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The value of uric acid/albumin ratio to predict cardioversion success in atrial fibrillation patients

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Abstract

Electrical cardioversion (EC) is a common procedure to restore sinus rhythm after atrial fibrillation (AF). Many factors predict EC success and long-term risk of AF recurrence. Uric acid functions as a pro-oxidant molecule at high concentrations and can trigger AF formation. Uric acid/albumin ratio (UAR) performs better than other inflammatory markers in predicting the development of AF. In this study, we aimed to evaluate the role of UAR in predicting AF recurrence after EC. Patients presenting with paroxysmal AF who underwent EC procedure for the first time were included in this study. The endpoint of the study was successful EC. All patients were monitored during the index hospitalization and routine 24-hour rhythm monitoring was performed at subsequent visits. Patients were divided into two groups according to whether they had successful EC or not. According to our data, successful EC was detected in 49 (61.3%) patients, while AF recurrence was documented in 31 (38.7%) patients during follow-up. Serum uric acid and UAR were significantly lower in patients with successful EC compared to patients with AF recurrence ($p<0.05$). To determine the UAR cut-off value for detecting EC success, the ROC curve was drawn and the best cut-off value was determined as 1.616 by using the Youden index, (AUC: 0.960, 95% CI: 0.923-0.998, $P<0.001$). Our findings suggest that UAR plays an independent role in the development of AF following successful EC.

Keywords: Atrial fibrillation, electrical cardioversion, uric acid/albumin ratio

Introduction

Electrical cardioversion (EC) is a common procedure to restore sinus rhythm (SR) after atrial fibrillation (AF) [1]. Several factors serve as predictors of successful EC and long-term risk of AF recurrence. These include the duration of AF, significant mitral valve disease, left atrial enlargement, presence of rheumatic valve disease, cardiac dimensions and function, as well as advanced age [2-4]. Nevertheless, the determinants facilitating patients' maintenance of SR following successful cardioversion, alongside the predictors of AF recurrence subsequent to successful electrical cardioversion, remain inadequately elucidated. Therefore, identifying who would benefit most from EC and treating reversible causes not only helps achieve successful EC but also reduces the risk of recurrence of AF.

Since there is a direct link between inflammation-related atrial fibrosis and conduction disorders, the relationship between various inflammatory markers and AF occurrence is frequently investigated [5,6]. Uric acid (UA), functions as an oxidant molecule when it exists at increased concentrations in the bloodstream [7]. Recent investigations have demonstrated that elevated plasma concentrations of uric acid can induce AF formation through mechanisms involving apoptosis, oxidative stress, and cardiomyocyte hypertrophy [8]. It has been determined that UAR, a new-generation inflammatory marker produced based on this thesis, performs better than other inflammatory markers in predicting the development of AF [9]. Our aim was to assess the role of UAR in predicting AF recurrence after EC.

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Material and Methods

Compliance with Ethical Standards

The ethics committee approval of the study was obtained with the decision number 2022/3976 of the Necmettin Erbakan University meeting dated 16 September 2022. Written informed consent was obtained from all participants. Artificial intelligence-supported technologies were not used in the study.

The study included patients with paroxysmal AF who underwent their first EC procedure between 2020 and 2022. Patients with persistent AF, atrial flutter (AFl), atrial tachycardia (AT), or those who had undergone ablation patients were excluded. Patients with moderate or more severe valvular heart disease, malignancy, sepsis, or conditions associated with inflammation were also excluded. Paroxysmal AF was defined as episodes spontaneously resolving within seven days, while persistent AF lasted more than 7 days but less than a year and required intervention for termination. The primary endpoint of the study was successful EC, defined as restoration of SR immediately after the EC and no documented recurrence of AF episodes during the subsequent one-year follow-up period. All patients were monitored during the index hospitalization and routine 24-hour rhythm monitoring was performed at subsequent visits. Symptomatic episodes necessitating intervention or asymptomatic instances of AF documented on 24-hour rhythm monitoring were classified as recurrences. Regardless of EC effectiveness, anticoagulation was adjusted according to individuals' CHA2DS2-VASC scores.

All patients underwent comprehensive transthoracic echocardiographic examination by an experienced cardiologist before EC. Additionally, transesophageal echocardiography was performed if necessary. All measurements were conducted in accordance with the criteria outlined by the American Society of Echocardiography [10]. Demographic and clinical characteristics, laboratory parameters, echocardiographic findings, and follow-up data were retrieved from medical records. Patients were stratified into two groups based on the success or failure of EC. The study protocol was approved by the ethics committee of our hospital.

Statistical Analysis

The study utilized SPSS software version 18.0 for Windows to analyze the data, employing various statistical methods including the Kolmogorov-Smirnov test, $\chi 2$ test, Fisher's exact test, Student's t-test, and Mann-Whitney U-test. Continuous variables were reported as mean±standard deviation for normal distribution and as median (25th-75th percentiles) for abnormal distribution. The predictive value of the uric acid ratio (UAR) in detecting EC success was assessed through area under the receiver operating characteristic (ROC) curves (AUCs), with the optimal cut-off value determined using the Youden index. A significance level of $p<0.05$ was maintained throughout the study.

Results

Between January 2020 and December 2022, a total of 80 eligible patients were enrolled in the study. Among them, 45% were male, with a mean age of 50.8±12.6 years. The average follow-up duration was 13±2.8 months. According to our data, successful EC was detected in 49 (61.3%) patients, while AF recurrence was documented in 31 (38.7%) patients during follow-up. The distribution of EC success by gender was statistically similar, and the mean age of both groups was similar ($p>0.05$). The patients' antiarrhythmic treatment histories were similar, and although the rate of use was higher in the group in which cardioversion was successful, no statistically significant difference was observed ($p>0.05$).

The baseline demographic and clinical characteristics of the study population are presented in Table 1. There were no statistically significant differences observed between the two groups regarding demographic and clinical characteristics. Regarding echocardiographic findings, both groups had similar characteristics (Table 2). Conversely, the estimated left ventricular ejection fraction (LVEF) was notably lower in patients who achieved successful electrical cardioversion compared to those who experienced atrial fibrillation recurrence (52.02±9.35 vs 56.00±8.16, $p<0.05$).

Table 1. Comparison of cardiovascular success rates according to demographic characteristics and chronic diseases

	Total (n=80)	CV success+ (n=49)	CV success- (n=31)	p
Sex; n (%)				
Female	44 (100.0)	26 (59.1)	18 (40.9)	0.661*
Male	36 (100.0)	23 (63.9)	13 (36.1)	
Age (years)	65.50±12.49 67.5 (31-88)	64.79±11.50 67 (40-88)	66.61±14.04 68 (31-88)	0.530**
HT; n (%)				
Yes	65 (100.0)	39 (60.0)	26 (40.0)	0.633*
No	15 (100.0)	10 (66.7)	5 (33.3)	
DM; n (%)				
Yes	17 (100.0)	12 (70.6)	5 (29.4)	0.373*
No	63 (100.0)	37 (58.7)	26 (41.3)	
Antiarrhythmic drug usage; n (%)				
Yes	27 (100.0)	13 (48.1)	14 (51.9)	0.133*
No	53 (100.0)	36 (67.9)	17 (32.1)	

*: Pearson Ki-square test, **: T-test in independent groups, HT: hypertension, DM: diabetes mellitus

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Table 2. Cardiovascular success based on echocardiographic findings

	Total (n=80)	CV success+ (n=49)	CV success- (n=31)	p
Heart rate	87.25±21.38 83 (54-140)	87.87±22.24 83 (54-140)	86.24±20.26 85 (60-140)	0.801*
EF	53.56±9.07 59 (25-60)	52.02±9.35 55 (30-60)	56.00±8.16 60 (25-60)	**0.013***
LVEDD	48.94±5.42 48 (41-68)	49.08±5.08 48 (41-60)	48.73±5.99 47.5 (41-68)	0.599*
LVESD	30.71±6.41 30 (22-56)	31.04±5.80 31 (22-46)	30.10±7.34 29 (22-56)	0.224*
LA	41.60±4.84 41.5 (31-55)	41.40±4.44 41 (33-49)	41.90±5.47 42 (31-55)	0.659**
Aort annulus diameter	27.47±2.52 27 (21-34)	27.77±2.70 28 (21-34)	27.00±2.16 27 (21-32)	0.182**
PAB	36.77±11.55 35 (20-70)	35.89±10.67 35 (20-70)	38.16±12.88 35 (20-70)	0.723*

*: Mann Whitney U test, **: T-test in independent groups, ***: Fisfer Exact test, ****: Pearson Ki-square test, EF: ejection fraction, LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter, LA: left atrium, PAB: pulmonary artery pressure

The baseline laboratory values for both groups are presented in Table 3. Our findings indicate that serum platelet and albumin levels were significantly elevated in patients who achieved successful electrical cardioversion compared to those who experienced atrial fibrillation recurrence ($p<0.05$). Conversely, serum uric acid and UAR were significantly lower in patients with successful electrical cardioversion compared to those with atrial fibrillation recurrence ($p<0.05$) (Table 3). To establish the optimal UAR cut-off value for detecting electrical cardioversion success, a ROC curve was generated, yielding a best cut-off value of 1.616 determined by the Youden index (AUC: 0.960, 95% CI: 0.923-0.998, $p<0.001$). Below this threshold, electrical cardioversion success could be identified with a sensitivity of 87.8% and a specificity of 87.1% (Figure 1).

Table 3. Comparison of hematological and biochemical data according to cardiovascular success status

	Total (n=80)	CV success+ (n=49)	CV success- (n=31)	p
Wbc	10.74±9.75 9.2 (5.2-68.8)	11.76±12.16 8.7 (5.2-68.8)	9.12±3.09 8.1 (5.2-16.5)	0.300*
Neutrophil	5.97±2.75 4.9 (2.6-15.1)	5.95±2.43 4.9 (2.6-13.1)	6.02±3.24 4.9 (2.6-15.1)	0.682*
Lymphocyte	2.28±0.94 2.1 (0.2-4.8)	2.34±0.89 2.1 (0.9-4.8)	2.19±1.02 2.1 (0.2-4.7)	0.486*
Hemoglobin	13.52±1.88 13.8 (10.3-16.9)	13.83±1.74 14.1 (10.3-16.9)	13.02±2.02 12.4 (10.3-16.8)	0.054*
Platelet	258.53±68.72 268 (46-385)	275.06±54.83 273 (147-385)	232.41±80.46 234 (46-381)	**0.006****
GFR	76.40±26.67 75.5 (5.1-125.9)	76.56±27.38 78.3 (5.1-118.0)	76.14±25.97 72.8 (40.6-125.9)	0.945**
Urea	42.25±19.05 38.0 (18.2-120.3)	40.90±17.32 37.6 (18.2-82.0)	44.40±21.63 39.3 (21.4-120.3)	0.465*
Creatinine	0.99±0.31 0.8 (0.6-1.8)	0.99±0.30 0.8 (0.6-1.8)	0.99±0.31 0.8 (0.6-1.7)	0.878*
Uric acid	6.11±1.34 6.2 (3.4-10.5)	5.41±0.97 5.6 (3.4-7.1)	7.22±1.08 7.0 (5.2-70.5)	**<0.001***
Albumin	3.90±0.49 4.0 (2.8-5.1)	4.13±0.38 4.1 (3.2-5.1)	3.55±0.44 3.5 (2.8-4.8)	**<0.001****
Uric acid/albumin	1.60±0.48 1.5 (0.8-3.0)	1.31±0.25 1.3 (0.8-1.8)	2.06±0.39 2.0 (1.4-3.0)	**<0.001****
TSH	2.39±1.62 2.0 (0.1-6.6)	2.23±1.54 2.0 (0.1-6.6)	2.64±1.74 2.2 (0.1-6.0)	0.260*

*: Mann Whitney U test, **: T-test in independent groups, ***: Fisfer Exact test, ****: Pearson Ki-square test, Wbc: white blood cell, GFR: glomerular filtration rate, TSH: thyroid-stimulating hormone

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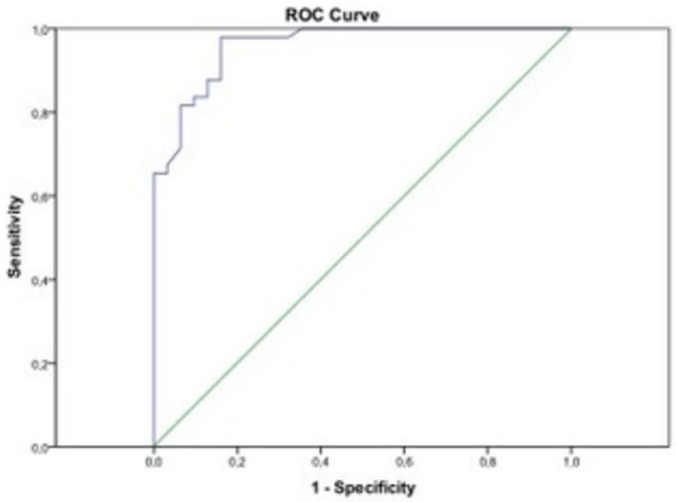

Figure 1. ROC curve of uric acid/albumin parameter

Discussion

To the best of our knowledge, this study represents the first investigation into the predictive role of uric acid ratio in anticipating AF recurrence subsequent to successful electrical cardioversion. The principal discovery of our study is that UAR emerged as an independent predictor of AF recurrence following successful EC. AF stands as the most prevalent cardiac conduction disorder globally and is linked with elevated risks of cardiac mortality and morbidity [11-13]. Although several studies reveal independent risk factors favoring AF, some of these studies are based on cross-sectional observations and do not examine the direct relationship between these risk factors and AF occurrence. Additionally, some of these studies did not exclude patients with increased cardiovascular risk factors, limiting the elucidation of independent risk factors for AF occurrence. Hence, the objective of this study was to explore an independent risk factor capable of predicting not only the success of EC but also the likelihood of AF recurrence.

Since the relationship between hyperuricemia and new-onset AF has been shown in many studies to be independent of gender, age, and race [14-16], we decided to use uric acid as the main parameter. The findings from our investigation validated that elevated serum uric acid levels and decreased serum albumin levels were correlated with a heightened risk of AF recurrence subsequent to successful EC. We also observed a direct link between the UAR and the risk of AF recurrence. When the data of our study were examined, significantly low albumin and high uric acid levels were detected in patients who developed AF following successful EC, and the proven relationship of these parameters with oxidative stress, neurohormonal, and inflammatory activation comes to the fore as the underlying mechanisms. Furthermore, reductions in nitric oxide levels, particularly subsequent to hyperuricemia, along with the shortening of the action potential plateau phase and acceleration of the repolarization rate, may serve as potential mechanisms underlying the onset of AF [17-19].

When all independent parameters evaluated in the study were examined, it was seen that the UAR was superior to other parameters in predicting AF recurrence. Our results were also consistent with Karataş et al.'s study showing a strong association between UAR and AF recurrence following successful catheter ablation [20]. In addition, it confirmed the proven prognostic value of UAR in various adverse cardiovascular conditions including ST elevation myocardial infarction, aortic stenosis, and aortic dissection [21-23].

Study Limitations

Our study has several limitations. The study's findings may be constrained by the modest sample size and the fact that it was conducted exclusively at a single center, potentially restricting the broader applicability of the results. Second, not all inflammatory parameters were included in the study and compared with UAR. Although patients are periodically monitored with rhythm monitoring, arrhythmic events may be missed due to incorrect Holter evaluation and/or technical reasons.

Conclusion

Our results indicate that uric acid ratio independently contributes to the occurrence of atrial fibrillation following successful electrical cardioversion, surpassing traditional inflammatory markers. From a clinical standpoint, we believe that UAR represents a straightforward, cost-effective, and promising predictive inflammatory parameter that could be integrated into cardiovascular assessments to identify individuals at elevated risk for AF recurrence among patients undergoing EC.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The ethics committee approval of the study was obtained with the decision number 2022/3976 of the Necmettin Erbakan University meeting dated 16 September 2022.

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