The association between serum uric acid and controlled attenuation parameter in United States adults without hepatitis B and C: a cross-sectional study

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Abstract

Background: Controlled attenuation parameter (CAP) is a kind of widespread popular parameter to evaluate various types of hepatic steatosis by liver ultrasound transient elastography. We investigated the relationship between serum uric acid (SUA) and CAP without hepatitis B and C virus-infected in the United States adults, data from National Health and Nutrition Examination Survey (NHANES).

Methods: The present study was cross-sectional research. 4319 American men and women participants ≥ 18 years old, without B and C hepatitis, were included in our analysis. There are some measures to evaluate the association between SUA and CAP by multivariate logistic regression analyses, fit smoothing curves, generalized additive models, two-piecewise linear regression model and subgroup analyses.

Results: There was a positive association between the value of SUA and CAP by multivariate logistic regression analyses after adjusting for various confounders. Besides, the inflection point of non-linear curve relationship was identified as 4.3 mg/dL, for SUA < 4.3 mg/dL, the effect size is 10.6 ($P < 0.01$); Correspondingly, SUA ≥ 4.3 mg/dL, the effect size is 4.3 ($P < 0.01$). Finally, SUA was positively associated with glycohemoglobin less than 6.5% individuals ($\beta = 7.3$, $P < 0.01$) and Fasting glucose less than 7.0 mmol/L individuals ($\beta = 6.8$, $P < 0.01$) in the subgroup analysis.

Conclusions: Our research found the relationship between SUA and CAP is non-linear. Subgroup analysis indicated that the positive association between SUA and CAP were showed in non-diabetic patients but not in diabetic.

Background

Hepatic steatosis, due to the unbalance of lipid metabolism in liver cells, various lipid substances appear in the cytoplasm of liver cells such as triglycerides, cholesterol etc. [1, 2]. The causes of hepatic steatosis include alcoholic, non-alcoholic, infected hepatitis B and C virus, etc. Among them, two main mortal reasons are the non-alcoholic and alcoholic fatty liver [3, 4]. In daily clinical practice, the paramount measure for diagnosing various kinds of fatty liver was pathologic findings, but its price and risk limited clinical application.

In non-invasive diagnostic methods, the value of controlled attenuation parameter (CAP) is a kind of widespread popular parameter to evaluate various types of hepatic steatosis for its convenience and accuracy, which measures ultrasound attenuation related to the presence of fatty liver tissue by liver ultrasound transient elastography [5, 6]. Serum uric acid (SUA) is an end product from adenine and guanine nucleotides metabolism by related oxidase enzyme [7]. Correspondingly, a large amount of clinical evidence shows that elevated SUA is a marker of heart failure [8], insulin resistance [9], gout and nephrolithiasis [10].

The traditional ultrasound diagnosis result of fatty liver has confirmed to be related to SUA [11]. As for assessing hepatic steatosis by ultrasound attenuation, Min-Sun Kwak et al [12] indicated the increase of CAP is likely to be a sign of early laboratory examination in liver steatosis with various abnormal metabolism of substances. However, the research that the association between SUA and CAP in the United States population infected without hepatitis B and C virus has limited. In our study, we analysed the data to evaluate the relationship between SUA and CAP without B, C hepatitis population, data from NHANES of the American National Center for Health Statistics.

Methods

Study population

We executed a cross-sectional study, data from NHANES that has collected data about health status, diet type and disease-related examination, by a cross-sectional investigation in the sample of United States population since 1970s [13]. Our study analysis based on data from the 2017–2018 year represents a cycle of the NHANES. Of the 9254 participants, we excluded 3398 participants with age ≥ 18 years, 737 participants missing CAP (controlled attenuation parameter) information, 299 participants missing SUA (serum uric acid) information, 378 participants indicating hepatitis B core antibody positive, 123 participants indicating hepatitis C antibody/cRNA positive or missing relative information about hepatitis C. Finally, in all of 4319 respondents ≥ 18 years old, without B and C hepatitis, were selected in our investigation.

Variables

SUA was regarded as an exposure variable of the study. Roche Cobas 6000 Chemistry Analyzer (Roche Diagnostics Corporation, Indianapolis, IN 46250) used to measure SUA. Reagents were supplied by Roche Cat. No. 03183807190, UA2 reagent kit (400 tests). The outcome variable was the CAP (controlled attenuation parameter) used to assess hepatic steatosis. The value of CAP was acquired by FibroScan® using ultrasound and the vibration controlled transient elastography (VCTETM). However, to ensure accuracy and security of the examination, individuals were excluded if they (1) were unable to cooperate with inspection, (2) were pregnant or unsure if no pregnant, (3) had an electronic medical device in the body, or (4) had lesions that cannot be checked.

Covariates

(1) Socio-demographic variables include age, gender, marital status, race and educational level. Except for age as continuous covariates, the others are all categorical variables. If participants were widowed, divorced, never married or separated were defined as single, while one participant refused to provide or missing information about marital status defined as other. (2) Smoking behaviour, alcohol intake and body mass index (BMI) are lifestyle variables defined as categorical variables. If an individual smoked more than 100 cigarettes in life, smoking behaviour defined as yes. Otherwise, it defined as no. The year before the survey, the amount of drink intake less than 17.01g, 17.01g–34.02g and more than 34.02g were

defined as low, medium and high, respectively. (3) Clinical and laboratory examination include glycohemoglobin, fasting glucose, albumin(Alb), globulin, serum creatinine (SCr), alanine aminotransferase (ALT), gamma-glutamyl transaminase (GGT), lactate dehydrogenase (LDH), total bilirubin (Tbi), high-density lipoprotein (HDL), cholesterol, liver stiffness measurement (LSM) and controlled attenuation parameter(CAP). Except for glycohemoglobin and fasting glucose as categorical variables, the others are continuous covariates. About the above variables and covariates, more details presented at <https://www.cdc.gov/nchs/nhanes/>.

Statistical analysis

Participants were categorized into quartiles according to SUA concentration. Descriptive characteristics of participants presented as percentages (categorical variables) and means $\pm$ standard deviations (continuous variables). The weighted Chi-square test and the one-way ANOVA or Kruskal Wallis H test were performed to compare descriptive characteristics among quartiles of SUA. A univariate and multivariate weighted linear regression model was used to assess the relationship between SUA and CAP in different models. Crude model adjusted for none. Model I adjusted for gender, age, race. Model II adjusted for gender, age, race, education level, marital status, ALT, ALB, SCr, globulin, GGT, LDH, Tbi, serum cholesterol, smoking behaviour, fasting glucose, HDL, LSM, alcohol intake, BMI, glycohemoglobin. Moreover, the non-linear relationship between SUA and CAP was found by smooth curve fittings and generalized additive models (GAM). The inflection point in the non-linear relationship was calculated using a two-piecewise linear regression model. Finally, subgroup analysis was performed to assess the association between SUA and CAP, and an interaction test was executed. All analysis use package R (<http://www.Rproject.org>) and EmpowerStats (<http://www.empowerstats.com>), with a *P*-value <0.05 defined as statistically significant.

Results

Baseline characteristics of individuals

The baseline characteristics of individuals according to quartiles of SUA are presented in Table 1. A total of 4319 participants, more than 18 years old, were included in our study, with those participants divided into four groups. There were notable differences in descriptive characteristics among the SUA quartiles, except race, education level, marital status, and globulin. Compared to the other groups (Q1-Q3), respondents located in the top group (Q4) of SUA were regarded to be male, black, and to have obesity ($BMI \geq 30$), the behavior of smoking, alcohol intake. Furthermore, compared with the other three SUA groups (Q1-Q3), patients had a significantly higher glycohemoglobin, Alb, SCr, ALT, GGT, LDH, cholesterol, LSM, and CAP in the top groups (Q4).

Univariate analysis for CAP

The results of univariate analysis for controlled attenuation parameter (CAP) were shown in Table 2. We found that there were statistically significant in univariate analyses for CAP, with the exception of alcohol

intake. Further, the results showed that BMI (≥ 30 kg/m²), glycohemoglobin ($\geq 6.5\%$), fasting glucose (≥ 7.0 mmol/L), Globulin, SCr, ALT, GGT, LDH, cholesterol, LSM, SUA were associated with higher CAP.

Positive relationship between SUA and CAP

The results of multivariate regression analysis after adjusting for various confounding factors were used to assess the relationship between SUA and CAP in different models, which are presented in Table 3. In the Crude Model that was unadjusted for confounders, SUA was a positive association with CAP ($\beta = 13.5$, 95%CI: 12.2-14.7, $P < 0.001$). With simple and full adjustment for confounders, the association was also positive in model 1 ($\beta = 11.8$, 95%CI: 10.4-13.2, $P < 0.001$) and model 2 ($\beta = 5.4$, 95%CI: 4.1-6.6, $P < 0.001$), respectively. After turning continuous variables SUA into categorical variables (quartiles), participants in the top of the serum uric acid group (Q4) had a 17.6 dB/m (95%CI: 12.7, 22.5, $P < 0.001$) greater CAP than those in the bottom group. Besides, we performed a trend test, which is also statistically significant ($P < 0.001$).

The analyses of non-linear relationship

In the investigation, the non-linear relationship was examined between SUA and CAP by smooth curve fittings and generalized additive models, which are shown in Figure 1. We found the non-linear relationship between SUA and CAP after adjusting related confounders. What's more, the inflection point of curve was identified as 4.3 mg/dL (Table 4) with a two-piecewise linear regression model. For SUA < 4.3 mg/dL, each additional 1 mg/dL SUA was associated with a 10.6 dB/m increase in CAP (95%CI: 6.3-14.8); However, SUA ≥ 4.3 mg/dL, each additional 1 mg/dL SUA was only associated with a 4.3 dB/m increase in CAP (95%CI: 2.9-5.8).

Subgroup analysis

Our subgroup analysis, stratified by age, gender, alcohol intake, smoking behavior, glycohemoglobin, and fasting glucose, as well as interaction test, showed in Table 5. Statistical significant interactions were detected between SUA and age, gender, glycohemoglobin, fasting glucose, respectively. Furthermore, it is surprising that SUA was positively associated with less than 6.5% group of glycohemoglobin ($\beta = 7.3$, 95%CI: 6.0- 8.6, $P < 0.001$) and less than 7.0 mmol/L group of Fasting Glucose ($\beta = 6.8$, 95%CI: 5.5- 8.0, $P < 0.001$) in the subgroup analysis.

Discussion

Our study revealed the positive association between SUA and CAP in non-hepatitis B and non-hepatitis C population by multivariate regression analysis, even without excluding the alcohol intake population. After adjusted gender, age, race, education level, marital status, ALT, albumin, SCr, globulin, GGT, LDH, TBI, cholesterol, smoking behaviour, fasting glucose, HDL, LSM, alcohol intake, BMI and glycohemoglobin, CAP increased by 5.4 dB/m stems from 1 mg/dL increase in SUA (95%CI: 4.1-6.6). Moreover, by a series of related non-linear relationship statistical model, we found the non-linear relationship between SUA and

CAP, as well as calculated inflection point. According to the diagnostic criteria for diabetes, fasting glucose ≥ 7.0 mmol/L or glycohemoglobin $\geq 6.5\%$ were diagnosed diabetes [14]. Consequently, with diabetes relative subgroup analysis, the relationship of SUA and CAP showed a positive association only in respondents with non-diabetes, but the difference between the two ways was not significant in patients with diabetes. However, in the subgroup analysis of alcohol intake, SUA and CAP showed a positive correlation in all subgroup ($p < 0.001$).

Searching for PubMed, we found a few articles that reported SUA and fatty liver showed a positive correlation. Roberto Catanzaro et al. [15] found a positive association between non-alcoholic fatty liver disease (NAFLD) and high concentration of SUA in the Mediterranean individual, and Xiaoya Zheng et al. [16] also reported the same relationship in non-obesity Chinese adults. However, they also used traditional abdominal ultrasound to evaluate NAFLD, which was lower accuracy than CAP [17, 18]. Similarly, CAP and alcoholic hepatic steatosis were positively associated. Jan Petrasek et al. [19] proved that uric acid and ATP were regarded as taking part in an inflammatory reaction between hepatocytes and inflammatory cells and play a pivotal role in liver inflammation in vitro experiments with alcohol participation. Maja Thiele et al. [20] pointed that for alcoholic fatty liver, or other causes for a fatty liver had an excellent diagnostic precision with CAP, even severe steatosis can also be applied. Whereas, the notable disadvantage was that the research sample size was too small, and NAFLD was also excluded from his study.

In our research, we did not exclude either NAFLD or alcoholic fatty liver disease (AFLD) in the study individuals but executed a subgroup analysis to evaluate the effect of alcohol on the relationship between SUA concentration and the value of CAP. We found that SUA and CAP showed a positive association in each alcohol intake subgroup, and the effect size was statistically significant. Our research is similar to the Victor de Lédighen et al. [21] result that the value of CAP was a significantly positive relationship with alcohol intake, which was attributed to the fatty liver diagnoses caused by drinking.

Ming-Hsiung Shih et al. [22] analysed 5370 participants from the NHANES III to conclude that respondents with a higher concentration of SUA had a higher incidence of NAFLD [assessed by traditional ultrasound evaluation], and it was not affected by gender factors. However, in the 4002 population based Chinese cohort, Xianghai Zhou et al. [23] found a higher concentration SUA for only women independently correlated with higher odds of NAFLD (assessed by unenhanced abdominal CT), which is consistent with our research. Performing gender subgroup analysis and interaction test, we found that its interaction was statistically significant ($p < 0.001$), and SUA was positively associated with CAP in female, with an effect size of 9.3 (95%CI: 7.4- 11.2).

Our research has many advantages. Firstly, we use generalized additive models to evaluate SUA and CAP based on smooth curve fittings, considering that GAM can better predict their nonlinear relationship. Secondly, to make our research results stable and reliable, we used some sensitivity analysis, such as trend test and interaction test. Thirdly, compared with traditional ultrasound, we chose CAP as the

outcome variable in the database, and it can not only qualitatively but also quantitatively diagnose hepatic steatosis, which makes the result more accurate[24, 25].

Our research also has some shortcomings. On the one hand, as a kind of observational study, the cross-sectional research only reveals a positive association rather than discovers the causal link between SUA and CAP. On the other hand, this study only based on the study of the American population, and the application in other countries will be limited due to the factor that NHANES is a survey aimed at collect data on the disease and nutrition of the American [26].

Conclusions

Our research found the relationship between SUA and CAP is non-linear. Significantly, the positive association between SUA and CAP were showed in non-diabetic patients but not in diabetic.

Abbreviations

CAP: Controlled attenuation parameter; SUA: Serum uric acid; BMI: Body mass index; Alb: Albumin; SCr: Serum creatinine; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transaminase; LDH: Lactate dehydrogenase; TBi: Total bilirubin; HDL: High-density lipoprotein; LSM: Liver stiffness measurement; NAFLD: Non-alcoholic fatty liver disease; AFLD: Alcoholic fatty liver disease

Declarations

Ethics approval and consent to participate

All NHANES data acquisition is approved by the ethics review board of the National Center for Health Statistics.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are available in the NHANES repository, <https://wwwn.cdc.gov/nchs/nhanes/Default.aspx>.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

M H, L C contributed to the design, data collection, analysis, writing of this study. Y W, H M made revisions for related content. All authors read and approved the final manuscript.

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Tables

Table 1 Baseline characteristics of participants (N =4319).

Characteristic	Serum uric acid Quartiles (mg/dL)				<i>P</i> value
	Q1	Q2	Q3	Q4	
No. of participants	1035	1055	1067	1162	
Age (years, mean $\pm$ sd)	45.24 $\pm$ 16.63	44.28 $\pm$ 17.27	48.95 $\pm$ 17.42	48.16 $\pm$ 18.18	<0.0001
Gender (%)					<0.0001
Male	14.80	39.08	60.74	77.73	
Female	85.20	60.92	39.26	22.27	
Race (%)					0.0759
Mexican American	10.45	9.20	9.25	9.55	
Other Hispanic	8.01	7.29	6.64	5.98	
Non-Hispanic White	63.19	63.89	66.53	61.37	
Non-Hispanic Black	10.41	9.81	8.90	11.35	
Other Race	7.95	9.81	8.69	11.76	
Marital status (%)					0.1955
Married or living with partner	62.89	57.44	60.44	60.99	
Single	33.75	38.47	36.69	35.66	
Other	3.36	4.08	2.87	3.36	
Education level (%)					0.0893
Below high school education	9.96	9.37	9.15	10.64	
High school graduate	22.89	26.55	29.25	24.99	
College graduate	63.78	59.99	58.64	60.98	
Not recorded	3.36	4.09	2.96	3.39	
BMI (%)					<0.0001
<30(kg/m ²)	72.74	61.89	52.05	43.61	
$\geq$ 30	27.26	38.11	47.95	56.39	
Smoking behavior (%)					<0.0001
Yes	33.84	40.59	44.12	43.24	
No	66.16	59.41	55.88	56.76	
Alcohol intake (%)					<0.0001
Low	28.35	29.17	24.52	24.73	
Medium	26.76	22.80	19.80	20.44	
High	44.89	48.03	55.68	54.83	
Glycohemoglobin (%)					0.0080
<6.5(%)	92.49	90.66	90.90	88.19	

≥6.5	7.51	9.34	9.10	11.81	
Fasting glucose (%)					0.0010
<7.0(mmol/L)	95.61	96.33	92.84	93.95	
≥7.0	4.39	3.67	7.16	6.05	
Alb (g/L, mean ± sd)	40.57 ± 3.03	40.86 ± 3.29	41.27 ± 3.08	41.36 ± 3.27	<0.0001
Globulin (g/L, mean ± sd)	29.93 ± 3.95	29.93 ± 3.95	29.83 ± 4.05	29.95 ± 4.03	0.8887
SCr (umol/L, mean ± sd)	66.48 ± 27.83	72.88 ± 19.69	80.15 ± 19.75	91.12 ± 43.23	<0.0001
ALT (IU/L, mean ± sd)	18.09 ± 12.55	20.61 ± 17.00	23.50 ± 13.67	28.70 ± 21.01	<0.0001
GGT (IU/L, mean ± sd)	23.77 ± 35.02	24.86 ± 31.06	28.73 ± 27.16	37.70 ± 53.24	<0.0001
LDH (IU/L, mean ± sd)	152.94 ± 29.16	155.82 ± 32.20	157.76 ± 30.12	159.54 ± 32.99	<0.0001
TBi (umol/L, mean ± sd)	6.90 ± 3.97	7.53 ± 4.36	8.94 ± 5.60	8.72 ± 4.69	<0.0001
HDL (mmol/L, mean ± sd)	1.52 ± 0.38	1.44 ± 0.40	1.32 ± 0.36	1.26 ± 0.37	<0.0001
Cholesterol (mmol/L, mean ± sd)	4.80 ± 0.97	4.88 ± 1.06	4.89 ± 1.02	4.97 ± 1.08	0.0022
LSM (kpa, mean ± sd)	4.98 ± 3.21	5.55 ± 4.99	5.91 ± 5.40	6.68 ± 5.94	<0.0001
CAP (dB/m, mean ± sd)	239.24 ± 57.55	253.91 ± 60.73	274.44 ± 62.01	286.39 ± 63.56	<0.0001

Abbreviations: BMI, body mass index; Alb, albumin; SCr, serum creatinine; ALT, alanine aminotransferase; GGT, gamma-glutamyl transaminase; LDH, lactate dehydrogenase; TBi, total bilirubin; HDL, high-density lipoprotein; LSM, liver stiffness measurement; CAP, controlled attenuation parameter.

Table 2: Univariate analysis for controlled attenuation parameter.

	Statistics, n (%)	β (95%CI)	P-value
Age[year]	48.8 $\pm$ 18.6	0.8 (0.7, 0.9)	<0.001
Gender			
Male	2088 (48.3%)	Reference	
Female	2231 (51.7%)	-21.0 (-24.7, -17.2)	<0.001
Race			
Mexican American	656 (15.2%)	Reference	
Other Hispanic	421 (9.7%)	-22.1 (-31.5, -12.7)	<0.001
Non-Hispanic White	1571 (36.4%)	-14.9 (-21.4, -8.3)	<0.001
Non-Hispanic Black	920 (21.3%)	-29.1 (-37.6, -20.6)	<0.001
Other Race	751 (17.4%)	-16.0 (-24.6, -7.4)	<0.001
Marital status			
Married or Living with partner	2417 (56.0%)	Reference	
Single	1677 (38.8%)	-17.6 (-21.6, -13.7)	<0.001
Other	225 (5.2%)	-48.1 (-58.5, -37.7)	<0.001
BMI (kg/m ²)			
<30	2510 (58.1%)	Reference	
$\geq$ 30	1809 (41.9%)	62.4 (59.0, 65.8)	<0.001
Smoking behavior			
Yes	1723 (39.9%)	Reference	
No	2596 (60.1%)	-13.9 (-17.8, -10.1)	<0.001
Alcohol intake			
Low	1053 (24.4%)	Reference	
Medium	843 (19.5%)	-3.6 (-9.1, 1.8)	0.191
High	2423 (56.1%)	3.5 (-1.0, 8.1)	0.126
Education level			
Below high school education	769 (17.8%)	Reference	
High school graduate	979 (22.7%)	3.1 (-4.0, 10.2)	0.392
College graduate	2343 (54.2%)	-4.8 (-11.3, 1.7)	0.149
Not recorded	228 (5.3%)	-44.2 (-56.0, -32.4)	<0.001

Glycohemoglobin (%)

<6.5	3732 (86.4%)	Reference	
≥6.5	587 (13.6%)	59.7 (53.5, 66.0)	<0.001

Fasting glucose(mmol/L)

<7.0	4000 (92.6%)	Reference	
≥7.0	319 (7.4%)	56.0 (47.7, 64.3)	<0.001

Albumin (g/L)	40.7 ± 3.3	-2.5 (-3.1, -1.9)	<0.001
Globulin (g/L)	30.8 ± 4.3	1.4 (1.0, 1.9)	<0.001
Scr (umol/L)	79.3 ± 41.4	0.1 (0.0, 0.2)	0.003
ALT (IU/L)	22.2 ± 17.2	1.1 (1.0, 1.2)	<0.001
GGT (IU/L)	30.5 ± 42.8	0.3 (0.3, 0.4)	<0.001
LDH (IU/L)	157.9 ± 33.6	0.2 (0.1, 0.2)	<0.001
TBi (umol/L)	7.9 ± 4.7	-0.5 (-0.9, -0.1)	0.008
Cholesterol (mmol/L)	4.8 ± 1.1	5.3 (3.5, 7.1)	<0.001
HDL (mmol/L)	1.4 ± 0.4	-52.9 (-57.5, -48.3)	<0.001
LSM(Kpa)	6.0 ± 5.3	3.4 (3.0, 3.7)	<0.001
SUA (mg/dL)	5.4 ± 1.5	13.5 (12.2, 14.7)	<0.001

Abbreviations: BMI, body mass index; Alb, albumin; SCr, serum creatinine; ALT, alanine aminotransferase; GGT, gamma-glutamyl transaminase; LDH, lactate dehydrogenase; TBi, total bilirubin; HDL, high-density lipoprotein; LSM, liver stiffness measurement; SUA, serum uric acid.

Table 3 Relationship between SUA and controlled attenuation parameter in different models.

Variable	Crude Model		Model Ⅰ		Model Ⅱ	
	β (95%CI)	P-value	β (95%CI)	P-value	β (95%CI)	P-value
SUA	13.5 (12.2, 14.7)	<0.001	11.8 (10.4, 13.2)	<0.001	5.4 (4.1, 6.6)	<0.001
SUA(quantile)						
Q1	Reference		Reference		Reference	
Q2	14.7 (9.5, 19.8)	<0.001	13.8 (8.7, 18.9)	<0.001	6.5 (2.3, 10.7)	0.002
Q3	35.2 (30.1, 40.4)	<0.001	29.0 (23.6, 34.3)	<0.001	14.7 (10.2, 19.3)	<0.001
Q4	47.2 (42.0, 52.3)	<0.001	40.4 (34.8, 46.1)	<0.001	17.6 (12.7, 22.5)	<0.001
Pfor trend	<0.001		<0.001		<0.001	

Abbreviations: CI, confidence interval; SUA, serum uric acid.

Crude model adjust for none. Model I adjust for gender, age, race. Model II adjust for gender, age, race, education level, marital status, alanine aminotransferase, albumin, serum creatinine, globulin, gamma-glutamyl transaminase, lactate dehydrogenase, total bilirubin, serum cholesterol, smoking behavior, fasting glucose, HDL-cholesterol, liver stiffness measurement, alcohol intake, body mass index, glycohemoglobin.

Table 4 Threshold effect analysis of serum uric acid and controlled attenuation parameter using a Piece-wise Linear Regression.

Inflection point (mg/dL)	Effect size (β)	95%CI	<i>P</i> value	log likelihood ratio
< 4.3	10.6	6.3 to 14.8	<0.001	0.012
≥ 4.3	4.3	2.9 to 5.8	<0.001	

Abbreviations: CI, confidence interval

Gender, age, race, marital status, alanine aminotransferase, albumin, serum creatinine, globulin, gamma-glutamyl transaminase, lactate dehydrogenase, total bilirubin, serum cholesterol, smoking behavior, liver stiffness measurement, HDL-cholesterol, alcohol intake, education level, body mass index, glycohemoglobin, fasting glucose were adjusted.

Table 5 Effect size of serum uric acid and controlled attenuation parameter in prespecified and exploratory subgroups in each subgroup

	N	β (95%CI)	P-value	P for interaction
Age (year)				0.0467
<60	2834	6.6 (5.1, 8.1)	<0.001	
≥ 60	1485	3.9 (1.9, 5.9)	<0.001	
Gender				0.0002
Male	2088	3.5 (1.7, 5.3)	<0.001	
Female	2231	9.3 (7.4, 11.2)	<0.001	
Smoking behavior				0.0445
Yes	1723	4.7 (2.7, 6.7)	<0.001	
No	2596	7.5 (5.9, 9.0)	<0.001	
Alcohol intake				0.1709
Low	1053	6.0 (3.5, 8.5)	<0.001	
Medium	843	7.8 (5.0, 10.7)	<0.001	
High	2423	5.8 (4.2, 7.4)	<0.001	
Glycohemoglobin (%)				0.0024
<6.5	3732	7.3 (6.0, 8.6)	<0.001	
≥ 6.5	587	2.0 (-0.8, 4.8)	0.162	
Fasting glucose (mmol/L)				0.0141
<7.0	4000	6.8 (5.5, 8.0)	<0.001	
≥ 7.0	319	0.6 (-3.4, 4.5)	0.784	

Abbreviations: CI, confidence interval.

Above model adjusted for race, education level, marital status, alanine aminotransferase, albumin, serum creatinine, globulin, gamma-glutamyl transaminase, lactate dehydrogenase, total bilirubin, serum cholesterol, HDL-cholesterol, liver stiffness measurement and body mass index except the subgroup variable.

Figures

Figure 1

The positive association between serum uric acid (SUA) and controlled attenuation parameter (CAP). A threshold, nonlinear association between SUA and CAP was found ($P < 0.001$) in a generalized additive model (GAM). The solid red line shows the smooth curve fit between variables. The blue dotted line indicates the 95% of confidence interval. Gender, age, race, marital status, alanine aminotransferase, albumin, serum creatinine, globulin, gamma-glutamyl transaminase, lactate dehydrogenase, total bilirubin, serum cholesterol, smoking behavior, liver stiffness measurement, HDL-cholesterol, alcohol intake, education level, body mass index, glycohemoglobin, fasting glucose were adjusted.