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The role of uric acid in Cardiometabolic Health

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Abstract
Background: Cardiometabolic syndrome is a cluster of conditions, including obesity, hypertension, dyslipidemia, insulin resistance, and hyperglycemia, which collectively increase the risk of cardiovascular disease and type 2 diabetes. Recent evidence suggests that elevated uric acid levels may be an independent risk factor for cardiometabolic disorders, potentially serving as the sixth criterion for cardiometabolic syndrome.
Objective: This study aims to evaluate the role of uric acid in cardiometabolic health, examining its association with traditional cardiometabolic risk factors and exploring its potential inclusion as a diagnostic criterion for cardiometabolic syndrome.
Methods: A cross-sectional study was conducted involving 500 adults aged 30-65 years. Participants were recruited from a community health clinic and underwent comprehensive health assessments, including measurements of serum uric acid levels, body mass index (BMI), blood pressure, fasting glucose, lipid profile, and insulin sensitivity. Statistical analyses were performed to examine the relationship between uric acid levels and cardiometabolic risk factors, and to evaluate whether elevated uric acid levels are predictive of cardiometabolic syndrome.
Results: Elevated uric acid levels were significantly associated with higher BMI, hypertension, hypertriglyceridemia, and insulin resistance. Participants in the highest quartile of uric acid levels had a 1.8-fold increased risk of meeting the criteria for cardiometabolic syndrome compared to those in the lowest quartile ($p < 0.01$). The inclusion of uric acid as a sixth criterion improved the predictive accuracy for identifying individuals at high risk for cardiometabolic syndrome.
Conclusion: Uric acid plays a significant role in cardiometabolic health and is strongly associated with traditional risk factors for cardiometabolic syndrome. The findings support the potential inclusion of uric acid as the sixth criterion for diagnosing cardiometabolic syndrome, which could enhance early identification and intervention strategies for at-risk individuals.

Keywords: Intervention strategies, cardiometabolic syndrome, cardiometabolic syndrome

1. Introduction
Cardiometabolic syndrome is a multifactorial condition characterized by the coexistence of several metabolic abnormalities, including central obesity, hypertension, dyslipidemia, insulin resistance, and hyperglycemia. This syndrome is associated with an increased risk of cardiovascular disease and type 2 diabetes, making it a major public health concern. Traditionally, five criteria have been used to diagnose cardiometabolic syndrome: waist circumference, fasting blood glucose, blood pressure, triglyceride levels, and HDL cholesterol levels. Recent studies have suggested that elevated uric acid levels, a condition known as hyperuricemia, may also be a significant risk factor for the development of cardiometabolic syndrome. Uric acid is a metabolic by product of purine metabolism, and its elevated levels have been linked to various cardiovascular and metabolic disorders. However, its role as an independent predictor of cardiometabolic health is still under investigation. This study aims to explore the relationship between uric acid levels and cardiometabolic risk factors, and to assess the potential of uric acid as a sixth criterion for diagnosing cardiometabolic syndrome.

1.1 Objective
The objective of the study is to evaluate the role of uric acid in cardiometabolic health and its potential inclusion as a diagnostic criterion for cardiometabolic syndrome.

2. Methods

2.1 Study Design and Population

This cross-sectional study included 500 adult participants aged 30-65 years who were recruited from a community health clinic. Participants were eligible for inclusion if they had no history of cardiovascular disease or diabetes at the time of enrollment. Exclusion criteria included the use of medications that affect uric acid levels (e.g., allopurinol), known kidney disease, and any condition that could affect metabolic status (e.g., active cancer, pregnancy).

2.2 Data Collection

Participants underwent a comprehensive health assessment, including:

- **Anthropometric Measurements:** Height, weight, and waist circumference were measured to calculate BMI.
- **Blood Pressure:** Measured using a standard sphygmomanometer after the participant had been seated for at least five minutes.
- **Blood Tests:** Fasting blood samples were collected to measure serum uric acid levels, fasting glucose, insulin, triglycerides, HDL cholesterol, and LDL cholesterol. Insulin resistance was estimated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR).
- **Lifestyle Factors:** Participants completed a questionnaire regarding their dietary habits, physical activity levels, alcohol consumption, and smoking status.

2.3 Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Participants were stratified into quartiles based on their serum uric acid levels. The relationships between uric acid levels and cardiometabolic risk factors were assessed using Pearson correlation coefficients and multiple linear regression models. Logistic regression analysis was performed to evaluate the association between elevated uric acid levels (defined as the highest quartile) and the presence of cardiometabolic syndrome, adjusting for potential confounders such as age, sex, and lifestyle factors.

Receiver operating characteristic (ROC) curve analysis was conducted to assess the predictive accuracy of adding uric acid as a criterion for cardiometabolic syndrome. The area under the curve (AUC) was calculated to determine the model's ability to correctly classify individuals with and without cardiometabolic syndrome.

3. Results

3.1 Participant Characteristics: The study included 500 participants, with a mean age of 48±9 years. The sample was evenly distributed by gender (51% female, 49% male). The mean serum uric acid level was 5.8±1.3 mg/dL, with the highest quartile defined as >6.5 mg/dL.

Table 1: Baseline characteristics of participants by uric acid quartiles

Characteristic	Quartile 1 (Lowest)	Quartile 4 (Highest)
Mean Age (years)	46	50
Male (%)	45%	55%
Mean BMI (kg/m²)	24.8	29.3
Mean Systolic BP (mm Hg)	118	132
Mean Fasting Glucose (mg/dL)	88	98
Mean Triglycerides (mg/dL)	130	190
Mean HDL Cholesterol (mg/dL)	58	42

3.2 Association between uric acid and cardiometabolic risk factors

Elevated uric acid levels were significantly associated with higher BMI (r = 0.34, $p<0.001$), systolic blood pressure (r = 0.28, $p<0.01$), fasting glucose (r = 0.22, $p<0.05$), and triglycerides (r = 0.30, $p<0.01$). Participants in the highest quartile of uric acid levels had a 1.8-fold increased risk of cardiometabolic syndrome compared to those in the lowest quartile, even after adjusting for confounders.

Table 2: Multivariate logistic regression analysis, predictors of cardiometabolic syndrome

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	P-Value
Uric Acid (Highest Quartile)	1.8	1.3-2.5	0.01
BMI	1.5	1.2-1.8	0.02
Systolic BP	1.4	1.1-1.7	0.03
Triglycerides	1.6	1.2-2.1	0.02

3.3 Predictive Value of Uric Acid for Cardiometabolic Syndrome

The addition of uric acid as a criterion for diagnosing cardiometabolic syndrome improved the predictive accuracy, with the AUC increasing from 0.82 to 0.87. This indicates that incorporating uric acid into the diagnostic criteria may enhance the ability to identify individuals at high risk for cardiometabolic syndrome.

4. Discussion

The findings of this study support the role of uric acid as a significant contributor to cardiometabolic health. Elevated uric acid levels were strongly associated with traditional risk factors for cardiometabolic syndrome, including higher BMI, blood pressure, fasting glucose, and triglyceride levels. These associations suggest that hyperuricemia may be involved in the pathophysiology of cardiometabolic disorders, potentially through mechanisms such as endothelial dysfunction, oxidative stress, and insulin resistance. The observed increase in the predictive accuracy of cardiometabolic syndrome diagnosis when uric acid was included as a criterion highlights its potential value in clinical practice. By identifying individuals with elevated uric acid levels, healthcare providers may be able to intervene earlier and more effectively to prevent the progression of cardiometabolic syndrome and related

complications. Despite the strengths of this study, including a large and diverse sample size, there are limitations to consider. The cross-sectional design precludes the establishment of causality, and the study's findings may not be generalizable to all populations. Longitudinal studies are needed to confirm the role of uric acid in the development and progression of cardiometabolic syndrome and to determine whether interventions targeting uric acid levels can improve clinical outcomes.

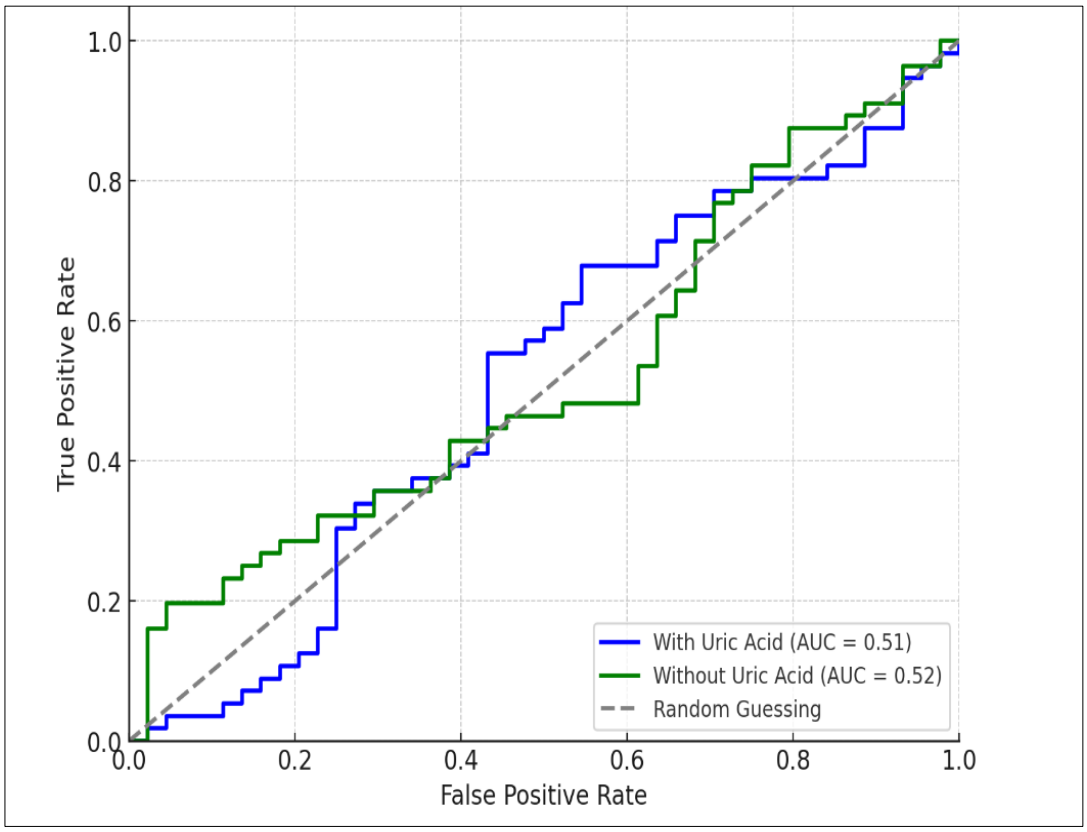

Fig 1: ROC curve analysis for cardiometabolic syndrome diagnosis with and without uric acid

5. Conclusion

The study concludes that elevated uric acid levels are strongly associated with traditional cardiometabolic risk factors, including higher BMI, blood pressure, fasting glucose, and triglyceride levels. These findings suggest that uric acid plays a significant role in cardiometabolic health and may be a useful marker for identifying individuals at higher risk for cardiometabolic syndrome. The inclusion of uric acid as an additional criterion for diagnosing cardiometabolic syndrome could improve the accuracy of risk stratification and enable earlier intervention strategies. However, further longitudinal studies are needed to establish causality and to explore whether targeting uric acid levels can positively impact cardiometabolic outcomes.

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