



## Are preoperative monocytes and HDL values an early predictor of recurrence in the surgical ablation treatment of atrial fibrillation?

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### Research Article

#### History

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#### ABSTRACT

**Background:** Monocyte HDL (high-density lipoprotein) cholesterol ratio has been accepted as a newly emerging cardiovascular prognostic marker. This study aims to investigate the determinants of monocyte and HDL cholesterol values in the early recurrence of atrial fibrillation (AF) treated with cryoablation and radiofrequency ablation.

**Methods:** This retrospective study was conducted between September 2006 and July 2014 in the Department of Cardiovascular Surgery, Adana City Hospital, Health Sciences University, including 100 patients who underwent surgical AF ablation with open heart surgery. Logistic regression analysis was used to determine monocytes and HDL cholesterol values, which are among the factors affecting recurrence in the first three months postoperatively.

**Results:** 100 patients who underwent surgical ablation together with open heart surgery were evaluated for early postoperative recurrence. According to the logistic regression analysis, the most effective features and measurements for early recurrence were diabetes mellitus (DM), AF duration, left atrial diameter, low HDL cholesterol, and high monocyte values before the procedure.

**Conclusion:** Preoperative low HDL and high monocyte values can be considered a determining factor for early recurrence in surgical ablation treatment of AF.

**Keywords:** Monocytes, ablation, atrial fibrillation

## Preoperatif monosit ve HDL değerleri atriyal fibrilasyonun cerrahi ablasyon tedavisinde rekürrensin erken belirleyicisi midir?

#### Süreç

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#### Öz

**Amaç:** Monosit HDL (high-density lipoprotein) kolesterol oranı yeni çıkan bir kardiyovasküler prognostik marker olarak kabul edilmiştir. Bu çalışmanın amacı kriyoablasyon ve radyofrekans ablasyon uygulanan atriyal fibrilasyon (AF) tedavisinde erken dönem rekürrensinde monosit ve HDL kolesterol değerlerinin belirleyiciliğini araştırmaktır.

**Yöntemler:** Bu retrospektif çalışmamız Eylül 2006 ile Temmuz 2014 tarihleri arasında, Sağlık Bilimleri Üniversitesi Adana Şehir Hastanesi Kalp ve Damar Cerrahisi kliniğinde açık kalp cerrahisi ile birlikte cerrahi AF ablasyonu uygulanan 100 hasta dahil edilerek yürütüldü. Postoperatif ilk 3 ay içinde rekürrensi etkileyen faktörlerden monosit ve HDL kolesterol değerlerinin belirleyiciliği için logistik regresyon analizi kullanıldı.

**Bulgular:** Açık kalp cerrahisi ile birlikte cerrahi ablasyon uygulanan 100 hasta postoperatif erken rekürrens açısından değerlendirildi. Logistik regresyon analizine göre erken rekürrensin görülmesine en etkili özellik ve ölçümler diabetes mellitus (DM), AF süresi, sol atriyum çapı ve işlem öncesi düşük HDL kolesterol ve yüksek monosit değerleri bulunmuştur.

**Sonuç:** Preoperatif düşük HDL ve yüksek monosit değerleri AF'nin cerrahi ablasyon tedavisinde erken rekürrensi belirleyici bir faktör olarak düşünülebilir.

**Anahtar sözcükler:** Monosit, ablasyon, atriyal fibrilasyon

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## Introduction

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia that develops as a result of the irregular electrical activity of the atria and is characterized by a loss of atrial mechanical function. The prevalence of AF is around 1.5-2% in adults, and it is known to increase with age. One of the most critical and devastating clinical conditions of AF is stroke. In addition, AF is a strong and independent risk factor for mortality and morbidity<sup>1</sup>. AF is particularly important for patients undergoing cardiac surgery because 30-84% of patients admitted for mitral valve surgery have chronic AF. This rate is 5% for coronary artery patients<sup>2</sup>. Although AF is so common, medical treatment has been tried for a long time, but the desired level of success has not been achieved. Different surgical techniques have been developed for this purpose. The Maze III procedure, which was developed and subsequently modified twice by James Cox et al., has become the gold standard. However, radiofrequency and cryoablation methods are widely used today because this procedure takes a lot of time, has a high risk of complications, and requires a lot of experience. However, recurrence of AF is common and frequently occurs in the first three months after ablation<sup>3</sup>.

Inflammation and oxidative stress have been shown to contribute significantly to the structural formation of AF. It has been shown that CRP, IL-1, IL-6, IL-8, and TNF are closely related to thrombogenesis and electrical and structural formation in AF. Recent studies have supported that the monocyte/HDL cholesterol (M/H) ratio is an inflammation and oxidative stress factor and can be a cardiovascular prognostic biomarker. Canpolat et al. evaluated the M/H value in late recurrence after catheter ablation in patients with non-valvular AF<sup>4</sup>. Adil et al. In another study conducted by Maze, they showed the prognostic M/H value that determines the recurrence in the early period after the procedure<sup>5</sup>. Our study investigated the determinants of preoperative monocytes and HDL cholesterol values in the early recurrence of AF after surgical ablation.

## MATERIALS AND METHODS

### Patients

In this study, 100 patients who underwent surgical AF with open heart surgery at the Department of Cardiovascular Surgery of Adana City Hospital, Health Sciences University, between September 2006 and July 2014 were retrospectively analyzed. Radiofrequency ablation methods were applied to the patients as surgical ablation. He was examined for early recurrence after the surgical procedure. The study was conducted according to the recommendations set by the Declaration of Helsinki for Human Subjects Biomedical Research, and the institutional ethics committee approved the protocol.

### Determination of Clinical Information and Risk Factors

Demographic data (age, gender, DM, HT, hyperlipidemia (HPL), smoking, and family history of coronary artery disease) of the patients included in the study were recorded. Diabetic patients using oral antidiabetic and/or insulin or fasting blood glucose levels above 126 mg/dL in at least two measurements were recorded as diabetic patients defined. The presence of HPL was defined in patients with total cholesterol of 200 mg/dL or a low-density lipoprotein (LDL) value of 100 mg/dL according to the 'Adult Treatment Panel III' guideline or in patients receiving lipid-lowering drug therapy.

Standard transthoracic echocardiography (TTE) examinations were performed with the EPIQ 7 TTE device. TTE examinations were performed with the patient in the supine position or lying on the left side using appropriate echocardiographic windows using Mmod, two-dimensional, color Doppler, and pulse wave Doppler echocardiography methods. Left ventricular and end-systolic dimensions, ejection fraction (EF), posterior wall thicknesses, interventricular septum thicknesses, and left atrium dimensions were measured.

### Surgical Ablation Methods and Follow-up

After the median sternotomy, bicaval cannulation was performed in all patients, and cardiopulmonary bypass (CPB) was performed. Antegrade and retrograde isothermal blood cardioplegia were used for myocardial protection. Medtronic Cardioblate BP ablation system (Cardioblate, Medtronic Inc, Minnesota, USA) was used for bipolar radiofrequency ablation. Thrombectomy was performed first in cases with thrombosis. Left pulmonary veins were explored and freed. Bipolar ablation was applied epicardially, and both pulmonary veins were isolated as islands. Then, the lesion was created by applying epicardial ablation to the left atrial appendage. A lesion was created around both right pulmonary veins by means of a bipolar catheter, and the left atriotomy incision was combined.

Amiodoron loading infusion (5 mg/kg/hour) was applied at the end of the CPB, and amiodarone maintenance (5 micrograms/kg/minute) treatment was applied in the intensive care unit. At discharge, the patients were given amiodoron therapy at a dose of 400 mg/day for 60 days. Electrocardiographs of the patients were evaluated for the first three months.

### Statistical analysis

IBM SPSS 20.0 statistical program was used to analyze the data. Categorical measurements were summarized as numbers and percentages, and numerical measurements as mean and standard deviation (median and minimum-maximum where appropriate). When comparing categorical measures across treatments, a Chi-square test statistic was used. T-test was used in independent groups to compare

numerical measurements between treatments. Logistic regression analysis was used to determine the most effective features and measures in determining the presence of recurrence. Statistical significance level was taken as 0.05 in all tests.

**Results**

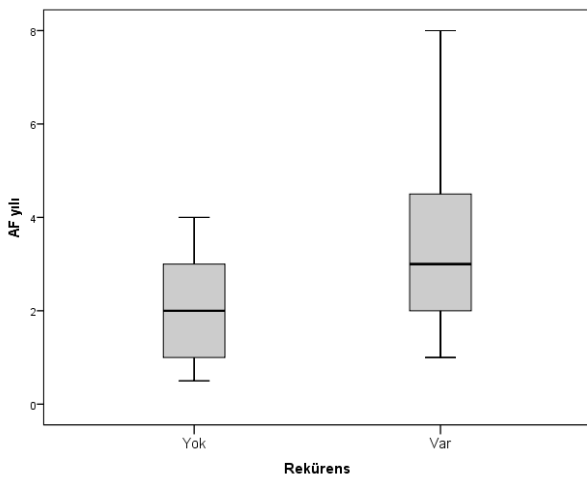
One hundred patients who underwent surgical AF ablation were included in our study. All patients were followed up after surgery. The patients' clinical, echocardiographic, and laboratory parameters were compared in both groups with and without early recurrence (Table 1). Smoking was found to be significant in those with recurrence (P: 0.022). In the

analysis of categorical and numerical measurements, the increase in AF year, left ventricular end-diastolic diameter (LVDd), left ventricular end-systolic diameter (LVSD), and left atrial diameter (LA diameter) was statistically significant (Table 2). According to the logistic regression analysis, recurrence was determined by the presence of DM in patients (P: 0.04), AF durations (every 1-year increase) (P: 0.03), and left atrial diameter (each 1 unit increase) (LA) ( P: 0.02) values. Every 0.1 unit increase in monocytes before surgical ablation (P: 0.03) and a decrease of 1 unit in preoperative HDL values (P: 0.009) were statistically significant (Table 3).

**Table 1: Analysis of categorical measures to detect early postoperative recurrence**

	recurrence		P	Odds Ratio (%95 GA)
	No	Yes		
Age, average±SS	56,2±13,9	61,4±15,9	0,116	--
Sex, average (%)			0,225	--
Male	37 (%51)	10 (%37)		
Female	36 (%49)	17 (%63)		
BMI, average±SS	25,5±3,9	26,2±3,5	0,369	--
Cigarette, number (%) *			0,022	2,85 (1,15-7,12)
Yes	53 (%80)	13 (%20)		
No	20 (%59)	14 (%41)		

BMI, body mass index; SS, standard deviation



**Recurrence**

**Graph 1: AF year in determining early recurrence in patients undergoing surgical ablation AF year**

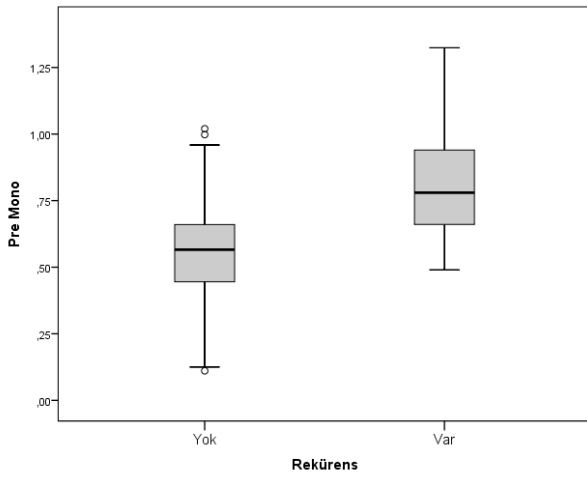
**Table 2: Analysis of risk factors in early recurrence detection**

	recurrence		P	Odds Ratio (%95 GA)
	No	Yes		
AF year, average±SS	2,2±1,0	3,4±1,9	0,001	1,99 (1,35-2,95)
median (min-max)	2 (1-4)	3 (1-8)		
EF, average±SS	52,3±7,4	48,9±12,2	0,183	--
LVDd, average±SS	4,8±0,4	5,1±0,4	0,007	4,76 (1,45-15,61)
LVSd, average±SS	3,7±0,4	4,1±0,5	<0,001	6,10 (2,13-17,48)
LA diameter, average±SS	4,9±0,5	5,4±0,5	<0,001	6,73 (2,63-17,25)

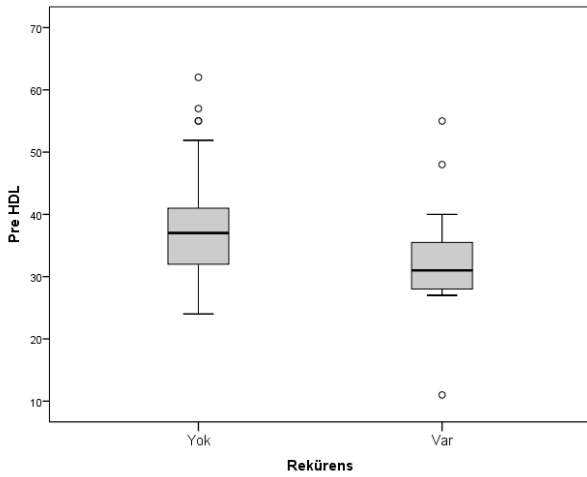
EF, ejection fraction; LVDd, left ventricular end-diastolic diameter; LVSd, left ventricular end-systolic diameter; LA, left atrium

**Table 3: The most effective features and measures in determining recurrence according to logistic regression analysis HDL, high-density lipoprotein**

	P	Odds Ratio	OR için %95 Güven aralığı
DM existance	0,041	6,72	1,08-41-75
AF period (every one year increase)	0,035	1,87	1,05-3,36
LA diameter (every 1 unit increment)	0,021	5,70	1,30-25,02
Preoperative monocytes (every 0.1 unit increase)	0,034	1,55	1,03-2,33
Preoperative HDL (every 1 unit decrease)	0,009	1,17	1,04-1,31



**Graph 2: The effect of preoperative monocytes and HDL values on recurrence**



**Graph 3: PreHDL Levels and Recurrence**

## Discussion

Inflammation and oxidative stress are essential in the pathogenesis of atrial fibrillation and cardiovascular diseases. Inflammatory mediators are closely related to the electrical and structural new formation of the atria 6. Experimental and clinical studies have shown that oxidative stress is closely related to AF 7. Monocytes are important sources of proinflammatory and pro-oxidant cytokines. It plays a key role in initiating, maintaining, and recurrence of AF triggered by inflammatory events. Monocytes and macrophage infiltration have been detected in the atria of patients with AF 8.

Dyslipidemia, especially high triglyceride (TG), high LDL cholesterol, and low HDL cholesterol levels, are risk factors for cardiovascular disease 9. HDL cholesterol has antioxidant, anti-inflammatory, and antithrombotic effects such as reducing macrophage accumulation,

inhibiting the transmigration of monocytes, increasing nitric oxide synthase expression in endothelial tissues, and protecting endothelial cells 10. However, the relationship between lipid profile and AF recurrence is inconsistent. Increased AF recurrence was demonstrated in patients with low blood HDL cholesterol levels and high TG levels. Still, no correlation was observed between total cholesterol or LDL cholesterol levels and AF 11.

Smoking; the relationship between systemic inflammatory response, vascular endothelial damage, and atherosclerosis has been defined by studies 12. In a study by Köylü et al., erythrocyte, hemoglobin, hematocrit, monocytes, HDL cholesterol, and monocyte/HDL averages were found to be significantly higher in non-smokers 13.

In this retrospective study, we analyzed the factors affecting early recurrence as an inflammatory parameter in 100 patients with AF who underwent surgical ablation with open heart surgery. Our study found that many factors, such as AF year, LVDd, LVSD, LA diameter, and the presence of Diabetes Mellitus (DM), significantly affect the early recurrence of AF. The relationship between inflammatory parameters, preoperative monocytes, HDL cholesterol levels, and early recurrence of AF was investigated. It was determined that every 0.1 unit increase in preoperative monocyte values and every 1 unit decrease in HDL cholesterol levels significantly affect the early recurrence of AF after surgical ablation.

In our study, early recurrence after surgical ablation was significantly higher in individuals who actively quit smoking before surgery but were ex-smokers.

Limitations of our study: Being a single-center study, insufficient measurement of serum HDL and monocyte levels at once and details of surgical procedures are the limitations of our study

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