Received: 16 Apr 2025 | **Accepted:** 29 May 2025 **Genel Tıp Derg. Volume** 35/**Issue** 5 (October), 922-933
DOI: 10.54005/geneltip. 1677988

ORIGINAL ARTICLE

Evaluating the Uric Acid/Albumin Ratio as a Biomarker for Disease Severity in Acute Myocarditis Patients

Akut Miyokardit Hastalarında Hastalığın Şiddetinin Biyobelirteci Olarak Ürik Asit/Albümin Oranının Değerlendirilmesi

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How to cite ?

Eyiol H., Eyiol A., Şahin A. T., Evaluating the Uric Acid/Albumin Ratio as a Biomarker for Disease Severity in Acute Myocarditis Patients, Genel Tıp Derg. 2025;35(5):922-933

ABSTRACT

Aim: Uric acid/albumin ratio (UAR) has recently emerged as a potential marker for oxidative stress and inflammation, the key components in the pathophysiology of myocarditis. Therefore, high UAR may reflect increased disease activity and severity in myocarditis patients. In this study, we aimed to evaluate the usability of UAR as a biomarker in determining disease severity in patients with acute myocarditis.
Methods: The study population was evaluated retrospectively. Laboratory parameters of the patients were examined. We classified the condition as severe myocarditis based on the presence of refractory chest pain, hypotension, detection of pericardial effusion with subsequent increase, a decrease in ejection fraction (EF), and lack of response to medical and symptomatic treatment. The primary outcome was the association between UAR and disease severity.
Results: The median age was 43.5 years. The UAR was significantly higher in females (0.10 vs. 0.10, p=0.003). Patients with pericardial effusion had significantly higher UARs (0.137 vs. 0.100, p<0.001), and those requiring intensive therapies such as inotropes, intravenous (IV) steroids, or intravenous immunoglobulin (IVIG) also showed elevated UARs.
Conclusion: Our study provides evidence supporting the use of UAR as a novel marker for assessing disease severity in acute myocarditis patients. By integrating markers of oxidative stress and nutritional/inflammatory status, UAR offers a comprehensive tool for risk stratification and management in clinical practice.

Keywords: Myocarditis, pericardial effusion, uric acid/albumin ratio

ÖZ

Amaç: Ürik asit/albümin oranı (UAR) son zamanlarda miyokarditin patofizyolojisinde önemli bileşenler olan oksidatif stres ve inflamasyon için potansiyel bir belirteç olarak ortaya çıkmıştır. Bu nedenle, yüksek UAR miyokardit hastalarında artmış hastalık aktivitesini ve şiddetini yansıtabilir. Bu çalışmada, akut miyokarditli hastalarda hastalık şiddetini belirlemede bir biyobelirteç olarak ürik asit/albümin oranının kullanılabilirliğini değerlendirmeyi amaçladık.
Yöntem: Çalışma popülasyonu retrospektif olarak değerlendirildi. Hastaların laboratuvar parametreleri incelendi. Durumu, dirençli göğüs ağrısı, hipotansiyon, daha sonra artış gösteren perikardiyal efüzyon tespiti, ejeksiyon fraksiyonunda (EF) azalma ve tıbbi ve semptomatik tedaviye yanıt eksikliği temelinde şiddetli miyokardit olarak sınıflandırdık. Birincil sonuç, UAR ile hastalık şiddeti arasındaki ilişkiydi.
Bulgular: Ortanca yaş 43,5 yıldı. UAR kadınlarda önemli ölçüde daha yüksekti (0,10'a karşı 0,10, p=0,003). Perikardiyal efüzyonlu hastalarda önemli ölçüde daha yüksek UAR'lar vardı (0,137'ye karşı 0,100, p<0,001) ve inotroplar, intravenöz (IV) steroidler veya intavenöz immünoglobulin (IVIG) gibi yoğun tedaviler gerektirenlerde de yüksek UAR'lar görüldü.
Sonuç: Çalışmamız, akut miyokardit hastalarında hastalık şiddetini değerlendirmek için yeni bir belirteç olarak UAR kullanımını destekleyen kanıtlar sunmaktadır. Oksidatif stres ve beslenme/iltihap durumu belirteçlerini entegre ederek, UAR klinik uygulamada risk sınıflandırması ve yönetimi için kapsamlı bir araç sunar

Anahtar kelimeler: Miyokardit, perikardiyal efüzyon, ürik asit/albümin oranı

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

INTRODUCTION

Myocarditis is an inflammatory disease of the heart muscle that can significantly impact cardiac function and overall patient prognosis(1, 2). It often presents with a wide range of clinical symptoms, from mild chest pain and fatigue to severe heart failure and sudden cardiac death (3). The diagnosis of myocarditis typically involves a combination of clinical assessment, imaging techniques such as echocardiography and cardiac MRI, and histological examination via endomyocardial biopsy(4, 5). However, the variability in clinical presentation and the invasiveness of some diagnostic methods underscore the need for reliable, non-invasive biomarkers to aid in the early detection and management of this condition.

The management of myocarditis largely depends on the severity of the disease, which can range from self-limiting to life-threatening(6). Treatment strategies vary accordingly and may include supportive care, immunosuppressive therapy, and in severe cases, mechanical circulatory support or heart transplantation(7, 8). Identifying factors determining disease severity is crucial for tailoring treatment plans and improving patient outcomes. Conventional markers such as troponins and natriuretic peptides have been used to assess myocardial injury and stress, yet there remains a need for additional biomarkers that can provide more comprehensive insights into disease activity and prognosis(9).

Uric acid and albumin levels have individually been associated with various cardiovascular conditions(10, 11). Uric acid, a product of purine metabolism, is known for its pro-inflammatory and pro-oxidative properties, which may exacerbate myocardial damage(12). Albumin, a major plasma protein, plays a critical role in maintaining oncotic pressure and has anti-inflammatory and antioxidant effects(13). The uric acid/albumin ratio (UAR) has recently emerged as a potential marker for oxidative stress and inflammation, both of which are key components in the pathophysiology of myocarditis. Elevated UAR may thus reflect heightened disease activity and severity in myocarditis patients.

In this study, we aim to evaluate the utility of UAR as a biomarker for determining disease severity in patients with acute myocarditis. We hypothesize that a higher UAR is associated with more severe disease manifestations and poorer clinical outcomes. By exploring this relationship, we hope to provide clinicians with a novel, non-invasive tool for assessing myocarditis severity, which could ultimately enhance patient management and prognostication.

MATERIAL and METHODS

Ethical Consideration

This study was approved by the Necmettin Erbakan University Ethics Committee (Date: 25.04.2024, Decision No: 2024/4975). The study was conducted under the principles of the Declaration of Helsinki.

Study Design

This retrospective study was conducted to evaluate the utility of UAR as a biomarker for determining disease severity in patients with acute myocarditis. The study included patients diagnosed with acute myocarditis between January 2015 and December 2022 at our institution. A total of 260 patients, including 154 males and 106 females, were enrolled. The diagnosis of acute myocarditis

was based on the combination of the following:

-Clinical presentation (e.g., chest pain, shortness of breath, palpitations),

-Elevated cardiac biomarkers (e.g., troponin I or T),

-Electrocardiographic changes (e.g., ST-T segment abnormalities, arrhythmias), and

-Echocardiographic findings (e.g., regional wall motion abnormalities, pericardial effusion, or reduced ejection fraction) in the absence of obstructive coronary artery disease.

To exclude ischemic heart disease, all patients underwent either coronary angiography or coronary computed tomography angiography (CCTA). Patients with confirmed obstructive coronary artery disease were excluded.

We defined the severe myocarditis group as patients presenting with refractory chest pain, hypotension, progressive pericardial effusion, marked reduction in ejection fraction, and poor response to standard medical and symptomatic treatment.

Patients aged 18 years or older with a confirmed diagnosis of acute myocarditis were included. Exclusion criteria were as follows: the presence of chronic kidney disease, liver disease, malignancy, or any condition known to significantly affect uric acid or albumin levels; incomplete medical records; and prior use of uric acid-lowering therapy or albumin supplementation before the diagnosis. These criteria were applied to ensure homogeneity and avoid confounding factors in the interpretation of UAR values.

Statistical Analysis

Statistical analyses in this study were conducted using the Statistical Package for Social Sciences for Windows, version 27.0 (SPSS, IBM Inc, Chicago, IL, USA). The normality of the distribution of numerical variables was assessed using the Kolmogorov-Smirnov test, histogram analyses, skewness/kurtosis data, and Q-Q plots. Descriptive statistics for the numerical and categorical variables obtained in the study were analyzed, with quantitative parameters expressed as median (IQR) [minimum-maximum] or mean ± standard deviation. Relationships between the two groups were examined using the Mann-Whitney U test or independent t-test. Correlations between quantitative parameters were evaluated using Pearson or Spearman correlation analyses. Throughout the study, a type I error rate of 5% ($\alpha = 0.05$) was used, and a p-value < 0.05 was considered statistically significant.

RESULTS

Table 1 summarizes the general distribution of quantitative parameters among myocarditis patients. The median age was 43.5 years, with a range from 18 to 74 years. Hemoglobin (Hb) levels ranged from 10.5 to 17.7 g/dL, with a mean of 14.4 g/dL. White blood cell (WBC) counts varied significantly, averaging 10.04 × 10^3/mL. Other notable findings include a mean platelet count of 244.34 × 10^3/mL, an average albumin level of 42.8 g/L, and a median ejection fraction (EF) of 60%. Troponin levels showed a wide range, from 48 to 50,000 ng/L, indicating diverse levels of myocardial injury. The median UAR was 0.102, ranging from 0.081 to 0.191. The median length of stay in the

Table 1. Summary of the general distribution of quantitative parameters and gender differences in myocarditis patients

					Sex		
					Male (n=154, 59.2%)	Female (n=106, 40.8%)	
Parameters	**Unit**	**Minimum**	**Maximum**	**Distribution†**	**Distribution***		**p-value**
Age	years	18	74	43.5 (18-74)	47 (18-74)	36 (18-65)	0.317
Hemoglobin	g/dL	10,5	17.7	14.4 (10.5-17.7)	15.1 (12.2-17.7)	13.3 (10.5-16.8)	**<0.001**
WBC	103/mL	8.01	23.82	10.04 (8.01-23.82)	9.82 (8.08-21.26)	11.23 (8.01-23.82)	**0.001**
Neutrophil	103/mL	3.62	19.93	7.32 (3.62-19.93)	6.92 (3.62-18.28)	8.43 (4.66-19.93)	**<0.001**
Monocyte	%	0.04	1.82	0.66 (0.04-1.82)	0.66 (0.04-1.82)	0.67 (0.28-1.8)	0.423
Lymphocyte	103/mL	0.40	4.78	2.07 (0.4-4.78)	2.05 (0.4-4.78)	2.09 (0.89-3.77)	0.924
Platelet	103/mL	146	366	244.34±50.02	238.0±48.0	254.0±51.0	**0.008**
RDW	%	11.2	17.7	13.45±1.06	13.5±1.0	13.3±1.2	0.115
Albumin	g/L	32.0	50.6	42.8±3.05	43.5±2.5	41.8±3.4	**<0.001**
ASO	IU/mL	111	387	205.87±69.29	207.0±67.0	204.0±73.0	0.790
EF	%	30	65	60 (30-65)	60 (30-65)	60 (45-65)	**<0.001**
Troponin	ng/L	48	50000	456 (48-50000)	579 (51-50000)	406 (48-38990)	0.220
CRP	mg/L	10	348	32 (10-348)	28 (10-348)	34 (11-256)	**0.029**
D-dimer	ng/mL	365	987	566 (365-987)	579 (367-987)	550 (365-790)	**0.032**
Ferritin	ng/mL	19	165	73 (19-165)	67 (19-165)	78 (24-144)	**0.022**
Fibrinogen	ng/dL	2.56	4.16	3.41 (2.56-4.16)	3.41 (2.56-4.16)	3.41 (2.66-4.01)	0.540
LDL	mg/dL	53	198	134 (53-198)	134 (53-196)	134 (71-198)	0.664
HDL	mg/dL	23	129	43 (23-129)	42 (23-65)	45 (26-129)	**<0.001**
TRG	mg/dL	72	307	126 (72-307)	123 (72-298)	128 (78-307)	**0.011**
Glucose	mg/dL	77	167	97 (77-167)	95 (78-132)	100 (77-167)	0.207
Uric acid	mg/dL	3.6	6.2	4.4 (3.6 – 6.2)	4.4 (3.6-6.2)	4.45 (3.6-6.1)	0.069
Uric acid/Albumin ratio		0.081	0.191	0.102 (0.081-0.191)	0.10 (0.08-0.16)	0.10 (0.08-0.19)	**0.003**
ICU time	day	1	10	1 (1-10)	1 (1-10)	1 (1-7)	0.604
Hospitalization time	day	1	14	3 (1-14)	3 (1-14)	3 (2-14)	0.372

†Parameters are expressed as IQR (Interquartile Range)[median. Min and max] or mean±SD.WBC: White blood cell, RDW: Red cell distribution width, ASO: Antistreptolysin O, EF: Ejection fraction, CRP: C-reactive protein, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TRG: Triglyceride; ICU: Intensive care unit

intensive care unit was one day (1-10) and the median length of stay in the hospital was three days (1-14).

Table 1 also compares parameters between male and female patients with myocarditis, revealing significant differences. Males had higher median Hb levels (15.1 g/dL vs. 13.3 g/dL, $p<0.001$) and lower WBC counts (9.82 × 10^3/mL vs. 11.23 × 10^3/mL, $p=0.001$) compared to females. Neutrophil counts were lower in males (6.92 × 10^3/mL vs. 8.43 × 10^3/mL, $p<0.001$). Females had higher platelet counts (254.0±51.0 × 10^3/mL vs. 238.0 ± 48.0 × 10^3/mL, $p=0.008$) and lower albumin levels (41.8±3.4 g/L vs. 43.5±2.5 g/L, $p<0.001$). The UAR was significantly higher in females (0.10 vs. 0.10, $p=0.003$). Additionally, differences in inflammatory markers such as CRP and ferritin were noted, with females exhibiting higher median levels. No significant difference was observed between the duration of intensive care and hospital stay in male and female patients.

Tables 2, 3, and 4 evaluate the UAR in the context of specific clinical conditions, hospital stay durations, and correlations with various parameters. Table 3 indicates that patients with pericardial effusion had significantly higher UARs (0.137 vs. 0.100, $p<0.001$), and those requiring intensive therapies such as inotropes, IV steroids, or IVIG also showed elevated UARs.

Table 3 shows that patients with longer hospital stays (>2 days) had higher median levels of WBC, neutrophils, CRP, and ferritin compared to those with shorter stays.

Table 4 presents correlations between UAR and other clinical parameters, finding significant associations with ICU stay duration, total hospital stay, and several hematological and biochemical markers, suggesting that UAR may serve as a useful indicator of disease severity and hospital outcomes in myocarditis patients. A strong negative correlation was observed between age and ASO, CRP, and ferritin levels. There was a moderate negative correlation between age and both ejection fraction (EF) and HDL levels. A moderate positive correlation was found between ICU stay duration and total hospital length of stay. Additionally, a strong positive correlation was observed between total hospital stay and troponin and fibrinogen levels. There was a moderate positive correlation between total hospital stay and both CRP and D-dimer levels. A strong positive correlation was found between UAR and triglyceride levels, while UAR showed a moderate positive correlation with WBC, neutrophil count, RDW, and glucose levels.

DISCUSSION

In this study, we examined the potential utility of UAR as a marker for determining disease severity in patients with acute myocarditis. Previous studies have shown that refractory chest pain, increased pericardial effusion, cardiac tamponade, hypotension, reduced ejection fraction, low cardiac output, and persistent ventricular arrhythmias in patients with acute myocarditis indicate a more severe, refractory, and rapidly progressing disease course(14). The Lombardy registry, a multicenter Italian study involving 443 patients hospitalized with confirmed myocarditis, identified severe hemodynamic impairment at hospital admission as being associated with the highest risk of cardiac death(15-17). Similarly, another study of 220 patients from 16 tertiary care hospitals, all with

Table 2. Comparison of uric acid/albumin values according to the presence of specific conditions

		Uric Acid/Albumin ratio	
Parameters		**Median (min-max)**	**p**
Pericardial Effusion	No (n=184)	0.100 (0.081-0.114)	<0.001
	Yes (n=74)	0.137 (0.125-0.191)	
Use of Beta Blocker	No (n=139)	0.104 (0.082-0.191)	0.018
	Yes (n=121)	0.102 (0.081-0.167)	
Use of ACEi/ARB	No (n=139)	0.104 (0.082-0.191)	0.018
	Yes (n=121)	0.102 (0.081-0.167)	
Inotrope Support	No (n=251)	0.103 (0.081-0.191)	<0.001
	Yes (n=9)	0.144 (0.137-0.191)	
Use of IV Steroid	No (n=248)	0.103 (0.081-0.191)	<0.001
	Yes (n=12)	0.142 (0.135-0.191)	
IVIG	No (n=255)	0.103 (0.081-0.191)	<0.001
	Yes (n=5)	0.147 (0.137-0.191)	
HT	No (n=139)	0.103 (0.082-0.191)	0.051
	Yes (n=121)	0.102 (0.081-0.167)	
HL	No (n=188)	0.102 (0.082-0.191)	0.323
	Yes (n=72)	0.104 (0.081-0.167)	
DM	No (n=208)	0.103 (0.082-0.191)	0.571
	Yes (n=52)	0.104 (0.081-0.167)	
Smoking	No (n=105)	0.104 (0.082-0.191)	0.062
	Yes (n=155)	0.102 (0.081-0.172)	
Family History	No (n=184)	0.103 (0.082-0.191)	0.723
	Yes (n=76)	0.103 (0.081-0.167)	
Obesity	No (n=102)	0.104 (0.082-0.191)	0.041
	Yes (n=158)	0.102 (0.081-0.167)	
Flu infection within 4 weeks	No (n=97)	0.103 (0.086-0.191)	0.425
	Yes (n=163)	0.103 (0.081-0.16)	
Tonsillitis	No (n=162)	0.103 (0.081-0.167)	0.124
	Yes (n=98)	0.103 (0.086-0.191)	
Gastroenteritis in 4 weeks	No (n=208)	0.103 (0.081-0.191)	0.294
	Yes (n=52)	0.103 (0.087-0.16)	
Coronary CT Angiography	No (n=197)	0.103 (0.081-0.172)	0.168
	Yes (n=63)	0.103 (0.082-0.191)	
Coronary Angiography	No (n=61)	0.103 (0.082-0.191)	0.139
	Yes (n=199)	0.103 (0.081-0.172)	

ACEi: Angiotensin converting enzyme inhibitor; ARB: Angiotensin reseptor blocker; IV: Intravenous; IVIG: Intravenous immunoglobulin; HT: Hypertension; HL: Hyperlipidemia; DM: Diabetes mellitus; CT: Computed tomography.

Table 3. Comparison of quantitative parameters with total hospital stay groups

		Total Hospitalization Time		
		1-2 days (n=127, 48.8%)	>2 days (n=133, 51.2%)	p
Parameters	**Unit**	**Distribution***		
Age	years	47 (19-68)	39 (18-74)	<0.001
Hemoglobin	g/dL	14.8 (10.5-17.7)	14.3 (10.5-17.7)	0.088
WBC	103/mL	9.66 (8.01-23.82)	11.4 (8.23-22.71)	0.005
Neutrophil	103/mL	6.51 (3.62-19.93)	8.27 (3.67-18.47)	0.008
Monocyte	%	0.65 (0.04-1.37)	0.67 (0.2-1.82)	0.211
Lymphocyte	103/mL	2.22 (0.82-4.78)	2.05 (0.4-3.95)	0.336
Platelet	103/mL	248±52	241±48	0.304
RDW	%	13.2±1.1	13.7±1	<0.001
Albumin	g/L	43±3.1	42.6±3	0.202
ASO	IU/mL	194±67	217±70	0.009
EF	%	60 (45-65)	60 (30-65)	<0.001
Troponin	ng/L	218 (48-18511)	3609 (51-50000)	0.013
CRP	mg/L	23 (10-203)	39 (10-348)	<0.001
D-dimer	ng/mL	510 (365-722)	590 (367-987)	0.793
Ferritin	ng/mL	67 (19-165)	77 (22-165)	<0.001
Fibrinogen	ng/dL	3.13 (2.56-3.87)	3.61 (2.88-4.16)	0.252
LDL	mg/dL	132 (53-191)	134 (71-198)	<0.001
HDL	mg/dL	43 (27-129)	43 (23-57)	<0.001
TRG	ng/dL	118 (72-290)	128 (77-307)	0.720
Glucose	mg/dL	93 (78-167)	100 (77-145)	0.041
Uric acid	mg/dL	4.3 (3.6-6.1)	4.7 (3.6-6.2)	0.163
Uric acid/Albumin ratio		0.101 (0.081-0.191)	0.105 (0.086-0.191)	0.249

†Parameters are expressed as IQR (Interquartile Range)[median, min and max] or mean±SD. WBC:White blood cell; RDW: Red cell distribution width; ASO: Antistreptolysin O; EF: Ejection fraction; CRP: C-reactive Protein; LDL: Low density lipoprotein; HDL: High density lipoprotein; TRG: Triglyceride; ICU: Intensive care unit

Tablo 4. Examining the correlations of quantitative parameters with age, ICU stay, total hospital stay, Uric Acid/Albumin ratio

		Age	ICU Time	Hospitalization Time	UAR
Age	ρ	-	-0.179	-0.136	-0.085
	P	-	0.004	0.028	0.171
ICU time	ρ	-0.179	-	0.444	0.337
	P	0.004	-	<0.001	<0.001
Hospitalization Time	ρ	-0.136	0.444	-	0.335
	P	0.028	<0.001	-	<0.001
UAR	ρ	-0.085	0.337	0.335	-
	P	0.171	<0.001	<0.001	-
Hemoglobin	ρ	0.025	-0.132	-0.151	-0.354
	P	0.692	0.033	0.015	<0.001
WBC	ρ	-0.316	0.271	0.381	0.534
	P	<0.001	<0.001	<0.001	<0.001
Neutrophil	ρ	-0.265	0.271	0.371	0.530
	P	<0.001	<0.001	<0.001	<0.001
Monocyte	ρ	-0.305	0.199	0.184	0.155
	P	<0.001	0.001	0.003	0.012
Lymphocyte	ρ	-0.025	-0.075	-0.064	0.026
	P	0.693	0.225	0.302	0.676
Platelet	ρ	0.095	-0.073	-0.058	0.137
	P	0.127	0.239	0.351	0.027
RDW	ρ	0.228	0.235	0.285	0.419
	P	<0.001	<0.001	<0.001	<0.001
Albumin	ρ	0.073	-0.223	-0.163	-
	P	0.24	<0.001	0.008	-
ASO	ρ	-0.734	0.117	0.15	0.074
	P	<0.001	0.06	0.016	0.232
EF	ρ	-0.449	-0.074	-0.247	-0.03
	P	<0.001	0.233	<0.001	0.629
Troponin	ρ	-0.365	0.241	0.652	0.113
	P	<0.001	<0.001	<0.001	0.069
CRP	ρ	-0.612	0.321	0.414	0.304
	P	<0.001	<0.001	<0.001	<0.001
D-dimer	ρ	-0.152	0.326	0.587	0.270
	P	0.014	<0.001	<0.001	<0.001
Ferritin	ρ	-0.602	0.288	0.172	0.317
	P	<0.001	<0.001	0.005	<0.001
Fibrinogen	ρ	-0.058	0.33	0.61	0.214
	P	0.349	<0.001	<0.001	<0.001
LDL	ρ	0.353	0.18	0.235	0.313
	P	<0.001	0.004	<0.001	<0.001
HDL	ρ	-0.456	-0.058	-0.044	-0.005
	P	<0.001	0.35	0.476	0.939
TRG	ρ	-0.008	0.308	0.374	0.620
	P	0.899	<0.001	<0.001	<0.001
Glucose	ρ	0.217	0.231	0.257	0.498
	P	<0.001	<0.001	<0.001	<0.001
Uric acid	ρ	-0.086	0.333	0.345	-
	P	0.169	<0.001	<0.001	-

ICU: Intensive care unit; UAR: Uric acid/albumin ratio; WBC:White blood cell; RDW: Red cell distribution width; ASO: Antistreptolysin O; EF: Ejection fraction; CRP: C Reactive protein; LDL: Low density lipoprotein; HDL: High density lipoprotein; TRG: Triglyceride

biopsy-confirmed myocarditis, found that hemodynamic impairment at presentation was the primary determinant of both short- and long-term prognosis(18-20). In fulminant myocarditis, symptoms typically emerge rapidly within two days to two weeks, leading to significant hemodynamic dysfunction and circulatory failure, often resulting in a sharp drop in blood pressure and the need for vasoactive medications. In advanced stages, mechanical circulatory support devices may be required(21-23).

In our study, we classified patients with refractory chest pain, hypotension, detection of pericardial effusion with subsequent increase, decreased ejection fraction, and lack of response to medical and symptomatic treatment as a severe patient group. In addition to standard and symptomatic treatment, we administered intravenous steroids and IVIG therapy when necessary in this group. Throughout our follow-up, there was no need for mechanical circulatory support devices.

Our findings indicate that higher UAR values are significantly associated with increased severity of myocarditis, evidenced by correlations with extended ICU stays, increased need for inotropic support, and elevated levels of inflammatory markers such as CRP and ferritin. These results align with previous research suggesting that oxidative stress and inflammation play crucial roles in the pathophysiology of myocarditis.

In addition to myocarditis, UAR has been investigated as a prognostic marker in several other inflammatory and cardiovascular diseases. Studies have shown that elevated UAR levels are associated with worse outcomes in patients with acute kidney injury, heart failure, coronary artery disease, pulmonary arterial hypertension, and even chronic inflammatory conditions such as rheumatoid arthritis. These findings support the hypothesis that UAR reflects both oxidative stress and systemic inflammation, mechanisms that are common across various disease processes. For instance, in patients with ST-elevation myocardial infarction (STEMI), a high UAR was linked to increased in-hospital mortality and poor short-term prognosis. Similarly, in chronic coronary artery disease, UAR was found to correlate with the extent of atherosclerosis. These associations suggest that UAR may serve as a generalizable marker of disease severity and adverse outcomes across a wide range of clinical conditions beyond myocarditis.

Several studies have reported elevated uric acid levels in patients with various cardiovascular conditions, including myocarditis(24, 25). Uric acid, a product of purine metabolism, is known to be a marker of oxidative stress and inflammation. Elevated serum uric acid levels have been associated with adverse cardiovascular outcomes, including heart failure and myocardial infarction. Our study expands on this by demonstrating that when adjusted for albumin levels, reflecting the body's nutritional and inflammatory status, the UAR provides a more nuanced assessment of myocarditis severity.

The albumin level is an established prognostic marker in various diseases, including cardiovascular disorders. Hypoalbuminemia is often observed in patients with severe inflammation and is associated with worse clinical outcomes. By combining uric acid and albumin levels into a single ratio, the UAR

accounts for both oxidative stress and nutritional/inflammatory status, providing a comprehensive marker that correlates well with disease severity in myocarditis patients.

In our cohort, patients with higher UAR values were more likely to experience complications such as pericardial effusion and required more intensive medical interventions, including IV steroids and inotropic support. These findings suggest that UAR can serve as a reliable marker for identifying patients at higher risk of severe disease who may benefit from closer monitoring and more aggressive treatment strategies. Additionally, the significant correlation between UAR and total hospital stay underscores its potential utility in predicting healthcare resource utilization. In general, we did not need MRI and endomyocardial biopsy because the patient's clinical course was not aggressive and they responded to treatment, especially those with severe course responded to IVIG and IV steroids. If the patient was resistant to treatment or the clinic worsened despite these treatments, we would consider MRI and endomyocardial biopsy.

Comparatively, few studies have specifically investigated the role of UAR in myocarditis. However, our findings are consistent with broader literature examining the prognostic value of uric acid and albumin in other cardiovascular and inflammatory conditions. For instance, studies have shown that high UAR values are predictive of poor outcomes in heart failure and coronary artery disease. These parallels highlight the potential of UAR as a universal marker of disease severity in various cardiac conditions.

Limitations

This study has several limitations that must be acknowledged. Firstly, the diagnosis of myocarditis in our cohort was based on clinical presentation and non-invasive tests rather than endomyocardial biopsy or cardiac MRI, considered gold standards for definitive diagnosis. The lack of these diagnostic modalities may have led to misclassification or underestimation of the disease's presence and severity. Secondly, we did not measure B-type natriuretic peptide (BNP) levels, a well-established biomarker in heart failure and myocarditis. BNP could have provided additional insights into the severity of myocardial dysfunction and the patients' hemodynamic status. The absence of BNP data may limit the comprehensive assessment of cardiac function in our study population.

Additionally, our study is retrospective, which inherently carries biases such as selection bias and recall bias. The reliance on medical records for data collection can result in incomplete or inaccurate information, potentially affecting the study's outcomes. Prospective studies would be needed to validate our findings and provide more robust evidence. Another limitation is the potential for confounding factors that were not accounted for in our analysis. Factors such as underlying comorbidities, medications, and lifestyle factors (e.g., diet, smoking) can influence uric acid and albumin levels, thereby affecting the UAR. A more comprehensive analysis controlling for these variables would strengthen the validity of our conclusions.

CONCLUSION

In conclusion, our study provides evidence supporting the use of UAR as a novel marker for assessing disease severity in acute myocarditis patients. By integrating markers of oxidative stress and nutritional/inflammatory status, UAR offers a comprehensive tool for risk stratification and management in clinical practice. Future studies should aim to validate these findings in larger, prospective cohorts and explore the mechanistic pathways linking UAR with myocarditis severity.

Funding: This study received no funding. In our article, no support was received from artificial intelligence-based assistive technologies.

Conflict of interest: The authors report no conflict of interest

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