

## RESEARCH ARTICLE

# Elevated Monocyte to High-density Lipoprotein Ratio Is a Risk Factor for New-onset Atrial Fibrillation after Off-pump Coronary Revascularization

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## Abstract

Atrial fibrillation (AF) is a common complication of coronary revascularization. Currently, the mechanisms of postoperative AF are unclear. This study was aimed at investigating the risk factors for new-onset AF (NOAF) after coronary revascularization and exploring the early warning effects of clinical inflammatory markers. A retrospective analysis was conducted on 293 patients with unstable angina pectoris who underwent coronary artery revascularization in Beijing Chao-Yang Hospital, Capital Medical University, between April 2018 and June 2021, including 224 patients who underwent coronary artery bypass grafting and 69 patients who underwent one-step hybrid coronary revascularization. Baseline data, clinical data, blood indicators and AF episodes within 7 days after the surgery were collected. Participants were divided into two groups according to whether AF occurred, and the data were analyzed between groups. In addition, multivariate logistic regression was used to explore the independent risk factors for developing AF post coronary revascularization. Aging, a larger left atrial inferior-superior diameter, use of an intra-aortic balloon pump, a greater blood volume transfused during perioperative period and a higher monocyte to high-density lipoprotein ratios on postoperative day 1 were independent risk factors for NOAF after coronary artery surgery.

**Keywords:** Atrial fibrillation; coronary revascularization; Neutrophils; High-density lipoprotein

**Significance Statement:** In this study, we calculated the monocyte to high-density lipoprotein ratio (MHR), according to the levels of monocytes and high-density lipoprotein, to investigate the previously unexplored role of the MHR in AF after off-pump CABG.

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## Introduction

Coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), and hybrid coronary revascularization (HCR) are common procedures for coronary revascularization. However,

patients after CABG and HCR are prone to atrial fibrillation (AF). Postoperative atrial fibrillation (POAF) has an incidence of approximately 20–40% and usually occurs 2–4 days after surgery [1]. HCR is a new procedure for treating multi-branch lesions in coronary artery disease. However, a meta-analysis including seven studies has indicated that the incidence of AF is not significantly lower after HCR than CABG [2]. POAF is associated with poor prognosis and is an independent predictor of complications such as infection, stroke, renal insufficiency, respiratory failure, and cardiac arrest [3]. Therefore, exploring the risk factors for POAF after coronary revascularization is important to identify POAF and enable early intervention for patients at risk.

The mechanism of POAF remains unclear. Dobrev et al. [4] have proposed a model of POAF, in which POAF occurrence is divided into three stages. The first stage involves preoperative atrial substrate with susceptibility to AF, which develops over several years and is often associated with factors included age, diabetes, and hypertension. The second stage involves atrial substrate changes in the perioperative period, which are often associated with surgery, extracorporeal circulation, and aseptic inflammation. The third stage involves atrial substrate changes in the postoperative period, which are evident within 5 days after surgery and often correlate with multiple triggers, such as sympathetic excitation, inflammation, oxidative stress, and surgical pain. The various triggers cause structural and electrophysiological changes in the atria, thus further increasing the susceptibility to, and likelihood of, AF. Studies are increasingly indicating that the inflammatory response correlates with POAF occurrence. Weymann et al. [5] have found that elevated preoperative and postoperative white blood cell count (WBC) is a risk factor for POAF, on the basis of 22 studies with a total of 6,098 patients who underwent CABG surgery. In a prospective cohort study, Gibson et al. [6] have included 275 patients undergoing non-emergency coronary artery bypass grafting and have found that an elevated neutrophil to lymphocyte ratio (NLR) pre- and postoperatively is associated with the incidence of POAF. Clinical composite indicators such as the NLR, platelet to lymphocyte ratio, and lymphocyte to monocyte ratio (LMR) are recently identified markers of systemic inflammation, which are

considered essential for prediction and prognosis in various cardiovascular diseases [7]. In summary, classical inflammatory cells, such as neutrophils, monocytes, and lymphocytes, are associated with the development of postoperative atrial fibrillation. Olesen et al. [8] have found that elevated postoperative C-reactive protein (CRP) levels after CABG surgery are associated with the development of POAF. Yilmaz et al. [9] have considered NLR as a predictor of AF, and Ertas et al. [10] have examined the role of red blood cell distribution width in postoperative AF and found that preoperative red blood cell distribution width (RDW) levels predict new-onset AF after CABG in patients without AF history. High-density lipoprotein (HDL) has anti-inflammatory and antioxidant effects, and studies have shown that HDL levels correlate with diminished atrial fibrillation risk.

In this study, we calculated the MHR according to the levels of monocytes and HDL to investigate the previously unstudied role of this ratio in AF after off-pump CABG.

## Methods

### Participants

This study examined patients with unstable angina who were admitted to Beijing Chao-Yang Hospital, Capital Medical University, for coronary revascularization between April 2018 and June 2021 and received off-pump CABG surgery or HCR surgery. The inclusion and exclusion criteria were as follows.

Inclusion criteria: (1) patients with unstable angina who underwent coronary revascularization at our institution, including off-pump CABG surgery or HCR surgery; and (2) procedures performed by the chief surgeon of the Second Ward of the Heart Center of Beijing Chao-Yang Hospital, Capital Medical University.

Exclusion criteria: (1) a history of preoperative AF or previous antiarrhythmic medication; (2) emergency CABG surgery, emergency HCR surgery, or off-pump CABG surgery with intraoperative transfer to extracorporeal circulation; (3) acute or chronic infection, valvular heart disease, or rheumatic cardiomyopathy; (4) benign or malignant

tumors, hematological disorders, or immune system disorders; (5) use of hormones, immunosuppressive drugs, or radiotherapy drugs; and (6) hepatic or renal insufficiency (glutathione > 2 times the upper limit of normal and blood creatinine > 177  $\mu\text{mol/L}$ ).

### Observational Indicators

The observational indicators were as follows: (1) Baseline information: sex, age, body mass index (BMI), history of smoking, alcohol drinking, hypertension, diabetes, stroke, heart attack, PCI, non-AF arrhythmias, and preoperative medication history (e.g., use of beta blockers or calcium channel blockers (CCB)). (2) Clinical data: cardiac ultrasound: preoperative cardiac echocardiographic indices, such as left ventricular end-diastolic diameter (LVEDd), left ventricular end-systolic diameter (LVESd), left ventricular ejection fraction (LVEF), anterior-posterior diameter of the left atrium, right-left diameters of the left atrium, inferior-superior diameters of the left atrium, inferior-superior diameters of the right atrium, and right-left diameters of the right atrium; operative data: operative time, number of vessels anastomosed, intraoperative bleeding, blood volume transfused during the perioperative period, and use of an intra-aortic balloon pump (IABP). (3) Hematological parameters: preoperative, immediate postoperative, and postoperative day 1 white blood cell count (WBC), neutrophil count (N), neutrophil percentage (N%), red blood cell distribution width-coefficient of variation (RDW-CV), platelet distribution width (PDW), mean platelet volume (MPV), NLR, MHR, M%HR, LMR, NHR, N%HR, and postoperative day 1 troponin (TnI).

### Definition of New-Onset AF

New-onset atrial fibrillation after surgery is defined as new onset atrial fibrillation following surgery in patients without prior history of atrial fibrillation. The diagnostic criteria for AF referred to the 2020 ESC Guidelines for *Atrial Fibrillation*.

This study complied with the review criteria established by the Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University, and was approved by the Ethics Committee (Ethics No.: 2021-ke-26).

### Statistical Analysis

Patients were divided into AF and non-AF groups according to the presence or absence of the first occurrence of AF within 7 days after surgery. SPSS 26.0 statistical software (IBM, Armonk, NY, USA) was used for statistical analysis. Count data are expressed as frequencies and percentages, and the chi-square test was used for comparison between groups. Continuous variables with a normal distribution are expressed as mean with standard deviation, and independent samples t-test was used for comparisons between groups. Continuous variables with a skewed distribution are presented as median and interquartile ranges [M (Q1, Q3)], and the Mann-Whitney U test was used for comparisons between groups. Variables with  $P < 0.1$  in the univariate analysis were included in the multivariate logistic regression analysis to analyze the risk factors for POAF after coronary revascularization.  $P < 0.05$  was considered statistically significant.

### Results

Baseline data: the incidence of AF after coronary revascularization was 28.0%. The mean age was significantly higher in the AF group than the non-AF group ( $65.9 \pm 8.3$  vs.  $61.2 \pm 8.6$ ,  $P < 0.001$ ). No statistical difference was observed between patients in the AF and non-AF groups in terms of sex, BMI, history of smoking, alcohol consumption, previous hypertension, diabetes mellitus, history of stroke, heart attack, and previous non-AF arrhythmias ( $P > 0.05$ ). The non-AF group had significantly higher use of preoperative  $\beta$ -blockers than the AF group ( $82.5\%$  vs.  $70.7\%$ ,  $P = 0.026$ ). No significant difference was observed between groups regarding the preoperative use of CCB drugs ( $P = 0.926$ ) (Table 1).

Table 2 shows the comparison of the clinical data of the two groups. The anterior-posterior diameter of the left atrium was greater in the AF group than the non-AF group ( $38.5 \pm 4.9$  mm vs.  $37.3 \pm 4.1$  mm,  $P = 0.042$ ). The right-left diameters of the left atrium were larger in the AF group than the non-AF group ( $39.6 \pm 5.3$  mm vs.  $38.2 \pm 4.9$  mm,  $P = 0.041$ ). The inferior-superior diameters of the left atrium were significantly wider in the AF group than the non-AF group ( $51.9 \pm 5.2$  mm vs.  $49.9 \pm 4.5$  mm,  $P = 0.001$ ).

**Table 1** Demographic Data and Clinical Characteristics of Patients Undergoing Coronary Revascularization.

Variables	AF group (n=82)	Non-AF group (n=211)	P value
Age (years old)	65.9±8.3	61.2±8.6	<0.001***
Male [n, (%)]	66 (80.5%)	168 (79.6%)	0.868
BMI	25.5 (23.8, 27.9)	25.6 (23.6, 27.7)	0.882
Smoking [n, (%)]	54 (65.9%)	120 (56.9%)	0.160
Drinking [n, (%)]	28 (34.1%)	74 (35.1%)	0.881
Medical history			
Hypertension [n, (%)]	56 (68.3%)	146 (69.2%)	0.881
Diabetes [n, (%)]	36 (43.9%)	81 (38.4%)	0.387
Stroke [n, (%)]	21 (25.6%)	35 (16.6%)	0.078
Myocardial infarction [n, (%)]	24 (29.3%)	47 (22.3%)	0.210
PCI [n, (%)]	13 (15.9%)	34 (16.1%)	0.957
Arrhythmia except for AF [n, (%)]	5 (6%)	10 (4.7%)	0.636

AF: atrial fibrillation; BMI: body mass index. \*\*\*P < 0.001.

**Table 2** Comparison of Clinical Data for Patients Undergoing Coronary Revascularization.

Variables	AF group (n=82)	Non-AF group (n=211)	P Value
LVEDd (mm)	49.4±7.0	48.9±5.4	0.522
LVESd (mm)	33.1±8.4	31.5±7.3	0.134
LVEF (%)	60.2±11.8	62.5±9.7	0.112
The anterior-posterior diameter of left atrium (mm)	38.5±4.9	37.3±4.1	0.042*
The right-left diameters of left atrium (mm)	39.6±5.3	38.2±4.9	0.041*
The inferior-superior diameters of left atrium (mm)	51.9±5.2	49.9±4.5	0.001
The right-left diameters of right atrium (mm)	34.4±3.5	33.6±3.7	0.097
The inferior-superior diameters of right atrium (mm)	45.6±4.1	44.6±3.9	0.044*
Preoperative medication			
β-Blocker [n, (%)]	58 (70.7%)	174 (82.5%)	0.026*
CCB [n, (%)]	31 (37.8%)	81 (38.4%)	0.926
Surgical classification [n, (%)]			
CABG [n, (%)]	68 (82.9%)	156 (73.9%)	0.103
HCR [n, (%)]	14 (17.1%)	55 (26.1%)	
Duration of operation (h)	4.2±0.9	4.4±0.8	0.139
Number of anastomotic vessels (n)	2.7±1.0	2.5±1.0	0.142
Use of IABP [n, (%)]	20 (24.4%)	20 (9.5%)	0.001**
Bleeding volume during operation (mL)	496.0±204.8	461.9±211.7	0.212
Perioperative blood transfusion volume (mL)	359.8±493.3	227.3±283.6	0.024*

LVEDd: left ventricular end-diastolic diameter; LVESd: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; CCB: calcium channel blockers; HCR: hybrid coronary revascularization; IABP: intra-aortic balloon pump; CABG: coronary artery bypass grafting. \*P < 0.05; \*\*P < 0.01.

The inferior-superior diameters of the right atrium were larger in the AF group than the non-AF group (45.6±4.1 mm vs. 44.6±3.9 mm, P=0.044). No statistical difference was observed between groups in LVEDd, LVESd, LVEF, and the right-left diameters of the right atrium (P>0.05). IABP was used in

a higher proportion of patients during surgery in the AF group than the non-AF group (24.4% vs. 9.5%, P=0.001). The perioperative transfusion volume was greater in the AF group than the non-AF group (359.8±493.3 mL vs. 227.3±283.6, P=0.024). No statistical difference was observed between the AF



**Table 3** Comparison of Preoperative Blood Parameters in Patients Undergoing Coronary Revascularization.

Variables	AF group (n=82)	Non-AF group (n=211)	P Value
WBC ( $\times 10^9/L$ )	6.9 $\pm$ 1.9	6.6 $\pm$ 1.5	0.210
N ( $\times 10^9/L$ )	4.3 $\pm$ 1.4	4.1 $\pm$ 1.2	0.268
N% (%)	61.5 (56.8, 66.3)	61.5 (55.3, 67.3)	0.752
RDW-CV (%)	12.8 $\pm$ 0.9	12.7 $\pm$ 0.7	0.273
PDW (fl)	12.7 $\pm$ 2.4	12.2 $\pm$ 2.0	0.053
MPV (fl)	10.6 $\pm$ 0.9	10.4 $\pm$ 0.9	0.118
NLR	2.5 $\pm$ 1.2	2.5 $\pm$ 1.8	0.820
MHR	0.6 $\pm$ 0.3	0.5 $\pm$ 0.2	0.088
M%HR	8.2 $\pm$ 3.2	7.8 $\pm$ 2.7	0.294
LMR	4.4 $\pm$ 1.7	4.6 $\pm$ 1.7	0.443
N%HR	73.0 $\pm$ 20.4	72.1 $\pm$ 21.8	0.761
NHR	5.2 $\pm$ 2.4	4.8 $\pm$ 2.0	0.215

WBC: white blood cell count; N: neutrophil count; N%: neutrophil percentage; RDW-CV: red blood cell distribution width level; PDW: platelet distribution width; MPV: mean platelet volume; NLR: neutrophil to lymphocyte ratio; MHR: monocyte to high density lipoprotein ratio; LMR: lymphocyte to monocyte ratio.

and non-AF groups regarding the operative time, number of anastomosed vessels, and intraoperative bleeding.

Hematological data: Peripheral blood was drawn preoperatively, immediately postoperatively, and on the morning of the first postoperative day. WBC, N, lymphocyte count, monocyte count, N%, percentage of monocytes, RDW-CV, PDW, MPV, and HDL were measured, and NLR, MHR, M%HR, LMR, N%HR and NHR were further calculated. As shown in Table 3, no statistically significant differences were observed between the AF and non-AF groups in any preoperative blood indicators ( $P > 0.05$ ). In the immediate postoperative blood indices (Table 4), RDW-CV was significantly higher in the AF group than the non-AF group (12.9% $\pm$ 1.3% vs. 12.5% $\pm$ 0.7%,  $P = 0.020$ ); no statistically significant difference was observed between groups in WBC, N, N%, PDW, MPV, NLR, MHR, M%HR, LMR, N%HR, and NHR ( $P > 0.05$ ). Among the patients' blood indicators on postoperative day 1 (Table 5), the RDW-CV levels were significantly higher in the AF group than the non-AF group (13.2 $\pm$ 1.3 vs. 12.8 $\pm$ 0.8,  $P = 0.013$ ); the MPV levels were significantly higher in the AF group than the non-AF group (10.9 $\pm$ 0.9 vs. 10.6 $\pm$ 0.9,  $P = 0.039$ ); and the TnI levels on postoperative day 1 were

markedly higher in the AF group than the non-AF group (16.5 $\pm$ 35.5 vs. 6.2 $\pm$ 16.0,  $P = 0.013$ ). No

**Table 4** Comparison of Immediate Postoperative Blood Parameters in Patients Undergoing Coronary Revascularization.

Variables	AF group (n=82)	Non-AF group (n=211)	P Value
WBC ( $\times 10^9/L$ )	11.4 $\pm$ 4.0	11.5 $\pm$ 3.4	0.819
N ( $\times 10^9/L$ )	9.4 $\pm$ 3.4	9.5 $\pm$ 3.0	0.775
N% (%)	82.0 $\pm$ 6.6	82.2 $\pm$ 5.9	0.807
RDW-CV (%)	12.9 $\pm$ 1.3	12.5 $\pm$ 0.7	0.020*
PDW (fl)	12.2 $\pm$ 2.4	11.8 $\pm$ 1.9	0.078
MPV (fl)	10.6 $\pm$ 0.9	10.5 $\pm$ 0.9	0.290
NLR	9.6 $\pm$ 11.3	8.0 $\pm$ 4.9	0.218
MHR	0.5 $\pm$ 0.3	0.5 $\pm$ 0.3	0.276
M%HR	4.4 $\pm$ 2.0	4.2 $\pm$ 2.0	0.353
LMR	4.0 $\pm$ 2.8	4.6 $\pm$ 4.3	0.256
N%HR	97.8 $\pm$ 26.9	96.8 $\pm$ 27.3	0.787
NHR	11.4 $\pm$ 5.6	11.2 $\pm$ 4.9	0.745

WBC: white blood cell count; N: neutrophil count; N%: neutrophil percentage; RDW-CV: red blood cell distribution width level; PDW: platelet distribution width; MPV: mean platelet volume; NLR: neutrophil to lymphocyte ratio; MHR: monocyte to high density lipoprotein ratio; LMR: lymphocyte to monocyte ratio. \* $P < 0.05$ .

**Table 5** Comparison of Blood Parameters on Postoperative Day 1 in Patients Undergoing Coronary Revascularization.

Variables	AF group (n=82)	Non-AF group (n=211)	P Value
WBC ( $\times 10^9/L$ )	10.9 $\pm$ 2.9	10.9 $\pm$ 2.8	0.991
N ( $\times 10^9/L$ )	9.4 $\pm$ 2.7	9.5 $\pm$ 2.6	0.882
N% (%)	86.1 $\pm$ 3.5	86.5 $\pm$ 3.6	0.305
RDW-CV (%)	13.2 $\pm$ 1.3	12.8 $\pm$ 0.8	0.013*
PDW (fl)	12.5 $\pm$ 2.2	12.1 $\pm$ 1.9	0.101
MPV (fl)	10.9 $\pm$ 0.9	10.6 $\pm$ 0.9	0.039*
NLR	14.5 $\pm$ 6.2	14.3 $\pm$ 6.2	0.762
MHR	0.9 $\pm$ 0.4	0.8 $\pm$ 0.4	0.088
M%HR	7.8 $\pm$ 2.9	7.1 $\pm$ 2.8	0.066
LMR	1.2 $\pm$ 1.4	1.2 $\pm$ 0.5	0.918
N%HR	102.7 $\pm$ 27.6	101.8 $\pm$ 27.3	0.798
NHR	11.5 $\pm$ 5.0	11.2 $\pm$ 4.3	0.587
TnI (ng/mL)	16.5 $\pm$ 35.5	6.2 $\pm$ 16.0	0.013*

WBC: white blood cell count; N: neutrophil count; N%: neutrophil percentage; RDW-CV: red blood cell distribution width level; PDW: platelet distribution width; MPV: mean platelet volume; NLR: neutrophil to lymphocyte ratio; MHR: monocyte to high density lipoprotein ratio; LMR: lymphocyte to monocyte ratio. \*P < 0.05.

statistically significant differences were observed in WBC, N, N%, PDW, NLR, MHR, M%HR, LMR, N%HR, and NHR between groups on postoperative day 1 (P > 0.05).

Variables with P < 0.1 in the univariate analysis were included in the multivariate logistic regression analysis model (Table 6). Age (OR = 1.09, P < 0.001, 95% CI: 1.05–1.13), inferior-superior diameter of the left atrium (OR = 1.08, P = 0.011, 95% CI: 1.02–1.15), use of IABP (OR = 2.48, P = 0.020, 95%

CI: 1.16–5.33), perioperative transfusion volume (OR = 1.00, P = 0.038, 95% CI: 1.000–1.002), and MHR level on postoperative day 1 (OR = 2.38, P = 0.023, 95% CI: 1.13–5.02) were independently associated with POAF after coronary revascularization (Figure 1).

## Discussion

The pathophysiological process of POAF is complex. Patients with POAF often present a preoperative AF-susceptible atrial stroma due to chronic atrial remodeling. On the basis of the preoperative atrial stroma, surgery-associated factors can trigger AF and facilitate atrial remodeling, thus perpetuating AF. These surgery-associated triggers include surgical trauma, ischemia-reperfusion injury, the inflammatory response, oxidative stress, and sympathetic activation [4].

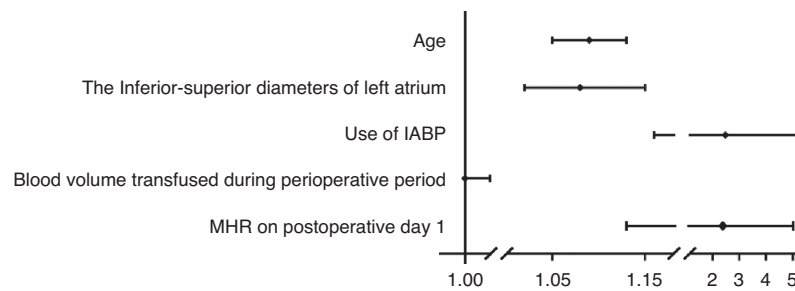
In the present study, we collected baseline data, preoperative clinical data, and blood indicators. Some indicators were independently associated with POAF after off-pump coronary revascularization, including age, upper and lower left atrial diameter, use of IABP, perioperative transfusion volume, and postoperative day 1 MHR level.

CABG surgery and PCI are the two main procedures currently used for coronary revascularization, and the incidence of AF after CABG is high. POAF has an incidence of approximately 20–40% and usually occurs 2–4 days after surgery [1]. Combining the advantages of surgical CABG and coronary medical intervention, HCR has emerged as a new procedure for revascularization in multi-vessel lesions in coronary atherosclerotic heart disease. However, the incidence of AF is not

**Table 6** Multivariate Logistic Regression Analysis of Risk Factors for POAF After Coronary Revascularization.

Variables	Multivariate logistic regression		
	OR	95% CI	P Value
Age (years old)	1.09	1.05–1.13	<0.001***
The Inferior-superior diameters of left atrium (mm)	1.08	1.02–1.15	0.011*
Use of IABP [n (%)]	2.48	1.16–5.33	0.020*
Blood volume transfused during perioperative period (mL)	1.00	1.000–1.002	0.038*
MHR on postoperative day 1	2.38	1.13–5.02	0.023*

IABP: intra-aortic balloon pump; MHR: monocyte to high density lipoprotein ratio. \*P < 0.05; \*\*\*P < 0.001.



**Figure 1** Forest Plot of Multivariate Logistic Regression Analysis.

Abbreviations: IABP, Intra-aortic balloon pump; MHR, Monocyte to high-density lipoprotein ratio.

significantly decreased after HCR. A meta-analysis including seven studies has indicated an incidence of POAF of 17% in the HCR group versus 19.2% in the CABG group, and no difference in the odds of POAF between the HCR group and the CABG group [2, 11]. Our study showed that the incidence of AF after coronary revascularization was 28.0%, with 30.3% after CABG and 20.2% after HCR. No statistical difference was observed in the incidence of POAF between CABG and HCR ( $P=0.103$ ), a finding generally consistent with those in other studies.

Advanced age was found to be a risk factor for the development of AF after coronary revascularization, in agreement with previous findings. Studies have shown that the incidence of POAF is five times higher in patients  $\geq 72$  than  $\leq 55$  years of age [12, 13]. A possible reason for the increased incidence of AF with advanced age is that aging-associated changes, such as myocardial fibrosis, amyloid deposition, dysregulation of connexins, abnormal calcium handling, and degenerative changes in the cardiac conduction system can occur. These changes lead to electrophysiological changes in the heart, such as shortening of the effective inactivity period, increased inactivity dispersion, and electrophysiological changes, such as delayed intra-atrial conduction and abnormal autoregulation, which in combination make older people prone to arrhythmias such as AF [14]. Older patients often have a combination of underlying diseases such as hypertension, diabetes mellitus, and coronary artery disease, thus leading to increased myocardial oxygen consumption, further decreased myocardial blood supply and induction of AF development.

In addition, trials have indicated that a history of hypertension, heart attack, or diabetes is a risk factor for POAF after cardiac surgery [3]. However, our study did not find differences between the AF and non-AF groups regarding the history of hypertension, heart attack, diabetes, and stroke, possibly because of an insufficient sample size.

In this study, the atrial diameters of patients were found to statistically significantly differ between the AF and non-AF groups, including left atrial inferior-superior diameters, left atrial left-right diameters, left atrial anterior-posterior diameters, and right atrial inferior-superior diameters. Left atrial volume accurately reflects the degree of left atrial enlargement, and increased volume is often closely associated with increased ventricular filling pressures and diastolic insufficiency. Osranek et al. [15] have prospectively observed 205 patients undergoing CABG and have found that the risk of AF in patients after CABG increases progressively with increasing left atrial volume, with a 5-fold increase in the risk of POAF when the left atrial volume is  $>32$  mL/m<sup>2</sup>. An increased left atrial volume index ( $28.6 \pm 12.3$  vs.  $37.9 \pm 15.5$ ;  $P < 0.01$ ) has been found to be a predictor of POAF after heart valve surgery and to be associated with longer length of stay and greater postoperative morbidity [16].

According to our surgical data, the probability of POAF was significantly higher in patients with intraoperative IABP (OR=2.48,  $P=0.020$ , 95% CI: 1.16–5.33), as also confirmed by several studies [13, 17, 18]. In addition, the higher the amount of perioperative blood transfusion, the more likely the patients were to develop AF. Alameddine et al. [19] have found that patients transfused with 1–3

units of red blood cells have an AF incidence of approximately 22%, whereas patients receiving 4–6 units show an incidence of POAF of 39%. The amount of blood transfused is often associated with advanced age, high blood loss, and poor cardiac function, thus predisposing patients to AF. Moreover, surgical blood transfusion can also induce an inflammatory state. Bilgin et al. [20] have found that blood transfusion during cardiac surgery can lead to the activation of WBCs and the production of inflammatory mediators, such as IL-6 and IL-12, thus further inducing the development of AF.

Among the clinical indicators on postoperative day 1, the inflammatory marker MHR was an independent risk factor for POAF after coronary revascularization. Canpolat et al. have found that elevated pre-ablation MHR is associated with AF recurrence after cryo-catheter ablation after a mean follow-up of  $20.6 \pm 6.0$  months [21]. Another study has found that higher pre-procedure MHR levels are independently associated with a significantly elevated risk of early AF recurrence after radiofrequency maze [22]. Suzuki et al. [23] have observed that the proportion of CD14++CD16+ monocytes in peripheral blood is significantly higher in patients with AF than controls, and that peripheral blood CD14++CD16+ intermediate type monocytes may be closely associated with the pathogenesis of AF. HDL has anti-inflammatory and antioxidant effects, including inhibiting monocyte transport of oxidized low-density lipoproteins, expression of endothelial adhesion proteins, and promotion of reverse transport of oxidized molecules [24]. Watanabe et al. [25] have studied the relationship between lipids and AF risk in the general population, and have found that lower HDL is associated with a greater risk of AF in women. In a case-control study, Annour et al. [26] reported that the risk of paroxysmal AF is 9.40 times higher in patients with low rather than normal HDL levels. MHR combines inflammation and oxidative stress processes, and is simple and easy to measure. Nonetheless, relatively few domestic and international studies have been performed on the correlation between MHR and POAF after coronary revascularization. The present study demonstrated the relationship between

this marker and POAF. These findings may provide theoretical support for the early identification of patients at high risk of POAF after coronary revascularization.

## Limitations

Owing to the limited availability of data from retrospective studies and the slightly different examinations that patients underwent preoperatively, we were unable to obtain all essential factors associated with POAF, for example, brain natriuretic peptide, the indicator of cardiac function; C-reactive protein; erythrocyte sedimentation rate; D-dimer; interleukin-6; tumor necrosis factor-alpha; and intraoperative aortic clamping time. In addition, owing to the relatively small number of patients undergoing the HCR procedure, the two procedures were not studied separately in this study. Our study was a single-center retrospective analysis with a small sample size. Future multicenter studies with expanded sample sizes are needed to validate the results of this study.

In conclusion, this study explored the risk factors for new-onset AF after coronary artery surgery and the early warning role of MHR in AF after off-pump GABG. Compared with patients who did not develop AF after surgery, patients with new-onset AF tended to be older, and to have larger inferior-superior diameters of the left atrium, greater use of IABP, greater blood volumes transfused during the perioperative period, and higher MHR values on postoperative day 1. This study provides a unique perspective on the early detection of new-onset AF in patients.

## Ethics Statement

This study complied with the review criteria established by the Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University and was approved by the Ethics Committee (Ethics No.: 2021-ke-26).

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None.

## Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Author Contributions

Yameng Mu: study concept and design; acquisition and analysis of data; drafting of the manuscript; critical revision of the manuscript. Jiayin Niu, Min Zhang, Pengfei Liu and Cuncun Hua: acquisition of data; drafting of the manuscript. Guangzhen Zhong and Yulin Guo: study concept and design; acquisition of data; drafting of the manuscript; critical revision of the manuscript.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Abbreviations

CABG	Coronary artery bypass grafting
HCR	Hybrid coronary revascularization
POAF	Postoperative atrial fibrillation
WBC	White blood cell count
N	Neutrophil count
N%	Neutrophilic granulocyte percentage
RDW-CV	Red blood cell distribution width-CV
PDW	Platelet distribution width
MPV	Mean platelet volume
NLR	Neutrophil to lymphocyte ratio
MHR	Monocyte to high-density lipoprotein ratio
M%HR	Monocyte percentage to high-density lipoprotein ratio
LMR	Lymphocyte to monocyte ratio
NHR	Neutrophil to high-density lipoprotein ratio
N%HR	Neutrophil percentage to high-density lipoprotein ratio
TnI	Troponin
BMI	Body mass index
CCB	Calcium channel blocker
LVEDd	Left ventricular end diastolic diameter
LVESd	Left ventricular end systolic diameter
LVEF	Left ventricular ejection fraction
IABP	Intra-aortic balloon pump
HDL	High-density lipoprotein

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