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Uric Acid and Grip Strength as Predictors of Mortality in Older Adults: A Sex-Stratified Analysis

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Abstract

Background

Sarcopenia and hyperuricemia correlate with negative outcomes in older adults, including increased mortality. While diminished muscle strength predicts functional deterioration and mortality, elevated serum uric acid's prognostic value remains controversial. This study investigated individual and combined effects of reduced handgrip strength and hyperuricemia on all-cause mortality, focusing on sex-specific differences.

Methods

This retrospective cohort study evaluated 910 individuals aged ≥ 60 years between 2020–2024 at a university hospital. Participants with confounding conditions or interfering medications were excluded. Uric acid was quantified enzymatically and classified into quartiles. Sarcopenia was defined using EWGSOP2 criteria, including handgrip strength and skeletal muscle mass index from bioelectrical impedance analysis. Cox regression and Kaplan-Meier analyses assessed mortality risk.

Results

The mean age was 71 years, with 66.9% of participants being female. Reduced handgrip strength and elevated UA levels were correlated with detrimental metabolic indicators. Univariate analysis indicated that both low handgrip strength (HR: 1.91, 95% CI: 1.15–3.18) and the highest quartile of uric acid (UA) levels (HR: 1.86, 95% CI: 1.13–3.08) were significant predictors of mortality. Nevertheless, these correlations diminished following multivariable correction. Sex-stratified studies indicated that hyperuricemia persisted as an independent predictor for mortality in females (HR: 3.08; 95% CI: 1.31–7.26; p = 0.010).

Conclusion

Both diminished grip strength and elevated uric acid levels are associated with increased mortality in older adults, particularly among females. Routine incorporation of sex-specific metabolic and physical performance assessments may enhance risk stratification strategies in geriatric populations.

INTRODUCTION

Sarcopenia, the age-associated reduction in skeletal muscle mass, strength, and functionality, significantly contributes to frailty, disability, and elevated mortality in older adults [1]. Among its diagnostic components, handgrip strength (HGS) has emerged as a simple yet highly predictive marker of functional decline and adverse outcomes [2]. This age-related muscle deterioration is driven by

multifactorial processes, including chronic low-grade inflammation, oxidative stress, hormonal dysregulation, and neuromuscular degeneration [3]. Elevated levels of inflammatory biomarkers such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) have been repeatedly associated with reduced muscle strength in older adults [4].

Uric acid (UA), the end product of purine metabolism, plays a complex role in human health. On one hand, elevated serum UA levels have been implicated in the pathogenesis of cardiovascular and cerebrovascular diseases, hypertension, metabolic syndrome, and increased all-cause mortality, likely due to their pro-inflammatory and oxidative effects [5, 6]. On the other hand, UA acts as a potent antioxidant, scavenging oxygen free radicals and mitigating oxidative stress, thereby potentially conferring neuroprotective effects [7]. Low serum UA levels have been linked to adverse outcomes including increased mortality and higher risk of neurodegenerative diseases such as Alzheimer's and Parkinson's disease [8].

Despite prior research investigating the relationship between UA levels and sarcopenia-related parameters, findings continue to be inconsistent and ambiguous. While some studies report that moderate UA levels are positively associated with muscle strength, others suggest a detrimental impact, particularly at higher UA concentrations [9, 10]. To our knowledge, no research has particularly investigated this association within Turkish older adults, a population characterized by unique dietary and metabolic profiles.

In this study, we aimed to evaluate the independent and combined associations of serum uric acid levels and handgrip strength with all-cause mortality among older adults. We also examined sex-specific differences to better elucidate the interaction between metabolic and functional determinants of survival in late life.

MATERIALS AND METHODS

Study population and setting

This retrospective cohort study examined the association between serum uric acid levels, handgrip strength, and all-cause mortality in older adults. A total of 910 older adults aged 60 years and above, who were evaluated at the Department of Geriatrics, University Hospital between 2020 and 2024, were included. Participants were primarily community-dwelling older adults undergoing routine health assessments. Exclusion criteria comprised: (1) active malignancy, infection, or recent surgery; (2) history of gout or the use of uric acid-lowering medications or diuretics; (3) end-stage renal disease (eGFR < 30 mL/min/1.73 m²); (4) conditions limiting handgrip strength evaluation (e.g., severe hand osteoarthritis, peripheral neuropathy, advanced dementia); and (5) contraindications to bioelectrical impedance analysis (e.g., cardiac pacemaker, metallic implants, generalized edema). This study was approved by the ethical review board of University Faculty of Medicine and complied with the Helsinki Declaration. All participating patients supplied formal informed consent to engage in the trial.

Laboratory and Clinical Assessments

The blood samples were collected after a 12 h overnight fast, on the same day that the bioimpedance was performed. Serum UA levels (mg/dL) were analyzed using enzymatic-colorimetric methods. Elevated UA was defined as > 7.0 mg/dL in male and > 6.0 mg/dL in females [11]. Participants were also stratified into UA quartiles based on the distribution of measured values. Anthropometric measurements included height, weight, body mass index (BMI), and waist circumference. BMI was calculated as weight (kg) divided by height squared (m^2), and waist circumference was measured at the midpoint between the lower costal margin and the iliac crest. A questionnaire assessing Activities of Daily Living (ADL) via the Katz index [12] and Instrumental Activities of Daily Living (IADL) using the Lawton scale [13] was administered to the patients. For the ADL and IADL assessments, scores of ≤ 6 points and ≤ 8 points indicated dependence, respectively. The nutritional status, depressive mood, cognitive functions, and frailty were evaluated using the Mini Nutritional Assessment (MNA) short form [14], Geriatrics Depression Scale (GDS) [15], Standardized Mini-Mental State Examination (SMMSE) [16], and the FRAIL scale [17], respectively. Concerning the MNA, GDS, MMSE, and FRAIL scores: for the MNA, scores below 8 indicate malnutrition, scores between 8 and 11 signify malnutrition risk, and scores above 11 are classified as normal; for the GDS, scores exceeding 14 denote a depressive mood; for the MMSE, scores below 24 indicate cognitive impairment; and for the FRAIL scale, scores of 0, 1–2, and 3 or more are categorized as nonfrail, prefrail, and frail, respectively.

Sarcopenia Assessment

Handgrip strength (HGS) was measured using a digital dynamometer (Takei TKK 5401, Japan). Three trials were performed on the dominant hand, with a minimum interval of one minute between attempts, and the average value was recorded. Muscle mass was assessed via bioelectrical impedance analysis (BIA) using the Bodystat QuadScan 1500. Electrodes were placed according to standard manufacturer guidelines. Skeletal muscle mass (SMM) was calculated using the Janssen equation and normalized by BMI to yield the skeletal muscle mass index (SMMI, kg/BMI). Sarcopenia was defined based on EWGSOP2 criteria as the presence of both low muscle strength and reduced muscle mass. The cut-off values used were: HGS < 32 kg for males and < 22 kg for females; SMMI < 1.049 kg/BMI for males and < 0.823 kg/BMI for females [18, 19]. Gait speed was also measured over a 4-meter walk, recorded in seconds.

Statistical Analysis

Data normality was assessed using histograms, Q–Q plots, and the Shapiro–Wilk test. Risk factors associated with all-cause mortality were first evaluated using univariate Cox proportional hazards regression models in the overall population, as well as separately in female and male participants. Serum uric acid levels were categorized into quartiles. Subsequently, multivariable Cox regression models were constructed to examine the associations between handgrip strength groups (high and low)

and serum uric acid quartiles, adjusting for age, sex, BMI, CKD, DM, and CHD. The proportional hazards assumption was checked using the Schoenfeld residuals and log-log plot. Differences in the levels of 18 clinical biomarkers of biological aging across handgrip strength and serum uric acid groups were assessed using one-way analysis of variance (ANOVA) and independent samples *t*-tests. The Benjamini–Hochberg procedure was applied to control the false discovery rate due to multiple comparisons. For post hoc pairwise comparisons, Tukey's test and Tamhane's T2 test were used, as appropriate. Kaplan–Meier survival curves were generated to illustrate differences in survival according to handgrip strength and serum uric acid quartiles. A significance level of $p < 0.05$ was considered statistically significant. All statistical analyses were performed using R software version 4.0.4 (www.r-project.org).

RESULTS

A total of 910 older adults (mean age: 71.0±6.9 years; 66.9% female) were included in the study. During a median follow-up of 48 months, 103 participants (11.3%) died. Mortality was significantly higher among males compared to females (20.9% vs. 6.6%, p<0.001). Males were older and exhibited significantly lower fat mass and higher muscle mass, skeletal muscle mass index, and handgrip strength compared to females.

The prevalence of geriatric syndromes showed substantial sex-based differences. Sarcopenia was more common among males (67.1%) than in females (32.9%, p<0.001), whereas malnutrition (70.9% vs. 29.1%, p = 0.017), polypharmacy (70.9% vs. 29.1%, p=0.017), depressive symptoms (78.5% vs. 21.5%, p<0.001), and frailty (72.3% vs. 27.7%, p<0.001) were more prevalent among females (Table 1). Participants with reduced HGS exhibited higher triglyceride levels, lower LDL cholesterol, and elevated white blood cell counts (adjusted p<0.05). Similarly, individuals in the highest quartile of serum uric acid (UA) showed higher triglyceride and urea levels and significantly lower HDL cholesterol, indicating a more adverse metabolic profile (Figure 1; Supplementary Table S1 and S2).

Survival Analyses

In univariate Cox regression models, low HGS was associated with an increased risk of all-cause mortality (HR = 1.91, 95% CI: 1.15–3.18, $p = 0.013$). Similarly, participants in the highest UA quartile (Q4) had a significantly elevated mortality risk compared to those in the lowest quartile (Q1) (HR: 1.86, 95% CI: 1.13–3.08, p = 0.015) (Figure 2). However, after adjustment for confounding variables including age, sex, BMI, CKD, diabetes mellitus, and CHD, these associations were attenuated and no longer statistically significant. Kaplan–Meier survival curves supported these findings demonstrating lower survival probabilities in individuals with reduced HGS (log-rank p = 0.011) and those in the highest UA quartile (log-rank p = 0.00023) (Figure 3). In sex-stratified multivariable Cox regression models, elevated UA (Q4) remained an independent predictor of mortality among females (HR: 3.08; 95% CI: 1.31–7.26; p = 0.010). In contrast, in males, hyperuricemia was not significantly associated with mortality. Instead, significant predictors of mortality in the male subgroup included CKD, CHD, frailty, malnutrition, and cognitive impairment (Table 2 and Table 3).

DISCUSSION

Low handgrip strength and elevated blood uric acid levels correlated with heightened all-cause mortality, according to this retrospective cohort study of community-dwelling Turkish older adults. The predictive impact of hyperuricemia was most pronounced in female patients, even after controlling for major confounders. These data indicate that muscle strength and metabolic condition, as shown by serum uric acid levels, may function as independent and sex-specific prognostic factors for survival in advanced age. Sarcopenia has repeatedly been associated with negative outcomes in older adults; nevertheless, the use of uric acid as a mortality risk biomarker remains contentious, as prior research has shown conflicting findings. Our findings enhance the existing research by emphasising the cumulative and perhaps collaborative impacts of functional decline and metabolic dysregulation on geriatric prognosis.

The literature exhibits conflicting evidence regarding the relationship between UA and muscle strength. Nahas et al. demonstrated a positive and independent correlation between blood uric acid levels and peak isokinetic muscular strength in older males and females, utilising data from the NHANES (1999–2002) cohort [20]. Individuals in the highest quartile of UA demonstrated approximately 2.2 kg more strength than those in the lowest quintile, indicating a possibly protective role of UA in muscular function. The authors warn that increased UA is linked to cardiovascular risk, suggesting its effects may vary based on the clinical endpoint.

Prior research presents inconclusive results concerning the association between serum uric acid and muscular strength. Huang et al. identified an inverted J-shaped correlation in Japanese males, indicating that both low and very high uric acid levels may adversely affect muscle function [21]. These findings indicate that UA may exert dual effects—offering antioxidative protection at physiological levels but contributing to oxidative stress and inflammation when elevated. Our study supports this dual-action hypothesis, as higher UA levels correlated with unfavorable metabolic markers and increased mortality, particularly in females. In contrast to Huang et al., who concentrated on middle-aged working males, our cohort comprised older individuals with a wider array of comorbidities and functional impairments, potentially elucidating some disparities in strength profiles among uric acid quartiles.

In contrast, Macchi et al. conducted a longterm analysis of the InCHIANTI cohort and found that elevated UA levels were prospectively linked to improved handgrip and knee extension strength over a three-year duration [22]. They suggested that UA might function as a compensatory antioxidant mechanism that mitigates oxidative damage in ageing muscle. The study, while not evaluating mortality, underscores a possible protective function of UA in the preservation of muscle mass.

Nonetheless, recent data from Korean cohorts have yielded inconsistent findings. Yi et al. and Suh et al. both established a negative connection between serum uric acid and relative handgrip strength in Korean females, even after controlling for metabolic variables [23, 24]. The findings indicate that the correlation between UA and muscle strength may differ according on sex, ethnicity, age, and the assessment of absolute versus relative strength. Suh et al. posited that estrogen-related alterations in uric acid clearance and muscle metabolism following menopause may intensify the identified negative

correlation in females. Our study significantly contributes to the existing literature by illustrating that diminished muscle strength and increased uric acid levels are together linked to mortality risk, reinforcing the idea that both factors should be evaluated simultaneously in older individuals.

Kawamoto et al. identified a favourable correlation between UA and handgrip strength in older females, indicating a possible advantageous role of UA in muscle preservation in later life. Nonetheless, their conclusions were restricted to functional outcomes and excluded survival data. The discrepancies among these studies may be ascribed to variations in study design (cross-sectional versus longitudinal), age distribution, comorbidities, and the UA thresholds utilised for analysis [25].

Collectively, our data substantiate the notion of UA as a dual-natured molecule—providing protection against age-related oxidative damage in muscle at modest concentrations, yet proving harmful when persistently raised, especially in susceptible subgroups. The noted sex-specific effects may indicate varying hormonal profiles, antioxidant capacities, or body compositions, all of which necessitate additional mechanistic exploration.

These investigations, together with our findings, indicate a limited optimum range for serum UA, wherein its antioxidant qualities may enhance muscular function. When UA levels beyond this physiological threshold, its pro-inflammatory and vasculotoxic actions may prevail, leading to vascular dysfunction and heightened mortality risk. The sex-specific correlation identified in our study—where hyperuricemia forecasted death solely in females—may be due to hormonal factors, sex-related disparities in UA metabolism, or differing endogenous antioxidant capacities, as previously suggested in the literature. This work contributes to existing evidence by showing that elevated UA levels and diminished muscle strength are independently linked to increased mortality risk in older adults, with potential synergistic effects observed in females. Due to the simplicity, affordability, and non-invasive nature of assessing both handgrip strength and serum UA levels, these metrics are promising as practical instruments for evaluating mortality risk in standard geriatric care. However, additional longitudinal and interventional studies are required to accurately delineate the UA threshold at which its function transitions from protective to detrimental, and to investigate whether UA-lowering therapies or muscle-strengthening interventions can significantly enhance survival outcomes in this at-risk population.

This research possesses numerous significant strengths. This study is one of the few to concurrently assess the predictive significance of blood uric acid levels and handgrip strength in forecasting all-cause mortality in older adults. Utilising a sex-stratified analytical method, our results underscore significant sex-specific correlations frequently neglected in geriatric prognostic models. A reasonably large cohort of community-dwelling older adults enhances the study, thereby augmenting its external validity. We conducted a comprehensive geriatric assessment that encompassed nutritional status, frailty, cognitive function, depression, and functional capacity, thereby facilitating rigorous multivariable adjustments and reducing residual confounding. Both blood uric acid and handgrip strength are cost-effective, non-invasive, and readily available clinical metrics, rendering the study's findings very relevant to standard geriatric care, especially in resource-constrained environments. However, it is important to acknowledge

certain limitations. The study's observational approach prevents causal conclusions. We assessed serum uric acid levels at a single time point, which may not accurately reflect long-term exposure or fluctuations. Furthermore, we did not have access to data regarding dietary purine consumption, alcohol use, or the administration of specific drugs that could affect UA levels (e.g., low-dose aspirin, corticosteroids). Finally, despite our adjustments for significant comorbidities, unmeasured variables may persist. Future longitudinal and interventional studies are needed to clarify causal relationships and to determine whether UA-lowering interventions or muscle-strengthening programs can improve survival in older adults.

Abbreviations

• UA
Uric acid
• HGS
Handgrip strength
• BMI
Body mass index
• EWGSOP2
European Working Group on Sarcopenia in Older People 2
• HR
Hazard ratio
• CI
Confidence interval
• ADL
Activities of Daily Living
• IADL
Instrumental Activities of Daily Living
• BIA
Bioelectrical impedance analysis
• SMM
Skeletal muscle mass
• SMMI
Skeletal muscle mass index

Declarations

Ethics Approval and Consent to Participate:

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Erciyes University Faculty of Medicine (decision number 2024/243). Written informed consent was obtained from all participants.

Consent for Publication:

Not applicable.

Competing Interests:

The authors declare that they have no competing interests.

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Author Contribution

ND: Data collection, investigation, writing-review and editing. SA: Conceptualization, methodology, investigation, writing-original draft, supervision. GZ: Statistical analysis, methodology, writing-review and editing. SIYT: Data collection, investigation, writing-review and editing. All authors read and approved the final manuscript.

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Availability of Data and Materials:

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1. Characteristics of subjects by gender.

Characteristics	Total n=910	Female n=609	Male n=301	p
Age, years	71 (66-76)	71 (66-76)	72 (67-78)	**0.002**
<74	604 (66.4)	420 (70)	184 (30)	**0.019**
>75	306 (33.6)	189 (61.8)	117 (38.2)	
Marital status n(%)				**<0.001**
Single	18 (2)	11 (61.2)	7 (38.8)	
Married	612 (67.3)	345 (56.4)	267 (43.6)	
Widow	280 (30.7)	253 (90.4)	27 (9.6)	
Income n(%)				0.922
Good	110 (12.1)	72 (65.5)	38 (34.5)	
Middle	700 (77)	469 (67)	231 (33)	
Bad	100 (10.9)	68 (68)	32 (32)	
Height, cm, medyan (IQR)	156 (151-163)	153 (150-157)	165 (161-170.5)	**<0.001**
Weight, kg, medyan (IQR)	75.05 (66.25-85)	75.1 (65-86)	75 (68-75)	0.548
BMI, kg/m^2 medyan (IQR)	30.3 (26.33-35)	32 (27.9-36)	27.4 (24.8-30.5)	**<0.001**
WC, cm, medyan (IQR)	105 (95-113)	107 (95-115)	101 (95-108)	**<0.001**
Hip circumference, cm, medyan (IQR)	110 (102-120)	115 (106-123)	104 (99-109)	**<0.001**
CC, cm, medyan (IQR)	37 (33-40)	37 (34-41)	35 (32.4-38)	**<0.001**
Muscle mass, kg, medyan (IQR)	20.28 (17.09-25.23)	18.36 (15.86-20.90)	26.04 (23.48-29.39)	**<0.001**
Fat-free mass, kg, medyan (IQR)	42 (37.4-49.9)	40 (35.4-44.6)	51.9 (46.9-58.6)	**<0.001**
Fat mass, kg, medyan (IQR)	31.2(23.1-38.87)	34.9 (28.1-42.1)	22.9 (18.3-27.4)	**<0.001**
Total fat mass, % medyan (IQR)	43.7 (33-49.3)	47 (42.7-50.7)	30.6 (26.8-34.9)	**<0.001**
Skeletal muscle mass index, medyan (IQR)	8.33 (0.53-0.89)	7.789 (6.862-8.765)	9.585 (8.802-10.576)	**<0.001**
4 m walking test, m/s, medyan (IQR)	0.72 (0.5-0.95)	0.69 (0.5-0.87)	0.8 (0.54-1)	**<0.001**
TUG, s, medyan (IQR)	11.5 (9-15)	12 (9.45-15.83)	10.6 (8.48-14)	**<0.001**

HGS, kg, medyan (IQR)	20 (15-28)	17.4 (13-22.1)	29 (22.15-35)	**<0.001**
GFR, ml/min/1.73m^2 medyan (IQR)	75.84 (63-88.89)	77 (63.5-89.7)	75 (61.3-87.5)	0.046
Glucose, mg/dL medyan (IQR)	108 (94-137.75)	107 (93-137)	111 (95.5-140.5)	0.068
LDL, mg/dL medyan (IQR)	113.7 (90.7-138.8)	118.4 (94.9-144.4)	106.9 (82.2-127)	**<0.001**
HDL, mg/dL medyan (IQR)	48.4 (40.85-58.5)	51.4 (43-60.4)	44.5 (37.4-51)	**<0.001**
TG, mg/dL medyan (IQR)	138 (102-191)	138 (105-191)	136.5 (95-192)	0.195
Albumin, g/dL medyan (IQR)	4.46 (4.26-4.68)	4.44 (4.27-4.65)	4.52 (4.21-4.73)	0.128
CRP, mg/L medyan (IQR)	2.9 (1.41-6.68)	3.01 (1.47-6.47)	2.64 (1.26-8.03)	0.867
Vitamin D, ng/mL medyan (IQR)	19 (12.45-28)	19 (11.9-29.1)	19.55 (14.08-26)	0.438
Uric acid, mg/dL medyan (IQR)	5.2 (4.27-6.2)	5 (4.1-6)	5.5 (4.75-6.6)	**<0.001**
Hyperuricemia, n (%)				**0.025**
Yes	213 (23.4)	156 (73.2)	57 (26.8)	
No	697 (76.6)	453 (65)	244 (35)	
Hypertension, n (%)				**<0.001**
Yes	617 (67.8)	446 (72.3)	171 (27.7)	
No	293 (32.2)	163 (55.6)	130 (44.4)	
CKD, n (%)				0.114
Yes	193 (21.2)	120 (67.2)	73 (37.8)	
No	717 (78.8)	489 (68.2)	228 (31.8)	
Diabetes, n (%)				0.228
Yes	437 (48)	301 (68.9)	136 (31.1)	
No	473 (52)	308 (65.1)	165 (34.9)	
Stoke history, n (%)				0.356
Yes	32 (3.5)	19 (59.4)	13 (40.6)	
No	878 (96.5)	590 (67.2)	288 (32.8)	
CHD, n(%)				0.096

Yes	183 (20.1)	113 (61.7)	70 (38.5)	
No	727 (79.9)	496 (68.2)	231 (31.8)	
SBP, mmHg, medyan (IQR)	130 (120-140)	130 (120-140)	130 (120-140)	0.307
DBP, mmHg, medyan (IQR)	80 (70-85)	80 (70-85)	80 (70-85)	0.334
ADL, dependent n(%)				0.168
Yes	524 (57.6)	341 (65.1)	183 (34.9)	
No	386 (42.4)	268 (69.4)	118 (30.6)	
IADL, dependent n(%)				0.827
Yes	582 (64)	388 (66.7)	194 (33.3)	
No	328 (36)	221 (67.4)	107 (32.6)	
Depressive mood, n(%)				**<0.001**
Yes	391 (43)	307 (78.5)	84 (21.5)	
No	519 (57)	302 (58.2)	217 (41.8)	
Cognitive impairment, n(%)				0.643
Yes	176 (19.6)	120 (68.2)	56 (31.9)	
No	725 (80.4)	481 (66.3)	244 (33.7)	
Sarcopenia, n(%)				**<0.001**
Yes	764 (84)	561 (73.4)	203 (26.6)	
No	146 (16)	48 (32.9)	98 (67.1)	
Malnutrition, n(%)				**0.017**
Yes	477 (53.5)	338 (70.9)	139 (29.1)	
No	415 (46.5)	263 (63.4)	152 (36.6)	
Polypharmacy, n(%)				**0.003**
Yes	463 (50.9)	331 (71.5)	132 (28.5)	
No	447 (49.1)	278 (62.2)	169 (37.8)	
Frailty, n(%)				**<0.001**
Non-frail	150 (16.5)	66 (44)	84 (56)	
Pre-frail	475 (52.2)	337 (71)	138 (29)	
Frail	285 (31.3)	206 (72.3)	79 (27.7)	
Mortality, n(%)				**<0.001**

Yes	103 (11.3)	40 (38.8)	63 (61.2)	
No	807 (88.7)	569 (70.5)	238 (29.5)	
Number of drugs, medyan (IQR)	4 (2-6)	4(2-6)	3 (1-5)	**0.002**

BMI: body mass index; TUG: Timed Up and Go test; LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; CRP: C-reactive protein; CKD: Chronic kidney disease; CHD: coronary heart disease; ADL: activities of daily living; IADL: instrumental activities of daily living. SBP: Systolic blood pressure; DBP: Diastolic blood pressure. CC:Calf circumference. Statistically significant *p* values are shown in bold.

Table 2. Univariate Cox regression analyses of overall survival among female participants.

Variables	Univariate Cox	
	HR (95%CI)	***p*-value**
Age, years	1.11(1.07-1.16)	**<0.001**
Marital status		
Single	1.00	-
Married	0.54(0.28-1.04)	0.064
Income		
High	1.00	-
Middle	2.66(0.64-11.09)	0.181
Low	4.13(0.86-19.87)	0.077
Height (cm)	0.90(0.86-0.95)	**<0.001**
Weight (kg)	0.97(0.95-0.99)	**0.009**
BMI (kg/m^2)	0.97(0.93-1.03)	0.318
Waist circumference (cm)	0.99(0.97-1.02)	0.915
Hip circumference (cm)	0.98(0.97-1.01)	0.294
Calf circumference (cm)	0.96(0.91-1.02)	0.212
Muscle mass (kg)	0.88(0.80-0.96)	**0.005**
Fat-free mass (kg)	0.92(0.88-0.96)	**<0.001**
Fat mass (kg)	0.99(0.96-1.01)	0.306
Total fat mass, %	1.04(0.99-1.09)	0.132
Skeletal muscle mass index	0.85(0.69-1.04)	0.119
4 m walking test (m/s)	0.35(0.09-1.36)	0.129
TUG, s	1.06(1.02-1.10)	**0.001**
HGS (kg)	0.94(0.89-0.99)	**0.014**
HGS (kg),		
High (females >22 kg, males >36 kg)	1.00	-
Low (females≤22 kg, males≤36 kg)	1.79(0.82-3.90)	0.142
GFR (ml/min/1.73) m^2)	0.97(0.96-0.98)	**<0.001**
Glucose (mg/dL)	1.00(0.99-1.01)	0.514

LDL cholesterol	0.99(0.98-1.00)	**0.028**
HDL cholesterol	0.96(0.94-0.99)	**0.009**
TG (mg/dL)	1.00(0.99-1.00)	0.848
Albumin (g/dL)	0.09(0.04-0.20)	**<0.001**
CRP (mg/L)	1.01(1.00-1.02)	**0.018**
Vitamin D (ng/mL)	0.97(0.94-1.01)	0.108
Uric acid (mg/dL)	1.29(1.11-1.50)	**0.001**
Uric acid (Quartile)		
1.Quartile	1.00	-
2.Quartile	0.71(0.23-2.25)	0.563
3.Quartile	0.96(0.34-2.74)	0.938
4.Quartile	3.08(1.31-7.26)	**0.010**
Hyperuricemia	3.46(1.86-6.44)	**<0.001**
Hypertension	1.80(0.79-4.06)	0.159
CKD	4.51(2.43-8.39)	**<0.001**
Diabetes mellitus	0.81(0.44-1.51)	0.508
Stoke history	2.76(0.98-7.76)	0.055
CHD	2.01(1.02-3.95)	**0.044**
Systolic blood pressure (mmHg)	0.99(0.98-1.02)	0.821
Diastolic blood pressure (mmHg)	0.99(0.95-1.02)	0.518
ADL, dependent	1.94(0.83-4.51)	0.124
IADL, dependent	1.54(0.67-3.55)	0.315
Depressive mood	1.31(0.70-2.46)	0.393
Cognitive impairment	2.08(1.07-4.04)	**0.032**
Sarcopenia	3.19(0.44-23.24)	0.252
Malnutrition	2.67(1.22-5.83)	**0.014**
Polypharmacy	1.83(0.94-3.55)	0.074
Frailty		
Non-frail	1.00	-

Pre-frail	1.49(0.34-6.51)	0.597
Frail	4.10(0.97-17.41)	0.056
Number of drugs	1.06(0.96-1.18)	0.263

BMI: body mass index; TUG: Timed Up and Go test; LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; CRP: C-reactive protein; CKD: Chronic kidney disease; CHD: coronary heart disease; ADL: activities of daily living; IADL: instrumental activities of daily living. Statistically significant *p* values are shown in bold.

Table 3. Univariate Cox regression analyses of overall survival among male participants.

Variables	Univariate Cox	
	HR (%95CI)	*p*-value*
Age, years	1.07(1.04-1.11)	**<0.001**
Marital status		
Single	1.00	-
Married	0.82(0.39-1.73)	0.605
Income		
High	1.00	-
Middle	0.77(0.40-1.48)	0.430
Low	0.75(0.28-2.04)	0.575
Height (cm)	0.99(0.96-1.02)	0.391
Weight (kg)	0.98(0.96-1.00)	**0.025**
BMI (kg/m^2)	0.96(0.91-1.01)	0.089
WC (cm)	0.99(0.97-1.01)	0.247
Hip circumference (cm)	0.98(0.96-0.99)	**0.003**
CC (cm)	0.96(0.92-1.01)	0.130
Muscle mass (kg)	0.95(0.90-1.01)	0.076
Fat-free mass (kg)	0.96(0.94-0.99)	**0.006**
Fat mass (kg)	1.00(0.96-1.03)	0.819
Total fat mass, %	1.04(1.00-1.07)	**0.048**
Skeletal muscle mass index	0.85(0.72-1.02)	0.077
4 m walking test (m/s)	0.53(0.23-1.23)	0.140
TUG, s	1.06(1.03-1.09)	**<0.001**
HGS (kg)	0.97(0.94-0.99)	**0.012**
HGS (kg),		
High (females >22 kg, males >36 kg)	1.00	-
Low (females≤22 kg, males ≤36 kg)	1.57(0.80-3.09)	0.192
GFR (ml/min/1.73) m^2)	0.98(0.97-0.99)	**<0.001**
Glucose (mg/dL)	1.00(0.99-1.00)	0.666

LDL (mg/dL)	0.99(0.98-1.00)	**0.027**
HDL (mg/dL)	1.00(0.98-1.03)	0.881
TG (mg/dL)	0.99(0.99-1.00)	**0.002**
Albumin (g/dL)	0.21(0.14-0.33)	**<0.001**
CRP (mg/L)	1.01(1.00-1.02)	**0.030**
Vitamin D (ng/mL)	1.01(0.99-1.04)	0.342
Uric acid (mg/dL)	1.09(0.94-1.26)	0.268
Uric acid (Quartile)		
1.Quartile	1.00	-
2.Quartile	0.82(0.42-1.61)	0.566
3.Quartile	0.47(0.20-1.08)	0.074
4.Quartile	1.40(0.74-2.66)	0.301
Hyperuricemia	1.72(0.99-3.00)	0.056
Hypertension	1.28(0.77-2.14)	0.336
CKD	2.12(1.26-3.57)	**0.004**
Diabetes mellitus	0.84(0.51-1.39)	0.497
Stoke history	0.75(0.24-2.39)	0.627
CHD	1.70(1.01-2.86)	**0.044**
SBP (mmHg)	0.99(0.97-1.01)	0.380
DBP (mmHg)	1.02(0.99-1.05)	0.124
ADL, dependent	2.38(1.00-5.66)	**0.050**
IADL, dependent	2.24(0.95-5.29)	0.067
Depressive mood	2.03(1.23-3.36)	**0.006**
Cognitive impairment	2.22(1.31-3.78)	**0.003**
Sarcopenia	1.13(0.64-1.97)	0.678
Malnutrition	2.15(1.28-3.64)	**0.004**
Polypharmacy	1.22(0.74-2.00)	0.435
Frailty		
Non-frail	1.00	-

Pre-frail	1.83(0.86-3.88)	0.115
Frail	3.48(1.63-7.42)	**0.001**
Number of drugs	1.05(0.97-1.14)	0.258

BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; CRP: C-reactive protein; CKD: Chronic kidney disease; CHD: coronary heart disease; ADL: activities of daily living; IADL: instrumental activities of daily living. Statistically significant *p* values are shown in bold.

Figures

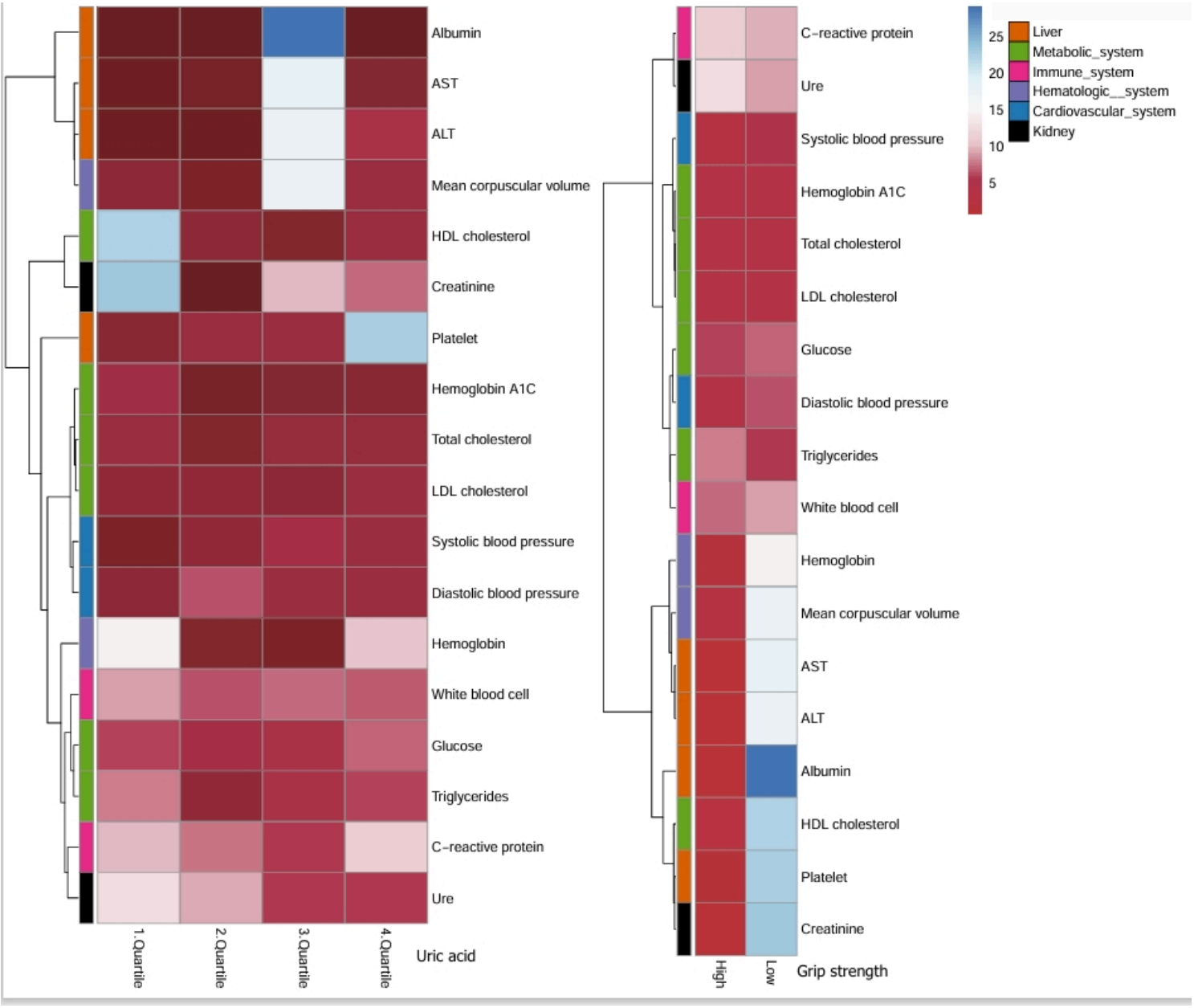


Figure 1

Heatmap displaying the distribution of laboratory parameters across uric acid quartiles (left) and grip strength levels (right).

Hierarchical clustering was applied to visualize the patterns of biomarker changes across quartiles of serum uric acid and dichotomized handgrip strength levels. Parameters are grouped by physiological systems (e.g., liver, kidney, cardiovascular) as indicated by the color-coded sidebar.

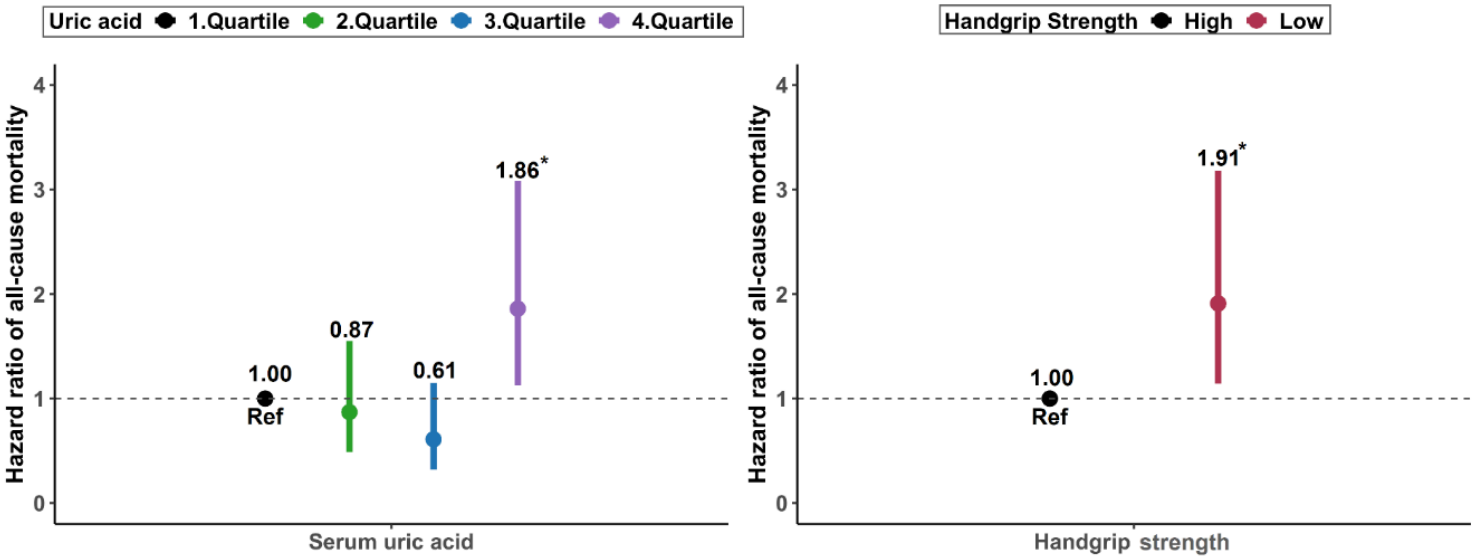


Figure 2

Adjusted Hazard Ratios for All-Cause Mortality According to Serum Uric Acid Quartiles and Handgrip Strength Categories

Forest plots display multivariate-adjusted hazard ratios (HRs) and 95% confidence intervals for all-cause mortality according to (A) serum uric acid quartiles and (B) handgrip strength categories. The first quartile of uric acid and the high handgrip strength group serve as reference categories (HR = 1.00). The highest uric acid quartile (Q4) and low handgrip strength group were significantly associated with increased mortality risk (*p < 0.05).

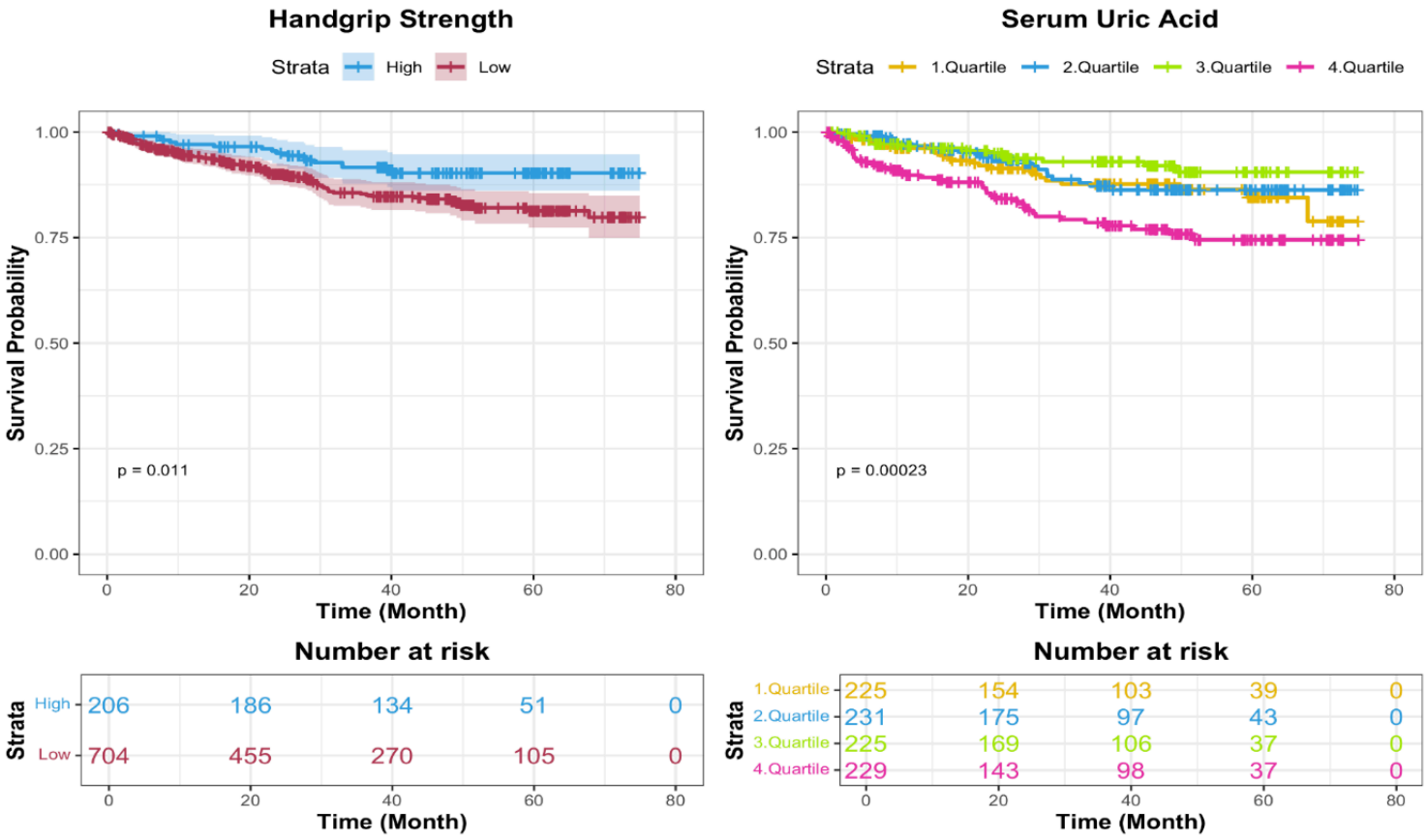


Figure 3

Kaplan–Meier Survival Curves According to Handgrip Strength and Serum Uric Acid Quartiles

Kaplan–Meier plots illustrating all-cause survival probability over time stratified by (A) handgrip strength (high vs. low) and (B) serum uric acid quartiles. Log-rank test showed significantly reduced survival in individuals with low handgrip strength (p = 0.011) and those in the highest uric acid quartile (p = 0.00023). The number of participants at risk during follow-up is presented below each plot.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTables.docx