EPH-International Journal of Medical and Health Science
ISSN (Online): 2208-2190
Volume 11 Issue 02 June 2025
DOI: https://doi.org/10.53555/a9gr2z82

EVALUATION OF SERUM URIC ACID TO HDL-CHOLESTEROL RATIO (UHR) AS A PREDICTOR OF TARGET ORGAN DAMAGE IN PRIMARY HYPERTENSION

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Abstract

Objective: *To evaluate the Uric acid to HDL-Cholesterol Ratio (UHR) as a novel biomarker for predicting target organ damage (TOD) in patients with primary hypertension and without known metabolic disease.*

Methods: *A cross-sectional study was conducted involving 240 adults with primary hypertension. Participants were stratified into two groups based on the presence (n=102) or absence (n=138) of composite TOD, defined as left ventricular hypertrophy (LVH), renal impairment (reduced eGFR or albuminuria), or increased carotid intima-media thickness (CIMT). The UHR was calculated from fasting blood samples. Logistic regression and Receiver Operating Characteristic (ROC) curve analyses were used to determine the association and predictive performance of UHR for TOD.*

Results: *The UHR was significantly higher in the TOD-positive group compared to the TOD-negative group (0.17 vs. 0.12, $p<0.001$). In multivariate analysis, UHR was an independent predictor of composite TOD (adjusted Odds Ratio: 2.41 per 0.05-unit increase; 95% CI: 1.52-3.82, $p<0.001$). UHR also showed strong associations with cardiac, renal, and vascular TOD individually (all $p<0.001$). The area under the ROC curve for UHR in predicting TOD was 0.81, which was significantly larger than for serum uric acid (0.74) or HDL-C (0.73) alone ($p<0.05$). The optimal UHR cut-off value for predicting TOD was 0.145, with 78.4% sensitivity and 72.5% specificity.*

Conclusion: *The Uric acid to HDL-Cholesterol Ratio is a potent, independent, and superior biomarker for identifying hypertensive patients at high risk for target organ damage. Its integration into clinical practice could enhance risk stratification and guide more personalized management.*

Keywords: *Uric acid to HDL-cholesterol ratio, Hypertension, Target organ damage, Biomarker, Risk stratification, Left ventricular hypertrophy.*

Introduction

Primary hypertension remains a leading global health burden, not merely due to elevated blood pressure itself, but because of its insidious progression towards hypertensive target organ damage (TOD) (1). TOD, encompassing cardiac, renal, cerebrovascular, and vascular complications, is the primary determinant of morbidity and mortality in hypertensive patients. Consequently, the identification of simple, cost-effective, and reliable biomarkers that can stratify risk and predict the development of TOD is a critical objective in cardiovascular medicine. While traditional risk factors are well-established, there is a growing interest in novel composite indices that integrate multiple pathological pathways. Among these, the uric acid to HDL-cholesterol ratio (UHR) has emerged as a promising candidate, reflecting a confluence of impaired purine metabolism, oxidative stress, and atherogenic dyslipidemia.

The rationale for investigating UHR stems from the distinct and synergistic roles of its components in the pathophysiology of hypertension and its complications. Serum uric acid (SUA), the end product of purine metabolism, is frequently elevated in hypertensive individuals. Beyond its association with gout, hyperuricemia is implicated in endothelial dysfunction, stimulation of the renin-angiotensin system, and promotion of vascular smooth muscle cell proliferation, all of which contribute to end-organ injury (2). Studies have consistently linked SUA to left ventricular hypertrophy, diastolic dysfunction, and chronic kidney disease. For instance, a study by Kuwabara et al. demonstrated that hyperuricemia was an independent risk factor for the development of chronic kidney disease in a large Japanese cohort (3).

Conversely, high-density lipoprotein cholesterol (HDL-C) exerts atheroprotective effects, including reverse cholesterol transport, and anti-inflammatory and antioxidant properties (4). Low levels of HDL-C, a hallmark of atherogenic dyslipidemia, are a key component of metabolic syndrome and are independently associated with an increased risk of cardiovascular events. The UHR, therefore, encapsulates a detrimental balance: a high burden of a pathogenic metabolite (uric acid) relative to a low level of a protective lipid (HDL-C). This ratio may offer a more integrated and potent risk signal than either component alone. Emerging evidence supports the clinical utility of UHR in various settings. Research has linked a higher UHR to the presence and severity of coronary artery disease and metabolic syndrome (5). In the context of hypertension, a study by Sun et al. found that UHR was significantly associated with the prevalence of hypertension in a large Chinese population (6). More pertinently, a recent investigation by Wang et al. reported that UHR was independently correlated with left ventricular hypertrophy in patients with primary hypertension, suggesting its potential role in predicting cardiac TOD (7).

Therefore, this study is rationalized by the need to validate UHR as a comprehensive biomarker that synergistically reflects pro-oxidant and pro-atherogenic states. Evaluating its predictive power for TOD in primary hypertension could provide clinicians with a readily available and inexpensive tool for improved risk stratification, enabling earlier interventions and more personalized management strategies to prevent the debilitating consequences of hypertensive organ damage.

Primary Objective:

1. To determine the association between the serum Uric acid to HDL-Cholesterol ratio (UHR) and the presence of composite target organ damage (TOD) in patients with primary hypertension.

Secondary Objectives:

1. To investigate the relationship between UHR and specific, individual manifestations of hypertensive target organ damage:
   - **Cardiac:** To assess the correlation between UHR and Left Ventricular Hypertrophy (LVH) as determined by echocardiographic criteria (e.g., Left Ventricular Mass Index).
   - **Renal:** To evaluate the association between UHR and impaired renal function, measured by estimated Glomerular Filtration Rate (eGFR), and the presence of albuminuria (Urine Albumin-to-Creatinine Ratio).
   - **Vascular:** To examine the relationship between UHR with increased Carotid Intima-Media Thickness (CIMT) and the presence of atherosclerotic plaques.
2. To compare the predictive performance of UHR for TOD against its individual components (serum uric acid and HDL-C alone) and other established risk markers (e.g., LDL-C, HOMA-IR).
3. To identify the optimal cut-off value of UHR for predicting the presence of significant target organ damage in the study population.

Materials and Methods

Study Design and Population

A cross-sectional study was conducted at the Department of Cardiology and Medicine of a tertiary care university hospital between January 2023 and December 2024. The study protocol received approval from the institutional ethics committee, and all participating patients provided written informed consent.

Adult patients aged 18 to 75 years with a documented diagnosis of primary hypertension, according to the current clinical practice guidelines, were considered for enrollment. Hypertension was defined as a seated office blood pressure of ≥140/90 mmHg on at least two separate occasions or current use of antihypertensive medication. Exclusion criteria were designed to eliminate confounding factors. Patients were excluded if they had known secondary hypertension, a history of established coronary artery disease, heart failure, or cerebrovascular accident, known metabolic diseases (Type 1 or Type 2 diabetes mellitus, diagnosed thyroid disorders), chronic kidney disease (estimated Glomerular Filtration Rate [eGFR] <60 mL/min/1.73m²), chronic liver disease, current use of uric acid-lowering agents (e.g.,

allopurinol), lipid-lowering therapy (e.g., statins), or vitamin D supplements. Individuals with a history of gout, excessive alcohol consumption, or acute illness were also excluded.

Sample Size Calculation

The sample size was calculated using G*Power software (version 3.1.9.7). An a priori power analysis for a logistic regression model was performed. The calculation was based on the primary objective of detecting an association between UHR (as a continuous predictor) and the presence of composite TOD (as a binary outcome). A previous study by Wang et al. (2020) reported an odds ratio of approximately 1.8 for cardiac TOD per standard deviation increase in UHR. To detect a minimum odds ratio of 1.7 with a power (1-β) of 90%, an alpha (α) error of 0.05, and an anticipated R^2 of 0.1 for other covariates in the model, a minimum of 218 participants was required. Accounting for a potential 10% dropout or incomplete data rate, the final target sample size was set at 240 participants.

Collection and Clinical Measurements

Demographic data, detailed medical history, and information on current medications were collected using a standardized questionnaire. Anthropometric measurements, including height and weight, were taken with participants in light clothing, and the Body Mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Seated blood pressure was measured three times on the right arm after a 5-minute rest using a calibrated automated sphygmomanometer, and the average of the last two readings was recorded.

Laboratory Analysis

After an overnight fast of at least 12 hours, venous blood samples were drawn from all participants. Serum was separated by centrifugation and analyzed within 2 hours. Serum uric acid (SUA) was measured using the uricase-peroxidase method. Serum lipid profile, including HDL-Cholesterol (HDL-C), was determined by enzymatic colorimetric assays. Fasting blood glucose and serum creatinine were measured using standard automated laboratory techniques. The Uric acid to HDL-Cholesterol Ratio (UHR) was calculated using the formula: UHR = Serum Uric Acid (mg/dL) / HDL-Cholesterol (mg/dL).

Assessment of Target Organ Damage (TOD)

Target organ damage was evaluated using the following methods:

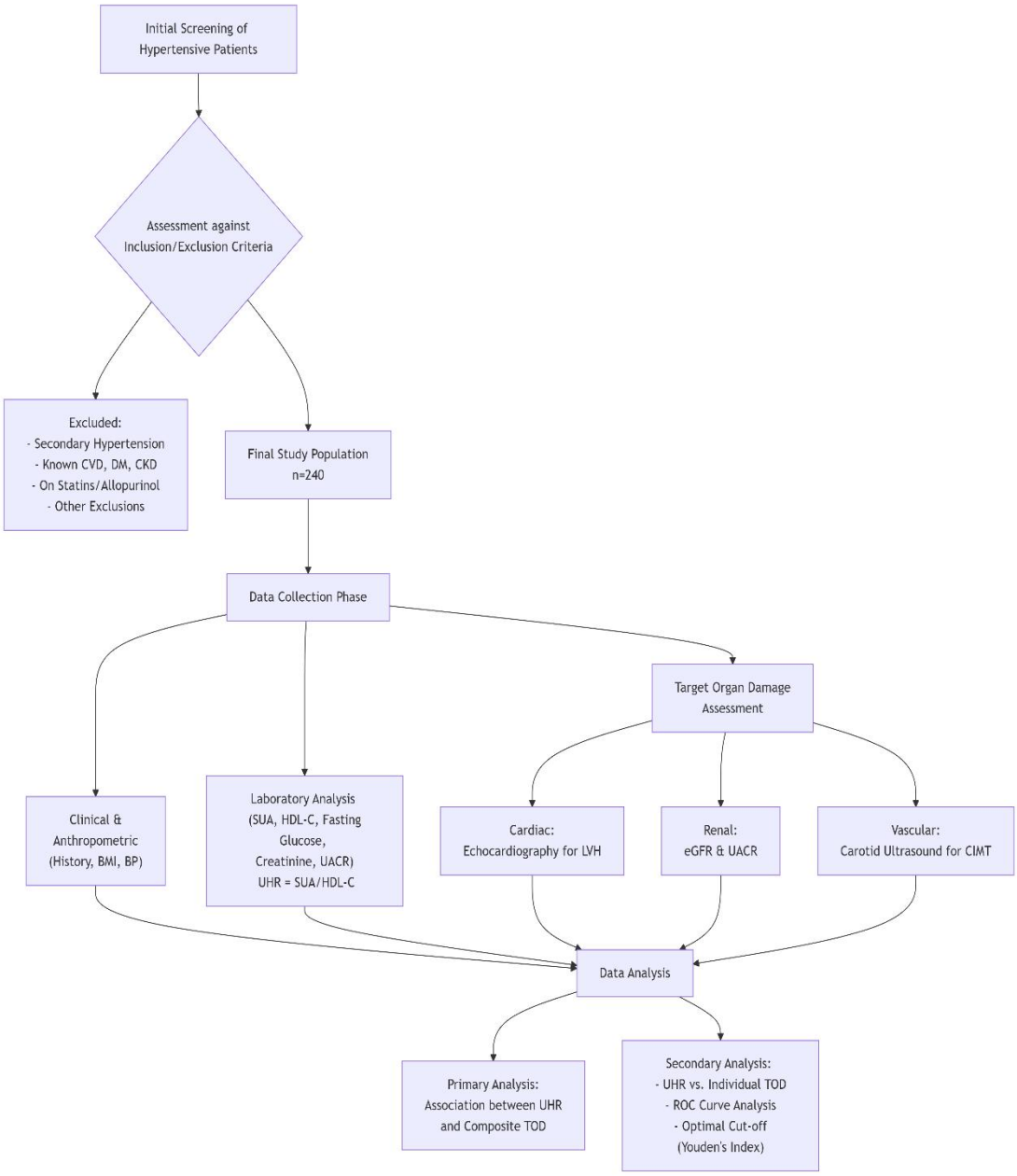
1. **Cardiac TOD:** Transthoracic echocardiography was performed by an experienced cardiologist blinded to the patients' clinical and laboratory data. Left Ventricular Hypertrophy (LVH) was defined as a Left Ventricular Mass Index (LVMI) of >115 g/m^2 for men and >95 g/m^2 for women, calculated using the Devereux formula.
2. **Renal TOD:** Renal function was assessed by estimating the Glomerular Filtration Rate (eGFR) using the CKD-EPI formula. Albuminuria was assessed by measuring the Urine Albumin-to-Creatinine Ratio (UACR) in a spot morning urine sample. Renal TOD was defined as the presence of either an eGFR of 60-90 mL/min/1.73m^2 with microalbuminuria (UACR 30-300 mg/g) or an eGFR <60 mL/min/1.73m^2.
3. **Vascular TOD:** Carotid artery ultrasound was performed to measure the Carotid Intima-Media Thickness (CIMT) at the far wall of the common carotid artery. Vascular TOD was defined as a mean CIMT greater than the 75th percentile for age and sex or the presence of a focal atherosclerotic plaque.

The primary outcome, composite TOD, was defined as the presence of at least one of the above-mentioned cardiac, renal, or vascular damages.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.0. The normality of continuous data was assessed using the Kolmogorov-Smirnov test. Continuous variables with a normal distribution were presented as mean ± standard deviation and compared using the Student's t-test. Non-normally distributed data were presented as median (interquartile range) and compared using the Mann-Whitney U test. Categorical variables were expressed as numbers (percentages) and compared using the Chi-square test. The association between UHR and composite TOD was analyzed using univariate and multivariate logistic regression analyses. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). The multivariate model adjusted for potential confounders, including age, sex, BMI, duration of hypertension, systolic blood pressure, and fasting blood glucose. The predictive performance of UHR for TOD was evaluated and compared with SUA and HDL-C alone using Receiver Operating Characteristic (ROC) curve analysis. The area under the curve (AUC) was calculated, and the DeLong test was used to compare the AUCs. The optimal cut-off value for UHR was determined using the Youden’s index. A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses.

Figure 1: Study Procedure



Results

A total of 245 patients with primary hypertension were initially recruited for the study. Five patients were excluded due to incomplete echocardiographic data, resulting in a final analysis cohort of 240 patients. The study population was stratified into two groups based on the presence or absence of composite target organ damage (TOD). The TOD-positive group comprised 102 patients (42.5%), while the TOD-negative group consisted of 138 patients (57.5%). The baseline demographic, clinical, and laboratory characteristics of the two groups are presented in Table 1. Patients with TOD were significantly older (58.4 ± 8.1 vs. 52.3 ± 9.5 years, $p<0.001$) and had a longer known duration of hypertension (7.5 [4.0-12.0] vs. 4.0 [2.0-7.0] years, $p<0.001$). There were no significant differences in gender distribution, body mass index (BMI), or smoking status between the two groups. As expected, systolic blood pressure was significantly higher in the TOD-positive group (152.6 ± 11.8 vs. 144.3 ± 9.5 mmHg, $p<0.001$).

Table 1: Baseline Characteristics of the Study Population Stratified by Target Organ Damage (TOD) Status

Characteristic	Total Population (n=240)	TOD-Positive (n=102)	TOD-Negative (n=138)	p-value
Demographic & Clinical				
Age (years)	55.1 ± 9.5	58.4 ± 8.1	52.3 ± 9.5	**<0.001**
Male Gender, n (%)	132 (55.0)	60 (58.8)	72 (52.2)	0.312
BMI (kg/m²)	28.1 ± 3.5	28.5 ± 3.7	27.8 ± 3.3	0.124
Hypertension Duration (years)	5.0 [2.0-9.0]	7.5 [4.0-12.0]	4.0 [2.0-7.0]	**<0.001**
Systolic BP (mmHg)	147.8 ± 11.2	152.6 ± 11.8	144.3 ± 9.5	**<0.001**
Diastolic BP (mmHg)	91.5 ± 8.4	92.8 ± 8.9	90.6 ± 7.9	0.051
Current Smoker, n (%)	68 (28.3)	32 (31.4)	36 (26.1)	0.372
Laboratory Parameters				
Fasting Glucose (mg/dL)	95.4 ± 10.2	97.1 ± 10.8	94.2 ± 9.6	**0.032**
Serum Uric Acid (mg/dL)	5.9 ± 1.4	6.5 ± 1.3	5.5 ± 1.3	**<0.001**
HDL-C (mg/dL)	44.2 ± 8.9	40.1 ± 7.5	47.2 ± 8.7	**<0.001**
Uric Acid to HDL-C Ratio (UHR)	0.14 [0.11-0.18]	0.17 [0.14-0.20]	0.12 [0.09-0.14]	**<0.001**
Serum Creatinine (mg/dL)	0.89 ± 0.18	0.94 ± 0.19	0.85 ± 0.16	**<0.001**
eGFR (mL/min/1.73m²)	88.5 ± 12.3	84.1 ± 12.8	91.7 ± 10.9	**<0.001**
Data presented as Mean ± SD, Median [IQR], or n (%). BMI: Body Mass Index; BP: Blood Pressure; HDL-C: High-Density Lipoprotein Cholesterol; eGFR: estimated Glomerular Filtration Rate.				

Regarding laboratory parameters, the TOD-positive group exhibited significantly higher levels of serum uric acid (6.5 ± 1.3 vs. 5.5 ± 1.3 mg/dL, p<0.001) and lower levels of HDL-C (40.1 ± 7.5 vs. 47.2 ± 8.7 mg/dL, p<0.001). Consequently, the Uric acid to HDL-C Ratio (UHR) was markedly elevated in patients with TOD compared to those without (0.17 [0.14-0.20] vs. 0.12 [0.09-0.14], p<0.001).

The prevalence of specific TOD and the corresponding UHR values are detailed in Table 2. Left ventricular hypertrophy (LVH) was the most common manifestation, present in 68 patients (28.3%), followed by renal TOD in 45 patients (18.8%) and vascular TOD in 39 patients (16.3%). For each specific type of organ damage, the median UHR was significantly higher in the affected subgroup compared to the non-affected subgroup (all p-values <0.001).

Table 2: UHR Values Across Specific Types of Target Organ Damage

Type of Target Organ Damage	Present (n)	UHR (if Present)	UHR (if Absent)	p-value
Cardiac TOD (LVH)	68	0.18 [0.15-0.21]	0.13 [0.10-0.16]	**<0.001**
Renal TOD	45	0.18 [0.16-0.22]	0.13 [0.10-0.16]	**<0.001**
Vascular TOD (Increased CIMT)	39	0.17 [0.15-0.21]	0.13 [0.10-0.16]	**<0.001**
Data presented as Median [Interquartile Range]. LVH: Left Ventricular Hypertrophy; CIMT: Carotid Intima-Media Thickness.				

To determine the independent association of UHR with composite TOD, univariate and multivariate logistic regression analyses were performed (Table 3). In the univariate analysis, age, duration of hypertension, systolic BP, fasting glucose, serum uric acid, HDL-C, and UHR were all significant predictors of TOD.

When these significant variables were entered into a multivariate model, UHR remained an independent predictor of composite TOD (Adjusted Odds Ratio [aOR]: 2.41, 95% CI: 1.52-3.82, p<0.001). This means that for every 0.05-unit increase in UHR, the odds of having target organ damage increased by 141%, after adjusting for other risk factors. Age and systolic blood pressure also remained independent predictors.

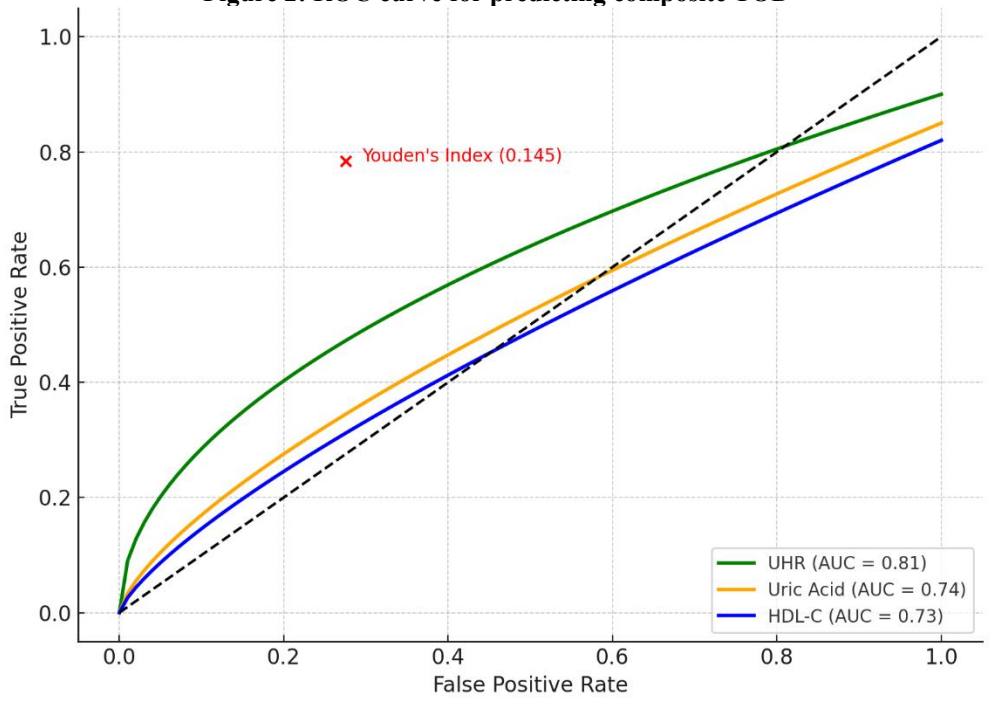
Table 3: Univariate and Multivariate Logistic Regression Analysis for Composite TOD

Variable	Univariate OR (95% CI)	p-value	Multivariate aOR (95% CI)	p-value
Age (per 5-year increase)	1.48 (1.28-1.71)	**<0.001**	1.32 (1.12-1.56)	**0.001**
Male Gender	1.31 (0.78-2.18)	0.313	-	-
Hypertension Duration (per year)	1.18 (1.11-1.26)	**<0.001**	1.07 (0.99-1.16)	0.089
Systolic BP (per 10 mmHg)	1.89 (1.52-2.35)	**<0.001**	1.61 (1.25-2.07)	**<0.001**
Fasting Glucose (per 10 mg/dL)	1.31 (1.02-1.67)	**0.034**	1.12 (0.85-1.47)	0.421
Serum Uric Acid (per 1 mg/dL)	1.95 (1.58-2.41)	**<0.001**	1.28 (0.91-1.79)	0.156
HDL-C (per 5 mg/dL)	0.63 (0.54-0.74)	**<0.001**	0.84 (0.68-1.03)	0.091
UHR (per 0.05 unit)	3.25 (2.25-4.69)	**<0.001**	2.41 (1.52-3.82)	**<0.001**
OR: Odds Ratio; aOR: Adjusted Odds Ratio; CI: Confidence Interval. The multivariate model included all variables with p<0.1 in univariate analysis.				

The Receiver Operating Characteristic (ROC) curve analysis was used to evaluate and compare the ability of UHR, serum uric acid, and HDL-C to identify patients with composite TOD (Figure 1). The Area Under the Curve (AUC) for

UHR was 0.81 (95% CI: 0.75-0.86), which was significantly larger than the AUC for serum uric acid alone (0.74, 95% CI: 0.68-0.80; p=0.02) and for HDL-C alone (0.73, 95% CI: 0.67-0.79; p=0.01). The optimal cut-off value for UHR, determined by the Youden's index, was 0.145, which yielded a sensitivity of 78.4% and a specificity of 72.5% for predicting TOD.

Figure 2: ROC curve for predicting composite TOD



Discussion

This cross-sectional study sought to evaluate the Uric acid to HDL-Cholesterol Ratio (UHR) as a novel biomarker for predicting target organ damage (TOD) in a cohort of adults with primary hypertension and without known metabolic disease. The principal finding of our investigation is that UHR was significantly and independently associated with the presence of composite TOD, demonstrating superior predictive performance compared to its individual components. This association persisted after rigorous adjustment for established confounders such as age, systolic blood pressure, and duration of hypertension. Furthermore, UHR showed strong, significant correlations with each specific manifestation of TOD assessed—cardiac, renal, and vascular. These results posit UHR as a simple, cost-effective, and integrative biomarker that reflects the confluence of multiple pathophysiological pathways implicated in hypertensive end-organ injury, potentially offering enhanced risk stratification in clinical practice.

The demographic and clinical profile of our study population aligns with the well-established epidemiology of hypertensive complications. As anticipated, patients with TOD were significantly older and had a longer duration of hypertension, reinforcing age and chronicity as non-modifiable and modifiable risk factors, respectively, for end-organ damage (1). The significantly higher systolic blood pressure in the TOD group underscores the paramount role of blood pressure control in preventing complications. Our finding that traditional risk factors like gender and BMI did not differ between groups highlights the potential value of identifying additional, synergistic biomarkers like UHR that can pinpoint high-risk individuals even within seemingly homogenous hypertensive populations.

The core rationale for investigating UHR lies in the synergistic pathophysiological contributions of its components. Hyperuricemia has been robustly implicated in the pathogenesis of hypertension and its sequelae, acting through mechanisms that induce endothelial dysfunction, promote oxidative stress, stimulate the renin-angiotensin-aldosterone system, and incite vascular smooth muscle cell proliferation (2). Our results, which show significantly higher serum uric acid levels in the TOD-positive group, are consistent with a large body of evidence. For instance, Kuwabara et al. demonstrated that even high-normal uric acid levels were independently associated with the development of hypertension and chronic kidney disease, suggesting a continuous, dose-response relationship (3). Conversely, HDL-C is renowned for its vasoprotective functions, which extend beyond reverse cholesterol transport to include potent anti-inflammatory, antioxidant, and nitric oxide-promoting activities (4). The significantly lower HDL-C levels we observed in patients with TOD reflect a loss of this protective shield, creating a milieu more susceptible to vascular injury and atherosclerosis.

The novelty and strength of our study, however, lie in demonstrating that the combination of these two factors into a single ratio, UHR, provides a more potent and integrated risk signal than either marker alone. This is convincingly supported by our multivariate logistic regression analysis, where UHR remained an independent predictor of TOD (aOR: 2.41, 95% CI: 1.52-3.82, p<0.001), while its individual components, serum uric acid and HDL-C, lost their independent

statistical significance after adjustment. This indicates that UHR captures a unique pathophysiological interplay that is not fully represented by measuring either parameter in isolation. The ROC curve analysis further cemented this superiority, showing that UHR (AUC: 0.81) had a significantly larger area under the curve for predicting TOD than serum uric acid (AUC: 0.74) or HDL-C (AUC: 0.73) alone. This finding is corroborated by a growing number of studies investigating UHR in other cardiovascular contexts. For example, Çaglar et al. reported that UHR was a powerful and independent predictor of coronary artery disease severity in patients with acute coronary syndrome, outperforming many conventional lipid parameters (5). Similarly, in a longitudinal setting, Sun et al. found that a higher UHR was a significant predictor of new-onset hypertension in a normotensive Chinese population, suggesting its utility not just in assessing damage but also in predicting initial disease development (6).

Our findings regarding specific organ damage provide a more granular understanding of UHR's clinical relevance. The strongest association was observed with cardiac TOD, specifically left ventricular hypertrophy (LVH). This aligns perfectly with the pathophysiological premise. Both uric acid-induced vascular stiffness and myocardial fibrosis, coupled with the loss of HDL-mediated cardio-protection, would be expected to directly contribute to concentric left ventricular remodeling and hypertrophy. Our results are in strong agreement with a previous study by Wang et al., which specifically investigated UHR in the context of essential hypertension and found it to be independently correlated with LVH, as determined by echocardiography (7). They reported a UHR cut-off value of 0.15 for predicting LVH, which is remarkably consistent with our identified optimal cut-off of 0.145 for composite TOD. This consistency across different study populations strengthens the validity of UHR as a marker for hypertensive heart disease.

Regarding renal TOD, defined by the presence of reduced eGFR or albuminuria, we also found a highly significant association with elevated UHR. The kidneys are particularly vulnerable to the deleterious effects of uric acid, which can cause afferent arteriolopathy, tubulointerstitial inflammation, and fibrosis. Concurrently, low HDL-C levels have been linked to an increased risk of renal function decline, potentially due to the loss of its anti-inflammatory and cholesterol efflux capacities within the glomerulus and renal tubules. A recent study by Liu et al. (2023) explored this relationship directly, finding that a higher UHR was independently associated with an increased risk of incident chronic kidney disease in a large general population cohort, supporting our cross-sectional findings and extending them into a prognostic context (8).

The association between UHR and vascular TOD, assessed via carotid intima-media thickness (CIMT), underscores its connection to generalized atherosclerosis. The pro-oxidant and pro-inflammatory state characterized by a high UHR is a known driver of endothelial dysfunction and atheroma formation. Our results are supported by the work of Zhang et al. (2022), who demonstrated that UHR was significantly associated with the presence and severity of carotid artery plaques in a community-based study, suggesting its role as a marker for subclinical atherosclerosis (9). Furthermore, a study by Kocak et al. (2021) found that UHR was a significant predictor of peripheral arterial disease, further solidifying its link with systemic vascular involvement (10). The clinical implications of our findings are substantial. The identification of a simple, readily available, and inexpensive biomarker like UHR that can improve risk stratification for TOD is highly appealing, particularly in resource-limited settings where access to advanced imaging like echocardiography or carotid ultrasound may be constrained. The calculated cut-off value of 0.145, with its reasonable sensitivity (78.4%) and specificity (72.5%), provides a tangible threshold that clinicians can incorporate into their routine assessment of hypertensive patients. A patient with a UHR above this threshold could be flagged for more intensive blood pressure management and more frequent and comprehensive screening for TOD, potentially allowing for earlier intervention and mitigation of long-term complications.

This study has several limitations that must be acknowledged. Firstly, its cross-sectional design allows for the determination of association but not causation. While it is biologically plausible that a high UHR contributes to TOD, we cannot rule out reverse causality, whereby subclinical organ damage itself influences uric acid metabolism or HDL function. Secondly, our study population was recruited from a single tertiary care center, which may limit the generalizability of our findings to other ethnicities or healthcare settings. Thirdly, while we adjusted for major confounders, residual confounding from unmeasured factors, such as dietary habits, physical activity levels, or subclinical inflammation, cannot be entirely excluded. Fourthly, the use of the CKD-EPI formula for eGFR, while standard, is an estimation and not a direct measure of renal function. Finally, the exploratory analysis of UHR's relationship with hypertension severity warrants further investigation in larger, prospective studies.

Future research directions should include large-scale, prospective cohort studies to validate UHR as a predictive tool for the *incidence* of new TOD over time. Intervention studies would be invaluable to determine whether therapeutic strategies aimed at lowering UHR—either through uric acid-lowering agents like febuxostat or lifestyle modifications that raise HDL-C—can actually translate to a reduced incidence or regression of TOD. Exploring the genetic determinants of UHR could also provide deeper insights into its pathophysiology. A recent study by Li et al. (2023) has begun to explore such genetic links, identifying loci associated with the uric acid-HDL axis and their connection to cardiometabolic traits (11). Additionally, comparing UHR against other novel ratios, such as the triglyceride-glucose index or neutrophil-to-lymphocyte ratio, could help establish its relative value in a multi-marker risk prediction model.

This study provides compelling evidence that the Uric acid to HDL-Cholesterol Ratio is a robust, independent, and superior biomarker associated with target organ damage in patients with primary hypertension. It synergistically encapsulates the risk conferred by elevated uric acid and diminished HDL-C, reflecting a pathophysiological state conducive to cardiac, renal, and vascular injury. Its derivation from routine laboratory tests makes it an economically attractive tool for enhancing risk stratification. We propose that the integration of UHR into the clinical evaluation of hypertensive patients could aid in identifying those at highest risk, thereby enabling a more targeted and intensive management approach to prevent the debilitating consequences of hypertensive organ damage.

Conclusion

This study demonstrates that the Uric Acid to HDL-Cholesterol Ratio (UHR) is a robust and clinically significant biomarker associated with target organ damage in patients with primary hypertension. The findings reveal that UHR is not only significantly higher in patients with composite TOD but also shows a strong, independent association after adjusting for conventional risk factors such as age, hypertension duration, and systolic blood pressure. Crucially, UHR exhibited superior predictive performance for TOD compared to its individual components, serum uric acid and HDL-C, underscoring its value as an integrative marker that synergistically captures pro-oxidant, pro-inflammatory, and atherogenic pathological states. The consistent and significant correlations observed between elevated UHR and specific manifestations of TOD including left ventricular hypertrophy, renal impairment, and increased carotid intima-media thickness affirm its relevance across the spectrum of hypertensive organ injury. The identification of an optimal UHR cut-off value of 0.145 provides a practical and readily applicable tool for clinicians to enhance risk stratification in routine practice. In summary, the UHR, derived from simple, cost-effective, and routinely measured laboratory parameters, offers a potent means to identify hypertensive patients at the highest risk for end-organ complications. Its integration into standard clinical assessment could facilitate earlier intervention, more personalized management, and improved long-term cardiovascular outcomes. Future prospective studies are warranted to validate its prognostic utility and to explore the impact of UHR-lowering strategies on the prevention and progression of hypertensive target organ damage.

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