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The role of systemic inflammatory response index to predict postoperative atrial fibrillation in patients undergoing coronary artery bypass grafting

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ABSTRACT

Objectives: The aim of the present study was to investigate the association between systemic inflammatory response index (SIRI) and the occurrence of postoperative atrial fibrillation (POAF) in patients undergoing coronary artery bypass grafting (CABG).

Patients and methods: Between September 2022 and July 2024, a total of 276 consecutive patients (189 males, 87 females; mean age: 62.6±7.3; range, 49 to 79 years) who underwent elective isolated CABG were included in this study. Clinical data and electrocardiograms of the patients were obtained. Based on the rhythm status during hospitalization after surgery, the patients were divided into two groups with POAF rhythm (n=78) and normal sinus rhythm (n=198). The SIRI index value was obtained based on the product of the number of neutrophils per monocyte divided by the lymphocyte count immediately before surgery.

Results: The mean value of preoperative SIRI in the group with POAF was 6.8±1.1, while it was 3.2±0.8 in the non-POAF group, indicating a significant difference (p=0.008). According to the receiver operating characteristic (curve analysis, a SIRI higher than 5.5 could predict POAF with a sensitivity of 79.2% and a specificity of 66.8%. Along with increased SIRI, advanced age, history of hypertension and smoking, as well as reduced left ventricular ejection fraction were other predictors of POAF.

Conclusion: Assessing preoperative SIRI index can predict the occurrence of POAF in CABG patients with acceptable sensitivity and specificity values.

Keywords: Coronary artery bypass grafting, postoperative atrial fibrillation, systemic inflammatory response index.

New-onset postoperative atrial fibrillation (POAF) is a frequent sequel after coronary artery bypass grafting (CABG), with an overall prevalence ranged between 11 and 50%.[1] The occurrence of this arrhythmic event is expected mostly during two to four days after operation.[2] Patients with POAF are at an increased risk for complications after surgery including brain stroke, prolonged hospitalization, myocardial infarction as well as early or long-term death mainly due to the likelihood of thromboembolic events.[3-5] The overall incidence of POAF has continued to rise, despite decades of attempts at therapeutic interventions.[6] The main mechanisms of POAF remains unclear; however, some risk profiles including hypertension, history of heart failure, obesity, and advanced age have been identified to be associated with this arrhythmia.[7,8] Moreover, some cardiac-related changes such as atrial fibrosis and atrial dilatation have been shown to be related to the risk for POAF.[9] Additionally, due to the close association of cardiac arrhythmia with the activation of inflammatory cascades, evidence regarding the relationship between the occurrence of this event and the activity of inflammatory markers has become extremely strong.[10]

The systemic inflammatory response index (SIRI) as the product of neutrophil count and monocyte count divided by lymphocyte count is currently identified as an applicable inflammatory index to describe the pathophysiological causes of many disorders with a strong inflammatory bed such

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as diabetes mellitus, rheumatological disturbances, metabolic disorders, cerebrovascular events, renal insufficiency and even cardiovascular disorders.[11-13] Recently, the association of increased SIRI and the risk for cardiac arrhythmias has strengthened.[14] From a pathophysiological perspective, as structural and electrophysiological properties in cardiac myocytes provide a meaningful response in the form of inflammatory responses to any pathological changes, a strong association of cardiac functional abnormalities including cardiac arrhythmia and systemic inflammatory responses is predictable. In this regard, the emergence of some anatomical and functional abnormal changes in heart tissue such as fibrosis, endothelial dysfunction, cellular apoptosis and even cardiac necrosis which are strongly associated with cardiac arrhythmias have a close link to inflammatory responses.[15] However, whether the occurrence of systemic inflammatory responses, particularly the SIRI index, can be an indicator of the risk of atrial fibrillation (AF), is still unclear. Evidences in this regard have recently been presented. It has been found an association of raising the serum levels of inflammatory markers such as C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) with the risk for AF.[16-18] Also, the association of SIRI with the risk for adverse outcomes following CABG has been also shown.[20] However, the association between SIRI and the occurrence of POAF remains uncertain. In the present study, we aimed to investigate the association between SIRI and the occurrence of POAF in patients undergoing CABG.

PATIENTS AND METHODS

This single-center, cross-sectional study was conducted at Okan University Hospital, Department of Cardiovascular Surgery between September 2022 and July 2024. A total of 276 consecutive patients (189 males, 87 females, mean age: 62.6±7.3, range, 49 to 79 years) who underwent elective isolated CABG and whose clinical data and electrocardiogram data of the patients were reached included. Patients under 18 years of age, patients undergoing concomitant cardiac procedures, those with chronic underlying disorders such as liver or kidney disorders, patients with underlying inflammatory diseases, a history of thyroid disorders, a history of cancer, or patients with a history of corticosteroid treatment within the past six months were excluded from the study. A written informed consent was obtained from each patient. The study protocol was approved by the Okan University Hospital Ethics Committee (date: 2022 February, no: TR.OK.REC.2025.121). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Based on the rhythm status during hospitalization after surgery, the patients were classified into two groups with POAF rhythm (n=78) and normal sinus rhythm (n=198). In this study, AF was defined as the presence of irregular RR intervals with the absence of discrete P waves complicated by fibrillatory waves. Also, new-onset AF (NOAF) was identified as the occurrence of an AF episode lasting at least 30 sec during the hospital stay.

Background data including demographic characteristics, clinical history, medication history, and laboratory findings were all extracted through a review of the patients' archived records. In this regard, the SIRI index value was obtained based on the product of the number of neutrophils per monocyte divided by the lymphocyte count. Finally, first, the mean of the index was compared between the two groups with and without POAF. Then, using a multivariate logistic regression model in the presence of confounding background factors, the difference in POAF between the two groups was re-evaluated. Then, based on the analysis of the area under the curve (AUC) of the receiver operating characteristics (ROC) curve, the value of POAF in distinguishing between the two rhythm states of POAF and sinus rhythm was determined, the most optimal cut-off value for POAF, and the sensitivity and specificity of this index in distinguishing POAF from sinus rhythm were evaluated.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency, where applicable. The t-test was used to compare quantitative variables and the chi-square test was used to compare qualitative variables. The difference in SIRI between the groups with and without POAF was assessed by the multivariate linear regression model with the presence of baseline variables. The area under the

ROC curve analysis was used to determine the diagnostic value of the SIRI scoring system in predicting POAF. A *p* value of <0.05 was considered statistically significant.

RESULTS

Of a total of 276 patients, 78 (28.2%) had POAF. Comparing baseline characteristics between the subgroups with and without POAF showed significantly higher mean age, as well as higher prevalence rates of hypertension and smoking in the group with POAF compared to the group with normal sinus rhythm (Table 1). With respect to cardiovascular parameters, those with POAF had significantly lower left ventricular ejection fraction (LVEF) on admission; however, no significant difference was revealed between the two groups in the number of coronary arteries involvement (p>0.05).

The mean value of preoperative SIRI in the group with POAF was 6.8±1.1, while it was 3.2±0.8 in the non-POAF group, indicating a significant difference (p=0.008). The multivariate linear regression model with the presence of baseline parameters showed a significant difference in SIRI between the groups with and without POAF (β=0.382, p=0.002) (Table 2). According to the ROC curve analysis, assessing the value of preoperative SIRI could effectively predict the occurrence of POAF (AUC=0.788, 95% confidence interval (CI): 0.603-0.973). The most optimal cut-off value of SIRI to predict POAF was 5.5, yielding a sensitivity of 79.2% and a specificity of 66.8% (Figure 1).

DISCUSSION

The cause of AF following major cardiac surgery is still unclear. However, based on available evidence, the role of activation of local and systemic inflammatory factors following surgical manipulation, as well as underlying dysfunction of the cardiac conduction system, is quite prominent.[7-10] Overall, the available evidence supports the central

Table 1
Comparing baseline characteristics between groups with and without POAF

	Group with POAF (n=78)			Group without POAF (n=198)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Sex							
Male	55	70.5		134	67.6		0.758
Mean age (year)			65.6±8.8			59.7±5.6	0.001
Mean BMI (kg/m^2)			27.4±1.5			26.6±1.2	0.223
History of hypertension (%)	44	56.4		56	28.3		0.001
History of diabetes (%)	22	28.2		44	22.2		0.656
History of hyperlipidemia (%)	17	21.8		41	20.7		0.779
Current smoking (%)	14	17.9		32	16.1		0.856
Preoperative LVEF (%)			48.6±6.2			53.4±7.8	0.024
Number of coronary arteries involved							0.835
One-vessel	6	7.7		15	7.6		
Two-vessel	22	28.2		61	30.8		
Three-vessel	50	64.1		122	61.6		
Using CPB (%)	49	62.8		122	61.6		0.779
CPB time (min)			96.6±35.3			95.0±33.6	0.079
Cross-clamp time (min)			78.2±28.4			77.2±32.2	0.275
The mean SIRI value			6.8±1.1			3.2±0.8	0.008

POAF: Postoperative atrial fibrillation; SD: Standard deviation; BMI: Body mass index; LVEF: Left ventricular ejection fraction; SIRI: Systemic inflammatory response index; CPB: Cardiopulmonary bypass.

Table 2

Multivariate linear regression analysis to determine the difference in SIRI between the groups with and without POAF

Items	Unstandardized coefficients		T score	Sig.
	Beta	SE		
Sex	0.395	0.402	0.982	0.335
Occurrence of POAF	0.382	0.113	3.387	0.002
Body mass index	0.014	0.087	0.166	0.869
Age	0.009	0.002	4.827	0.001
Hypertension	0.003	0.119	0.022	0.983
Diabetes mellitus	0.099	0.111	0.886	0.383
Hyperlipidemia	0.133	0.113	1.172	0.251
Smoking	-0.614	0.001	-0.735	0.468
Three-vessel disease	0.003	0.002	1.445	0.159
CPB	0.0001	0.001	-1.737	0.093
CPB time	-0.007	0.016	-0.427	0.672
Cross-clamp time	-0.107	0.183	-0.587	0.562
LVEF	0.053	0.130	0.409	0.686

SIRI: Systemic inflammatory response index; POAF: Postoperative atrial fibrillation; SE: Standard error; CPB: Cardiopulmonary bypass; LVEF: Left ventricular ejection fraction.

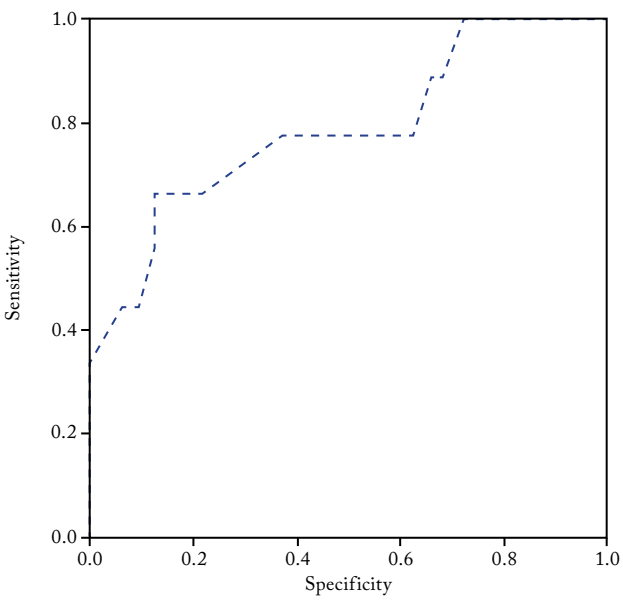

Figure 1. The area under the ROC curve indicates high value of SIRI to discriminate POAF from non-POAF groups (AUC=0.889).

ROC: Receiver operating characteristic; SIRI: Systemic inflammatory response index; POAF: Postoperative atrial fibrillation; AUC: Area under the curve.

role of immune remodeling in the development of AF after surgery. Immune remodeling mainly refers to the impairment of atrial composition due to the activation of immune cells following cardiac manipulations.[19] Indeed, immune remodeling flare alterations in structural and conductive systems of the atrium which may ultimately lead to atrial-related arrhythmias such as AF. In other words, any abnormal changes in heart architecture such as due to metabolic disturbances, heart failure, ischemic cardiac events and even following cardiac interventions can activate inflammatory factors such as neutrophils, proinflammatory biomarkers, platelets, lymphocytes, and macrophages which predispose the heart to abnormal cardiac remodeling and, thus, to arrhythmias including AF.[20] In this regard, the activation of neutrophils and macrophages can result in production and secretion of some cytokines such as interleukin (IL)-1B, IL-6, IL-17A, and tumor necrosis factor-alpha (TNF-α) that may lead to appear atrial fibrosis, the main basis for the development of atrial arrhythmias. Based on the confirmed role of inflammatory factors in

the development of AF and also considering the prominent role of SIRI in the occurrence of cardiac arrhythmic disorders, currently the hypothesis of a relationship between the occurrence of AF and SIRI has gained great strength, particularly in the context of cardiac interventions.[21,22] To illustrate, as indicated by Wang et al.,[23] SIRI could effectively predict new-onset in patients with ST-segment elevation myocardial infarction following percutaneous coronary intervention. In another study, Hinoue et al.[24] showed that preoperative SIRI was a useful prognostic biomarker for predicting POAF in patients undergoing cardiac surgery using cardiopulmonary bypass (CPB). Also, Luo et al.[25] revealed that the increased SIRI could predict an increased risk of the POAF and independently predicted the late recurrence of AF after CryoMaze concomitant with mitral valve surgery. As shown in the present study, preoperative assessment of SIRI can be effective in predicting the occurrence of postoperative AF. In this context, values higher than 5.5 with acceptable sensitivity and specificity can be more likely to occur with this postoperative complication. Of note, it should be kept in mind that this cut-off value may vary greatly based on the underlying characteristics of the patients as well as the type of procedure performed.

As another finding of the study, and in line with previous studies, the main predictors of POAF occurrence, in addition to SIRI index, were old age, history of hypertension, and history of smoking. Other studies have also pointed to some background parameters, as well as procedure-related variables as predictors of this complication. In a study by Lotter et al.,[26] advanced age, a P-wave duration of ≥100 ms, chronic obstructive pulmonary disease (hypertension <1 point>, age >75 years <1 point>, stroke or transient ischemic attack <2 points>, chronic obstructive pulmonary disease <1 point>, and heart failure <2 points> [HATCH]) score, and CPB time ≥100 min were associated with POAF. Erdolu and As[27] also reported that higher age and increased atrial volume along with reduced LVEF were all associated with the risk for POAF. Apart from the role of underlying risk factors, intraoperative characteristics have also been suggested as significant factors associated with the occurrence of AF. In this context, although in the present study, we did not find a relationship between CPB or cross-clamp time, both factors have been identified in some studies as important and influential factors on the occurrence of this arrhythmia. Overall, the occurrence of this complication can be considered the result of a multifactorial interaction between preoperative and intraoperative factors. Therefore, in addition to the role of inflammatory factors such as SIRI, special attention should be paid to preoperative factors and procedural parameters.

Nonetheless, there are some limitations to this study. First, the predictive value of SIRI was only evaluated in predicting the occurrence of postoperative atrial fibrillation, and the role of this marker in predicting the occurrence of long-term arrhythmias (through long-term follow-up of patients) was not evaluated. Second, the predictive value of SIRI was not compared with other inflammatory and proinflammatory factors. Finally, due to the possibility of differences in atrial fibrillation rates in different surgical techniques, the difference in the value of SIRI in predicting arrhythmias between off-pump and on-pump types was not compared.

In conclusion, POAF is a common postoperative complication after CABG which can be induced by the activation of different inflammatory processes. Therefore, the role of SIRI index to predict the occurrence of POAF is mostly highlighted in recent years. Our study results suggest that increased SIRI along with other parameters such as advanced age, history of hypertension, smoking and reduced LVEF can effectively predict POAF in CABG patients. Further large-scale, prospective studies are needed to draw more reliable conclusions on this subject.

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