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The relationship between uric acid albumin ratio (UAR) and prognosis in patients with atrial fibrillation hospitalized in intensive care unit

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ABSTRACT

Aims: Recent studies have demonstrated an association between uric acid (UA) albumin ratio (UAR), and newly developing atrial fibrillation (AF) and also AF recurrence. We conducted a study to examine the prognostic value of UAR in critically ill patients with AF.

Methods: A retrospective examination was conducted on patients diagnosed with AF based on electrocardiography, who admitted to the intensive care unit (ICU) from the emergency department during the period from January 1st to May 1st, 2024. UAR levels were calculated by dividing the amount of UA by the amount of albumin. Based on the cut-off value, UAR levels were categorized into two groups: low UAR and high UAR. A comprehensive comparison was conducted on all the data between these two groups.

Results: The high UAR (UAR>0.231) group exhibited significantly higher UA, vasopressor requirement, mechanical ventilation support, length of stay in ICU, and in-hospital mortality rate compared to the low UAR (UAR≤0.231) group. Conversely, albumin levels were significantly lower ($p<0.001$ for all). The UAR cut-off value was 0.231, with a sensitivity of 97.3% and a specificity of 96.7% (The area under the curve (AUC):0.995, $p<0.001$). The mortality prediction ability of UAR was superior to that of albumin and UA alone (AUC: 0.995, 0.956, 0.981, respectively).

Conclusion: UAR is a cost-effective, easily accessible, useful marker for assessing the prognosis of critically ill patients with AF in ICU.

Keywords: Uric acid albumin ratio, atrial fibrillation, intensive care unit, prognosis, mortality

INTRODUCTION

Atrial fibrillation (AF) is the most common form of arrhythmia observed in one out of every six patients hospitalized in the intensive care unit (ICU).[1] Early identification of AF in patients hospitalized in the ICU is crucial since it is linked to several complications including ischemia, stroke, hemodynamic instability, mortality, and prolonged hospitalization. AF can be initiated in ICU patients by infection, inflammation, and arrhythmogenic triggers.[2]

Inflammation-induced fibrosis contributes to the initiation and perpetuation of AF. Several markers of inflammation have been demonstrated to be linked with the development of AF.[3] The last metabolite of purine, uric acid (UA), is catalyzed by xanthine oxidase, the main source of reactive oxygen species. UA, a molecular indicator of inflammation and oxidative stress, is linked to the development and progression of AF.[4] Studies have indicated that albumin, a potent anti-inflammatory and antioxidant substance, is linked to several inflammatory markers found in the bloodstream.[5] It has been suggested that the relationship between low serum albumin and AF may have a strong predictive value in patients with high comorbidities.[6]

The uric acid albumin ratio (UAR), a recently identified measure, has demonstrated its predictive power in several studies on inflammation.[7,8] Two recent studies have demonstrated that UAR has a superior ability to predict the development of newly emerging AF and AF recurrence.[3,9] Nevertheless, thus far, no study has been conducted to examine the correlation between UAR and the prognosis of patients with critical AF admitted to the ICU. Hence, our study aimed to examine the predictive capability of UAR in critically ill patients with AF.

METHODS

Study Design and Patient Population

A retrospective examination was conducted on patients who were admitted to ICU from the emergency department (ED)

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for various causes over the period of 01 January to 01 May 2024. The study comprised male and female patients who were over 18 years old, as well as patients diagnosed with AF based on electrocardiography (ECG). The study excluded individuals who had cancer, were pregnant, had hematological, rheumatological, oncological or infectious diseases, were undergoing immunosuppressive treatments, or had incomplete laboratory information. The study retrospectively collected data from the hospital system on patients' age, gender, UA and albumin levels at the time of admission to the ED, whether they required mechanical ventilation (MV) or vasopressor during their hospital stay, the length of their hospital stay (LOHS), the length of their ICU stay (LOS-ICU), and their outcomes (discharge or exitus). The evaluation of mortality was determined by the occurrence of death while patients was hospitalized. UAR levels were calculated by dividing the amount of UA by the amount of albumin.[9] Based on the cut-off value, UAR levels were categorized into two groups: low UAR and high UAR. A comprehensive comparison was conducted on all the data between these two groups, and receiver operating characteristic (ROC) analysis was applied to those that were associated with mortality. The study was initiated with the approval of the Necmettin Erbakan University Medical Faculty Clinical Researches Ethics Committee (Date: 28/06/2024, Decision No: 2024/5038). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Biochemical Analysis

During admission to the ED, blood samples were collected to assess UA and albumin values. The measurement was conducted using the Mindray chemistry analyzer BS-2000M device (Shenzhen, China).

Statistical Analysis

Statistical analyses in the study were performed using the SPSS 27.0 (IBM Inc., Chicago, IL, USA) program. The Kolmogrov-Smirnov test, histogram analysis, skewness/kurtosis data, and Q-Q plots were used to evaluate the assumptions of normal distribution. Descriptive statistics of the numerical and categorical data obtained in the study were analysed, and the parameters were expressed as IQR [median (minimum- maximum)]. Relationships between the two groups were examined with the Mann-Whitney U test. Relationships between categorical (nominal) parameters were examined with Pearson's chi-square analysis. ROC analysis was performed to determine predictive value and cut-off value for appropriate parameters. In the entire study, the type-I error rate was taken as 5% (α=0.05) and $p<0.05$ was accepted as the significant limit.

RESULTS

Table 1 presents a comparison of the characteristics of patients who survived and those who did not survive. Compared to the survivors, the deceased patients had significantly higher age, UA, UAR, vasopressor requirement, MV support, and LOS-ICU. On the other hand, albumin and LOSH were significantly lower in the deceased patients ($p<0.001$ for all). There was not a significant relationship between these two groups in terms of gender (p=0.841).

Table 1. Comparison of the clinical features of survivor and non-survivor patients

Variables	Survivors (n=271, 64.5%)	Non-survivors (n=149, 35.5%)	p value
Age, years	73 (18-98)	78 (19-103)	<0.001
Gender			
Male, n (%)	141 (52.03%)	76 (51.01%)	0.841
Female, n (%)	130 (47.97%)	73 (48.99%)	
Laboratory parameters			
Uric acid, (mg/dl)	5.3 (2-9.8)	9.2 (5.2-17.7)	<0.001
Albumin (g/L)	38.3 (21.1-50.2)	26.9 (18.2-36.1)	<0.001
UAR	0.14 (0.06-0.35)	0.37 (0.19-0.8)	<0.001
MV support, n (%)			
No	207 (76.38%)	17 (11.41%)	<0.001
Yes	64 (23.62%)	132 (88.59%)	
Vasopressor support			
No	160 (59.04%)	24 (16.11%)	<0.001
Yes	111 (40.96%)	125 (83.89%)	
LOHS (day)	14 (4-27)	11 (1-70)	<0.001
LOS-ICU (day)	7 (4-19)	11 (1-70)	<0.001

UAR: Uric acid albumin ratio, MV: Mechanical ventilation, LOHS: Length of hospital stay, LOS-ICU: Length of ICU stay, ICU: intensive care unit

Table 2 presents the overall characteristics of all patients as per the UAR. The high UAR (UAR >0.231) group exhibited significantly higher age, UA levels, vasopressor requirement, MV support, LOS-ICU, and in-hospital mortality rate compared to the low UAR (UAR ≤0.231) group. Conversely, albumin levels and LOSH were significantly lower ($p<0.001$ for all). There was not a significant relationship between the two groups in terms of gender (p=0.47).

The ROC analysis of UA, albumin, and UAR in predicting mortality is shown in Table 3. While the UA cut off value was 7.35, it had 94% sensitivity and 95.2% specificity (AUC: 0.981, $p<0.001$). While the albumin cut-off value was 31.9, it had 93.3% sensitivity and 90.4% specificity (AUC: 0.956, $p<0.001$). While the UAR cut-off value was 0.231, it had 97.3% sensitivity and 96.7% specificity (AUC: 0.995, $p<0.001$). The mortality prediction ability of UAR was higher to that of albumin and UA alone (AUC: 0.995, 0.956, 0.981, respectively).

DISCUSSION

In critically ill patients, early detection of AF is essential due to the high risk of mortality and long-term complications.[1] While the exact mechanism remains uncertain, it is well-established that both inflammatory response and oxidative stress contribute to the development of AF. Inflammation can result in the degeneration, necrosis, apoptosis and fibrosis of atrial myocytes, hence, can change the electrical structure of the atrium.[4] Numerous alternative strategies have been suggested to date in order to predict the development of AF, such as the investigation of inflammation-related biomarkers.[2]

Table 2. Characteristics of patients according to UAR groups

Variables	Low group (UAR≤0.231) (n=266, 63.3%)	High group (UAR>0.231) (n=154, 36.7%)	p value
Age, years	73 (18-98)	78 (19-103)	<0.001
Gender			
Male, n (%)	141 (53.01%)	76 (49.35%)	0.470
Female, n (%)	125 (46.99%)	78 (50.65%)	
Laboratory parameters			
Uric acid, (mg/dl)	5.3 (2-8.6)	9.1 (5.2-17.7)	<0.001
Albumin (g/L)	38.6 (21.1-50.2)	26.9 (18.2-36.1)	<0.001
MV support, n (%)			
No	204 (76.69%)	20 (12.99%)	<0.001
Yes	62 (23.31%)	134 (87.01%)	
Vasopressor support			
No	153 (57.52%)	31 (20.13%)	<0.001
Yes	113 (42.48%)	123 (79.87%)	
LOHS (day)	14 (4-27)	11 (1-70)	<0.001
LOS-ICU (day)	7 (4-19)	11 (1-70)	<0.001
In-hospital mortality			
No	262 (98.5%)	9 (5.84%)	<0.001
Yes	4 (1.5%)	145 (94.16%)	

UAR: Uric acid albumin ratio, MV: Mechanical ventilation, LOHS: Length of hospital stay, LOS-ICU: Length of ICU stay, ICU: intensive care unit

Table 3. ROC analysis of parameters in mortality prediction

	AUC	95% CI		Cut-off	Sensitivity (%)	Specificity (%)	
		Lower limit	Upper limit				p
Uric acid	0.981	0.969	0.993	7.35	94.0%	95.2%	<0.001
Albumin*	0.956	0.938	0.975	31.9	93.3%	90.4%	<0.001
UAR	0.995	0.991	0.999	0.231	97.3%	96.7%	<0.001

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, *Lower values are associated with positive (exitus) results. UAR: Uric acid albumin ratio

The significance of UA metabolism in numerous diseases that occur alongside chronic inflammation should not be underestimated.[10] By causing atrial remodeling induced by inflammation, oxidative stress, and fibrosis, UA contributes to the pathophysiology of AF.[11] Multiple meta-analyses have demonstrated the correlation between hyperuricemia and AF.[4,10] A study revealed that patients with AF exhibited significantly elevated levels of UA in comparison to those without AF. This study highlighted the positive correlation between increasing levels of UA and the incidence of AF.[12] In a separate study that included patients with new-onset, paroxysmal, and persistent AF, it was verified that UA levels were directly correlated with the duration of AF and were significantly higher in those with persistent AF than in the other groups.[4] A recent study including 1484 patients with coronary artery disease (CAD) indicated that levels of UA were higher in patients with new-onset atrial fibrillation (NOAF) compared to those without NOAF.[9] Our study found that levels of UA were significantly higher in patients who died in contrast to those who survived. Furthermore, UA demonstrated a high level of accuracy in predicting mortality in critically ill AF patients who were admitted to the ICU. Thus, UA could serve as a marker linked to adverse outcomes for these patients.

Serum albumin, the most important protein found in human serum, performs a multitude of essential physiological functions. Albumin, with its various effects including the maintenance of colloid osmotic pressure, anti-platelet aggregation, anti-inflammatory, antioxidant and anticoagulant effects, may also contribute to the pathophysiological process of AF.[5,13] Currently, numerous studies have proven that the likelihood of AF increases as albumin levels decrease.[14,15] A meta-analysis shown that a concentration of 10 g/L serum albumin resulted in a 36% decrease in the incidence of AF. Furthermore, a significant relationship between serum albumin and AF was seen.[4] According to Zhao et al.,[13] patients with persistent AF had lower levels of albumin compared to patients with paroxysmal AF. Our study revealed that the albumin levels of patients who died were significantly lower than those who survived. Furthermore, albumin demonstrated a high AUC for the prediction of mortality in patients with critical AF. Consequently, the levels of albumin in these patients may serve as an indicator of the intensity of the inflammatory response and the severity of the disease.

Currently, UAR, which has recently been identified as a new marker for inflammation and oxidative stress, has been the subject in numerous studies.[9] Two recent studies have demonstrated a correlation between UAR and mortality in patients who have acute renal failure.[16,17] Another study demonstrated that UAR exhibited a stronger predictive capacity compared to UA and albumin in forecasting the likelihood of developing contrast-related nephropathy in patients diagnosed with ST-segment elevation myocardial infarction (STEMI).[7] A study of 402 individuals with CAD found that there were significantly higher levels of UAR in patients in the medium-high cardiac surgery scores group compared to patients in the low cardiac surgery scores group. Furthermore, it has been highlighted that UAR can be utilized with confidence to estimate the magnitude of CAD.[8] A study involving 4599 patients with STEMI found that UAR could serve as an easily accessible parameter for identifying high-risk patients and predicting mortality.[18] Selçuk et al.[9] discovered that the levels of serum UAR were elevated in patients with NOAF compared to those without NOAF. Based on the logistic regression model, it has been demonstrated that UAR is an independent predictor of NOAF in STEMI patients. Karataş et al.[3] conducted a study to assess the efficacy of UAR in predicting the recurrence of AF following a successful catheter ablation procedure. During ROC analysis, when the UAR value >1.67, it accurately predicted the occurrence of recurrence with a sensitivity of 77% and a specificity of 57% (AUC 0.68, p<0.01). Our study found that the UAR was significantly higher among individuals who

died compared to those who survived. The high UAR group exhibited significantly greater requirements for vasopressor use, MV support, LOS-ICU, and in-hospital mortality rate, in comparison to the low UAR group. In addition, when compared to albumin and UA, UAR had exceptional predictive ability for mortality (AUC: 0.956, 0.981, 0.995, respectively). Thus, UAR serves as a closely linked marker for predicting the prognosis of patients with critical AF.

Limitations

Initially, this study was a single-center retrospective study with a small sample size. Secondly, since the patient data in the study were based on medical records, information such as medications used, body-mass index, smoking, alcohol consumption, malnutrition, etc. could not be fully provided. Third, it should be noted that the data collection was limited to the time of admission to ED, and any subsequent changes that occurred during the patient's stay were not analyzed. Fourth, it was not possible to track the long-term results of critically ill patients with AF who were admitted to the ICU. To summarize as this is the initial study examining the correlation between UAR and prognosis in patients with critical AF, it is necessary to carry out prospective and multicenter studies to validate our findings.

CONCLUSION

UAR serves as a cost-effective, easily accessible, and useful marker in the prognostic assessment of critically ill AF patients admitted to the ICU. In addition, UAR had a higher predictive efficacy in predicting mortality in these patients, as compared to albumin and UA.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the Necmettin Erbakan University Faculty of Medicine Clinical Researches Ethics Committee (Date: 28/06/2024, Decision No: 2024/5038).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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