Is There Any Association Between Uric Acid to High-density Lipoprotein Cholesterol Ratio and Erectile Dysfunction?

Ürik Asitin Yüksek Yoğunluklu Lipoprotein Kolesterole Oranı ile Erektil Disfonksiyon Arasında Bir İlişki Var mı?

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Abstract

Objective: Elevated uric acid (UA) and low levels of high-density lipoprotein (HDL) cholesterol are associated with cardiovascular events and mortality. Erectile dysfunction (ED) has been considered an early marker of cardiovascular disease (CVD). Therefore, this study aimed to investigate the uric acid/ HDL ratio (UHR) as a nowel marker in patients with ED.

Materials and Methods: The study included 147 patients with a mean age of 50 years (range 32-76 years). Retrospective analyses were performed on the patients who were admitted to urology outpatient clinics. The laboratory parameter results were retrieved from the hospital medical records, and the UHR value was calculated. Patients were categorized into three groups according to the International Index of Erectile Function (IIEF) score. UHR was compared between groups, and its predictive value was evaluated using regression analysis and ROC curve analysis.

Results: Age was found to be significantly different in all three groups (Groups 1-2, p=0.001; Groups 1-3, p=0.000; Groups 2-3, p=0.001). It was observed that the degree of ED increased with age. The values of UA and HDL were similar in all groups (p>0.05). In contrast, the UHR value was statistically significantly higher 0.15 (0.083-0.288, p =0.047) in the moderate-severe ED (Group 3). ROC curve analyses revealed that UHR predicted severe ED (IIEF 5-11) with 42.9% sensitivity and 87.3% specificity (AUC:0.66, CI 95% 0.538-0.781, p=0.019).

Conclusion: UHR may serve as a severe ED indicator in patients admitted to the cardiology outpatient clinic since it has a significant association with a low IIEF score.

Keywords: erectile dysfunction, uric acid, high-density lipoprotein, uric acid/ HDL ratio

Öz

Amaç: Yüksek ürik asit (UA) ve düşük yüksek yoğunluklu lipoprotein (HDL) kolesterol seviyeleri kardiyovasküler olaylar ve mortalite ile ilişkilidir. Erektil disfonksiyon (ED), kardiyovasküler hastalığın erken bir belirteci olarak kabul edilmiştir. Bu nedenle, bu çalışmada ED'li hastalarda bir yeni belirteç olarak ürik asit/HDL oranını (UHR) araştırmayı amaçladık.

Gereçler ve Yöntemler: Çalışmaya yaş ortalaması 50 (32-76 yaş aralığında) olan 147 hasta dahil edildi. Üroloji polikliniğine başvuran hastaların retrospektif analizleri yapıldı. Hastaların laboratuvar parametreleri hastane tıbbi kayıtlarından alındı ve UHR değerleri hesaplandı. Hastalar Uluslararası Erektil Fonksiyon İndeksi (IIEF) skoruna göre üç gruba ayrıldı. UHR gruplar arasında karşılaştırıldı; prediktif değeri regresyon analizi ve ROC eğrisi analizi ile değerlendirildi.

Bulgular: Her üç grupta da yaş anlamlı olarak farklı bulundu (Grup 1-2, p=0,001; Grup 1-3, p=0,000; Grup 2-3, p=0,001). ED derecesinin yaşla birlikte arttığı gözlendi. Ürik asit ve HDL değerleri üç grup arasında anlamlı farklılık göstermedi (p>0,05). Buna karşılık, orta-şiddetli ED'de (Grup 3) UHR değeri istatistiksel olarak anlamlı derecede yüksekti 0.15 (0.083-0.288, p=0,047). ROC eğrisi analizi, UHR'nin % 42.9 duyarlılık ve % 87.3 özgüllükle (AUC: 0.66, CI %95 0.538-0.781, p=0.019) şiddetli ED'yi (IIEF 5-11) öngördüğünü ortaya koydu.

Sonuç: UHR, düşük IIEF skoru ile anlamlı bir ilişkisi olduğu için kardiyoloji polikliniğine başvuran hastalarda ciddi bir ED göstergesi olarak kullanılabilir.

Anahtar kelimeler: erektil disfonksiyon, ürik asit, yüksek yoğunluklu lipoprotein, ürik asit/HDL oranı

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Introduction

Sexual health is one of the essential components of global health and good life of quality. Atherosclerotic cardiovascular disease (ASCVD) and vascular sexual dysfunction have similar pathogenesis [1]. Erectile dysfunction (ED) is defined as the inability of erection to last long enough to start and maintain sexual intercourse. About 1/4 to 1/3 of adult men experience this problem [2,3]. ED may develop due to many reasons such as genetic, organic, anatomical disorders, systemic diseases, lifestyle, and environmental factors. Usually, the underlying cause is not single but a combination of several factors [4].

Vascular damage due to endothelial dysfunction prevents adequate vasodilation of the penile vessels in response to sexual stimulation and causes ED. Therefore, vascular ED may be an early manifestation of CVD and is associated with vascular risk factors such as hipertension (HT), diabetes mellitus (DM), dyslipidemia and, smoking [5].

The enzyme xanthine oxidase synthesizes uric acid [6]. Uric acid (UA) to high-density lipoprotein (HDL)-cholesterol ratio (UHR) is a new parameter, which has been investigated in patients with type 2 diabetes mellitus with metabolic syndrome [7]. HDL cholesterol levels are negatively correlated with oxidative stress and the degree of inflammation in chronic diseases [8]. Several epidemiological studies showed significant relationship between serum UA levels and various cardiovascular conditions such as HT, metabolic syndrome, coronary artery disease (CAD), cerebrovascular (CV) disease, and dementia. [9-12].

Studies concluded that there is a significant relationship between uric acid and inflammation. It has been claimed that the effects of uric acid on mortality and poor prognosis occur through its pro-inflammatory mechanism [13]. High uric acid and low HDL lead to poor cardiovascular outcomes by increasing endothelial dysfunction and oxidative stress. Studies have shown that the combined effect of the two causes more damage [14,15]. The related literature shows that, there is limited knowledge about the relationship between UHR and ED. Considering the strong relationship between erectile dysfunction and cardiac diseases, it was hypothesized that the uric acid to HDL ratio, associated with cardiovascular mortality, could predict erectile dysfunction.

Material and Method

This single-center study was conducted on a total of 147 patients with a mean age of 50 years (range 32-76 years). Retrospective analyses were performed on the patients who have been admitted to urology outpatient clinics between 2015 and 2019. The detailed medical history of the study population was retrieved from the hospital medical records. Patients were categorized into three groups according to the IIEF score. Group 1 was formed of patients with an IIEF score of 22-25, without erectile dysfunction, Group 2 of patients with moderate-to-mild ED with an IIEF score of 12-24, and Group 3 of those with an IIEF score of 5-11 with moderate-to-severe ED.

Exclusion criteria were as follows; active malignant disease, systemic inflammatory or infectious disease, surgery or trauma within one month, end-stage renal failure (eGFR<15 ml/min/1.73m^2), liver failure, patients taking medications that may affect serum uric acid levels such as thiazides, furosemide, acetylsalicylic acid, etc. and medicines that may affect serum lipid levels such as statins, fibrates, niacin, etc., and that may affect erectile dysfunction such as beta-blockers, thiazide diuretics, and those with erectile dysfunction due to psychogenic and hormonal reasons.

Age, gender, smoking, and IIEF scores were recorded from the patient files and hospital medical records. Laboratory parameters, such as blood uric acid, total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglyceride (TG), were measured using an automatic biochemical analyzer (Architect C8000, USA), and results were obtained from the same database and patient files. The uric acid to HDL ratio (UHR) is calculated by dividing serum uric acid level by HDL cholesterol.

Hypertension was accepted as systolic blood pressure (BP) of ≥140 mmHg or diastolic BP of ≥90 mmHg or both or the use of antihypertensive drugs. DM was defined as the use of anti-diabetic medications or fasting plasma glucose levels ≥126 mg/dL in at least two measurements or a glycated hemoglobin ratio (HbA1c) of ≥6.5%. The study was approved by the Institutional Review Board Ethics Committee of Dr. Sadi Konuk Training and Research Hospital (Approval no: 2021/342). Written informed consent was obtained from all patients.

Evaluation of Erectile Function

ED was evaluated by the Turkish version of the International Index of Erectile Function with five questions (IIEF-5) [16]. This is a self-administered questionnaire in which patient responses are based on their experience during the last four weeks and are scored on a 5-point Likert scale, with lower values representing the poorer sexual function. Total scores are classified as; 22-25: No erectile dysfunction; 17-21: Mild erectile dysfunction; 12-16: Mild to moderate erectile dysfunction; 8-11: Moderate erectile dysfunction; and 5-7: Severe erectile dysfunction [17]. This questionnaire has been shown to provide data on ED 98% sensitivity and 88% specificity [18].

Statistically Analysis

All statistical calculations were made using IBM SPSS statistics vn.25 software. The normality of data distribution was assessed with the Shapiro-Wilk test. Skewed data were expressed as median and minimum-maximum values. Since the data were not normally distributed, the Kruskal-Wallis test was used to compare the groups. ROC curve analysis was used to assess the predictive ability of UHR for ED. Univariate and Multivariate Logistic regression analyses were performed to investigate predictors of ED.

Results

The demographic and clinical data of patients are summarized in **Table 1**. Age was found to be significantly different in all three groups (Groups 1-2, p=0.001; Groups 1-3, p=0.000; Groups 2-3, p=0.001). The degree of ED was observed to increase with age. A statistically significant difference was determined between the three groups in respect of total cholesterol values. Post hoc analyses showed that this difference was between Group 1 (normal patients with IIEF 22-25) and Group 2 (patients with moderate-mild IIEF 12-21) (p=0.036). DM was observed at a higher rate in Group 3. No significant difference was determined between the groups in respect of triglyceride, LDL cholesterol, HDL cholesterol, and UA values (p>0.05 for all).

The laboratory data of the study groups are summarized in **Table 2**. The values of uric acid and HDL were similar in all groups (p>0.05). The UHR value was determined to be statistically significantly higher 0.15 (0.083-0.288, p=0.047) in Group 3 (moderate-severe ED).

Multiple logistic regression analysis was also performed to define the predictive value of variables for the presence of ED. UHR was not found to be an independent predictor of ED [p=0.216, 95% CI for OR:748.11, (0.021-2664.8)], but age predicted ED [p=0.002, 95% CI for OR:1.130 (1.044-1.233)] **(Table 3)**.

ROC curve analyses revealed that UHR predicted severe ED (IIEF 5-11) with 42.9 % sensitivity and 87.3 % specificity (AUC:0.66, CI 95 % 0.538-0.781, p=0.019) **(Figure 1).**

Discussion

The principal finding of the present study was that UHR was statistically significantly higher in patients with moderate-severe ED than in those with mild and mild to moderate ED. Also, UHD predicted severe ED.

Table 1. Clinical characteristics of the study population

	Mean ± SD	Median (min-max)
Age	49.93±9.24	50.00 (32-76)
Smoking (n)	62	42.2
Diabetes Mellitus (n)	39	24.5
Hypertension (n)	61	41.5
IIEF -5	16.90±4.758	18.00 (5-25)
Triglyceride (mg/dl)	159.80±83.373	136.00 (32-422)
HDL-C (mg/dl)	45.25±13.841	42.00 (25-136)
LDL-C (mg/dl)	123.98±37.407	127.80 (41-230)
TC (mg/dl)	198.85±42.621	205.00 (96-314)
Uric acid (mg/dl)	5.61±1.184	5.60 (3-13)
UHR (%)	0.13±0.049	0.12 (0.033-0.288)

IIEF: international index of erectile function; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; UHR: uric acid to hdl-cholesterol ratio

Table 2. Clinical characteristics and laboratory parameters of the study groups

	Group 1 (n=24)	Group 2 (n=102)	Group 3 (n=21)	P- value
Age	41.00 (32-57)	50.00 (33-75)	58.00 (43-76)	0.000
Smoking (n, %)	16 (66.7)	39 (39.0)	7 (33.3)	0.031
Hypertension (n, %)	3 (12.5)	41 (41.0)	17 (27.9)	0.000
Diabetes Mellitus (n, %)	2 (8.3)	21 (21.0)	13 (61.9)	0.000
TG (mg/dl)	140.00 (58-386)	131.50 (32-422)	141.00 (64-350)	0.841
HDL-C (mg/dl)	42.50 (32-136)	42.55 (25-113)	40.00 (28-50)	0.092
LDL-C (mg/dl)	102.00 (30-188)	130.60 (41-230)	120.20 (64-188)	0.103
TC (mg/dl)	170.50 (108-252)	211.00 (96-314)	196.00 (119-253)	0.029
UA (mg/dl)	5.30 (3-9)	5.60 (3-9)	6.12 (4-13)	0.599
UHR (%)	0.11 (0.033-0.201)	0.12 (0.347-0.270)	0.15 (0.083-0.288)	0.047

TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; UA: uric acid; UHR: uric acid to HDL-cholesterol ratio

Table 3. Univariate and multivariate logistics regression analysis for independent predictors of erectile dysfunction

Parameter	Univariate		Multivariate	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Age	1.157 (1.074-1.247)	0.000	1.130 (1.044-1.233)	0.002
Smoking	0.307 (0.122-0.773)	0.012	0.456 (0.166-1.253)	0.128
HT	6.444 (1.826-22.747)	0.004	3.171 (0.826- 12.172)	0.093
UHR	63.42 (0.039-1042.8)	0.193	748.11 (0.021-2664.8)	0.216

HT: hypertension; UHR: uric acid to HDL-cholesterol ratio
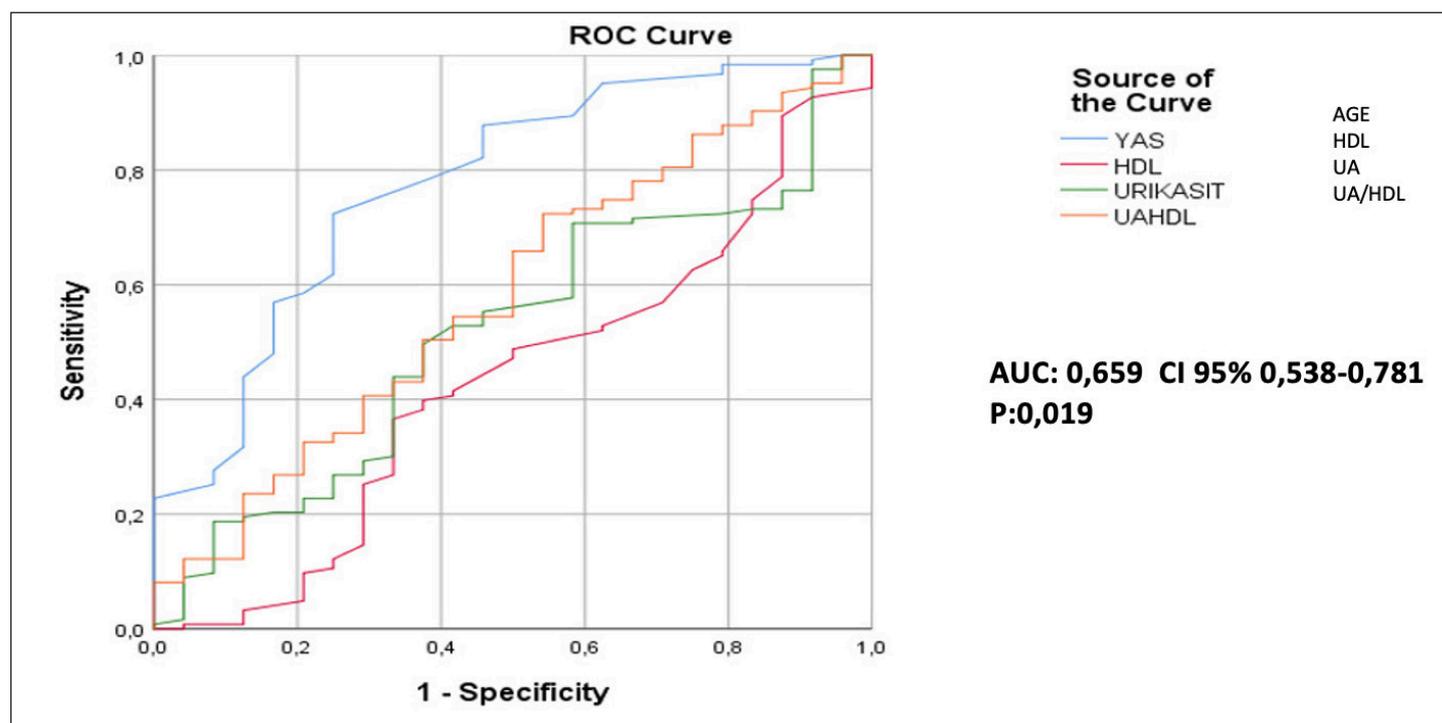
Figure 1. ROC curve of the study parameters in predicting severe ED

Multiple mechanisms such as androgen hormone levels, psychosocial factors, vascular damage, and endothelial dysfunction play a key role in the pathogenesis of ED. It is thought that uric acid may be associated with ED since it affects endothelial and vascular functions [19,20].

Meta-analyses have shown that UA is also a predictor of cardiovascular risk factors such as insulin resistance, HT and the development of renal disease (20-23). Therefore, all these risk factors that cause endothelial and vascular damage are also associated with ED.

UHR is a new marker consisting of two values, namely UA and HDL cholesterol. Using UHR, the degree of inflammation and endothelial dysfunction can be determined which may be involved in ED, indicated by a higher level of UA or a lower level of HDL cholesterol, or both. In a recent study, UHR was reported to be a predictor of metabolic syndrome in type 2 DM patients and was suggested as a marker of high sensitivity and specificity for the control of diabetes. Another study by Ruihua Liu et al. showed a significant association of UHR with cardiovascular mortality in peritoneal dialysis patients with age >65 years, malnutrition, DM, and CVD history [24].

ED may be an early predictor of CVD; thus, it may provide insight for clinicians in investigating risk factors. It was thought that the patients admitted to the cardiology department were reluctant to express complaints of ED. Therefore, it may be important to refer patients with high UHR to urology outpatient clinics for early diagnosis of ED. Thus, early detection of high-risk patients for ED and an early start to treatment will increase their quality of life, and most importantly, reduce the risk of CVD. Thus, early diagnosis of ED can accelerate the diagnosis and treatment of underlying risk factors and prevent major adverse cardiocerebrovascular events [5]. Our study is the first to examine the relationship between uric acid/HDL ratio and erectile dysfunction to the best of our knowledge.

Limitations of the study: The cross-sectional and retrospective design of the study and the limited number of patients can be considered limitations of this study.

Conclusion

UHR may serve as an indicator of severe ED in patients admitted to the cardiology outpatient clinic since it has a significant association with a low IIEF score. More comprehensive prospective cohort studies may yield different results and show that UHR may be a predictor of ED.

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