Correlation Between Carotid Intima Media Thickness and Serum Uric Acid, Results From 15843 Subjects in 2016-2020

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Abstract

Objective: Uric acid is thought to be associated with the occurrence of atherosclerosis, which is closely related to cardio-cerebrovascular disease. However, the present study examined serum uric acid (SUA) and its correlation with carotid intima-media thickness (CIMT), which is a major issue. The purpose of this paper is to examine serum uric acid concentration and its correlation with carotid artery atherosclerosis according to age and sex groups.

Methods: Individuals who underwent physical examinations at the First Affiliated Hospital of Chongqing Medical University from 2016 to 2020 were selected. The physical examination information of the subjects was recorded, and biochemical indexes such as blood uric acid levels were collected. The intima media thickness of the carotid artery was measured by ultrasound. Using traditional atherosclerosis risk factors as adjustment variables, the association between blood uric acid levels and atherosclerosis was assessed by logistic regression analysis.

Results: A total of 15,843 subjects (73.90% male) were included, with an average age of 52 ± 12 (20-92) years. The prevalence of CIMT thickened was 9.51%, and the plaque prevalence was 28.59%. Univariate analysis results showed that there were significant differences in CIMT thickening and plaque occurrence among different SUA level groups in both men and women ($P < 0.0001$). After adjustment for conventional cardiovascular risk factors, increased SUA levels were significantly associated with an increased risk of CIMT thickening (male: ≤ 220 $\mu\text{mol/L}$ as the reference group, 220-290 $\mu\text{mol/L}$: OR=1.591, 95% CI: 1.069-2.367; 290-360 $\mu\text{mol/L}$: OR=1.65, 95% CI: 1.127-2.415; 360-430 $\mu\text{mol/L}$: OR=1.634, 95% CI: 1.116-2.393; >430 $\mu\text{mol/L}$: OR=1.857, 95% CI: 1.264-2.73; $P < 0.05$. female: ≤ 210 $\mu\text{mol/L}$ as the reference group, 260-310 $\mu\text{mol/L}$: OR=1.419, 95% CI: 1.059-1.901; 310-360 $\mu\text{mol/L}$: OR=1.432, 95% CI: 1.048-1.957; >360 $\mu\text{mol/L}$: OR=1.557, 95% CI: 1.113-2.177; $P < 0.05$). Correlation analysis in each age subgroup showed that CIMT was significantly associated with SUA in men ≥ 60 years old and women 45-60 years old and ≥ 60 years old (male: ≤ 220 $\mu\text{mol/L}$ as the reference group, >430 $\mu\text{mol/L}$: OR=1.972, 95% CI: [1.2,3.238]. female: ≤ 210 $\mu\text{mol/L}$ as the reference group, >360 $\mu\text{mol/L}$ (45-60 years old): OR=1.77, 95% CI:[1.107,2.832]; > 360 $\mu\text{mol/L}$ (≥ 60 years old), OR = 1.65, 95% CI: [1.067, 2.551]. $P < 0.05$).

Conclusions: In both men and women, increased SUA levels are closely associated with thickened CIMT, which is associated with a higher risk of cardio-cerebrovascular disease. The age at which this association was observed in women was lower than in men, and whether this result is due to changes in hormone levels before and after menopause remains to be prospectively studied.

Introduction

In recent years, with the improvement of people's living standards and changes in the diet, the incidence of atherosclerosis has shown an increasing trend each year and has begun to occur in increasingly younger individuals, resulting in higher mortality worldwide [1]. Atherosclerosis is a result of lipid metabolic disorders when fat lesions form on the arterial wall lining, and thickening and hardening of the arterial wall and narrowing of the vascular lumen are the main causes of cardio-cerebrovascular disease [2, 3]. Carotid intima thickness has been suggested to be a marker of atherosclerosis sensitivity and has been increasingly used as a proxy indicator for atherosclerosis [4, 5]. Several studies have shown that increased carotid intima thickness is closely associated with plaque occurrence and an increased risk of future cardio-cerebrovascular disease (including stroke and coronary heart disease) [6, 7].

Uric acid is a normal metabolite of purine nucleotides and may cause atherosclerosis by acting as a mediator of inflammation, inducing endothelial dysfunction and stimulating smooth muscle hyperplasia[8]. SUA is closely related to many traditional cardiovascular risk factors, such as age, hypertension, obesity, diabetes, etc. [9, 10]. In previous studies, the association between increased SUA and cardiovascular and cerebrovascular diseases is considered to be an epigenetic phenomenon rather than a causal relationship [11]. However, increasing evidence supports that hyperuricemia is one of the possible risk factors for atherosclerosis and is closely related to the morbidity and mortality of cardio-cerebrovascular disease, suggesting that uric acid, a biomarker, could be a target for therapeutic intervention [12–16]. Many studies not only support this relationship but also indicate that uric acid is an independent risk factor for cardiovascular and cerebrovascular events, including in high-risk populations such as individuals with coronary heart disease, congestive heart failure, diabetes, hypertension, etc. [17–19]. However, the importance of the association between high uric acid and cardiovascular and cerebrovascular events in the general population remains to be clarified.

In this study, we examined the relationship between serum uric acid levels and atherosclerosis in the general checkup population and determined whether this relationship varies with population status. This study aimed to provide new evidence on the relationship between uric acid and cardio-cerebrovascular disease and to clarify the role of uric acid in the occurrence and development of cardio-cerebrovascular disease.

Participants And Methods

2.1 Population Selection

Data collected from the Health Management Center of the First Affiliated Hospital of Chongqing Medical University from 2016 to 2020 were used; adults older than 18 years old were included, and those with incomplete physical examination data, malignant tumors, severe liver or kidney diseases, other metabolic diseases, or recent drug use affecting uric acid metabolism were excluded. After 8–12 hours of overnight fasting, 5 mL venous blood samples were extracted from all subjects, and urine samples were collected the next morning. Biochemical indexes were detected by an automatic biochemical analyzer in the biochemical laboratory.

2.2 General physical measurement and biochemical analysis

The general physical examination was performed by a professional physician. The participants took off their shoes and wore light clothing when their height and weight were measured. After three measurements were obtained, the average value was taken, which was accurate to 0.1cm(kg). BMI was calculated as weight (kg)/height (m)². Waist circumference was measured by placing a soft tape measure around the waist at the navel level. Abdominal central obesity

was defined as waist circumference ≥ 90 cm in men and ≥ 85 cm in women [20]. The systolic blood pressure and diastolic blood pressure (SBP and DBP, respectively) were measured by two highly trained nurses at 8 to 10 a.m., and the average of the six measurements was taken as the final value. Adult hypertension was defined as SBP/DBP $\geq 140/90$ mm Hg or use of antihypertensive drugs [21]. Creatinine, fasting blood glucose, HDL-C, LDL-C, hemoglobin, mean platelet volume, globulin, total cholesterol, triglycerides, alanine transaminase, glutamic-oxalacetic transaminase, glutamyltransferase, urea and urine pH indexes were measured in strict accordance with the standard procedures by the automatic biochemical instrument laboratory of the First Affiliated Hospital of Chongqing Medical University. The laboratory has obtained ISO15189 standard certification. Blood uric acid was measured by the Roche C701 uricase colorimetric method. The source of the SUA reference interval was obtained from the reagent manufacturer's instructions and approved by clinical verification.

2.3 Ultrasound examination of carotid intima media thickness

The intima media thickness of the common carotid artery was measured by Toshiba Aplio 500 color Doppler ultrasonography. The vertical distance between the upper endometrial margin and the upper endometrial margin was measured at the distal common carotid artery (1.0-1.5 cm below the level of bifurcation) and the carotid bulb (where the initial segment of the internal carotid artery was relatively enlarged). Normal was defined as $IMT < 1.0$ mm, and thickened was defined as $1.0 \text{ mm} \leq IMT < 1.5 \text{ mm}$. A plaque was defined as a focal structure invading the arterial lumen greater than 50% of the peripheral IMT value or $IMT \geq 1.5 \text{ mm}$ [22].

2.4 Covariable selection

By consulting experts in the field of cardiovascular and cerebrovascular diseases and referring to relevant information, 51 factors that may be related to atherosclerosis were selected. Combined with our data, 26 variables were retained, and 20 covariates were finally included after variables with more than 30% missing data were eliminated. The included factors were sex, age, BMI, central obesity, hypertension, pulse, creatinine(Cre), fasting blood glucose(FBG), HDL-C, LDL-C, hemoglobin, mean platelet volume(MPV), globulin, total cholesterol(TC), triglycerides(TG), Aspartate aminotransferase(AST), glutamate pyruvic transa(ALT), gamma-glutamyltransferase(GGT), SUA, and urine pH.

2.5 Statistical analysis

Categorical variables are presented as frequencies (relative frequencies), while continuous variables are presented as the mean $\pm$ standard deviation. The Wilcoxon rank sum test was used to compare the rates of each variable between the normal, thickened and plaque groups, and $P < 0.05$ was considered to be statistically significant. The reference intervals of all physical examination variables were in accordance with the physical examination standards of the First Affiliated Hospital of Chongqing Medical University (Appendix 1). SUA was divided into categories. Since the critical value of hyperuricemia was $428 \mu\text{mol/L}$ for males and $357 \mu\text{mol/L}$ for females, after rounding up, $> 430 \mu\text{mol/L}$ and $> 360 \mu\text{mol/L}$ were used as the highest SUA levels in the male and female groups, respectively, and the group intervals were $70 \mu\text{mol/L}$ for males and $50 \mu\text{mol/L}$ for females. The population was divided into five groups according to the serum uric acid level (male: Group1: $\leq 220 \mu\text{mol/L}$, Group2: $220-290 \mu\text{mol/L}$, Group3: $290-360 \mu\text{mol/L}$, Group4: $360-430 \mu\text{mol/L}$, Group5: $>430 \mu\text{mol/L}$; female: Group1: $\leq 210 \mu\text{mol/L}$, Group2: $210-260 \mu\text{mol/L}$, Group3: $260-310 \mu\text{mol/L}$, Group4: $310-360 \mu\text{mol/L}$, Group5: $>360 \mu\text{mol/L}$). Four ordered logistic regression models were constructed: Model 1 was the unadjusted single factor model, Model 2 was adjusted for age, Model 3 was adjusted for age, BMI, central obesity and hypertension, and Model 4 was adjusted for all covariates. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and R 4.0.4 software.

Results

3.1 CIMT thickened and plaque prevalence in males and females

A total of 15,843 persons (73.90% male, mean age 52 ± 12 (20–92)) who met the inclusion and exclusion criteria were selected. According to the classification standard of carotid intima media thickness, 61.90% of the people had normal CIMT. Thickened was found in 9.51% of the participants, and the plaque prevalence was 28.59%. The prevalence of CIMT thickened and plaque in the male population was higher than that in the female population ($P < 0.0001$), and the specific proportion distribution is shown in Fig. 1.

3.2 Baseline characteristics and univariate analysis

Table 1 shows the distribution of various variables in the normal, thickened and plaque groups of CIMT in different male and female populations. With increasing age, the incidence of thickened and plaque in CIMT gradually increased. The thickened rate of CIMT in patients with central obesity and hypertension was significantly higher than that in patients without central obesity and hypertension. Univariate analysis showed that age, BMI, central obesity, hypertension, FBG, urine pH, TC, TG, LDL-C, hemoglobin, AST, ALT, urea, Cre, and SUA had significant effects on CIMT in the male population. In the female population, the variables that had a significant influence on CIMT were age, BMI, central obesity, hypertension, pulse, FBG, urine pH, TC, TG, HDL-C, LDL-C, hemoglobin, ALT, GGT, urea, Cre, and SUA.

Table 1
Relevant baseline variables according to CIMT

Male(n = 11708)				Female(n = 4135)		
	CIMT			CIMT		
			<i>P^a</i>			<i>P^a</i>
	Normal(59.35%)	Thickened(10.13%)	Plaque(30.52%)	Normal(69.12%)	Thickened(7.76%)	Plaque(23.12%)
Age(years)						
18–45	2948(89.14)	125(3.78)	234(7.08)	937(95.61)	13(1.33)	30(3.06)
45–60	3171(59.36)	641(12)	1530(28.64)	1366(76.02)	139(7.74)	292(16.25)
≥ 60	830(27.13)	420(13.73)	1809(59.14)	555(40.87)	169(12.44)	634(46.69)
BMI (kg/m²)						
< 18.5	79(54.86)	10(6.94)	55(38.19)	174(84.47)	6(2.91)	26(12.62)
18.5–24	2757(59.92)	426(9.26)	1418(30.82)	1968(72.11)	210(7.7)	551(20.19)
24–28	3252(58.21)	608(10.88)	1727(30.91)	579(60.06)	81(8.4)	304(31.54)
≥ 28	861(62.57)	142(10.32)	373(27.11)	137(58.05)	24(10.17)	75(31.78)
Central obesity						
Yes	2600(56.93)	532(11.65)	1435(31.42)	403(52.34)	75(9.74)	292(37.92)
No	4349(60.9)	654(9.16)	2138(29.94)	2455(72.96)	246(7.31)	664(19.73)
Hypertension						
Yes	1440(44.99)	422(13.18)	1339(41.83)	473(47.68)	104(10.48)	415(41.83)
No	5509(64.76)	764(8.98)	2234(26.26)	2385(75.88)	217(6.9)	541(17.21)
Pulse (counts per minute)						
Lower	498(59)	84(9.95)	262(31.04)	124(60.78)	22(10.78)	58(28.43)
Normal	6229(59.48)	1062(10.14)	3182(30.38)	2619(69.52)	293(7.78)	855(22.7)
Higher	222(56.78)	40(10.23)	129(32.99)	115(70.12)	6(3.66)	43(26.22)
FBG (mmol/l)						
Lower/Normal	5760(63.7)	868(9.6)	2415(26.71)	2600(72.67)	261(7.29)	717(20.04)
Higher	1189(44.62)	318(11.93)	1158(43.45)	258(46.32)	60(10.77)	239(42.91)
Urine PH	6.35(0.54)	6.31(0.54)	6.28(0.51)	6.42(0.61)	6.35(0.60)	6.33(0.60)
TC (mmol/L)						
Lower	27(44.26)	7(11.48)	27(44.26)	-	-	-
Normal	4223(61.63)	665(9.71)	1964(28.66)	1612(73.67)	132(6.03)	444(20.29)
Higher	2699(56.29)	514(10.72)	1582(32.99)	1246(64)	189(9.71)	512(26.3)
TG (μmol/l)						
Lower/Normal	3659(57.18)	655(10.24)	2085(32.58)	2266(71.37)	232(7.31)	677(21.32)
Higher	3290(61.97)	531(10)	1488(28.03)	592(61.67)	89(9.27)	279(29.06)
HDL-C (mmol/L)						
Lower	2624(60.45)	454(10.46)	1263(29.09)	540(63.75)	75(8.85)	232(27.39)
Normal	2461(59.02)	433(10.38)	1276(30.6)	862(69.63)	82(6.62)	294(23.75)
Higher	1864(58.3)	299(9.35)	1034(32.34)	1456(71.02)	164(8)	430(20.98)

Male(n = 11708)				Female(n = 4135)		
LDL-C (MMOL/L)				< 0.0001		< 0.0
Normal	4590(61.39)	737(9.86)	2150(28.75)	2031(73.83)	173(6.29)	547(19.88)
Higher	2359(55.76)	449(10.61)	1423(33.63)	827(59.75)	148(10.69)	409(29.55)
Hemoglobin(g/L)				< 0.0001		0.0
Lower	66(39.05)	18(10.65)	85(50.3)	109(81.34)	5(3.73)	20(14.93)
Normal	6631(59.5)	1131(10.15)	3383(30.35)	2589(69.02)	288(7.68)	874(23.3)
Higher	252(63.96)	37(9.39)	105(26.65)	160(64)	28(11.2)	62(24.8)
MPV(f1)				0.6268		0.1
Lower/Normal	6460(59.26)	1115(10.23)	3327(30.52)	2632(68.85)	299(7.82)	892(23.33)
Higher	489(60.67)	71(8.81)	246(30.52)	226(72.44)	22(7.05)	64(20.51)
Globulin(g/L)				0.0735		0.6
Lower	55(58.51)	12(12.77)	27(28.72)	-	-	-
Normal	6867(59.43)	1168(10.11)	3520(30.46)	2831(69.15)	318(7.77)	945(23.08)
Higher	27(45.76)	6(10.17)	26(44.07)	27(65.85)	3(7.32)	11(26.83)
ALT(U/L)				< 0.0001		0.7
Lower	69(46.31)	13(8.72)	67(44.97)	41(71.93)	2(3.51)	14(24.56)
Normal	6042(58.34)	1065(10.28)	3250(31.38)	2636(69.26)	291(7.65)	879(23.1)
Higher	838(69.72)	108(8.99)	256(21.3)	181(66.54)	28(10.29)	63(23.16)
AST(U/L)				< 0.0001		0.0
Lower	234(48.45)	61(12.63)	188(38.92)	61(82.43)	1(1.35)	12(16.22)
Normal	6354(59.61)	1076(10.09)	3229(30.29)	2653(69.11)	300(7.81)	886(23.08)
Higher	361(63.78)	49(8.66)	156(27.56)	144(64.86)	20(9.01)	58(26.13)
GGT(U/L)				< 0.0001		0.0
Lower	15(50)	6(20)	9(30)	129(81.65)	5(3.16)	24(15.19)
Normal	5565(57.84)	1005(10.44)	3052(31.72)	2599(68.92)	294(7.8)	878(23.28)
Higher	1369(66.59)	175(8.51)	512(24.9)	130(63.11)	22(10.68)	54(26.21)
Urea (mmol/L)				< 0.0001		< 0.0
Lower	326(63.67)	50(9.77)	136(26.56)	-	-	-
Normal	6585(59.31)	1126(10.14)	3392(30.55)	2741(69.89)	303(7.73)	878(22.39)
Higher	38(40.86)	10(10.75)	45(48.39)	117(54.93)	18(8.45)	78(36.62)
Cre (μmol/l)				< 0.0001		0.0
Lower	70(42.94)	18(11.04)	75(46.01)	16(59.26)	2(7.41)	9(33.33)
Normal	6805(59.92)	1148(10.11)	3404(29.97)	2663(69.91)	288(7.56)	858(22.53)
Higher	74(39.36)	20(10.64)	94(50)	179(59.87)	31(10.37)	89(29.77)
SUA (μmol/l)				< 0.0001		< 0.0
Group1	2181(61.89)	337(9.56)	1006(28.55)	333(59.89)	50(8.99)	173(31.12)
Group2	2437(61.31)	393(9.89)	1145(28.81)	511(64.6)	69(8.72)	211(26.68)
Group3	1796(56.34)	333(10.45)	1059(33.22)	876(67.91)	113(8.76)	301(23.33)
Group4	460(51.74)	107(12.04)	322(36.22)	828(75.41)	60(5.46)	210(19.13)

Male(n = 11708)				Female(n = 4135)		
Group5	75(56.82)	16(12.12)	41(31.06)	310(77.5)	29(7.25)	61(15.25)

Notes: (1) Due to the low cell frequency, the male group with lower FBG, TG and MPV was combined with the Normal group; The female group with lower FBG, TC, TG, MPV, globulin and urea was combined with the Normal group.

(2) “a” represents the Kruskal-Wallis rank sum test.

3.3 Correlation between serum uric acid and carotid intima media thickness

The correlation analysis results of SUA and CIMT are shown in Fig. 2. Since sex had a significant effect on the correlation between the two, males and females were analyzed separately. The results showed that in the male population, the risk of CIMT thickening was not significantly different in the group with higher SUA compared to the group with the lowest in the unadjusted Model 1. However, after adjusting for age (Model 2) and for age, BMI, central obesity, and hypertension (Model 3), the risk of CIMT thickening was significantly increased in the group with higher SUA levels. After adjustment for all risk factors, the risk of CIMT thickening increased significantly with the increase in SUA level ($\leq 220\text{ }\mu\text{mol/L}$ as the reference group, $220\text{--}290\text{ }\mu\text{mol/L}$: OR = 1.591, 95% CI: 1.069–2.367; $290\text{--}360\text{ }\mu\text{mol/L}$: OR = 1.65, 95% CI: 1.127–2.415; $360\text{--}430\text{ }\mu\text{mol/L}$: OR = 1.634, 95% CI: 1.116–2.393; $>430\text{ }\mu\text{mol/L}$: OR = 1.857, 95% CI: 1.264–2.73; $P < 0.05$) (Fig. 2 Male). In the female population, the risk of CIMT thickening was significantly increased in the high SUA group compared to that in the low SUA group whether the univariate model or all risk factors were included in the adjustment ($\leq 210\text{ }\mu\text{mol/L}$ as the reference group, $260\text{--}310\text{ }\mu\text{mol/L}$: OR = 1.419, 95% CI: 1.059-1.901; $310\text{--}360\text{ }\mu\text{mol/L}$: OR = 1.432, 95% CI: 1.048–1.957; $>360\text{ }\mu\text{mol/L}$: OR = 1.557, 95% CI: 1.113–2.177; $P < 0.05$) (Fig. 2 Female).

3.4 Stratified analysis according to age

The overall analysis showed that the relationship between SUA and CIMT tended to be stable after age was included in the model (Model 2, Model 3, and Model 4) (Fig. 2). Obviously, age had a significant influence on the correlation between SUA and CIMT, so we further analyzed the correlation between these variables in each age group. The result is shown in Fig. 3. We found no association between SUA and CIMT in male and female aged 18–45 years. In male ≥ 60 years old, an increase in SUA concentration significantly increased the risk of CIMT thickening ($\leq 220\text{ }\mu\text{mol/L}$ as the reference group, $> 430\text{ }\mu\text{mol/L}$: OR = 1.972, 95% CI:[1.2,3.238]; $P < 0.05$) (Fig. 3 Male). There was a significant correlation between SUA and CIMT in female aged 45–60 years and ≥ 60 years ($\leq 210\text{ }\mu\text{mol/L}$ as the reference group, $> 360\text{ }\mu\text{mol/L}$ (45–60 years old): OR = 1.77, 95% CI:[1.107,2.832]; $> 360\text{ }\mu\text{mol/L}$ (≥ 60 years old) OR higher, OR = 1.65, 95% CI: [1.067, 2.551]. $P < 0.05$) (Fig. 3 Female).

Discussion

In this cross-sectional study, we investigated the association between SUA and CIMT in adults. Overall, the analysis results showed that an increased risk of CIMT thickening was significantly associated with higher SUA in both men and women after adjustment for traditional atherosclerosis risk factors. The results of subgroup analysis by age showed that there was a significant correlation between SUA and CIMT only in men aged ≥ 60 years and in women aged 45–60 years and ≥ 60 years. Therefore, this study suggests that high blood uric acid levels may be a risk factor for atherosclerosis and that the age associated with carotid intima thickness is lower in women than in men.

Many previous studies have also explored the relationship between SUA and CIMT and found that elevated blood uric acid levels are associated with a variety of cardiovascular and cerebrovascular diseases [23]. Most studies have shown that increased SUA levels are positively correlated with atherosclerosis [24, 25]. This study is consistent with the results of previous studies, as well as the results of our published meta-analysis and another systematic review [26, 27].

The mechanism by which uric acid leads to atherosclerosis is considered to be a pathophysiological process. Previous studies have suggested that uric acid can be used as a danger signal to promote the proliferation of vascular smooth muscle cells and oxidative stress [28] and induce inflammation. The occurrence of this process involves a variety of reactions, including oxidation of low-density lipoprotein [29] and inhibition of nitric oxide production and endothelial dysfunction, which eventually leads to atherosclerosis [30–32]. However, it is not clear whether uric acid has a pathogenic role in the development of atherosclerosis or is merely a marker of the atherosclerotic process. Therefore, it is necessary to conduct a large cohort study to investigate the role of uric acid levels in the progression of atherosclerosis.

This study assessed the correlation between SUA and CIMT in individuals according to sex. The results showed that although SUA was significantly associated with CIMT in both men and women after adjustment for conventional cardiovascular risk factors, higher SUA levels were not significantly associated with CIMT thickening in men in the univariate model, whereas associations were present in women in both univariate and multivariate models. In previous studies on the relationship between SUA and atherosclerosis, sex differences also existed in the risk of atherosclerosis associated with SUA [33, 34]. Studies have shown that uric acid is a multifactorial trait that is controlled by strong genes in addition to environmental factors [35, 36], and there are significant differences in blood uric acid concentrations between males and females [37]. In addition, studies have shown that the biological effects of uric acid in men and women are different; there are many differences in the influence on the different developmental stages of carotid artery atherosclerosis [38–40]. Therefore, women are more prone to vascular injury than men and have a higher risk of asymptomatic cerebral infarction [41]. We believe that the differences identified between men and women in this study are also related to these reasons.

In men, no significant association was found in the single-factor model, and no correlation was found in the two-factor model adjusted for BMI, hypertension, and central obesity. However, in the model adjusted for age alone, the risk of CIMT thickening was significantly increased in the high SUA group, suggesting that age may be an important factor affecting the correlation between SUA and CIMT. Further analysis stratified by age showed that the risk of CIMT thickening and plaque associated with high SUA was higher in men ≥ 60 years old and women 45–60 years old and ≥ 60 years old. Therefore, the correlation between blood uric acid and carotid atherosclerosis may be different in different age groups. Elderly individuals compose the population most commonly

affected by atherosclerosis. With increasing age, the function of the human body declines, and the effect of uric acid in the human body also changes, which may be the reason for the occurrence of this result. It has been reported that serum uric acid levels are higher in postmenopausal women than in premenopausal women [42, 43]. Our study shows that SUA exhibits an association with CIMT at a younger age in females than in men, menopause may play a role in uric acid's effect in the body perhaps due to female hormone level changes before and after menopause [44].

This study aimed to explore the relationship between SUA and CIMT. The main limitations of this study are as follows: first, due to the limitations of physical examination data, all risk factors for atherosclerosis, such as smoking, drinking and disease history, were not included in the multifactor regression model, which may introduce some bias to the results. Second, although our study concluded that serum uric acid levels were associated with carotid intima thickness, the cross-sectional nature of the study makes it impossible to elucidate a cause-effect relationship. Third, our study was single centered, and the participants were all Chinese, so the applicability of the findings to other ethnic groups may be limited. Fourth, since female hormone levels were not included in the physical examination data, the differences between male and female results in terms of age could not be further explored. We will conduct prospective studies in this regard in the future. Despite these limitations, we believe that the conclusion of this study provides theoretical support for further clinical studies and have important implications for the clinical prevention and treatment of carotid atherosclerosis.

Conclusion

In summary, in this study, we explored the correlation between SUA and CIMT in detail by gender and age and found that after adjusting for traditional cardiovascular risk factors, both men and women with high uric acid had a significantly increased risk of CIMT thickening and plaque. In the subgroup analysis by age, a significant association was found only in men ≥ 60 years and women 45–60 and ≥ 60 years. It is suggested that uric acid is closely related to the occurrence and development of carotid atherosclerosis, which may be a cause of cardiovascular events. This relationship may be strengthened with increasing age, and the degree of association in the female population is greater than that in the male population.

Abbreviations

CIMT: carotid intima media thickness; SUA: serum uric acid; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; TC: total cholesterol; BMI: body mass index; ALT: glutamate pyruvic transa; AST: Aspartate aminotransferase; GGT: Gamma-glutamyltransferase; FBG: Fasting blood glucose; TC: total cholesterol; Cre: Creatinine; MPV: mean platelet volume; TG: triglycerides

Declarations

Ethics approval and consent to participate

Since our study used physical examination data in hospital, this study was exempt from ethical approval from Chongqing Medical University Institutional Review Board. The requirement for informed consent was waived as the database was constructed after anonymization according to strict confidentiality guidelines.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated during and/or analysed during the current study are not publicly available due the fact that its copyright belongs to the First Affiliated Hospital of Chongqing Medical University but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

MM participated in the design of the study and drafted the manuscript. MZM and LXW contributed to the study design, performed statistical analyses and revised the manuscript. XNZ substantively revised the manuscript. LZ and RC performed data collection. LFL participated in the data analysis. All authors read and approved the final manuscript.

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Figures

Figure 1

Normal, thickened and plaque incidence of CIMT in males and females

Figure 2

Forest map of correlation analysis between SUA and CIMT

Figure 3

Forest map of correlation analysis stratified by age Notes: (1) There were too few males 18-45 years old with a level ≤ 220 $\mu\text{mol/L}$, so this population was combined with the 220-290 $\mu\text{mol/L}$ population. (2) There were too few females 18-45 years old with a level ≤ 210 $\mu\text{mol/L}$, so this population was combined with the 210-260 $\mu\text{mol/L}$ population.

Supplementary Files

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- [Appendix1.docx](#)