ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

The Hemoglobin, Albumin, Lymphocyte, and Platelet Score as a Simple Blood-Based Predictor of Residual Coronary Disease Burden in Diabetic Patients with Non-ST-Elevation Myocardial Infarction

Diyabetik Non-ST Elevasyonlu Miyokard Enfarktüsü Hastalarında Rezidüel Koroner Hastalık Yükünü Öngörmede Hemoglobin, Albümin, Lenfosit ve Trombosit Skorunun Basit Bir Kan Testi Belirteci Olarak Değeri

ABSTRACT

Objective: Patients with type 2 diabetes mellitus (T2DM) and non-ST-elevation myocardial infarction (NSTEMI) are at increased risk of incomplete revascularization and adverse outcomes. Simple biomarkers to predict residual disease burden and prognosis are clinically valuable. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score reflects inflammation and nutritional status. This study evaluated the association of the HALP score with the residual Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score (rSS) and 12-month major adverse cardiovascular events (MACE) in T2DM patients with NSTEMI.

Method: This retrospective study included 210 diabetic patients. Participants were stratified into three groups based on rSS (0, 1–8, > 8). HALP scores were calculated from admission laboratory values, and outcomes were followed for 12 months. Associations between HALP and rSS were assessed using Spearman correlation and multivariable regression. Receiver operating characteristic (ROC) analysis identified a HALP cut-off value for predicting high rSS. The prognostic value for MACE was evaluated using Cox regression and Kaplan-Meier analysis.

Results: HALP scores were significantly lower in patients with rSS > 8 ($P < 0.001$) and were negatively associated with rSS ($\beta = -0.344$, $P < 0.001$). The optimal HALP score cut-off for predicting rSS > 8 was 2.96, with 78% sensitivity and 77% specificity. Patients with HALP ≤ 2.96 had a higher prevalence of rSS > 8 (43.7% vs. 6.5%) and experienced more MACE over 12 months (29.6% vs. 13.7%, $P = 0.005$). In Cox analysis, a low HALP score (≤ 2.96) was an independent predictor of MACE, along with age and C-reactive protein (CRP) levels (hazard ratio = 1.916, $P = 0.045$).

Conclusion: Lower HALP scores are associated with higher residual disease burden and worse outcomes. The HALP score may serve as a practical tool for risk stratification in patients with diabetic NSTEMI.

Keywords: Hemoglobin, albumin, lymphocyte, and platelet score, major adverse cardiovascular events, non-ST-elevation myocardial infarction, residual SYNTAX score, type 2 diabetes mellitus

ÖZET

Amaç: Tip 2 diabetes mellitus (T2DM) ve non-ST elevasyonlu miyokard enfarktüsü (NSTEMI) olan hastalar, yetersiz koroner revaskülarizasyon ve olumsuz klinik sonuçlar açısından artmış risk taşır. Rezidüel hastalık yükünü ve prognozu öngörebilecek basit biyobelirteçlerin belirlenmesi klinik açıdan önemlidir. Hemoglobin, albümin, lenfosit ve trombosit düzeylerine dayanan HALP skoru, inflamasyon ve beslenme durumunu yansıtan yeni bir göstergedir. Bu çalışma, HALP skorunun rezidüel SYNTAX skoru (rSS) ile ilişkisini ve T2DM'li NSTEMI hastalarında 12 aylık majör advers kardiyovasküler olaylar (MACE) üzerindeki prognostik değerini değerlendirmeyi amaçladı.

Yöntem: Bu retrospektif çalışmaya, NSTEMI tanısıyla perkütan koroner girişim (PCI) uygulanan 210 T2DM hastası dahil edildi. Hastalar, rSS değerlerine göre üç gruba ayrıldı (0, 1–8, >8). HALP skorları yatış laboratuvar verilerinden hesaplandı ve hastalar 12 ay boyunca takip edildi. HALP ile rSS arasındaki ilişkiler Spearman korelasyonu ve çok değişkenli regresyon analizi ile

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

İlke Erbay

Pelin Aladağ

Department of Cardiology, Bülent Ecevit University Faculty of Medicine, Zonguldak

Corresponding author:
İlke Erbay
✉ ilkeerbay@gmail.com

Received: June 24, 2025
Accepted: August 03, 2025

Cite this article as: Erbay İ, Aladağ P. The Hemoglobin, Albumin, Lymphocyte, and Platelet Score as a Simple Blood-Based Predictor of Residual Coronary Disease Burden in Diabetic Patients with Non-ST-Elevation Myocardial Infarction. *Turk Kardiyol Dern Ars.* 2025;53(6):000-000.

DOI: 10.5543/tkda.2025.71080

değerlendirildi. ROC analizi, yüksek rSS öngörüsü için optimal HALP eşik değerini belirledi. MACE öngörüsüne yönelik analizlerde Cox regresyonu ve Kaplan–Meier yöntemleri kullanıldı.

Bulgular: HALP skoru, rSS >8 olan hastalarda anlamlı olarak daha düşüktü (p<0,001). Çok değişkenli doğrusal regresyon analizinde HALP, rSS ile negatif yönde bir ilişki gösterdi (β = –0,344, p<0,001). HALP skoru için 2,96'lık eşik değeri, rSS >8'i %78 duyarlılık ve %77 özgüllükle öngördü. HALP ≤2,96 olan hastalarda, HALP>2,96 olanlara göre rSS >8 prevalansı (43,7% vs. 6,5%) ve 12 ay içinde MACE sıklığı (29,6% vs. 13,7%, P = 0,005) daha yüksekti. Cox analizinde düşük HALP skoru (HALP ≤2,96), yaş ve CRP düzeyleriyle birlikte 12 aylık MACE için bağımsız bir öngörücü olarak bulundu (HR=1,916, P = 0,045).

Sonuç: Düşük HALP skorları, daha fazla rezidüel koroner hastalık yükü ve kötü klinik sonuçlarla ilişkili bulunmuştur. HALP skoru, T2DM'li NSTEMI hastalarında risk sınıflandırması için pratik ve erişilebilir bir araç olabilir.

Anahtar Kelimeler: Hemoglobin, albümin, lenfosit ve trombosit skoru, majör kardiyovasküler olaylar, tip 2 diabetes mellitus; non-ST elevasyonlu miyokard enfarktüsü, rezidüel SYNTAX skoru

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, despite considerable advances in diagnosis and therapeutic strategies.[1] Among CVDs, coronary artery disease (CAD) is the most common and is often complicated by comorbid conditions such as type 2 diabetes mellitus (T2DM), which significantly worsens clinical outcomes.[2] Non-ST-elevation myocardial infarction (NSTEMI), a common manifestation of acute coronary syndromes, is frequently observed in diabetic patients and is associated with a higher risk of adverse cardiovascular events and poorer long-term prognosis compared to non-diabetic individuals.[3] However, there remains a clinical need for a simple, accessible, and reliable prognostic marker to help predict adverse outcomes in this high-risk population.

In recent years, inflammation- and nutrition-based indices, such as the systemic immune-inflammation index, the prognostic nutrition index, and the C-reactive protein (CRP) to albumin ratio, have been increasingly used to predict clinical outcomes in patients with acute coronary syndromes. These markers reflect the complex interplay between systemic inflammation, immune dysregulation, and nutritional status, which is particularly relevant in patients with diabetes and CAD.[4-7] Among these indices, the hemoglobin, albumin, lymphocyte, and platelet (HALP) score has garnered interest due to its prognostic relevance in systemic diseases.

The HALP score is a novel composite biomarker that reflects both systemic inflammation and nutritional status. Originally investigated in oncology, it has recently been shown to predict adverse outcomes in CVDs.[8] Each of its components has been individually associated with cardiovascular risk. Anemia and hypoalbuminemia, commonly observed in T2DM patients, reflect malnutrition and chronic inflammation and have been independently linked to poor outcomes after myocardial infarction (MI).[9,10] Low lymphocyte counts have been reported to be associated with increased mortality in patients with CAD.[11] In addition, platelet hyperactivity, which is common in diabetic patients, contributes to atherothrombosis and increases vascular inflammation, potentially worsening clinical outcomes in acute coronary syndrome.[12]

While the HALP score reflects systemic inflammation and nutritional status, the anatomical extent of CAD is better assessed using angiographic tools such as the residual Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score (rSS). Residual CAD after the index event is a known predictor of poor outcomes, and the rSS is a validated tool used to quantify this burden.[13,14] In addition to anatomical complexity, residual coronary disease may also be influenced by systemic factors such as inflammation and nutritional status.[15] Despite growing recognition of the role of systemic factors in post-MI outcomes, their relationship with residual CAD burden remains unclear in diabetic patients.

The aim of this study was to evaluate the association between the HALP score and the rSS after primary percutaneous coronary intervention (pPCI), as well as to assess its prognostic value in predicting major adverse cardiovascular events (MACE) in patients with T2DM and NSTEMI.

ABBREVIATIONS

AUC	Area under the curve
bSS	Baseline SYNTAX score
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CI	Confidence interval
CRP	C-reactive protein
CVD	Cardiovascular disease
DAPT	Dual antiplatelet therapy
GRACE	Global Registry of Acute Coronary Events
HALP	Hemoglobin, albumin, lymphocyte, and platelet score
HbA1c	Glycated hemoglobin
HR	Hazard ratio
IRA	Infarct-related artery
IQR	Interquartile range
LAD	Left anterior descending (artery)
LDL-C	Low-density lipoprotein cholesterol
LMCA	Left main coronary artery
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
NSTEMI	Non-ST-elevation myocardial infarction
PCI	Percutaneous coronary intervention
ROC	Receiver operating characteristic
rSS	Residual SYNTAX score
SD	Standard deviation
STEMI	ST-elevation myocardial infarction
T2DM	Type 2 diabetes mellitus

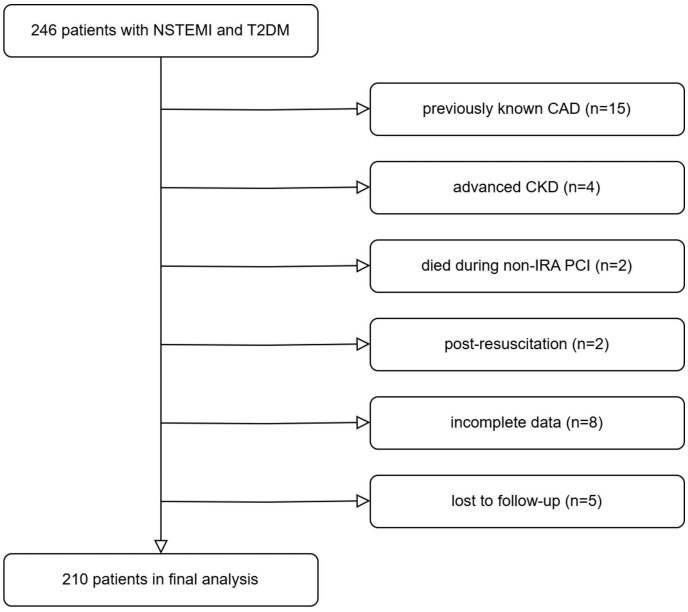

Figure 1. Study flow chart.

CAD, Coronary artery disease; CKD, Chronic kidney disease; IRA, Infarct-related artery; NSTEMI, Non–ST-segment elevation myocardial infarction; PCI, Percutaneous coronary intervention; T2DM, Type 2 diabetes mellitus.

Materials and Methods

Study Design and Population

This retrospective observational study included 246 consecutive patients with a diagnosis of NSTEMI and a known history of T2DM who were admitted to the emergency department of Bülent Ecevit University Hospital and underwent pPCI between January 2022 and January 2024.

Patients were excluded if they had a known history of CAD, active or chronic inflammatory disorders, hematologic malignancies, severe hepatic or renal dysfunction, ongoing chemotherapy or immunosuppressive therapy, chronic glucocorticoid use, cardiogenic shock, cardiopulmonary arrest requiring resuscitation, pregnancy, use of thrombolytic agents, referral for emergency coronary artery bypass grafting (CABG) surgery, underwent surgical revascularization during follow-up, or had missing data, including blood count parameters. After applying these exclusion criteria, 210 patients were included in the final analysis (Figure 1).

Baseline demographic, clinical, and laboratory data were retrospectively collected from the hospital's electronic medical records. The HALP score was calculated using complete blood count and biochemical parameters. All patients were followed for 12 months after discharge for the occurrence of clinical outcomes.

Laboratory Measurements and HALP Score Calculation

Hemoglobin, lymphocyte, and platelet counts were measured using an automated hematology analyzer (UniCel DxH 800, Beckman Coulter, USA), and serum albumin levels were measured using standard automated biochemistry analyzers available in the hospital laboratory. Blood samples for these measurements were obtained on the day of admission, prior to coronary angiography. The HALP score was calculated using the following formula:

HALP = hemoglobin (g/L) × albumin (g/L) × lymphocyte count (10^3/μL) / platelet count (10^3/μL).

Angiographic Evaluation and Percutaneous Coronary Intervention

All patients underwent coronary angiography via the femoral or radial artery upon admission. In accordance with current guidelines for NSTEMI, routine pre-angiography loading with dual antiplatelet therapy (DAPT) was not performed. Instead, 300 mg of acetylsalicylic acid and a loading dose of either 600 mg clopidogrel or 180 mg ticagrelor were administered during or immediately after the procedure, based on the revascularization strategy and clinical judgment.[16] Unfractionated heparin was administered intravenously during the procedure at a dose of 70–100 U/kg, with additional doses given as needed to maintain adequate anticoagulation. Primary percutaneous coronary intervention was performed based on angiographic findings, targeting only the culprit lesion or lesions deemed responsible for the acute presentation. Treatment involved either balloon angioplasty alone or drug-eluting stent implantation, according to the operator's discretion and lesion characteristics.

Definitions

Non-ST-elevation myocardial infarction was defined as chest pain or angina-equivalent symptoms without persistent ST-segment elevation on electrocardiography, accompanied by elevated cardiac troponin levels above the 99th percentile upper reference limit, with a dynamic change indicative of acute myocardial injury.[16]

The baseline SYNTAX score (bSS) and rSS were calculated by summing the individual scores of all coronary lesions with ≥ 50% diameter stenosis in vessels measuring at least 1.5 mm. Residual SYNTAX scores were classified as follows: a score of 0 indicated complete revascularization; scores of 1–8 were defined as low-to-moderate residual disease burden; and scores greater than 8 were considered high residual disease burden, as previously described.[17] All angiographic variables relevant to the bSS and rSS were assessed by two experienced cardiologists trained in SYNTAX scoring, who were blinded to procedural data and clinical outcomes. In case of disagreement, the final score was determined by consensus.

In our study, rSS was calculated after infarct-related artery (IRA) revascularization and, when applicable, following any additional non-IRA PCI procedures performed prior to discharge. If no further revascularization was planned after discharge, the same rSS value was used for follow-up analysis. In patients who underwent staged PCI on non-IRA vessels after discharge, the final rSS was recalculated based on the most recent angiographic procedure and used to assess follow-up outcomes. These elective interventions were typically performed within 10 to 30 days after the index procedure. In total, 35.2% (n = 74) of patients underwent staged PCI either during hospitalization or within the early post-discharge period.

Type 2 diabetes mellitus was defined as a prior diagnosis of diabetes treated with oral hypoglycemic agents and/or insulin, or based on laboratory criteria at admission: random plasma glucose ≥ 200 mg/dL or glycated hemoglobin (HbA1c) ≥ 6.5%.[18] Hypertension was defined as a prior diagnosis of hypertension,

use of antihypertensive medications, or a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg. Hyperlipidemia was defined as a known diagnosis of dyslipidemia, use of lipid-lowering therapy, or total cholesterol ≥ 200 mg/dL, low-density lipoprotein cholesterol (LDL-C) ≥ 130 mg/dL, or triglycerides ≥ 150 mg/dL. Smoking was defined as current smoking or a history of smoking with a cumulative exposure of at least 10 pack-years, regardless of current status.

Follow-up and Outcomes

Follow-up began after completion of the full revascularization strategy, including staged PCI procedures when applicable. For patients who did not undergo further intervention after discharge, follow-up was initiated at the time of hospital discharge. All patients were followed for 12 months to assess the occurrence of MACE.

The primary outcome was the occurrence of MACE, defined as a composite of all-cause mortality and non-fatal myocardial infarction during the follow-up period. Outcome data were obtained retrospectively through review of hospital records, outpatient follow-up notes, and the national electronic health record system when available.

The study protocol was approved by the Ethics Committee of Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Committee (Approval Number: 2025/10, Date: 21.05.2025), and all procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki. Informed consent was waived due to the retrospective design of the study. The authors confirm that no artificial intelligence (AI)-assisted technologies (such as large language models [LLMs], chatbots, or image generators) were used in the production of this manuscript.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Variables with a normal distribution were expressed as mean ± standard deviation (SD), while those with a non-normal distribution were presented as median with interquartile range (IQR). Categorical variables were reported as frequencies and percentages. Patients were categorized into three groups based on their rSS (rSS = 0, rSS = 1-8, and rSS > 8), and baseline clinical, laboratory, and angiographic characteristics were compared across groups using one-way analysis of variance (ANOVA) or the Kruskal-Wallis test for continuous variables, and the chi-square or Fisher's exact test for categorical variables. To assess the relationship between HALP score and rSS, Spearman correlation analysis was performed. Additionally, multivariable linear regression analysis was conducted to identify independent predictors of rSS, including variables with a p-value < 0.10 in univariable analysis. Receiver operating characteristic (ROC) curve analysis was used to evaluate the performance of the HALP score in predicting high residual coronary disease burden (rSS > 8). The optimal HALP cut-off value of 2.96, determined using the Youden index, was used to stratify patients into two groups (HALP ≤ 2.96 and HALP > 2.96) for further analyses. The prognostic value of the HALP score for predicting 12-month MACE was assessed using Cox proportional hazards regression analysis. Variables with a p-value < 0.10 in univariable analysis were entered into the multivariable model. Kaplan-Meier survival curves were generated according to HALP categories, and survival differences were evaluated using the log-rank test. A two-tailed p-value < 0.05 was considered statistically significant.

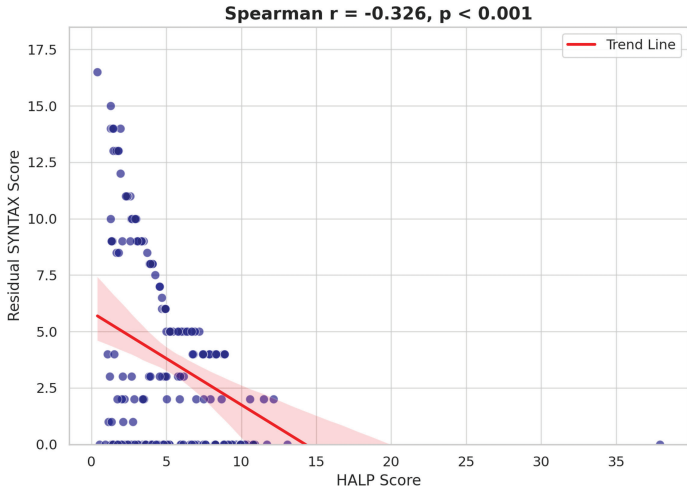

Figure 2. Association between HALP score and residual SYNTAX score.

HALP, Hemoglobin, albumin, lymphocyte, and platelet.

Results

A total of 210 patients with T2DM and NSTEMI were divided into three groups based on rSS: rSS = 0 (n = 86), rSS = 1-8 (n = 84), and rSS > 8 (n = 40). Baseline demographic, clinical, angiographic, and laboratory characteristics according to rSS groups are summarized in Table 1. Patients with rSS > 8 were significantly older and had higher Global Registry of Acute Coronary Events (GRACE) scores (P < 0.001). Angiographically, these patients had higher bSS, more frequent involvement of the left main coronary artery (LMCA) and left anterior descending artery (LAD), and a higher rate of staged PCI (all P < 0.001). Laboratory analyses showed that patients in the rSS > 8 group had significantly lower lymphocyte counts and HALP scores (P = 0.013 and P < 0.001, respectively), as well as higher levels of HbA1c, CRP, and LDL-C (P < 0.001, P = 0.001, and P = 0.006, respectively).

Association Between HALP Score and rSS

Spearman correlation analysis revealed a significant inverse relationship between HALP score and rSS (r = -0.326, P < 0.001) (Figure 2). In the multivariable linear regression analysis, the HALP score was independently associated with rSS (β = -0.344, P < 0.001) (Table 2).

Predictive Performance of the HALP Score for High rSS

ROC curve analysis was performed to evaluate the ability of the HALP score to predict high residual coronary disease burden, defined as rSS > 8. The analysis showed that the HALP score had an area under the curve (AUC) of 0.848 (P < 0.001) for predicting rSS > 8. The optimal cut-off value of HALP 2.96 provided a sensitivity of 78% and a specificity of 77% (Figure 3).

Table 1. Baseline characteristics according to residual synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score groups

	rSS = 0 (n = 86)	rSS = 1–8 (n = 84)	rSS > 8 (n = 40)	P
Age, years	66.0 (59.0–69.3)	62.5 (53.0–69.0)	75.0 (68.0–77.7)	< 0.001
Male sex, n (%)	64 (74.4)	59 (70.2)	23 (57.5)	0.156
BMI, kg/m²	28.1 (26.3–31.9)	28.2 (25.9–30.9)	27.1 (25.0–30.3)	0.249
Smoking status, n (%)	52 (60.5)	42 (50.0)	30 (75.0)	0.028
HT, n (%)	64 (74.4)	55 (65.5)	34 (85.0)	0.067
HL, n (%)	50 (58.1)	53 (63.1)	30 (75.0)	0.188
COPD, n (%)	5 (5.8)	9 (10.7)	7 (17.5)	0.121
History of stroke, n (%)	7 (8.1)	7 (8.3)	1 (2.5)	0.447
CKD, n (%)	20 (23.3)	24 (28.6)	21 (52.5)	0.004
AF, n (%)	8 (9.3)	6 (7.1)	2 (5.0)	0.683
GRACE score	120.8 ± 16.1	124.3 ± 20.4	137.3 ± 23.5	< 0.001
bSS	7.0 (4.7–9.0)	9.5 (7.0–13.0)	18.5 (16.6–20.0)	< 0.001
rSS	0.0 (0.0–0.0)	4.0 (3.0–5.0)	10.0 (9.0–13.0)	< 0.001
HR, beats/min	82.5 ± 11.2	81.8 ± 15.1	78.9 ± 14.9	0.375
Diastolic BP, mmHg	80.6 ± 10.0	77.6 ± 15.6	78.8 ± 10.7	0.306
Systolic BP, mmHg	137.2 ± 19.2	136.2 ± 22.0	139.8 ± 21.2	0.668
Killip class				0.017
Class I, n (%)	80 (93.0)	74 (88.1)	29 (72.5)	
Class II, n (%)	6 (7.0)	9 (10.7)	8 (20.0)	
Class III, n (%)	0 (0.0)	1 (1.2)	3 (7.5)	
Infarct-related artery involvement				
LMCA, n (%)	0 (0.0)	0 (0.0)	2 (5.0)	0.014
LAD and/or its branches, n (%)	40 (46.5)	26 (31.0)	23 (57.5)	0.007
Cx and/or its branches, n (%)	27 (31.4)	20 (23.8)	5 (12.5)	0.071
RCA and/or its branches, n (%)	19 (22.1)	38 (45.2)	12 (30.0)	0.108
Other affected vessels				
LMCA, n (%)	0 (0.0)	1 (1.2)	4 (10.0)	< 0.001
LAD and/or its branches, n (%)	0 (0.0)	25 (29.8)	7 (17.5)	0.008
Cx and/or its branches, n (%)	0 (0.0)	33 (39.3)	17 (42.5)	< 0.001
RCA and/or its branches, n (%)	0 (0.0)	18 (21.4)	12 (30.0)	< 0.001
PCI performed at different time, n (%)	0 (0.0)	46 (54.8)	28 (70.0)	< 0.001
LVEF, %	50.0 (45.7–55.0)	50.0 (45.0–55.0)	48.0 (42.0–50.0)	0.006
LV-EDD, mm	50.0 (47.0–53.0)	50.5 (48.0–55.0)	50.0 (45.0–52.7)	0.157
LA, mm	39.0 (36.0–41.0)	39.0 (36.2–41.0)	38.5 (37.0–41.0)	0.630
Hemoglobin, g/dL	13.3 ± 2.0	13.4 ± 1.6	12.9 ± 1.8	0.304
RBC, $\times 10^6$/μL	4.6 ± 0.5	4.5 ± 0.6	4.6 ± 0.6	0.517
WBC, $\times 10^3$/μL	8.6 (7.1–11.4)	8.3 (7.0–10.6)	8.8 (7.0–11.1)	0.754
Neutrophil, $\times 10^3$/μL	5.9 (4.6–8.9)	5.7 (4.6–8.9)	5.7 (4.4–7.7)	0.843
Lymphocyte, $\times 10^3$/μL	1.7 (1.2–2.4)	1.7 (1.4–2.3)	1.4 (1.0–1.7)	0.013
Monocyte, $\times 10^3$/μL	0.6 (0.4–0.7)	0.5 (0.4–0.7)	0.6 (0.5–0.8)	0.418
Platelet, $\times 10^3$/μL	228.0 (175.0–278.2)	230.0 (188.2–265.5)	233.5 (192.5–270.7)	0.795
Albumin, g/dL	41.0 (39.0–43.2)	41.0 (39.0–44.0)	41.0 (40.0–43.0)	0.686
HALP score	4.9 (2.4–9.0)	5.0 (3.9–6.8)	2.3 (1.5–2.9)	< 0.001
Creatinine, mg/dL	0.9 (0.8–1.1)	1.0 (0.9–1.2)	1.1 (0.8–1.6)	0.023

Table 1 (cont). Baseline characteristics according to residual synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score groups

	rSS = 0 (n = 86)	rSS = 1–8 (n = 84)	rSS > 8 (n = 40)	P
eGFR, mL/min/1.73 m²	72.3 ± 14.1	68.6 ± 14.6	64.9 ± 17.7	0.033
Glucose, mg/dL	155.5 (118.7–225.7)	167.0 (122.2–240.2)	230.0 (131.2–293.0)	0.043
HbA1c, %	7.6 (6.8–9.1)	8.1 (6.9–9.7)	9.4 (8.4–10.6)	<0.001
CRP, mg/L	4.0 (2.0–7.0)	4.8 (2.3–10.5)	9.3 (4.2–16.5)	0.001
ALT, U/L	21.5 (15.0–31.2)	19.5 (14.0–29.0)	18.0 (12.0–26.7)	0.158
Total cholesterol, mg/dL	202.5 ± 39.4	202.1 ± 42.5	221.9 ± 45.8	0.030
Non-HDL cholesterol, mg/dL	143.4 ± 43.2	145.8 ± 44.1	172.7 ± 48.7	0.002
LDL, mg/dL	126.0 ± 31.3	132.7 ± 36.8	147.8 ± 39.8	0.006
HDL, mg/dL	40.0 (35.0–46.0)	38.5 (34.0–45.7)	39.5 (34.2–44.7)	0.894
TG, mg/dL	157.0 (107.7–213.5)	135.5 (92.5–233.0)	187.0 (155.5–287.7)	0.003

AF, Atrial fibrillation; ALT, Alanine aminotransferase; BMI, Body mass index; BP, Blood pressure; bSS, Baseline SYNTAX score; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; CRP, C-Reactive protein; Cx, Circumflex artery; eGFR, Estimated glomerular filtration rate; GRACE, Global registry of acute coronary events; HbA1c, Hemoglobin A1c; HDL, High-density lipoprotein; HL, Hyperlipidemia; HR, Heart rate; HT, Hypertension; LA, Left atrial diameter; LAD, Left anterior descending artery; LDL, Low-density lipoprotein; LV-EDD, Left ventricular end-diastolic diameter; LVEF, Left ventricular ejection fraction; Non-HDL, Non-high-density lipoprotein; PCI, Percutaneous coronary intervention; RBC, Red blood cell count; RCA, Right coronary artery; rSS, Residual SYNTAX score; TG, Triglycerides; WBC, White blood cell count.

Table 2. Multivariable linear regression analysis for predictors of residual synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score

	Beta coefficient	95% CI	P
Age, years	0.049	0.003–0.095	0.037
Male sex□	0.114	-1.068–1.296	0.849
HT□	0.732	-0.470–1.933	0.231
CRP, mg/L	0.062	0.012–0.112	0.016
LVEF, %	-0.042	-0.122–0.039	0.305
eGFR, mL/min/1.73 m²	-0.020	-0.056–0.016	0.277
HbA1c, %	0.422	0.136–0.708	0.004
HALP score	-0.344	-0.488– -0.201	< 0.001

Model R^2 = 0.249; Adjusted R^2 = 0.219. □: Retained in the model due to clinical relevance despite non-significance. Other variables with P < 0.10 in univariate analysis were included in the multivariate model. CI, Confidence interval; CRP, C-Reactive protein; eGFR, Estimated glomerular filtration rate; HALP, Hemoglobin, albumin, lymphocyte, and platelet score; HbA1c, Glycated hemoglobin; HT, Hypertension; LVEF, Left ventricular ejection fraction.

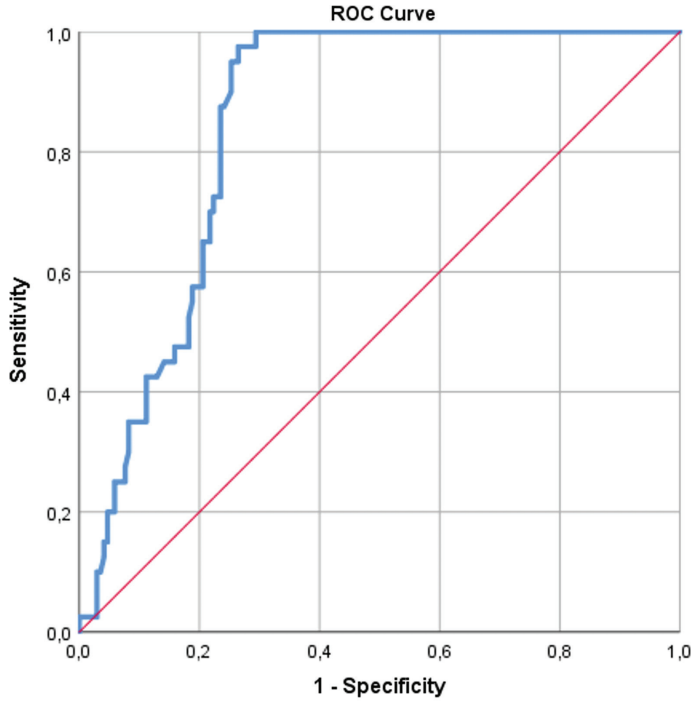

Figure 3. ROC curve analysis of the HALP score for predicting residual SYNTAX score > 8. At the optimal cut-off value of HALP < 2.96, the AUC was 0.848, with a sensitivity of 78%, specificity of 77% (95% CI: 0.802–0.901, P < 0.001).

AUC, Area under the curve; HALP, Hemoglobin, albumin, lymphocyte, and platelet; ROC, Receiver operating characteristic.

Clinical Outcomes According to HALP Score

Based on the ROC-derived cut-off, patients were categorized into two groups: HALP > 2.96 (n = 139) and HALP ≤ 2.96 (n = 71). As shown in Table 3, the proportion of patients with rSS > 8 was significantly higher in the HALP ≤ 2.96 group (43.7% vs. 6.5%, P < 0.001). During the 12-month follow-up, MACE occurred more frequently in the low HALP group (29.6% vs. 13.7%, P = 0.005). Non-fatal MI was also more common (15.5% vs. 6.5%, P = 0.035), while the difference in all-cause mortality was not statistically significant (14.2% vs. 7.1%, P = 0.108).

Prognostic Value of HALP Score for 12-Month Outcome

According to univariate Cox regression analysis, age, CRP level, rSS > 8, HALP ≤ 2.96, and the presence of an LMCA lesion were all significantly associated with MACE. In the multivariable model, HALP ≤ 2.96 remained an independent predictor of MACE (hazard ratio [HR] = 1.916, 95% confidence interval [CI]: 1.013–3.621, P = 0.045), along with age (HR = 1.036, P = 0.026) and CRP (HR = 1.026, P = 0.011) (Table 4).

Table 3. Comparison of residual synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score and clinical outcomes based on receiver operating characteristic (ROC)-derived hemoglobin, albumin, lymphocyte, and platelet (HALP) score cut-off

	HALP score > 2.96 (n = 139)	HALP score ≤ 2.96 (n = 71)	P
rSS group, n (%)			< 0.001
rSS = 0	59 (42.4)	27 (38.0)	
rSS = 1-8	71 (51.1)	13 (18.3)	
rSS > 8	9 (6.5)	31 (43.7)	
Non-fatal MI, n (%)	9 (6.5)	11 (15.5)	0.035
All-cause mortality, n (%)	10 (7.1)	10 (14.2)	0.108
MACE*, n (%)	19 (13.7)	21 (29.6)	0.005

*MACE was defined as a composite of non-fatal myocardial infarction and all-cause mortality. HALP, Hemoglobin, albumin, lymphocyte, and platelet score; MACE, Major adverse cardiovascular events; MI, Myocardial infarction; ROC, Receiver operating characteristic; rSS, Residual SYNTAX score.

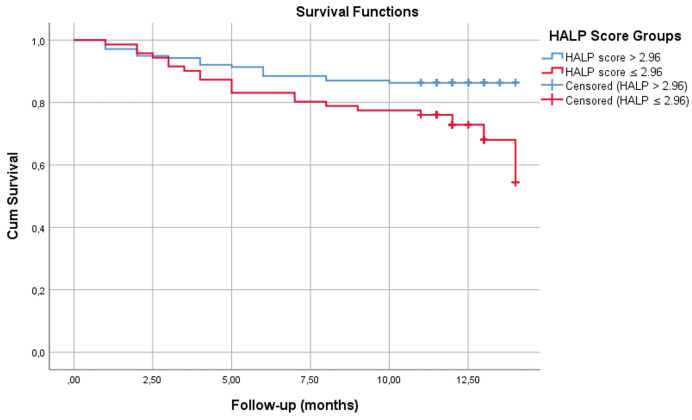

Figure 4. Kaplan-Meier survival curves based on HALP score groups over a 12-month follow-up period. Patients with a HALP score ≤ 2.96 had significantly lower cumulative survival compared to those with a HALP score > 2.96 during the follow-up period (Log-rank test: χ^2=6.951, df=1, P = 0.008).

HALP, Hemoglobin, albumin, lymphocyte, and platelet; Cum Survival, Cumulative survival.

Table 4. Cox regression analysis for determining the risk factors associated with 12-month major adverse cardiovascular events (MACE)

	Univariate analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age, years	1.044 (1.012–1.076)	0.006	1.036 (1.004–1.068)	0.026
Male sex□	0.823 (0.430–1.577)	0.557		
Smoking	1.878 (0.937–3.762)	0.076		
HT□	0.949 (0.474–1.901)	0.883		
CRP, mg/L	1.026 (1.007–1.045)	0.006	1.026 (1.006–1.047)	0.011
LVEF, %	0.981 (0.939–1.024)	0.382		
eGFR, mL/min/1.73 m²	0.995 (0.975–1.016)	0.651		
HbA1c, %	1.012 (0.861–1.189)	0.888		
rSS >8	2.844 (1.508–5.363)	0.001		
HALP score ≤ 2.96	2.243 (1.206–4.174)	0.011	1.916 (1.013–3.621)	0.045
LMCA lesion	2.617 (1.094–6.258)	0.031		

The final Cox model had a –2 log likelihood of 411.835. □: Included variables had P < 0.10 in univariate analysis or were retained based on clinical relevance. HR, Hazard ratio; CI, Confidence interval; CRP, C-reactive protein; eGFR, Estimated glomerular filtration rate; HALP, Hemoglobin, albumin, lymphocyte, and platelet score; HbA1c, glycated hemoglobin; HT, Hypertension; LMCA, Left main coronary artery; LVEF, Left ventricular ejection fraction; MACE, Major adverse cardiovascular events; rSS, Residual SYNTAX score.

Kaplan-Meier analysis showed a significant difference in cumulative survival between the two HALP groups at 12 months. Patients with HALP ≤ 2.96 had a lower survival rate compared to those with HALP > 2.96 (log-rank test: χ^2 = 6.951, P = 0.008) (Figure 4).

Discussion

This study evaluated the relationship between the HALP score, a composite biomarker reflecting systemic inflammation and nutritional status, and residual coronary disease burden, as measured by the rSS, in patients with T2DM and NSTEMI. Our main findings demonstrated that lower HALP scores were significantly associated with higher rSS values. A HALP score below the ROC-derived threshold of 2.96 independently predicted high residual disease burden (rSS > 8). Furthermore, patients with HALP ≤ 2.96 experienced a significantly higher incidence of MACE over the 12-month follow-up. In multivariable Cox regression analysis, a low HALP score remained an independent predictor of MACE, alongside older age and elevated CRP levels.

The important role of inflammation and nutritional status in the development of diabetes mellitus (DM) and CVD is well established.[19] In patients with T2DM, persistent low-grade inflammation, immune dysregulation, and metabolic disturbances lead to characteristic alterations in hematologic and biochemical parameters.[20-22] Among these, anemia, reflected by low hemoglobin levels, has been associated with increased cardiovascular mortality.[23] Similarly, hypoalbuminemia has been identified as a predictor of adverse cardiovascular outcomes in diabetic patients.[24] Lymphopenia, as also observed in our study

among patients with high rSS (rSS > 8), has been associated with increased cardiovascular risk in individuals with T2DM.[25] Elevated platelet counts, reflecting a prothrombotic and inflammatory state, have also been implicated in the development of atherosclerosis and cardiovascular events in this population.[26]

The HALP score is a novel biomarker that integrates hemoglobin and albumin levels with lymphocyte and platelet counts, reflecting both nutritional and inflammatory status. Although each of these components has been individually associated with cardiovascular outcomes in patients with T2DM, their combined relationship with angiographic disease burden has not previously been investigated in this population.

Recent studies have further highlighted the prognostic value of the HALP score in diabetic populations. Lower HALP scores have been identified as independent risk factors for microvascular complications such as diabetic nephropathy and retinopathy and have shown a negative association with both glomerular filtration rate and retinal vascular damage.[27] More importantly, a large-scale cohort analysis demonstrated that the HALP score was independently and inversely correlated with both all-cause and cardiovascular mortality in individuals with diabetes or prediabetes.[28] In line with these findings, our results showed that patients with higher rSS had significantly lower HALP values, highlighting a possible mechanistic pathway through which systemic metabolic imbalance contributes to incomplete coronary revascularization.

Systemic disturbances in patients with T2DM contribute to vascular dysfunction and progressive atherosclerosis.[29,30] A significant relationship was identified between lower HALP scores and higher rSS, which proved to be robust in multivariable linear regression analysis. Given that the rSS reflects the extent of unrevascularized coronary atherosclerosis, the HALP score may serve as an indirect indicator of diffuse atherosclerotic burden in diabetic patients.

A cut-off value of 2.96 demonstrated the HALP score's ability to distinguish patients with rSS > 8 in our study. A recent study by Ilis et al.[31] also showed that the HALP score had prognostic value in patients with NSTEMI, independent of diabetes status, reporting that a threshold of 2.62 predicted in-hospital mortality. In our study, patients with HALP scores ≤ 2.96 experienced significantly higher rates of non-fatal MI and overall MACE during the 12-month follow-up. Given its previously reported association with in-hospital mortality,[31,32] the HALP score may also be useful in identifying long-term risk in diabetic patients with NSTEMI.

Our multivariable Cox regression analysis showed that the HALP score was an independent predictor of 12-month MACE, while HbA1c was not. This discrepancy may be explained by collinearity, as the HALP score includes hemoglobin and albumin, parameters influenced by both glycemic control and nutritional status. Moreover, markers of inflammation and nutrition may provide prognostic information that extends beyond traditional glycemic metrics in diabetic patients with acute coronary syndromes. A recent meta-analysis by Pan et al.[33] demonstrated that HbA1c was not significantly associated with short-term mortality in diabetic patients with acute coronary syndrome, suggesting that conventional glycemic markers may not fully capture cardiovascular risk in this population.[34] In contrast, composite indices such as the HALP score have been shown to reflect both inflammation and systemic resilience. For example, Liu et al.[35] reported that the HALP score independently predicted no-reflow and long-term MACE in patients with ST-segment elevation myocardial infarction (STEMI), while Zhao et al.[28] found an inverse relationship between HALP and cardiovascular mortality in a large diabetic cohort from the National Health and Nutrition Examination Survey (NHANES) database. These findings support the idea that the HALP score, previously linked to in-hospital mortality in acute coronary syndrome patients, may also help identify diabetic patients with NSTEMI who are at increased risk of long-term adverse cardiovascular outcomes. In our study, this was reflected by a significantly higher incidence of MACE, primarily driven by non-fatal MI.

This study has certain limitations. The data were collected retrospectively, so not all potential confounding factors could be controlled. The results reflect the experience of a single center and may not be generalizable to other clinical settings. The HALP score was calculated only at admission; therefore, we were unable to evaluate changes over time. We included only patients with NSTEMI and T2DM, allowing for a focused analysis but limiting the applicability of the findings to broader populations. Variations in the timing of staged PCI procedures (typically 10 to 30 days post-procedure) may have introduced heterogeneity in rSS calculation. Additionally, follow-up began after PCI procedures for non-IRAs, which may have contributed to variability in follow-up timing. Finally, the strict exclusion criteria, including the absence of previously known CAD, resulted in a more homogeneous but smaller study population.

Conclusion

In patients with NSTEMI and T2DM, lower HALP scores were independently associated with both higher residual coronary disease burden and an increased risk of adverse cardiovascular events. Integrating the HALP score into clinical workflows, alongside tools such as the GRACE score, may offer a practical approach to identifying high-risk diabetic patients with NSTEMI.

Ethics Committee Approval: Ethics committee approval was obtained from Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Committee (Approval Number: 2025/10, Date: 21.05.2025).

Informed Consent: Informed consent was waived due to the retrospective design of the study.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: The authors confirm that no artificial intelligence (AI)-assisted technologies (such as large language models [LLMs], chatbots, or image generators) were used in the production of this manuscript.

Author Contributions: Concept – İ.E.; Design – İ.E., P.A.; Supervision – İ.E.; Resource – İ.E., P.A..; Materials – P.A.; Data Collection and/or Processing – İ.E., P.A.; Analysis and/or Interpretation – İ.E.; Literature Review – İ.E., P.A.; Writing – İ.E.; Critical Review – P.A.

Peer-review: Externally peer-reviewed.

References

1. Roth GA, Mensah GA, Johnson CO, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: Update from the GBD 2019 study. *J Am Coll Cardiol*. 2020;76(25):2982–3021. [CrossRef]
2. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: A systematic literature review of scientific evidence from across the world in 2007–2017. *Cardiovasc Diabetol*. 2018;17(1):83. [CrossRef]
3. Skoda R, Nemes A, Bárczi G, et al. Survival of myocardial infarction patients with diabetes mellitus at the invasive era (Results from the városmajor myocardial infarction registry). *J Clin Med*. 2023;12(3):917. [CrossRef]
4. Luo J, Qin X, Zhang X, et al. Prognostic implications of systemic immune-inflammation index in myocardial infarction patients with and without diabetes: Insights from the NOAFCAMI-SH registry. *Cardiovasc Diabetol*. 2024;23(1):41. [CrossRef]
5. Peng Y, Lin A, Luo B, Chen L, Lin Y. The effect of prognostic nutritional index on diabetic patients with myocardial infarction. *Diabetol Metab Syndr*. 2024;16(1):179. [CrossRef]
6. Li T, Yuan D, Wang P, et al. Association of prognostic nutritional index level and diabetes status with the prognosis of coronary artery disease: A cohort study. *Diabetol Metab Syndr*. 2023;15(1):58. [CrossRef]
7. Li J, Zhu P, Li Y, et al. A novel inflammatory biomarker, high-sensitivity C-reactive protein-to-albumin ratio, is associated with 5-year outcomes in patients with type 2 diabetes who undergo percutaneous coronary intervention. *Diabetol Metab Syndr*. 2023;15(1):14. [CrossRef]
8. Pan H, Lin S. Association of hemoglobin, albumin, lymphocyte, and platelet score with risk of cerebrovascular, cardiovascular, and all-cause mortality in the general population: Results from the NHANES 1999–2018. *Front Endocrinol (Lausanne)*. 2023;14:1173399. [CrossRef]
9. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in The Atherosclerosis Risk in Communities (ARIC) study. *J Am Coll Cardiol*. 2002;40(1):27–33. [CrossRef]
10. Oduncu V, Erkol A, Karabay CY, et al. The prognostic value of serum albumin levels on admission in patients with acute ST-segment elevation myocardial infarction undergoing a primary percutaneous coronary intervention. *Coron Artery Dis*. 2013;24(2):88–94. [CrossRef]
11. Ommen SR, Gibbons RJ, Hodge DO, Thomson SP. Usefulness of the lymphocyte concentration as a prognostic marker in coronary artery disease. *Am J Cardiol*. 1997;79(6):812–814. [CrossRef]
12. Angiolillo DJ, Bernardo E, Sabaté M, et al. Impact of platelet reactivity on cardiovascular outcomes in patients with type 2 diabetes mellitus and coronary artery disease. *J Am Coll Cardiol*. 2007;50(16):1541–1547. [CrossRef]
13. Farooq V, Serruys PW, Bourantas CV, et al. Quantification of incomplete revascularization and its association with five-year mortality in the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) trial validation of the residual SYNTAX score. *Circulation*. 2013;128(2):141–151. [CrossRef]
14. Yan L, Li P, Wang Y, et al. Impact of the residual SYNTAX score on clinical outcomes after percutaneous coronary intervention for patients with chronic renal insufficiency. *Catheter Cardiovasc Interv*. 2020;95(Suppl 1):606–615. [CrossRef]
15. Altunova M, Karakayalı M, Kahraman S, et al. Systemic immune-inflammatory index is associated with residual SYNTAX score in patients with ST-segment elevation myocardial infarction. *Anatol J Cardiol*. 2023;27(8):472–478. [CrossRef]
16. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023;44(38):3720–3826. [CrossRef]
17. Généreux P, Palmerini T, Caixeta A, et al. Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: The residual SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) score. *J Am Coll Cardiol*. 2012;59(24):2165–2174. [CrossRef]
18. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes–2024. *Diabetes Care*. 2024;47(Suppl 1):S20–S42. [CrossRef]
19. Zhang J, Fan X, Xu Y, et al. Association between inflammatory biomarkers and mortality in individuals with type 2 diabetes: NHANES 2005–2018. *Diabetes Res Clin Pract*. 2024;209:111575. [CrossRef]
20. Tsalamandris S, Antonopoulos AS, Oikonomou E, et al. The role of inflammation in diabetes: Current concepts and future perspectives. *Eur Cardiol*. 2019;14(1):50–59. [CrossRef]
21. Li H, Zou L, Long Z, Zhan J. Immunometabolic alterations in type 2 diabetes mellitus revealed by single-cell RNA sequencing: Insights into subtypes and therapeutic targets. *Front Immunol*. 2025;15:1537909. [CrossRef]
22. Pellegrini V, La Grotta R, Carreras F, et al. Inflammatory trajectory of type 2 diabetes: Novel opportunities for early and late treatment. *Cells*. 2024;13(19):1662. [CrossRef]
23. Zoppini G, Targher G, Chonchol M, et al. Anaemia, independent of chronic kidney disease, predicts all-cause and cardiovascular mortality in type 2 diabetic patients. *Atherosclerosis*. 2010;210(2):575–580. [CrossRef]
24. Jhund PS, McMurray JJ, Chaturvedi N, et al. Mortality following a cardiovascular or renal event in patients with type 2 diabetes in the ALTITUDE trial. *Eur Heart J*. 2015;36(36):2463–2469. [CrossRef]
25. Zidar DA, Al-Kindi SG, Liu Y, et al. association of lymphopenia with risk of mortality among adults in the US general population. *JAMA Netw Open*. 2019;2(12):e1916526. [CrossRef]
26. Colwell JA, Nesto RW. The platelet in diabetes: Focus on prevention of ischemic events. *Diabetes Care*. 2003;26(7):2181–2188. [CrossRef]
27. Tel BMA, Tel MR, Bilgin S, Duman TT, Aktas G. Diagnostic value of HALP score in detecting diabetic nephropathy in patients with type 2 diabetes mellitus. *Ibnosina J Med Biomed Sci*. 2024;16(3):116–122. [CrossRef]
28. Zhao P, Zhang Z, Li M, Hao J, Wang Y. Association between hemoglobin-albumin-lymphocyte-platelet score and all-cause or cardiovascular mortality in patients with diabetes or prediabetes: Mediated effects of renal function. *BMC Cardiovasc Disord*. 2025;25(1):331. [CrossRef]
29. Wang S, Jia B, Niu S, Chen S. Relationship between the hemoglobin, albumin, lymphocyte count, platelet count (HALP) score and type 2 diabetes retinopathy. *Diabetes Metab Syndr Obes*. 2024;17:2693–2706. [CrossRef]
30. Paneni F, Beckman JA, Creager MA, Cosentino F. Diabetes and vascular disease: Pathophysiology, clinical consequences, and medical therapy: Part I. *Eur Heart J*. 2013;34(31):2436–2443. [CrossRef]
31. Ilis D, Arslan A, Artac I, et al. Prognostic value of HALP score in predicting in-hospital mortality in patients with NSTEMI. *Biomark Med*. 2025;19(5):139–147. [CrossRef]
32. Karakayali M, Omar T, Artac I, et al. The prognostic value of HALP score in predicting in-hospital mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Coron Artery Dis*. 2023;34(7):483–488. [CrossRef]
33. Pan W, Lu H, Lian B, Liao P, Guo L, Zhang M. Prognostic value of HbA1c for in-hospital and short-term mortality in patients with acute coronary syndrome: A systematic review and meta-analysis. *Cardiovasc Diabetol*. 2019;18(1):169. [CrossRef]
34. Zheng Y, Huang Y, Li H. Hemoglobin albumin lymphocyte and platelet score and all-cause mortality in coronary heart disease: A retrospective cohort study of NHANES database. *Front Cardiovasc Med*. 2023;10:1241217. [CrossRef]
35. Liu H, Zhang F, Li Y, et al. The HALP score predicts no-reflow phenomenon and long-term prognosis in patients with ST-segment elevation myocardial infarction after primary percutaneous coronary intervention. *Coron Artery Dis*. 2025;36(4):273–280. [CrossRef]