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Retrospective Evaluation of the Relationship Between Systemic Inflammation Index, Left Ventricular Functions, and Prevalence of Coronary Artery Disease in Patients with Chronic Atrial Fibrillation

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ABSTRACT

Objective: The relationship between 'atrial fibrillation (AF)' and 'coronary artery disease (CAD)' has been identified, and they share a vast array of overlapping risk determinants. Inflammation is of paramount importance in the occurrence and spread of both AF and CAD. The objective of the present study was to clarify the relationship between the level of the 'systemic inflammation index (SII)' and 'left ventricular functions' and the prevalence of CAD in patients with chronic AF.

Methods: The research was conducted using records of 271 patients diagnosed with chronic AF and 301 patients with sinus rhythm in the cardiology outpatient clinic of a university hospital. Patients' socio-demographic data, comorbidities, laboratory results, echocardiographies, and coronary angiography were evaluated. 'NLR (neutrophil-lymphocyte ratio),' 'PLR (platelet-lymphocyte ratio),' and 'LMR (lymphocyte-monocyte ratio)' were computed using hemogram and biochemistry results.

Results: Increased 'uric acid,' 'C-reactive protein,' and 'left atrial diameter' were associated with an increased likelihood of AF. Increased uric acid and SII were associated with an increased risk of having a SYNTAX score ≥23. In the mortality follow-up of the AF group, an increased NLR was associated with an increased probability of mortality. Additionally, whereas a positive correlation was identified between the 'left ventricular end-diastolic diameter' and 'left ventricular end-systolic diameter' and SII, NLR, and PLR, a negative correlation with LMR was found ($p<0.05$).

Conclusions: The study results clearly demonstrate the roles of NLR, SII, and uric acid in predicting mortality and CAD in AF patients, highlighting the practical benefit of integrating these markers into existing risk scores to determine coronary risk and optimize treatment strategies.

Keywords: Atrial fibrillation, coronary artery disease, systemic inflammation index.

1. INTRODUCTION

Atrial fibrillation (AF) is a frequently observed, life-threatening rhythm disorder that occurs in every 3-5 individuals after the age of 40 (1). AF, which has a higher actual prevalence, was reported in 33.5 million in 2010 (1), 37.574 million in 2017 (2), and 59 million in 2019 (1).

AF has recently become a significant cause of hospitalizations and increased healthcare costs (3,4). Additionally, it is a condition linked to adverse clinical outcomes (morbidity and mortality), causing a significant burden on the healthcare system (1). Echocardiography and Doppler echocardiography are fundamental diagnostic approaches to assess the structural and functional status of the heart after electrocardiographic evaluation in patients with AF (5,6). Echocardiography is critical to assessing hemodynamics and prognosis in patients with AF (5). However, the cause of AF is complex and not fully understood (2,7,8).

Patients with AF have been reported to have a quite high incidence of coronary artery disease (CAD) (9,10). CAD increases atrial excitability due to ischemia and electrical imbalance, thereby adversely impacting AF. On the other hand, AF accelerates atherosclerosis formation through endothelial dysfunction and inflammation and causes micro – and macro-thrombus formation with increased

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thrombogenicity and hypercoagulability (10). The co-occurrence of AF and CAD, which have many risk factors in common, in the same individuals threatens life considerably (8,9). Furthermore, inflammation is fundamental to the occurrence of both AF and CAD (8,11).

Inflammation causes the formation of AF by leading to a series of changes in the atrium's structure and electrical activity (12). Whereas elevated platelets and reduced lymphocytes are associated with a poor prognosis in cardiovascular diseases, other inflammatory markers increase susceptibility to thrombosis in AF (13,14).

The literature has identified new systemic inflammatory markers based on the ratios of leukocyte subtypes, such as neutrophils, lymphocytes, and monocytes, to assess systemic inflammatory response (15). Inflammatory indices such as 'neutrophil-lymphocyte ratio (NLR),' 'platelet-lymphocyte ratio (PLR),' 'lymphocyte-monocyte ratio (LMR),' and 'systemic inflammation index (SII)' are cost-effective and simple measures of inflammation that can be easily obtained (16). As seen from the current data, these markers help determine the prognosis and risk profile of many cardiovascular diseases, such as CAD, hypertension, and pulmonary embolism (17).

Although some studies have examined the relationship among AF, CAD, and inflammation, the underlying mechanism remains incompletely understood. The present work aimed to reveal the relationship between the 'systemic inflammation index (SII)' and 'left ventricular functions' and CAD prevalence in patients with chronic AF.

2. METHODS

This retrospective and single-center study examined the records of 271 patients with chronic AF and 301 patients with sinus rhythm (SR). The patient groups consisted of patients followed up in the cardiology outpatient clinic of a university hospital between January 2015 and July 2022. Ethics committee approval for the study was obtained from Uludağ University Faculty of Medicine Clinical Research Ethics Committee (date: 27.07.2022, number: 2022-15/17), and the research was conducted in accordance with the principles specified in the Declaration of Helsinki.

The researcher scanned patients' files retrospectively. During scanning, 271 patient files that met the predefined inclusion criteria for the AF group were identified. Three hundred and one patients without AF but with SR were randomly included in the control group.

The study sample was created by retrospectively reviewing the records of patients who underwent elective or emergency coronary angiography (CAG) at our center during the specified time period. The study included patients over 18 years of age with chronic AF and a control group of patients over 18 years of age without AF. Individuals who had undergone transthoracic echocardiography and CAG within the last 3 months, had complete routine examinations and medical history were included. Figure 1 details the patient selection process.

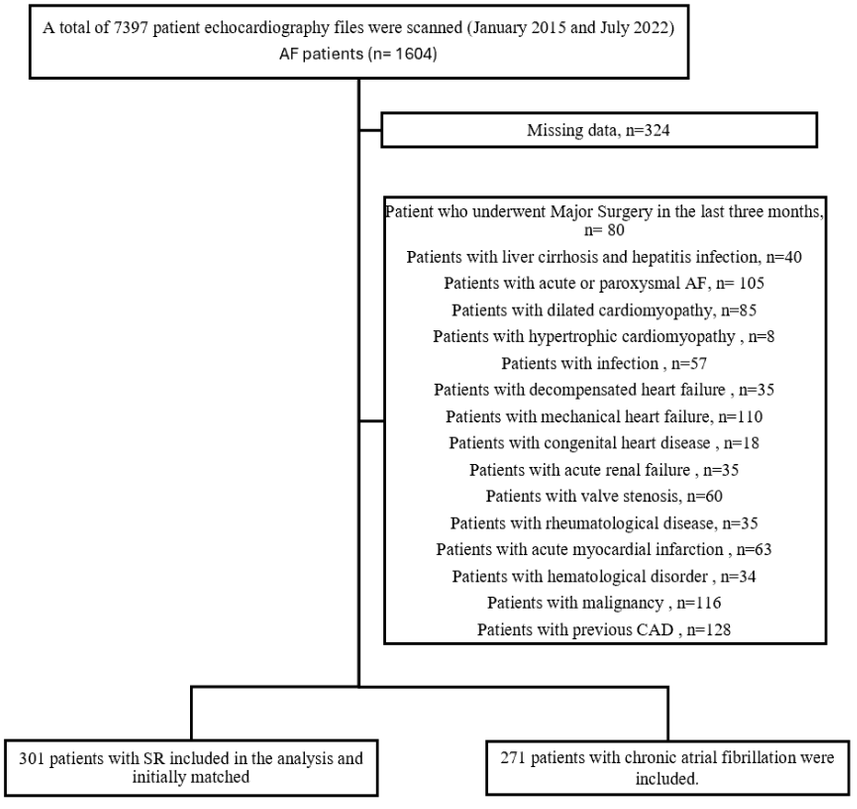


Figure 1. *Patient flow diagram*

The database used at the university hospital was scanned to include patients in the study. A total of 7397 patient echocardiography files were scanned. Of these, 1604 were AF patients. Three hundred twenty-four patients with missing data and a total of 1009 patients, including 'patients who underwent major surgery in the last three months (n=80),' 'patients with liver cirrhosis and hepatitis infection (n=40),' 'patients with acute or paroxysmal AF (n=105),' 'patients with dilated cardiomyopathy (n=85),' 'patients with hypertrophic cardiomyopathy (n=8),' 'patients with infection (n=57),' 'patients with decompensated heart failure (n=35),' 'patients with mechanical heart failure (n=110),' 'patients with congenital heart disease (n=18),' 'patients with acute renal failure (n=35),' 'patients with valve stenosis (n=60),' 'patients with rheumatological disease (n=35),' 'patients with acute myocardial infarction (n=63),' 'patients with hematological disorder (n=34),' 'patients with malignancy (n=116),' and 'patients with previous CAD (n=128),' were excluded from the research. Patients enrolled in the study were over 18 years of age.

The patient group consisted of 271 patients with chronic AF. The control group comprised 301 patients with SR. Patients in both groups were matched on some sociodemographic characteristics (age, sex, etc.). Furthermore, patients with chronic or acute AF who fulfilled the exclusion criteria for the AF group were excluded in the SR group's matching. Finally, the mortality status of patients in the AF group was checked on 15.06.2023 from the patient files.

2.1. Coronary Angiography (CAG) and Echocardiography Evaluation

During the scanning, patients' socio-demographic data, comorbidities, and laboratory results were retrieved from the hospital's database, and their CAG was evaluated. In the CAG evaluation, patients for whom the standard Seldinger technique was used were preferred. Patients who underwent CAG were classified into two groups: those with lesion stenosis of 50% and above (CAD group) and those with lesion stenosis of less than 50% (non-CAD patient group). NLR, PLR, and LMR were computed using hemogram and biochemistry results. The SII was calculated with 'platelet count*neutrophil/lymphocyte ratio (P*NLR).' Additionally, the absolute values used in the formulae are expressed in $10^3/\mu L$, and the indices obtained are presented as dimensionless ratios.

In the echocardiographic evaluation, 'left atrial diameter (LAD),' 'left ventricular end-systolic diameter (LVESD),' 'left ventricular end-diastolic diameter (LVEDD),' 'interventricular septum thickness in diastole (IVSD),' 'posterior wall thickness,' 'ascending aorta diameter,' 'left ventricular ejection fraction (LVEF)' (using the 'modified Simpson method in the apical four-chamber examination'), and valve regurgitation flows were measured by standard 2D and color Doppler examination.

The prevalence of CAD in the patient groups was evaluated based on the SYNTAX score. Parameters, such as dominance, number of lesions, trifusion, the presence of bifurcation, and calcification, were considered when computing the score. The total score was obtained by summing the scores of each lesion (18). Based on the SYNTAX score, patients were divided into four subgroups: 0, 1-22, 23-31, and 32 and above. Two experienced cardiologists, unaware of patients' clinical status, performed assessments.

2.2. Statistical Analysis

The 'Shapiro-Wilk test' and the 'Kolmogorov-Smirnov test' investigated the suitability of variables to normal distribution. For comparisons between two groups, the 't-test' and 'Mann-Whitney U test' were applied based on the data distribution. As descriptive statistics, 'mean ± standard deviation' and 'median (minimum – maximum)' values were given. 'Pearson's chi-square test' was performed for the inter-group comparison of categorical variables. 'Categorical variables' were expressed as n (%). Relationships between variables were determined using 'Spearman's rank correlation coefficients.' The 'Binary Logistic Regression Analysis Forward LR and Backward LR method' was employed to identify risk factors associated with AF and with SYNTAX score ≥23. 'The Binary Logistic Regression Analysis Backward LR method' was employed to determine the factors affecting mortality in patients in the AF group. Statistical analysis was conducted using the program SPSS version 22.0 (Chicago, USA). For statistical analysis, significance was set at $p < .05$.

3. RESULTS

The study presented some sociodemographic results, comorbidities, smoking, family history, and the treatment method applied according to the angiography results of the AF and SR groups. No significant difference was revealed between the groups in terms of age, sex, some comorbidities (hypertension, diabetes mellitus, and obstructive sleep apnea syndrome), smoking, family history, and treatment method applied according to angiography results (Table 1).

Table 2 compares the inflammatory parameters of the AF and SR groups. Accordingly, the uric acid (6.7 mg/dL), 'red cell distribution width (RDW)' (13.4%), 'C-reactive protein (CRP)' (3 mg/L), NLR (2.3), and SII (492) values of the AF group were statistically higher than the uric acid (5.8 mg/dL), RDW (12.7%), CRP (2 mg/L), NLR (2.1), and SII (463) values in the control group ($p < 0.05$). The albumin (40 g/L) and LMR (3.3) values of the AF group were statistically lower than the albumin (42 g/L) and LMR (3.8) values of the control group ($p < .05$) (Table 2).

Table 3 compares the echocardiography findings of the AF and SR groups. The LVEDD, LVESD, LAD, ascending aorta width, and 'Systolic Pulmonary Artery Pressure (sPAP)' averages were higher in the AF group in comparison with the SR group ($p<.05$). In the AF group, 19.6% of patients had an LVEF of 40 and below, 17.3% had an LVEF between 41 and 49, and 63.1% had an LVEF of 50 and above. In the control group, 9.6% of patients had an LVEF of 40 and below, 18.0%

had an LVEF between 41 and 49, and 72.4% had an LVEF of 50 and above. Of patients in the AF group, 57.6% had moderate mitral valve regurgitation, while 8.8% had severe mitral valve regurgitation. Conversely, the majority of patients in the control group (73.1%) had mild mitral valve regurgitation. Of patients in the AF group, 34.3% had mild aortic valve regurgitation, whereas 14.8% and 0.7% had moderate and severe aortic valve regurgitation, respectively. On the other hand, most patients in the control group (72.8%) did not have aortic valve regurgitation. In the AF group, moderate tricuspid valve regurgitation was present in 43.9%, and severe in 10.7%. On the contrary, the vast majority of patients (84.4%) in the control group had mild mitral valve regurgitation (Table 3).

Table 1. *Clinical characteristics of the control and patient groups*

Characteristics		Patient group (AF) (n=271)		Control group (SR) (n=301)		p
		Mean±SD		Mean±SD		
Age		69.41±8.15		68.46±8.21		.164
		n	%	n	%	
Sex	Female	120	44.3	123	40.9	.409
	Male	151	55.7	178	59.1	
Hypertension	Absent	42	15.5	58	19.3	.236
	Present	229	84.5	243	80.7	
Diabetes Mellitus	Absent	160	59.0	183	60.8	.669
	Present	111	41.0	118	39.2	
Peripheral Artery Disease	Absent	243	89.7	265	88.0	.537
	Present	28	10.3	36	12.0	
Smoking	Absent	153	56.5	185	61.5	.224
	Present	118	43.5	116	38.5	
Family History	Absent	219	80.8	261	86.7	.055
	Present	52	19.2	40	13.3	
Hyperlipidemia	Absent	101	37.3	57	18.9	**<.001**
	Present	170	62.7	244	81.1	
Pulmonary Embolism	Absent	258	95.2	296	98.3	**.032**
	Present	13	4.8	5	1.7	
Cerebrovascular Disease	Absent	208	76.8	275	91.3	**<.001**
	Occlusive	61	22.5	24	8.0	
	Hemorrhagic	2	0.7	2	0.7	
Chronic Kidney Disease	Absent	191	70.5	251	83.4	**<.001**
	Present	80	29.5	50	16.6	
COPD	Absent	218	80.4	273	90.7	**<.001**
	Present	53	19.6	28	9.3	
OSAS	Absent	257	94.8	293	97.3	.121
	Present	14	5.2	8	2.7	
Treatment method applied according to angiography results	Medical Treatment (Patients without serious coronary artery disease)	102	37.6	106	35.2	.393
	PCI	91	33.6	112	37.2	
	CABG	78	28.8	83	27.6	

CABG = Coronary Artery Bypass Graft, COPD = Chronic Obstructive Pulmonary Disease, OSAS= Obstructive Sleep Apnea Syndrome, PCI = Percutaneous Coronary Intervention, Chi-Square Analysis; Values in bold are statistically significant at p < .01.

Table 2. *Inflammatory parameters of the control and patient groups*

	Patient group (AF) (n=271)	Control group (SR) (n=301)	p
Albumin (g/L)	40(28-52)	42(30-51)	**<.001***
Total Protein (g/L)	70(51-87)	70(41-86)	.884*
Uric Acid (mg/dL)	6.7(3.1-15.9)	5.8(2.3-14.1)	**<.001***
MPV (fL)	8.4(5.5-15.5)	8.1(5.6-13.3)	.223*
RDW (%)	13.4(9.1-23)	12.7(9.5-19.4)	**<.001***
CRP (mg/L)	3(1-5)	2(1-5)	**<.001***
NLR	2.3(0.8-8.9)	2.1(0.9-5.9)	**.001***
PLR	107.3(49-344)	104.6(45-383)	.257*
LMR	3.3(0.7-18.9)	3.8(1.3-18.4)	**<.001***
SII	492(148-2083)	463(129.9-1774)	**.023***

*MPV: mean platelet volume, RDW: red cell distribution width, CRP: C-reactive protein, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, LMR: lymphocyte-monocyte ratio, SII: systemic inflammation index.*Mann-Whitney U test, Median (Min-Max); Values in bold are statistically significant at p < .05.*

The LVEDD, LVESD, LAD, ascending aorta width, and sPAP averages were higher in the AF group in comparison with the SR group. The mean LVEDD value for the AF group was 51.37 ± 7.13 mm, while the value for the SR group was measured as 48 ± 6.49 mm. The mean LVESD value for the AF and SR group was 35.66 ± 9.14 mm and 32.31 ± 7.96 mm, respectively. The mean LAD value for the AF group was 47.29 ± 5.74 mm, whereas the value for the SR group was measured as 38.69 ± 5.36 mm. The mean sPAP in the AF and SR group was 37.63 ± 12.93 mmHg and 26.42 ± 9.89 mmHg, respectively. The mean ascending aorta width was 35.66 ± 4.46 mm in the AF group and 34.47 ± 4.50 mm in the SR group. Table 3 compares the SYNTAX score between the AF and SR groups. No statistically significant difference was found between the AF and SR groups in terms of the SYNTAX groups and SYNTAX scores (p>.05) (Table 3).

Table 4 shows the relationship between the SYNTAX score, LAD, LVEDD, LVESD, sPAP, IVSD, and posterior wall thickness and SII, NLR, PLR, LMR, mean platelet volume (MPV), RDW, CRP, total protein, albumin, and uric acid values in the AF group. The SYNTAX score correlated positively with SII, NLR, PLR, and RDW and negatively with albumin and LMR (p<.05). LAD correlated positively with NLR and RDW and negatively with albumin (p <.05). LVEDD and LVESD were found to correlate positively with SII, NLR, PLR, RDW, and uric acid ratio and negatively with LMR (p<.05). The sPAP ratio correlated positively with SII, NLR, PLR, RDW, and uric acid ratio and negatively with LMR (p<.05) (Table 4).

Table 3. *Transthoracic echocardiography findings of the control and patient groups*

n(%)		Patient group (AF) (n=271)	Control group (SR) (n=301)	p
		n(%)	n(%)	
Left Ventricular Ejection Fraction (%)	50 and above	171(63.1)	218(72.4)	0.003*
	41-49	47(17.3)	54(18.0)	
	40 and under	53(19.6)	29(9.6)	
Left Ventricular Hypertrophy	Present	144(53.1)	139(46.2)	0.097*
Degree Mitral Valve Regurgitation	Absent	1(0.4)	0(0)	<0.001*
	Mild	90(33.2)	220(73.1)	
	Moderate	156(57.6)	73(24.2)	
	Severe	24(8.8)	8(2.7)	
Degree of Aortic Valve Regurgitation	Absent	136(50.2)	219(72.8)	<0.001*
	Mild	93(34.3)	56(18.6)	
	Moderate	40(14.8)	23(7.6)	
	Severe	2(0.7)	3(1)	
Degree of Tricuspid Valve Regurgitation	Absent	3(1.1)	0(0)	<0.001*
	Mild	120(44.3)	254(84.4)	
	Moderate	119(43.9)	41(13.6)	
	Severe	29(10.7)	6(2)	
Ventricular End-Diastolic Diameter (mm)		51.37±7.13	48±6.49	<0.001**
Left Ventricular End-Systolic Diameter (mm)		35.66±9.14	32.31±7.96	<0.001**
Left Atrial Diameter (mm)		47.29±5.74	38.69±5.36	<0.001**
Interventricular Septum Thickness (mm)		11.69±1.77	11.43±1.55	0.065**
Posterior Wall Thickness (mm)		11. 42±1.65	11.20±1.41	0.089**
Ascending Aortic Diameter (mm)		35.66±4.46	34.47±4.50	0.002**
Systolic Pulmonary Artery Pressure (mmHg)		37.63±12.93	26.42±9.89	<0.001**
SYNTAX score		16(0-50)	15(0-52)	0.884
SYNTAX group	0	98±36.2	97±32.2	0.362
	1-22	66±24.4	91±30.2	
	23-31	54±19.9	63±20.9	
	>32	53±19.6	50±16.6	

n (%), *Mean±SD, *Chi-Square Analysis, **Independent Samples t-test, * Median (Min-Max).*
Values in bold are statistically significant at p < .01.

In the AF and SR groups, the effects of urea, uric acid, total protein, albumin, CRP, MPV, RDW, NLR, MLR, PLR, and SII variables on AF were evaluated. According to the analysis results, elevated uric acid, CRP, and LAD were associated with an increased likelihood of AF. The model explained 53.4% of the variance in having AF (Nagelkerke R^2) (Table 5).

In the AF group, the effects of age, urea, uric acid, total protein, albumin, CRP, MPV, RDW, NLR, MLR, PLR, and SII variables on the SYNTAX score ≥23 were evaluated, and increased uric acid and SII were associated with an increased likelihood of having a SYNTAX score ≥23. The model explained 11.6% of the variance in having a SYNTAX score ≥23 (Nagelkerke R^2) (Table 5).

Mortality status was checked in patients in the AF group on 15.06.2023 from patient files. The effect of PLR, NLR, LMR, and SII variables on mortality status was evaluated. The model's correct classification rate was computed at 79.3%. According to the analysis results, increased NLR in patients in the AF group was associated with a higher probability of mortality. The model explained 2.3% of the variance in mortality status (Nagelkerke R^2) (Table 5).

Table 4. *Relationship between the SYNTAX score and inflammatory parameters of left ventricular functions in patients with AF (n=271)*

		SYNTAX Score	LAD	LVEDD	LVESD	sPAP	IVSD	Posterior Wall Thickness
Albumin (g/L)	r	-0.155*	-0.144*	-0.021	-0.111	-0.115	-0.035	-0.051
	p	.011	0.018	0.730	0.068	0.059	0.571	0.408
Total Protein (g/L)	r	-0.101	-0.100	-0.023	-0.034	-0.050	-0.139*	– 0.165**
	p	.096	0.100	0.712	0.580	0.408	0.023	0.007
Uric Acid (mg/dL)	r	0.119	0.083	0.204**	0.162**	0.166**	-0.031	-0.053
	p	.051	0.172	0.001	0.008	0.006	0.609	0.386
MPV (fL)	r	-0.008	0.024	-0.031	0.045	-0.034	-0.052	0.00
	p	.90	0.695	0.607	0.464	0.572	0.396	0.995
RDW (%)	r	0.154*	0.134*	0.145*	0.222**	0.227**	-0.015	0.015
	p	.011	0.028	0.017	<0.001	<0.001	0.808	0.812
CRP (mg/L)	r	0.030	0.023	-0.023	-0.040	-0.070	-0.008	-0.037
	p	.619	0.702	0.710	0.507	0.249	0.901	0.547
NLR	r	0.328**	0.124*	0.271**	0.268**	0.277**	-0.036	-0.023
	p	<.001	0.041	<0.001	<0.001	<0.001	0.554	0.703
PLR	r	0.250**	0.118	0.181**	0.199**	0.278**	-0.035	-0.025
	p	<.001	0.052	0.003	0.001	<0.001	0.569	0.682
LMR	r	-0.190**	-0.078	-0.189**	-0.201**	-0.235**	0.063	0.036
	p	.002	0.200	0.002	0.001	<0.001	0.303	0.559
SII	r	0.340**	0.063	0.228**	0.229**	0.224**	-0.080	-0.056
	p	<.001	0.298	<0.001	<0.001	<0.001	0.192	0.357

*LAD: Left Atrial Diameter, LVEDD: Ventricular End-Diastolic Diameter, LVESD: Left Ventricular End-Systolic Diameter, sPAP: Systolic Pulmonary Artery Pressure, IVSD: interventricular septum thickness in diastole, MPV: mean platelet volume, RDW: red cell distribution width, CRP: C-reactive protein, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, LMR: lymphocyte-monocyte ratio, SII: systemic inflammation index. **p<.01, *p<.05.*

Table 5. *Risk factors affecting AF and risk factors affecting the SYNTAX score ≥23 and mortality in patients with AF*

	B	S.E.	Wald	df	p	Exp(B)	95% C.I.	
							Lower	Upper
Risk factors affecting AF (n=572)								
Uric Acid (mg/dL)	0.148	0.068	4.702	1	.030*	1.159	1.014	1.325
CRP (mg/L)	0.358	0,108	11.047	1	.001**	1.430	1.158	1.766
LAD	0.289	0.026	125.803	1	.000**	1.335	1.269	1.404
Constant	-14.350	1.199	143.320	1	.000**	0.000		
Omnibus, Chi-Square=292.132, df=3, p<.001; Hosmer-Lemeshow=14.935, df=8, p>.05								
Nagelkerke R2=0.534								
Risk factors affecting the SYNTAX score ≥23 in patients with AF (n=271)								
SII	0.002	0.000	14.773	1	.000**	1.002	1.001	1.003
Uric Acid (mg/dL)	0.142	0.071	4.068	1	.044**	1.153	1.004	1.324
Constant	-2.578	0.561	21.100	1	.000**	0.076		
Omnibus, Chi-Square=24.032, df=2, p<.001; Hosmer-Lemeshow=0.083, df=8, p>.05								
Nagelkerke R^2=0.116								
Mortality in patients with AF (n=271)								
NLR	0.296	0.116	6.493	1	.011*	1.345	1.071	1.689
Constant	-2.199	0.355	38.355	1	.000**	0.111		
χ2=Chi-square, Classification Overall Percentage =79.3, Hosme-Lemeshow=12.399, df=8, p=.134								
Nagelkerke R Square= 0.037,								
Cox & Snell R Square=0.023,								

*C.I.=Confidence Interval, OR= Odds Ratio, CRP: C-reactive protein, LAD: Left Atrial Diameter, NLR: neutrophil-lymphocyte ratio, SII: systemic inflammation index.**p<.01; *p<.05; Model =Forward LR*

4. DISCUSSION

This study, which evaluated the relationship between the SII level and left ventricular functions and the prevalence of CAD in patients with chronic AF, found a positive correlation between the SII level and the SYNTAX score, LVEDD, LVESD, and sPAP in patients with AF. Furthermore, the study found that uric acid, CRP, and LAD were associated with AF, whereas uric acid and SII were associated with CAD (i.e., SYNTAX score ≥23) in AF patients. The current study provides important new information to understand the etiology of AF and CAD better.

The SII level is a marker created by combining neutrophil, lymphocyte, and platelet values to assess the body's inflammatory response (19,20). It has been stressed that the clinical outcomes of diseases may be worse due to high inflammatory activity at high SII values. It has been determined that a high SII level significantly affects survival in cancer patients (21), prognosis and mortality in patients with chronic heart failure (22) and hospitalizations due to non-fatal myocardial infarction, stroke, and heart failure (23,24). The SII level is valuable in predicting the prevalence of CAD, especially in comparison with traditional risk factors (24-26). Although the current study found a significant relationship between the SII and SYTAX score (≥23), the OR value obtained (1.002) was quite low and had quite limited clinical significance. The finding above supports the relationship between the SII and SYNTAX score. However, it also indicates that it is insufficient on its own to predict high complexity, and the results must be interpreted with caution. On the contrary, the 'CHA_2DS_2-VASc score' is employed to determine thromboembolic risk in AF patients (27), whereas the 'GRACE risk score' is used to identify acute ischemic risk (28). While the current scores focus on demographic and hemodynamic data, SII focuses on chronic systemic inflammation, a common denominator of AF and CAD. Additionally, SII combines not only inflammation (neutrophils and lymphocytes) but also pro-thrombotic status (platelets), which is critical to the pathophysiology of AF, into a single parameter (29). These scores suggest that the addition of an inflammatory parameter, such as SII, would have a higher predictive power in CAD diagnosis and could be utilized as a cost-effective 'early warning system' in the early diagnosis of CAD.

The present study found that 'uric acid levels' were significantly associated with the presence of both AF and CAD. Additionally, patients with AF were determined to have higher uric acid levels. The study results support our findings, and serum uric acid levels were found to be higher in patients with AF and patients with CAD and useful in predicting AF and CAD (30,31). Hyperuricemia and gout have pro-oxidant effects. It reduces the bioavailability of nitric oxide in the vascular wall, ultimately causing inflammation and endothelial dysfunction. This may increase the cardiovascular incidence of AF, such as hypertension, metabolic syndrome, and diabetes, by causing changes in conduction pathways (31,32).

Some studies in the literature have evaluated the effects of inflammatory parameters, such as 'CRP,' 'tumor necrosis factor-alpha,' 'interleukin-1,' and 'interleukin-6 levels,' on the development of AF (33,34). The observational and meta-analysis study by Li et al. (35) emphasized that a high serum CRP level predicted AF and serial CRP measurements should be considered in predicting AF. Although the underlying mechanism remains unclear, CRP binds to myocardial cell membranes, thereby activating the complement cascade and causing tissue damage (36).

NLR was found to be elevated in the AF group and was associated with mortality. However, the Nagelkerke R^2 (0.037) and Cox & Snell R^2 (0.023) values were quite low, indicating the limited explanatory power of the model. The literature has found that neutrophils increase atherosclerosis and inflammation by triggering the disintegration and death of smooth muscle cells (37). Lymphocytes are an important parameter of the inflammatory response and the atherosclerotic process. In atherosclerotic lesions, the atherosclerotic plaque grows, and the lipid core develops after lymphocyte apoptosis, leading to plaque rupture and thrombus formation (25). NLR is an important indicator of oxidative stress damage and the prognosis of mortality in cardiac and non-cardiac patients (38,39). The current information explains high NLR values in patients with AF and increased mortality in patients with AF in our study.

Although it was not found to be significant in the model established in the research, a study found high LMR and albumin levels to be associated with a reduced risk of AF and high SII levels to be associated with an increased risk of AF (33). LMR is determined from lymphocyte and monocyte counts, which are important for leukocyte differentiation. Lymphopenia indicates a physiological stress response, while monocytosis reflects chronic systemic inflammation (40). It has been revealed that the infiltration of inflammatory cells (monocytes, lymphocytes, etc.) increases in the atrial myocardium or appendage tissues of patients with AF. Furthermore, it has been shown that a higher proportion of activated T lymphocytes is detected in patients with paroxysmal or permanent AF. Monocyte infiltration in the left atrium has been reported to be accompanied by thromboembolic events caused by AF (41).

Albumin is a very important antioxidant in circulation. Free radical-related damage plays an important role in the pathology of AF (42). It has been found that hypoalbuminemia is involved in the onset and progression of AF by adversely affecting anti-inflammatory and antioxidant activities (19,33). The current findings support a negative correlation between albumin level and LAD.

Our study identified a positive correlation between LAD and NLR, a negative correlation between LAD and albumin, a positive correlation between LVED and LVESD and NLR, PLR, and SII, and a negative correlation with LMR in patients with AF. Zhang et al. (33) detected a positive correlation between NLR and LAD and a negative correlation between LMR and LA and LVEDD, but did not find a correlation between PLR

and LA and LVEDD. Since the study by Zhang et al. (33) did not provide explanatory information about the medications patients used, the difference in study results is thought to have originated from differences in patient characteristics, such as age and sex.

4.1. Limitations

The present research is a single-center retrospective study. The study used a 12-lead ECG to evaluate patients' permanent AF. However, Holter or continuous monitoring was not performed. Methods such as 'intravascular ultrasound' and 'optical coherence tomography' were not employed to evaluate the prevalence of CAD. Furthermore, the SII is a systemic inflammation score computed from the number of peripheral blood cells. It should be kept in mind that this may vary depending on patients' daily medication use and the time interval between blood collection and the time of measurement. Another limitation of our research is the significant differences between the AF and control groups in some clinical characteristics ('chronic obstructive pulmonary disease,' 'chronic kidney disease,' and 'cerebrovascular diseases') and LVEF values. This shows a higher disease burden in the AF group than in the control group. The potential impacts of these comorbidities and low LVEF values on systemic inflammation could not be completely ruled out statistically. Hence, it should be considered that a part of the inflammatory increase may be due to these comorbidities. There is a need for future prospective studies in which these parameters are more homogeneously distributed or in which specific subgroup analyses can be conducted. However, the findings from our study provide important new information to understand the underlying etiology of AF and CAD. The current study's findings are particularly significant for the retrospective evaluation of the relationship between specific biochemical parameters and angiographic findings in patients with AF and SR.

5. CONCLUSIONS

Consequently, our study demonstrated the critical role of inflammatory and metabolic markers in predicting different clinical risks in AF patients. LAD, CRP, and uric acid strongly correlated with AF, whereas SII and uric acid were determined to be predictive values in detecting the presence of concomitant CAD in this patient group. Moreover, NLR comes to the fore as a determinant of mortality in AF patients. Therefore, incorporating inflammatory parameters, such as SII, into the scores used in practice (CHA_2DS_2, GRACE, etc.) could help assess coronary risk and optimize treatment strategies.

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