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ORIGINAL RESEARCH

Evaluation of the prognostic value of systemic inflammation indexes in patients diagnosed with acute coronary syndrome in the emergency department

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Abstract

Background: Cardiovascular diseases progress through inflammation. The aim of this study was to determine the prognostic value of systemic inflammation markers in predicting mortality in patients with acute coronary syndrome (ACS). **Methods**: This retrospective cross-sectional study included patients who presented at the Emergency Department (ED) with ACS (ST segment elevation myocardial infarction (STEMI)-Myocardial infarction without ST segment elevation (NSTEMI)). Patients who met the study inclusion criteria were selected retrospectively and data were retrieved from the hospital's automated records system. Systemic inflammatory indexes, including the Systemic inflammation response index (SIRI), Systemic immune-inflammation index (SII) and Aggregate index of systemic inflammation (AISI) were calculated. The patients were grouped according to mortality status and were examined in two groups as STEMI and NSTEMI. **Results**: The study included 509 patients, comprising 77.2% males and 22.8% females with a mean age of 57.7 years. STEMI was diagnosed in 309 patients and NSTEMI in 200. The most common comorbidities were hypertension in 27.4% of cases, coronary artery disease in 19.4%, and diabetes mellitus in 16.8%. Mortality occurred in 14.3% of the cases. The mean age was found to be significantly higher in the NSTEMI group than in the STEMI group ($p < 0.05$). The neutrophil value, SII, SIRI and AISI values were significantly higher in the NSTEMI group than in the STEMI group ($p < 0.05$ for all). The Neutrophil to Lymphocyte ratio (NLR), SIRI, SII and AISI values were also markedly higher in the exitus patient group than in the survivors group ($p < 0.05$ for all). The multivariate regression analysis results showed that the NLR, SIRI and AISI values had an independent and significant impact on distinguishing survivors from deceased the patients ($p < 0.05$). **Conclusions**: Systemic inflammation indexes were found to be significant predictors of mortality in patients with ACS.

Keywords

STEMI-NSTEMI; Systemic inflammation indexes; Mortality

1. Introduction

Cardiovascular diseases (CVD), particularly coronary heart disease, are complex chronic conditions, with multiple risk factors. including dyslipidemia, hypertension, insulin resistance, hypercoagulability and inflammatory responses [1]. Although great advances have been made in the prevention and treatment of CVDs, they remain a leading cause of death and disability worldwide [2].

To mitigate the impact of CVDs on public health, researchers have increasingly focused on the role of low-grade inflammatory markers in the disease process [3]. Evidence suggests that patients with systemic inflammatory diseases are at much greater risk of developing CVD than the general population [4]. Moreover, inflammatory variables have been identified as potential predictive markers for CVD. In acute coronary syndrome (ACS), cytokines such as interleukin and white blood cell subclusters contribute to endothelial dysfunction, and these markers are used for risk classification [5]. It has also been reported that the balance of lymphocyte subgroups is impaired due to increased expression of interferon and chemokines by proinflammatory cell subclusters [6]. Atherosclerotic plaque become more prone to rupture and thromboses are formed as a result of intensified inflammation. Given the established relationship between high blood inflammatory markers and the development and progression of disease of CVD, the peripheral blood count serves as a simple yet valuable significant tool [7]. White blood cell counts and subcluster counts, and acute phase proteins obtained from routine blood tests are commonly used

as markers of systemic inflammation in clinical practice [8]. Additionally, immunological inflammatory cells have been identified as predictive factors related to the formation and progression of CVDs. Counts of neutrophil, lymphocyte and thrombocyte, as well as the ratios between these cell types, calculated from routine blood tests, have been extensively studied as prognostic tools. Research indicates that the predictive value of these ratios for all-cause mortality and mortality related to major cardiovascular events is superior to that of white blood cell counts and the subcluster counts directly obtained from routine blood tests [9].

The aim of this study was to investigate the prognostic value of the Systemic inflammation response index (SIRI), Systemic immune-inflammation index (SII) and Aggregate index of systemic inflammation (AISI) inflammatory indexes in patients diagnosed with STEMI and NSTEMI.

2. Materials and methods

Approval for this retrospective, cross-sectional, single-centre study was granted by the Clinical Research Ethics Committee of the Application and Research Centre of Health Sciences University Şişli Hamidiye Eftal Training and Research Hospital (decision no: 3884, dated: 18 April 2023). Patients were selected from those aged >18 years who presented at Şişli Hamidiye Eftal Training and Research Hospital between 2019 and 2023.

2.1 Study inclusion criteria

The patients included in the study were those who presented to the Emergency Department (ED) with symptoms of chest pain, shortness of breath and fainting, were diagnosed with ACS, and were subsequently found to have critical coronary narrowing on coronary angiography. The entire patient cohort consisted of individuals with a Synergy Between Taxus and percutaneous coronary intervention (PCI) and Cardiac Surgery Prolonged Survival (SYNTAX) score of moderate to high (>22) and necessitating revascularisation [10].

2.2 Study exclusion criteria

- Age <18 years,
- Findings of sepsis and septic shock,
- The presence of hemolytic anemia, autoimmune disease or advanced grade malignancy,
- Pregnancy,
- The presence of end-stage chronic kidney or liver failure,
- Incomplete data in the hospital records.

Patient data were retrieved from the hospital automated records system in respect of demographic characteristics (age, gender, exitus status), clinical characteristics, length of hospital stay, comorbidities, smoking status, family history, vital signs, biochemical parameters, hemogram test parameters and the inflammation markers (NLR, SII, SIRI, AISI) calculated from these parameters. Inflammation indices of the patients were calculated from blood analyses taken at the time of presentation to the emergency department. Patients who presented at ED were diagnosed with ACS and admitted to the Coronary Intensive Care Unit (ICU) were examined in two groups of STEMI and NSTEMI according to the European Society of Cardiology (ESC) 2023 guidelines.

The inflammatory parameters were calculated as follows:

- NLR = Neutrophil count/lymphocyte count,
- SII = Platelet count × neutrophil count/lymphocyte count,
- SIRI = Neutrophil count × monocyte count/lymphocyte count,
- AISI = Neutrophil count × platelet count × monocyte count/lymphocyte count.

2.3 Statistical analysis

Data obtained in the study were analyzed using SPSS version. 28.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as mean ± standard deviation, median, maximum and minimum values for continuous variables and as number (n) and percentage (%) for categorical variables. Conformity of the data to normal distribution was examined with the Kolmogorov-Smirnov test. For the analysis of independent quantitative data, the Mann Whitney U-test was used, and the Chi-square test was applied to categorical data. The effect of independent variables on dependent variables was calculated with Binary Logistic Regression Analysis. Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the predictive value of variables. A value of $p < 0.05$ was considered statistically significant.

3. Results

A total of 509 patients who were diagnosed with ACS and admitted to the coronary ICU were evaluated, comprising 393 (77.2%) males and 116 (22.8%) females with a mean age of 57.7 years. A diagnosis of STEMI was made in 309 cases and NSTEMI in 200.

In the STEMI patients, the electrocardiography (ECG) findings showed anterior STEMI in 144 (46.6%) and inferior STEMI in 144 (46.6%). The risk factors most often determined were hypertension (HT) (n = 211, 27.4%), coronary artery disease (CAD) (n = 149, 19.4%) and diabetes mellitus (DM) (n = 129, 16.8%) (Table 1).

The median thrombolysis in myocardial infarction (TIMI) and History, Electrocardiogram, Age, Risk factors, and Troponin (HEART) scores of the patients were 3 and 5, respectively, placing them in the moderate risk group. The median values of the vital and hematological parameters were found to be within the normal cut-off range. The median length of hospital stay was 3 days. A total of 73 patients were determined as exitus in the NSTEMI and STEMI groups (Table 2).

The age of patients at presentation was significantly higher in the NSTEMI group compared to the STEMI group ($p < 0.05$). Similarly, the proportion of female patients was significantly higher in the NSTEMI group than in the STEMI group ($p < 0.05$). In terms of comorbidities, the rates of CAD, HT, DM, congestive heart failure (CHF) and coronary artery bypass graft (CABG) were significantly higher in the NSTEMI group than in the STEMI group ($p < 0.05$). However, there was significant difference between the NSTEMI and STEMI groups in the rates of cerebrovascular disease (CVD), hyperlipidemia (HL), chronic renal failure (CRF) and chronic

TABLE 1. Demographic information, comorbidities and ECG characteristics of the patients.

	Min–Max	Median	Mean ± standard deviation (SD)/n (%)
Age on presentation (yr)	28.0–93.0	57.0	57.7 ± 12.0
Gender			
Male			393 (77.2%)
Female			116 (22.8%)
Comorbidities			
HT			211 (27.4%)
CAD			149 (19.4%)
DM			129 (16.8%)
CABG			32 (4.2%)
CRF			22 (2.9%)
COPD			20 (2.6%)
HL			20 (2.6%)
CHF			16 (2.1%)
CVD			7 (0.9%)
Smoking status			
(−)			381 (74.9%)
(+)			128 (25.1%)
Family history			
(−)			384 (75.4%)
(+)			125 (25.6%)
Anterior MI			
(−)			165 (53.4%)
(+)			144 (46.6%)
Inferior MI			
(−)			165 (53.4%)
(+)			144 (46.6%)
Posterior MI			
(−)			284 (91.9%)
(+)			25 (8.1%)
Lateral MI			
(−)			298 (96.4%)
(+)			11 (3.6%)
AVR Elevation			
(−)			307 (99.4%)
(+)			2 (0.6%)
Group			
STEMI			309 (60.7%)
NSTEMI			200 (39.3%)

Min: minimum; Max: maximum; HT: Hypertension; CAD: Coronary artery disease; DM: Diabetes mellitus; CABG: Coronary artery bypass graft; CRF: Chronic renal failure; COPD: Chronic obstructive pulmonary disease; HL: Hyperlipidemia; CHF: Congestive heart failure; CVD: Cerebrovascular disease; MI: Myocardial infarction; AVR: Lead augmented vector right; STEMI: ST segment elevation myocardial infarction; NSTEMI: Myocardial infarction without ST segment elevation.

TABLE 2. Analyses of the inflammation indexes with the vital and clinical characteristics and hematological parameters of the patients.

	Min–Max	Median	Mean ± SD/n (%)
TIMI Score	0.0–6.0	3.0	3.1 ± 1.6
HEART Score	2.0–9.0	5.0	5.4 ± 1.7
Systolic Blood Pressure	75.0–230.0	128.0	136.2 ± 31.7
Pulse	45.0–149.0	89.0	92.5 ± 24.5
Temperature	35.7–37.4	36.8	36.6 ± 0.5
WBC	1.1–25.1	10.6	11.1 ± 3.9
Neutrophils	0.4–34.2	12.2	12.9 ± 6.9
Lymphocytes	0.2–6.9	2.3	2.6 ± 1.4
Monocytes	0.2–2.8	1.1	1.2 ± 0.4
RBC	0.1–6.3	4.8	4.7 ± 0.7
HGB	68.0–197.0	145.0	141.0 ± 19.9
HCT	20.9–93.6	43.3	42.7 ± 6.5
MCV	29.6–120.0	90.4	89.7 ± 7.3
PLT	108.0–629.0	315.0	345.0 ± 104.2
MPV	6.7–14.3	9.9	10.0 ± 1.2
PDW	0.3–19.9	16.2	16.2 ± 1.1
RDW	1.4–36.7	13.3	13.7 ± 1.7
Urea	14.0–205.0	33.0	37.6 ± 19.6
Creatinine	0.4–6.7	0.9	1.0 ± 0.7
CRP	0.1–301.1	4.8	16.5 ± 38.9
LDH	102.0–4081.0	230.0	283.2 ± 243.0
Lactate	0.3–16.7	2.3	2.6 ± 1.6
Troponin	2.4–9870.3	64.0	367.6 ± 931.5
Glucose	73.0–583.0	138.5	164.2 ± 78.2
HDL	16.0–118.0	39.0	40.9 ± 11.8
LDL	23.0–400.0	128.0	133.0 ± 65.1
Cholesterol	22.0–458.0	192.0	194.7 ± 52.1
Triglycerides	26.0–1434.0	128.5	161.7 ± 128.6
NLR	0.5–96.1	5.0	7.1 ± 8.2
SIRI	0.4–163.3	5.6	8.2 ± 10.6
SII	144.5–53,798.6	1639.6	2456.0 ± 3287.6
AISI	76.1–91,457.7	1828.2	2887.9 ± 4826.6
Duration of chest pain (mins)	15.0–10,080.0	255.0	819.6 ± 1243.4
Length of hospital stay (CICU + ward)	1.0–24.0	3.0	4.0 ± 2.9
Length of hospital stay (CICU + ward)			
1–3 d			307 (60.3%)
>4 d			202 (39.7%)
Exitus			
(–)			436 (85.7%)
(+)			73 (14.3%)

Min: minimum; Max: maximum; SD: standard deviation; SIRI: Systemic inflammation response index; SII: Systemic immune-inflammation index; TIMI: Thrombolysis in myocardial infarction; HEART: History, Electrocardiogram, Age, Risk factors, and Troponin; WBC: White blood cells count; RBC: Red blood cells count; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; PLT: Platelet; MPV: Mean platelet volume; PDW: Platelet distribution width; RDW: Red cell distribution width; CRP: C reactive protein; LDH: Lactate dehydrogenase; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; NLR: Neutrophil to Lymphocyte ratio; AISI: Aggregate index of systemic inflammation; CICU: Cardiac intensive care unit.

obstructive pulmonary disease (COPD) ($p > 0.05$).

No significant difference was observed between the NSTEMI and STEMI groups with respect to smoking status or family history ($p > 0.05$ for both) (Table 3).

No significant difference was found in systolic blood pressure values between the STEMI and NSTEMI groups ($p > 0.05$). However, the pulse rate was significantly higher in the NSTEMI group than in the STEMI group ($p < 0.05$). No significant difference was seen between the groups regarding body temperature values ($p > 0.05$).

The white blood cells count (WBC), neutrophil count, lymphocyte count, red blood cells count (RBC), hemoglobin (HGB), hematocrit (HCT) and mean corpuscular volume (MCV) values were significantly lower in the NSTEMI group than in the STEMI group ($p < 0.05$ for all). No significant difference was observed between the groups for monocyte and platelet (PLT) values ($p > 0.05$) (Table 4a).

There was no significant difference between the STEMI and NSTEMI groups in terms of the mean platelet volume (MPV), creatinine, C reactive protein (CRP), high-density lipoprotein (HDL), and cholesterol values ($p > 0.05$). However, the values of PDW, Lactate dehydrogenase (LDH), lactate, glucose and low-density lipoprotein values (LDL) were significantly lower in the NSTEMI group compared to the STEMI group ($p < 0.05$). Conversely, the values of red cell distribution width (RDW), urea, troponin, triglycerides, and NLR values were markedly higher in the NSTEMI group than in the STEMI group ($p < 0.05$) (Table 4a).

The SIRI, SII and AISI values were significantly higher in the NSTEMI group than in the STEMI group ($p < 0.05$). The duration of chest pain was also longer in the NSTEMI group than in the STEMI group ($p < 0.05$).

No significant difference was observed between the groups with respect to the total length of hospital stay ($p > 0.05$). A statistically significantly higher rate of patients in the NSTEMI group had a length of stay >4 days ($p < 0.05$). No significant difference was noticed between the groups regarding the rate of exitus patients ($p > 0.05$) (Table 4b).

In the exitus group, the lactate, troponin, and glucose values were significantly higher than in the survivors group ($p < 0.05$). No significant difference was observed between the exitus and survivors groups in terms of the HDL values ($p > 0.05$).

The LDL, cholesterol and triglycerides values were significantly lower in the exitus group compared to the survivors group ($p < 0.05$). The NLR, SIRI, SII, and AISI values were

TABLE 3. Analyses of the sociodemographic data between the STEMI and NSTEMI groups.

	STEMI Group		NSTEMI Group		*p*
	Mean ± SD/n (%)	Median	Mean ± SD/n (%)	Median	
Age on presentation (yr)	55.9 ± 11.4	55.0	60.6 ± 12.4	60.0	<0.001†
Gender					
Male	253 (81.9%)		140 (70.0%)		0.002‡
Female	56 (18.1%)		60 (30.0%)		
Comorbidities					
CAD	61 (19.7%)		88 (44.0%)		<0.001‡
HT	105 (34.0%)		106 (53.0%)		<0.001‡
DM	60 (19.4%)		69 (34.5%)		<0.001‡
CHF	3 (1.0%)		13 (6.5%)		<0.001‡
CVD	3 (1.0%)		4 (2.0%)		0.330‡
HL	14 (4.5%)		6 (3.0%)		0.385‡
CRF	11 (3.6%)		11 (5.5%)		0.293‡
CABG	8 (2.6%)		24 (12.0%)		<0.001‡
COPD	8 (2.6%)		12 (6.0%)		0.053‡
Smoking status					
(–)	226 (73.1%)		155 (77.5%)		0.268‡
(+)	83 (26.9%)		45 (22.5%)		
Family History					
(–)	235 (76.1%)		149 (74.5%)		0.691‡
(+)	74 (23.9%)		51 (25.5%)		

†*Mann-Whitney U-test*/‡*Chi-square test.*

SD: standard deviation; STEMI: ST segment elevation myocardial infarction; CAD: Coronary artery disease; HT: Hypertension; DM: Diabetes Mellitus; CHF: Congestive heart failure; CVD: Cerebrovascular disease; HL: Hyperlipidemia; CRF: Chronic renal failure; CABG: Coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; NSTEMI: Myocardial infarction without ST segment elevation.

TABLE 4a. Analysis of the vital and hematological parameters between the groups.

	STEMI Group		NSTEMI Group		*p*
	Mean ± SD	Median	Mean ± SD	Median	
Systolic blood pressure	136.1 ± 32.6	127.0	136.2 ± 30.3	129.0	0.576†
Pulse	86.5 ± 22.2	84.0	101.6 ± 25.2	100.0	<0.001†
Temperature	36.6 ± 0.5	36.8	36.6 ± 0.5	36.8	0.133†
WBC	11.8 ± 4.0	11.5	10.0 ± 3.3	9.7	<0.001†
Neutrophils	10.4 ± 5.9	8.4	16.7 ± 6.7	17.1	<0.001†
Lymphocytes	2.8 ± 1.5	2.6	2.3 ± 1.1	2.2	0.001†
Monocytes	1.2 ± 0.4	1.1	1.2 ± 0.4	1.1	0.686†
RBC	4.8 ± 0.7	4.9	4.7 ± 0.6	4.7	0.023†
HGB	143.5 ± 19.7	147.0	137.1 ± 19.7	140.0	<0.001†
PLT	344.9 ± 104.2	315.0	345.1 ± 104.4	317.0	0.770†
Urea	36.8 ± 19.6	33.0	38.7 ± 19.5	36.0	0.027†
Creatinine	1.03 ± 0.64	0.90	1.05 ± 0.73	0.90	0.636†
CRP	15.9 ± 38.6	4.7	17.4 ± 39.4	5.1	0.248†
LDH	294.3 ± 179.2	239.0	265.2 ± 320.2	214.0	<0.001†
Lactate	2.8 ± 1.8	2.5	2.2 ± 1.0	2.1	<0.001†
Troponin	246.1 ± 505.8	46.0	557.6 ± 1330.8	100.7	0.005†
Glucose	166.8 ± 79.5	142.0	160.3 ± 76.2	130.0	0.041†
HDL	41.4 ± 12.2	39.0	40.3 ± 11.2	39.0	0.454†
LDL	135.8 ± 58.5	130.0	128.9 ± 73.5	124.5	0.016†
Cholesterol	199.4 ± 53.3	192.0	187.8 ± 49.6	192.0	0.055†
Triglycerides	152.3 ± 115.9	122.0	175.4 ± 144.4	146.0	0.005†
NLR	5.5 ± 6.1	3.4	9.6 ± 10.2	7.4	<0.001†

†*Mann-Whitney U-test.*

SD: standard deviation; STEMI: ST segment elevation myocardial infarction; NSTEMI: Myocardial infarction without ST segment elevation; WBC: White blood cells count; RBC: Red blood cells count; HGB: Hemoglobin; PLT: Platelet; CRP: C reactive protein; LDH: Lactate dehydrogenase; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; NLR: Neutrophil to Lymphocyte ratio.

TABLE 4b. Analysis of the inflammatory indexes, duration of chest pain, and exitus status between the groups.

	STEMI Group		NSTEMI Group		*p*
	Mean ± SD/n (%)	Median	Mean ± SD/n (%)	Median	
SIRI	6.2 ± 6.9	3.9	11.2 ± 14.1	8.3	<0.001†
SII	1869.0 ± 2084.5	1095.0	3362.9 ± 4416.3	2469.7	<0.001†
AISI	2133.9 ± 2316.7	1265.8	4052.7 ± 6993.9	2762.0	<0.001†
Duration of chest pain	287.8 ± 292.2	185.0	1641.2 ± 1642.2	1220.0	<0.001†
Hospitalization duration	3.7 ± 2.5	3.0	4.3 ± 3.4	3.0	0.210†
Length of hospital stay					
1–3 d	201 (65.0%)		106 (53.0%)		0.007‡
>4 d	108 (35.0%)		94 (47.0%)		
Exitus					
(−)	269 (87.1%)		167 (83.5%)		0.264‡
(+)	40 (12.9%)		33 (16.5%)		

†*Mann-Whitney U-test*/‡*Chi-square test.*

SD: standard deviation; SIRI: Systemic inflammation response index; SII: Systemic immune-inflammation index; STEMI: ST segment elevation myocardial infarction; NSTEMI: Myocardial infarction without ST segment elevation; AISI: Aggregate index of systemic inflammation.

statistically significantly higher in the exitus group than in the survivors group ($p < 0.05$) (Table 5a).

In the univariate model, the effect of the NLR, SIRI, SII and AISI values was found to have a significant impact on the differentiation of exitus and surviving patients ($p < 0.05$). In the multivariate model, the values of NLR, SIRI and AISI were observed to have an independent significant effect on the differentiation of exitus and surviving patients ($p < 0.05$) (Table 5b).

The NLR value had a significant effect in differentiating between exitus and surviving patients (Area under the curve (AUC): 0.811; 95% Confidence interval (CI): 0.764–0.857). The cutoff value of 6.137 for NLR was associated with an (AUC: 0.747; 95% CI: 0.690–0.804), sensitivity of 83.6%, Positive predictive values (PPV) 29.0%, specificity 65.8% and Negative predictive values (NPV) 96.0% (Table 6a).

The SIRI value was determined to have a significant effect in distinguishing between exitus and surviving patients (AUC: 0.802; 95% CI: 0.755–0.848). The cutoff value of 5.087 for SIRI had an (AUC: 0.730; 95% CI: 0.677–0.782) with sensitivity of 91.8%, PPV 25.1%, specificity 54.1% and NPV 97.5% (Table 6b).

The SII also demonstrated a significant effect in the differentiation of exitus and surviving patients (AUC: 0.793; 95% CI: 0.744–0.841). The cutoff value of 1792 for SII yielded an AUC of 0.738 (95% CI: 0.683–0.792) with sensitivity of 87.7%, PPV 26.8%, specificity 59.9% and NPV 96.7% (Table 6c).

The AISI value was had a significant effect on the differentiation of exitus and surviving patients (AUC: 0.780; 95% CI: 0.729–0.830). The cutoff value of 2622 for AISI corresponded to an (AUC: 0.720; 95% CI: 0.656–0.783) with sensitivity of 74.0%, PPV 29.2%, specificity 70.0% and NPV 94.1% (Table 6d). Fig. 1 shows the ROC curve of inflammation indices in terms of mortality.

4. Discussion

The results of this study, which investigated the inflammation indices of patients diagnosed with ACS and critical narrowing as determined by angiography, demonstrated a clear relationship between inflammation and mortality.

Inflammation plays an important role in the formation and development of atherosclerosis. Increased arterial stiffness, driven by heightened oxidative and inflammatory damage, is influenced by both an increase in neutrophils, which promote oxidative damage in the vascular wall, and a decrease in lymphocytes [11]. The NLR has been shown to be independently associated with coronary artery calcification, and this increases the risk of CAD. Several previous studies have reported that the NLR serves as a prognostic marker for CAD, correlating with the risk, severity, and outcomes of the disease [12]. SIRI, SII and AISI have also gained increasing attention as predictive

TABLE 5a. Comparisons of hematological and derived inflammatory indexes in the exitus and surviving groups.

	Exitus (−)		Exitus (+)		*p*
	Mean ± SD	Median	Mean ± SD	Median	
Lactate	2.5 ± 1.2	2.3	3.4 ± 3.0	2.6	0.031†
Troponin	326.2 ± 785.8	54.0	612.8 ± 1518.6	125.0	0.034†
Glucose	157.6 ± 69.3	135.0	203.8 ± 110.8	167.0	0.002†
HDL	40.8 ± 11.4	39.0	41.9 ± 14.1	39.0	0.759†
LDL	136.9 ± 66.8	130.0	107.5 ± 45.2	95.0	<0.001†
Cholesterol	197.9 ± 50.9	197.0	172.8 ± 55.2	159.0	<0.001¶
Triglycerides	167.8 ± 134.6	135.0	120.2 ± 61.6	106.0	0.009†
NLR	5.9 ± 6.4	4.2	14.2 ± 13.0	10.9	<0.001†
SIRI	6.9 ± 9.6	4.6	15.6 ± 12.8	12.0	<0.001†
SII	2097.6 ± 3046.6	1411.1	4596.9 ± 3841.3	3660.1	<0.001†

¶*Independent Samples t-test/*†*Mann-Whitney U-test, Logistic Regression (Forward LR).*
SD: standard deviation; SIRI: Systemic inflammation response index; SII: Systemic immune-inflammation index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; NLR: Neutrophil to Lymphocyte ratio.

TABLE 5b. Regression analysis of inflammation index parameters in respect of mortality.

	Univariate Model			Multivariate Model		
	OR	95% CI	*p*	OR	95% CI	*p*
NLR	1.141	1.094–1.190	<0.001	1.166	1.075–1.266	<0.001
SIRI	1.084	1.052–1.118	<0.001	1.116	1.016–1.225	0.021
SII	1.000	1.000–1.000	<0.001	-	-	-
AISI	1.000	1.000–1.000	<0.001	1.000	1.000–1.000	<0.001

SIRI: Systemic inflammation response index; SII: Systemic immune-inflammation index; OR: Odds ratio; CI: Confidence interval; NLR: Neutrophil to Lymphocyte ratio; AISI: Aggregate index of systemic inflammation.

TABLE 6a. ROC analysis of NLR in respect of mortality.

	AUC		95% CI	*p*
NLR	0.811		0.764–0.857	<0.001
NLR cut off 6.137	0.747		0.690–0.804	<0.001
	EX (−)	EX (+)		%
NLR				
<6.137	287	12	Sensitivity	83.6%
≥6.137	149	61	Positive Predictive Value	29.0%
			Specificity	65.8%
			Negative Predictive Value	96.0%

AUC: Area under the curve; CI: Confidence interval; NLR: Neutrophil to Lymphocyte ratio; EX: Exitus.

TABLE 6b. ROC analysis of SIRI in respect of mortality.

	AUC		95% CI	*p*
SIRI	0.802		0.755–0.848	<0.001
SIRI cut Off 5.087	0.730		0.677–0.782	<0.001
	EX (−)	EX (+)		%
SIRI				
<5.087	236	6	Sensitivity	91.8%
≥5.087	200	67	Positive Predictive Value	25.1%
			Specificity	54.1%
			Negative Predictive Value	97.5%

SIRI: Systemic inflammation response index; AUC: Area under the curve; CI: Confidence interval; EX: Exitus.

TABLE 6c. ROC analysis of SII in respect of mortality.

	AUC		95% CI	*p*
SII	0.793		0.744–0.841	<0.001
SII cut off 1792	0.738		0.683–0.792	<0.001
	EX (−)	EX (+)		%
SII				
≤1792	261	9	Sensitivity	87.7%
>1792	175	64	Positive Predictive Value	26.8%
			Specificity	59.9%
			Negative Predictive Value	96.7%

SII: Systemic immune-inflammation index; AUC: Area under the curve; CI: Confidence interval; EX: Exitus.

TABLE 6d. ROC analysis of AISI in respect of mortality.

	AUC		95% CI	*p*
AISI	0.780		0.729–0.830	<0.001
AISI cut off 2622	0.720		0.656–0.783	<0.001
	EX (−)	EX (+)		%
AISI				
≤2622	305	19	Sensitivity	74.0%
>2622	131	54	Positive Predictive Value	29.2%
			Specificity	70.0%
			Negative Predictive Value	94.1%

AISI: Aggregate index of systemic inflammation; AUC: Area under the curve; CI: Confidence interval; EX: Exitus.

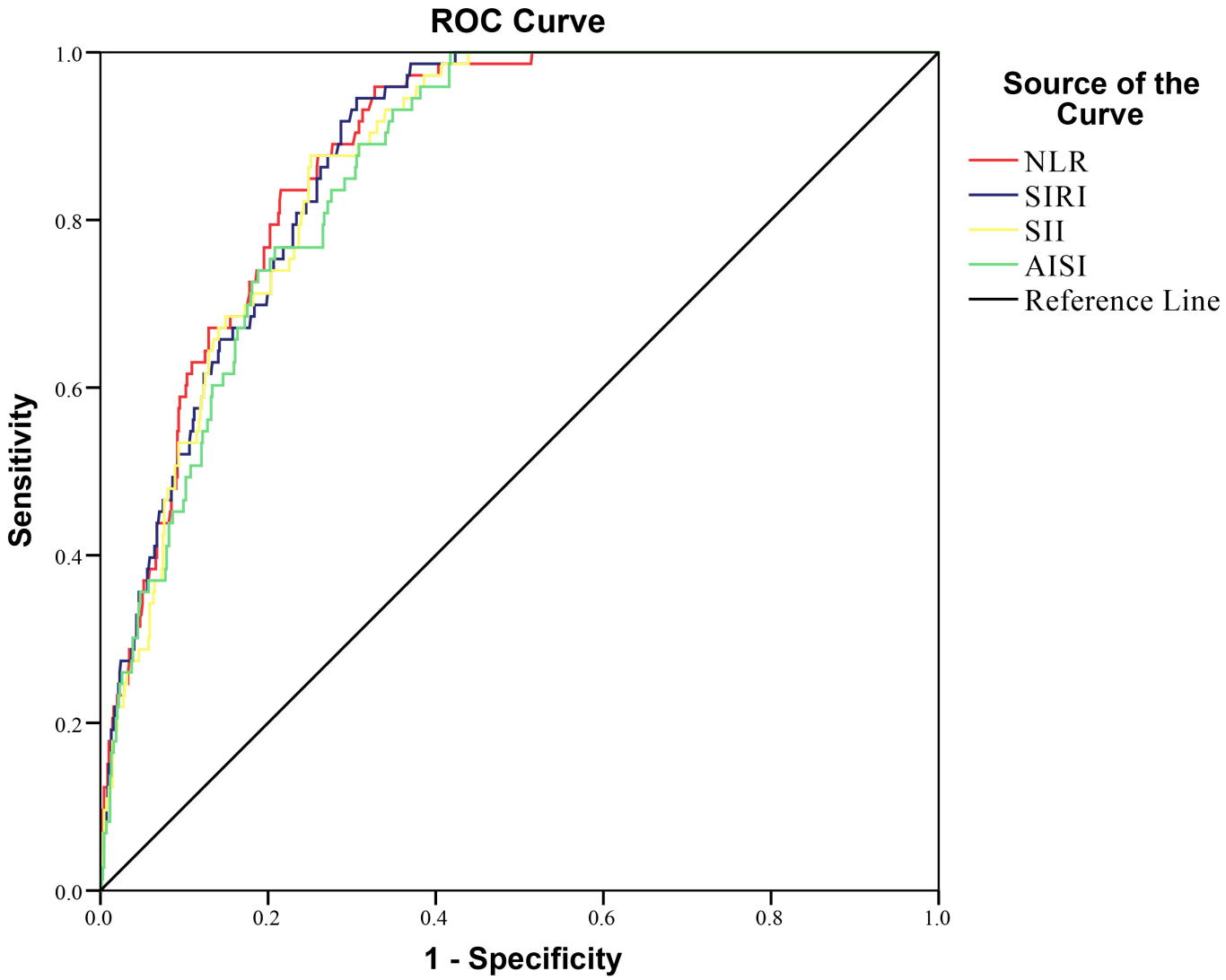

FIGURE 1. ROC curve of inflammation indices in terms of mortality. ROC: Receiver Operating Characteristic; SIRI: Systemic inflammation response index; SII: Systemic immune-inflammation index; NLR: Neutrophil to Lymphocyte ratio; AISI: Aggregate index of systemic inflammation.

biomarkers.

In a study by Sari *et al.* [13], a significant difference in NLR values between patients with normal and abnormal coronary angiography results was found, underscoring the ability of NLR to detect coronary artery abnormalities. Similarly, Tangjitgamol *et al.* [14] demonstrated the value of NLR in predicting the presence of severe atherosclerosis and CAD. Another study by Yoon *et al.* [15], showed that NLR could predict the coronary thrombus load. In the current study results, the NLR value was determined to be statistically significantly higher in the NSTEMI group than in the STEMI group. It was concluded that this was related to the higher mean age of the NSTEMI group and the higher rate of chronic disease than the STEMI group.

Choi *et al.* [16] found that NLR >2.8 was an independent determinant of major adverse cardiac events (MACE) in CAD patients undergoing percutaneous coronary intervention (PCI) A similar result was found by Li *et al.* [17] that NLR ≥2.83 could predict the development of MACE. In a study of ACS by Fan *et al.* [18], high NLR, PLR and derived neutrophil-lymphocyte ratio (dNLR) values were shown to be associated with a higher risk of MACE. In the current study, the NLR was found to be higher in the NSTEMI patient group and was significant in respect of MACE. This result was taken as evidence that the formation of MACE is triggered by inflammatory parameters.

Recent studies have proven that inflammatory cells could be beneficial in predicting the prognosis of patients with ACS. However, inflammatory predictors based on one or two components are considered weak and insufficient for accurately predicting the prognosis of ACS [19]. Therefore, the SII contains three types of inflammatory cell, provides a comprehensive representation of the body's inflammatory status [20]. A positive correlation between the SII and the SYNTAX score has been previously shown, and this can be used for CAD risk classification after PCI and for prognosis prediction. Jin *et al.* [21] reported that high rates of stroke and all-cause deaths corresponded to high SII and SIRI levels, and only a high SIRI value was found to be independently associated with a high MI risk. Li *et al.* [17] found that the predictive ability of

SIRI for MACE was better than that of SII. An increase in SII has been shown to be associated with poor outcomes in CVDs. Yang *et al*. [22] reported a relationship between high SII levels in CAD and poor clinical results. In a study by Dey *et al*. [23], a correlation was reported between high SII and poor results after elective CABG operations, and Huang *et al*. [24] showed that a high SII predicted poor clinical results in elderly patients after ACS. A large-scale study involving 3561 patients by Zhao *et al*. [25] concluded that SII serves as a low-cost, rapid, and easily accessible parameter that effectively predicts prognosis in patients undergoing revascularisation for three-vessel coronary disease.

In a study examining the NSTEMI coronary thrombus load, Özkan *et al*. [26] showed that a high SII score was an independent determinant of high coronary thrombus load. W. Fan *et al*. [18] reported that a high SII value was associated with a high risk of MACE in a study of 1553 ACS patients. In a study by Huang *et al*. [24], the mean SII was calculated to be 1645.60 in patients with STEMI and 1057.95 in patients with NSTEMI, and no significant difference was determined between the two groups. In another study of 843 STEMI patients, Saylık *et al*. [27] reported that patients with high SII (>554.9) had higher PCI and lower direct stent implantation (without predilatation) compared to patients with low SII. A high SII was also found to be significant with respect to MACE and showed better prognostic value than the NLR and PLR [27]. The results of the current study showed that the SII value was significantly effective in predicting mortality.

In a study by Dziedzic *et al*. [28], the SII and SIRI values in a group of 244 elderly postmenopausal females diagnosed with ACS were found to be significantly higher compared to those of females with stable CAD. The highest values were observed in the females with NSTEMI [28]. In the current study, the SII, SIRI and AISI values were also found to be statistically significantly high in the patients with NSTEMI.

According to the data of the Framingham Heart Study, the lifetime risk of developing symptomatic CAD after the age of 40 years is 49% for males and 32% for females [29]. In a study of patients aged >65 years with ACS, Huang *et al*. [24] reported that 66.9% of the patients were male. Mahmoud Barbarawi *et al*. [30] conducted a meta-analysis of NSTEMI patients and found that 78% were male and the mean age was 63.8 $\pm$ 12.8 years. STEMI patients evaluated in a study by Ply Chichareon *et al*. [31] had a mean age of 60.7 years and 77.3% were male. The current study patient group comprised 77.2% males and the mean age was 57.7 years. The mean age of the NSTEMI patients was higher. That the majority of patients were male and of an older age was consistent with the literature on ACS. In the comparisons of the STEMI and NSTEMI patients in the current study, there was found to be a significantly higher rate of female patients in the NSTEMI group.

In previous studies comorbidities have been reported as HT 12.9%, DM 6.2%, and other ischaemic heart disease 27.6% by Costache *et al*. [32], and as HT 25%, ischaemic heart disease 20%, and DM 15% by D'Ippoliti *et al*. [33]. Huang *et al*. [24] reported the most common comorbidity to be HT at 59.49%, followed by DM at 25.18%. In parallel with these findings in literature, the most common comorbidity in the current study was HT (27.4%).

Ouyang *et al*. [34] found that high lactate values were a marker of poor prognosis and high mortality. Liang *et al*. [35] stated that an increase in lactate level showed an increase in narrowing in the coronary arteries of patients. The current study results showed that the lactate values were higher in the patient group that developed mortality. In our study, although lactate was significantly higher in the STEMI group, we did not find a difference in hospitalization times between the STEMI and NSTEMI groups. However, lactate levels were higher in the group with a higher mortality rate, consistent with the literature.

Clonal hematopoiesis of indeterminate potential (CHIP) is a condition associated with leukemia in individuals without evidence of hematologic malignancy, dysplasia or cytopenia, but it poses an increased risk of cardiovascular disease as a result of increased inflammation [36, 37]. One of the issues that needs to be investigated is whether ACS patients with high inflammation index have cardiovascular diseases due to CHIP.

5. Limitations

This study had certain limitations. Primarily the retrospective design and relatively low sample size may have introduced selection bias and limit the generalizability of the findings. In addition, the effects of the inflammation indices on long-term mortality (beyond one month) could not be evaluated, restricting the understanding of their predictive value over extended periods.

6. Conclusions

The results of this study demonstrated that the SII, SIRI and AISI values serve as significant predictors of mortality in ACS patients. A high NLR values were associated with a poor prognosis. The inflammation indices were higher in patients of advanced age and those with chronic diseases, highlighting the potential role of systemic inflammation in the progression and outcomes of ACS.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available for sharing by the corresponding author upon request.

AUTHOR CONTRIBUTIONS

BDS—provided the main framework, identified and organized primary materials, and collaborated in writing the manuscript. AM and UK—identified appropriate references and collaborated on the writing of the manuscript. EA—reviewed and contributed to drafting sections of the manuscript. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was performed after the approval of institutional ethics committee (University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital Health Application and Research Center Clinical Research Ethics Committee, decision no: 3884, dated: 18 April 2023) in accordance with the Declaration of Helsinki. Participation was voluntary and informed consent was obtained from all participants.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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