Multi-inflammatory index as a novel predictor of new-onset atrial fibrillation after off-pump coronary artery bypass grafting

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ABSTRACT

Background: To our knowledge, a possible predictive relationship of the multi-inflammatory index (MII) with new-onset atrial fibrillation (AF) after off-pump coronary artery bypass grafting (CABG) has not yet been studied in the literature.

Aims: We aimed to investigate whether the MII is a novel group of hematological markers for predicting postoperative new-onset AF in patients undergoing off-pump CABG.

Methods: A total of 427 patients undergoing isolated off-pump CABG between October 2021 and December 2023 were enrolled in this retrospective observational cohort study and allocated to two groups: the AF group (n = 108) and the non-AF group (n = 319). The groups were compared in terms of baseline clinical patient characteristics, laboratory parameters, and operative and postoperative data.

Results: The median values of age, length of hospital stay, platelet and neutrophil count, C-reactive protein level, systemic immune-inflammation index, MII-1, MII-2, and MII-3 were significantly greater in the AF group compared to the non-AF group in univariate analyses. In multiple explanatory variable logistic regression analysis, MII-1, MII-2, and MII-3 were determined to be significant hematological variables, and thereby these indices were considered the independent predictors of postoperative new-onset AF. Receiver operating characteristic curve analyses showed that to predict postoperative new-onset AF, MII-1 of 22.47 constituted the cut-off value with 62.0% sensitivity and 57.0% specificity, MII-2 of 141.77 constituted the cut-off value with 43.5% sensitivity and 76.8% specificity, and MII-3 of 5669 constituted the cut-off value with 63.8% sensitivity and 58.3% specificity.

Conclusion: This study demonstrated for the first time that all MIIs predicted new-onset AF after off-pump CABG.

Key words: atrial fibrillation, coronary artery bypass grafting, multi-inflammatory index, off-pump, predictor

INTRODUCTION

Atrial fibrillation (AF) is one of the most important and widespread complications following coronary artery bypass grafting (CABG) with an incidence of 10% to 40% [1–3]. It has been shown that new-onset AF after CABG is linked to significant morbidity, mortality, prolonged hospital stay, and increased healthcare costs [4, 5]. To decrease these unfavorable outcomes and costs, it is critical to identify the patients at high risk of postoperative new-onset AF and implement appropriate procedures to prevent it. Therefore, to achieve these goals, we need readily accessible, reliable, and affordable biomarkers that can be used in routine clinical practice.

Even though it is known that a wide variety of etiologic factors such as surgical trauma,

WHAT'S NEW?

The multi-inflammatory index (MII) is a newly developed index group composed of several inflammatory indices including the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and systemic immune-inflammation index, combined with C-reactive protein. The prognostic and/or predictive capacity of MII has been recently examined in various conditions such as cardiovascular diseases, metastatic colorectal cancer, COVID-19, degenerated intervertebral disc, and erectile dysfunction. However, to the best of our knowledge, there is no study examining a possible relationship between MII and atrial fibrillation (AF) in the literature. Therefore, in this study, we aimed to examine whether there was a possible predictive relationship between the MIIs and postoperative new-onset AF in patients undergoing off-pump coronary artery bypass grafting and showed for the first time that all MIIs predicted new-onset AF after off-pump coronary artery bypass grafting.

extracorporeal circulation, electrolyte imbalance, and hypoxia are implicated in the pathogenesis of postoperative atrial fibrillation (POAF), electro-patho-physiological molecular mechanisms of POAF are less well understood. Nonetheless, inflammation is one of the pathophysiological factors known to contribute to the development of AF [6–8]. Many inflammatory indicators such as C-reactive protein (CRP), white blood cell (WBC) counts, and interleukin (ILs) levels, have been thoroughly investigated regarding POAF [9]. Moreover, various inflammatory parameters derived from a simple complete blood count (CBC) analysis such as the neutrophil/lymphocyte ratio (NLR) [10, 11], platelet/lymphocyte ratio (PLR) [11], and systemic immune-inflammation index (SII) [12–14] have been recently studied as possible predictive indicators of POAF after CABG.

Multi-inflammatory index (MII) is a novel index group consisting of a combination of several hematological inflammatory indices such as the NLR, PLR, and SII, with CRP. This novel index group, including MII-1, MII-2, and MII-3, was first studied in patients with metastatic colorectal cancer, and all MII indices were found to be useful prognostic biomarkers of that cancer [15]. Afterward, the prognostic and/or predictive abilities of the MII were also studied in other diseases such as acute coronary syndrome (ACS) [16], acute ischemic stroke (AIS) [17], pulmonary embolism (PE) [18], and in critically ill COVID-19 patients [19]. On the other hand, to the best of our knowledge, there has been no study investigating the possible relationship between the MII and AF reported in the literature. Therefore, we hypothesized that the MII, a novel inflammatory indicator, could be a predictor of new-onset AF following off-pump CABG, and this study was designed to examine whether there was a possible predictive relationship between the MII and POAF in patients undergoing off-pump CABG. In addition, other possible predictors and postoperative outcomes of new-onset AF following off-pump CABG were also examined.

METHODS

Ethical considerations

The study protocol was approved by the institutional scientific research ethics committee. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was taken from all patients after giving them detailed information about the surgery and postoperative period.

Study population and design

This was a retrospective observational cohort study conducted in patients undergoing isolated off-pump CABG between October 2021 and December 2023. A total of 427 patients with available medical records were included in the study, and were assigned to two groups according to the development of postoperative new-onset AF: the AF group (n = 108) and the non-AF group (n = 319). Preoperative basic demographic features, comorbidities and laboratory parameters, operative data, and postoperative results and complications were screened, recorded for analysis, and then compared between the groups. Therefore, the predictors as well as postoperative outcomes of new-onset AF after off-pump CABG were identified. The exclusion criteria were as follows: a history of previous paroxysmal, persistent or permanent AF, conventional on-pump CABG, emergency surgery, redo surgery, and concomitant surgery such as carotid endarterectomy and cardiac valve surgery.

Surgical procedure

All patients were operated through median sternotomy under general anesthesia. The internal thoracic artery, great saphenous vein, and radial artery were the most commonly used bypass grafts. Unfractionated heparin at a dose of 200 IU/kg was administered intravenously with targeting for an activated clotting time of more than 300 seconds. During the distal anastomoses, an octopus tissue stabilizer was used to ensure the appropriate position on the beating heart as well as a bulldog clamp accompanied by blowing air to supply the bloodless area and an intracoronary shunt to maintain the myocardial perfusion when necessary. During the proximal anastomoses, an aortic side-biting clamp was used to supply the bloodless area and appropriate position on the ascending aorta. Distal anastomoses were performed with either 7/0 or 8/0 propylene sutures while proximal anastomoses with either 6/0 or 7/0. The "no-touch aorta" procedure was performed in cases with severe calcifica-

tion or porcelain aortas. Protamine infusion with a rate of 1/1 was administered intravenously to neutralize the effect of unfractionated heparin after completing all anastomoses.

Postoperative rhythm monitoring

Continuous electrocardiogram (ECG) monitoring was provided to all patients for the first 48 hours after the surgery. Standard 12-lead ECGs were taken every day for the remaining days till discharge to evaluate the heart rhythms of patients. Additionally, the radial pulse was palpated at least once every four hours to evaluate the heart rate and dysrhythmias. In the event of tachycardia, palpitations, or a suspicion of an abnormal heart rhythm, a second 12-lead ECG was taken and examined. The diagnosis of new-onset AF was made with the presence of uneven RR intervals and lack of P waves on the ECG.

Laboratory analysis

Before the surgical procedure, peripheral venous blood samples were collected. The samples were put into sterile tubes with a set quantity of anticoagulant and then transported to the laboratory for analysis. An automatic CBC analysis device (Beckman Coulter Inc., CA, US) was used to detect the values of preoperative CBC test parameters. The CBC parameters included in the study were as follows: hemoglobin, hematocrit, mean corpuscular volume, red cell distribution width (RDW), WBC, platelet (PLT), neutrophil (NEU), lymphocyte (LYM), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit, as well as the NLR, PLR, and SII. Moreover, MII-1, MII-2, and MII-3 were also included in the analysis, with the addition of CRP.

We used the following formulas in the study:

$$NLR = NEU / LYM;\ PLR = PLT / LYM;$$
$$\text{and } SII = PLT \times NEU / LYM.$$
$$MII\text{-}1 = NLR \times CRP;\ MII\text{-}2 = PLR \times CRP;$$
$$\text{and } MII\text{-}3 = SII \times CRP$$

Statistical analysis

The Shapiro–Wilk test was used to evaluate the normality of variables. Continuous variables were presented as median (min.–max.) values while categorical variables were expressed as numbers (percentages). Continues variables were analyzed using the Mann-Whitney U test while categorical variables were analyzed using the χ^2 test. Multiple explanatory variable logistic regression analysis was conducted to determine independent predictors of POAF. Receiver-operating characteristic (ROC) curve analyses were conducted to determine the cut-off values of selected variables with sensitivity and specificity rates, via logistic regression, for POAF from the area under the curve. ROC curve analysis was performed using the "Optimal Cutpoints" library of R software [20]. R software was used to perform the statistical analyses (R Core Team, 2021) [21]. A *P*-value <0.05 was regarded as statistically significant for all analyses.

RESULTS

This study included 108 patients with POAF (74 males and 34 females) and 319 patients without POAF (231 males and 88 females), and POAF incidence was calculated as 25.3%. Patients with POAF were significantly older than those without POAF, and the median ages were 67 and 63 years for the AF group and non-AF group, respectively ($P = 0.003$). No significant differences were detected for other clinical features and comorbid conditions between the groups (Table 1). As laboratory parameters of the patients were compared between the groups, the median values of PLT, NEU, SII, CRP, MII-1, MII-2, and MII-3 in the AF group were detected to be significantly greater than those in the non-AF group (Table 2). When we considered intraoperative data, postoperative outcomes, and complications, only the median value of the length of hospital stay in the AF group was detected to be significantly greater than in the non-AF group. There were no significant differences with regard to the other intraoperative and postoperative variables between both groups (Table 3).

After identifying the significant risk factors in univariate analyses, the multiple explanatory variable logistic regression analysis was conducted to determine the independent predictors of POAF by adjusting for significant variables. According to the multiple explanatory variable logistic regression analysis; age, MII-1, MII-2, and MII-3 were found to be independent predictors of POAF (Table 4).

ROC curve analyses showed that for predicting POAF development, age of 64 constituted the cut-off value with 67.6% sensitivity and 53.6% specificity, MII-1 of 22.47 constituted the cut-off value with 62.0% sensitivity and 57.0% specificity, MII-2 of 141.77 constituted the cut-off value with 43.5% sensitivity and 76.8% specificity, and MII-3 of 5669 constituted the cut-off value with 63.8% sensitivity and 58.3% specificity (Table 5). The ROC curves of these determined independent predictors of POAF are presented in Figure 1.

DISCUSSION

The present study demonstrated that patients with new-onset POAF were significantly older and had longer hospital stays compared to patients without new-onset POAF. Among laboratory parameters, PLT, NEU, SII, CRP, MII-1, MII-2, and MII-3 values in the AF group were significantly greater than those in the non-AF group according to the univariate analysis. However, in the multiple explanatory variable logistic regression analysis, PLT, NEU, SII, and CRP lost statistical significance, and only MII-1, MII-2, and MII-3 remained significant. Therefore they were considered the relevant predictive indices for new-onset POAF. The most interesting finding of our study was that all these MII indices independently predicted new-onset POAF following off-pump CABG, which was confirmed for the first time.

Identifying the predictors of new-onset AF after heart surgery is essential because it makes it possible to

Table 1. Demographics, clinical characteristics and comorbidities

Variable	Non-AF group (n = 319)	AF group (n = 108)	*P*-value
Age, years	63 (41–84)	67 (47–83)	0.003
Sex (female)	88 (27.5%)	34 (31.4%)	0.27
Weight, kg	77 (50–122)	77 (55–122)	0.54
Height, cm	169 (145–190)	168 (145–190)	0.98
BMI, kg/m^2	27.4 (18.5–39.8)	26.9 (18.5–39.4)	0.52
Obesity	78 (24.4%)	20 (18.5%)	0.26
LVEF level	55 (25–70)	55 (30–65)	0.69
Hypertension	212 (66.4%)	63 (58.3%)	0.16
Diabetes mellitus	119 (37.3%)	45 (41.6%)	0.49
Hyperlipidemia	125 (39.1%)	37 (34.2%)	0.42
Myocardial infarction	108 (33.8%)	38 (35.1%)	0.89
COPD	22 (6.9%)	5 (4.6%)	0.54
Peripheral arterial disease	35 (10.9%)	10 (9.2%)	0.75
Chronic renal failure	20 (6.2%)	7 (6.4%)	1.00
Chronic hepatic failure	1 (0.3%)	0 (0.0%)	1.00
Previous PCI	46 (14.4%)	16 (14.8%)	1.00
Previous CVE	22 (6.9%)	8 (7.4%)	1.00
Smoking	118 (37.0%)	29 (26.8%)	0.07

Abbreviations: AF, atrial fibrillation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVE, cerebrovascular event; LA, left atrium; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention

Table 2. Laboratory parameters

Variable	Non-AF group (n = 319)	AF group (n = 108)	*P*-value
HGB, g/dl	13.0 (8.4–19.0)	13.0 (9.5–18.0)	0.44
HCT, %	39.0 (24.8–55.0)	39.8 (27.2–54.0)	0.53
MCV, fl	87.7 (65.9–103.3)	87.2 (65.9–99.2)	0.85
RDW, %	16 (13.2–30.8)	16 (13.3–23.1)	0.19
WBC, 10^3/µl	9 (2.6–30.5)	9 (4.4–28.6)	0.66
PLT, 10^3/µl	235 (93–719)	254 (103–745)	0.04
NEU, %	70.2 (27.8–92.1)	74.5 (37.1–92.0)	0.01
LYM, %	17.0 (5.0–54.2)	15.6 (5.3–42.0)	0.51
MPV, fl	8 (3.2–18.3)	8 (5.4–12.5)	0.82
PDW, %	17.5 (15.4–20.9)	17.6 (15.7–20.7)	0.38
PCT, %	0.170 (0.020–0.640)	0.174 (0.060–0.510)	0.19
NLR	3.900 (1.104–15.038)	4.379 (1.415–17.019)	0.09
PLR	14.254 (3.333–67.600)	16.39 (3.25–65.06)	0.06
SII, 10^3/µl	987.6 (196.3–4895.4)	1204.7 (211.5–5120.1)	0.001
CRP, mg/l	4.3 (0.4–143.0)	6.55 (0.3–37.2)	0.004
MII-1, mg/l	18.47 (0.85–321.03)	28.53 (1.73–231.44)	<0.001
MII-2, mg/l	67.52 (2.68–1469.7)	106.0 (3.9–994.6)	<0.001
MII-3, g/l	4599 (147–81863)	7646 (254–83748)	<0.001

Abbreviations: CRP, C-reactive protein; HCT, hematocrit; HGB, hemoglobin; LYM, lymphocyte; MCV, mean corpuscular volume; MII, multi-inflammatory index; MPV, mean platelet volume; NEU, neutrophil; NLR, neutrophil-to-lymphocyte ratio; PCT, plateletcrit; PDW, platelet distribution width; PLT, platelet; PLR, platelet-to-lymphocyte ratio; RDW, red cell distribution width; SII, systemic immune-inflammation index; WBC, white blood cell; other — see Table 1

create preventative strategies and provide required early interventions. Even though a large number of different predictors of new-onset POAF have been reported in various studies, advanced age is the most well-known predictor that has been identified by most studies [1–5]. As previously documented, our study also confirmed that advanced age was a significant and independent predictor of new-onset POAF.

The number of studies examining hematological indices derived from basic blood tests to predict new-onset POAF following heart surgery has risen in the last years, and these hematological indices have gained increasing popularity in relevant subjects because these tests are low-cost, reliable, fast, and easily accessible. In fact, many hematological indices obtained from the CBC analysis, such as PLT, RDW, MPV, WBC, NLR, PLR, and SII, have been thoroughly examined, and the predictive values of these indices for new-onset POAF have been demonstrated. However, these different studies have often shown inconsistent and inconclusive results due to methodological differences, heterogeneity of patient selection, and potential bias. In a systematic review and meta-analysis study including a total of 6098 patients from 22 studies, the predictive roles of hematological indices in new-onset POAF were investigated after isolated CABG, valve surgery, or combined procedures. That study reported that preoperative PLT,

Table 3. Operative data and postoperative outcomes

Variable	Non-AF group (n = 319)	AF group (n = 108)	*P*-value
LITA usage	302 (94.6%)	102 (94.4%)	1.00
Complete revascularization	300 (94.0%)	100 (92.5%)	0.76
Number of distal bypass	3 (1–6)	4 (1–6)	0.08
Length of ICU stay, hour	24 (14–360)	27 (14–192)	0.55
Length of hospital stay, day	6 (3–27)	7 (5–19)	0.006
Inotrope requirement	60 (18.8%)	20 (18.5%)	1.00
IABP requirement	9 (2.8%)	6 (5.5%)	0.30
Low cardiac output syndrome	9 (2.8%)	6 (5.5%)	0.30
Myocardial infarction	12 (3.7%)	4 (3.7%)	1.00
Cerebrovascular event	13 (4.0%)	2 (1.8%)	0.43
Reintubation	14 (4.3%)	4 (3.7%)	0.98
Pneumonia	8 (2.5%)	5 (4.6%)	0.43
Mediastinitis	8 (2.5%)	4 (3.7%)	0.75
Reexploration for bleeding	10 (3.1%)	3 (2.7%)	1.00
AKI requiring hemodialysis	7 (2.1%)	2 (1.8%)	1.00
Gastrointestinal bleeding	2 (0.6%)	0 (0.0%)	0.99
In-hospital mortality	5 (1.5%)	2 (1.8%)	1.00

Abbreviations: AKI, acute kidney injury; IABP, intraaortic balloon pump; ICU, intensive care unit; LITA, left internal thoracic artery; other — see Table 1

Table 4. Results of the multiple explanatory variable logistic regression analysis for predicting the independent risk factors

Variable	Odds ratio (95% CI)	*P*-value
Age, year	1.0405 (1.0133–1.0683)	0.003
PLT, 10^3/μl	1.0172 (0.9008–1.1448)	0.78
NEU, %	0.9911 (0.9662–1.0153)	0.47
CRP, mg/l	1.0079 (0.9879–1.0278)	0.40
SII, 10^3/μl	1.0502 (0.9735–1.1305)	0.11
MII-1, mg/l	1.0064 (1.0009–1.0119)	0.003
MII-2, mg/l	1.0020 (1.0007–1.0034)	0.02
MII-3, g/l	1.0000 (1.0000–1.0000)	0.002

Abbreviations: CI, confidence interval; other — see Table 2

RDW, MPV, WBC, and NLR, as well as postoperative WBC and NLR, were significant hematological indices associated with POAF [22]. In our study, we found that preoperative PLT, NEU, SII, and CRP were significant markers in the univariate analysis; however, in the logistic regression model, these indices did not reach statistical significance and were not considered significant predictive markers for new-onset AF after off-pump CABG.

Among the hematological indices derived from the CBC test, the SII is one of the relatively novel and most frequently studied markers that has been shown to have a predictive and/or prognostic value in various cardiovascular diseases [23]. The SII consists of the combination of three inflammatory peripheral cell counts (platelets, neutrophils, and lymphocytes), with a formula (SII = PLT × NLR) and simultaneously reflects the inflammatory and immune status of patients. Considering the role of inflammatory and immune mechanisms in AF pathogenesis, it was thought that the SII might have a predictive value in the development of AF, and studies investigating the relationship between the SII and AF were designed based on this hypothesis.

In a recent study involving 622 patients diagnosed with ACS, the relationship between the SII and new-onset AF was investigated. Thirty-five (5.6%) of these patients developed new-onset AF during a two-year follow-up period, and they were in the study group. In the study, SII was significantly increased in the study group compared to the control group, and the multivariate logistic regression analysis indicated that the SII was an independent predictor of new-onset AF in ACS patients [24]. In another study, Bağcı et al. [25] examined whether SII predicted new-onset AF after ST-segment elevation MI, and demonstrated the predictive ability of the SII for new-onset AF in this group of patients. The authors concluded that the SII could be used as an independent predictor of new-onset AF after ST-segment elevation MI.

In addition, the predictive role of the SII in predicting new-onset POAF in patients undergoing CABG was also investigated in several recent studies. Yilmaz et al. [12] and Uğuz et al. [13] demonstrated the predictive value of the SII for new-onset POAF in on-pump CABG patients while

Table 5. Results of the ROC curve analysis for the determined independent predictors

	Optimum cut-off value	AUC (95% CI)	Sensitivity (%)	Specificity (%)
Age, year	64	0.595 (0.535–0.655)	67.6	53.6
MII-1, mg/l	22.47	0.614 (0.554–0.674)	62.0	57.0
MII-2, mg/l	141.77	0.624 (0.563–0.686)	43.5	76.8
MII-3, g/l	5669	0.637 (0.576–0.698)	63.8	58.3

Abbreviations: AUC, area under the curve; ROC, receiver-operating characteristic; other — see Tables 2 and 4

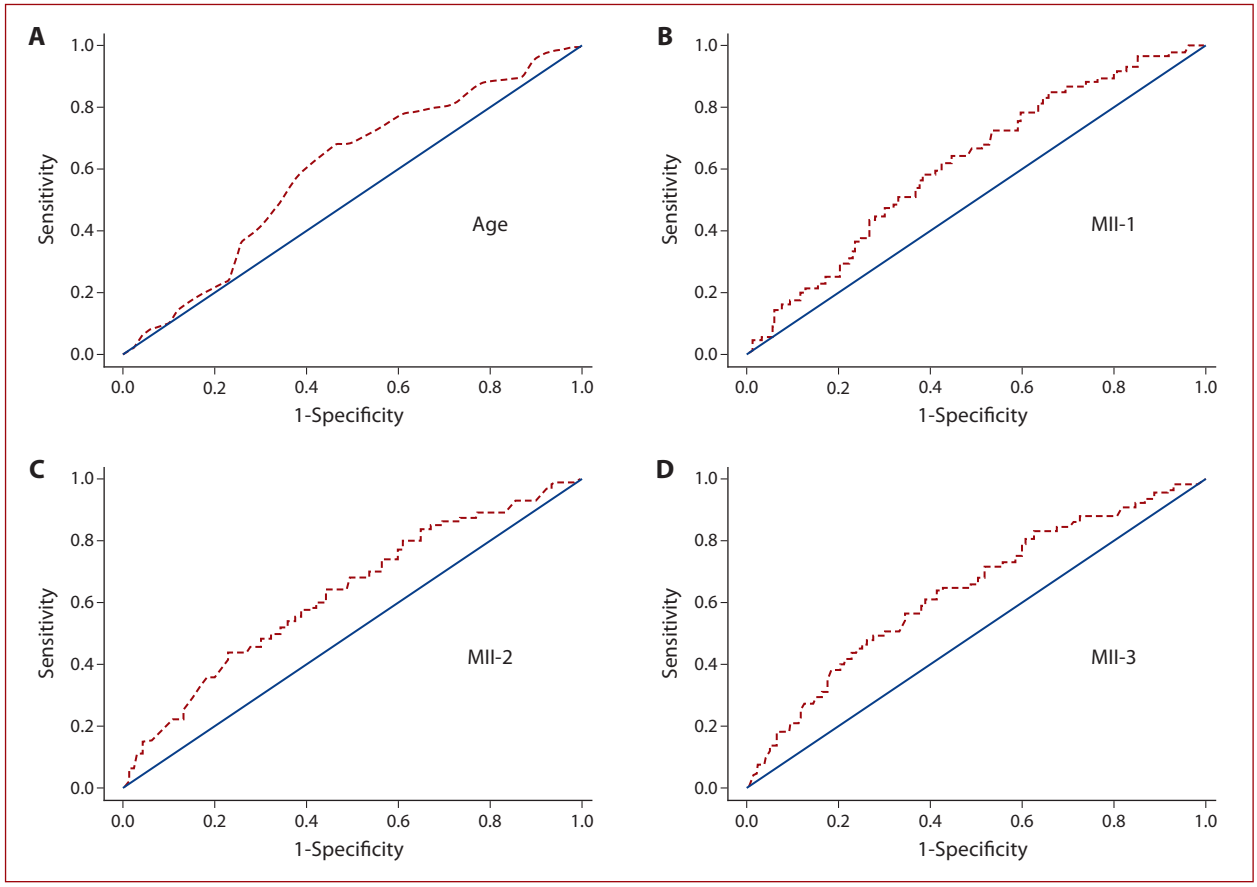

Figure 1. Receiver operating characteristic curves of the determined independent predictors

Topal et al. [14] reported similar findings in off-pump CABG patients. Moreover, a systematic review and meta-analysis study evaluating the SII for predicting POAF after cardiac surgery has just been published. In this recent article, 3245 patients from 8 studies were included (6 studies involved CABG, 1 mitral valve surgery, and another 1 various cardiac procedures). The study indicated that an elevated SII was significantly associated with increased risk of POAF after cardiac surgery, highlighting its utility as a predictive biomarker [26].

In our study, even though SII was detected as a significant variable in the univariate analysis, in the logistic regression analysis model, it dropped from the model at the last stage of analysis. Therefore, even though the odds ratio of SII was very close to 1, we could not accept SII as a significant and independent marker in the prediction of POAF. In fact, if the MIIs, which we thought to be stronger indices (e.g., MII-3 = SII × CRP), had not been included in the logistic regression analysis, SII would probably not have dropped out of the model and would have been identified as a significant and independent predictor of POAF.

The MII is a newly developed index group composed of several inflammatory indices including the NLR, PLR, and SII, in combination with CRP. MII was first described by Casadei Gardini et al. [15], and its prognostic capacity was evaluated in patients with metastatic colorectal cancer undergoing first-line chemotherapy. The authors reported that all MIIs were useful prognostic markers in this patient population. Afterward, the prognostic and/or predictive capacity of MII was investigated in different conditions such as cardiovascular disorders, COVID-19, degenerated intervertebral disc, and erectile dysfunction. Gozdas et al. [19] studied the effects of many hematological markers on prognosis in critically ill COVID-19 patients, by comparing the results of laboratory parameters between survivors and non-survivors. In the study, among all inflammatory hematological markers, MII showed the best performance in predicting mortality. Therefore, it was concluded that MII could be useful in the early determination of poor prognosis in COVID-19 patients. In other studies, the diagnostic efficiency of MII was also shown in patients with degenerated intervertebral discs [27] and erectile dysfunction [28].

Recently, studies investigating the prognostic and/or predictive role of MII in various cardiovascular diseases such as ACS, AIS, and PE have been conducted, and the results of these studies have been published. In a recent study conducted by Doğanay et al. [16], the prognostic role of MII in acute stent thrombosis and in-hospital mortality was evaluated on 1488 ACS patients undergoing percutaneous coronary intervention. The study demonstrated that MII-3 exhibited better diagnostic performance than other inflammatory indices and concluded that MII-3 was a strong predictor of acute stent thrombosis after percutaneous coronary intervention, and it was related to the subsequent

increased risk of mortality. In the study, it was also indicated that MII could be an essential prognostic screening tool to identify high-risk patients before the intervention. Demirel et al. [17] examined the possible relationship between MIIs and the severity of AIS in 452 patients with ischemic stroke, who were admitted to the hospital within 72 hours of the onset of symptoms, by comparing the results of many laboratory parameters including all MIIs (MII-1, MII-2, and MII-3) between survivors and non-survivors. In the study, according to the simple and multiple logistic regression analyses for identifying mortality predictors, all MIIs were detected as significant variables and thereby were considered novel predictors of in-hospital mortality in AIS. A study conducted by Boyuk [18] investigated the roles of MII-1 and MII-2 in differential diagnosis of massive and non-massive PE and concluded that these inflammatory indices showed a strong ability to distinguish massive and non-massive PE compared to the previously studied classical inflammatory indices. In another study, the prognostic and predictive abilities of MII-1 and MII-2 for acute symptomatic seizures in patients with cerebral venous sinus thrombosis (CVST) were searched. In the study, MII-1 and MII-2 were detected to significantly predict the occurrence of seizures in CVST, and it was stated that these indices could be utilized as novel prognostic and predictive hematological markers of acute symptomatic seizures in CVST patients [29].

Furthermore, apart from these aforementioned studies related to the prognostic and/or predictive role of MII in various cardiovascular diseases, another interesting study investigated the relationship of MII-1 and MII-2 with mortality in patients operated for Stanford type A aortic dissection. Many hematological markers including MII-1 and MII-2 were compared between survivors and non-survivors, and, surprisingly, none of the studied hematological markers were found to be related to mortality [30]. Our study demonstrated that all MIIs including MII-1, MII-2, and MII-3 were detected to be significant variables in the univariate analysis of laboratory parameters, and even in the multiple explanatory variable logistic regression analysis for identifying the independent predictors of POAF. Therefore, we consider MIIs to be useful hematological markers for predicting new-onset AF after off-pump CABG.

The role of different inflammatory biomarkers, such as CRP and ILs, in predicting POAF after cardiac surgery was also extensively investigated. In a systematic review and meta-analysis evaluating the relationship of several inflammatory markers such as CRP and ILs with POAF following cardiac operations including isolated CABG, isolated valve surgery, and combined cardiac procedures, the baseline levels of CRP and IL-6, postoperative levels of CRP, IL-6, IL-8, and IL-10 were found to be relevant inflammatory parameters significantly associated with POAF [9]. In our study, CRP was found to be a significant variable in the univariate analysis, however, it dropped from the model in the logistic regression analysis. Therefore, we could not accept CRP as a significant and independent marker in the prediction of POAF. On the other hand, ILs were not studied in our study.

Study limitations

This study had some important limitations. The most important limitations were that it was retrospectively designed and data were collected and analyzed from a single center. Another important limitation was that we did not conduct a correlation analysis with other classical inflammatory biomarkers. In addition, after the intensive care unit stay, we did not conduct continuous cardiac rhythm monitoring in the acute inpatient ward. There was a probability of undetected brief episodes of asymptomatic AF in the acute inpatient ward even though cardiac rhythm was regularly monitored with conventional ECGs at least twice a day, and extra ECGs were taken from the patients when any irregularities in cardiac rhythm were suspected.

CONCLUSIONS

To the best of our knowledge, this study is the first clinical investigation of the predictive role of MII in new-onset POAF patients undergoing off-pump CABG. Our study showed, for the first time in the literature, that MIIs, a novel hematological index group involving MII-1, MII-2, and MII-3, predicted POAF in patients undergoing off-pump CABG. Therefore, all MIIs could be used as novel and promising markers for predicting new-onset AF after off-pump CABG. However, further large-scale prospective studies are necessary to support the findings of our study and achieve more valuable scientific information.

Article information

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