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RESEARCH ARTICLE

Can the systemic immune inflammation index (SII) and the systemic inflammation response index (SIRI) predict the severity of coronary artery disease?

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ABSTRACT

Aim: To examine the relationship between complete blood count metrics and the severity of coronary artery disease (CAD) in patients undergoing coronary angiography.

Methods: Patients diagnosed with stable angina pectoris or acute coronary syndrome by coronary angiography between October 2018 and February 2019 were included in the study. Based on their angiography results, patients were divided into two groups: one with severe CAD (n=258) and one with non-severe CAD (n=219). The initial clinical characteristics, along with data from laboratory tests and complete blood counts, were recorded and compared between the two groups.

Results: The Wight Blood Cell (WBC) count, Neutrophil (NEU) count, Monocyte/Lymphocyte Ratio (MLR), Neutrophil/Lymphocyte Ratio (NLR), Monocyte/High-Density Lipoprotein Cholesterol Ratio (MHR), systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) were each significantly higher in the group with severe CAD than in the group without severe CAD. The analysis utilized logistic regression, factoring in recognized CAD risk factors such as age, gender, diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), and smoking, identified NLR, MHR, MLR, SII, and SIRI as notable and independent indicators of severe CAD.

Conclusion: Our study showed that since it was an independent predictor of CAD, SII and SIRI could be utilized as a novel indicator for assessing the severity of CAD.

Keywords: complete blood count, coronary artery disease, inflammation, systemic immune inflammation index, systemic inflammation response index

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INTRODUCTION

Coronary artery disease (CAD), characterized by a prolonged progression over time and primarily attributed to atherosclerosis, stands as the primary cause of mortality globally, accounting for more than 30% of deaths beyond the third decade of life (1). Known for its latent development over an extended duration, atherosclerosis eventually manifests clinically and contributes notably to CAD. The recognized risk factors for atherosclerosis such as diabetes mellitus (DM), hypertension (HT), dyslipidemia, and smoking, are at least one risk factor in most individuals with CAD, and the presence of more than one of these risk factors creates a synergistic effect (2). When atherosclerotic plaques are examined, they have lipid deposits and foam cells in the center, a cap of smooth muscle cells, and a core region surrounded by a collagen-rich matrix. T cells, macrophages, and mast cells infiltrate the atherosclerotic lesion play a role in its growth, and produce inflammatory cytokines with signs of activation. These inflammatory cytokines and acute phase reactants produced and released into the circulation pose a risk for CAD (3,4). Recent studies have highlighted cost-effective. Hemogram (CBC) parameters that provide critical diagnostic and prognostic insights for diseases related to chronic inflammation, including CAD (5,6). In addition, recent studies have demonstrated the potential of inflammatory hematologic ratios including the NLR, platelet/lymphocyte ratio (PLR), and monocyte/lymphocyte ratio, which are both cost-effective and readily accessible, as well as reflecting the degree of systemic inflammation, and have shown a correlation between the severity, prognosis, and presence of CAD (7). The newly established SII and SIRI are also shown to improve risk prediction in CAD (8,9). In our study, we aimed to compare systemic inflammation indices in patients with and without severe CAD by coronary angiography (CAG).

METHODS

Study design and patient selection

This analysis, performed as a retrospective cohort study, was carried out in the cardiology department of a tertiary referral hospital in Türkiye, with the approval of the local ethics committee. Patients diagnosed with stable angina pectoris or acute coronary syndrome by coronary angiography between October 2018 and February 2019 were included in the study. Exclusion criteria were a recent history of acute coronary syndrome (ACS) before CAG or coronary artery bypass graft (CABG), major valvular heart condition, unstable heart failure, stroke, kidney and liver disease, acute and ongoing infection and inflammatory conditions, oncologic disease, poor nutritional status, hematologic conditions, low platelet count, symptomatic peripheral artery disorder, immune system diseases, pregnancy, and chronic lung disease.

All patients undergoing CAG were tested and categorized into two groups based on the findings of the CAG examination. Group 1 includes the severe CAD group, and Group 2 consists of the non-severe CAD group. All demographic information and laboratory parameters of all patients were obtained from their files by screening. The following laboratory parameters were analyzed: basic biochemical tests; CBC parameters of white blood cell (WBC), neutrophil (NEU), lymphocytes (LYM), platelet count (PLT), mean platelet volume (MPV), NLR, PLR, MLR, and monocyte/high-density lipoprotein cholesterol ratio (MHR). SII is calculated by the formula: (P×N)/L where P, N, and L stand for peripheral platelet, neutrophil, and lymphocyte counts, respectively. SIRI was calculated by the formula (N×M)/L, where N is the peripheral count of neutrophils, and M is the peripheral count of monocytes. A comparison of these recorded data was conducted between the groups. We further analyzed the role of SII and SIRI in predicting the severity of CAD after adjustment for age, sex, DM, HT, and smoking status.

Statistical analysis

SPSS version 15.0 was used to analyze the data. The Kolmogorov-Smirnov method was used for normality tests of the variables. The Student t-test was used to compare normally distributed variables, and these data are shown as mean ± SD. The comparison of non-normally distributed variables was performed using the Mann-Whitney test, and these data are shown as median (IQR). The comparison of categorical variables was done using the chi-square test. Univariate analyses were complemented by multivariate logistic regression analysis to determine the independent variables associated with severe CAD, adjusting for

Table 1. Baseline characteristics of the groups

	Severe CAD (+) n=258	Severe CAD (-) n=219	p value
Age (years)	65±11	61±12	p<0.001
Gender (F/M), n	65/193	94/125	p<0.001
HT, n	159	111	p=0.02
DM, n	131	72	p<0.001
HL, n	78	48	p=0.05
Family History, n	107	70	p=0.04
Smoking, n	112	65	p=0.02
BMI, kg/m^2	29.06±4.9	29.80±5.3	p=0.14
Waist Circumference, cm	106.1±13.8	105.12±15.1	p=0.60

HT: Hypertension, DM: Diabetes Mellitus, HL: Hyperlipidemia, BMI: Body Mass Index, CAD: Coronary artery disease.

Table 2. Laboratory findings of the groups

	Severity CAD (+) n=258	Severity CAD (-) n=219	P Value
HbA1c	7.02±1.7	6.50±1.3	<0.001
Urea	37.69±17.22	33.00±10.6	0.001
Creatinine	0.97±0.50	0.84±0.15	<0.001
GFR	81.03±18.93	87.6±14.9	0.002
Glucose	146.3±69	115.8±51.3	<0.001
TSH	1.17±1.02	2.46±7.17	0.013
HDL, mg/dl	42.33±9.69	46.41±11.16	<0.001
LDL, mg/dl	116.47±39.18	112.93±37.10	0.355
TC, mg/dl	186.88±44.76	187.22±45.42	0.973
TG	152.15±107.10	143.29±94.44	0.461
WBC	8.95±3.11	7.58±2.05	<0.001
NEU	6.0±2.97	4.69±1.68	<0.001
MONO	0.56±0.25	0.49±0.20	<0.001
NLR	3.50±3.10	2.58±1.97	0.001
PLR	138.72±80.38	133.84±68.94	0.794
RPR	0.066±0.018	0.065±0.018	0.678
MPR	0.034±0.011	0.034±0.011	0.363
MLR	0.29±0.17	0.25±0.15	0.004
MHR	0.014±0.007	0.011±0.006	<0.001
SII plt × neu/lym	883.41±829.70	639.32±467.67	0.03
SIRI neu × mono/lym	1.95±1.97	1.27±1.22	<0.001

CAD: Coronary artery disease, HbA1c: hemoglobin A1c, GFR: glomerular filtration rate, TSH: thyroid-stimulating Hormone, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TC: total cholesterol, TG: trigliceride, WBC: wight blood cell, NEU: Neutrophil, MONO: Monocyte, LYM: lymphocyte, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, RPR: red blood cell distribution width/platelet ratio, MPR: mean platelet volume/platelet ratio, MLR: monocyte/lymphocyte ratio, MHR: monocyte/high-density lipoprotein cholesterol ratio, SII: systemic immune inflammation index, SIRI: systemic inflammation response index.

other variables. Statistical significance was defined as a P value of less than 0.05.

RESULTS

A total of 477 patients were enrolled in the study. Group 1 consisted of 258 patients, while Group 2 consisted of 219 patients. A significant difference in gender distribution was observed between the two groups (p<0.001). Group 1 consisted of 75% male and 25% female patients, while Group 2 comprised 57% male and 43% female patients (p<0.001). The mean age of patients in Group 1 was higher than in Group 2. (p<0.001). The general characteristics of the study groups are summarized in Table 1. The groups did not differ significantly in other study data, including height (p=0.03), weight (p=0.95), body mass index (BMI) (p=0.11), and waist circumference (p=0.60), LDL-cholesterol (p=0.36), total cholesterol (p=0.97), LYM (p=0.85), mean corpuscular volume (MCV) (p=0.44), PLT (p=0.96), mean platelet volume (MPV) (p=0.11), and platelet-to-lymphocyte ratio (PLR) (p=0.79).

Compared to Group 2, Group 1 had significantly elevated levels of height, glucose, hemoglobin A1c (HbA1c), urea, creatinine, serum aspartate transferase (AST), potassium (K), WBC, NEU, NLR, MLR, MHR, SII, and SIRI (all p<0.05). Conversely, Group 1 had significantly lower levels of glomerular filtration rate (GFR), thyroid-stimulating hormone (TSH), and high-density lipoprotein (HDL) compared to Group 2 (all values p<0.05) (Table 2). The analysis utilized logistic regression, factoring in recognized CAD risk factors such as age, gender, DM, HT, HL, and smoking, identified NLR, MHR, MLR, SII, and SIRI as notable and independent indicators of severe CAD (Table 3).

Table 3. Independent predictors of coronary artery disease by logistic regression analysis

Variables	p value*	Odds ratio (95% CI)
Age (years)	<0.001	1.036 (1.018, 1.053)
Gender (F/M)	<0.001	2.233 (1.515, 3.292)
HT	0.016	1.563 (1.085, 2.251)
DM	<0.001	2.106 (1.450, 3.058)
HL	0.041	1.544 (1.018, 2.340)
Smoking	0.002	1.817 (1.242, 2.659)
NLR	<0.001	1.169 (1.072, 1.275)
MHR	<0.001	2.225 (7.490, 6.608)
MLR	0.010	5.040 (1.473, 17.246)
SII	<0.001	1.001 (1.000, 1.001)
SIRI	<0.001	1.334 (1.160, 1.535)
PLR	0.482	1.001 (0.998, 1.003)

CI: confidence interval, DM: diabetes mellitus, HL: hyperlipidemia, HT: Hypertension, MHR: monocyte count/HDL cholesterol ratio, MLR: monocyte/lymphocyte ratio, NLR: neutrophil/lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: (Platelet x neutrophil)/ lymphocytes, SIRI: (Neutrophil x monocyte)/ lymphocytes.

*Results of multivariate logistic regression analysis of significant coronary artery disease as the dependent variable.

Bold values indicate p<0.05.

DISCUSSION

Our study revealed that recognized CAD risk factors, including HT, DM, and dyslipidemia, were more prevalent, and certain CBC parameters, including WBC, Neu, Monocyte (MONO), NLR, and MLR, were significantly elevated in patients with severe CAD compared to those without severe CAD. Logistic regression analysis of these parameters, including well-known risk factors for CAD, showed that NLR, MHR, MLR, SII, and SIRI were all significant and independent predictors of substantial CAD, which would label these parameters and indices as an independent predictor of the severity of CAD.

Asymptomatic inflammation is now recognized as pivotal in CAD pathogenesis and progression, involving costly and limited availability of agents like growth factors, cytokines, and adhesion molecules (10). In contrast, CBC parameters, being simple, inexpensive, and easily accessible, have gained traction in recent research for their diagnostic potential.

In various studies, NLR emerged as a determinant of severe CAD, predicting cardiac risk in patients (11). Elevated NLR values correlated with advanced CAD and poorer prognosis (12). Meta-analyses further confirmed the predictive value of NLR for cardiovascular events and all-cause mortality, particularly in groups with progressive atherosclerosis (13). Consistent with the existing literature, our study also found significantly higher NLR levels in Group 1.

Recently, MLR has garnered attention as a notable CBC parameter. Previous studies have shown that MLR levels can help identify fragile plaques in patients with stable angina pectoris and have been proven to independently predict the presence and severity of CAD. Similarly, our study found that MLR was higher in Group 1.

Another inflammation parameter, MHR, has been defined as a new and dramatic marker of cardiovascular diseases in recent years and associated with SYNergy between PCI with TAXUS and Cardiac Surgery' (SYNTAX) and Gensini scores, and is thought to be related to the burden of coronary atherosclerosis. MHR was significantly higher in Group 1 in our study as well.

The recently described SII and SIRI are new inflammatory biomarkers. In a study of 85,154 patients, Jin et al.[8] investigated the associations between SII and SIRI with cardio vasculer diseases (CVD) and all-cause mortality risks, and both indices showed positive associations with stroke risk and all-cause mortality risk. In addition, higher SIRI was associated with a higher risk of MI, whereas SII was not.

Yildiz et al.[9] examined coronary CT angiography data from 1456 patients and observed higher SIRI and SII values in mixed plaque types. They identified SII and SIRI as independent predictors of one-year major adverse cardiac events (MACE), with SIRI enhancing risk prediction in CAD.

Based on the hypothesis that chronic low-grade inflammation is associated with a variety of diseases, Xia et al.[14] recently made an effort to assess the SII, SIRI, and the risk of all-cause mortality and cardiovascular mortality in 42,875 adults during a follow-up of 20 years. They showed higher levels of SII and SIRI associated with higher all-cause and cardiovascular mortality compared to lower levels of SII and SIRI. In a recent study, Wei et al.[15] studied the correlation of SII and SIRI to clinical risk factors that included Global Registry of Acute Coronary Events (GRACE), Gensini, and QTc in 310 patients with AMI. They found that major adverse cardiac events were higher in those with higher levels of SII and SIRI. Moreover, SII was associated with SIRI and potential post-infarction risk factors. Dziedzic et al.[16] aimed to analyze the relationship of inflammation intensity by SII and SIRI with CAG-measured CAD burden and the ACS or stable CAD diagnosis in 699 patients. Stable CAD and ACS patients showed significant differences in SII. The ACS population had significantly higher values, while there was no significant difference among ST elevation myocard infarction (STEMI), non ST elevation myocard infarction (NSTEMI), unstable angina pectoris (USAP) patients. Besides, no such significant relationship was found for SII and SIRI with the severity of CAD.

In a cohort of 669 individuals with stable CAD, Candemir et al.[17] demonstrated a positive correlation between SII and CAD severity as measured by the SYNTAX scale. Similarly, in a study involving 400 patients who underwent coronary angiography, Liu et al.[18] identified a correlation between SII and the Gensini scale of CAD severity. They characterized SII as an independent variable for diagnosing and gauging the severity of CAD.

In our study, both SII and SIRI levels were higher in the group with severe CAD compared to the group without severe CAD.

Finally, logistic regression analysis showed that biomarkers such as NLR, MHR, MLR, SII, and SIRI were significant and independent predictors of CAD. This emphasizes the importance of evaluating markers of inflammation as predictors of disease beyond traditional CAD risk factors.

These findings not only contribute to the understanding of CAD pathophysiology and risk factors but may also help to improve risk prediction and treatment strategies in future clinical practice. However, more prospective studies and further research are needed to integrate these biomarkers into clinical practice.

The retrospective design and the relatively small number of patients are limitations of this study. Nonetheless, it aligns with other studies in the literature. Gensini or Syntax scores were not applied to the study population, which could be the other limitation.

Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date 04/07/2023, number 2023/232). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: MFB; Concept: MFB, MC; Design: MFB, MC; Data Collection or Processing: MC; Analysis or Interpretation: MC; Literature Search: MFB; Writing: MFB, MC. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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