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Assessment of the Efficacy of the Hemoglobin, Albumin, Lymphocyte, and Platelet Score in Predicting Recurrence of Atrial Fibrillation Following Cryo-Balloon Ablation

Kriyobalon Ablasyonu Sonrası Atriyal Fibrilasyon Rekürrensini Tahmin Etmede Hemoglobin, Albümin, Lenfosit, Trombosit Skorunun Etkinliğinin Değerlendirilmesi

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score has gained interest as a potential predictive biomarker for various clinical outcomes across multiple diseases. This study aimed to evaluate the efficacy of the HALP score in predicting the recurrence of atrial fibrillation (AF) following cryo-balloon ablation (CBA).

Method: A total of 399 patients who underwent CBA for AF were included in the study. Patients were divided into three equal groups based on their HALP scores, and post-procedural AF recurrence was evaluated retrospectively across these groups.

Results: After adjusting for confounding independent variables, patients in Tertile 1 had 2.1-fold higher rate of AF recurrence compared to those in Tertile 3, which served as the reference group. Receiver operating characteristic (ROC) curve analysis showed that the HALP score predicted AF recurrence with an area under the curve (AUC) of 0.69, 65% sensitivity, and 65% specificity (hazard ratio [HR]: 0.69, 95% confidence interval [CI]: 0.63-0.74, P < 0.001).

Conclusion: This study suggests that the HALP score may serve as an independent predictor of AF recurrence following CBA.

Keywords: Atrial fibrillation, cryo-balloon ablation, HALP score

ÖZET

Amaç: Hemoglobin, Albümin, Lenfosit, Trombosit (HALP) skoru, bir çok hastalıkta çeşitli klinik sonuçları tahmin etmek için potansiyel bir öngörücü biyobelirteç olarak kullanılmaktadır. Bu çalışma, kriyobalon ablasyonundan (KBA) sonra atriyal fibrilasyonun (AF) rekürrensini tahmin etmede HALP skorunun etkinliğini değerlendirmeyi amaçlamıştır.

Yöntem: Çalışmaya AF nedeniyle KBA yapılan ve HALP skorlarına göre üç eşit gruba ayrılan 399 hasta dahil edildi ve işlem sonrası AF rekürrensi gruplar arasında retrospektif olarak değerlendirildi.

Bulgular: Karışıklığa neden olan bağımsız parametreler çıkarıldıktan sonra, Tertil 1'e dahil edilen hastaların, referans grup olarak varsayılan Tertil 3'e kıyasla AF tekrarlama oranlarının 2,1 kat daha yüksek olduğu bulundu. ROC eğrisi analizi, HALP skorunun AF rekürrensini 0,69 AUC, %65 duyarlılık ve %65 özgüllükle öngördüğünü gösterdi. (HR: 0.69, 95% CI: 0.63-0.74, P < 0.001).

Sonuç: Bu çalışma, HALP skorunun KBA'dan sonra AF tekrarının bağımsız bir öngörücüsü olarak işlev görebileceğini ortaya koydu.

Anahtar Kelimeler: Atriyal fibrilasyon, kriyobalon ablasyonu, HALP skoru

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Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with an increased risk of stroke, heart failure, and sudden death.[1] AF is a chronic, progressive condition characterized by episodes of exacerbation and remission. Initially, the pulmonary veins (PV) are primarily responsible for triggering AF through rapid, repetitive discharges, while micro-reentrant circuits near the PV-left atrial

(LA) junction and within the atrial body contribute to its maintenance.[2] With advances in cardiac electrophysiology, pulmonary vein isolation (PVI) has emerged as an effective treatment for AF and remains the cornerstone of catheter ablation (CA) for all types of AF. Current guidelines recommend CA for patients who exhibit symptoms and are resistant to pharmacological therapy, regardless of AF subtype.[3] Compared to rate control strategies with antiarrhythmic drugs, CA has been shown to significantly reduce both mortality and morbidity.[4] Patients with persistent AF who undergo cryo-balloon ablation (CBA) with PVI have shown a 40% recurrence rate of atrial arrhythmias within one year.[5] The likelihood of AF recurrence and procedural complications after CBA may vary depending on patient-specific characteristics. In this context, biomarkers such as the hemoglobin, albumin, lymphocyte, and platelet (HALP) score may be useful in predicting treatment outcomes. The HALP score has emerged as an immune-nutritional biomarker, utilizing commonly measured parameters to provide a single composite score that reflects a patient's overall health status.[6] These four parameters are important for evaluating both immunological and nutritional status, and their combination offers a more accurate prediction of inflammatory prognosis than any single marker alone. Originally developed by Chen et al.[7] to predict outcomes in gastric cancer, the HALP score is calculated using the formula: {hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L)} / platelets (/L). These values are easily obtainable from standard laboratory tests used in routine clinical practice. Recent studies have also shown that the HALP score may predict mortality risk in patients with cardiovascular disease.[8,9] This study aims to evaluate the utility of the HALP score in predicting AF recurrence after CBA in patients with nonvalvular atrial fibrillation (NVAF).

Materials and Methods

Study Population and Design

This retrospective, single-center study included 399 patients who underwent CBA for nonvalvular AF between January 2019 and June 2022. Exclusion criteria were: severe valvular disease; recent myocardial infarction (MI) or percutaneous coronary intervention (PCI) within the previous three months; prior AF ablation; the need for additional ablation procedures such as those for atrial tachycardia or atrial flutter; inflammatory conditions (e.g., sepsis, malignancy, rheumatologic disorders); recent stroke within the past month; severe anemia; ejection fraction below 30%; and acute kidney injury. Demographic information, preoperative transthoracic echocardiography (TTE) and electrocardiographic (ECG) findings, laboratory values, medications, procedural characteristics, and complications were collected from hospital medical records and the National Health Database. Long-term follow-up data were obtained through periodic patient evaluations documented in hospital records. All procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki and its subsequent amendments. The study received approval from the Health Sciences University Hamidiye Scientific Research Ethics Board (Approval Number: 14/18, Date: 28.11.2024), and written informed consent was obtained from all patients prior to undergoing CBA (HFM No: 24/570).

ABBREVIATIONS

AF	Atrial fibrillation
CA	Catheter ablation
CBA	Cryo-balloon ablation
CI	Confidence interval
ECG	Electrocardiography
HALP	Hemoglobin, Albumin, Lymphocyte, and Platelet
HDL-C	High-density lipoprotein cholesterol
HR	Hazard ratio
HT	Hypertension
LA	Left atrium
LAAP	Left atrial anteroposterior diameter
LDL-C	Low-density lipoprotein cholesterol
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
NOAC	Novel oral anticoagulant
NVAF	Nonvalvular atrial fibrillation
PCI	Percutaneous coronary intervention
PV	Pulmonary veins
ROC	Receiver operating characteristic
TEE	Transesophageal echocardiography
TSH	Thyroid-stimulating hormone
TTE	Transthoracic echocardiography
VKA	Vitamin K antagonist

Definitions and Study Outcome

AF was defined as the absence of P waves and the presence of irregular RR intervals lasting more than 30 seconds, as observed on a standard 12-lead ECG or during 24-hour rhythm monitoring. Paroxysmal AF was characterized as an arrhythmia that terminates spontaneously or with intervention within seven days of onset. In contrast, chronic AF was defined as an arrhythmia persisting for more than seven days and resolved with cardioversion (either pharmacological or electrical) after this period.[10] HALP scores were calculated using laboratory data from the most recent blood samples obtained immediately prior to the CBA procedure. All blood samples were collected from the antecubital vein following at least 8 hours of fasting and were analyzed at a single clinical laboratory. Serum levels of glucose, thyroid-stimulating hormone (TSH), albumin, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides were measured using a Cobas c 501 analyzer (Roche Diagnostics, Mannheim, Germany). Complete blood counts, including hemoglobin, white blood cell count (neutrophils and lymphocytes), and platelet measurements, were performed using the Sysmex K-1000 Hematology Analyzer (Guangdong, China). Serum creatinine levels were measured using the kinetic alkaline picrate (Jaffe) method. The HALP score was calculated using the following formula: hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L) ÷ platelets (/L).[7]

All patients underwent TTE to assess valvular disease, left ventricular ejection fraction (LVEF), and LA dimensions prior to the CBA procedure. Transesophageal echocardiography (TEE) was performed in all patients 6-12 hours before CBA to exclude intracardiac thrombi, using deep sedation without intubation. The CBA procedures were conducted by two operators and

Table 1. Comparison of Demographic and Clinical Characteristics of Patients Categorized by HALP Score Tertiles

	HALP Score Tertiles			
	Tertile 1 (n = 133)	**Tertile 2 (n = 133)**	**Tertile 3 (n = 133)**	**P**
Age, years	62 (55-68)	59 (50-66)	58 (47-63)	<0.001
Male Gender	72 (54.1%)	80 (60.2%)	89 (66.9%)	0.103
Hypertension	63 (47.4%)	53 (39.8%)	44 (33.1%)	0.059
Diabetes Mellitus	29 (21.8%)	21 (15.8%)	27 (20.3%)	0.433
Smoking	11 (8.3%)	12 (9.0%)	13 (9.8%)	0.912
Chronic Renal Failure	11 (8.3%)	11 (8.3%)	8 (6.0%)	0.715
Congestive Heart Failure	9 (6.8%)	7 (5.3%)	8 (6.0%)	0.875
Chronic Obstructive Pulmonary Disease	15 (11.3%)	19 (14.5%)	19 (14.4%)	0.682
Obstructive Sleep Apnea Syndrome	36 (27.1%)	28 (21.2%)	28 (21.2%)	0.427
Coronary Artery Disease	27 (20.3%)	16 (12.0%)	24 (18.0%)	0.176
Percutaneous Coronary Intervention	14 (10.5%)	7 (5.3%)	12 (9.0%)	0.256
Coronary Artery Bypass Grafting	4 (3.0%)	2 (1.5%)	5 (3.8%)	0.494
Cerebrovascular Accident	2 (1.5%)	2 (1.5%)	6 (4.5%)	0.218
Atrial Fibrillation Type				
Paroxysmal	61 (45.9%)	74 (55.6%)	83 (62.4%)	0.024
Persistent	25 (18.8%)	22 (16.5%)	28 (21.1%)	0.642
Long Persistent	47 (35.3%)	37 (27.8%)	22 (16.5%)	0.002
Follow-up, months	12 (4-26)	17 (7-25)	21 (12-28)	
Perioperative Medication				
Beta-Blockers	79 (61.2%)	70 (54.3%)	84 (65.6%)	0.171
ACEIs or ARBs	43 (33.3%)	31 (24.0%)	37 (29.1%)	0.256
Spironolactone	4 (3.1%)	8 (6.2%)	7 (5.5%)	0.462
Class I Antiarrhythmic Drugs	46 (35.9%)	46 (35.9%)	42 (32.8%)	0.832
Sotalol	7 (5.4%)	9 (7.0%)	7 (5.5%)	0.839
Amiodarone	27 (20.9%)	23 (17.8%)	32 (25.0%)	0.370
Warfarin	27 (20.9%)	21 (16.2%)	23 (18.0%)	0.607
New Oral Anticoagulants	82 (63.6%)	83 (64.3%)	83 (64.3%)	0.989

Continuous variables are presented as median and interquartile range. Nominal variables are presented as frequency (%). ACEIs, Angiotensin-Converting Enzyme Inhibitors; AF, Atrial Fibrillation; ARBs, Angiotensin II Receptor Blockers.

included continuous invasive arterial blood pressure monitoring, oxygen saturation measurement, and ECG monitoring. Unfractionated heparin was administered via intravenous boluses after transseptal puncture to maintain an active clotting time of 300-350 seconds. Transseptal puncture was performed using a steerable 12 F sheath (FlexCath Advance, AchieveTM; Medtronic, Minneapolis, MN, USA) to access the LA. The Achieve Mapping Catheter was used to guide the Arctic Front Advance Cryoablation Catheter (Medtronic, Minneapolis, MN, USA) through the FlexCath sheath into the antrum of each PV. Following contrast injection and confirmation of PV obstruction, a freeze-thaw-freeze protocol was applied, with each freeze lasting 240 seconds, to achieve PVI. To prevent phrenic nerve injury during cryoenergy delivery to the right PVs, a 6-F decapolar coronary sinus catheter was positioned in the superior vena cava, and diaphragmatic movement was monitored both manually and fluoroscopically. Successful PVI was defined as the elimination of all PV potentials recorded by the Achieve mapping catheter, along with demonstration of either: (1) pacing from the electrode catheter positioned in the coronary sinus with no conduction to the Achieve mapping catheter in the PV (entry block maneuver), or (2) pacing from the circular mapping catheter in the PV with no conduction to the electrode catheter in the coronary sinus (exit block maneuver).

Follow-Up and Medical Treatment

At the conclusion of the procedure, TTE was performed to rule out pericardial effusion. Post-procedure, all patients were monitored for at least 24 hours using telemetric ECG. They were prescribed oral anticoagulant therapy for a minimum of three months, using either a vitamin K antagonist (VKA) or a novel oral anticoagulant (NOAC). At the three-month follow-up, the decision to continue long-term NOAC therapy was based on each patient's CHA_2DS_2-VASc score (Valvular Congestive Heart failure, Hypertension, Age ≥ 75, Diabetes, Stroke – Vascular disease, Age 65–74, and Sex category score). Antiarrhythmic medications administered before the procedure were continued after treatment. Patients were evaluated at our outpatient clinic at one, three, six, and twelve months post-procedure, and annually thereafter. Patients were assessed for symptoms at each follow-up visit, and a 12-lead ECG was performed. When clinically indicated, 24-hour Holter monitoring and TTE were also conducted. During follow-up, any episode of AF lasting at least 30 seconds was considered a recurrence. The first three months following ablation were designated as the blanking period, and recurrences occurring within this timeframe were classified as early recurrences. During this period, several episodes resolved spontaneously with a return to sinus rhythm, while others required electrical or pharmacological cardioversion. An AF episode lasting at least 30 seconds after the blanking period following CBA was defined as a long-term recurrence.

Statistical Analysis

At admission, HALP scores were used to categorize the study population into tertiles. Comparisons between groups were made with respect to medical treatments, echocardiographic parameters, laboratory values, and baseline characteristics. Normality was assessed using the Kolmogorov-Smirnov test. For numerical variables, data are presented as median and interquartile range. The Kruskal-Wallis test revealed that all continuous variables had skewed distributions. Categorical variables are presented as numbers and percentages, and were analyzed using Pearson's chi-square test. A multivariable model was used to compare the three groups. To assess AF recurrence in comparison to tertile 3, a forward Cox regression analysis was performed. The hazard ratio (HR) was used to indicate the relative risk of AF recurrence compared to tertile 3. Additionally, a model was constructed to evaluate the influence of potential confounders on the association between HALP score and AF recurrence. Each model was either (1) unadjusted or (2) adjusted for age, left atrial anteroposterior diameter, and AF type. All HRs were reported with 95% confidence intervals (CIs), and a two-tailed p-value of less than 0.05 was considered statistically significant. The optimal cut-off values for the HALP score in predicting AF recurrence were determined using nonparametric receiver-operating characteristic (ROC) curve analysis. Statistical analyses were performed using the Statistical Package for the Social Sciences, version 20.0 (IBM Corp., Armonk, New York, USA).

Results

The study population included 399 patients who had undergone CBA for AF. Patients were divided into three equal tertiles based on HALP score, ranging from lowest to highest. The median HALP score was 0.33 (0.26-0.40) in tertile 1, 0.57 (0.51-0.62) in tertile 2, and 0.87 (0.76-1.08) in tertile 3. here were no significant differences in comorbidities among the three groups, except for mean age and rates of long-term AF: age: 62 (55-68), 59 (50-66), 58 (47-63); long-term AF: 74 (55.6%), 43 (32.3%), 34 (25.6%) (P < 0.001). Patients in the lowest HALP tertile were older and had a higher prevalence of long-term AF compared to those in other groups. The average follow-up duration was 12 months for tertile 1, 17 months for tertile 2, and 21 months for tertile 3. The demographic and clinical characteristics of patients, categorized by HALP scores, are presented in Table 1. No differences were observed between the groups regarding the initiation of anticoagulation or antiarrhythmic medications during the periprocedural interval.

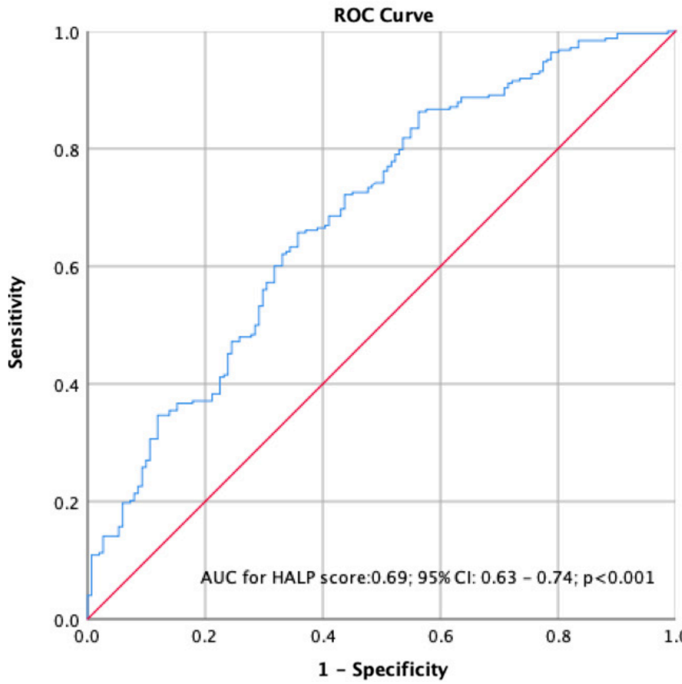

Figure 1. Receiver operating characteristic (ROC) curve analysis of the HALP score (hemoglobin, albumin, lymphocyte, and platelet score) for predicting AF recurrence after CBA.

Table 2 provides a comparison of laboratory and TTE parameters among the groups. No substantial differences were noted in TTE parameters between the groups. However, in the low HALP score group (tertile 1), hemoglobin, lymphocyte count, platelet count, and albumin levels were lower compared to the other two groups.

As summarized in Table 3, univariate Cox proportional regression analysis of clinical, echocardiographic, and laboratory data identified age, hypertension (HT), male sex, left atrial anteroposterior diameter (LAAP), paroxysmal AF, and HALP score as statistically significant factors associated with long-term AF recurrence. In the multivariate analysis, age, LAAP, paroxysmal AF, and HALP score emerged as independent predictors.

Cox regression models for AF recurrences based on HALP score tertiles are shown in Table 4. AF recurrence occurred in 55.6% of patients in tertile 1, 32.3% in tertile 2, and 25.6% in tertile 3 following CBA. After adjusting for confounding independent variables, including age, LA anteroposterior diameter, and AF type, patients in tertile 1 were found to have 2.1-fold higher risk of long-term AF recurrence compared to those in tertile 3.

The ROC curve analysis indicated that a HALP score of 0.53 demonstrated 65% sensitivity and 65% specificity, with an area under the curve (AUC) of 0.69 for predicting AF recurrence after CBA (HR: 0.69, 95% CI: 0.63-0.74, P < 0.001) (Figure 1). When

Table 2. Comparison of Laboratory and Echocardiographic Parameters of Patients According to Tertiles Determined by the HALP Score

	HALP Score Tertiles			
	Tertile 1 (n = 133)	Tertile 2 (n = 133)	Tertile 3 (n = 133)	P
Laboratory Variables at Implantation				
Hb (g/dL)	12.3 (11.5-13.9)	13.8 (12.5-14.8)	14.8 (13.5-15.5)	< 0.001
Neutrophils (cells/μL)	4.1 (3.2-5.3)	4.4 (3.5-5.0)	4.1 (3.4-5.0)	0.424
Lymphocytes	1.7 (1.4-2.2)	2.3 (2.0-2.7)	3.0 (2.3-3.6)	< 0.001
Platelet count (/mm^3)	266 (227-331)	230 (197-266)	195 (163-218)	< 0.001
Creatinine (mg/dL)	0.8 (0.7-0.9)	0.8 (0.7-1.0)	0.8 (0.7-0.9)	0.842
Urea (mg/dL)	14 (12-18)	13 (12-17)	15 (13-17)	0.261
TSH	1.6 (0.9-3.1)	1.3 (0.9-2.4)	1.4 (0.8-2.7)	0.386
AST	19 (15-22)	19 (16-26)	19 (17-24)	0.531
ALT	17 (12-22)	18 (14-26)	17 (13-24)	0.260
Glucose (mg/dL)	97 (90-110)	97 (92-113)	95 (89-105)	0.223
Albumin	3.9 (3.8-4.1)	4.0 (3.8-4.2)	4.1 (3.9-4.4)	< 0.001
Triglycerides	129 (91-194)	141 (102-196)	143 (101-217)	0.275
LDL	113 (93-136)	112 (87-135)	111 (92-139)	0.928
HDL	41 (35-51)	40 (35-50)	40 (35-50)	0.261
HALP Score	0.33 (0.26-0.40)	0.57 (0.51-0.62)	0.87 (0.76-1.08)	< 0.001
Echocardiographic Variables at Implantation				
LVEF (%)	60 (55-60)	60 (55-60)	60 (55-60)	0.789
LVEDD (mm)	48 (43-50)	48 (45-51)	48 (45-50)	0.260
LVESD (mm)	30 (26-34)	30 (27-35)	29 (26-34)	0.615
LAAP (mm)	40 (37-44)	40 (37-43)	41 (36-44)	0.607

ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; Hb, Hemoglobin; HALP, Hemoglobin, Albumin, Lymphocyte, and Platelet; HDL, High-Density Lipoprotein; LAAP, Left Atrial Anteroposterior Diameter; LDL, Low-Density Lipoprotein; LVEF, Left Vetricular Ejection Fraction; LVEDD, Left Ventricular End-Diastolic Dimension; LVESD, Left Ventricular End-Systolic Dimension; TSH, Thyroid-Stimulating Hormone.

Table 3. Univariable and Multivariable Cox Proportional Regression Analyses of Long-Term Atrial Fibrillation Recurrence After the Procedure Based on Baseline Clinical, Echocardiographic, and Laboratory Data

Univariable Analysis	P	HR (95% CI)	Multivariable Analysis	P	OR (95% CI)
Age, years	0.004	1.023 (1.007-1.039)	Age	0.012	1.012 (1.005-1.032)
Hypertension	0.037	1.408 (1.020-1.944)	Hypertension	0.248	1.240 (0.861-1.785)
Male Gender	0.043	1.425 (1.011-2.010)	Male Gender	0.175	1.013 (0.994-1.031)
Left Atrial Anteroposterior Diameter	0.001	1.052 (1.022-1.083)	Left Atrial Anteroposterior Diameter	0.011	1.040 (1.009-1.072)
Atrial Fibrillation Type (Paroxysmal)	0.004	0.605 (0.429-0.854)	Atrial Fibrillation Type (Paroxysmal)	0.043	0.805 (0.682-0.980)
HALP Score	<0.001	0.169 (0.087-0.329)	HALP Score	< 0.001	0.200 (0.103-0.389)

All clinically relevant variables were included in the model. Only variables that were statistically significant in univariate analysis (P < 0.05) are shown on the left. CI, Confidence Interval; HR, Hazard Ratio.

the study population was divided into tertiles, Kaplan-Meier analysis showed that patients in tertile 3 had a lower rate of AF recurrence during long-term follow-up compared to the other tertiles (Figure 2).

Discussion

This study demonstrated that the HALP score serves as an independent predictor of AF recurrence following CBA. This study is the first study to evaluate the HALP score in this context, making it a novel contribution to the field.

With the increasing use of AF ablation due to its effectiveness in rhythm management, CBA has emerged as a key treatment modality.[11] However, AF recurrence after ablation is a major limitation, with recurrence rates reported as high as 50% within the first year post-procedure.[12] Therefore, predicting the risk of recurrence following ablation is crucial. The mechanism of AF recurrence after CBA is influenced by both anatomical and physiological factors in the ablation area, as well as specific patient characteristics. Early recurrence often occurs during the postoperative blanking period following CBA; however,

Table 4. Cox Regression Models for Atrial Fibrillation Recurrence by HALP Score Tertile

	HALP Score Tertiles		
	T1 (n = 133)	T2 (n = 133)	T3 (n = 133)
Atrial Fibrillation Recurrences			
Number of Patients with Recurrence	74	43	34
Recurrence Rate (%)	55.6	32.3	25.6
HR for Atrial Fibrillation Recurrences (95% CI)			
Model 1: Unadjusted	2.7 (1.3-10.5)	1.9 (0.7-5.3)	1 [Reference]
Model 2: Adjusted for All Covariates[a]	3.1 (1.8-16.2)	2.5 (0.9-6.2)	1 [Reference]

CI, Confidence Interval; HR, Hazard Ratio; HALP, Hemoglobin, Albumin, Lymphocyte, and Platelet Score; [a]Only parameters that reached statistical significance in the multivariate analysis were age, left atrial anteroposterior diameter, and atrial fibrillation (AF) type.

the underlying mechanisms of this early recurrence are not yet fully understood. Research suggests a strong association with inflammation resulting from ablation-induced lesions.[13] Therefore, in our study, patients who experienced recurrence beyond the first three months, referred to as the blanking period, were considered to have an AF recurrence.

The development and maintenance of arrhythmia depend on both structural and electrical remodeling. Inflammation is recognized as a major contributor to structural remodeling, including myocyte degeneration and interstitial fibrosis.[14] Inflammation-induced fibrosis leads to conduction abnormalities that can initiate and sustain arrhythmias. Additionally, systemic inflammatory changes have been linked to prothrombotic indices, indicating that inflammation may also contribute to the hypercoagulable condition observed in AF.[15] Several studies have indicated that the HALP score may be useful in diagnosing and predicting the prognosis of various inflammatory diseases.[16-18] According to a study by Pan et al.,[9] the HALP score may also serve as a predictor of mortality in patients with cardiovascular disease. Among patients who underwent primary percutaneous intervention for ST-segment elevation myocardial infarction, a recent study found that the HALP score significantly predicted the no-reflow phenomenon and short-term mortality.[19] The HALP score is calculated by combining four hematological parameters: hemoglobin, lymphocyte count, platelet count, and albumin levels. Recent studies suggest that low hemoglobin levels and anemia may be associated with the development of new-onset AF. Furthermore, patients with anemia may have an increased risk of clinical AF recurrence.[20-22] Albumin is a protein produced by the liver that functions as a negative acute-phase reactant; decreased serum levels indicate an inflammatory condition. Albumin levels are also influenced by a patient's nutritional status and metabolic demands.[23] Hypoalbuminemia has been associated with a higher prevalence of AF.[24] Lymphocytes and platelets are essential components of the immune system. A reduced lymphocyte count and elevated platelet count may reflect compromised immunity and an increased susceptibility to infection.[25] In a study by Kutlay et al.,[26] the platelet-to-lymphocyte ratio (PLR) was found to be elevated in the AF group, emphasizing its significance in predicting the early onset of AF.

Our study corroborated previous research demonstrating a statistically significant decrease in hemoglobin, albumin, and lymphocyte levels, and an increase in platelet levels, in the group

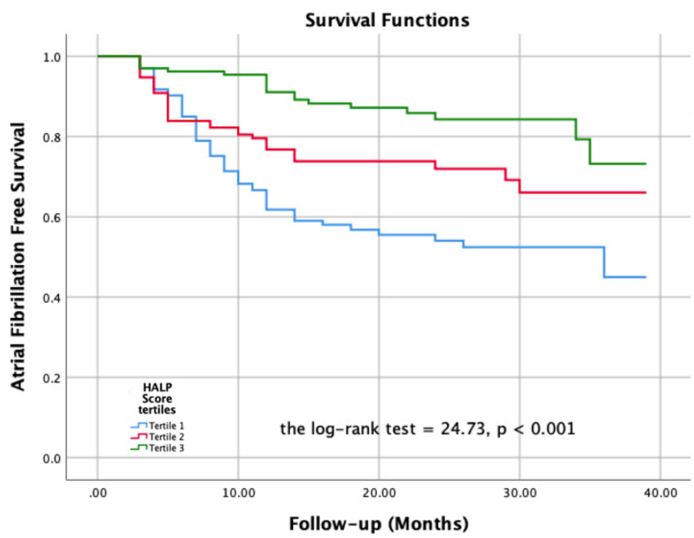

Figure 2. Kaplan-Meier curve illustrating atrial fibrillation recurrence according to HALP score (hemoglobin, albumin, lymphocyte, and platelet score) tertiles.

with the highest incidence of AF recurrence following CBA. Another key finding is that the HALP score, which incorporates parameters independently recognized as strong predictors of AF recurrence, was able to predict post-CBA AF with an AUC of 0.69. Follow-up durations in our study were shortest in the cohort with the lowest HALP score and the highest frequency of AF recurrence, while the longest follow-up durations were observed in the cohort with the highest HALP score. This was because patients who experienced AF recurrence were not followed further. Given the design of the study, this limitation is not believed to have influenced the overall outcomes. Although CBA is a widely used and effective technique for patients with AF, it is an invasive procedure that carries potential risks. Therefore, it is essential to identify patients who may be at risk of recurrence after the procedure. We believe our results are clinically applicable, as the HALP score can be easily derived from routine laboratory data. By using this score, clinicians can identify patients at high risk of long-term AF recurrence who may benefit from closer monitoring. However, our findings must be confirmed in randomized controlled studies before being implemented in routine clinical practice.

Limitations

The main limitations of our study were its retrospective design and the use of single-center data. Although all patients were followed through regular clinical visits, and those with symptoms suggestive of arrhythmia underwent thorough evaluations, advanced methods, such as remote arrhythmia monitoring, were not utilized due to the retrospective nature of the study. It is also known that patients' laboratory values can fluctuate over time, potentially affecting their HALP scores. Unfortunately, our study was based on a single set of laboratory values. Therefore, prospective studies that include multiple laboratory measurements over time may provide more accurate results. Finally, additional prospective and randomized studies are needed to validate our findings.

Conclusion

This study demonstrated that the HALP score, a reliable, simple, easily accessible, and cost-effective biomarker, can be used to predict AF recurrence following CBA.

Ethics Committee Approval: Ethics committee approval was obtained from Health Sciences University Hamidiye Scientific Research Ethics Board (Approval Number: 14/18, Date: 28.11.2024).

Informed Consent: Written informed consent was obtained from all patients included in this retrospective analysis.

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