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ORIGINAL ARTICLE

Cross-sectional and longitudinal associations between serum uric acid and metabolic syndrome

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Abstract Research on the importance of serum uric acid (SUA) as a contributing metabolic factor to cardiovascular diseases has conducted to conflicting results, with most studies assuming a cross-sectional design. The aim of this study was to evaluate the association of SUA and metabolic syndrome (MetS) and its features. A representative sample of 2,485 individuals aged ≥18 years was randomly selected from the non-institutionalized resident population of Porto, Portugal. A total of 1,054 eligible subjects were included for the longitudinal analyses. Hyperuricemia was defined as SUA ≥70 mg/L in men and ≥60 mg/L in women. MetS was defined according the Joint Interim (2009) criteria. Associations were estimated using Poison regression and binomial models. In the cross-sectional analysis, subjects with hyperuricemia had a 2.10-fold increased risk of MetS as compared with normouricemic subjects (PR = 2.10, 95% CI: 1.68–2.63). Among MetS features, high triglycerides presented the strongest association with hyperuricemia (PR = 2.32, 95% CI: 1.84–2.91). The MetS crude incidence rate was 4.5/100 person-year (95% CI: 3.9–5.2) in normal uricemic and 13.0/100 person-year (95% CI: 8.5–20.0) in hyperuricemic participants. Using a multivariate longitudinal approach, hyperuricemia was positively associated with MetS incidence rate ratios (IRR = 1.73, 95% CI: 1.08–2.76). One standard deviation increase of SUA concentration was associated with a 1.22-fold increase in MetS risk (IRR = 1.22, 95% CI: 1.05–1.42). Elevated SUA presented the strongest association with high-triglycerides concentration (IRR = 1.44, 95%: 1.22–1.71) and waist circumference (IRR = 1.25, 95%: 1.05–1.49). The independent positive association between SUA and MetS suggested by this longitudinal study supports that SUA might be a risk factor for MetS.

Keywords Uric acid · Metabolic syndrome · Incidence rate ratio · Prevalence rate

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Introduction

The prevalence of hyperuricemia has been increasing in recent years, in both developed and developing countries [1]. Previous epidemiological studies showed that increased serum uric acid (SUA) levels are independent markers of increased cardiovascular disease risk [2, 3] and also reported a relation between SUA levels and several cardiovascular outcomes, including metabolic syndrome (MetS) and its features [1, 4, 5]. Currently, there is no clear explanation for this relationship [6]. Several authors assume that hyperuricemia is a secondary phenomenon to MetS (acting as a risk marker), and others, based on prior evidence from experimental studies in human and animal models, suggest that SUA may be likely a risk factor to the syndrome [7, 8]. Possible explanations for the role of SUA as risk marker include early renal impairment in hypertension, confounding by diuretics, alcohol intake, and hyperinsulinemia, which enhance tubular reabsorption of sodium and uric acid [9]. The decline in renal function contributes to elevated SUA. Hyperuricemia, however,

may be present together with MetS in people who are not overweight or obese, and often precedes the development of hyperisulinemia and renal function impairment [10], obesity [11], and diabetes [12, 13].

Uric acid may play a role in the pathogenesis of MetS, because hyperuricemia is associated with deleterious effects on endothelial function, platelet adhesion and aggregation, and oxidative metabolism [14]. It has been suggested that SUA may play a role in the pathogenesis of early-onset of hypertension [15]. Other mechanisms could be related with inflammatory and oxidative changes that uric acid induces in adipocytes [16]. The enzyme that generates uric acid from xanthine (xanthine oxidoreductase) is expressed in adipocytes and is critical to the adipogenesis process [17].

The strongest evidence of SUA as a risk factor for the development of MetS is from studies in animal models showing that a decrease in uric acid levels can prevent or reverse features of the MetS [18]. However, in human populations, the association between SUA and MetS has been mostly provided by cross-sectional studies. In these studies, MetS prevalence increased substantially with increasing levels of SUA [19, 20]. Some cohort studies have further evaluated the incidence of MetS and its risk factors [21–24], but data describing the effect of SUA on the MetS incidence are still scarce [22].

The aim of this study was to evaluate the cross-sectional and longitudinal associations between SUA and MetS in Portuguese adults.

Methods

Subjects

Participants are part of a cohort study, the EPIPorto study, which comprises a representative sample of 2,485 Portuguese adults (61.8% women) aged 18–92 years and living in Porto, an urban center in northwest Portugal. The baseline evaluation was conducted during 1999–2003 (participation proportion of 70%), and 66.1% of the cohort was re-evaluated during 2005–2008. As previously described [25], participants were recruited by random digit dialing using households as the sampling unit.

The local ethics committee approved the study protocol. All participants gave informed written consent to participate in the study, which was carried out in accordance with the Helsinki Declaration.

Data collection

Data on socio-demographic, personal and family medical conditions, and behavioral characteristics (including smoking habits, alcohol consumption, physical activity, and diet) were collected by trained interviewers, using structured standard questionnaires.

Age and education were recorded as completed years of age and schooling, respectively.

All participants were asked to bring their current medication, a posteriori codified by a trained pharmacist, who classified all the medications according to the WHO Anatomical Therapeutic Chemical (ATC) classification system [26].

Anthropometric data were obtained after a 12-h fasting, with the subject in light clothing and barefoot. Body weight was measured to the nearest 0.1 kg using a digital scale (Tanita®) and height to the nearest centimeter in the standing position using a wall stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by square height in meters. Waist and hip circumferences were measured to the nearest centimeter, with the subject standing, using a flexible and non-distensible tape and avoiding exertion of pressure on tissues. Waist circumference (WC) was measured midway between the lower limit of the rib cage and the iliac crest. Hip circumference was considered as the maximal circumference over the femoral trochanters. Waist-to-hip circumference ratio was calculated (WHR).

Blood pressure was measured on a single occasion using a standard mercury sphygmomanometer with the cuff on the right upper arm. Two blood pressure readings were taken after the participant had rested for 10 min, and the mean of the two readings was calculated.

Blood was sampled after a 12-h overnight fast. SUA, glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides were measured using automatic standard enzymatic methods.

Hyperuricemia was defined as SUA $\geq$70 mg/L in men and SUA $\geq$60 mg/L in women [27].

Tobacco consumption was registered as daily (at least one cigarette/day), occasional (less than one cigarette/day), former (quit for at least 6 months), or never smoking. For analyses, only two categories were considered: current smoking (daily and occasional smoking) and non-smoking (never and former smoking). Dietary intake, including alcohol consumption, was assessed by face-to-face interviewers using a validated semi-quantitative food frequency questionnaire, concerning the previous 12 months [28, 29]. Food consumption was converted into total energy and nutrients intake using the Food Processor Plus software (version 7.02, ESHA Research, Salem, Oregon, 1997), adapted to Portuguese foods and dishes. Total physical activity was quantified in metabolic equivalent per hour, using a validated questionnaire [30] that included a detailed recall of all professional, domestic, and leisure-time physical activities.

MetS definition

In the present study, the definition of MetS was based on the Joint Interim criteria [31, 32]. According to these criteria, MetS is identified when at least three of the following conditions are present in the same subject: WC $\geq$ 102 cm in men or $\geq$88 cm in women, serum triglycerides $\geq$1.695 mmol/L^{-1} (150 mg/dL) and/or drug treatment for elevated triglycerides, HDL cholesterol <1.036 mmol/L^{-1} (40 mg/dL) in men and <1.295 mmol/L^{-1} (50 mg/dL) in women and/or drug treatment for reduces HDL cholesterol, blood pressure $\geq$130 and/or $\geq$85 mmHg or pharmacological treatment for hypertension, and plasma glucose $\geq$5.6 mmol/L^{-1} (100 mg/dL) and/or antidiabetic pharmacological treatment.

Statistical analysis

Comparisons between continuous variables were performed using the Student *t* test or non-parametric equivalent tests. Categorical variables were compared using the χ^2 test.

In this study, the cross-sectional and the longitudinal effects of SUA on MetS and its metabolic features were assessed.

For the longitudinal analysis, time at risk was considered as the number of years between the first and second visit to the Department (follow-up time) in those who did not develop the MetS. In individuals who developed MetS, time at risk was estimated as the mid-point the period between the two visits. Since the follow-up time is different between participants, we have calculated incidence rate ratios (IRR) as a measure of association instead of relative risks. Poisson regression with offset in *ln* (neperian logarithm) time at risk was used to estimate the IRR and respective 95% confidence intervals (95% CI). Two approaches were used to analyze the effect of SUA: one using the usual cut-off points for hyperuricemia and the other using SUA as a continuous variable. When SUA was used as a continuous variable, a *z*-score transformation was performed by subtracting the mean to the observed value and dividing by the standard deviation, thus representing the change in the incidence by one standard deviation of SUA.

In order to compare the longitudinal effect with the cross-sectional effect of SUA on MetS and its features, prevalence ratios (PR) were used as measures of association, instead of odds ratios. Poisson regression was used to estimate PR and respective 95% CI.

Statistical analyses were performed using SPSS (version 18.0, SPSS Inc., Chicago, IL, USA, 2010) and R Statistical Software (version 2.7.1, R Foundation for Statistical Computing, Austria, 2008).

Results

The cross-sectional analyses were performed with 2,275 participants, who presented baseline information on both MetS (195 missing) and SUA (15 missing). After excluding participants who presented MetS at the baseline ($n = 641$), 1,634 participants remained for the longitudinal analyses. During the observation period, there were 535 losses to follow-up and 45 participants had missing information on MetS features (two or more) and for that reason were excluded, remaining 1,054 participants eligible for the longitudinal analyses.

The median follow-up time was 5 years (inter-quartile range = 4.5). The main characteristics of participants at baseline and at follow-up are presented in Table 1. In comparison with individuals who refused or did not complete the follow-up evaluation, eligible participants for the longitudinal analyses had a similar sex distribution (female 59.7 vs. 60.6%, $p = 0.725$), mean age (50.1 vs. 49.6 years, $p = 0.626$), and education level (9.4 vs. 8.9 years, $p = 0.101$). Also, no significant differences between groups for smoking, alcohol consumption, BMI, total physical activity, energy intake, and all MetS features were observed.

Cross-sectional analysis

Subjects with hyperuricemia had higher prevalence of each individual MetS feature and a 2.43-fold increased risk of MetS as compared with normouricemic subjects (PR = 2.43, 95% CI: 1.97–2.99) (Table 2).

In multivariate models, adjusting for age, sex, and education (model 1) or model 1 plus energy expenditure, smoking, alcohol, protein, and total energy intake (model 2), hyperuricemia remained significantly and positively associated with MetS (PR = 2.10, 95% CI: 1.68–2.63) and each MetS feature. Among the MetS features, high triglycerides presented the strongest association with hyperuricemia (PR = 2.32, 95% CI: 1.84–2.91) (Table 2).

Longitudinal analysis

The incidence rate of MetS was 4.5/100 persons-year (95% CI: 3.9–5.2) in normouricemic participants and 13.0/100 persons-year (95% CI: 8.5–20.0) in hyperuricemic subjects. A positive association of hyperuricemia with MetS incidence was found (crude IRR = 2.88, 95% CI: 1.83–4.51) (Table 3). A subsequent model was employed, utilizing model 2 from above with the addition of the presence of one or two features of MetS at baseline evaluation). Using this model, hyperuricemia remained positively and significantly associated with MetS incidence. Hyperuricemic subjects presented 1.73 times more risk of developing MetS compared with normouricemic participants (model 3 adjusted IRR = 1.73, 95% CI: 1.08–2.76).

Table 1 Comparison of characteristics between eligible and non-eligible participants of the EPIPorto cohort at baseline (Porto, Portugal 1999–2003) and follow-up evaluations (Porto, Portugal 2005–2008)

		Cross-sectional analyses ($n = 2485$)			Longitudinal analyses ($n = 1634$)		
		Non-eligible participants[a] $n = 210$ n (%)	Eligible participants $n = 2275$ n (%)	p Value	Non-eligible participants[b] $n = 580$ n (%)	Eligible participants $n = 1054$ n (%)	p Value
Sex	Female	138 (65.6)	1,401 (61.6)	0.266	355 (59.7)	639 (60.6)	0.725
Smoking	Current smokers	78 (41.9)	1,007 (44.8)	0.743	108 (18.1)	210 (19.9)	0.419
Alcohol	Current drinkers	149 (80.1)	1,833 (81.6)	0.870	309 (51.9)	501 (47.5)	0.105
WC	(♂ ≥ 102♀ ≥ 88 cm)	78 (40.8)	731 (32.2)	0.015	384 (64.5)	715 (67.8)	0.431
Blood pressure	(≥130/85 mmHg)	134 (79.8)	1,461 (66.6)	0.001	264 (44.4)	496 (47.1)	0.500
Triglycerides	(≥150 mg/dL)	13 (22)	540 (23.8)	0.756	53 (8.9)	111 (10.5)	0.355
HDL cholesterol	(♂ < 40 ♀ < 50 mg/dL)	20 (43.5)	628 (27.8)	0.019	85 (14.3)	129 (12.2)	0.177
Glucose	(≥100 mg/dL)	19 (26.4)	524 (23.3)	0.539	70 (11.8)	99 (9.4)	0.095
		Mean (SD)	Mean (SD)	p Value	Mean (SD)	Mean (SD)	p Value
Age	years	57.8 (16.5)	52.5 (15.3)	0.001	50.1 (17.5)	49.6 (14.7)	0.626
Education	years	7.52 (5.2)	8.67 (5.2)	0.003	8.9 (5.2)	9.4 (5.2)	0.101
Uric acid	mg/L	48.6 (15.1)	45.6 (13.8)	0.123	43.4 (13.2)	43.6 (12.4)	0.705
BMI	kg/m^2	34.0 (17.8)	28.7 (13.7)	0.032	26.5 (11.7)	26.6 (11.8)	0.917
Total physical activity	met/h	1.53 (0.310)	1.54 (0.360)	0.356	1.55 (0.296)	1.57 (0.320)	0.288
Total energy intake	kcal/day	2271.0 (651.7)	2237.7 (640.9)	0.492	2303 (662.7)	2269 (637.1)	0.875
Protein intake	g/day	101.8 (29.2)	100.1 (29.3)	0.788	101.6 (29.8)	102 (29.7)	0.822

SD standard deviation

[a] Participants with missing information on MetS or SUA levels at baseline

[b] Participants with MetS at baseline and those with missing information on two or more MetS features

Analyzing SUA as a continuous variable, one standard deviation increase of SUA concentration was significantly associated with a 1.22-fold increase in MetS risk (IRR = 1.22, 95% CI: 1.05–1.42) (model 3, Table 3).

Regarding the associations between hyperuricemia and the MetS features, hyperuricemia presented the strongest crude association with the occurrence of high-blood pressure (IRR = 2.33, 95%: 1.09–4.99), which became non-significant after adjustment for potential confounders. Only high WC remained significantly and positively associated with hyperuricemia, after adjustment for the same set of variables as in model 2 plus have one or two features of MetS at baseline evaluation (IRR = 1.73, 95% CI: 1.00–3.01).

One standard deviation increase of SUA concentration (each 12 mg/L increase) was significantly associated with high-WC (IRR = 1.25, 95%: 1.05–1.49) and high-triglycerides levels (IRR = 1.44, 95%: 1.22–1.71) and even after adjustment for several confounders.

Discussion

In this adult population, an independent positive effect of SUA on MetS was observed. A more than twofold increased risk of MetS was found for hyperuricemic subjects as compared with the normouricemic counterparts. Other researchers reported similar magnitude of cross-sectional associations between hyperuricemia and MetS [19, 20, 33].

With these cross-sectional observations, we could argue that hyperuricemia is very likely a marker for Mets occurrence. However, in order to answer to the main question under research: Is SUA an independent risk factor of MetS or merely a risk marker? The present study estimated the MetS incidence according to SUA levels and hyperuricemia. Hyperuricemic status was associated with a 1.73-fold increase in MetS risk, independently of other risk factors. To our knowledge, few studies have been conducted to estimate IRR of MetS in relation to SUA status. The relative role of SUA for MetS incidence was estimated by Ryu et al. [22] in a Korean cohort population. According to this study, ~1.6-fold increased risk for MetS was observed in subjects with SUA levels in the highest quintile compared with the lowest one. Beside these results, the strongest evidence of the role of uric acid in the development of MetS has been provided by experimental studies in animal models showing that a decrease in SUA levels can reverse features of the MetS [18].

Table 2 Cross-sectional association of hyperuricemia with MetS and its features (Joint Interim criteria)

	SUA (mg/L)		PR (95% CI)
	♂ < 70 ♀ < 60 *n* = 2,090 (%)	♂ ≥ 70 ♀ ≥ 60 *n* = 185 (%)	
High WC	633 (30.6)	98 (53.8)	
Model 0[a]			1.76 (1.42–2.18)
Model 1[b]			1.71 (1.38–2.13)
Model 2[c]			1.60 (1.28–2.01)
High blood pressure	1277 (64.4)	166 (92.7)	
Model 0[a]			1.44 (1.22–1.69)
Model 1[b]			1.22 (1.03–1.43)
Model 2[c]			1.21 (1.02–1.43)
High triglycerides	431 (20.8)	103 (56.0)	2.69 (2.17–3.34)
Model 0[a]			2.69 (2.17–3.34)
Model 1[b]			2.26 (1.82–2.82)
Model 2[c]			2.32 (1.84–2.91)
Low-HDL cholesterol	556 (27.1)	64 (35.8)	
Model 0[a]			1.32 (1.02–1.71)
Model 1[b]			1.30 (0.99–1.68)
Model 2[c]			1.36 (1.04–1.79)
High glucose	437 (21.1)	82 (44.3)	
Model 0[a]			2.10 (1.66–2.66)
Model 1[b]			1.63 (1.28–2.07)
Model 2[c]			1.65 (1.29–2.12)
MetS	505 (24.7)	106 (59.9)	
Model 0[a]			2.43 (1.97–2.99)
Model 1[b]			2.07 (1.67–2.57)
Model 2[c]			2.10 (1.68–2.63)

MetS is identified when at least three of the following conditions are present in the same subject

High WC (♂ ≥ 102, ♀ ≥ 88 cm); high blood pressure (≥130/85 mmHg or pharmacological treatment for hypertension); high triglycerides (≥150 mg/dL); low-HDL cholesterol (♂ < 40 ♀ < 50 mg/dL); high glucose (≥100 mg/dL or antidiabetic treatment)

PR prevalence ratios

[a] Crude PR

[b] Adjusted for age, age^2, sex, and education (continuous)

[c] Adjusted for the same set of variables as in model 1 plus smoking (current smoker), alcohol (current drinker), protein and total energy intake (continuous), and total physical activity (continuous)

Among MetS features, the strongest cross-sectional and longitudinal association found in our study was between serum triglycerides and SUA levels. The same effect has been previously found in several groups of patients [34, 35] and also in healthy subjects [36]. Although genetic factors have been associated with the occurrence of gout and hypertriglyceridemia [37], the underlying mechanism for the association of triglycerides with SUA levels is still not

Table 3 Longitudinal association of hyperuricemia and continuous uric acid levels with MetS and its features (Joint Interim criteria)

	SUA (mg/L) (*n* = 1,054)	
	♂ ≥ 70	♀ ≥ 60 *n* = 185 IRR (95% CI)	SUA (continuous) Mean (SD) = 44(12) IRR (95% CI)
High WC		
Model 0[a]	1.63 (0.98–2.72)	0.93 (0.81–1.08)
Model 1[b]	2.17 (1.29–3.67)	1.30 (1.10–1.52)
Model 2[c]	2.29 (1.35–3.88)	1.34 (1.14–1.59)
Model 3[d]	1.73 (1.00–3.01)	1.25 (1.05–1.49)
High blood pressure		
Model 0[a]	2.33 (1.09–4.99)	1.23 (1.04–1.45)
Model 1[b]	2.01 (0.93–4.33)	1.23 (1.00–1.50)
Model 2[c]	2.02 (0.93–4.43)	1.21 (0.99–1.49)
Model 3[d]	1.76 (0.79–3.96)	1.13 (0.91–1.41)
High triglycerides		
Model 0[a]	1.99 (1.13–3.50)	1.34 (1.22–1.59)
Model 1[b]	1.81 (1.02–3.20)	1.45 (1.25–1.68)
Model 2[c]	1.91 (1.02–3.51)	1.51 (1.30–1.76)
Model 3[d]	1.66 (0.89–3.08)	1.44 (1.22–1.71)
Low-HDL cholesterol		
Model 0[a]	1.87 (1.20–2.90)	1.28 (1.14–1.45)
Model 1[b]	1.55 (0.99–2.41)	1.25 (1.10–1.44)
Model 2[c]	1.48 (0.93–2.36)	1.24 (1.10–1.44)
Model 3[d]	1.09 (0.67–1.77)	1.11 (0.95–1.30)
High glucose		
Model 0[a]	1.80 (1.18–2.73)	1.30 (1.17–1.45)
Model 1[b]	1.39 (0.91–2.13)	1.19 (1.05–1.35)
Model 2[c]	1.32 (0.85–2.05)	1.17 (1.03–1.33)
Model 3[d]	1.01 (0.64–1.60)	1.05 (0.91–1.21)
MetS		
Model 0[a]	2.88 (1.83–4.51)	1.38 (1.22–1.56)
Model 1[b]	2.46 (1.55–3.90)	1.44 (1.25–1.65)
Model 2[c]	2.43 (1.52–3.88)	1.46 (1.26–1.69)
Model 3[d]	1.73 (1.08–2.76)	1.22 (1.05–1.42)

MetS is identified when at least three of the following conditions are present in the same subject

High WC (♂ ≥ 102, ♀ ≥ 88 cm); high blood pressure (≥130/85 mmHg or pharmacological treatment for hypertension); high triglycerides (≥150 mg/dL); low-HDL cholesterol (♂ < 40 ♀ < 50 mg/dL); high glucose (≥100 mg/dL or antidiabetic treatment)

SD standard deviation, *IRR* incidence rate ratio, *95% CI* 95% confidence intervals, *SUA* serum uric acid

[a] Crude IRR

[b] Adjusted for age, age^2, sex, and education (continuous)

[c] Adjusted for the same set of variables as in model 1 plus smoking (current smoker), alcohol (current drinker), protein and calories consumption (continuous), and total physical activity (continuous)

[d] Adjusted for the same set of variables as in model 2 plus have one or two features of MetS at baseline evaluation

clear. About half of hyperuricemic patients with gout have high-triglycerides levels and in these patients a higher prevalence of the E2 allele of apoliprotein E (ApoE) has reported [38]. ApoE plays an important role in the modulation of lipoprotein metabolism. It has a reduce capacity to the remnants receptor (ApoB/E), which would result in a decrease clearance rate of the very low-density lipoprotein (VLDL) and consequent higher mean levels of VLDL cholesterol and VLDL triglycerides [39].

In the present study, high-WC and high-blood pressure were also positively associated with hyperuricemia but in multivariate analysis only central obesity remained significantly associated.

Some studies showed that SUA level is independently associated with serum leptin level and suggested that leptin could be a factor responsible for hyperuricemia in obese patients [40] and with insulin resistance syndrome [41].

Studies of uric acid levels and the development of hypertension have been consistent in showing positive associations [42–44]. One study showed that elevated uric acid concentrations did not predict the development of hypertension [42].

Comparison of our results with other studies should consider the discussion on differences between PR and prevalence odds ratio (POR) [45, 46]. PR and POR are similar for a rare disease, but they could be very different for a common disease, such as MetS and its features. In the present cross-sectional analysis, subjects with hyperuricemia had a PR for MetS of 2.10 (95% CI: 1.68–63), but a POR of 4.33 (95% CI: 3.03–6.18) (data not shown). Other authors concluded that PR are more consistent, conservative, and interpretable for estimating the true effect of IRR (incidence rate ratio) [47] and even should be used in preference to the POR [48]. In the present study, the use of PR is more adequate and more comparable to IRR than POR. Also, the existence of several MetS definitions and cut-points of hyperuricemic status could explain the differences among studies. Recently, the Joint Interim proposes a single set of cut-points for all components except WC in an attempt to unify criteria and facilitate international comparisons.

Other strengths and limitations of this study deserve further discussion.

In this study, we have used a longitudinal approach to clarify the effect of SUA as predictor of MetS. Accordingly, we estimated the effect of SUA at baseline on incident cases of MetS. Although this procedure could have minimized some of the problem of reverse causality, we cannot exclude this possibility.

Although our analyses considered the adjustment for several potential confounders, the possibility of residual confounding cannot be excluded, namely considering missing variables, such as fasting insulin concentration or renal function. Information on the use of drugs that interfere in SUA concentration (thiazides, furosemide, and allopurinol) was obtained, but the final models did not include these medications as confounders because a restricted number of participants used hyperuricemic drugs.

Results from the present study support that a high concentration of SUA is a risk factor for MetS development. Attending the increasing trends of MetS worldwide, more emphasis should be put in SUA as an additional link to cardiovascular disease.

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