DOI: 10.14744/ejmi.2020.65402
EJMI 2020;4(1):61–65

Research Article

Association of Monocyte-to-HDL Ratio With Postoperative Atrial Fibrillation After Coronary Artery Bypass Surgery

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Abstract

Objectives: In this study, we aimed to show whether high monocyte/HDL ratio (MHR), which is an important marker of inflammation, predicts atrial fibrillation after coronary artery bypass surgery.

Methods: A total of 1980 patients with preoperative sinus rhythm who underwent CABG operation between May 2012 and March 2014; 256 patients who developed POAF and 256 patients who did not develop POAF in the same period were included in the study. Retrospective demographic data, laboratory findings, mortality and morbidity records were compared.

Results: In this study, 256 patients were included in each group. The patients with POAF were similar to those without POAF in terms of preoperative and operative characteristics. Comparison of laboratory data of the patients is given in the table, only significant difference was observed in terms of monocyte count and MHR (p<0.001, p=0.005). It was determined a cut-off level of 0.022 for MHR level for predicting POAF with a sensitivity of %71.2 and a specificity of %51.4, in receiver operating charactheristic (ROC) curve analysis; area under the curve: 0.737, %95 CI: 0.628-0.836, p=0.003).

Conclusion: This study will contribute to previous studies on prediction and prevention of POAF development.

Keywords: Atrial fibrillation, coronary artery bypass surgery, monocyte-to-HDL ratio

Cite This Article: *Erol G, Demirdas E, Mungan U, Kartal H, Sicim H, Arslan G. Association of Monocyte-to-HDL Ratio With Postoperative Atrial Fibrillation After Coronary Artery Bypass Surgery. EJMI 2020;4(1):61–65.*

Atrial fibrillation (AF) is the most common cardiac arrhythmia. Due to the increasing elderly population, it has become a serious public health problem that causes increases in health expenditures. The prevalence of AF in the general population has been reported as 2%.[1]

Postoperative atrial fibrillation (POAF) is the most common type of arrhythmia after coronary artery bypass grafting (CABG), and the incidence of AF after coronary artery bypass grafting (CABG) is between 15% and 50%.[2]

Postoperative atrial fibrillation (POAF) that develops early after CABG is mostly short-term, but can sometimes resolve spontaneously. It is not a fatal complication, but it has been shown to be associated with severe hemodynamic deterioration, prolonged hospital stay, increased early and late mortality and morbidity in thromboembolic events. The release of inflammatory mediators and oxidative stress are the most cited factors in POAF.[2]

Inflammation, oxidative stress, platelet activation and endothelial dysfunction have an important role in the development, progression and prevalence of atherosclerosis.[3]

Inflammatory cells such as monocytes, lymphocytes, eosinophils and neutrophils have been found to be associated with coronary artery disease.[4]

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Submitted Date: December 06, 2019 **Accepted Date:** January 24, 2020 **Available Online Date:** February 17, 2020

Monocyte cells are an important component of the inflammatory process in atherosclerotic plaque formation, and monocyte counts that are found to be high in the acute phase of myocardial infarction have been associated with plaque progression and have been identified as an independent risk marker for acute myocardial infarction (AMI) and coronary artery disease (CAD).[5]

During atherosclerosis, monocytes migrate to the subendothelial area. This migration ability of monocytes plays an important role in atherosclerotic plaque formation. Previous studies have shown that monocytes have better migration ability in hypercholesterolemic environment.[6]

In this study, we aimed to show whether high monocyte/HDL ratio (MHR), which is an important marker of inflammation, predicts atrial fibrillation after coronary artery bypass surgery.

Methods

1980 patients with preoperative sinus rhythm who underwent CABG operation between May 2012 and March 2014 at a Cardiovascular Surgery Clinic; 256 patients who developed POAF and 256 patients randomly selected from patients who did not develop POAF in the same period were included in the study. Retrospective demographic data, preoperative risk factors, preoperative medication, postoperative data, postoperative complications, laboratory findings, observed mortality and morbidity records were obtained from patient files and hospital database.

Postoperative intubation, length of stay in ICU and length of hospital stay, age, gender, height, weight, diabetes mellitus (DM), hypertension, chronic obstructive pulmonary disease (COPD), preoperative arrhythmia and echocardiography findings, drug use coronary angiography (CAG) findings, number of coronary bypass grafts, coronary bypass grafts, aortic crossclamp and total CPB duration under standard cardiopulmonary bypass (CPB), postoperative drainage and total red blood product amount and treatment of patients who developed atrial fibrillation were evaluated retrospectively.

Patients with sinus rhythm in the preoperative period, who had a history of entering the rhythm of AF, underwent emergency CABG, additional procedures for CABG operations, reoperations and open heart surgery other than CABG were excluded from the study.

In the ICU, ECG monitoring with D-II derivation with a 6-channel, 3-lead monitor and invasive arterial monitoring from the radial artery was performed for 3 days. In the ICU, the presence of acid-base imbalance, electrolyte imbalance, partial oxygen and carbon dioxide pressure was monitored hourly, and second and later days every four hours.

Fever, pulse, arterial blood pressure, and oxygen saturation were monitored at four-hour intervals. Standard 12-lead ECG was recorded once daily for the patients who were routinely monitored in the ICU and in the service. In addition, standard 12-lead ECG was recorded in patients who had arrhythmia during routine postoperative follow-up.

Operative Technique

Median sternotomy was performed in all CABG patients. All CABG cases were performed by aortic-right atrial cannulation. After cardiac arrest with antegrade and retrograde cold crystalloid cardioplegia and topical hypothermia, continuation of the arrest was provided with intermittent retrograde cold blood cardioplegia. Operations were completed under moderate hypothermia (28 °C). In all 512 patients who underwent CABG, left internal mammary artery (LIMA) was used in the left anterior descending artery position. Hot blood cardioplegia was given before the cross clamp was removed.

Statistical Analysis

Statistical analyzes were performed using SPSS (version 15, SPSS Inc., Chicago, IL, USA) statistical program. All continuous variables were expressed as the mean±SD.

Categorical variables were compared in the two groups using the test2 test; Fisher's–Whitney U-test and independent samples t-test were used to assess differences in non-categorical or continuous variables between the two groups.

The AF variables were investigated using univariate analysis. P-value <0.25 on univariate analysis, P-value <0.05 was considered to be significant.

Results

In this study, 256 patients were included in each group. Preoperative and operative data of the patients are summarized in Table 1. The patients with POAF were similar to those without POAF in terms of preoperative and operative characteristics. Comparison of laboratory data of the patients is given in Table 2, only significant difference was observed in terms of monocyte count and MHR ($p<0.001$, $p=0.005$).

Risk factors for POAF development were included in univariate logistic regression analysis. In univariate logistic regression analysis, POAF was significantly correlated with MHR level p=0.012, OR: 1.589; CI 95%: (0.543-4.346), monocyte number p=0.001, OR: 1.137; CI 95%: (0.593-2.356) and age >60 years p=0.027; OR: 0.396; CI 95%: (0.159-0.921). But POAFwasn't correlated with sex p=0.412, OR: 1.096; CI 95%: (0.504-2.324), hypertension p=0.472, OR: 1.507; CI

Table 1. Comparison of preoperative and operative characteristics of patients

Variables	POAF (+) n=256	POAF (-) n=256	p
Age (Mean±SD)	59.3±8.57	60.5±9.12	0.162
Gender (male/female) n (%)	175/81	183/73	0.117
Diabetes mellitus n (%)	97	89	0.532
Hypertension, n (%)	121	115	0.453
COPD n (%)	72	63	0.197
Body mass index (kg/m^2)	25.6±3.5	24.7±2.6	0.179
LVEF (%±SD)	44.7±8.9	45.4±9.1	0.876
Left atrial diameter (mm±SD)	46.7±8.4	48.3±.9.2	0.563
Cross-clamp time (min)	61.3±15.7	59.7±14.42	0.456
Cardiopulmonary bypass time (min)	90.07±21.41	87.9±18.86	0.731
Operation duration (min)	245.2±66.1	237.4±59.6	0.647
Total amount of cardioplegia used (ml)	1552±461	1527±443	0.842

Table 2. Comparison of laboratory values of patients

	POAF (+) n=256	POAF (-) n=256	p
Hematocrit (%±SD)	39.5±5.3	41.2±4.5	0.021
WBC count (10^3/ul±SD)	9.4±2.3	9.6±2.7	0.225
Platelet count (10^3/ul±SD)	255.3±66.5	261.4±63.7	0.678
Monocyte count (10^3/ul±SD)	1.0±0.3	0.8±0.2	<0.001
MHR	0.032±0.014	0.022±0.007	0.005
Neutrophil count (10^3/ul±SD)	8.3±3.5	7.1±3.1	0.121
Lymphocyte count (10^3/ul±SD)	2.2±0.9	2.3±0.8	0.586
Urea (mg/dl)	36.9±25	29.3±15.4	0.166
Serum creatinine (mg/dl)	1.2±0.8	1.1±0.6	0.367
HbA1c (%)	7.1±1.9	6.5±1.5	0.143
Total cholesterol (mg/dl)	143±52	167±78	0.335
LDL	118±40	125±41	0.461
HDL	35±14	36±9	0.224
TG	140±49	163±76	0.115

95% (0.715-3.213), diabetes mellitus p=0.294, OR: 1.478; CI 95%: (0.704-2.659), ejection fraction p=0.434; OR: 0.523; CI 95%: (0.152-1.745), and cardiopulmonary bypass (CPB) time p=0.357; OR: 1.097; CI 95%: (1.082-1.124) (Table 3).

Similar to the results in univariate analysis, MHR level p=0.005, OR: 1.215; CI 95%: (0.593-2.356), monocyte number p=0.023, OR: 1.645; CI 95%: (1.063-2.654) and age> 60 years p=0.034; OR: 1.223; CI 95%: (1.027-1.783) was defined as an independent predictor of postoperative AF after CABG surgery in multivariate analyzes (Table 4).

Additionally, it was determined a cut-off level of 0.022 for MHR level for predicting POAF with a sensitivity of %71.2 and a specificity of %51.4, in receiver operating characteristic (ROC) curve analysis; area under the curve: 0.737, %95 CI: 0.628-0.836, p=0.003) (Fig. 1).

Discussion

Atrial fibrillation occurs in approximately 60%, depending on the type of operation after open heart surgery, and usually occurs on the second or third postoperative day. Postoperative atrial fibrillation is associated with increased morbidity and mortality.[7] Cardiac surgery is associated with systemic inflammatory response, including increased cytokines and activation of endothelial and leukocyte responses.

Previous studies have reported several inflammatory markers, such as CRP, interleukin-6, interleukin-8, interleukin-6, and complement, associated with an increased incidence of POAF.[8]

Inflammatory mediators due to CPB and ischemia repurfusion may cause myocardial depression and apoptosis. The re-

Table 3. Results from ROC analysis

Cutt-of point	Specificity	Sensitivity	AUC	p	95% CI
0.022	51.4%	71.2%	0.737	0.003	0.628-0.836

Table 4. Patients' data analysis.

	Univariate		Multivariate
	ODDS (%95C.I.Lower Upper)	p	ODDS (%95C.I.Lower Upper)
MHR	1.589 (0.543-4.346)	0.012	1.215 (0.593-2.356)
Monocyte count (10^3/ul±SD)	1.137 (0.635-2.406)	0.001	1.645 (1.063-2.654)
Age >60	0.396 (0.159-0.921)	0.026	1.223 (1.027-1.783)
Sex	1.096 (0.504-2.324)	0.412	
Hypertension	1.507 (0.715-3.213)	0.472	
DiabetesMellitus	1.478 (0.704-2.659)	0.294	
LVEF	0.523 (0.152-1.745)	0.434	
CPB time	1.097 (1.082-1.124)	0.357	

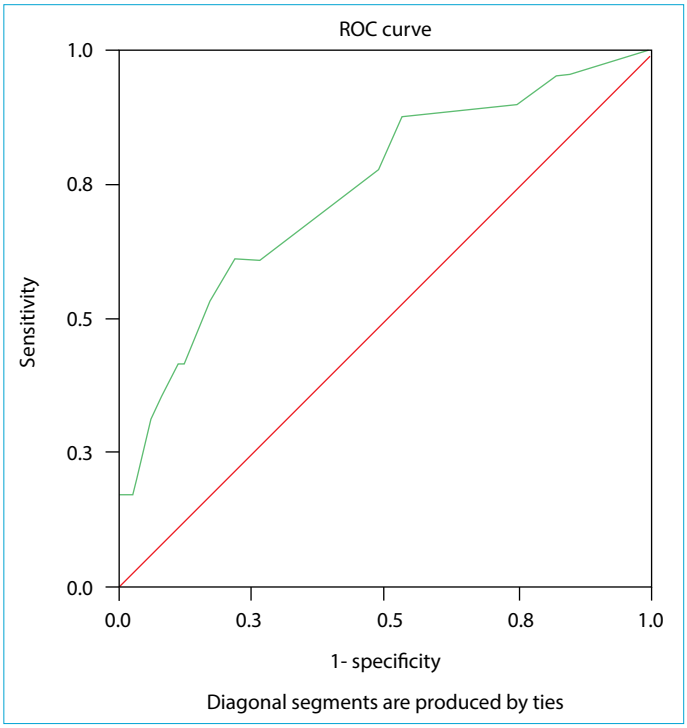

Figure 1. ROC curve analysis.

sulting changes may cause deterioration of the electrical activity of the heart and trigger the development of POAF.[9–11]

The relationship of HDL with AF due to its anti-inflammatory and antioxidant effects has been investigated many times.[12] However, few studies have investigated the link between monocyte levels and atrial fibrillation.

In this study, we evaluated the effect of MHR levels on POAF development in patients undergoing CABG. In this study, a correlation was found between high MHR values and POAF.

MHR levels and monocyte counts were significantly higher in patients with POAF than those with sinus rhythm. This supports the role of inflammation in AF after open heart surgery.

Remodeling caused by atrial fibrosis plays an important prognostic and therapeutic role in atrial fibrillation. Atrial fibrosis is thought to result from inflammation and oxidative stress. Monocytes are the most important source of proinflammatory and prooxidative cytokines and monocytes play an important role in atrial electrical and structural remodeling.[13] Therefore, MHR combines two main processes, inflammation and oxidative stress.

In a study, left atrial dimensions and monocyte levels of persistent AF patients were found to be greater than those of paroxysmal AF patients.[14]

A recent study showed that MHR may be an important biomarker in addition to AF history and LA diameters.[15]

Conclusion

This study, which provides additional evidence for the relationship between inflammation and POAF, will contribute to previous studies on prediction and prevention of POAF development.

Disclosures

Ethics Committee Approval: The Ethics Committee of Lokman Hekim University provided the ethics committee approval for this study (25.12.2019-2019037).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – G.E., E.D.; Design – E.D., U.M.; Supervision – G.A., C.B.; Materials – E.D.; Data collection &/or processing – E.D., H.S.; Analysis and/or interpretation – H.K., H.S.; Literature search – G.E., H.K.; Writing – E.D., G.E.; Critical review – C.B.

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