ORIGINAL RESEARCH

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The Association Between the HALP Score and Disease Severity in Patients with Diabetic Foot Disease Presenting to the Emergency Department: A Prospective Observational Study

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Abstract

Objective: Rapid assessment of disease severity in diabetic foot disease is essential in the emergency department. While the Wagner classification reflects local wound severity, the HALP score reflects systemic inflammatory and nutritional status. This study evaluated the association between the HALP score and Wagner stage and assessed its ability to identify advanced disease.

Materials and Methods: This prospective, single-center observational study included 130 patients with diabetic foot disease. The primary outcome was the association between the HALP score and Wagner stage. Secondary outcomes included amputation, in-hospital mortality, and 28-day mortality. Group comparisons, ROC analysis, DeLong's test, and multivariable logistic regression were performed.

Results: The median age was 66 years, and 65.4% of the patients were male. Amputation was performed in 48.5% of patients, and the median Wagner stage was 4 (3–5). HALP scores did not differ according to amputation status (p=0.212) but were significantly lower in Wagner grade 5 than in grades 1–2, 3, and 4 (all adjusted p≤0.026). HALP demonstrated good discrimination for Wagner grade 5 disease (AUC=0.790, 95% CI, 0.712–0.868), outperforming hemoglobin, lymphocyte count, and platelet count while performing similarly to albumin. Lower HALP scores remained independently associated with Wagner grade 5 disease (adjusted OR=0.857, 95% CI, 0.794–0.925; p<0.001).

Conclusion: Lower HALP scores were independently associated with advanced diabetic foot disease. Rather than replacing the Wagner classification, the HALP score may serve as a complementary biomarker during the initial emergency department assessment.

Keywords: Amputation, Diabetic Foot, Emergency Medicine, HALP Score

Introduction

Diabetic foot disease is one of the most common and serious complications of diabetes mellitus (DM) and a significant cause of emergency department presentations. It is associated with high morbidity, mortality, and impaired quality of life. Diabetic foot ulcers affect millions of people worldwide and represent a leading cause of diabetes-related hospitalizations [1]. Approximately 80% of nontraumatic lower extremity amputations are attributable to diabetic foot disease, and the lifetime risk of limb loss is markedly higher in patients with DM than in the nondiabetic population [2].

Accurate assessment of disease severity in patients presenting to the emergency department is essential for clinical decision-making and prognostic evaluation. The Wagner classification, based on ulcer depth and the presence of infection and gangrene, remains one of the most widely used systems because of its simplicity and prognostic utility [3]. Higher Wagner stages are associated with more severe infection, increased need for surgical intervention, and poorer clinical outcomes, including amputation [4].

Peripheral neuropathy, vascular insufficiency, chronic inflammation, and malnutrition play interconnected roles in the pathophysiology of diabetic foot disease. Neuropathy increases susceptibility to trauma, while hyperglycemia-related metabolic dysfunction impairs wound healing and immune responses. Systemic

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inflammation and poor nutritional status further reduce tissue repair capacity [5,6]. Therefore, while the Wagner classification remains the cornerstone of local disease severity assessment, additional biomarkers reflecting systemic inflammatory and nutritional status may provide complementary information regarding the overall disease burden.

The HALP score, consisting of hemoglobin, albumin, lymphocyte, and platelet parameters, reflects nutritional status, systemic inflammation, and immune response and was initially described as a prognostic marker in oncology [7]. Its prognostic value has also been demonstrated in nonmalignant conditions, including cardiovascular and inflammatory diseases [8,9]. Given the central roles of systemic inflammation, immune dysfunction, and malnutrition in diabetic foot disease, the HALP score may provide complementary information beyond local wound assessment by reflecting the patient's overall physiological status.

The primary aim of this prospective study was to investigate the association between the HALP score and diabetic foot disease severity according to the Wagner classification in patients presenting to the emergency department. We further evaluated whether the HALP score could provide complementary information beyond the Wagner classification by examining its discriminative performance for identifying advanced disease, comparing its performance with that of its individual laboratory components, and assessing its independent association with Wagner grade 5 disease after adjustment for clinically relevant covariates.

Materials and Methods

Study Design and Setting

This study was designed as a single-center, prospective, observational study conducted in the Emergency Medicine Department of a tertiary care center. Patient recruitment began on August 15, 2024, and continued for approximately one year until the predetermined sample size was reached. Adult patients aged ≥18 years who presented to the emergency department with clinical findings suggestive of diabetic foot disease were enrolled. This study was conducted after obtaining approval from the local ethics committee and in accordance with the Declaration of Helsinki. Written informed consent, including the patient's name, surname, and signature, was obtained from all patients or their legally authorized representatives.

Participant Selection

A total of 158 patients presenting to the emergency department with clinical findings suggestive of diabetic foot disease were assessed for eligibility. Based on the inclusion and exclusion criteria, 28 patients were excluded, and 130 patients constituted the final analysis cohort. The numbers of included and excluded patients, reasons for exclusion, and the patient selection process are presented in Figure 1.

The diagnosis of diabetic foot disease was established based on the presence of previously diagnosed type 2 diabetes mellitus together with pathological clinical findings in the foot, such as ulceration, infection, gangrene, or deformity, and confirmation that these findings were associated with peripheral neuropathy

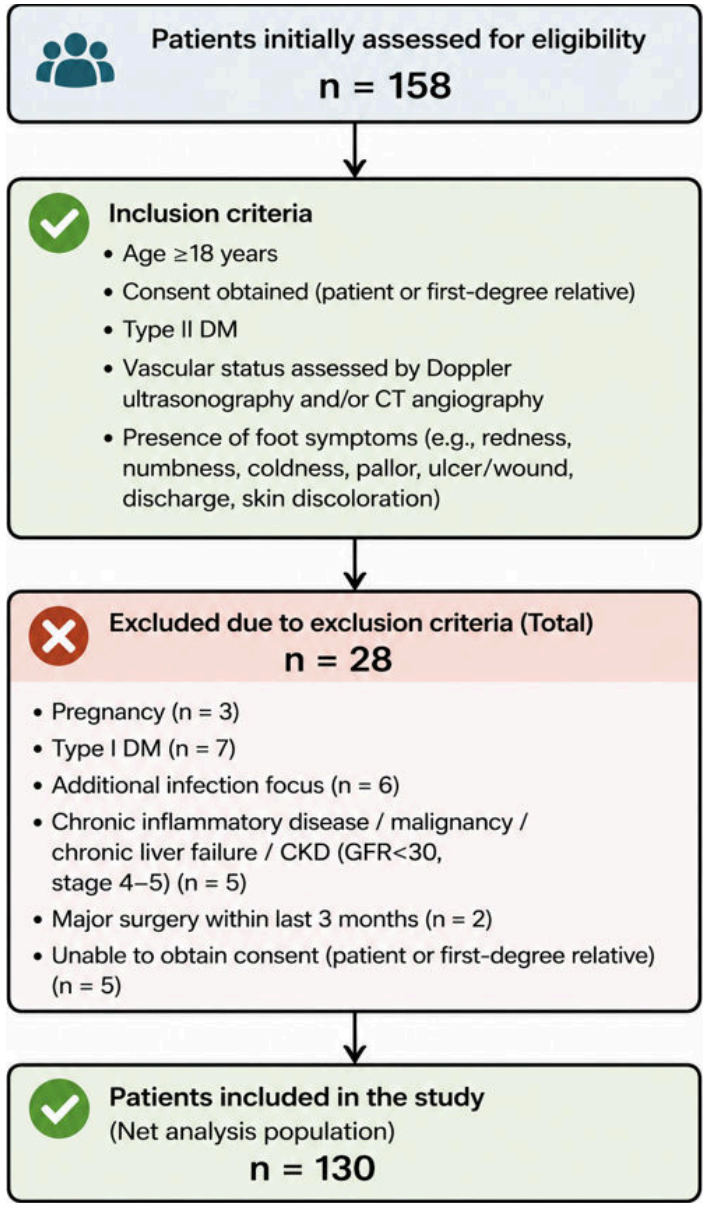

Figure 1. Flowchart of the patient selection. Of 158 patients assessed for eligibility, 28 were excluded based on predefined exclusion criteria, and 130 patients were ultimately included in the final analysis.

and/or peripheral vascular insufficiency. Peripheral neuropathy was assessed based on the presence of sensory loss and/or loss of reflexes on clinical examination. Peripheral vascular insufficiency was evaluated based on palpation of peripheral pulses and ischemic findings such as coldness of the foot and color changes. Patients who met the inclusion criteria were enrolled in the study, as shown in the study flowchart (Fig. 1).

Data Collection

The parameters evaluated in the study included patients' sociodemographic characteristics (age, sex, and comorbidities), vital signs (systolic and diastolic blood pressure, body temperature, heart rate, respiratory rate, and fingertip oxygen saturation [SpO_2]), Glasgow Coma Scale (GCS) score, complete blood count and biochemical parameters, as well as radiological imaging findings, including plain radiography, Doppler ultrasonography, and/or computed tomography angiography. Data on clinical outcome variables, including the need for amputation, in-hospital mortality, and 28-day mortality, were obtained from the hospital's electronic medical record system.

Definitions

The HALP score was calculated using hemoglobin (g/dL), albumin (g/dL), lymphocyte count (/mm^3), and platelet count (/mm^3) values according to the following formula: HALP=(hemoglobin×albumin×lymphocyte count)/platelet count [7]. Patients were classified according to the Wagner Diabetic Foot Classification as follows: Stage 0 (high-risk foot without an open ulcer), Stage 1 (superficial ulcer confined to the skin), Stage 2 (deep ulcer extending to the tendon, capsule, or bone), Stage 3 (deep ulcer accompanied by abscess, osteomyelitis, or severe infection), Stage 4 (localized gangrene involving part of the foot), and Stage 5 (extensive gangrene involving the entire foot) [3].

For ROC curve and multivariable logistic regression analyses, Wagner stage 5 was defined as advanced diabetic foot disease and compared with Wagner stages 1–4. Owing to the small number of patients in Wagner stages 1 and 2, these categories were combined for nonparametric comparisons across Wagner stages.

Sample Size

An a priori sample size calculation was performed in accordance with the planned statistical analyses. Assuming an effect size of 0.5, a two-sided alpha level of 0.05, and a statistical power of 80%, a minimum of 128 patients was calculated to be sufficient to meet the study objectives. The sample size calculation was performed using G*Power software (version 3.1).

Outcomes

The primary outcome of the study was the association between the HALP score and diabetic foot disease severity according to the Wagner classification. Secondary outcomes included the need for amputation, the level of amputation, in-hospital mortality, and 28-day mortality.

Statistical Analysis

All statistical analyses were performed using Jamovi software (The Jamovi Project, version 2.7.31.0). Data distribution was assessed using visual methods (histograms and Q–Q plots) and the Shapiro–Wilk test. Continuous variables were expressed as medians and interquartile ranges (IQRs), and categorical variables as numbers and percentages.

Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Continuous variables between two independent groups were compared using the Mann–Whitney U test, with rank-biserial correlation (r_rb) reported as the effect size when applicable. Differences in HALP scores across Wagner stages were analyzed using the Kruskal–Wallis test, and the effect size was reported as epsilon-squared (ε^2). When significant, pairwise comparisons were performed using Dunn's post hoc test with Bonferroni correction.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the ability of the HALP score and its individual components to discriminate Wagner grade 5 disease. The optimal cutoff value was determined using Youden's index. Areas under the ROC curves (AUCs) were compared using DeLong's test. To evaluate the independent association between the HALP score and Wagner grade 5 disease, multivariable binary logistic regression analysis was performed, including clinically relevant covariates. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. All tests were two-sided, and $p<0.05$ was considered statistically significant.

Results

The median age of the 130 patients included in the study was 66 years (59–72), and 65.4% were male. The most common comorbidities were hypertension (67.7%), coronary artery disease (41.5%), and heart failure (30.8%). Vital signs at emergency department presentation were generally stable, and the median Glasgow Coma Scale (GCS) score was 15 in all patients. Laboratory evaluations revealed marked hyperglycemia, elevated inflammatory markers, and low albumin levels. On radiological assessment, vascular pathology was detected on Doppler ultrasonography in 77.7% of patients, while findings consistent

with osteomyelitis were present on plain radiography in 75.4%. During follow-up, 48.5% of the patients underwent amputation; the rates of intensive care unit admission, in-hospital mortality, and 28-day mortality were 10.0%, 7.7%, and 6.9%, respectively. According to the Wagner classification, the median stage was 4 (3–5). The demographic, clinical, and laboratory characteristics of the study population are summarized in Table 1.

Table 1. Baseline demographic, clinical, laboratory, and imaging characteristics of the study population (n=130)

Age, years	66.0 (59.0–72.0)
Male sex, n (%)	85 (65.4)
Co-morbidities	
Hypertension, n (%)	88 (67.7)
Coronary artery disease, n (%)	54 (41.5)
Heart failure, n (%)	40 (30.8)
Chronic kidney disease, n (%)	28 (21.5)
Cerebrovascular disease, n (%)	12 (9.2)
Other comorbidities, n (%)	92 (70.8)
Vital signs	
Body temperature, °C	36.7 (36.5–37.1)
Heart rate, /min	85.0 (74.3–95.0)
Respiratory rate, /min	20.0 (20.0–22.0)
SpO_2, %	95.0 (93.0–96.0)
Systolic BP, mmHg	129 (116–142)
Diastolic BP, mmHg	73.5 (65.0–81.0)
GCS score	15 (15–15)
Laboratory parameters	
Glucose, mg/dL	220 (148–349)
Creatinine, mg/dL	1.21 (0.85–1.83)
eGFR, mL/min/1.73 m^2	62.5 (37.3–84.0)
Urea, mg/dL	55.1 (37.4–91.0)
C-reactive protein, mg/L	157 (54.0–256)
Procalcitonin, ng/mL	0.29 (0.08–1.14)
Albumin, g/L	32.9 (27.8–36.4)
WBC, $\times10^3$/µL	14.8 (9.66–18.5)
Hemoglobin, g/dL	11.3 (9.72–12.4)
Platelet count, $\times10^3$/µL	336 (234–418)
Neutrophil count, $\times10^3$/µL	12.0 (7.07–15.7)
Lymphocyte count, $\times10^3$/µL	1.32 (0.96–1.95)
Monocyte count, $\times10^3$/µL	0.89 (0.63–1.13)
Radiologic assessment	
Doppler ultrasound pathology present, n (%)	101 (77.7)
CT angiography performed, n (%)	21 (16.2)
Osteomyelitis on plain radiography, n (%)	98 (75.4)
Outcome	
Amputation during follow-up, n (%)	63 (48.5)
ICU admission, n (%)	13 (10.0)
In-hospital mortality, n (%)	10 (7.7)
28-day mortality, n (%)	9 (6.9)
Wagner classification	4 (3–5)

Continuous variables are presented as median (interquartile range), and categorical variables as number (%). Laboratory and vital signs correspond to measurements obtained at emergency department presentation. Radiologic variables indicate whether the examination was performed and/or pathology was detected, regardless of specific anatomical distribution. ICU admission refers to admission during the index hospitalization. GCS: Glasgow Coma Scale; CT: Computed tomography

According to Doppler ultrasonography findings, no vascular pathology was detected in 22.3% of patients, whereas the most frequently observed flow pattern was monophasic flow (51.5%); arterial occlusion was present in 13.8% of patients. The most commonly affected vessels on Doppler ultrasonography were the posterior tibial artery (23.8%) and the anterior tibial artery (16.9%). Computed tomography angiography was performed in 16.2% of patients, and arterial occlusion was detected in 18 patients (13.8% of the overall cohort). On CT angiography, occlusion was most frequently observed in the superficial femoral artery and anterior tibial artery segments. On plain radiographic examination, findings consistent with osteomyelitis were present in 75.4% of patients. Detailed radiological findings are presented in Table 2.

Wagner stage was significantly higher in patients who underwent amputation. The median Wagner stage was 4 (4–5) in the amputation group, compared with 3 (3–4) in patients without amputation ($p<0.001$). When the distribution across Wagner stages was examined, most patients who underwent amputation were classified as stages 4 and 5, whereas patients who did not undergo amputation were predominantly clustered in stage 3. No statistically significant difference was found in HALP scores between patients with and without amputation ($p=0.212$) (Table 3A).

Due to the very small number of patients in Wagner stage 1 (n=2) and the limited number in stage 2 (n=8), these two stages were combined into a single group (grades 1–2) for statistical comparisons. Overall, HALP scores differed significantly across Wagner groups (Kruskal–Wallis $H=27.9$, $df=3$, $p<0.001$), with a moderate effect

Table 2. Radiologic findings of diabetic foot patients (n=130)

Doppler ultrasound findings	
No vascular pathology	29 (22.3)
Monophasic flow	67 (51.5)
Biphasic flow	9 (6.9)
Triphasic flow	7 (5.4)
Arterial occlusion	18 (13.8)
Arterial segments involved on Doppler ultrasound*	
No arterial segment involvement	35 (26.9)
Common femoral artery	10 (7.7)
Superficial femoral artery	12 (9.2)
Deep femoral artery	1 (0.8)
Popliteal artery	7 (5.4)
Posterior tibial artery	31 (23.8)
Anterior tibial artery	22 (16.9)
Dorsalis pedis artery	12 (9.2)
CT angiography findings	
CT angiography performed	21 (16.2)
Arterial occlusion detected	18 (13.8)
Affected vessels on CT angiography*	
Superficial femoral artery	5 (3.8)
Popliteal artery	2 (1.5)
Anterior tibial artery	6 (4.6)
Posterior tibial artery	4 (3.1)
Dorsalis pedis artery	1 (0.8)
No arterial segment involvement	3 (2.3)
Plain radiography findings	
Osteomyelitis present	98 (75.4)

Values are presented as number (%). Percentages are calculated based on the total study population (N = 130). Percentages may exceed 100% as multiple vascular segments could be involved in the same patient. CT: Computed tomography.

Table 3. Distribution of Wagner classification by amputation status and post-hoc pairwise comparisons of HALP scores across Wagner grades

A) Wagner classification according to amputation status (n=130)

Wagner grade	No amputation (n=67)	Amputation (n=63)	Total n (%)
Grade 1	2 (3.0%)	0 (0.0%)	2 (1.5%)
Grade 2	8 (11.9%)	0 (0.0%)	8 (6.2%)
Grade 3	28 (41.8%)	7 (11.1%)	35 (26.9%)
Grade 4	21 (31.3%)	28 (44.4%)	49 (37.7%)
Grade 5	8 (11.9%)	28 (44.4%)	36 (27.7%)
Wagner classification, median (IQR)	3 (3–4)	4 (4–5)	<0.001

B) Dunn post-hoc pairwise comparisons of HALP scores across Wagner groups*

Wagner group comparison	z	Adjusted p (Bonferroni)
Grade 1–2 vs Grade 3	0.546	1.000
Grade 1–2 vs Grade 4	−0.305	1.000
Grade 1–2 vs Grade 5	2.848	0.026
Grade 3 vs Grade 4	−1.363	1.000
Grade 3 vs Grade 5	3.464	0.003
Grade 4 vs Grade 5	5.120	< 0.001

Values are presented as n (%) unless otherwise stated. Percentages in the "No amputation" and "Amputation" columns are calculated within each amputation group, whereas total percentages are calculated based on the overall study population (n=130). Wagner classification is presented as median (IQR) and compared between amputation groups using the Mann–Whitney U test. *Pairwise comparisons were performed using Dunn's test with Bonferroni correction following a significant Kruskal–Wallis test for HALP scores across Wagner grades. Wagner grades 1 (n=2) and 2 (n=8) were combined due to small sample sizes. Kruskal–Wallis H=27.9, df=3, p<0.001, ε^2=0.216

size (ε^2=0.216). Bonferroni-corrected Dunn post hoc analysis demonstrated that HALP scores in patients with Wagner grade 5 disease were significantly lower than those in patients with grades 1–2, 3, and 4 (adjusted p=0.026, p=0.003, and p<0.001, respectively). No statistically significant differences in HALP scores were observed among grades 1–2, 3, and 4 (Table 3B).

To further evaluate the discriminatory performance of the HALP score, receiver operating characteristic (ROC) curve analyses were performed to identify Wagner grade 5 disease. The HALP score demonstrated the highest discriminative performance among the evaluated laboratory markers, with an AUC of 0.790 (95% CI, 0.712–0.868; p<0.001). Albumin also showed good discriminative ability (AUC=0.757, 95% CI, 0.664–0.850; p<0.001), whereas platelet count, lymphocyte count, and hemoglobin demonstrated lower AUC values (Table 4, Figure 2). The optimal HALP cutoff value was 15.09, corresponding to a sensitivity of 88.9% and a specificity of 61.7%.

Pairwise comparisons of ROC curves using DeLong's test demonstrated that the HALP score had significantly greater discriminatory performance than hemoglobin (ΔAUC=0.182, p<0.001), lymphocyte count (ΔAUC=0.177, p<0.001), and platelet count (ΔAUC=0.153, p=0.016), whereas no statistically significant difference was observed between the HALP score and

Table 4. Receiver operating characteristic (ROC) analysis of the HALP score and its individual components for identifying Wagner grade 5 diabetic foot disease

Marker	AUC	95% CI	p
HALP	0.790	0.712–0.868	<0.001
Albumin	0.757	0.664–0.850	<0.001
Platelet	0.637	0.529–0.746	0.013
Lymphocyte	0.613	0.501–0.725	0.048
Hemoglobin	0.607	0.499–0.715	0.051

AUC: Area under the receiver operating characteristic (ROC) curve; CI: Confidence interval. ROC analyses were performed to evaluate the discriminatory performance of the HALP score and its individual components for identifying Wagner grade 5 disease. P values indicate the statistical significance of each AUC compared with the null hypothesis (AUC=0.50).

albumin (ΔAUC=0.033, p=0.447) (Table 5). Among the individual components, albumin demonstrated the highest discriminatory performance, whereas the composite HALP score showed the greatest overall discriminative performance.

To account for potential confounding factors, a multivariable logistic regression analysis was performed including the HALP score, age, chronic kidney disease, and C-reactive protein. The overall model was statistically significant (Omnibus χ^2=37.7, p<0.001; Nagelkerke R^2=0.364). After adjustment for these clinically relevant covariates, lower HALP scores remained independently associated with Wagner grade 5 disease (adjusted OR=0.857, 95% CI, 0.794–0.925; p<0.001). Chronic kidney disease was also independently associated with Wagner grade 5 disease (adjusted OR=0.245, 95% CI, 0.074–0.813; p=0.022), whereas age and C-reactive protein were not significantly associated with the outcome (Table 6).

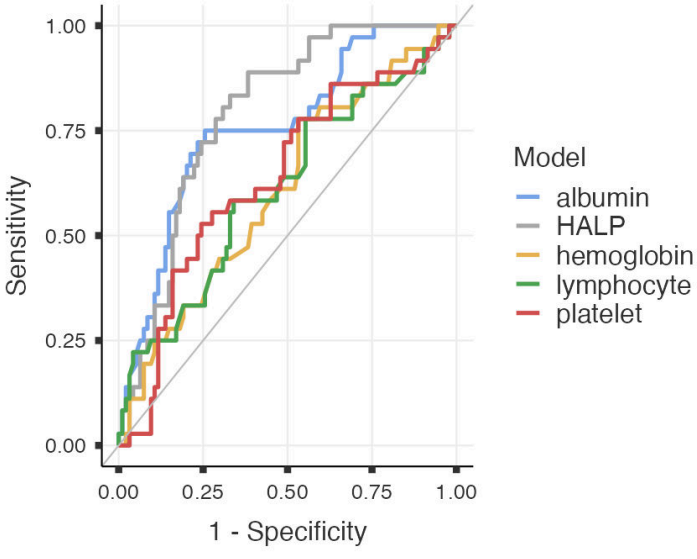

Figure 2. Receiver operating characteristic (ROC) curves of the HALP score and its individual components for identifying Wagner grade 5 diabetic foot disease.

Table 5. Pairwise comparison of the ROC curves of the HALP score and its individual components using DeLong's test

Comparison	ΔAUC	95% CI	z	p
HALP vs Hemoglobin	0.182	0.077 to 0.288	3.401	<0.001
HALP vs Albumin	0.033	–0.052 to 0.118	0.761	0.447
HALP vs Lymphocyte	0.177	0.076 to 0.277	3.449	<0.001
HALP vs Platelet	0.153	0.028 to 0.277	2.404	0.016

ΔAUC indicates the difference in area under the receiver operating characteristic (ROC) curve between the HALP score and each individual component. Pairwise comparisons were performed using DeLong's test. Positive ΔAUC values indicate superior discriminatory performance of the HALP score.

Table 6. Multivariable logistic regression analysis for factors independently associated with Wagner grade 5 diabetic foot disease

Variable	Adjusted OR	95% CI	p
HALP	**0.857**	**0.794–0.925**	**<0.001**
Age	1.004	0.958–1.052	0.867
Chronic kidney disease	0.245	0.074–0.813	0.022
C-reactive protein	1.002	0.998–1.006	0.319

OR: Odds ratio; CI: Confidence interval; AIC: Akaike information criterion. Variables entered into the multivariable logistic regression model were HALP, age, chronic kidney disease, and C-reactive protein. The overall model was statistically significant (Omnibus χ^2=37.7, df=4, p<0.001), with a Nagelkerke R^2 of 0.364 (AIC=126; n=130).

Additional analyses were performed to explore the association between the HALP score and mortality outcomes. Median HALP scores were lower among patients who died during hospitalization or within 28 days than among survivors; however, these differences did not reach statistical significance (Mann–Whitney U=452, p=0.197 and Mann–Whitney U=363, p=0.097, respectively).

Discussion

When evaluating patients with diabetic foot disease in the emergency department, rapid assessment of disease severity is essential for appropriate risk stratification and timely clinical decision-making. In the present study, lower HALP scores were significantly associated with increasing diabetic foot disease severity, with the most pronounced decline observed in patients with Wagner grade 5 disease. ROC analysis further demonstrated that the HALP score showed good discriminative performance for identifying Wagner grade 5 disease and outperformed most of its individual components, while multivariable logistic regression

confirmed that this association remained significant after adjustment for clinically relevant covariates. Rather than serving as a substitute for the Wagner classification, which primarily reflects local tissue involvement, the HALP score may provide complementary information by reflecting the patient's systemic inflammatory and nutritional status.

In this study, a substantial proportion of patients exhibited elevated inflammatory markers, low albumin levels, and radiological evidence of significant vascular pathology and osteomyelitis. These findings are consistent with previous studies reporting that advanced diabetic foot disease is frequently accompanied by systemic inflammation and malnutrition [2,10]. Likewise, high rates of osteomyelitis and peripheral arterial disease have been reported in patients managed at tertiary referral centers, and our radiological findings are consistent with these observations [11,12]. Nearly half of the patients underwent amputation, and the median Wagner stage was 4, indicating that our cohort predominantly consisted of patients with advanced diabetic foot disease. This likely reflects the tertiary referral nature of our institution, where patients are commonly referred after unsuccessful treatment elsewhere or because of severe disease requiring specialized care. Previous studies have consistently demonstrated that higher Wagner stages are associated with increased rates of amputation and mortality, particularly in patients with Wagner grades 4 and 5 [4,13]. In contrast, substantially lower amputation rates have been reported in centers with well-established multidisciplinary diabetic foot programs [14]. Therefore, our findings should primarily be interpreted within the context of patients with advanced diabetic foot disease managed in tertiary care settings, where rapid risk stratification and early multidisciplinary intervention remain particularly important.

The key components of the HALP score—hemoglobin, albumin, lymphocytes, and platelets—play critical roles in the pathophysiology of diabetic foot disease. Hemoglobin is a fundamental parameter that determines the oxygen-carrying capacity of the blood; anemia may impair adequate oxygen delivery to tissues, leading to local hypoxia, which can trigger an inflammatory response and thereby exacerbate disease severity. In a meta-analysis, a significant association was demonstrated between anemia and diabetic foot ulcers, and a one-unit decrease in hemoglobin level was reported to markedly increase the risk of diabetic foot ulceration [15]. Albumin is one of the most important indicators of nutritional status and plays a critical role in protein synthesis required for wound healing, immune function, and tissue repair [16]. Moreover, one study demonstrated that an albumin level of ≤28 g/L in patients with pneumonia was associated with a more severe and potentially fatal course of infection [17]. Malnutrition has been reported in 15–62% of patients with diabetic foot ulcers, and by delaying wound healing, it increases the risk of amputation by approximately threefold [18]. Lymphocytes are key components of the adaptive immune response and play a critical role in host defense against infections. A reduction in lymphocyte count may weaken the immune response to infection and thereby contribute to accelerated disease progression in diabetic foot disease, particularly in clinical presentations complicated by infection [19]. Platelets play a central role in hemostasis and endothelial function and help prevent infection by initiating blood coagulation during the early phase of wound healing. In patients with diabetic foot disease, a decrease in platelet count may adversely affect the wound-healing process and contribute to weakened defense against infection. In the study by Yang et al. [20], a linear relationship was demonstrated between platelet count and wound-healing outcomes, and a low platelet count was reported to predict poorer wound-healing outcomes. In addition, platelets regulate the inflammatory response and support tissue repair by secreting proinflammatory cytokines and growth factors. By integrating these parameters into a single composite index, the HALP score provides a more comprehensive reflection of nutritional status, systemic inflammation, immune competence, and hemostatic function than any individual component alone.

Within this framework, we further evaluated the relationship between the HALP score and Wagner stage. Post hoc analyses demonstrated that HALP scores remained comparable across Wagner grades 1–4 but declined significantly in patients with Wagner grade 5 disease. These findings suggest that the HALP score is more useful for identifying end-stage diabetic foot disease than for discriminating incremental differences across intermediate Wagner stages. Consistent with this observation, ROC analysis demonstrated good discriminative performance of the HALP score for identifying Wagner grade 5 disease. Furthermore, comparison with its individual components showed that the HALP score outperformed hemoglobin, lymphocyte count, and platelet count while demonstrating discriminative performance comparable to that of albumin alone. These findings support the concept that combining multiple laboratory parameters into a composite index may better reflect the complex systemic alterations accompanying advanced diabetic foot disease than most individual biomarkers. Previous studies have similarly reported that lower HALP scores are associated with more advanced Wagner stages and worse clinical outcomes in diabetic foot disease [21–23].

In agreement with previous reports, a strong association was observed between the Wagner classification and the need for amputation in our cohort, reinforcing its established role

in reflecting local tissue destruction and guiding surgical management [13,24]. The significantly higher Wagner stages among patients who underwent amputation further support the clinical utility of the Wagner classification in identifying patients requiring surgical intervention. In contrast, HALP scores did not differ significantly between patients with and without amputation, suggesting that the HALP score should not be interpreted as a direct predictor of surgical intervention. Likewise, no significant association was observed between the HALP score and short-term mortality, although median HALP values tended to be lower among nonsurvivors. Nevertheless, our stage-based analyses demonstrated that HALP scores declined markedly in patients with Wagner grade 5 disease, and multivariable logistic regression further confirmed that this association remained significant after adjustment for clinically relevant covariates. Taken together, these findings suggest that the HALP score primarily reflects the systemic disease burden accompanying advanced diabetic foot disease rather than individual clinical outcomes such as amputation or short-term mortality. From a practical perspective, the HALP score can be readily calculated from routine laboratory parameters obtained during the initial emergency department evaluation and therefore requires no additional testing, cost, or equipment. Accordingly, it may provide complementary information regarding the patient's systemic inflammatory burden and nutritional status when interpreted alongside the Wagner classification. Therefore, rather than replacing the Wagner classification, the HALP score may serve as a complementary biomarker for identifying patients with advanced diabetic foot disease when interpreted alongside established clinical assessment tools.

Study Limitations

This study has several limitations. First, the HALP score was calculated using laboratory parameters obtained only at emergency department presentation and therefore does not reflect dynamic changes during the course of the disease. Second, although multivariable analyses were performed to adjust for selected clinically relevant covariates, several important factors known to influence diabetic foot disease severity, including diabetes duration, glycemic control (e.g., HbA1c), smoking status, peripheral neuropathy, previous diabetic foot disease, and prior amputation history, were unavailable and could not be incorporated into the analyses. Therefore, residual confounding cannot be excluded. In addition, the study population predominantly consisted of patients with advanced diabetic foot disease treated at a tertiary referral center, while Wagner grades 1 and 2 were underrepresented, which may limit the generalizability of our findings to patients with less severe disease. Future multicenter studies including primary care, secondary care, and outpatient diabetic foot clinics are warranted to evaluate the clinical utility of the HALP score across the full spectrum of diabetic foot disease. Finally, the decision to perform amputation was influenced by multiple clinical factors, including local wound characteristics, vascular status, and multidisciplinary clinical judgment, which could not be fully standardized. Nevertheless, the prospective study design and inclusion of consecutive patients presenting to the emergency department provide valuable insight into the potential role of the HALP score as a complementary biomarker in the initial assessment of diabetic foot disease.

Conclusion

In this prospective study, lower HALP scores were associated with advanced diabetic foot disease, with the most pronounced decline observed in patients with Wagner grade 5 disease. Although the HALP score was not associated with amputation or short-term mortality, it remained independently associated with Wagner grade 5 disease after adjustment for clinically relevant covariates. Rather than replacing the Wagner classification, the HALP score may serve as a complementary biomarker reflecting systemic inflammatory burden, nutritional status, and physiological reserve. Given that it can be readily calculated from routine laboratory parameters, the HALP score may assist in the initial assessment of patients presenting to the emergency department with diabetic foot disease. Further multicenter studies with larger and more diverse patient populations are warranted to validate these findings and better define the clinical role of the HALP score in diabetic foot disease.

Ethics Committee Approval: This study was approved by The Ankara Etlik City Hospital Clinical Research Ethics Committee (Approval no: 2024-696 – 31.07.2024)

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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