metabolic parameters were compared between patients with and without progression. Multivariable logistic regression was performed to identify independent predictors.

Results: Amputation progression occurred in 64 patients (42.3%). Patients with progression had significantly lower GNRI scores and levels of albumin, cholesterol, and lymphocytes, and significantly higher levels of C-reactive protein, HbA1c, and serum creatinine. In multivariable analysis, serum creatinine [odds ratio (OR): 4.06, 95% confidence interval (CI): 2.04-8.09, $p<0.001$], GNRI (OR: 2.72, 95% CI: 1.30-5.65, $p=0.008$), and Wagner grade ≥ 3 (OR: 3.25, 95% CI: 1.07-9.83, $p=0.037$) were independently associated with amputation progression.

Conclusion: Poor nutritional status, renal dysfunction, and advanced ulcer severity are independently associated with an increased risk of progression to a higher level of amputation in patients with DFUs. GNRI may serve as a practical and accessible tool for early risk stratification and clinical decision-making.

Keywords: Amputation, diabetic foot ulcer, malnutrition, nutritional status, risk assessment

ÖZ

Amaç: Diyabetik ayak ülserleri (DAÜ), alt ekstremite ampütasyonlarının başlıca nedenlerinden biridir ve daha proksimal ampütasyon düzeylerine ilerleme riski taşıyan hastaların belirlenmesi önemli bir klinik zorluk olmaya devam etmektedir. Bu çalışmanın amacı, DAÜ nedeniyle cerrahi tedavi uygulanan hastalarda nütrisyonel durum ile ampütasyon düzeyi progresyonu arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif kohort çalışmasına, 2020-2025 yılları arasında DAÜ nedeniyle cerrahi ampütasyon uygulanan 151 hasta dahil edildi. Nütrisyonel durum, Geriatrik Nütrisyonel Risk İndeksi (GNRI) ve *Controlling Nutritional Status* skoru kullanılarak değerlendirildi. Birincil sonlanım noktası, minör ampütasyondan majör ampütasyona veya daha proksimal bir ampütasyon düzeyine geçiş olarak tanımlanan ampütasyon progresyonuydu. Progresyon gelişen ve gelişmeyen hastalar klinik, laboratuvar ve metabolik parametreler açısından karşılaştırıldı. Bağımsız belirleyicileri saptamak amacıyla çok değişkenli lojistik regresyon analizi yapıldı.

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Received: 16.06.2026
Accepted: 03.08.2026
Publication Date: 25.09.2026

Cite as: Altuntaş Y, Bozca MA, İpek E, Balkanlı B, Alibakan G, Demirkale İ. Association between nutritional status and proximal re-amputation in patients undergoing amputation for diabetic foot ulcers: the role of GNRI and CONUT scores. Med J Bakirkoy. 2026;22(Suppl 1):71-78

ÖZ

Bulgular: Ampütasyon progresyonu 64 hastada (%42,3) gözlendi. Progresyon gelişen hastalarda GNRI skorları, albümin, total kolesterol ve lenfosit düzeyleri anlamlı olarak daha düşük; C-reaktif protein, HbA1c ve serum kreatinin düzeyleri ise daha yüksekti. Çok değişkenli analizde serum kreatinin düzeyi [olasılık oranı (OR): 4,06; %95 güven aralığı (GA): 2,04-8,09; p<0,001], GNRI (OR: 2,72; %95 GA: 1,30-5,65; p=0,008) ve Wagner evresi ≥3 olması (OR: 3,25; %95 GA: 1,07-9,83; p=0,037) ampütasyon progresyonu ile bağımsız olarak ilişkili bulundu.

Sonuç: Kötü nütrisyonel durum, böbrek fonksiyon bozukluğu ve ileri ülser şiddeti, DAÜ olan hastalarda ampütasyon düzeyi progresyonu riskinde artış ile bağımsız olarak ilişkilidir. GNRI, erken risk sınıflandırması ve klinik karar verme süreçlerinde kullanılabilecek pratik ve kolay uygulanabilir bir araç olabilir.

Anahtar Kelimeler: Ampütasyon, diyabetik ayak ülseri, malnütrisyon, nütrisyonel durum, risk değerlendirmesi

INTRODUCTION

Diabetes mellitus remains a major global health challenge, with an estimated 537 million adults affected worldwide, a number that continues to rise and reflects the increasing burden of diabetes-related complications (1). Among these complications, diabetic foot ulcers (DFUs) are particularly devastating, leading to substantial morbidity, reduced quality of life, recurrent hospitalizations, and significant healthcare expenditure (2,3). The lifetime risk of developing a DFU ranges between 19% and 34% among individuals with diabetes, emphasizing its global impact (4). DFU-related infections contribute to approximately 85% of non-traumatic lower extremity amputations (5), and patients who undergo amputation face five-year mortality rates comparable to many malignant diseases (6). Identifying factors associated with progression to higher amputation levels is therefore crucial for improving clinical outcomes in this high-risk population.

The clinical trajectory of DFUs is shaped by a multifactorial interplay, including glycemic control, infection severity, vascular insufficiency, systemic inflammation, and overall disease burden (7). Recently, the influence of nutritional status on wound healing, immune function, and infection control has gained increasing recognition. Malnutrition is known to impair immune responses, delay tissue repair, and contribute to adverse outcomes in individuals with chronic wounds (8). Objective nutritional assessment tools such as the Geriatric Nutritional Risk Index (GNRI) and the Controlling Nutritional Status (CONUT) score have emerged as practical, laboratory-based measures reflecting systemic nutritional impairment. Previous studies have demonstrated associations between poor nutritional scores and unfavorable clinical outcomes—including mortality, prolonged hospitalization, and delayed wound healing—in patients with DFUs (9-11). In diabetic foot surgery, determining the appropriate level of amputation is a central concern for orthopedists, and evaluating nutritional impairment may provide valuable prognostic insight. Despite increasing recognition of nutritional status as a prognostic factor, the potential role of GNRI and CONUT in predicting amputation progression—particularly from minor to major amputation—remains insufficiently explored, leaving a notable gap in the current literature.

Therefore, this study was designed to evaluate the association of GNRI and CONUT scores with progression in amputation level among patients undergoing surgical treatment for DFUs. The research question of this study was whether preoperative nutritional status, measured using the GNRI and CONUT scores, predicted progression of amputation level in patients undergoing amputation for DFUs. Specifically, we evaluated whether patients who progressed from minor to major amputation differed from those who did not progress with respect to these nutritional indices. We aimed to determine whether these nutritional indices could serve as reliable predictors of adverse surgical trajectories. We hypothesized that lower GNRI and higher CONUT scores would be associated with an increased likelihood of amputation progression.

METHODS

This study was approved by the University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital Health Practice and Research Center Clinical Research Ethics Committee (approval no: 5001, date: 05.08.2025), and all procedures were conducted in accordance with the Declaration of Helsinki. This retrospective cohort study was conducted at a tertiary referral center between January 2020 and January 2025. During this period, all patients who underwent surgical amputation due to DFU were screened. Demographic characteristics (age, sex), metabolic parameters (glucose, HbA1c, total cholesterol), nutritional indicators (albumin, lymphocyte count, hemoglobin), inflammatory markers [C-reactive protein (CRP), white blood cell (WBC)], and renal function parameters [serum creatinine, estimated glomerular filtration rate (eGFR)] were extracted from electronic medical records. Additional clinical information, including diabetes duration, smoking status, comorbidities such as end-stage renal disease (ESRD), cardiovascular or cerebrovascular disease, and body mass index (BMI), was also recorded. Ulcer severity was assessed using the Wagner classification and dichotomized as Wagner grades <3 for low-to-moderate severity and ≥3 for limb-threatening ulcers, as commonly applied in previous literature.

A total of 216 patients who underwent surgical amputation for DFU between January 2020 and January 2025 were identified, and their medical records, operative notes, laboratory data, and follow-up information were retrospectively reviewed. After this evaluation, 65 patients were excluded for the following reasons: missing laboratory data preventing calculation of the CONUT or GNRI scores; insufficient follow-up or lack of postoperative control records; death during treatment before progression assessment; primary presentation with major amputation precluding evaluation of progression; coexistence of non-diabetic foot conditions such as traumatic injuries, vasculitis, tumors, or non-diabetic Charcot; being under 18 years of age; or having inconsistent clinical data. Following these exclusions, 151 patients met all criteria and constituted the final analytical cohort. The inclusion criteria were: a diagnosis of type 2 diabetes mellitus; a DFU requiring surgical amputation; availability of complete preoperative laboratory parameters; and a minimum of one month of postoperative follow-up. The exclusion criteria were: age under 18 years; primary major amputation at presentation; missing clinical or laboratory data; pregnancy; and non-diabetic foot pathology (Figure 1).

Amputation levels were categorized as minor when the procedure was performed distal to the ankle joint (including toe, ray, and transmetatarsal amputations) and as major when the procedure occurred through or proximal to the ankle joint (including below-knee and above-knee amputations). Amputation progression, defined as the primary outcome, referred exclusively to the transition from a minor amputation to a major amputation or the advancement of a major amputation to a more proximal level. Changes between minor amputation types (e.g., transitions from toe to ray or from ray to transmetatarsal amputation), were not considered progression because such revisions typically reflect limited local tissue loss or management of localized infection rather than clinically meaningful deterioration. In contrast, progression to a major amputation reflects a substantial increase in limb-loss severity and a significant decline in function; therefore, it was deemed an appropriate indicator of true progression. Accordingly, patients were classified into two groups: those with no progression, defined as having experienced no shift to a more proximal amputation level; and those with progression, defined as having undergone a minor-to-major or a major-to-more-proximal amputation.

Nutritional status was evaluated using the CONUT and GNRI scores. The CONUT score was calculated from serum albumin, total lymphocyte count, and total cholesterol values, and categorized as normal (0-1), mild malnutrition (2-4), moderate malnutrition (5-8), or severe malnutrition (9-12). The GNRI score was computed using the formula GNRI=1.489×albumin (g/L)+41.7×(current weight/ideal body weight), with ideal body weight calculated using the Lorentz formula. GNRI categories included: no nutritional risk (>98), mild risk (92-98), and moderate-to-severe risk (<92). Clinical variables collected for analysis included age, sex, BMI, duration of diabetes, comorbidities (ESRD, cardiovascular and cerebrovascular disease), smoking status, and Wagner grade. Laboratory parameters included albumin, CRP, hemoglobin, glucose, HbA1c, total cholesterol, lymphocyte count, WBC, serum creatinine, and eGFR.

Statistical Analysis

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation, and categorical variables as numbers and percentages. Differences between groups were assessed using the Mann-Whitney U test for continuous variables and the chi-

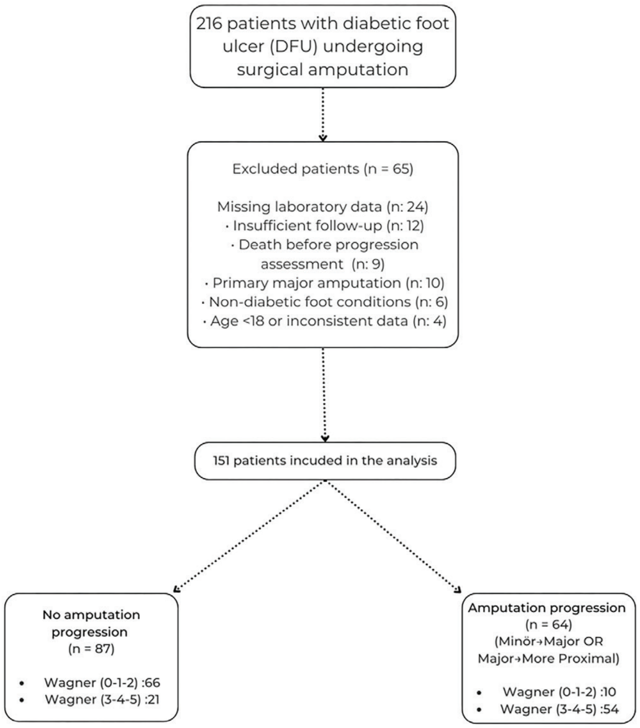

Figure 1. Study flow diagram. Flow diagram of patient selection. Of 216 patients with diabetic foot ulcer (DFU), 151 met inclusion criteria and were analyzed. Patients were categorized into groups with and without amputation progression, with corresponding Wagner grade distributions

square test for categorical variables. Variables associated with amputation progression in univariate analyses at a significance level of $p<0.10$, or those deemed clinically relevant, were entered into a multivariable logistic regression model. This model was developed using the backward stepwise likelihood ratio (Backward LR) method. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Model fit was assessed using the Hosmer-Lemeshow test, and explanatory power was evaluated using Nagelkerke R^2. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 151 patients who underwent surgical amputation for DFUs were included in the analysis. The mean age of the cohort was 66.9±9.2 years, 61.5% (n=93) were male, and the mean BMI was 28.09±4.6 kg/m^2. The mean duration of diabetes was 11.85±2.6 years. Laboratory parameters showed a mean albumin level of 2.97±0.64 g/dL, CRP of 108±39 mg/L, HbA1c of 10.1±1.47%, and total cholesterol of 142±41 mg/dL. The mean lymphocyte count was 1307±392/µL, serum creatinine was 2.04±1.03 mg/dL, and the mean eGFR was 46±19 mL/min. Baseline characteristics of the study population are summarized in Table 1.

Of the 151 patients, 64 (42.3%) experienced amputation progression and 87 (57.7%) did not. Patients with progression were older, had lower BMI , and had a longer duration of diabetes than those without progression. Albumin levels, lymphocyte counts, and total cholesterol concentrations were lower in the progression group. CRP and WBC values were higher among patients with progression. Glucose and HbA1c levels were also higher in this group. Serum creatinine levels were higher and eGFR values were lower in patients with progression. Hemoglobin levels were lower in the progression group. Significant associations were observed among CONUT scores, Wagner grade, GNRI categories, and amputation progression (all $p<0.001$). Higher CONUT scores were more frequent among patients with higher Wagner grades (3-5), higher GNRI-defined nutritional risk categories, and higher progression rates. A significant association was observed between CONUT and GNRI classifications (χ^2=198.1, $p<0.001$). These relationships are illustrated in Figures 2, 3, and 4.

Table 1. Baseline demographic and laboratory characteristics of the study population by amputation progression status

Characteristic	Total (n=151)	No progression, (n=87) mean±SD	Progression, (n=64) mean±SD	p-value
Age (years), mean±SD	66.9±9.2	65.0±8.7	69.8±9.2	0.024
BMI (kg/m^2), mean±SD	28.09±4.6	30.20±3.43	25.23±4.33	<0.001
Duration of DM (years), mean±SD	11.85±2.6	11.06±1.59	12.69±3.10	<0.001
Gender, n (%)				
Male	93 (61.5)	49 (%56)	44 (%69)	0.167[a]
Female	58 (38.5)	38 (%44)	20 (%31)	
Smoking, n (%)				
Yes	60 (40)	40 (%46)	20 (%31)	0.097[a]
No	91 (60)	47 (%54)	44 (%69)	
Albumin (g/dL)	2.97±0.64	3.31±0.39	2.48±0.57	<0.001
CRP (mg/L)	108±39	88.7±34.1	136.6±26.9	<0.001
HbA1c (%)	10.1±1.47	9.21±1.46	11.49±0.96	<0.001
Total cholesterol (mg/dL)	142±41	160.9±34.2	114.8±34.0	<0.001
Lymphocyte count(/µL)	1307±392	1496±318	1020±298	<0.001
Serum creatinine (mg/dL)	2.04±1.03	1.42±0.52	2.87±0.96	<0.001
Glucose (mg/dL)	248±52	227.2±40.0	281.0±51.8	0.031
Hemoglobin (g/dL)	9.9±1.07	10.43±0.90	9.10±0.77	<0.001
WBC (×10^3/µL)	8.17±2.71	7.17±2.12	9.54±2.67	<0.001
eGFR (mL/min)	46±19	56.6±17.6	32.4±12.2	<0.001

Values are expressed as mean ± SD. Mann-Whitney U test was used for continuous variables
[a]: Pearson Chi-Square Test, p<0.05 considered statistically significant
Comparison of patients with and without amputation progression. The "total" column reflects the overall study population (n=151), while the "no progression" and "progression" columns present subgroup characteristics. p-values represent comparisons only between the two subgroups (progression vs. no progression)
Continuous variables are shown as mean±SD and compared using the Mann-Whitney U test; categorical variables were analyzed using Pearson's chi-square test
SD: Standard deviation, WBC: White blood cell, eGFR: Estimated glomerular filtration rate, CRP: C-reactive protein, BMI: Body mass index, DM: Diabetes mellitus

In the multivariable logistic regression model, serum creatinine, GNRI, and Wagner classification were independently associated with amputation progression. Serum creatinine was associated with progression (OR: 4.06, 95% CI: 2.04-8.09, p<0.001). GNRI was also associated with amputation progression (OR: 2.72, 95% CI: 1.30-5.65, p=0.008). Wagner grade ≥3 was independently associated with progression (OR: 3.25, 95% CI: 1.07-9.83, p=0.037). The final regression model demonstrated good calibration (Hosmer-Lemeshow p=0.786) with a Nagelkerke R^2 of 0.651 (Table 2). CONUT was associated with progression in univariate analyses but was not retained in the multivariable model.

DISCUSSION

DFUs represent a complex clinical condition associated with substantial morbidity, mortality, and a frequent need for surgical intervention (12). Despite increasing awareness of the role of systemic factors in DFU outcomes, the impact of nutritional status on amputation level progression has not been clearly defined. The potential effects of malnutrition, inflammation, and metabolic disturbances on wound healing are well established (13). The present study aimed to evaluate the association of GNRI and CONUT scores with progression in amputation level in patients undergoing surgical treatment for DFUs. The findings support our initial hypothesis and demonstrate that impaired nutritional

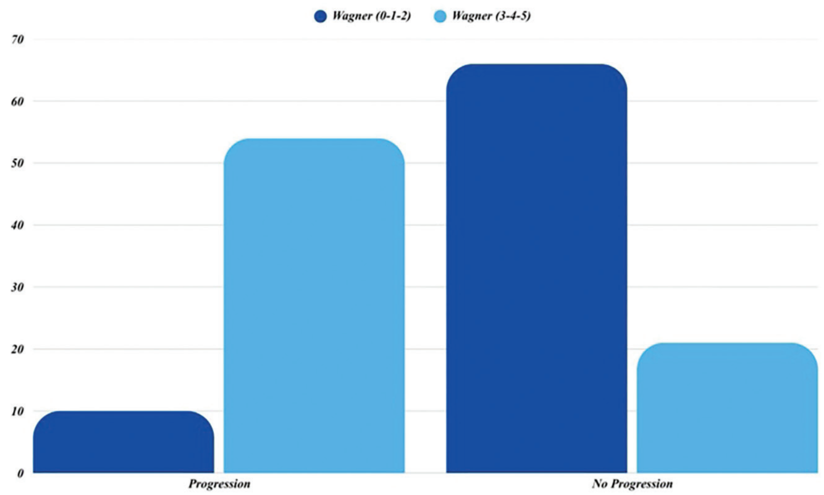

Figure 2. Distribution of Wagner ulcer grades by amputation progression status. This bar chart illustrates the distribution of Wagner grades (0-1-2 vs. 3-4-5) among patients with and without amputation progression. Higher-grade ulcers (Wagner 3-5) were notably more frequent in the progression group, whereas lower-grade ulcers (Wagner 0-2) were predominantly observed in patients without progression

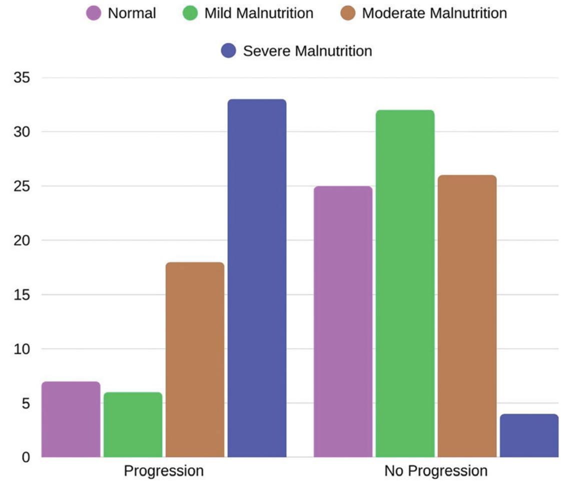

Figure 3. CONUT-based nutritional status categories in patients with and without amputation progression. This figure shows the distribution of nutritional status according to CONUT scoring (normal, mild malnutrition, moderate malnutrition, and severe malnutrition). Severe malnutrition was more common in the progression group, while normal and mild malnutrition categories were more prevalent among patients without progression

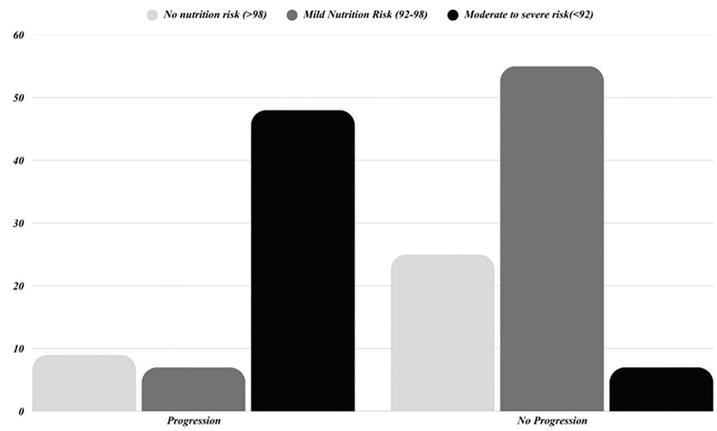

Figure 4. GNRI-based nutritional risk categories by amputation progression status. This bar graph presents the frequency of GNRI nutritional risk levels (no nutrition risk, mild nutrition risk, and moderate-to-severe nutrition risk) across the two patient groups. Moderate-to-severe nutrition risk (<92) was markedly higher in the progression group, whereas mild or no nutrition risk was more common in patients without progression
GNRI: Geriatric Nutritional Risk Index

Table 2. Independent predictors of amputation progression

Variable	OR	95% CI	p-value
Serum creatinine	4.06	2.04-8.09	<0.001
GNRI	2.72	1.30-5.65	0.008
Wagner grade ≥3	3.25	1.07-9.83	0.037

The multivariable logistic regression model identified serum creatinine, GNRI, and Wagner grade ≥3 as independent predictors of amputation progression. Higher serum creatinine levels and poorer nutritional status were associated with a significantly increased risk of progression. The final model demonstrated good calibration (Hosmer-Lemeshow p=0.786) and strong explanatory power (Nagelkerke R^2=0.651)
GNRI: Geriatric Nutritional Risk Index, OR: Odds ratio, CI: Confidence interval

status, along with adverse metabolic and inflammatory profiles, is significantly associated with an increased likelihood of progression to amputation. Notably, patients with progression exhibited poorer nutritional indices, greater inflammatory burden, worse glycemic control, and more pronounced renal dysfunction compared with those without progression.

The pathophysiology of DFUs is multifactorial, primarily driven by peripheral neuropathy, ischemia related to peripheral arterial disease, and superimposed infection (14). In addition to these mechanisms, systemic metabolic disturbances play a critical role in determining wound healing capacity. Reductions in albumin, cholesterol, and lymphocyte levels reflect impaired immune competence, diminished tissue repair capacity, and reduced metabolic reserve (15,16). The elevated CRP and WBC levels observed in patients with amputation progression are indicative of an intensified inflammatory response, which is known to adversely affect wound healing (17,18). Furthermore, renal dysfunction contributes to this process by impairing immune function, promoting systemic inflammation, and disrupting microvascular circulation (19). Anemia, commonly observed in chronic disease states, further compromises tissue oxygenation and healing potential (15). Persistent hyperglycemia, reflected by elevated HbA1c and glucose levels, remains a central driver of metabolic dysregulation, impairing leukocyte function and collagen synthesis, thereby delaying wound healing (20). Collectively, these findings demonstrate that the clinical and biochemical differences observed between groups are physiologically plausible and consistent with established mechanisms.

In addition to systemic factors, local wound characteristics are critical determinants of clinical outcomes. The Wagner classification remains one of the most widely used systems for assessing DFU severity (21,22). Although lower Wagner grades are generally associated with favorable outcomes, grades ≥3 indicate advanced tissue involvement and a higher risk of adverse progression. In the present study, higher Wagner grades were independently associated with amputation progression, consistent with previous reports emphasizing the prognostic significance of ulcer severity (22). The combined predictive value of GNRI, serum creatinine, and Wagner classification suggests that both systemic and local factors should be considered when evaluating the risk of disease progression.

From a clinical perspective, these findings highlight the importance of incorporating nutritional assessment into routine DFU management. Early identification of patients at nutritional risk, using simple and accessible tools such as GNRI, may facilitate timely intervention. Multidisciplinary approaches, including formal dietary consultation, individualized nutritional supplementation, and patient education, may help improve overall outcomes and potentially reduce the risk of progression to amputation. In addition, close monitoring and optimization of renal function and glycemic control appear essential in this high-risk population.

The present study has several strengths. The simultaneous evaluation of GNRI and CONUT scores in relation to amputation level progression provides a novel contribution to the literature, as most previous studies have focused primarily on mortality or major amputation outcomes rather than progression patterns (9,23-28) . The inclusion of comprehensive biochemical and clinical parameters allowed for a multidimensional assessment of the interplay between nutritional status, inflammation, renal function, and metabolic control. Furthermore, the use of multivariable regression analysis enabled the identification of independent predictors, enhancing the robustness of the findings and their potential clinical applicability.

Study Limitations

However, several limitations should be acknowledged. First, the retrospective, single-center design limits causal inference and may affect the generalizability of the results. Second, although multiple clinical and laboratory variables were included, important confounding factors such as peripheral arterial disease status, vascular imaging findings, and revascularization procedures were not systematically assessed, representing a significant limitation given their known impact on DFU outcomes. Third, standardized wound classification systems that incorporate infection and ischemia severity, such as the Wound, Ischemia, and foot Infection classification, were not available in this dataset, potentially limiting the ability to fully account for disease complexity. Fourth, information regarding in-hospital nutritional support or supplementation was not consistently available, precluding assessment of its potential modifying effect on outcomes. Fifth, although amputation progression was selected as a clinically meaningful endpoint reflecting functional deterioration, it may be influenced by surgeon decision-making and patient-related factors, thereby introducing potential subjectivity. Finally, collinearity between nutritional indices such as GNRI and CONUT limited their simultaneous inclusion in multivariable models; therefore, the independent contribution of each index should be interpreted with caution.

CONCLUSION

Poorer nutritional status, impaired renal function, and higher Wagner grade were associated with an increased likelihood of progression to a higher amputation level among patients with DFUs. Future research should incorporate prospective multicenter designs and more standardized analytical methods to refine risk prediction models and validate the clinical utility of nutritional indices in this population.

ETHICS

Ethics Committee Approval: This study was approved by the University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital Health Practice and Research Center Clinical Research Ethics Committee (approval no: 5001, date: 05.08.2025).

Informed Consent: Patient consent was waived due to the retrospective nature of this study.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: Y.A., E.İ., B.B., İ.D., Concept: Y.A., M.A.B., E.İ., B.B., G.A., İ.D., Design: Y.A., M.A.B., E.İ., B.B., G.A., İ.D., Data Collection or Processing: Y.A., E.İ., B.B., G.A., Analysis or Interpretation: M.A.B., B.B., İ.D., Literature Search: Y.A., M.A.B., İ.D., Writing: Y.A., M.A.B., E.İ., B.B., G.A., İ.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

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