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Systemic immune-inflammation index predicted presence and severity of coronary artery disease

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Abstract

Aim: We investigate whether the systemic immune-inflammation index (SII), an easily evaluated inflammatory and immune response marker, is associated with the SYNTAX score (SS) in patients admitted with suspected CAD who underwent coronary angiography (CAG).

Materials and Methods: Evaluated retrospectively were 456 patients who underwent CAG in the cardiology outpatient clinic between January 2020 and January 2022. The SII was calculated by the following formula: neutrophils × platelets / lymphocytes. SS values were divided into 3 groups; low group (<22), intermediate group (22-32) and, high group (≥32). Those with SS values of 0 were taken as the control group.

Results: The median SII value was higher in the CAD group compared to the control group (631.0 vs. 381.5, $p<0.001$) and a positive correlation was found between the SS and SII ($r=0.578$, $p<0.001$). Median SII values increased from the low SS group to the high SS group ($p<0.05$ for each SS group). The cut-off value of the SII in predicting the presence of CAD was >594.2, with 56.7% sensitivity and 91.1% specificity (AUC±SE: 0.807±0.020, $p<0.001$). In addition, it was found that the SII predicted low SS compared to the control group (OR=1.06; $p<0.001$), intermediate SS compared to the low SS group (OR=1.03; $p<0.001$), and high SS compared to the intermediate SS group (OR=1.04; $p<0.001$).

Conclusion: The SII has the potential to be a screening marker for the presence and severity of CAD before CAG. This study demonstrates that the SII is independently associated with coronary atherosclerosis burden.

Introduction

Coronary artery disease (CAD) is an atherosclerotic disease caused by complex and long processes that involve genetic and environmental factors [1]. The interaction of immune mechanisms with metabolic risk factors may lead to the initiation and progression of atherosclerosis. In the atherosclerotic process, inflammation affects the onset and progression of the disease, as well as plays an important role in plaque rupture and thrombus formation [2]. Atherosclerosis induces adhesion molecules followed by accumulation of inflammatory cells involved in the production of inflammatory mediators including cytokines and C-reactive protein (CRP) [3].

Previous studies have shown that indicators of inflammation are associated with the extent and severity of CAD as assessed by the SYNTAX score (SS) [4-6]. The inflammatory response is associated with the infiltration of platelets and leukocytes, and this relationship is the driving force of atherosclerotic lesions [7]. Neutrophils are the first line of defense under inflammatory conditions and are involved in the entry of immune cells such as monocytes into atherosclerotic lesions [8]. Platelets regulate the effector functions of neutrophils and macrophage [9]. However, lymphocytes are involved in the healing process by inducing pro- and anti-inflammatory cytokines [10]. These mechanisms support the hypothesis that the inflammatory response mediated by the innate or adaptive immune system has an important role in the onset and severity of

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CAD. In addition, a high SS value is potentially a predictor of poor prognosis [11]. Therefore, identifying high-risk patients with a simple, easy, and inexpensive prognostic marker may play a key role in the management of CAD. Recent studies suggest that the systemic immune-inflammation index (SII) better demonstrates the relationship between inflammatory response and immune response in patients with CAD (12). However, there are limited studies evaluating its relationship with the presence and severity of CAD and conflicting results have been shown regarding its diagnostic performance [12-14]. Therefore, in this study, we aimed to investigate the prognostic role of the SII in predicting the presence and severity of CAD in patients admitted with suspected CAD who underwent coronary angiography (CAG).

Materials and Methods

Study population

In this study, 3150 patients over the age of 18 who underwent CAG after ischemia detected by myocardial perfusion scintigraphy between January 2020 and January 2022 in a cardiology clinic were evaluated retrospectively. In previous studies, the prevalence of CAD in outpatients was found to be approximately 20% [15, 16]. According to this, the necessary study sample size was determined to be at least 281 patients with a 5% margin of error and 90% power. Patients were excluded according to the following criteria: presence of acute coronary syndrome, any history of revascularization (previous percutaneous coronary intervention or coronary artery bypass grafting) or peripheral artery disease, left ventricular ejection fraction measured to be lower than 50%, presence of advanced valvular heart disease, possible acute or chronic infections, a previous diagnosis of any autoimmune or systemic inflammatory diseases, the use of any glucocorticoid therapies within the past 3 months, any trauma or recent major surgeries, presence of active malignancies or hematological disease, hypo- or hyperthyroidism, and advanced/end-stage liver or renal failure. After applying the exclusion criteria, 456 patients were included in the study. Written informed consent was obtained from all participants. Local ethics committee approval was granted by the Lokman Hekim University Non-Interventional Clinical Research Ethics Committee with decision date and number 12.2021-2021/159.

Demographic characteristics and laboratory findings of the patients were recorded from their files. Smoking, hyperlipidemia (total cholesterol of ≥200 mg/dL), hypertension (systolic blood pressure of ≥140 and/or diastolic blood pressure of ≥90 mmHg and/or patient receiving anti-hypertensive therapy), and diabetes mellitus (fasting blood glucose of ≥126 or glucose of ≥200 mg/dL in a 2-hour oral glucose test or use of anti-diabetic medication) were evaluated as potential risk factors for CAD.

Laboratory measurements

For all patients, standardized lipid panel and blood chemistry measurements were performed in the morning hours. A Beckman Coulter LH 780 device (Mervue Laboratories, Galway, Ireland) was employed to obtain all necessary complete blood count and lipid parameters. The platelet-to-lymphocyte ratio (PLR) was obtained by division of the platelet count by lymphocyte count, the neutrophil-to-lymphocyte ratio (NLR) was obtained by division of the neutrophil count by the lymphocyte count, and the SII was calculated according to the following formula: neutrophils × platelets / lymphocytes. All index values were obtained from the same blood sample for each patient.

Angiography

CAG was performed using the standard Judkins techniques. CAD was defined as coronary stenosis of ≥50% of the lumen diameter narrowing in quantitative CAG. Patients with vessels with diameter of less than 1.5 mm and/or with less than 50% stenosis were considered as the control group. The SS was calculated for all coronary lesions with ≥50% diameter stenosis in a vessel greater than 1.5 mm (www.syntaxscore.com) [17]. SS values were divided into three groups as <22 (low), 22-32 (intermediate), and ≥32 (high) [18]. SS score was independently assessed by 2 experienced interventional cardiologists. Inter-observer variability in estimating the SYNTAX score was 0.74, while the intra-observer variability was 0.87.

Statistical analysis

All of the data obtained as described above were analyzed using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA) and Medcalc 11.4.2 (MedCalc Software, Mariakerke, Belgium) program. Normally distributed data were analyzed with Kolmogorov-Smirnov tests. Categorical variables were presented as numbers and percentages, and comparisons between groups were performed using Chi-square (post-hoc: cell-wise test) and Fisher Exact tests. The normal distribution of numerical variables was evaluated with Kolmogorov-Smirnov tests and results with normal distribution were shown as mean±standard deviation, while those with non-normal distribution were shown as median (interquartile range (IQR): 25-75 percentiles). Comparisons of numerical variables between CAD and control groups were performed with Student T-test or Mann-Whitney U test. Comparisons of numerical variables between SS groups were analyzed with ANOVA test (post-hoc: Bonferroni test) or Kruskal-Wallis test (post-hoc: Dunn's test). Independent predictors of presence and severity of CAD were evaluated by stepwise multivariate logistic regression analysis. Diagnostic performance evaluation was analyzed by ROC analysis, and cut-off values was analyzed by Youden index method. Value of $p < 0.05$ were recognized as statistically significant.

Results

CAG was applied for all of the patients in the study. The mean age of the patients was 63.2±10.5 years, 39.3% (n: 179) were male, 39.9% (n: 182) had diabetes mellitus, 69.1% (n: 315) had hypertension, 55% (n: 251) had hyperlipidemia, and 60.7% (n: 277) had CAD. The demographic and laboratory findings are shown in Table 1. The mean age, female gender ratio, and comorbidities ratio were higher in the CAD group compared to the control group ($p<0.05$). The median NLR (2.6 vs. 1.8, $p<0.001$), median PLR (124.4 vs. 96.6, $p<0.001$), and median SII

Table 1. Demographic and laboratory findings associated with the presence of CAD.

Variables	All population n=456	Control group n=179	CAD group n=277	p
Demographic findings				
Age, years	63.2±10.5	60.1±10.7	64.4±10.3	<0.001*
Gender, n(%)				
Male	179(39.3)	92(51.4)	87(31.4)	<0.001*
Female	277(60.7)	87(48.6)	190(68.6)	
Diabetes mellitus, n(%)	182(39.9)	58(32.4)	124(44.8)	0.008*
Hypertension, n(%)	315(69.1)	101(56.4)	214(77.3)	<0.001*
Hyperlipidemia, n(%)	251(55.0)	63(35.2)	188(67.9)	<0.001*
Laboratory findings				
Hemoglobin, g/dL	13.2±1.6	13.3±1.4	13.2±1.7	0.691
Neutrophil, x10^9/L	4.8±1.4	4.1±1.0	5.3±1.4	<0.001*
Platelet, x10^9/L	242.5±66.7	226.5±59.2	252.8±69.3	<0.001*
Lymphocyte, x10^9/L	2.1±0.6	2.3±0.6	2.0±0.6	<0.001*
Monocyte, cells/μL	0.6±0.2	0.6±0.2	0.7±0.2	<0.001*
RDW, %	13.9±1.3	13.8±1.3	13.9±1.4	0.740
PDW, %	12.5±2.3	12.8±2.6	12.4±2.0	0.050*
MPV, fL	10.5±1.0	10.5±1.1	10.4±0.9	0.322
LDL-C, mg/dL	122(94-148)	115(85-144)	127(90-150)	0.275
HDL-C, mg/dL	48.1±11.7	57.8±8.7	41.8±8.7	<0.001*
Triglyceride, mg/dL	131(96-197)	125(90-179)	140(97-205)	0.045*
NLR	2.2(1.7-2.8)	1.8(1.5-2.2)	2.6(2.1-3.4)	<0.001*
PLR	111.4(89-145)	96.6(78.3-116.3)	124.4(99-158.6)	<0.001*
SII	521(368-728)	381.5(307-523)	631(470-831)	<0.001*
Multivessel disease, n(%)	118(25.9)	-	118(42.6)	-
Location of lesions, n(%)				
LMCA	11(2.4)	-	11(4.0)	–
LAD	87(19.1)	-	87(31.4)	
Cx	76(16.7)	-	76(27.4)	
RCA	103(22.6)	-	103(37.2)	
SYNTAX score	6(0-47)	0	13(7-23)	<0.001*

Numerical variables were shown as mean ± standard deviation or median (IQR). Categorical variables were shown as numbers (%). * P <0.05 shows statistical significance.

Abbreviations: Cx, circumflex artery; HDL, high density lipoprotein; LAD, left anterior descending artery; LDL, low density lipoprotein; LMCA, left main coronary artery; MPV, mean platelet volume; MHR, monocyte to HDL ratio; NLR, neutrophil to lymphocyte ratio; PDW, platelet distribution width; PLR, platelet to lymphocyte ratio; PNR, platelet to neutrophil ratio; RCA, right coronary artery; RDW, red cell distribution width; SII, systemic immune-inflammation index.

(631.0 vs. 381.5, p<0.001) were higher in the CAD group compared to the control group, while mean high-density lipoprotein cholesterol (HDL-C) was lower (41.8±8.7 vs. 57.8±8.7, p<0.001) (Table 1).

The distribution of demographic data were similar in the SS groups. Median NLR, PLR, and SII values were found to be higher as SS values increased (p<0.05 for each SS group) (Table 2) (Figure 1A). A positive correlation was found between SS values and NLR (r=0.545, p<0.001), PLR (r=0.394, p<0.001), and SII (r=0.578, p<0.001) (Figure 1B).

The results of univariable regression analysis of potential risk factors that were previously associated with the presence of CAD (Table 1) are shown in Table 3. Increased age (OR=1.07, p<0.001), increased monocyte (OR=1.05, p<0.001), increased SII (OR=1.07, p<0.001) and decreased HDL-C (OR=0.78, p<0.001) levels were found to be an independent predictor of the presence of CAD (Table 3).

The results of univariable regression analysis of potential risk factors that were previously associated with the severity of CAD (Table 2) are shown in Table 4-6. Increased SII value predicted low SS compared to the control group (OR=1.06; p<0.001) (Table 4), intermediate SS compared to the low SS group (OR=1.03; p<0.001) (Table 5), and high SS compared to the intermediate SS group (OR=1.04; p<0.001) (Table 6).

In predicting CAD, the SII exhibited superior diagnostic performance compared to the PLR and NLR (Figure 2). The cut-off value of the SII in predicting the presence of CAD was >594.2, with 56.7% sensitivity and 91.1% specificity (AUC±SE: 0.807±0.020; the positive predictive

Table 2. Demographic and laboratory findings associated with the severity of CAD.

Variables	Control group n=179	SYNTAX Score			p
		Low n=204	Intermediate n=46	High n=27	
Demographic findings					
Age, years	60.1±10.7[bcd]	64.1±10.3[a]	64.4±10.1[a]	65.2±9.5[a]	<0.001*
Gender, n(%)					
Male	92(51.4)[bcd]	70(34.3)[a]	10(21.7)[a]	7(25.9)[a]	<0.001*
Female	87(48.6)[bcd]	134(65.7)[a]	36(78.3)[a]	20(74.1)[a]	
Diabetes mellitus, n(%)	58(32.4)[bcd]	95(46.6)[a]	18(39.1)[a]	11(40.7)[a]	0.046*
Hypertension, n(%)	101(56.4)[bcd]	159(77.9)[a]	36(78.3)[a]	19(70.4)[a]	<0.001*
Hyperlipidemia, n(%)	63(35.2)[bcd]	144(70.6)[a]	31(67.4)[a]	13(48.1)[a]	<0.001*
Laboratory findings					
Hemoglobin, g/dL	13.3±1.4	13.2±1.7	13.2±1.4	13.5±1.7	0.766
Neutrophil, x10^9/L	4.1±1.0[bcd]	5.0±1.2[acd]	5.4±1.4[abd]	6.8±1.3[abc]	<0.001*
Platelet, x10^9/L	226.5±59.2[bcd]	245.4±62.4[ad]	261±68.2[ad]	300.7±75.1[abc]	<0.001*
Lymphocyte, x10^9/L	2.3±0.6[bcd]	2.1±0.6[ad]	2.0±0.7[ad]	1.6±0.3[abc]	<0.001*
Monocyte, cells/µL	0.6±0.2[bcd]	0.7±0.2[ad]	0.7±0.2[ad]	0.8±0.2[abc]	<0.001*
RDW, %	13.8±1.3	13.9±1.4	13.7±1.1	14.3±1.3	0.337
PDW, %	12.8±2.6	12.3±2.1	12.3±1.8	12.4±1.8	0.231
MPV, fL	10.5±1.1	10.4±0.9	10.5±0.8	10.5±0.8	0.745
LDL-C, mg/dL	115(85-144)	125(86-142)	130.5(97-156)	136(117-164)	0.446
HDL-C, mg/dL	57.8±8.7[bcd]	42.2±8.7[a]	40.6±8.2[a]	40.9±9.0[a]	<0.001*
Triglyceride, mg/dL	125(90-179)	136(99-204)	153(105-248)	146(88-255)	0.141
NLR	1.8(1.5-2.2)[bcd]	2.4(2.0-3.0)[acd]	2.7(2.2-3.9)[abd]	4.2(3.6-4.9)[abc]	<0.001*
PLR	96.6(78.3-116.3)[bcd]	115.7(94-143)[acd]	136.6(105-189.4)[abd]	175(153-209)[abc]	<0.001*
SII	381.5(307.6-523)[bcd]	577.5(447.2-750.2)[acd]	762.6(541.3-1001.5)[abd]	1263.6(953.8-1462.3)[abc]	<0.001*
Multivessel disease, n(%)	0	71(34.8)[cd]	29(63.0)[b]	18(66.7)[b]	<0.001*

Numerical variables were shown as mean ± standard deviation or median (IQR). Categorical variables were shown as numbers (%). * P <0.05 shows statistical significance. Post-hoc analyzes were expressed as follows: a: P <0.05 vs. control group, b: P <0.05 vs. low SS group, c: P <0.05 vs. intermediate SS group, d: P <0.05 vs. high SS group.
Abbreviations: see Table 1.

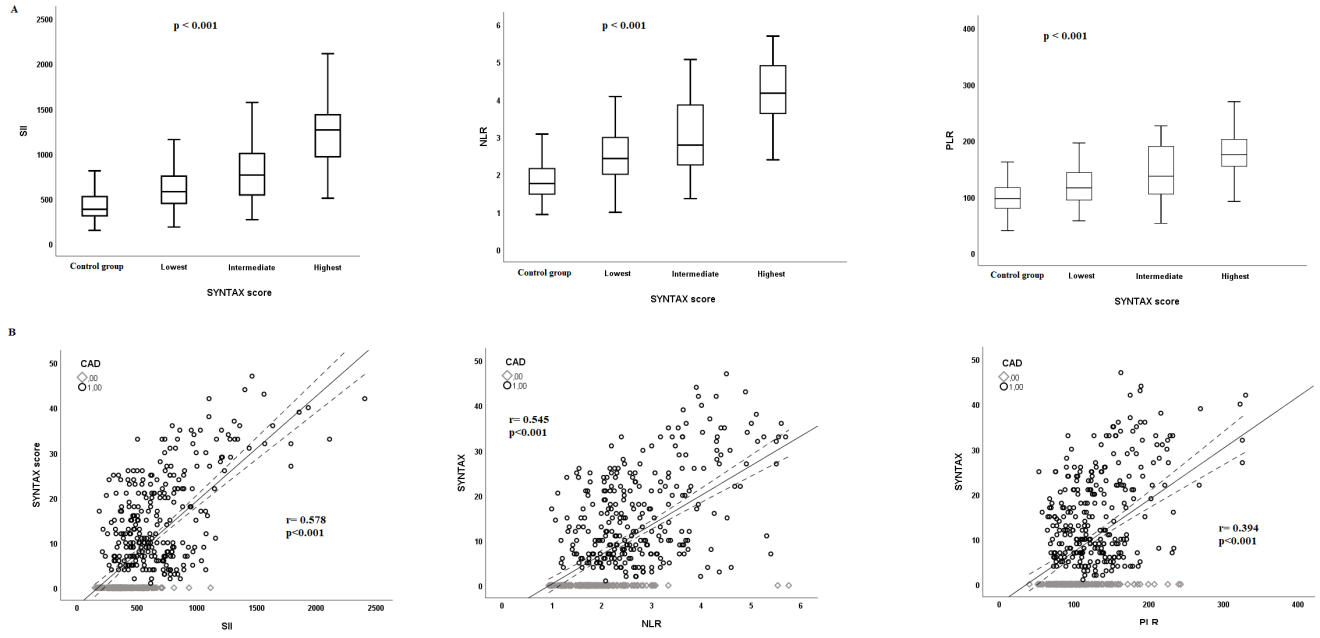


Figure 1. Relationship between SII and CAD severity (A) and SS (B).

Table 3. Independent predictors of the presence of CAD.

Variables	Univariable Regression				Multivariable Regression			
	OR	95% CI		p	OR	95% CI		p
		lower	upper			lower	upper	
Demographic findings								
Age	1.04	1.02	1.06	<0.001*	1.07	1.03	1.10	<0.001*
Gender								
Male	ref				-	-	-	-
Female	2.31	1.57	3.40	<0.001*	-	-	-	-
Diabetes mellitus	1.69	1.14	2.50	0.008*	-	-	-	-
Hypertension	2.62	1.74	3.94	<0.001*	-	-	-	-
Hyperlipidemia	3.89	2.61	5.79	<0.001*	-	-	-	-
Laboratory findings								
Neutrophil	2.29	1.88	2.79	<0.001*	-	-	-	-
Platelet	1.02	1.01	1.03	<0.001*	-	-	-	-
Lymphocyte	0.49	0.36	0.67	<0.001*	-	-	-	-
Monocyte	1.08	1.05	1.11	<0.001*	1.05	1.02	1.07	<0.001*
PDW	0.92	0.85	0.99	0.050*	-	-	-	-
HDL-C	0.81	0.78	0.84	<0.001*	0.78	0.74	0.82	<0.001*
Triglyceride	1.03	1.01	1.09	0.045*	-	-	-	-
NLR	1.15	1.06	1.25	<0.001*	-	-	-	-
PLR	1.03	1.01	1.05	<0.001*	-	-	-	-
SII	1.05	1.01	1.09	<0.001*	1.07	1.04	1.09	<0.001*
								Nagelkerke R^2= 0.778, p<0.001

* P <0.05 shows statistical significance. Abbreviations: see Table 1; CI, confidence intervals; OR, odds ratio, ref, reference.

Table 4. Independent predictors of the low SYNTAX score than control group.

Variables	Univariable Regression				Multivariable Regression			
	OR	95% CI		p	OR	95% CI		p
		lower	upper			lower	upper	
Demographic findings								
Age	1.03	1.01	1.05	<0.001*	1.06	1.03	1.10	<0.001*
Gender								
Male	ref				-	-	-	-
Female	1.54	1.18	2.02	<0.001*	-	-	-	-
Diabetes mellitus	1.64	1.18	2.27	0.047*	-	-	-	-
Hypertension	1.57	1.23	2.02	<0.001*	-	-	-	-
Hyperlipidemia	2.29	1.70	3.07	<0.001*	-	-	-	-
Laboratory findings								
Neutrophil	1.07	1.03	1.12	0.002*	-	-	-	-
Platelet	1.02	1.01	1.04	0.004*	-	-	-	-
Lymphocyte	0.52	0.40	0.65	0.001*	-	-	-	-
Monocyte	1.06	1.03	1.10	<0.001*	1.04	1.02	1.06	<0.001*
HDL-C	0.81	0.78	0.85	<0.001*	0.78	0.74	0.83	<0.001*
NLR	1.19	1.09	1.30	<0.001*	-	-	-	-
PLR	1.04	1.01	1.09	0.007*	-	-	-	-
SII	1.07	1.03	1.11	<0.001*	1.06	1.04	1.08	<0.001*
								Nagelkerke R^2= 0.749, p<0.001

* P <0.05 shows statistical significance. Abbreviations: see Table 1; CI, confidence intervals; OR, odds ratio, ref, reference.

value was 90.8% and the negative predictive value was 57.6%; p<0.001). One or more lesions were detected in 90.8% (n: 157) of 173 patients with SII values of >594.2. On the other hand, 163 (57.6%) of the patients with SII values of <594.2 did not have any lesions, which accounted for 35.7% of the entire study population.

Table 5. Independent predictors of the intermediate SYNTAX score than low SYNTAX score.

Variables	Univariable Regression				Multivariable Regression			
	OR	95% CI		p	OR	95% CI		p
		lower	upper			lower	upper	
Demographic findings								
Gender								
Male	ref				-	-	-	-
Female	1.88	0.88	4.01	0.102	-	-	-	-
Diabetes mellitus	0.74	0.38	1.42	0.361	-	-	-	-
Hypertension	1.02	0.47	2.21	0.962	-	-	-	-
Hyperlipidemia	0.86	0.43	1.71	0.669	-	-	-	-
Laboratory findings								
Neutrophil	1.28	1.00	1.65	0.049*	-	-	-	-
NLR	1.09	1.02	1.17	<0.001*	-	-	-	-
PLR	1.01	1.01	1.02	<0.001*	-	-	-	-
SII	1.03	1.02	1.04	<0.001*	1.03	1.02	1.04	<0.001*
								Nagelkerke R^2= 0.402, p<0.001

* P <0.05 shows statistical significance. Abbreviations: see Table 1; CI, confidence intervals; OR, odds ratio, ref, reference.

Table 6. Independent predictors of the high SYNTAX score than intermediate SYNTAX score.

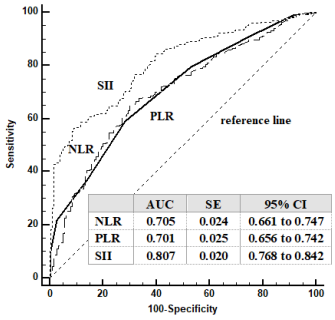
Variables	Univariable Regression				Multivariable Regression			
	OR	95% CI		p	OR	95% CI		p
		lower	upper			lower	upper	
Demographic findings								
Gender								
Male	ref				-	-	-	-
Female	0.79	0.26	2.41	0.683	-	-	-	-
Diabetes mellitus					-	-	-	-
Hypertension	0.66	0.22	1.95	0.452	-	-	-	-
Hyperlipidemia	0.45	0.17	1.19	0.080	-	-	-	-
Laboratory findings								
Neutrophil	1.97	1.33	2.93	<0.001*	-	-	-	-
Platelet	1.02	1.01	1.03	0.042*				
Lymphocyte	0.30	0.11	0.86	0.025*				
Monocyte	1.07	1.03	1.12	0.038*				
NLR	3.02	1.70	5.35	<0.001*	-	-	-	-
PLR	1.02	1.01	1.03	0.018*	-	-	-	-
SII				<0.001*	1.04	1.01	1.07	<0.001*
								Nagelkerke R^2= 0.410, p<0.001

* P <0.05 shows statistical significance. Abbreviations: see Table 1; CI, confidence intervals; OR, odds ratio, ref, reference.

Discussion

The striking findings of our study were as follows: [1] SII values were significantly different between groups according to both the presence and severity of CAD; [2] the SII exhibited superior diagnostic performance compared to the PLR and NLR; and [3] using the SII threshold level, 27% of patients with suspected CAD could avoid unnecessary CAG.

The SS evaluates the anatomy and character of lesions detected during CAG and it predicts prognosis and the need for revascularization [19]. A high SS value is associated with more adverse cardiovascular outcomes [20]. Therefore, biomarkers that can be obtained easily and cheaply attract increasing interest for the classification of patients suspected of CAD in clinical practice. Atherosclerosis, the most common cause of CAD, has a long development period and the diseases that it causes have acute onset and generally poor prognosis [21]. In atherosclerosis, lipid accumulation in the arterial intima, activation of inflammatory cells such as monocytes and T lymphocytes, accumulation of smooth muscle cells, and production of collagen and matrix proteins play important roles [22,23]. When tissue damage occurs, macrophages accumulate in the damaged tissue due to the inflammatory re-



Pairwise comparison of ROC curves

NLR vs PLR	
Difference between areas	0.005
Standard Error	0.031
95% Confidence Interval	-0.057 to 0.067
p value	0.881
NLR vs SII	
Difference between areas	0.102
Standard Error	0.030
95% Confidence Interval	0.043 to 0.161
p value	0.001
PLR vs SII	
Difference between areas	0.107
Standard Error	0.017
95% Confidence Interval	0.072 to 0.141
p value	< 0.001

Figure 2. Diagnostic performance evaluation of SII in predicting the presence of CAD.

sponse. During this process, IL-6 and TNF-α are secreted, and CRP synthesis is induced and increases with the progression of atherosclerosis [24]. Therefore, inflammatory reactions play key roles in atherosclerosis and CAD [25].

In ischemic myocardial tissue, secreted pro-inflammatory chemokines activate leukocytes, leading to leukocyte migration. Neutrophils are the first leukocytes found in these damaged tissues [26]. The activation of neutrophils may lead to the exacerbation of inflammatory responses via secretion of assorted mediators of inflammation [27]. In contrast to neutrophils, lymphocytes infiltrating the tissues of ischemic myocardium signify the regulation of cytotoxic and inflammatory responses. Reduced lymphocyte counts are considered as a response to physiological stressors in the face of myocardial ischemia. A surge in the numbers of apoptotic lymphocytes and secretions of various pro-inflammatory cytokines both lead to notable reductions in lymphocyte counts in the presence of acute stress [28]. Platelets are also of critical importance in myocardial ischemic processes. The accumulation of platelets are associated with the presence of ischemic and necrotic areas [29,30]. Based on these mechanisms, indices obtained from neutrophil, lymphocyte, and platelet counts are thought to better reflect atherosclerotic processes. Previous studies have shown that the PLR and NLR, which are indicators of subclinical inflammation, predict the presence and severity of CAD [31,32]. In previous studies where the PLR and NLR were evaluated together, conclusions about the superior of the two ratios differed [33,34]. This is probably due to the different mechanisms of their components. However, the components of the SII, a new marker of inflammation, include all components of both the NLR and PLR. Therefore, the SII may be a better prognostic indicator than the NLR or PLR.

The SII, as a new index based on circulating immune-inflammatory cells, is an indicator of immune-inflammatory response [12]. Limited studies have evaluated the prognostic role of the SII in CAD patients. Yang et al. [12] showed that increased SII values were associated with adverse events including cardiac death, myocardial infarction, stroke, and chronic heart failure in CAD patients. Yehong et al. [14] found that the SII predicted the presence and severity of CAD in 395 patients who underwent CAG. Candemir et al. [13] showed that in patients with stable angina pectoris, SII values were positively correlated with the SS and independently predicted high SS values. The current findings suggest that the SII is an independent predictor of the presence and severity of CAD. In addition, the SII exhibits superior diagnostic performance compared to the PLR and NLR. Furthermore, the SII can provide a separate cut-off value for the presence of CAD, and this cut-off value could save 35.7% of patients with suspected CAD from unnecessary CAG. To the best of our knowledge, this result has been shown here for the first time in the literature.

The main strength of this study was that the subjects comprised a homogeneous cohort of consecutive unselected patients and the study population was relevant to most patients with chest pain and suspected CAD in the general population. The primary limitation of the study was that the results were the reflection of a single-center experience. The second limitation is that comorbid conditions may exacerbate inflammation. Although confounding factors were adjusted in the regression analysis, their presence may have triggered the underlying mechanisms. Therefore, the prognostic role of the SII should be evaluated in future studies with larger sample sizes.

Conclusion

The SII is an important biomarker that predicts the presence and severity of CAD. Thus, it has the potential to be a screening marker for CAD before CAG. Furthermore, the SII threshold level can be used to avoid unnecessary CAG for a significant proportion of patients with suspected CAD.

Ethics approval

The study was performed in accordance with the Declaration of Helsinki, and approved by Clinical Research Ethics Committee of the Lokman Hekim University (Decision Date/No: 23.12.2021 / 2021/159).

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