


ORIGINAL ARTICLE

Characteristics of hyperuricemia in older adults in China and possible associations with sarcopenia

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Abstract

Objective: This cross-sectional study aimed to investigate the characteristics and epidemiology of hyperuricemia in older adults in China and evaluate possible associations between hyperuricemia and sarcopenia.

Methods: Three hundred and eighty-eight study subjects (>60 years old) meeting the inclusion criteria received blood tests and standardized examinations for bone mineral density, muscle mass, muscle strength, and physical performance. Data including demographic and clinical characteristic and comorbidity were also collected. All data were analyzed retrospectively.

Results: In the study population, higher uric acid levels were significantly correlated with higher muscle mass, grip strength, and bone density, but were unrelated to physical performance. When uric acid levels were separated into quartiles and the population was divided by sex, the correlation of uric acid to muscle mass was retained in some quartiles for both men and women, and the correlation to handgrip was only retained for one quartile for men. The correlation to bone density was retained in women in all analyses.

Conclusion: In the population as a whole, higher uric acid levels were significantly correlated with higher muscle mass, grip strength, and bone density, but had no relationship to physical performance. Differences between men and women in these relationships need to be studied further.

KEYWORDS

bone mineral density, hyperuricemia, muscle mass, older adults, sarcopenia, uric acid

1 | INTRODUCTION

Sarcopenia is the term used to describe the decrease in voluntary muscle mass, strength, and/or performance that occurs during aging,^{1,2} and has been associated with an increased risk of falling, fractures, loss of mobility and function, and loss of independence in the elderly.¹⁻⁴ Its prevalence is increasing along with the worldwide increase in the elderly population. In Japan, the prevalence of

sarcopenia among older adults was 8.2% for men and 6.8% for women.⁵ The insulin resistance and chronic inflammation that increase with aging are thought to be significant contributors to the development of age-related sarcopenia.^{1,6} The prevalence of chronic kidney disease (CKD) also increases in aging and can result in sarcopenia. Chronic low-grade inflammation and insulin resistance are thought to contribute to the development of CKD-related as well as age-related sarcopenia.⁷

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Hyperuricemia, a chronic elevation of serum uric acid levels, causes deposition of urate crystals and resulting gouty arthritis in some, although not all, individuals. It has been reported to be a risk factor for hypertension, cardiovascular disease, and renal disease, although it is not completely clear whether hyperuricemia itself is a cause or an accompaniment of these conditions.^{8–11} The prevalence of hyperuricemia and gout has increased over time in a number of countries.^{12,13} In the United States, the prevalence was reported to be 21.2% for men and 21.6% for women,¹³ and to have increased over a 20-year period, an increase believed to be related to the accompanying increase in the prevalence of obesity and hypertension.¹³ In China, the prevalence of hyperuricemia varies widely by age and gender and is reported to be 21.6% in males and 8.6% in females.¹⁴

Uric acid is best known for the tissue damage caused by deposits of crystals or microcrystals of this compound. However, it has potential beneficial and detrimental effects that are unrelated to crystal deposition and could affect the development of sarcopenia. An increase in the prevalence of metabolic syndrome (and therefore of insulin resistance) has been shown to accompany the increased prevalence of hyperuricemia, and this increase might contribute to an increase in sarcopenia.¹ However, the most important physiological property of uric acid is that it is a strong antioxidant^{11,15} and is responsible for about 60% of the antioxidant activity of serum. This antioxidant activity would decrease the development of sarcopenia. But the intracellular action of uric acid is inflammatory, and increased serum uric acid has been shown to be associated with increased inflammatory markers in serum under some conditions, an association that would increase the development of sarcopenia.^{16,17}

Previous studies have reported that increased hyperuricemia both increased^{18,19} and decreased²⁰ muscle strength as estimated by the handgrip test. One study has associated hyperuricemia with a decrease in skeletal muscle mass.²¹ These studies are difficult to compare to each other because they use different cutoff points to define hyperuricemia, the age range of the populations studied varies, and some studies include and some exclude subjects with CKD. And although clinical observation may reveal that weak patients have poor muscle strength and poor bone mineral density (BMD), patients' physical performance ability may still allow them to carry out daily activities. This suggests that muscle strength, muscle mass, and physical performance, as measurable factors for sarcopenia, may need to be regarded as separate criteria. This study therefore aimed to investigate hyperuricemia among older adults in China and to evaluate possible associations between hyperuricemia and each of 3 components of sarcopenia: muscle mass, muscle strength, and physical performance.

2 | PATIENTS AND METHODS

2.1 | Patients

A total of 899 adult subjects from First Affiliated Hospital of Medicine School, Zhejiang University in Hangzhou, China, during the

period from November 2013 to February 2015 were recruited for this study. Most of the subjects were from routine health checkups at the hospital and were not ill. Inclusion criteria were patients aged 60 years and older¹⁹ with or without hyperuricemia (uric acid >7 mg/dL) and availability of complete demographic and clinical data to evaluate hyperuricemia, CKD, and sarcopenia. Subjects younger than age 60 or who were missing data of sex, age, weight, height, uric acid, eGFR, Skeletal Muscle Index (SMI), Short Physical Performance Battery (SPPB), muscle strength, or whole-body total bone mass density (BMD) were excluded. All included patients provided signed informed consent to participate in the study. The Internal Review Board of First Affiliated Hospital of Medicine School, Zhejiang University, reviewed and approved the study protocol.

2.2 | Methods

In this cross-sectional study, patients who met the inclusion criteria had received routine blood tests and urinalysis and standardized examinations for bone mineral density (BMD), muscle mass and strength, and physical performance. Muscle mass was measured as SMI, using the method described by the consensus of the diagnosis of sarcopenia in Europe. Strength was measured as handgrip strength. Physical performance was determined by SPPB scores for lower extremity function, as described previously.²² The SPPB is a simple test to measure lower extremity function using tasks that mimic daily activities. The SPPB examines 3 areas of lower extremity function: static balance, gait speed, and getting in and out of a chair. Dual X-ray absorptiometry (Discovery DXA, Hologic Company, USA) was performed according to the manufacturer's instructions. An automatic biochemical analyzer (3600-310+ISE+ID, Roche Company) was used to perform the biochemical measurements. All data, including demographic and clinical characteristics and comorbidities, were collected and retained for retrospective analysis. Due to data limitations, our analyses did not separate subjects with sarcopenia from those without; instead, the diagnostic components of sarcopenia were each analyzed individually to determine possible associations with hyperuricemia. Renal function was categorized for analysis as stages of CKD: Stage I, eGFR >90; Stage II, eGFR >60 and <90; Stage III, eGFR >30 and <60; Stage IV, eGFR >15 and <30; and Stage V, eGFR <15.

2.3 | Statistical analysis

Subjects' demographics, clinical characteristics, and sarcopenia components are summarized as mean \pm standard deviation (SD) or median with interquartiles (IQR: 1st and 3rd quartiles) for continuous data, according to the normality of the data, and n (%) for categorical data by sex. Differences between sexes were compared using two-sample *t* test or Mann-Whitney U test for continuous data with or without normal distribution; Pearson's chi-square or Fisher's exact test was applied for categorical data.

A partial correlation with adjustment for age was performed to identify the correlation of sarcopenia components with subjects'

demographics and other characteristics in the total population and when subjects were separated according to sex. Results were presented as coefficient of correlation. A simple linear regression in which uric acid levels were divided into quartiles was performed to test the relationship between sarcopenia components and the subjects' demographics and other characteristics by sex, and results were represented as β -values with *P*-values. A simple logistic regression was performed for men and women to identify the association of each of the 4 study parameters (SMI, handgrip strength, SPPB, and BMD) with uric acid levels segregated into quartiles. The 3 sarcopenia components and BMD were stratified into low (\leq median value) and high ($>$ median value) groups before proceeding with this, and results were presented as odds ratio (OR) with corresponding 95% confidence intervals (CI). Finally, a multiple logistic regression was used to identify the association of the high/low sarcopenia component and BMD groups with respect to the uric acid quartiles after adjusting for age and BMI in females and males, separately. All statistical analyses were carried out using IBM SPSS statistical software version 22 for Windows (IBM Corp., Armonk, New York, USA).

3 | RESULTS

3.1 | Subjects

Of the of 899 subjects recruited, 388 with missing data for sex, age, weight, height, uric acid, eGFR, SMI, SPPB, muscle strength, or whole-body total BMD and 133 subjects with either age <60 years or poor kidney function (eGFR <30 per 10 mL/min/1.73 m²) were excluded (Table S1). The data of the remaining 378 subjects (231 males and 147 females) with complete demographic and clinical information were analyzed.

3.2 | Demographics and characteristics by sex

Men were older and more likely to smoke and drink than women, and of the 4 parameters studied, men had greater muscle mass, grip strength, and bone density than women, but similar physical performance scores (Table 1). Uric acid, BUN, and creatinine were higher in men than in women. And in the blood, lipid values (cholesterol, HDL, and LDL) and platelets, total protein, and globulin were lower in men.

3.3 | Relationship of the four study parameters with patient demographics and characteristics

Table 2 examines relationships between study parameters and patient demographics and characteristics in the total population and in men and women separately.

All 4 study parameters, after adjustment for age, were significantly related to smoking and drinking in the total population, but not, with one exception (drinking and BMD in males), when the population was separated according to sex.

3.3.1 | Muscle mass (SMI)

Both BMI and waist/hip ratio were significantly correlated with muscle mass both in the total population and in the male and female subsets. The significant correlation of creatinine and uric acid with muscle mass seen in the total population was lost when the male and female populations were considered separately. Of the blood values, the significant relationship, in the population as a whole, of platelets, hematocrit, and hemoglobin with muscle mass was lost in women, but retained in men. And a significant relationship between 2 factors related to metabolic syndrome (fasting glucose and HbA1c) and muscle mass was seen in men, but not in women or the total population.

3.3.2 | Handgrip strength

Handgrip strength was not related to either BMI or waist/hip ratio except for a mildly significant relation between BMI and grip strength seen only in the total population and not when the population was divided by sex. Creatinine, BUN, and uric acid lost their correlation with grip strength seen in the total population when the population was divided by sex. And in the blood, all parameters related to grip strength in the total population (platelets, hemoglobin, hematocrit, total protein, cholesterol, HDL, and LDL) also lost any significant relationship to grip strength when the population was divided by sex.

3.3.3 | Physical performance (SPPB)

Physical performance, as described previously, was related to smoking and drinking in the total population. It was also related to hemoglobin in women and triglycerides in both men and women. No other correlations were observed.

3.3.4 | Bone density (BMD)

Bone density in the total population was related to the same parameters as handgrip strength: platelets, hemoglobin, total protein, globulin, cholesterol, and LDL in blood, and creatinine and uric acid in urine. And as expected, bone density was related to urinary calcium and inorganic phosphate, a relationship not seen in any of the 3 components of sarcopenia. When the population was divided by sex, however, these relationships were lost, and the only relationships seen (besides the previously mentioned relationship to BMI) were a relationship to fasting insulin in females and to fasting glucose in males.

3.4 | Comparison of uric acid quartiles with study parameters

Table 3 shows results for simple linear regression analysis for males and females for the 3 diagnostic components of sarcopenia and bone marrow density. In this analysis, uric acid levels were stratified into 4

TABLE 1 Demographics and other characteristics by sex

Variables	Total (n = 378)	Females (n = 147)	Males (n = 231)	P-value
Demographics				
Age, years	75.3 ± 9.3 (60-100)	73.4 ± 8.5 (60-93)	76.6 ± 9.6 (60-100)	.001 <.001
Weight, kg	60.5 ± 10.6	55.2 ± 9.4	63.8 ± 10.0	<.001
Height, cm	162.7 ± 8.2	155.7 ± 6.1	167.1 ± 6.0	.761
Waist/hip ratio	22.8 ± 3.3	22.7 ± 3.3	22.8 ± 3.3	.946
BMI, kg/m ²				.699
Low (BMI < 18.5)	40 (10.6)	15 (10.2)	25 (10.8)	
Normal	157 (41.5)	65 (44.2)	92 (39.8)	
Obese (BMI ≥ 27.5)	181 (47.9)	67 (45.6)	114 (49.4)	
Characteristics				
Smoking	133 (53.4)	6 (9.1)	127 (69.4)	<.001
Drinking	90 (39.3)	9 (13.2)	81 (50.3)	<.001
Menopause	143 (37.8)	143 (97.3)	0 (0)	—
Diabetes mellitus	88 (40.0)	40 (48.8)	48 (34.8)	.040
Hypertension	227 (60.1)	91 (61.9)	136 (58.9)	.558
Thyroid disease	30 (7.9)	17 (11.6)	13 (5.6)	.037
Gastrectomy	11 (2.9)	2 (1.4)	9 (3.9)	.153
Chronic gastritis	25 (6.6)	12 (8.2)	13 (5.6)	.334
Chronic liver disease	20 (5.3)	7 (4.8)	13 (5.6)	.714
COPD	31 (8.2)	6 (4.1)	25 (10.8)	.020
Cardiac failure	0 (0)	0 (0)	0 (0)	—
Chronic renal disease	14 (3.7)	5 (3.4)	9 (3.9)	.804
Rheumatoid arthritis	5 (1.3)	3 (2.0)	2 (0.9)	.381
Cancers	109 (28.8)	31 (21.1)	78 (33.8)	.008
Sarcopenia-related components				
SMI	5.3 ± 1.0 5.2 (4.6-6.1)	4.8 ± 0.8 4.7 (4.3-5.2)	5.7 ± 0.9 5.7 (5.0-6.3)	<.001
Handgrip strength	20.8 ± 6.9 19.4 (16.1-23.7)	17.4 ± 4.1 17.5 (14.6-20.1)	23.0 ± 7.5 21.3 (17.3-28.4)	<.001
Total whole-body BMD	1.0 ± 0.1 1.0 (0.9-1.1)	0.9 ± 0.1 0.88 (0.83-0.95)	1.1 ± 0.1 1.07 (0.99-1.14)	<.001
SPPB score	9.0 ± 3.3 11.0 (6.0-12.0)	8.9 ± 3.3 11.0 (6.0-12.0)	9.1 ± 3.2 11.0 (7.0-12.0)	.243
Laboratory examination				
WBC	5.9 (4.7-7.53)	6.1 (4.8-7.4)	5.7 (4.5-7.7)	.291
PLT	180.5 (140-224)	196 (155-247)	168 (129-215)	<.001
Hemoglobin	123 (106-134)	120 (104-129)	124 (106-138)	.024
MCV	91 (88.2-93.8)	90 (87.6-92.8)	91.7 (88.4-94.8)	.001
Hct	36.45 (31.9-39.8)	35.8 (32.1-38.7)	37 (31.9-40.7)	.035
Total protein (g/dL)	64.65 (60.4-69.63)	66.2 (61.7-72.1)	63.4 (59.2-68.3)	<.001
Albumin	38.5 (35.08-41.5)	38.7 (36.2-42.4)	38.2 (34.3-40.8)	.026
Globulin	26.25 (23.28-29.2)	27.3 (24.4-30)	25.4 (22.5-28.6)	.001
ALT	16 (11-25)	14 (10-24)	17 (11-26)	.129
AST	21 (17-27)	20 (17-28)	21 (16-27)	.788
Total bilirubin	11 (8-15)	11 (8-15)	11 (8-15)	.191
Direct bilirubin	4 (3-6)	4 (3-5)	5 (3-6)	.002

(Continues)

TABLE 1 (Continued)

Variables	Total (n = 378)	Females (n = 147)	Males (n = 231)	P-value
hsCRP ^a	5.1 (2.2-19.82)	4.8 (2.15-20.05)	5.3 (2.2-19.7)	.806
Fasting glucose, mmol/L	4.89 (4.39-5.72)	4.95 (4.35-6.05)	4.86 (4.45-5.48)	.409
Fasting insulin ^b	10.1 (6.7-14.8)	9.8 (7.5-14.2)	10.1 (6.3-15.13)	.582
HbA1c	5.9 (5.6-6.4)	5.9 (5.6-6.5)	5.8 (5.5-6.2)	.093
Cholesterol	3.99 (3.24-4.69)	4.26 (3.65-5.06)	3.74 (3.11-4.49)	<.001
Triglyceride	1.07 (0.86-1.47)	1.13 (0.92-1.58)	1.06 (0.79-1.4)	.009
HDL	1.1 (0.88-1.35)	1.18 (0.99-1.42)	1.03 (0.86-1.29)	.001
LDL	2.18 (1.59-2.8)	2.45 (1.86-2.94)	1.98 (1.49-2.62)	<.001
Urine analysis				
Creatinine	70 (58-85)	58 (50-68)	79 (67-91)	<.001
BUN (mg/dL)	5.4 (4.4-7.13)	5.2 (4-6.8)	5.5 (4.5-7.4)	.020
Sodium	142 (139-143)	142 (139-143)	142 (139-143)	.883
Potassium	4.14 (3.87-4.38)	4.14 (3.84-4.33)	4.14 (3.88-4.4)	.408
Chloride	104 (102-106)	104 (102-106)	104 (102-106)	.995
Calcium	2.18 (2.08-2.26)	2.2 (2.09-2.3)	2.15 (2.08-2.24)	.007
Inorganic phosphate	1.12 (0.98-1.27)	1.19 (1.03-1.32)	1.08 (0.95-1.21)	<.001
Urine microalbumin ^b	12 (4-24)	9 (2.76-19.6)	13 (5.08-26.05)	.127
Uric acid	4.46 (3.43-5.7)	4.19 (3.23-5.33)	4.62 (3.51-5.82)	.013
eGFR (per 10 mL/min/1.73 m ²)				.179
Stage I (eGFR > 90)	178 (47.1)	78 (53.1)	100 (43.3)	
Stage II (eGFR >60 and ≤90)	162 (42.9)	58 (38.1)	106 (45.9)	
Stage III (eGFR ≥ 30 and ≤60)	38 (10.0)	13 (8.8)	25 (10.8)	

SMI, Skeletal Muscle Indices, measurement of muscle mass calculated from ASM (Appendicular Skeletal Muscle)/height² (kg/m²), ASM = sum of lean value in left arm, right arm, left leg, and right leg. SPPB, Short Physical Performance Battery, measurements of physical performance; BMD, bone mineral density. Data are summarized as mean ± SD with range (min, max.) for age, mean ± SD for weight, height, and ratio of waist and hip, median (IQR) for sarcopenia components, laboratory examination, and urine analysis data, and n (%) for categorical data. Bold value indicated significance (P-value <.05) between females and males.

^aSubjects with hsCRP < 1 were not included

^bMissing rate >50%.

quartiles (G1 [≤1st quartile], G2 [>1st quartile and ≤median], G3 [>median and ≤3rd quartile], and G4 [>3rd quartile]). The cutoff values for these quartiles were calculated separately for men and women (Table S2). In both men and women, quartile G2 was significantly correlated with lower muscle mass than quartile G4, and in women, quartiles G1, G2, and G3 of uric acid were all significantly correlated with lower bone density than quartile G4.

In Table 4, each of the study parameters was divided into a low (≤ median) and high (>median) group and uric acid levels were again stratified by quartile as in Table 3. Each uric acid quartile was then compared to G4 (crude model 1), G3 (crude model 2), and G2 (crude model 3) in the proportions of this quartile that were in the low (≤median) group of each of the 4 study parameters. In these comparisons, men and women in quartile G2 had a significantly greater probability of being in the low muscle mass group compared to men and women (respectively) in G4. Men in quartile G2 also had a greater probability of being in the low muscle mass group than men in G3. Men in quartile G2 had a greater probability of being in the lower handgrip strength group than men in G3. Women in the G1, G2, and G3 quartiles had a greater probability of being in the low

bone density group than women in G4. No relationship was seen between uric acid levels and physical performance. However, in this comparison, all the “above median” subjects had the top score¹² and large numbers of “≤ median” subjects had the median score,¹¹ so, because of the lop-sided distribution of the data, analysis by this method did not really address the question of low and high physical performance.

When the relationship between uric acid quartiles and study parameters was adjusted for both age and BMI (Table 5), no quartile, compared to quartile G4, increased or decreased the odds of higher muscle mass, handgrip, or bone density scores. But females with the lowest uric acid levels (quartile G1) had a significantly higher OR for better physical performance than those in G4 (OR 12.29, 1.95-77.66).

4 | DISCUSSION

In the study population as a whole, higher uric acid levels were significantly correlated with higher muscle mass, grip strength, and

TABLE 2 Partial correlation of sarcopenia components with subjects' demographics and other characteristics with adjusted age

Variables	Total (n = 378)			Females (n = 147)			Males (n = 231)					
	SMI	Handgrip strength	Whole-body total BMD	SPPB, score	SMI	Handgrip strength	Whole-body total BMD	SPPB, score	SMI	Handgrip strength	Whole-body total BMD	SPPB, score
Demographics												
Waist/hip ratio	0.275***	0.08	0.051	0.004	0.377***	0.155	0.15	0.061	0.296**	0.114	0.034	-0.028
BMI, kg/m ²	0.519***	0.120*	0.222***	0.035	0.543***	0.105	0.316***	0.058	0.606***	0.157	0.246***	0.038
Characteristics												
Smoking	0.220**	0.389***	0.322***	0.165*	-0.017	0.092	-0.031	-0.188	-0.142	-0.027	-0.028	0.107
Drinking	0.157*	0.278***	0.339***	0.198**	0.041	0.047	0.172	0.122	-0.090	-0.003	0.211**	0.113
Laboratory examination												
WBC	0.026	-0.040	-0.022	-0.034	0.061	-0.049	-0.070	0.003	-0.055	-0.015	0.031	-0.051
PLT	-0.189***	-0.143**	-0.158**	-0.083	-0.088	-0.059	-0.046	-0.109	0.148*	-0.023	-0.070	0.017
Hemoglobin	0.208***	0.123*	0.142**	0.024	0.116	0.184*	0.081	0.245**	0.199**	0.011	0.084	-0.124
MCV	0.031	0.058	0.021	0.037	-0.017	-0.008	-0.019	0.048	-0.011	0.003	-0.063	0.014
Hct	0.170**	0.057	0.092	-0.029	0.07	0.066	0.015	0.131	0.173**	-0.059	0.059	-0.129
Total protein (g/dL)	-0.051	-0.121*	-0.108*	-0.002	0.001	0.016	0.043	0.114	0.072	0.015	-0.012	0.012
Albumin	-0.003	-0.065	-0.041	0.058	0.044	-0.017	0.066	0.083	0.061	0.032	-0.008	0.072
Globulin	-0.048	-0.102*	-0.105*	-0.054	-0.043	0.039	-0.006	0.073	0.068	-0.016	-0.008	-0.045
ALT	-0.042	0.011	-0.026	0.011	-0.078	-0.061	-0.102	-0.010	-0.008	0.115	0.035	0.011
AST	-0.031	-0.009	0.017	0.001	-0.039	-0.032	-0.057	0.041	-0.041	-0.012	0.046	-0.039
Total bilirubin	0.023	0.059	0.046	-0.037	0.056	-0.044	0.116	-0.044	-0.011	0.044	0.017	-0.082
Direct bilirubin	0.018	0.062	0.044	-0.053	0.008	-0.079	-0.140	-0.071	-0.015	0.049	0.014	-0.100
hsCRP ^a	-0.009	0.02	0.086	-0.025	-0.103	-0.072	0.035	-0.203	0.005	0.013	0.102	0.039
Fasting glucose, mmol/L	0.077	-0.070	-0.019	0.015	0.11	-0.011	-0.103	0.04	0.175**	0.034	0.133*	0.003
Fasting insulin ^b	0.006	-0.049	-0.003	-0.018	0.072	0.118	0.299*	-0.004	0.045	0.047	-0.158	0.015
HbA1c	0.017	-0.092	-0.034	-0.014	0.023	-0.010	-0.036	0.043	0.176*	0.043	0.162*	-0.011
Cholesterol	-0.088	-0.195***	-0.146**	-0.087	0.012	0.045	0.053	0.119	0.061	-0.049	-0.018	-0.120
Triglyceride	-0.045	-0.017	-0.024	-0.068	0.027	0.069	0.039	0.170*	-0.011	0.081	0.07	-0.158*
HDL	-0.016	-0.123*	-0.087	0.005	0.048	0.014	0.101	0.066	0.091	-0.011	-0.045	0.018
LDL	-0.098	-0.189***	-0.129*	-0.060	0.001	0.084	0.042	0.103	0.022	-0.105	-0.018	-0.080
Urine analysis												
Creatinine	0.275***	0.320***	0.320***	0.033	0.081	0.114	0.02	-0.067	0.088	0.003	0.109	-0.089
BUN (mg/dL)	0.058	0.134***	0.038	-0.042	0.057	0.129	-0.029	-0.031	-0.003	0.089	-0.024	-0.082
Sodium	0.022	0.026	-0.005	0.003	0.173*	0.039	0.123	0.127	-0.078	-0.011	-0.100	-0.055

(Continues)

TABLE 2 (Continued)

Variables	Total (n = 378)				Females (n = 147)				Males (n = 231)			
	SMI	Handgrip strength	Whole-body total BMD	SPPB, score	SMI	Handgrip strength	Whole-body total BMD	SPPB, score	SMI	Handgrip strength	Whole-body total BMD	SPPB, score
Potassium	0.089	0.023	0.057	0.014	-0.060	0.037	-0.035	-0.032	0.146*	-0.074	0.097	0.066
Chloride	0.029	0.006	0.054	-0.025	0.135	-0.004	0.064	0.049	-0.064	-0.019	-0.137*	-0.041
Calcium	-0.006	-0.120*	-0.108*	-0.038	0.07	-0.075	-0.005	0.07	0.077	-0.014	-0.021	-0.021
Inorganic phosphate	-0.019	-0.116*	-0.137**	-0.025	0.07	0.052	-0.027	0.138	0.081	-0.015	-0.035	-0.027
Urine microalbumin ^b	0.075	0.02	0.038	-0.025	0.028	-0.030	-0.003	-0.030	0.128	0.071	0.098	-0.001
Uric acid	0.171**	0.170**	0.191***	0.048	0.154	0.071	0.225**	0.142	0.078	0.067	0.08	-0.027
eGFR (per 10 mL/min/1.73 m ²)	-0.138**	-0.096	-0.061	0.097	-0.162	-0.108	-0.049	0.033	-0.080	-0.005	-0.018	0.126

Results were presented as coefficient of correlation *r*.

P* < .05, *P* < .01, and ****P* < .001 indicate statistical significance.

^aSubjects with hsCRP < 1 were not included

^bMissing rate >50%.

bone density, but were not related to physical performance. When the population was divided by sex, the only correlation that was retained was the correlation between increased uric acid levels and increased bone density in women.

A number of previous studies have investigated the relationship between uric acid levels and the 3 components of sarcopenia,^{16,18-21} but this is the first study to examine the 3 components (muscle mass, muscle strength, and physical performance) and the age-related parameter, bone mineral density, in the same population. Of the 3 sarcopenia components, the correlation of uric acid to muscle mass was the strongest, for it was retained in some comparisons when uric acid quartiles were examined in both men and women, while the correlation to handgrip was only retained in one quartile comparison in men. And correlation to physical performance was “weakest,” for it was not seen. The correlation to the other age-related parameter, bone density, which has been related to uric acid concentrations in other studies²³ was retained in women in all analyses.

One explanation for the differences in the strength of the relationship between uric acid and the age-related parameters examined here is the differences in the number of confounding factors. Muscle mass is also related to BMI, handgrip is related both BMI and physical conditioning, and physical performance is related to BMI, muscle conditioning, and neurological function. Bone density is related to estrogen level instead of the factors confounding the relationship between uric acid and the 3 sarcopenia parameters, and the relationship between uric acid and bone density in women was the most clearly delineated in this study.

Another reason for the differences in the relationship between uric acid and the 3 components of sarcopenia might be that the criteria for sarcopenia may be divided into 2 parts, the quantitative (muscle mass) and qualitative (strength/performance) features of skeletal muscle, and these differ in underlying mechanisms. This question needs further study.

Because uric acid has both protective and harmful effects, previous studies have investigated whether its helpful, antioxidant effect is overwhelmed by its harmful inflammatory effect at higher concentrations. Beavers et al²¹ reported that very high UA levels (>8 mg/dL) were twice as likely to be associated with lower muscle mass than UA levels <6 mg/dL. Our study, covering a lower range of uric acid levels (<3.25 to >5.82), reported increases in UA to be associated with increased muscle mass throughout.

A similar dichotomy has been reported for handgrip results. Our study reported uric acid levels to be positively associated with increased handgrip strength, as did other studies using a similar concentration range for uric acid.^{18,24} Studies extending into a higher UA range (>6.8 mg/dL) reported grip strength to increase with increasing uric acid levels at lower levels and then to decrease when levels exceeded 6.8 mg/dL. These results lend credence to the hypothesis that uric acid's antioxidant effect predominates at lower levels and its inflammatory effect predominates at higher levels.

Increased uric acid has previously been linked to increased prevalence of metabolic syndrome and increased risk of type 2

TABLE 3 Simple linear regression models testing the relationship between diagnostic components of sarcopenia with patients' demographics and characteristics by sex

Variables	Males (n = 231)							
	SMI	Handgrip strength	Whole-body total BMD	SPPB, score	SMI	Handgrip strength	Whole-body total BMD	SPPB, score
Demographics								
Age	-0.010 (0.215)	-0.351 (<.001)	-0.0003 (0.767)	-0.334 (<.001)	-0.041 (<.001)	-0.661 (<.001)	-0.002 (0.010)	-0.267 (<.001)
Waist/hip ratio	5.994 (<.001)	7.632 (0.142)	0.247 (0.155)	1.698 (0.563)	4.221 (0.001)	8.278 (0.210)	0.067 (0.708)	-0.779 (0.756)
BMI, kg/m ²	0.137 (<.001)	0.090 (0.208)	0.010 (<.001)	0.032 (0.489)	0.160 (<.001)	0.189 (0.017)	0.008 (<.001)	0.023 (0.568)
Characteristics								
Smoking vs non-smoking	-0.044 (0.891)	0.873 (0.467)	-0.012 (0.805)	1.298 (0.133)	-0.287 (0.056)	-0.258 (0.714)	-0.007 (0.704)	0.509 (0.152)
Drinking vs non-drinking	0.087 (0.741)	0.366 (0.706)	-0.053 (0.164)	0.704 (0.327)	-0.163 (0.258)	-0.030 (0.967)	0.050 (0.007)	0.500 (0.153)
Laboratory examination								
WBC	0.018 (0.465)	-0.051 (0.556)	-0.003 (0.400)	0.002 (0.971)	0.018 (0.403)	-0.023 (0.816)	0.001 (0.640)	-0.037 (0.442)
PLT	-0.001 (0.291)	-0.002 (0.476)	-0.00005 (0.584)	-0.002 (0.190)	-0.002 (0.025)	-0.001 (0.732)	-0.0001 (0.287)	0.0004 (0.793)
Hemoglobin	0.006 (0.163)	0.030 (0.026)	0.001 (0.329)	0.025 (0.003)	0.008 (0.002)	0.002 (0.874)	0.0004 (0.204)	-0.011 (0.061)
MCV	-0.003 (0.843)	-0.005 (0.924)	-0.0004 (0.818)	0.018 (0.566)	-0.001 (0.868)	0.002 (0.967)	-0.001 (0.345)	-0.004 (0.838)
Hematocrit	0.009 (0.403)	0.029 (0.426)	0.0002 (0.858)	0.036 (0.114)	0.019 (0.009)	-0.029 (0.376)	0.001 (0.374)	-0.032 (0.051)
Total protein (g/dL)	0.0002 (0.988)	0.007 (0.852)	0.001 (0.603)	0.031 (0.172)	0.009 (0.275)	0.009 (0.820)	-0.0002 (0.861)	0.004 (0.856)
Albumin	0.007 (0.597)	-0.010 (0.836)	0.001 (0.431)	0.031 (0.319)	0.011 (0.353)	0.027 (0.628)	-0.0002 (0.910)	0.031 (0.274)
Globulin	-0.007 (0.606)	0.023 (0.638)	-0.0001 (0.938)	0.027 (0.382)	0.012 (0.302)	-0.013 (0.804)	-0.0002 (0.902)	-0.018 (0.498)
ALT	-0.002 (0.351)	-0.005 (0.467)	-0.0003 (0.219)	-0.001 (0.904)	-0.0004 (0.903)	0.025 (0.082)	0.0002 (0.594)	0.001 (0.866)
AST	-0.002 (0.639)	-0.006 (0.701)	-0.0004 (0.495)	0.005 (0.620)	-0.002 (0.594)	-0.003 (0.851)	0.0003 (0.491)	-0.005 (0.553)
Total bilirubin	0.008 (0.503)	-0.020 (0.600)	-0.002 (0.162)	-0.013 (0.596)	-0.0003 (0.863)	0.006 (0.504)	0.00006 (0.796)	-0.005 (0.213)
Direct bilirubin	0.002 (0.922)	-0.062 (0.341)	-0.004 (0.091)	-0.035 (0.394)	-0.0005 (0.826)	0.007 (0.461)	0.00006 (0.634)	-0.008 (0.129)
hsCRP ^a	-0.004 (0.227)	-0.009 (0.400)	0.0002 (0.683)	-0.017 (0.016)	0.0002 (0.937)	0.002 (0.846)	0.0004 (0.130)	0.003 (0.557)
Fasting glucose, mmol/L	0.056 (0.184)	-0.019 (0.893)	-0.007 (0.214)	0.044 (0.636)	0.100 (0.008)	0.089 (0.608)	0.010 (0.045)	0.004 (0.959)
Fasting insulin ^b	0.007 (0.607)	-0.035 (0.397)	0.004 (0.028)	-0.001 (0.979)	0.007 (0.665)	0.036 (0.652)	-0.003 (0.131)	0.005 (0.888)
HbA1c	0.014 (0.788)	-0.020 (0.910)	-0.003 (0.671)	0.055 (0.615)	0.180 (0.010)	0.195 (0.532)	0.022 (0.019)	-0.026 (0.874)
Cholesterol	0.010 (0.883)	0.125 (0.586)	0.006 (0.528)	0.208 (0.154)	0.055 (0.355)	-0.200 (0.459)	-0.002 (0.791)	-0.247 (0.069)
Triglyceride	0.034 (0.742)	0.287 (0.410)	0.006 (0.637)	0.454 (0.040)	-0.015 (0.874)	0.527 (0.221)	0.013 (0.294)	-0.516 (0.017)
HDL	0.111 (0.565)	0.112 (0.865)	0.030 (0.226)	0.332 (0.430)	0.216 (0.171)	-0.124 (0.864)	-0.014 (0.496)	0.101 (0.781)
LDL	0.001 (0.995)	0.279 (0.315)	0.005 (0.611)	0.218 (0.217)	0.025 (0.742)	-0.536 (0.114)	-0.003 (0.790)	-0.204 (0.231)
Urine analysis								
Creatinine	0.004 (0.329)	0.020 (0.169)	0.0001 (0.810)	-0.008 (0.420)	0.003 (0.183)	0.001 (0.960)	0.0005 (0.100)	-0.007 (0.179)
BUN (mg/dL)	0.021 (0.493)	0.159 (0.121)	-0.001 (0.729)	-0.204 (0.709)	-0.001 (0.962)	0.104 (0.176)	-0.001 (0.715)	-0.048 (0.216)
Sodium	0.046 (0.037)	0.036 (0.636)	0.004 (0.140)	0.074 (0.127)	-0.020 (0.236)	-0.013 (0.665)	-0.003 (0.130)	-0.032 (0.411)

(Continues)

TABLE 3 (Continued)

Variables	Females (n = 147)				Males (n = 231)			
	SMI	Handgrip strength	Whole-body total BMD	SPPB, score	SMI	Handgrip strength	Whole-body total BMD	SPPB, score
Potassium	-0.119 (0.475)	0.255 (0.654)	-0.009 (0.673)	-0.140 (0.699)	0.308 (0.027)	-0.714 (0.262)	0.027 (0.142)	0.321 (0.316)
Chloride	0.034 (0.103)	-0.003 (0.962)	0.002 (0.443)	0.027 (0.555)	-0.008 (0.603)	-0.021 (0.778)	-0.004 (0.038)	-0.023 (0.536)
Calcium	0.357 (0.399)	-1.309 (0.366)	-0.003 (0.952)	0.779 (0.399)	0.497 (0.245)	-0.405 (0.832)	-0.017 (0.755)	0.310 (0.753)
Inorganic phosphate	0.270 (0.403)	0.687 (0.534)	-0.014 (0.748)	1.162 (0.098)	0.337 (0.224)	-0.280 (0.821)	-0.019 (0.594)	-0.261 (0.683)
Urine microalbumin ^b	0.0003 (0.829)	-0.001 (0.816)	-0.000005 (0.981)	-0.001 (0.816)	0.002 (0.165)	0.005 (0.445)	0.0002 (0.289)	-0.00004 (0.991)
Uric acid	0.074 (0.064)	0.117 (0.394)	0.014 (0.006)	0.150 (0.087)	0.036 (0.237)	0.140 (0.311)	0.005 (0.225)	-0.028 (0.684)
G1 vs G4	-0.314 (0.100)	0.721 (0.454)	-0.059 (0.016)	0.721 (0.359)	-0.208 (0.239)	-1.051 (0.453)	-0.012 (0.577)	-0.088 (0.884)
G2 vs G4	-0.377 (0.049)	0.556 (0.563)	-0.052 (0.033)	1.046 (0.185)	-0.441 (0.013)	-2.244 (0.109)	-0.028 (0.191)	-0.535 (0.373)
G3 vs G4	-0.290 (0.129)	0.132 (0.891)	-0.052 (0.035)	0.451 (0.566)	-0.078 (0.658)	-0.085 (0.951)	0.007 (0.760)	0.897 (0.135)
eGFR (per 10 mL/min/1.73 m ²)	-0.005 (0.050)	-0.011 (0.195)	-0.0002 (0.557)	0.002 (0.695)	-0.002 (0.225)	-0.001 (0.944)	-0.00006 (0.782)	0.008 (0.057)

Results are shown as β (P-value).

Uric acid was stratified into 4 groups, G1 (\leq 1st quartile), G2 ($>$ 1st quartile and \leq median), G3 ($>$ median and \leq 3rd quartile), and G4 ($>$ 3rd quartile). The population was divided by sex.

^aSubjects with hsCRP $<$ 1 were not included

^bMissing rate $>$ 50%.

diabetes,^{3,25,26} conditions that have also been linked to sarcopenia.^{27,28} In our study, waist/hip ratio was significantly related to muscle mass in both men and women, but although men and women had similar mean fasting glucose, fasting insulin, and HbA1c levels, these parameters were significantly linked to muscle mass only in men. Further studies are needed to explore this gender difference.

In clinical practice, it is not entirely understood why we sometimes observe weak older adult patients with poor muscle strength and poor BMD, but their physical performance remains adequate, allowing the performance of daily activities. The results of a study in Taiwan found that skeletal muscle mass was significantly associated with handgrip strength in elderly Taiwanese patients, while the relationship with walking speed as an indicator of physical performance level was not significant.⁴ The authors of that study therefore suggested that physical performance should be a separate measurement beyond muscle mass measurements. Our study found physical performance (SPPB scores) decreased with age, but no relationship between uric acid levels and this estimate of physical performance was seen except for an inexplicable OR of 12 (in age- and BMI-adjusted data) in females for the link between the lowest uric acid quartile and SPPB score.

The choice of measurement methods is especially important when evaluating sarcopenia.²⁹ Grip strength was an important indicator in this study, a simple examination that has been used frequently in sarcopenia research. It is a fast, easy, inexpensive test compared with other tests of physical performance, but it is especially relevant in a balanced approach to identifying components of sarcopenia among patients with hyperuricemia.²⁹ We measured physical performance using the standard composite measure of the SPPB to evaluate balance, gait, strength, and endurance. This test examines the patient's ability to stand with feet together in different positions (side by side, semi-tandem, tandem), time to walk eight feet, and time to get up from a seated position 5 times. Gait speed is an important aspect of sarcopenia because it can readily demonstrate poor performance of lower extremity function and is considered predictive of the onset of disability in frail older adults.³⁰ Other studies have used impaired lower extremity function as criterion for sarcopenia diagnosis³¹ but have also included smoking, general health status, and lower physical activity.

In the present study, although we measured weight, we did not consider sarcopenic obesity, that is, loss of lean body mass and increase in fat mass. One opinion is that age-related weight loss and muscle mass loss are responsible for muscle weakness in older people due to changes in muscle composition when fatty tissue infiltrates into muscle and lowers its ability to perform.³² As such, we might suggest that both hyperuricemia and sarcopenia or the muscle strength component of sarcopenia are influenced by fat consumption along with other factors they have in common, including decreased physical activity, low protein intake, changes in hormone levels, and elevated markers of inflammation.¹ Studies have shown, for example, that age-associated fat accumulation is associated independently

TABLE 4 Association of sarcopenia components with uric acid in females and males, separately

Dependent variables	Females				Males				
	Independent variables ^a	Subjects with		Crude model III ^c	Subjects with		Crude model I ^c	Subjects with	
		≤median ^b	>median ^b		≤median ^b	>median ^b			
SMI		(n = 75)	(n = 72)		(n = 118)	(n = 113)		(n = 113)	
	G1	20 (54.1)	17 (45.9)	2.08 (0.81, 5.32)	30 (52.6)	27 (47.4)	1.32 (0.63, 2.77)	1.51 (0.73, 3.14)	0.63 (0.30, 1.33)
	G2	24 (64.9)	13 (35.1)	3.27 (1.25, 8.52)*	37 (63.8)	21 (36.2)	2.10 (0.99, 4.43)	2.40 (1.14, 5.04)*	1
							[P = .052]	[P = .021]	
Handgrip strength	G3	18 (48.6)	19 (51.4)	1.68 (0.66, 4.28)	25 (42.4)	34 (57.6)	0.88 (0.42, 1.83)	1	
	G4	13 (36.1)	23 (63.9)	1	26 (45.6)	31 (54.4)	1		
		(n = 73)	(n = 74)		(n = 116)	(n = 115)			
	G1	22 (59.5)	15 (40.5)	0.43 (0.17, 1.11)	27 (47.4)	30 (52.6)	0.93 (0.45, 1.94)	1.31 (0.63, 2.74)	0.51 (0.24, 1.08)
G2	18 (48.6)	19 (51.4)	0.67 (0.26, 1.70)	37 (63.8)	21 (36.2)	1.82 (0.87, 3.85)	2.57 (1.22, 5.42)*	1	
G3	19 (51.4)	18 (48.6)	0.60 (0.24, 1.53)	24 (40.7)	35 (59.3)	0.71 (0.34, 1.48)	1		
G4	14 (38.9)	22 (61.1)	1	28 (49.1)	29 (50.9)	1			
	(n = 72)	(n = 75)		(n = 116)	(n = 115)				
Whole-body total BMD	G1	22 (59.5)	15 (40.5)	3.33 (1.27, 8.76)*	33 (57.9)	24 (42.1)	1.33 (0.63, 2.78)	1.88 (0.89, 3.91)	1.38 (0.66, 2.87)
				[P = .015]					
	G2	19 (51.4)	18 (48.6)	2.40 (0.92, 6.25)	29 (50)	29 (50.0)	0.97 (0.46, 2.01)	1.36 (0.66, 2.82)	1
	G3	20 (54.1)	17 (45.9)	2.67 (1.02, 6.98)*	25 (42.4)	34 (57.6)	0.71 (0.34, 1.48)	1	
			[P = .045]						
G4	11 (30.6)	25 (69.4)	1	29 (50.9)	28 (49.1)	1			
	(n = 105)	(n = 42)		(n = 138)	(n = 93)				
SPPB score	G1	26 (70.3)	11 (29.7)	1.04 (0.38, 2.83)	34 (59.6)	23 (40.4)	1.07 (0.51, 2.27)	1.09 (0.52, 2.28)	0.84 (0.40, 1.79)
	G2	26 (70.3)	11 (29.7)	1.04 (0.38, 2.83)	37 (63.8)	21 (36.2)	1.28 (0.60, 2.71)	1.30 (0.62, 2.73)	1
	G3	28 (75.7)	9 (24.3)	1.37 (0.49, 3.84)	34 (57.6)	25 (42.4)	0.99 (0.47, 2.07)	1	
	G4	25 (69.4)	11 (30.6)	1	33 (57.9)	24 (42.1)	1		

^aIndependent variable was set as uric acid, and it was subgrouped into 4 groups, G1 (≤1st quartile), G2 (>1st quartile and ≤median), G3 (>median and ≤3rd quartile), and G4 (>3rd quartile). The population was divided by sex.

^bIndicates the numbers of subjects with median value given dependent variables by sex.

^cCrude models I, II, and III were performed for the association of dependent variables (≤median) and independent variables utilizing the binary logistic regression model with setting the reference group as uric acid G4, G3, and G2, separately. Results were presented as odds ratio (95% CI).

*P < .05 indicates significant association.

TABLE 5 Multiple binary logistic regression analysis of association of sarcopenia components with uric acid adjusting age and BMI in females and males, separately

Dependent variables ^a	Sex	Uric acid groups ^b			
		G1	G2	G3	G4
SMI	Females	1.02 (0.27, 3.77)	1.08 (0.28, 4.17)	1.47 (0.41, 5.33)	Reference
	Males	0.49 (0.14, 1.77)	0.68 (0.19, 2.42)	0.47 (0.14, 1.58)	Reference
Handgrip strength	Females	0.58 (0.13, 2.54)	1.04 (0.28, 3.85)	0.70 (0.19, 2.53)	Reference
	Males	1.09 (0.31, 3.78)	1.61 (0.44, 5.94)	0.75 (0.22, 2.55)	Reference
Whole-body total BMD	Females	2.74 (0.96, 7.81)	2.07 (0.75, 5.72)	2.62 (0.97, 7.09)	Reference
	Males	1.11 (0.51, 2.41)	0.70 (0.32, 1.53)	0.60 (0.28, 1.31)	Reference
SPPB score	Females	12.293 (1.95, 77.66)*	3.717 (0.763, 18.11)	4.48 (0.91, 22.02)	Reference
	Males	1.49 (0.36, 6.21)	0.48 (0.11, 2.11)	1.95 (0.46, 8.26)	Reference

^aDependent variables were set subjects > median value as reference.

^bUric acid was subgrouped into 4 groups, G1 (\leq 1st quartile), G2 (>1st quartile and \leq median), G3 (>median and \leq 3rd quartile), and G4 (>3rd quartile). The population was divided by sex.

Results were presented as odds ratio (95% CI) via binary logistic regression analysis with adjusting age and BMI.

* $P < .05$ indicates significant association.

with metabolic abnormalities such as insulin resistance as well as reduced strength and physical performance.³³

4.1 | Limitations

This study is not without limitations. First, although our sample size was large, this cross-sectional study used retrospective data, limiting analysis of cause. Second, as noted in the published literature, current criteria for sarcopenia are often defined as being below certain thresholds set against normal ranges obtained from healthy, young populations. This made it difficult in the present study to determine which patients in the older adult population of our dataset were sarcopenic. And we did not have data on the current medications or the sugar, carbohydrate, and fat content in the diet of the subjects.

5.1 | CONCLUSION

We were able to determine in a fairly large sample of older adult Chinese that within the concentration range studied, higher uric acid levels were associated with higher muscle mass, handgrip strength, and bone marrow density, but were not related to physical performance. However, there were distinct differences when these relationships were studied in men and women separately, and the reasons for these differences need to be examined in future studies.

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CONFLICT OF INTEREST

The authors have no conflict of interests to disclose.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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