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Systemic Immune-Inflammation Index: A Novel Predictor for Risk of Postoperative Atrial Fibrillation in Patients Undergoing Isolated Coronary Artery Bypass Grafting

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ABSTRACT

Objective: To investigate the utility of systemic immune-inflammation index (SII) and inflammatory panel in predicting the risk of postoperative atrial fibrillation (PoAF) among patients undergoing elective isolated coronary artery bypass grafting (CABG).

Methods: A total of 116 patients (mean age: 61.9 ± 9.8 years, 78.4% were males) undergoing isolated CABG were included in this retrospective study. Patients were divided into two groups, including those who developed PoAF (N = 26) and those without PoAF (N = 90). Inflammatory panel was evaluated in both groups.

Results: Patients with PoAF had significantly higher values for P-wave dispersion (PWD; 53.9 ± 5.9 versus 40.2 ± 5.1, $P < .001$), HATCH score (2.4 ± 1.3 versus 1 ± 1.1, $P < .001$), and left atrial dimension (4.0 ± 0.3 versus 3.8 ± 0.2 cm, $P = .003$). In the multivariate analysis with inclusion of PWD, HATCH score and SII, only SII (OR 1.007, 95% CI 1.002 to 1.012, $P = .003$) and PWD (OR 1.86, 95% CI 1.225 to 2.757, $P = .002$) were shown to be independent predictors of increased risk for PoAF.

Conclusion: Preoperative SII seems to be a non-invasive readily available marker that significantly predicts the risk of PoAF in patients undergoing isolated CABG.

INTRODUCTION

Postoperative atrial fibrillation (PoAF) is the most commonly encountered cardiovascular complication following cardiac surgery, including coronary artery bypass grafting (CABG) [Maisel 2001; Saxena 2012; Lomivorotov 2016]. The estimated incidence of PoAF is considered to range from 20% to 40%, depending on the age and severity of comorbidity [Maisel 2001; Saxena 2012; Lomivorotov 2016; Shen 2011; Filardo 2018].

PoAF typically occurs within the first four days after the intervention and has been associated with longer hospital stay and increased morbidity (i.e., hemodynamic instability, thromboembolic events, heart failure, neurological, renal, and infectious complications) [Maisel 2001; Saxena 2012; Lomivorotov 2016; Racca 2020; Lowres 2018; Eikelboom 2021; Villareal 2004]. In this regard, identification of patients at high risk of PoAF is considered critical to take due precautions in the preoperative period [Racca 2020; Selcuk 2021; Achmad 2021; Emren 2016; Hashemi 2012].

Although the exact mechanisms of PoAF following cardiac surgery are complex and remain unknown, systemic inflammation consistently has been reported to be associated with emergence and recurrence of PoAF in patients undergoing cardiac surgery, including CABG [Selcuk 2021; Hu 2015; Jacob 2014; Gibson 2010]. In fact, systemic inflammation is suggested to have a central role in cardiovascular disease and to be closely related to the pathogenesis of AF, while the cardiac surgery itself is considered an acute stressful event, generating a chain of inflammatory reactions [Racca 2020; Aviles 2003; Adegbala 2019].

Accordingly, inflammation and immune-based prognostic scores, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), as well as established pro-inflammatory biomarkers such as C-reactive protein (CRP) levels have been shown to predict mortality and morbidity after cardiac surgery [Iliopoulos 2020; Weedle 2019; Yoon 2021]. Recently, systemic immune-inflammation index (SII), which is an integrated indicator of neutrophil, platelet, and lymphocyte levels, has emerged as a prognostic factor for cardiovascular disease, including coronary artery disease (CAD), myocardial infarction, and chronic heart disease [Yoon 2021; Candemir 2021; Huang 2019; Dey 2021; Seo 2018].

Although high SII scores also have been suggested to be a potential hematologic biomarker of postoperative complications in patients undergoing CABG, the usefulness of SII in predicting the risk of PoAF in patients after cardiac surgery, especially in those undergoing an isolated CABG has not been extensively studied [Selcuk 2021; Dey 2021; Ata 2021].

In addition to inflammation and immune-based prognostic scores, some specific predictors, such P-wave dispersion (PWD) and HATCH score, can also be used for identification of patients at risk of PoAF [Achmad 2021; Emren 2016; Hashemi 2012; Savran 2021]. PWD, defined as the difference between the widest and the narrowest P-wave duration recorded from the 12 electrocardiography (ECG) leads, is a noninvasive ECG marker for atrial remodeling and a sensitive and specific predictor for AF [Selcuk 2021; Achmad 2021; Pérez-Riera 2016]. PWD commonly has been used in

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the assessment of the risk for AF in patients without apparent heart disease, in hypertensives, in patients with CAD, and in patients undergoing CABG [Achmad 2021; Hashemi 2012; Dilaveris 2001; Chandy 2004]. The HATCH scoring system, comprised of easily calculated clinical parameters (ie, hypertension, age, chronic obstructive pulmonary disease (COPD), heart failure (HF), and ischemic cerebrovascular event) is shown to predict the progression of paroxysmal AF (PAF) to persistent AF, while it also is considered to be a valuable parameter for the prediction of PoAF after CABG surgery [Emren 2016; Savran 2021; De Vos 2010; Erdolu 2020; Engin 2021; Chen 2015].

Given the mainstay role of systemic inflammation in the initiation of PoAF in patients following cardiac surgery [Racca 2020; Selcuk 2021; Achmad 2021; Emren 2016], the use of preoperative inflammatory or specific biomarkers is considered to help clinicians in identifying patients at higher risk to develop PoAF and thus suitable for prophylactic anti-arrhythmic interventions [Racca 2020; Selcuk 2021; Achmad 2021; Emren 2016].

However, there is limited data on the relation of PWD and HATCH score with post-CABG AF [Hashemi 2012; Savran 2021], while no study to date has investigated the SII in relation to PWD and HATCH score as predictors of PoAF after CABG.

Therefore, this study aimed to investigate the utility and diagnostic performance of SII in relation to AF-specific markers (PWD and HATCH score) in predicting the risk of PoAF among patients undergoing elective isolated CABG.

METHODS

Study population

A total of 116 patients (mean ± SD age: 61.9 ± 9.8 years, 78.4% were males) who underwent isolated CABG at a tertiary care hospital between April 2021 and July 2021 were included in this retrospective study. Patients were divided into two groups based on development of PoAF, including those with PoAF (N = 29) and those without PoAF (N = 90). Patients with emergency operations, significant valvular disease, autoimmune and inflammatory disease, end-stage renal failure or malignancy, or any condition that could affect the inflammatory status and those with previous history of AF and preoperative amiodarone therapy as well as those underwent off pump revascularization were excluded from the study. All surgeries (on-pump revascularization) were performed by the same and experienced cardiac surgeon team.

Written informed consent was obtained from each subject, following a detailed explanation of the objectives and protocol of the study, which was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the Bursa City Hospital Ethics Committee (2021-15/7).

Study parameters

Data on patient demographics (age, gender), smoking status, body mass index (BMI, kg/m^2), co-morbid diseases, and previous history of percutaneous coronary intervention and development of PoAF were recorded in each patient. Data on complete blood count (CBC) and blood biochemistry findings, inflammation, and immune-based prognostic markers (erythrocyte sedimentation rate (ESR), CRP, DDimer), cardiovascular risk markers (B-type natriuretic peptide (BNP), troponin), AF-specific markers (PWD, HATCH score, left ventricular ejection fraction (LVEF) and left atrial dimension (LAD), the SII and a composite SII-PWD score were recorded in patients with versus without PoAF. Correlation between SII, PWD and HATCH score was analyzed, and the multivariate logistic regression analysis was performed to investigate independent predictors of increased risk of PoAF. The receiver operating characteristics (ROC) curve was plotted to determine the role of SII and the composite SII-PWD score in identification of PoAF risk with calculation of area under curve (AUC) and cut-off value via ROC analysis.

Table 1. Demographic and clinical characteristics (N = 116)

Age (year), mean ± SD (min-max)	61.9 ± 9.8 (37-86)
Gender, n (%)	
Male	91 (78.4)
Female	25 (21.6)
BMI (kg/m^2), mean ± SD	27.8 ± 4.1
Active smoking, n (%)	41 (25.3)
Co-morbid diseases, n (%)	
Hypertension	65 (56.0)
Diabetes	43 (37.1)
Chronic obstructive pulmonary disease	16 (13.8)
Chronic kidney failure	3 (2.6)
Cerebrovascular event	6 (5.2)
Previous PCI, n (%)	6 (5.2)
PoAF, n (%)	
Yes	26 (22.4)
No	90 (77.6)

BMI, body mass index; PCI, percutaneous coronary intervention; PoAF, postoperative atrial fibrillation

AF-specific markers: HATCH score, a non-invasive marker for risk prediction of subsequent AF after ablation of typical AFL, was calculated based on hypertension (1 point), age ≥75 years (1 point), transient ischemic attack or stroke (2 points), chronic obstructive pulmonary disease (1 point), and heart failure (EF ≤ 40%, 2 points) [Emren 2016; Chen 2015].

PWD, a noninvasive ECG marker for atrial remodeling and predictor for AF, was obtained from the preoperative ECG results and defined as the difference between the widest and the narrowest P-wave duration in milliseconds (ms) recorded from the 12 ECG leads [Achmad 2021; Pérez-Riera 2016].

On blood samples obtained 24 hours prior to surgery, SII was calculated using the following formula: SII = platelet

Table 2. Laboratory findings with respect to postoperative atrial fibrillation

Laboratory parameters, median (min-max)		Postoperative atrial fibrillation		
		No (N = 90)	Yes (N = 26)	*P*-value
Hemoglobin (g/dL)	Preoperative	13.4 (0-17.2)	12.5 (8.8-17)	.032
	Postoperative 72 h	9.2 (6.8-12.8)	8.9 (7.6-11.4)	.386
WBC (10^3/μL)	Preoperative	9.5 (4.3-23.7)	9.3 (5.1-20.5)	.817
	Postoperative 72 h	12.4 (3.3-23.9)	11.7 (8.1-16.4)	.356
Platelet (10^3/μL)	Preoperative	246.5 (126-467)	240 (163-564)	.657
	Postoperative 72 h	184 (49-360)	197.5 (111-428)	.470
Neutrophil (10^3/μL)	Preoperative	5.7 (2.1-20.0)	6.4 (3.5-18.1)	.049
	Postoperative 72 h	10.7 (2.2-20.2)	10.7 (6.6-139.0)	.703
Lymphocyte (10^3/μL)	Preoperative	2.5 (1-5.3)	1.3 (0.4-2.8)	<.001
	Postoperative 72 h	0.8 (0.2-3.9)	0.6 (0.1-2.5)	.057
Monocyte (10^3/μL)	Preoperative	0.7 (0.3-2.2)	0.7 (0.4-1.5)	.728
	Postoperative 72 h	0.9 (0-3)	1.0 (0.5-1.6)	.894
Eosinophil (10^3/μL)	Preoperative	0.2 (0-0.7)	0.2 (0-0.5)	.549
	Postoperative 72 h	0 (0-0.5)	0 (0-0.3)	.237
Urea (mg/dL)	Preoperative	36.9 (17.8-304)	41.2 (14.7-128.2)	.073
	Postoperative 72 h	40.9 (16.9-131.6)	49.9 (26.3-131.4)	.004
Creatinine (mg/dL)	Preoperative	0.9 (0.5-42.4)	0.9 (0.7-5.1)	.861
	Postoperative 72 h	1.1 (0.6-5.1)	1.2 (0.7-5.9)	.265
GFR (mL/min/1.73m^2)	Preoperative	85 (1-128)	81 (10-109)	.175
	Postoperative 72 h	67.5 (9-127)	59 (8-97)	.093
AST (IU/L)	Preoperative	21 (9-245)	20.5 (13-43)	.920
	Postoperative 72 h	47 (10-891)	40 (21-284)	.188
ALT (U/L)	Preoperative	21 (8-347)	18 (5-67)	.203
	Postoperative 72 h	28 (9-355)	22.5 (10-147)	.121
Cholesterol (mg/dL)	Preoperative	200 (90-343)	185 (135-325)	.079
Triglyceride (mg/dL)	Preoperative	226 (75-758)	185 (82-555)	.577
HDL (mg/dL)	Preoperative	32 (18-69)	37 (22-58)	.193
LDL (mg/dL)	Preoperative	116 (48-237)	100 (34-237)	.032
TSH (μIU/L)	Preoperative	1.2 (0-7.3)	2 (0.1-4.8)	.639
T3 (pg/mL)	Preoperative	2.9 (1.5-4.4)	2.7 (1.3-3.1)	.143
T4 (ng/dL)	Preoperative	1.2 (0.1-2.1)	1.1 (0.9-1.5)	.609
Uric acid (mg/dL)	Preoperative	5.6 (2.7-9.7)	5.6 (4.3-9.3)	.855
ESR (mm/h)	Preoperative	22 (2-91)	20.5 (2-51)	.987
DDimer (ug/mL FEU)	Preoperative	0.4 (0-31.2)	0.4 (0-1.2)	.747
CRP (mg/L)	Preoperative	6.8 (0.6-121.1)	6.6 (1.2-67.1)	.866
	Postoperative 72 h	61.6 (1.4-327.4)	49.8 (9.4-219.9)	.369
Troponin (ng/L)	Preoperative	46.2 (3.9-3671)	173.5 (6.5-1470)	.408
	Postoperative 72 h	455.5 (35.8-9875)	668 (13.2-5297)	.318
BNP (ng/L)	Preoperative	316 (24-4811)	279 (162-3044)	.591
	Postoperative 72 h	995 (12-5000)	919 (99-31478)	.808

WBC, white blood cell; GFR, glomerular filtration rate; AST, aspartate transaminase; ALT, alanine transaminase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TSH, thyroid stimulating hormone; T3, triiodothyronine; T4, thyroxine; ESR, erythrocyte sedimentation rate; BNP, B-type natriuretic peptide; CRP, C-reactive protein

Table 3. Potential AF-specific markers with respect to postoperative atrial fibrillation

	Postoperative atrial fibrillation		
	No (N = 90)	Yes (N = 26)	*P*-value
AF-specific markers			
PWD (ms), mean ± SD	40.2 ± 5.1	53.9 ± 5.9	<.001
HATCH score, mean ± SD	1 ± 1.1	2.4 ± 1.3	<.001
LVEF (%), mean ± SD	50.0 ± 9.1	49.6 ± 10.4	.930
LAD (cm), mean ± SD	3.8 ± 0.2	4.0 ± 0.3	.003
SII, median (min-max)			
Preoperative	562.1 (165.2-2305.4)	1144 (783-10236.1)	<.001
Postoperative 72 h	2599.2 (282.2-7958.3)	3535.1 (1082.3-23562.2)	.020
Survivorship status, n (%)			
Survivor (N = 106)	84 (93.3)	22 (88.0)	.406
Non-survivor (N = 9)	6 (6.7)	3 (12.0)	

AF, atrial fibrillation; PWD, P-wave dispersion; LVEF, left ventricular ejection fraction; LAD, left atrial dimension; SII, Systemic immune-inflammation index

count × neutrophil count/lymphocyte count [Selcuk 2021; Yoon 2021]. A composite SII-PWD score also was calculated using the y values estimated from the regression model formed via coefficients revealed in the logistic regression analysis (y=-38.885 ± 0.007 x SII ± 0.621 x P-wave).

Transthoracic echocardiography was performed to determine the LVEF according to Simpson's method and the left anteroposterior atrial diameter (LAD) in parasternal long axis view.

The incidence of PoAF was detected by ECG and rhythm monitoring during the hospitalization period until discharge, with consideration of new-onset PoAF in case of the fibrillation rhythm lasting more than 10 minutes or the need for urgent intervention due to unstable hemodynamic status [Filardo 2018; Emren 2016; Filardo 2009].

Statistical analysis

Statistical analysis was made using MedCalc® Statistical Software version 19.7.2 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021). Shapiro Wilks test was used to investigate normal distribution. Descriptive statistics were reported for categorical data. Chi-square test (Yates continuity correction or Fisher Exact test, where available) was used for analysis of categorical variables. Mann-Whitney U test was used to compare two independent non-normally distributed variables. Spearman correlation test was performed to test relationships in ordinal or quantitative variable with non-normal distribution. ROC curve was plotted to determine performance of SII and SII-PWD composite score in identification of postoperative AF risk with calculation of AUC values and ideal cut-off value via ROC analysis. Variables having *P* value <.05 in univariate analysis were analyzed further in a multivariate regression model to identify statistically significant risk factors for AF development. Data were expressed as "mean ± standard deviation (SD), median (min-max), 95% confidence interval (CI) and percent (%), where appropriate. $P < .05$ was considered statistically significant.

RESULTS

Demographic and clinical characteristics

The mean ± SD patient age was 61.9 ± 9.8 years and 78.4% of patients were males. Hypertension (56.0%) was the most common comorbid disease. PoAF occurred in 26 (22.4%) of 116 CABG patients (Table 1).

Laboratory findings with respect to development of PoAF: Preoperative levels for hemoglobin (12.5 (8.8-17) versus 13.4(0-17.2), $P = .032$), lymphocyte (1.3(0.4-2.8) versus 2.5 (1-5.3), $P < .001$), and LDL (100(34-237) versus 116 (48-237), $P = .032$) were significantly lower, whereas postoperative 72 h urea levels (49.9 (26.3-131.4) versus 40.9 (16.9-131.6), $P = .004$) were significantly higher in patients with versus without PoAF. No significant difference was noted in inflammatory (ESR, CRP, DDimer) or cardiovascular risk (BNP, troponin) markers between patients with versus without PoAF (Table 2).

Potential AF-specific markers with respect to development of PoAF: Patients with versus without PoAF had significantly higher mean±SD values for PWD (53.9 ± 5.9 versus 40.2 ± 5.1, $P < .001$), HATCH score (2.4 ± 1.3 versus 1 ± 1.1, $P < .001$), and LAD (4.0 ± 0.3 versus 3.8 ± 0.2 cm, $P = .003$) (Table 3).

Median(min-max) SII values in the preoperative (1144 (783-10236.1) versus 562.1 (165.2-2305.4), $P < .001$) and postoperative (3535.1 (1082.3-23562.2) versus 2599.2 (282.2-7958.3), $P = .020$) period also were significantly higher in patients with versus without PoAF (Table 3).

Mortality rate was similar in patients with and without PoAF (12.0 versus 6.7%, $P = 0.406$) (Table 3).

Table 4. Correlation of systemic immune-inflammation index (SII) with P-wave dispersion (PWD) and HATCH score

	Systemic immune-inflammation index (SII)	
	Preoperative	Postoperative 72 h
P-wave dispersion (PWD)		
r	0.512	0.268
p	<.001	0.005
HATCH score		
r	0.393	0.138
p	<0.001	0.154

Spearman correlation analysis r: correlation coefficient

Correlation of SII with PWD and HATCH score

SII was positively correlated with both PWD (r=0.512, $P < .001$) and HATCH score (r=0.393, $P < .001$) in the preoperative period, whereas positively correlated only with PWD (r=0.268, $P = .005$) in the postoperative 72-h (Table 4).

Logistic regression analysis for independent predictors of postoperative AF

Amongst the variables significantly associated with postoperative AF in the univariate analysis (PWD, HATCH score and SII), only SII (OR 1.007, 95% CI 1.002 to 1.012, $P = .003$) and PWD (OR 1.86, 95% CI 1.225 to 2.757, $P = .002$) were shown to be independent predictors of increased risk for postoperative AF (Table 5).

ROC analysis for diagnostic performance of SII and composite SII-PWD score in predicting the PoAF

ROC analysis revealed a preoperative SII cut-off value >866.04 (AUC [95% CI]: 0.946 [0.887 to 0.979], $P < .001$) to be a potential marker of postoperative AF with a sensitivity of 92.31% and specificity of 1.1% (Figure 1).

ROC analysis revealed a composite SII-PWD score cut-off value >-3.311 (AUC (95% CI): 0.994 (0.957 to 1.000), $P < .001$) to be a potential marker of postoperative AF with a sensitivity of 100.0% and specificity of 99.29% (Figure 2).

DISCUSSION

Our findings revealed the development of PoAF in 22.4% of patients undergoing isolated CABG. Although higher values for LAD, PWD, HATCH score, and SII were associated with an increased risk of PoAF in the univariate analysis, multivariate analysis confirmed only PWD (OR 1.86) and SII (OR 1.007) as significant determinants of PoAF risk. ROC analysis also revealed the diagnostic performance of preoperative SII (cut-off value >866.04, AUC: 0.946, sensitivity: 92.31%) and composite SII-PWD score (cut-off value >-3.311, AUC: 0.994, sensitivity: 100%) in discriminating patients at risk of PoAF.

Table 5. Multivariate logistic regression analysis for independent predictors of postoperative AF

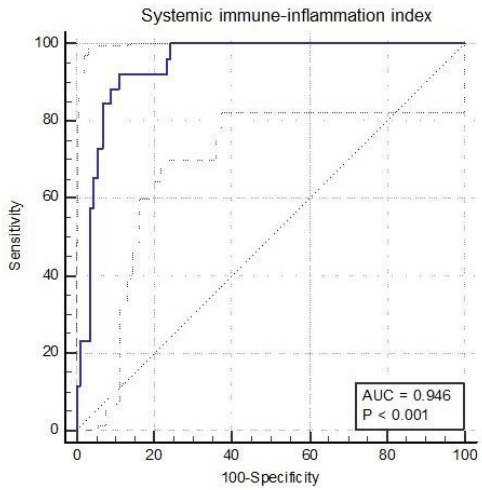
	B	OR (95% CI)	P
Systemic immune-inflammation index (SII)	0.007	1.007 (1.002-1.012)	.003
HATCH score	0.715	2.044 (0.683-6.115)	.201
P-wave dispersion (PWD)	0.621	1.86 (1.255-2.757)	.002
Constant	-38.885	-	.001

CI, confidence interval; OR, odds ratio

The prevalence of PoAF in the current study (22.4%) is in line with the reported range of PoAF (up to 30%) in previous studies with patients (mean age ~60 years) undergoing CABG [Selcuk 2021; Achmad 2021; Hashemi 2012; Ata 2021; Omae 2012]. Nonetheless, higher rates of PoAF have been reported in elderly (>70 years) patient populations, in accordance with the estimated 25% increase in the risk of new onset PoAF with each additional 5-year [Chandy 2004; Osranek 2006; Aranki 1996; El-Chami 2010].

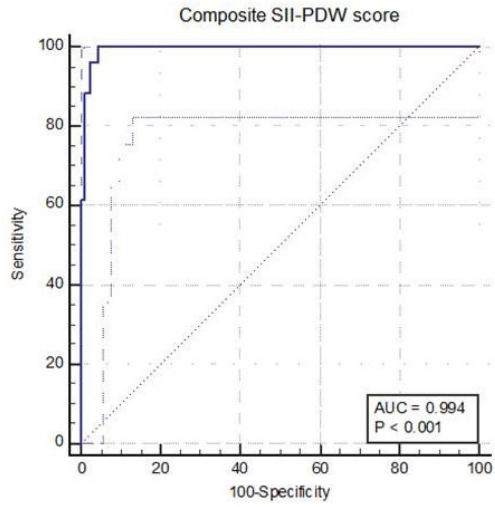
Similar to our findings, in a past study with 391 patients undergoing isolated CABG, SII was reported to be independent predictor of PoAF (OR 1.002) in multivariate logistic regression analysis, and SII cut-off value >807.8 (AUC: 0.7107) was shown to detect PoAF with 60.8% sensitivity and 80.9% specificity [Selcuk 2021]. In another study with 283 patients who underwent isolated CABG, SII (OR 1.548) as well as advanced age (OR 2.816), hypertension (OR 0.896) and preoperative right coronary Gensini score (OR 2.112) were reported to be independent predictors of PoAF [Ata 2021]. In a retrospective risk-prediction study in 1,007 patients undergoing off-pump CABG, SII (OR 1.01) was reported to be amongst the independent predictors of poor postoperative outcome and a SII cut-off value of 878.06 (AUC 0.984, 97.6% sensitivity, 91%, specificity) was determined to predict the incidence of complications, such as AF, intra-aortic balloon pump requirement, vasoactive-ionotropic score >20 and infections [Dey 2021]. The predictive value SII (a cut-off value of 1228.0, 60% sensitivity and 78.1% specificity) also was reported in detecting new-onset atrial fibrillation (NOAF) following ST segment elevation myocardial infarction (STEMI) [Bağcı 2021].

The PWD also has been reported to predict the risk of PoAF in patients undergoing CABG [Achmad 2021; Hashemi 2012; Pérez-Riera 2016; Ceylan 2010], as well as to predict PAF in acute ischemic stroke patients [Dogan 2012]. In a study among 42 patients, who underwent CABG, the authors reported significantly longer PWD in patients with PoAF and indicated PWD to be a significant predictor of PoAF (HR 1.05) [Achmad 2021]. In a study with 81 patients undergoing CABG, increased PWD (OR 1.17), absence of beta-blocker treatment (OR 8.88), and diabetes-hypertension combination (OR 1.45) were reported to be independent predictors of PoAF [Ceylan 2010]. In a study with 52 patients undergoing isolated CABG, the authors noted that minimum P-wave duration, PWD, and low ejection fraction were good



Area under the ROC curve (AUC)	0.946
Standard Error	0.0204
95% Confidence interval	0.887 to 0.979
z statistic	21.820
Significance level P (Area=0.5)	<0.0001
Youden index J	0.8120
Associated criterion	>866.04
Sensitivity	92.31
Specificity	1.11

Figure 1. ROC curve analysis for diagnostic performance of systemic immune-inflammation index in predicting the postoperative atrial fibrillation after CABG.



Area under the ROC curve (AUC)	0.994
Standard Error	0.0049
95% Confidence interval	0.957 to 1.000
z statistic	100.167
Significance level P (Area=0.5)	<0.0001
Youden index J	0.9556
Associated criterion	>-3.311
Sensitivity	100.00
Specificity	99.29

Figure 2. ROC analysis for diagnostic performance of composite SII-PWD score in predicting the postoperative atrial fibrillation after CABG. A composite SII-PWD score was calculated using the y values estimated from the regression model formed via coefficients revealed in the logistic regression analysis (y=-38.885 ± 0.007 x SII ± 0.621 x P-wave).

predictors of PoAF and can be used for patient risk stratification of PoAF after CABG [Hashemi 2012]. In a study among 400 acute ischemic stroke patients, PAF was detected in 40 patients on 24-hour Holter monitoring, while PWD (cut-off value 57.5 ms, AUC: 0.80, sensitivity: 80% specificity: 73%) on a single 12-lead ECG obtained within 24 hours of an acute ischemic stroke was reported to predict PAF and reduce the risk of recurrent strokes [Dogan 2012].

SII is considered to be an innovative inflammatory biomarker that combines neutrophil, lymphocyte, and platelet counts to reflect the overall inflammatory status of the body [Selcuk 2021], while presence of neutrophilia, thrombocytosis and lymphopenia in patients with high preoperative SII scores is considered to indicate the likelihood of an interplay between inflammation and impaired adaptive immune response [Yoon 2021; Aziz 2019]. Accordingly, SII was shown to predict PoAF better than either NLR or PLR in patients who underwent an isolated CABG [Selcuk 2021], and to have higher predictive power than CRP in detecting NOAF following STEMI [Bağcı 2021]. Also, SII was reported to predict severe coronary obstruction better than NLR or PLR, and the major cardiovascular events better than traditional risk factors in patients with the coronary syndrome [Erdoğan 2020; Yang 2020].

The association of higher PWD, as a marker of atrial depolarization heterogeneity, with increased risk of PoAF is suggested to be related to atrial stretching due to volume overload and atrial ischemia-induced during CABG yielding an increased dispersion of atrial refractoriness [Achmad 2021; Hashemi 2012; Chandy 2004]. Nonetheless, while the greater PWD indicates dispersion of atrial refractoriness and favors a re-entry mechanism and is therefore considered essential for the development of sustained arrhythmia in patients with PAF, the effect of increased PWD in the incidence of post-CABG AF has been reported to be moderate [Hashemi 2012; Chandy 2004].

In the current study, both PWD and SII were determined as significant predictors of PoAF risk after CABG, whereas using a composite SII-PWD score (cut-off > -3.311, AUC: 0.994) rather than SI alone (cut-off >866.04, AUC: 0.946) revealed a stronger predictive performance in identification of CABG patients at high risk of PoAF. Accordingly, our findings indicate favorable utility of SII-based risk stratification, alone or complementary to PWD, by clinicians to identify high-risk patients before CABG surgery. This supports the consideration of SII, as a non-invasive readily available marker incorporating both pro-inflammatory and pro-thrombotic corpuscular lines, to have a significant potential of assisting the clinicians in identifying patients vulnerable to poor outcomes after CABG and in making better medical decisions by more appropriate selection of candidates for selective prophylaxis [Selcuk 2021; Hashemi 2012; Dey 2021].

Indeed, postoperative 72-h SII values also were higher in our patients with versus without PoAF and were positively correlated with PWD values. Hence given that most episodes of postoperative AF occur by postoperative days 2 or 3, our finding support that screening for SII in the early postoperative period may also confer a useful strategy in predicting PoAF, enabling the likelihood of biatrial pacing during CABG operation to be activated as anti-arrhythmia pacing or use of magnesium as protective strategies reducing the occurrence of AF [Hashemi 2012; Fan 2000].

Some studies also reported higher HATCH scores in patients with versus without PoAF and indicated HATCH score (72% sensitivity and 75% specificity for a cut-off value >2 and 42% sensitivity 70% specificity for a cut-off value >1) to predict the development of PoAF (OR 1.334 to2.590) [Emren 2016; Savran 2021; Selvi 2018]. In the current study, HATCH scores were significantly higher in patient with versus without PoAF, supporting that patients with elevated preoperative HATCH score may have higher risk for AF after CABG surgery [Emren 2016; Savran 2021; Selvi 2018], whereas HATCH score was not found amongst the significant determinants of PoAF risk in the multivariate analysis.

An increase in LAD is considered a risk factor for AF [Osranek 2006; Vaziri 1994; Pritchett 2003]. Although LAD significantly was higher in our patients with PoAF compared with those who did not develop AF after CABG, multivariate analysis did not confirm the significant role of LAD in predicting PoAF in CABG patients.

In addition, our findings revealed no significant association of preoperative or postoperative CRP levels, troponin, or BNP with the development of PoAF in CABG patients. Indeed, CRP, natriuretic peptides and cardiac troponin have been shown to be the most promising biomarkers in the setting of AF [Noubiap 2021]. However, while CRP levels are increased in patients with AF [Zhou 2020], CRP and AF have been reported to be not correlated when measured before cardioversion, and thus CRP is considered not to be pathogenic in AF and not helpful when used to predict postoperative AF [Zhou 2020; Zarauza 2006]. Hence, given that AF is a complex disease with a multifactorial etiology, the likelihood of different relationships between AF and inflammation has been suggested depending on the type of inflammation and the inciting cause or longevity of the AF [Zhou 2020].

The retrospective single center design seems to be the major limitation of the present study preventing the establishing the temporality between cause and effect as well as generalizing our findings. Lack of data on follow up after discharge is another limitation that otherwise would extend the knowledge achieved in the current study. Also, despite its well-known interaction with certain laboratory markers, there is no consistent treatment to prevent or reduce PoAF, which seems to limit the clinical relevance of our findings, in terms of resulting in changes in preoperative or postoperative care by surgeons who are considering CABG. Nevertheless, as the first study addressing SII in relation to PWD and HATCH score in terms of PoAF risk isolated CABG patients, our findings represent a valuable contribution to the literature.

In conclusion, our findings indicate the potential of preoperative SII, as a non-invasive readily available marker, in predicting the PoAF risk in patients undergoing an isolated CABG. This emphasizes the favorable utility of a SII-based risk stratification, alone or complementary to PWD, in identifying patients at high risk of PoAF before CABG surgery and thus enabling better medical decisions regarding the prophylactic antiarrhythmic interventions in clinical practice.

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