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Is there a relationship between serum uric acid and prostate-specific antigen in middle-aged and elderly Chinese men?

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Abstract

Hyperuricemia may be one of the risk factors for the development of prostate cancer. We evaluated the association between serum uric acid (SUA) and elevated prostate-specific antigen (PSA) in the middle-aged and elderly Chinese men, and the adjustment effects of age, glycolipid metabolism and renal function. From January 2019 to December 2024, 967 participants from the middle-aged and elderly Chinese men who attended the urology outpatient clinic of Shuguang Hospital (Shanghai, China) were recruited in this cross-sectional study. Blood samples from participants were collected for the determinations of SUA, PSA, fasting blood glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol, creatinine, blood urea nitrogen and glomerular filtration rate. After adjusting for age, glycolipid metabolism and renal function, the odds ratios (95% confidence interval) of elevated PSA across increasing quartiles of SUA were 1.00, 1.42 (0.97–2.08), 1.45 (0.98–2.13) and 1.26 (0.83–1.90), respectively (*P* for trend = 0.259). The regression spline showed that the risk of elevated PSA tended to a slow but linear increase for SUA levels greater than about 443 μmol/L (*P* for non-linearity = 0.431). The stratified analyses suggested that the associations were significant for participants at least 75 years (*P* for trend = 0.015), but not for those less than 68 (*P* for trend = 0.162) and 68–74 years (*P* for trend = 0.761). Moreover, HDL-C was significantly interacted with SUA (*P* for interaction = 0.046). The associations were more evident in participants with high HDL-C levels (*P* for trend = 0.007) than in those with low (*P* for trend = 0.943) and median HDL-C levels (*P* for trend = 0.176). Our study for the first time demonstrates that SUA levels are unlikely to be associated with the risk of elevated PSA in the middle-aged and elderly Chinese men. Yet the associations between SUA and elevated PSA could be significant for participants at least 75 years. Notably, HDL-C may modify the associations.

Keywords Serum uric acid, Prostate-specific antigen, The middle-aged and elderly, Prostate cancer, Glycolipid metabolism, Renal function

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Introduction

Prostate-specific antigen (PSA), as a blood-based tumor biomarker, is the most widely used in all the major management stages of clinical prostate cancer, such as screening, surveillance following diagnosis, risk stratification for recurrence, and monitoring therapy [1]. Accumulated evidences suggested that benign prostatic hyperplasia (BPH) growth rate, prostate gland volume, obesity, end-stage renal disease, hypertension, hyperinsulinemia, dyslipidemia, hyperuricemia and high alanine aminotransferase levels may be risk factors for the development of patients with prostate cancer [2, 3]. Most notably, many observational studies have discussed the relationship between serum uric acid (SUA) and prostate cancer [4–7], although no consensus has been reached. However, data on the association between SUA and PSA are limited [8, 9], particularly in non-Caucasian ethnicities.

Moreover, SUA levels were correlated with indicators of glycolipid metabolism and renal function [10–12]. To our knowledge, studies on the relative importance of the connections of glycolipid metabolism, renal function and SUA in relation to prostate cancer are still lacking. And few studies have explored the potential interactions between glycolipid metabolism, renal function and SUA. Furthermore, the incidence of prostate cancer increased with age; they occurred in 30% of men over 50 years, and virtually all of men more than 90 years [13]. Therefore, the effect of age also needs to be considered.

In the current study, we analyzed the relationships between SUA levels and risk of elevated PSA in the middle-aged and elderly Chinese men. We especially examined the interplays between glycolipid metabolism, renal function and SUA; and the adjustment effect of age.

Materials and methods

Participants and ethics

In this cross-sectional study, we performed a survey for the middle-aged and elderly Chinese men who visited the urology outpatient clinic of Department of Urology, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine (Shanghai, China) from January 2019 to December 2024. For the study, we included the middle-aged and elderly participants (≥ 40 years) who were successfully measured for SUA, PSA, fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), creatinine (Cr), blood urea nitrogen (BUN) and glomerular filtration rate (GFR) (N = 1022). We excluded the participants who suffered from gout (N = 5), chronic kidney disease (CKD) (N = 9), severe cardiovascular and cerebrovascular disease (N = 8) within the last year, or undergone prostatectomy (N = 12), or attended the urology outpatient clinic for the second or above time (N = 21). Finally, a total of 967 participants were recruited in the study (Fig. 1).

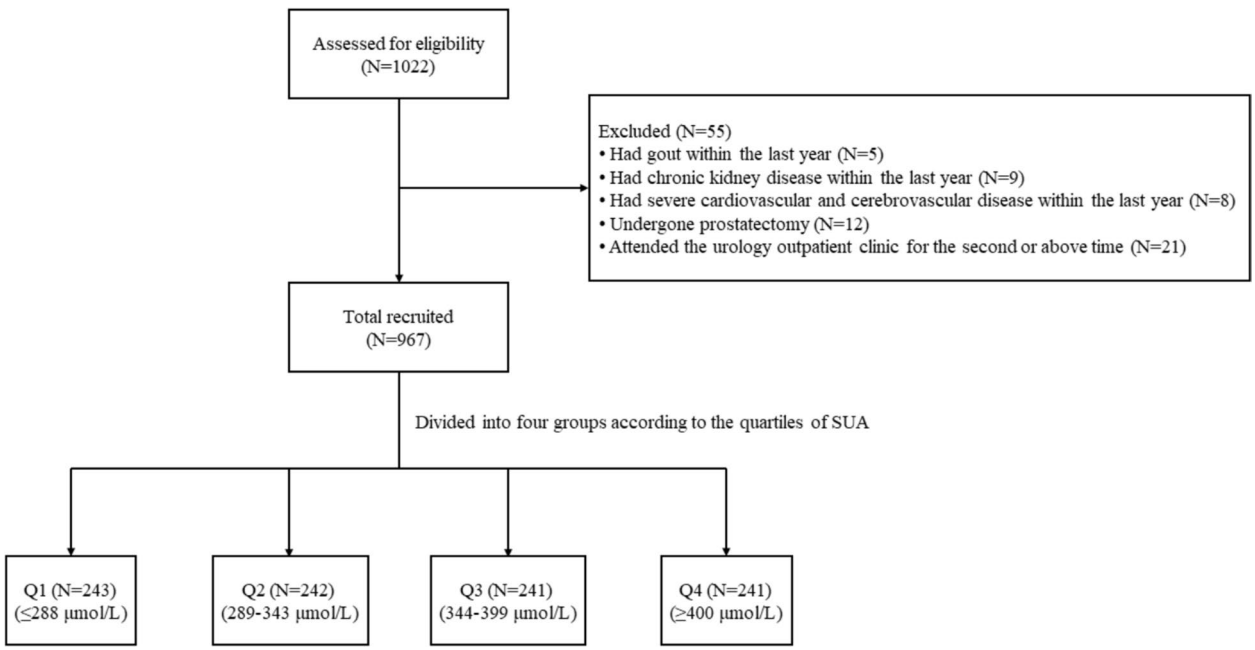

Fig. 1 The flow diagram of participant recruitment in this cross-sectional study. SUA, serum uric acid

The Ethics Committee of Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine reviewed and approved this study (Approval NO.2024–1592-175–01), and permitted the waiver of the requirement for written informed consents from all participants. The protocol of the present study was conducted in accordance with the principles of the Declaration of Helsinki (7 th revised edition in Brazil in 2013).

Detection of PSA and biochemical indicators

After overnight fasting for at least 8 h, blood samples of antecubital veins were drawn from all participants into plastic centrifuge tubes containing ethylenediaminetetraacetic acid. The samples in tubes were allowed to clot at room temperature, and immediately spun at 3,000 rpm for 15 min in the Allegra® X-12R benchtop centrifuge (Beckman Coulter Inc., Brea, CA, USA) to obtain serum for the determinations of SUA, PSA, FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR. Then, SUA was estimated by the uricase method, with the uric acid assay kit (Wako Pure Chemical Industries, Ltd., Tokyo, Japan). PSA was measured by the electrochemiluminescence method, using the PSA quantitative assay kit (Roche Diagnostics GmbH, Mannheim, Germany). The glucose assay kit (Wako Pure Chemical Industries, Ltd., Tokyo, Japan), by the hexokinase method, was used to determine the FBG. The concentrations of TC, TG, HDL-C and LDL-C were tested by the Hitachi 7600 automatic biochemical analyzer (Hitachi Ltd., Tokyo, Japan) with reagents obtained from Wako Pure Chemical Industries Ltd. (Tokyo, Japan). Cr was detected by the F-DAOS enzymatic reagent kit (Wako Pure Chemical Industries, Ltd., Tokyo, Japan). BUN was determined by the urease-glutamate dehydrogenase method, with the BUN assay kit (Wako Pure Chemical Industries, Ltd., Tokyo, Japan). GFR was calculated, using the simplified Modification of Diet in Renal Disease formula modified by the Chinese in 2006, as follows:

$$\mathrm{GFR}\left(\mathrm{mL/min\ per\ 1.75\ m^2}\right) = 175 \times \left[\mathrm{Cr}(\mu\mathrm{mol/L})\right]^{-1.154} \times \left[\mathrm{age(years)}\right]^{-0.203}$$

Statistical analysis

All data were analyzed with the SPSS 26.0 statistical software package (IBM Corp., Armonk, NY, USA). Continuous variables with normal distribution were presented as mean ± standard deviation, and categorical variables were expressed as number (percentage). The normality of continuous variables was rigorously assessed using the Shapiro–Wilk test (P < 0.05 indicating non-normality). For skewed distributions variables, non-parametric statistics (median and interquartile range) were applied in subgroup analyses and regression models to ensure robustness. Logarithmic transformation was performed for skewed variables in sensitivity analyses, which yielded results consistent with untransformed parametric tests. Participants were divided into four groups according to the quartiles of SUA, and the age, PSA and biochemical characteristics between the groups were compared by One-Way ANOVA. Unconditional logistic regressions were conducted to evaluate odds ratios (ORs) with 95% confidence interval (CI) for the risk of elevated PSA, after stepwise adjustment for covariates, including age, FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR. The interactions between SUA and other factors were assessed using the likelihood ratio test. The multivariable-adjusted restricted cubic spline regression was performed to model the relationship between SUA as continuous variable and the risk of elevated PSA. Two-sided *P* values < 0.05 were accepted as statistically significant.

Results

The mean age of 967 participants was 71.27 ± 8.07 years, with an age range of 43–98 years. A total of 633 (65.46%) participants had elevated PSA levels (normal range, 0.00–4.00 ng/mL). Table 1 presents the age, PSA and biochemical characteristics of all participants by the quartiles of SUA levels. Participants with higher SUA levels had higher PSA ($P = 0.019$), TG ($P = 0.002$), LDL-C ($P = 0.033$), Cr ($P < 0.001$) and BUN ($P < 0.001$), but lower FBG ($P = 0.003$), HDL-C ($P < 0.001$) and GFR ($P < 0.001$).

We assessed the associations between SUA levels and the risk of elevated PSA (Table 2). In the unadjusted crude model (Model 1), the ORs (95% CI) of elevated PSA across increasing quartiles of SUA levels were 1.00, 1.47 (1.01–2.12), 1.57 (1.08–2.28), and 1.57 (1.08–2.28), respectively (*P* for trend = 0.016). Then, after adjusting for age and FBG (Model 2), the ORs (95% CI) were 1.00, 1.44 (0.99–2.09), 1.53 (1.05–2.22), and 1.51 (1.04–2.20), respectively (*P* for trend = 0.029). After further adjusting for TC, TG, HDL-C and LDL-C (Model 3), the ORs (95% CI) were 1.00, 1.42 (0.98–2.06), 1.45 (0.99–2.13), and 1.41 (0.96–2.08), respectively (*P* for trend = 0.083). Based on Model 2, after additional adjusting for Cr, BUN and GFR (Model 4), the ORs (95% CI) were 1.00, 1.45 (0.99–2.11), 1.52 (1.04–2.23), and 1.35 (0.90–2.03), respectively (*P* for trend = 0.120). After adjusting for above multiple variables, including age, FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR (Model 5), the ORs (95% CI) were 1.00, 1.42 (0.97–2.08), 1.45 (0.98–2.13), and 1.26 (0.83–1.90), respectively (*P* for trend = 0.259). We also used the multivariable-adjusted restricted cubic spline regression with

Table 1 Age, PSA and biochemical characteristics of all participants by SUA levels (in quartiles)

Variables	SUA (μmol/L) (in quartiles)				*P*
	Q1 (N = 243) (≤ 288)	Q2 (N = 242) (289–343)	Q3 (N = 241) (344–399)	Q4 (N = 241) (≥ 400)	
Age (years)	71.44 ± 7.71	71.00 ± 7.53	70.95 ± 8.31	71.68 ± 8.71	0.708
PSA (ng/mL)	8.67 ± 11.11	12.13 ± 18.41	17.49 ± 55.62	18.94 ± 55.32	0.019
Biochemical measures					
FBG (mmol/L)	5.80 ± 1.97	5.58 ± 1.52	5.45 ± 1.12	5.33 ± 0.97	0.003
TC (mmol/L)	4.23 ± 0.86	4.23 ± 0.84	4.35 ± 0.91	4.33 ± 0.88	0.248
TG (mmol/L)	1.18 ± 0.71	1.38 ± 0.94	1.49 ± 1.50	1.56 ± 1.32	0.002
HDL-C (mmol/L)	1.35 ± 0.36	1.30 ± 0.32	1.27 ± 0.31	1.23 ± 0.27	< 0.001
LDL-C (mmol/L)	2.37 ± 0.67	2.38 ± 0.62	2.50 ± 0.72	2.51 ± 0.70	0.033
Cr (μmol/L)	70.44 ± 14.50	74.37 ± 14.26	76.81 ± 21.04	94.07 ± 37.76	< 0.001
BUN (mmol/L)	5.56 ± 1.43	5.99 ± 1.48	6.15 ± 1.95	6.92 ± 2.18	< 0.001
GFR (mL/min per 1.75 m^2)	99.93 ± 21.26	93.85 ± 19.87	91.19 ± 19.39	76.75 ± 24.16	< 0.001

SUA, serum uric acid; PSA, prostate-specific antigen; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Cr, creatinine; BUN, blood urea nitrogen; GFR, glomerular filtration rate

Table 2 Association between SUA and PSA

SUA (μmol/L)	Elevated PSA	Normal PSA	OR (95% CI)				
			Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]
Quartile 1 (≤ 288)	141(58.02%)	102(41.98%)	1.00	1.00	1.00	1.00	1.00
Quartile 2 (289–343)	162(66.94%)	80(33.06%)	1.47 (1.01–2.12)	1.44 (0.99–2.09)	1.42 (0.98–2.06)	1.45 (0.99–2.11)	1.42 (0.97–2.08)
Quartile 3 (344–399)	165(68.46%)	76(31.54%)	1.57 (1.08–2.28)	1.53 (1.05–2.22)	1.45 (0.99–2.13)	1.52 (1.04–2.23)	1.45 (0.98–2.13)
Quartile 4 (≥ 400)	165(68.46%)	76(31.54%)	1.57 (1.08–2.28)	1.51 (1.04–2.20)	1.41 (0.96–2.08)	1.35 (0.90–2.03)	1.26 (0.83–1.90)
P for trend			0.016	0.029	0.083	0.120	0.259

SUA, serum uric acid; PSA, prostate-specific antigen; OR, odds ratios; CI, confidence interval; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Cr, creatinine; BUN, blood *urea nitrogen*; GFR, glomerular filtration rate

[a] Model 1: Crude model, no adjustment

[b] Model 2: Adjusted for age and FBG

[c] Model 3: Based on Model 2, additionally adjusted for TC, TG, HDL-C and LDL-C

[d] Model 4: Based on Model 2, additionally adjusted for Cr, BUN and GFR

[e] Model 5: Based on Model 3, further adjusted for Cr, BUN and GFR

four knots at the 5th, 35 th, 65 th, and 95 th centiles to continuously model the association of SUA and PSA (Fig. 2). The regression spline indicated that, when SUA levels were greater than about 443 μmol/L, the risk of elevated PSA tended to a slow but linear increase (*P* for non-linearity = 0.431).

We next analyzed the associations between SUA and elevated PSA in different age groups (tertiles): below 68, 68–74, and at least 75 years (Table 3). The results showed that the associations were significant for participants at least 75 years (*P* for trend = 0.015), but not for those less than 68 (*P* for trend = 0.162) and 68–74 years (*P* for trend = 0.761). The interaction between SUA and age was not significant (*P* for interaction = 0.443).

Likewise, we performed a series of stratified analyses to examine the interactions between SUA and biochemical indicators, including FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR (Table 3). Considering the sufficient power of stratified analyses, we classified the strata factors-FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR-into three categories (tertiles): low, median, and high levels. The results of stratified analyses showed a significant interaction between SUA and HDL-C in relation to the risk of elevated PSA (*P* for interaction = 0.046). The associations between

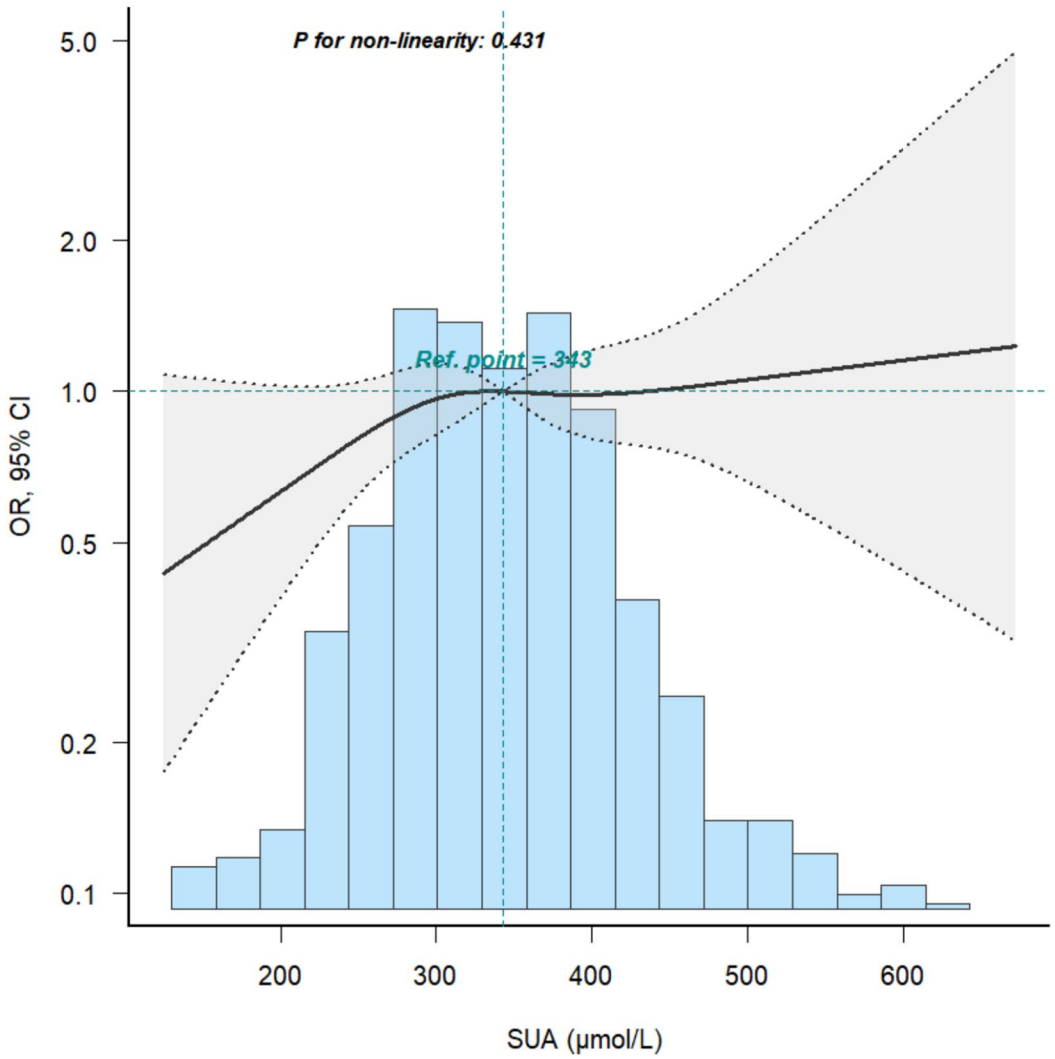

Fig. 2 Risks of elevated PSA according to SUA concentration as a continuous variable. The ORs were assessed by logistic regression modeling, adjusting for age, FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR. The gray-shaded area represents the 95% CIs. PSA, prostate-specific antigen; SUA, serum uric acid; ORs, odds ratios; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Cr, creatinine; BUN, blood urea nitrogen; GFR, glomerular filtration rate; CIs, confidence intervals

SUA and elevated PSA were more evident in participants with high HDL-C levels (P for trend $=0.007$) than in those with low (P for trend $=0.943$) and median HDL-C levels (P for trend $=0.176$). The interaction tests for FBG, TC, TG, LDL-C, Cr, BUN and GFR were not significant (P for interaction $=0.095$, 0.243, 0.477, 0.126, 0.202, 0.133 and 0.375, respectively).

Discussion

Our study, for the first time, demonstrated that SUA was univariately associated with the risk of elevated PSA in the middle-aged and elderly Chinese men, but not after further adjusting for multiple factors, including age, glycolipid metabolism, and renal function. However, the stratified analyses revealed that the associations between SUA and elevated PSA were significant for participants at least 75 years. Remarkably, we

Table 3 Stratified associations between SUA and PSA by age and biomarkers

Variables	SUA (μmol/L) (in quartiles)				*P* for trend	*P* for interaction
	Q1	Q2	Q3	Q4		
Age (years)						
< 68; N = 345	1.00	1.02(0.54–1.94)	1.27(0.67–2.42)	1.37(0.68–2.77)	0.162	0.443
68–74; N = 308	1.00	1.48(0.74–2.93)	1.55(0.75–3.19)	0.68(0.32–1.47)	0.761	
≥ 75; N = 314	1.00	2.13(1.08–4.21)	1.48(0.73–3.03)	2.11(1.01–4.42)	0.015	
FBG (mmol/L)						
Low (≤ 4.86); N = 329	1.00	1.52(0.80–2.91)	1.76(0.91–3.40)	1.48(0.73–2.99)	0.016	0.095
Median (4.87–5.52); N = 318	1.00	1.27(0.63–2.56)	1.75(0.82–3.74)	1.62(0.72–3.67)	0.111	
High (≥ 5.53); N = 320	1.00	1.62(0.83–3.13)	1.15(0.60–2.22)	0.88(0.43–1.80)	0.996	
TC (mmol/L)						
Low (≤ 3.85); N = 323	1.00	0.91(0.48–1.71)	0.96(0.50–1.85)	1.37(0.66–2.84)	0.460	0.243
Median (3.86–4.60); N = 323	1.00	2.27(1.15–4.47)	1.56(0.78–3.13)	1.00(0.49–2.04)	0.334	
High (≥ 4.61); N = 321	1.00	1.55(0.76–3.16)	2.43(1.19–4.95)	1.55(0.73–3.30)	0.023	
TG (mmol/L)						
Low (≤ 0.95); N = 327	1.00	0.60(0.32–1.13)	1.01(0.51–2.00)	0.82(0.38–1.76)	0.279	0.477
Median (0.96–1.38); N = 324	1.00	3.19(1.63–6.23)	2.51(1.28–4.91)	2.32(1.12–4.83)	0.004	
High (≥ 1.39); N = 316	1.00	1.73(0.80–3.73)	1.22(0.59–2.52)	1.09(0.52–2.30)	0.865	
HDL-C (mmol/L)						
Low (≤ 1.13); N = 334	1.00	1.20(0.61–2.35)	1.26(0.64–2.50)	0.93(0.46–1.86)	0.943	0.046
Median (1.14–1.38); N = 323	1.00	1.45(0.72–2.90)	1.50(0.74–3.03)	1.40(0.67–2.94)	0.176	
High (≥ 1.39); N = 310	1.00	1.71(0.90–3.25)	1.52(0.78–3.00)	1.79(0.81–4.00)	0.007	
LDL-C (mmol/L)						
Low (≤ 2.10); N = 326	1.00	0.99(0.53–1.84)	0.89(0.46–1.72)	1.15(0.56–2.34)	0.403	
Median (2.11–2.68); N = 323	1.00	1.58(0.81–3.07)	1.13(0.55–2.32)	0.77(0.37–1.61)	0.908	0.126
High (≥ 2.69); N = 318	1.00	1.95(0.93–4.09)	3.30(1.64–6.65)	2.28(1.07–4.86)	0.003	
Cr (μmol/L)						
Low (≤ 68); N = 328	1.00	1.55(0.86–2.77)	1.34(0.72–2.50)	1.81(0.74–4.44)	0.064	0.202
Median (69–80); N = 319	1.00	1.60(0.82–3.14)	1.91(0.97–3.74)	1.41(0.70–2.83)	0.197	
High (≥ 81); N = 320	1.00	0.96(0.41–2.28)	0.94(0.40–2.23)	0.79(0.35–1.77)	0.847	
BUN (mmol/L)						
Low (≤ 5.26); N = 324	1.00	1.68(0.87–3.24)	1.24(0.66–2.34)	1.07(0.50–2.29)	0.279	0.133
Median (5.27–6.62); N = 323	1.00	1.46(0.77–2.76)	1.25(0.63–2.45)	1.01(0.51–2.00)	0.650	
High (≥ 6.63); N = 320	1.00	1.36(0.63–2.94)	2.08(0.95–4.56)	1.98(0.88–4.43)	0.002	
GFR (mL/min per 1.75 m^2)						
Low (≤ 82.19); N = 324	1.00	1.01(0.44–2.30)	0.92(0.40–2.12)	0.87(0.40–1.89)	0.833	0.375
Median (82.20–99.50); N = 321	1.00	1.78(0.92–3.45)	2.15(1.10–4.17)	1.48(0.74–2.97)	0.105	
High (≥ 99.51); N = 322	1.00	1.35(0.74–2.46)	1.17(0.61–2.22)	1.54(0.64–3.68)	0.107	

Analyses were adjusted for covariates age and biomarkers when they were not the strata variables. SUA, serum uric acid; PSA, prostate-specific antigen; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Cr, creatinine; BUN, blood *urea nitrogen*; GFR, glomerular filtration rate

found an interaction between SUA and HDL-C in relation to risk of elevated PSA.

Prostate cancer is one of malignancies with the highest incidence for urinary system in elderly men [14, 15]. The development of prostate cancer may be a combined result of personal factors, such as age, obesity, metabolic syndrome, genetics and family history, and environmental factors, such as infection, diet and lifestyle [6]. SUA is the end product of purine metabolism, generated through the hydrolysis, deamination and oxidation of purine compounds in the human liver [6, 16]. SUA deposition inside the prostate may give rise to tissue damage, inflammation and elevated PSA, and in longtime may eventually cause cancer [9]. Brys et al. [5] reported that the levels of SUA were significantly higher in patients with prostate cancer (Group I = 100,

Gleason score = 2–4, SUA = 5.6 ± 3.0 mg/dL; Group II = 155, Gleason score = 5–7, SUA = 8.2 ± 2.3 mg/dL; Group III = 49, Gleason score = 8–10, SUA = 8.8 ± 2.5 mg/dL) than in healthy individuals (Control group = 233, Gleason score = 0, SUA = 3.5 ± 1.2 mg/dL), and further proposed that there was a significantly positive correlation between increased amount of SUA and oxidative stress in patients with prostate cancer (Group I: r = 0.778; Group II: r = 0.765; Group III: r = 0.619). On the contrary, Benli et al. [7] revealed that SUA levels were significantly lower in patients with prostate cancer (Group 1 = 117, SUA = 5.05 ± 1.14 mg/dL) than those without prostate cancer (Group 2 = 114, SUA = 6.04 ± 1.12 mg/dL), and suggested that low SUA levels could be a risk factor for patients with prostate cancer. Furthermore, Wang et al. [4] demonstrated that the levels of SUA were unlikely to influence the development of prostate cancer (N = 6,574, $P_{\text{trend for quartiles}} = 0.3$). However, the reasons for this contradictory phenomenon remain unclear and need to further clarify.

To date, PSA is the most widely used serum biomarker for the diagnosis of prostate cancer, which has a great predictive value in clinical practice [6, 17]. To our knowledge, only two literatures evaluating the association between SUA and PSA were previously published [8, 9]. Akinloye et al. [8] reported that prostate cancer patients with PSA levels of 11–20 ng/mL (N = 45, SUA = 2.18 ± 0.77 mg/dL) and > 20 ng/mL (N = 42, SUA = 2.33 ± 0.41 mg/dL) had significantly lower SUA levels, compared with those with PSA levels of 5–10 ng/mL (N = 33, SUA = 3.80 ± 1.06 mg/dL) and healthy subjects with PSA levels of < 3.0 ng/mL (N = 50, SUA = 3.62 ± 0.88 mg/dL). Interestingly, Siroosbakht et al. [9] revealed that SUA was significantly positively related to PSA in patients with BPH (N = 910, r = 0.156). In addition, hyperuricemia was significantly positively correlated with PSA (crude OR = 0.585, 95% CI 0.241–1.421); after additional adjusting for age, body mass index (BMI) and prostate volume, there was still a significantly positive correlation (adjusted OR = 0.647, 95% CI 0.254–1.645). However, data on the association of SUA and PSA are still lacking in the oriental men. In the present study, we found that participants with higher SUA levels had significantly higher levels of PSA (Table 1). Furthermore, univariate analysis (Model 1) showed that SUA was significantly associated with the risk of elevated PSA; conversely, further multivariate analysis (Model 2–5) revealed that, after stepwise adjusting for age, FBG, TC, TG, HDL-C, LDL-C, Cr, BUN and GFR, the significance of these associations gradually disappeared (Table 2). Meanwhile, the regression spline manifested that the risk of elevated PSA tended to a slow but linear increase for SUA levels more than about 443 μmol/L (*P* for non-linearity = 0.431) (Fig. 2).

Over the last century, the mean levels of SUA have progressively increased in the general population, and the prevalence of hyperuricemia increased with age and was higher in men than premenopausal women, because the estrogen increased urate excretion by the kidneys [18, 19]. Interestingly, a cross-sectional study revealed that adjusted by gender, SUA was negatively correlated with age [20]. In our study, the results of stratified analyses suggested that the associations between SUA and elevated PSA were statistically significant for participants at least 75 years, but not for those less than 68 and 68–74 years. Besides, we found that there may not be an interaction between SUA and age (Table 3). Of note, this is the first study which has specifically investigated the associations between SUA and the risk of elevated PSA in the middle-aged and elderly Chinese men, so that the findings for this age subgroup of the men may not be directly compared with any existing literature.

HDL-C was well known for its protective properties [21]. In addition to being involved in the inverse transport of cholesterol in the liver, HDL-C particles possess anti-inflammatory, antioxidant and antithrombotic properties that may protect against the development of cardiovascular disease and atherosclerosis [22]. A previous study suggested that higher SUA levels were closely associated with altered lipoprotein metabolism, which may be an early sign of atherosclerosis in participants [23]. In our study, the associations between SUA and elevated PSA were more evident in participants with high levels of HDL-C than in those with low and median levels of HDL-C; additionally, we also found that HDL-C was significantly interacted with SUA (Table 3). This may be related to the higher prevalence of overall cardiovascular disease, especially heart disease, among the middle-aged and elderly in China [24–27]. In contrast, we did not observe the interactions between TC, TG, LDL-C and SUA in this study (Table 3). These results were consistent with data from the previous study [22]. Moreover, a prospective study on SUA and the risk of diabetes showed that SUA was positively associated with the incidence of type 2 diabetes among Chinese adults [24]. Alternatively, we did not note an interaction between SUA and FBG in the study (Table 3).

Uric acid produced by the human body is mainly excreted through the kidneys, and any abnormality of renal function may touch off a marked decrease of urate excretion, which in turn leads to an increased level of SUA [19]. Additionally, several studies indicated that elevated SUA levels were associated with the increased risks of rapid GFR decline, acute kidney injury and CKD [28–30]. In the current study, we observed that participants with higher SUA levels had significantly higher levels of Cr and BUN, but lower levels of GFR (Table 1).

Nevertheless, we did not find the interactions between Cr, BUN, GFR and SUA in this study (Table 3).

As a major strength of this study, the large sample size (N = 967) ensures study power in exploration of complex interactions between SUA and other factors, including age, glycolipid metabolism and renal function. Nevertheless, the cross-sectional nature of the present study does not allow us to infer the causality for the effects. Moreover, other possible factors affecting SUA and PSA, such as BMI, blood pressure, and prostate gland volume, are not available in the current study.

Conclusions

Our study clearly demonstrates that SUA levels are unlikely to be associated with the risk of elevated PSA in the middle-aged and elderly Chinese men. However, the associations between SUA and elevated PSA could be significant for participants at least 75 years. It's worth noting that HDL-C may modify the associations. The causality of the associations between SUA and elevated PSA needs to be further verified in prospective studies and the underlying molecular mechanism remains to be elucidated.

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Author contributions
Yan Wang and Dongdong Guo participated in study design, data acquisition and interpretation, and drafting of the manuscript. Yan Wang and Cheng Ma participated in data acquisition. Cheng Ma and Xiangyang Zhan participated in the analysis, interpretation of data, and drafting of the manuscript. Dongliang Xu and Dongdong Guo participated in critical revision. Xinyu Zhai, Chuanmin Chu, Guanqun Ju, Mingyue Tan and Jianyi Gu participated in data collection. All authors have read and agreed to the published version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate
This study was approved by the Ethics Committee of Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine (Approval NO. 2024-1592-175-01). All procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki (7 th revised edition, 2013). Written informed consent was waived by the Ethics Committee of Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, as this study utilized anonymized clinical data collected during routine outpatient visits.

Consent for publication
Not applicable. No individual-level data or identifying information are included in this manuscript.

Competing interests
The authors declare no competing interests.

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