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Associations Between Variability of Serum Uric Acid Level and Comprehensive Geriatric Assessment Outcomes in Older Adults

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Abstract

Objective: Serum uric acid (SUA) is a marker with both antioxidant and prooxidant properties. While abnormal SUA levels have been linked to adverse outcomes, the effects of long-term intra-individual SUA fluctuations, particularly in older adults, remain unclear. This study examined the relationship between SUA variability and various components of the comprehensive geriatric assessment (CGA), including functional status, cognition, nutrition, and mood.

Materials and Methods: The study population consisted of 102 patients aged 65 years and older who were evaluated in a geriatric outpatient clinic. Uric acid coefficient of variation (SUA-CV) was calculated using four SUA measurements over a 12-year period. Participants were classified into low and high SUA-CV groups. All participants underwent CGA.

Results: Higher SUA-CV was significantly associated with lower activities of daily living, instrumental activities of daily living, mini-mental state examination, and mini nutritional assessment-short form scores, and with higher GDS scores, polypharmacy, and comorbidities ($p < 0.05$). Correlation analysis revealed significant associations between SUA-CV and various CGA parameters, particularly those reflecting functional and nutritional decline.

Conclusion: Increased variability in SUA levels is associated with poor functional, cognitive, nutritional, and mood status in older adults. SUA-CV may be a novel and cost-effective biomarker for systemic vulnerability in aging and may help guide individualized geriatric care.

Keywords: Uric acid, comprehensive geriatric assessment, variability, older adults

Introduction

Uric acid is the end product of purine metabolism. It has been increasingly recognized for its dual role in human physiology — acting both as a powerful antioxidant and, paradoxically, as a pro-oxidant under certain pathological conditions (1). The normal reference range for serum uric acid (SUA) in humans is between 3.0 and 6.8 mg/dL. However, these values are influenced by demographic factors such as age and sex, as well as various pathological conditions (2). High SUA levels have been associated with many age-related diseases, including cardiovascular disease, hypertension, metabolic syndrome, and neurodegenerative disorders such as Alzheimer's disease (3,4). Although the pathophysiological role of uric acid has been extensively investigated across a broad spectrum of disease processes, a comprehensive and definitive understanding remains elusive. Additionally, recent investigations have increasingly focused on the pathophysiological consequences of hypouricemia, and it has been suggested that both elevated and low SUA levels may be risk factors for comorbidities and all-cause mortality (2,5,6). Findings from small-sample studies suggest that mortality risk follows a U-shaped pattern in relation to SUA levels (5,6). However, beyond absolute uric acid levels, the variability of SUA over time has emerged as a potentially essential but underexplored marker of systemic homeostasis and metabolic resilience, particularly in older adults. In a recent large prospective study, greater variability in SUA levels was associated with an increased risk of cardiovascular disease during a six-year follow-up (7).

Comprehensive geriatric assessment (CGA) is an interdisciplinary and multidimensional approach aimed at assessing the medical,

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psychosocial, functional, and nutritional conditions of older adults (8). CGA helps predict health outcomes, guide therapeutic decisions, and optimize individualized care plans for older adults. Identifying novel, easily measurable biomarkers that correlate with CGA parameters could enhance early risk stratification and management strategies in geriatric care.

Recent studies have suggested that fluctuations in specific metabolic markers, such as glucose and cholesterol, may provide prognostic information beyond static values (9,10). In this context, SUA variability may reflect underlying inflammatory activity, fluctuations in renal function, or oxidative stress—all of which are relevant to geriatric syndromes such as frailty, cognitive decline, and functional impairment. There are no studies in the literature that have examined this subject in older adults.

The study investigates, in a cohort of older adults, the link between SUA variability and various domains of CGA, including functional status, cognitive function, nutritional status, and mood. We hypothesize that greater variability in uric acid levels may be associated with poorer outcomes in CGA parameters, suggesting its potential role as a surrogate biomarker in geriatric assessment.

Materials and Methods

Study Population

The study population consisted of individuals aged 65 years and older who were evaluated in the geriatric outpatient clinic of (Gazi University) Hospital from January to March 2021. Patients with stage 4 or 5 chronic kidney failure, malignancy, chronic liver disease, or systemic inflammatory disease were excluded from the study. Baseline data on participants' age, sex, educational level, comorbid conditions, and number of prescribed medications were collected. Each participant also underwent a CGA.

Comprehensive Geriatric Assessment

Participants' dependence in performing daily activities was evaluated using the Katz et al. (11) activities of daily living (ADL) and the Lawton instrumental ADL (IADL) scales (12,13). Mood was assessed using the geriatric depression scale—short form (GDS); a score of ≥5 was considered indicative of depression (14). Cognitive impairment was detected by the standardized mini-mental state examination (MMSE) and defined as an MMSE score of <24 and recall of ≤2 words in the three-word recall test (15). Nutritional risk status was assessed using the mini nutritional assessment-short form (MNA-SF) and malnutrition was defined as an MNA-SF score <8 (16,17). Polypharmacy was defined as the regular use of five or more medications.

Participants' height and weight were measured. To measure height, participants stood upright with their back and legs straight against the wall, and a pencil was placed on top of their heads to mark the height on a wall-mounted ruler. Body weight was measured using a Tanita BC 418 device. Body mass index was determined as body weight (kg) divided by the square of height (m^2).

SUA values were retrieved from the hospital records of patients included in the study. The study included 102 patients whose four uric acid measurements were available in the hospital records between 2008 and 2020. There is at least a two-year gap between each SUA. The variability of SUA was calculated from four different values for each patient. The following parameter was calculated for uric acid variability: the uric acid coefficient of variation (uric acid-CV).

Ethical approval for this study was obtained from the Gazi University Ethics Committee (decision number: 682, date: 02.11.2020), and the research was conducted in accordance with the ethical standards of the Declaration of Helsinki. Each participant provided written informed consent before participation.

Statistics

The categorical were reported as numbers and percentages (n,%). The Statistical Package for the Social Sciences (SPSS) version 22.0 was used for the statistical analyses. The Kolmogorov-Smirnov test and histograms were used to verify the normality of the distribution of numeric variables. Data were presented as numbers and percentages for categorical variables, mean ± standard deviation (SD) for normally distributed continuous variables, and median (minimum-maximum) for non-normally distributed continuous variables. The comparison of numerical parameters that followed a normal distribution between two independent groups was performed using the Student's t-test. The intergroup comparisons of numeric variables with non-normal distributions were performed using the Mann-Whitney U test. Spearman's rank correlation coefficient was used for parameters that were not normally distributed. The variability of SUA was calculated with four different values for each patient. The CV is a statistical measure that describes the relative dispersion of parameter values. CV is calculated by dividing the SD of the parameters by their mean value. The following parameter was calculated for uric acid variability: the uric acid-CV. Uric acid variability was categorized into low- and high-variability groups based on the median of the variability distribution in our study population. The median-based cut-off approach has commonly been used in previous studies evaluating biological variability indices and is therefore considered appropriate for the current analysis. We performed a post-hoc power analysis using G*Power version 3.1.9.4. Based on the observed effect size and sample size, the G*Power output yielded a non-centrality parameter (δ) of 3.87, a critical value of 1.98, degrees of freedom (df) of 95, and an estimated statistical power (1–β) of 0.96.

Results

A total of 102 patients (mean age 74.2 years; 64.7% female) were included in the study. When participants were stratified into low- and high-CV groups, significant differences were observed between the groups in ADL, IADL, MNA-SF, GDS, number of medications, and comorbidity count (Table 1).

Geriatric syndromes differed significantly between groups with low and high uric acid variability. Polypharmacy was more common in the high-variability group (78.4%) than in the low-variability group (52.9%) ($p = 0.011$). Similarly, malnutrition (13.7% vs. 2.0%, $p = 0.032$) and depression (43.1% vs. 23.5%, $p = 0.029$) were more frequent among participants with greater variability in uric acid levels. Cognitive impairment also differed markedly, with 39.2% in the high-variability group vs. 5.9% in the low-variability group ($p < 0.001$) (Table 1).

In the correlation analysis, negative correlations were found between SUA-CV and ADL, IADL, MNA-SF, and the number of comorbidities. In contrast, a positive correlation was found among the number of medications, GDS, and SUA-CV (Table 2).

Discussion

In this study, we observed significant correlations between SUA-CV and several CGA parameters, including ADL, IADL, MNA-SF, GDS, and the number of medications and comorbidities. The present study suggests that SUA-CV might serve as an informative biomarker for assessing both general health and functional capacity in older individuals.

Previous studies have primarily focused on hyperuricemia and its associations with adverse geriatric outcomes. For instance, observational cohort studies in older adults have linked elevated SUA levels with an increased risk of frailty (18,19). Conversely, in another cohort, hyperuricemia has paradoxically been associated with greater muscle mass and strength, suggesting a protective role against sarcopenia under certain conditions (20,21).

Table 1. Baseline demographic and clinical characteristics of groups defined by serum uric acid variability (CV).

Characteristics	Total (n = 102)	Low CV (n = 51)	High CV (n = 51)	p-value
Age, years	74.2 ± 6.3	73.4 ± 5.8	75 ± 6.7	0.204
Female, n (%)	66 (64.7%)	28 (54.9%)	38 (74.5%)	0.006
BMI, kg/m^2	27.9 (19.8–39.7)	27.7 (20–35.5)	28.5 (19.8–39.7)	0.434
High school or above, n (%)	25 (24.5%)	11 (21.5%)	14 (27.5%)	0.396
HTN, n (%)	66 (64.7%)	33 (64.7%)	33 (64.7%)	0.528
DM, n (%)	43 (42.1%)	22 (43.1%)	21 (41.2%)	0.500
COPD, n (%)	11 (10.8%)	4 (7.8%)	7 (13.7%)	0.262
CAD, n (%)	24 (23.5%)	10 (19.6%)	14 (27.5%)	0.241
Dyslipidemia, n (%)	19 (18.6%)	6 (11.8%)	13 (25.4%)	0.062
ADL	6 (1–6)	6 (1–6)	5 (2–6)	**0.000**
IADL	8 (1–8)	8 (1–8)	7 (1–8)	**0.000**
MNA-SF	12 (5–14)	13 (7–14)	11 (5–14)	**0.000**
MMSE	28 (10–30)	28 (18–30)	26 (10–30)	**0.005**
GDS	3 (0–14)	2 (0–10)	4 (0–14)	**0.001**
Number of medications	5 (0–14)	4 (0–14)	6 (0–12)	**0.002**
Polypharmacy, n (%)	67 (65.7%)	27 (52.9%)	40 (78.4%)	**0.011**
Malnutrition, n (%)	8 (7.8%)	1 (2%)	7 (13.7%)	**0.032**
Depression, n (%)	34 (33.3%)	12 (23.5%)	22 (43.1%)	**0.029**
Cognitive impairment, n (%)	23 (22.5%)	3 (5.9%)	20 (39.2%)	**0.000**
Fall, n (%)	23 (22.5%)	10 (19.6%)	13 (25.4%)	0.318
Urinary incontinence, n (%)	33 (32.3%)	14 (27.5%)	19 (37.3%)	0.211
Number of comorbidities	3 (0–7)	2 (0–5)	3 (0–7)	**0.007**
Sleep duration	6 (3–10)	7 (4–10)	6 (3–10)	0.908
SUA-CV	0.18 (0.04–0.57)	0.13 (0.04–0.18)	0.29 (0.19–0.57)	**0.000**

Categorical variables are presented as counts and percentages, normally distributed continuous variables as mean ± SD, and non-normally distributed continuous variables as median (range).
SD: Standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MNA-SF: Mini nutritional assessment-short form, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, SUA-CV: Serum uric acid-coefficient of variation.

Table 2. The results of the correlation analysis between the parameters and SUA-CV.

		SUA-CV	Number of medications	Number of comorbidities	ADL	IADL	MMSE	MNA-SF	GDS
SUA-CV	Rho coefficient	1							
	p								
Number of medications	Rho coefficient	0.266	1						
	p	**0.008**							
Number of comorbidities	Rho coefficient	-0.102	-0.222	1					
	p	0.321	**0.029**						
ADL	Rho coefficient	-0.365	-0.283	0.415	1				
	p	**0.000**	**0.004**	**0.000**					
IADL	Rho coefficient	-0.333	-0.013	-0.442	0.353	1			
	p	**0.001**	0.898	**0.000**	0.000				
MMSE	Rho coefficient	-0.097	0.217	-0.754	-0.151	0.648	1		
	p	0.330	**0.030**	**0.000**	0.130	**0.000**			
MNA-SF	Rho coefficient	-0.240	-0.117	-0.512	0.076	0.422	0.433	1	
	p	**0.017**	0.255	**0.000**	0.457	**0.000**	**0.000**		
GDS	Rho coefficient	0.413	0.361	-0.271	-0.475	-0.196	0.045	-0.352	1
	p	**0.000**	**0.000**	**0.007**	**0.000**	**0.048**	0.651	**0.000**	

ADL: Activities of daily living, IADL: Instrumental activities of daily living, MNA-SF: Mini nutritional assessment-short form, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, SUA-CV: Serum uric acid-coefficient of variation.

With regard to cognitive outcomes, elevated SUA appears to confer neuroprotective effects in conditions like. Alzheimer's or Parkinson-related dementia; however, findings remain inconsistent across subtypes, and some evidence suggests potential harm in vascular dementia (22,23). While most previous studies have relied on a single-time-point SUA measurement, our study considered intra-individual variability in SUA levels over a 12-year period. Although we did not control for potential confounding factors such as medication use or comorbidities, and we did not perform regression analyses, our descriptive findings may reflect potential associations between long-term SUA fluctuations and geriatric assessment outcomes.

Tian et al. (24) investigated the impact of visit-to-visit variability in SUA on all-cause mortality in a large general-population cohort and reported that greater SUA variability was independently associated with an increased risk of all-cause mortality. Their findings underscore the clinical relevance of longitudinal SUA fluctuations beyond single-time-point measurements. Although our study does not focus on mortality outcomes, it examines long-term SUA variability and explores its potential associations with CGA parameters.

From a geriatric clinical perspective, asymptomatic or non-specific hyperuricemia generally does not require pharmacological treatment. Current guidelines highlight that starting urate-lowering therapy in older adults solely based on elevated SUA levels—without gout, nephrolithiasis, or urate-related complications—offers no clear benefit and may increase the risk of medication-related adverse events, especially in individuals with multimorbidity and polypharmacy (25,26). This conservative approach underscores the importance of avoiding unnecessary treatment in geriatric practice. In this context, focusing on SUA variability rather than absolute SUA elevations may provide a more nuanced understanding of physiological instability without prompting unwarranted interventions. Our findings, therefore, complement existing clinical perspectives by suggesting that long-term fluctuations in SUA may be more relevant than isolated hyperuricemia in older adults.

Hypouricemia may reduce antioxidant capacity and is often associated with insufficient dietary intake of protein and purine-rich nutrients, as seen in malnourished individuals, and has been suggested in several studies to be a nutritional marker (6,27). This is particularly relevant in the geriatric population, where reduced appetite, chronic illness, and functional decline may limit adequate dietary intake (28). In our study, the observed association between higher SUA variability and lower MNA-SF scores supports the hypothesis that fluctuations in SUA levels—especially those trending toward hypouricemia—may serve as indirect markers of malnutrition or nutritional instability. Further research is needed to determine whether SUA variability precedes or follows nutritional decline.

This is the first study to examine the relationship between SUA variability and CGA domains in older adults. SUA is a low-cost biomarker commonly measured in clinical biochemical assays. Therefore, we believe that these findings are clinically relevant. Monitoring SUA variability may serve as an additional, readily available tool for risk assessment and early identification of vulnerable individuals among older adults.

Study Limitations

Nevertheless, our study has several limitations. First, the retrospective design and the relatively small sample size of this study may restrict the generalizability of the findings. Second, although we used four SUA measurements over a long period, these measurements were infrequent and unevenly distributed, which may have led to the omission of short-term fluctuations or acute changes. Third, dietary habits, hydration status, and medication use influence uric acid levels; however, these factors were not assessed in the study participants. Future research involving larger prospective cohorts is necessary to both verify these findings and examine the mechanisms underlying them.

Conclusion

Increased SUA variability is associated with negative geriatric outcomes, including functional decline, malnutrition, and depressive symptoms. SUA variability may serve as an underrecognized biomarker of systemic instability and aging-related vulnerability. Incorporating dynamic biochemical markers such as SUA-CV into routine geriatric assessments may improve the identification of at-risk individuals and support personalized interventions.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Gazi University Ethics Committee (decision number: 682, date: 02.11.2020), and the research was conducted in accordance with the ethical standards of the Declaration of Helsinki.

Informed Consent: Each participant provided written informed consent before participation.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.Y.B., Ç.Ç., İ.İ., Concept: F.Y.B., Ç.Ç., B.G., Design: F.Y.B., Ç.Ç., B.G., Data Collection or Processing: F.Y.B., Ç.Ç., İ.İ., Analysis or Interpretation: Ç.Ç., B.G., Literature Search: F.Y.B., İ.İ., Writing: F.Y.B., Ç.Ç., İ.İ., B.G.

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