

Association of uric acid and glucose disposal rate value in euglycemic Chinese subjects

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Research

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Abstract

Background: We aimed to examine the relationship between serum uric acid (SUA) levels and glucose disposal rate value (M value) evaluated by hyperinsulinemic euglycemic clamp technique in euglycemic Chinese subjects.

Methods: There were 19 non-diabetic Chinese subjects included in this study. The participants accepted physical examination, laboratory examination and standardized questionnaire. Insulin resistance was evaluated by M value. Some other indices were also calculated by data obtained from 3-hour oral glucose tolerance test (OGTT). Subjects were divided into two groups based on the median of SUA levels.

Results: The level of systolic blood pressure (SBP) ($P=0.035$), waist circumference ($P=0.009$), waist-to-hip ratio ($P=0.004$), Chinese visceral adiposity index (CAVI) ($P=0.028$), weight ($P=0.01$), serum creatinine (Cr) ($P=0.05$) and the percentage of drinking habits ($P=0.03$) were all significantly increased in high SUA group. The level of M value and high-density lipoprotein cholesterol (HDL-c) were significantly decreased in high SUA group ($P=0.041$ for M value and $P=0.09$ for HDL-c). There were no significant differences between those indirect insulin resistance indices and SUA. In addition, the SUA levels were inversely correlated with M value ($r=-0.666$, $P=0.002$) and HDL-c ($r=-0.619$, $P=0.005$), positively correlated with waist circumference ($r=0.615$, $P=0.005$), CVAI ($r=0.630$, $P=0.004$), SBP ($r=0.521$, $P=0.022$) and Cr ($r=0.550$, $P=0.015$) levels. Analysis of stepwise multiple regression showed the independent association between SUA and M value in both male and female euglycemic subjects.

Conclusions: There is a significant correlation between SUA levels and glucose disposal rate value in euglycemic Chinese subjects, which suggested that UA played an important role on insulin resistance even in those non-diabetic subjects

Background

Uric acid (UA) is the final metabolic product of purine compounds. Because of the lack of the uricase, humans mainly excreted UA by kidneys and gastrointestinal tract to maintain homeostasis[1]. In recent years, a large body of studies have proved the clinical significance of UA in development of various metabolic diseases, including gout, hypertension, coronary artery disease and metabolic syndrome[2–4]. Insulin resistance is a kind of dysregulation of insulin signaling system, which represents a reduced sensitivity of peripheral tissues, including adipose, skeletal muscle and liver tissues to respond to the physiological levels of insulin[5, 6]. The results of insulin resistance include glucose intolerance and hyperglycemia, and subsequent type 2 diabetes mellitus (T2DM)[6]. Classically, the gold standard for evaluating insulin resistance is the hyperinsulinemic euglycemic clamp technique, which was first improved and applied to human body by an American scholar Ralph a. DeFronzo in 1979[7]. It adopts the constant infusion of insulin to inhibit the liver gluconeogenesis, and the speed of glucose infusion to maintain the normal blood glucose level is used to reflect the ability of the organism to process or utilize glucose when the blood glucose level reaches a steady state. The hyperinsulinemic euglycemic clamp

technique can be widely used in populations with various glucose metabolism conditions because it can avoid the interference caused by endogenous insulin deficiency, it also plays an important role in researches on insulin resistance. However, since the technique is expensive and complicated to operate, there are some simple methods or formulas for insulin sensitivity evaluation having been put forward, including Quantitative Insulin Sensitivity Check Index (QUICKI)[8], Minimal model analysis[9], insulin sensitivity index proposed by Matsuda et al. (ISIMatsuda)[10], homeostasis model assessment of insulin resistance (HOMA-IR) [11], the reciprocal of the product of fasting insulin and blood glucose (IAI) and the ratio of area under curve of glucose and insulin (AUC_{Glu}/AUC_{Ins}) in oral glucose tolerance test (OGTT)[12]. These indices can evaluate insulin sensitivity at some time but may lead to misjudgment when the islet β -cell secretion function is defect, which results in limitations of applicable population. At present, the hyperinsulinemic euglycemic clamp technique is still an irreplaceable gold standard for the accurate determination of insulin sensitivity[13].

In recent years, the positive association between the level of serum uric acid (SUA) and insulin resistance has been reported[14, 15]. However, on the one hand, insulin resistance in most previous studies were evaluated by simple indices, only several researches in Western populations used the gold standard, hyperinsulinemic euglycemic clamp technique, to evaluate the degree of insulin sensitivity. On the other hand, most studies focused on subjects with diabetes mellitus (DM) or impaired glucose tolerance (IGT) but not populations with normal glucose tolerance (NGT) and normal fasting blood glucose.

In this study, we aimed to explore the relationship between SUA levels and insulin resistance measured by hyperinsulinemic euglycemic clamp technique in euglycemic Chinese subjects, to evaluate whether the correlation has existed in subjects without DM or IGT.

Methods

Participants

A total of 28 Chinese subjects were recruited in this study. After excluding 5 subjects with IGT and 4 subjects with DM based on the WHO 1997 criteria[16]. There were 19 participants with NGT and normal fasting blood glucose (8 males and 11 females) were included in the study.

This study was approved by the Peking Union Medical College Hospital (PUMCH) Ethics Committee and followed the ethical standards of the responsible committee on human experimentation (institution and national) and with the Helsinki Declaration of 1964, as revised in 2013. All participants signed written informed consent.

Anthropometric measurements

Anthropometric measurements were collected by well-trained examiners at study entry, including age, weight, height, waist circumference, thigh circumference and blood pressure. Blood pressure was measured three times after five minutes' rest and was recorded as the mean value of three times

measurements. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height in meters (m²). Chinese visceral adiposity index (CAVI) was calculated according to the formula in previous article[17] to evaluate visceral fat distribution.

General laboratory measurements

General laboratory measurements were collected after fasting for 8 to 12 hours including common blood counts, fasting blood glucose, SUA, blood urea nitrogen, serum creatinine (Cr), total serum cholesterol (TC), high- and low-density lipoprotein cholesterol (HDL-c and LDL-c), triglyceride (TG) and glycosylated hemoglobin A1c (HbA1c). Blood samples were collected in 3-hour OGTT from forearms to assay serum glucose, insulin and C-peptide at fasting (0-minute), 30-minute, 60-minute, 120-minute and 180-minute after 75g anhydrous glucose load by oral. Those data were measured by Beckman automatic biochemical analyzer AU5800.

QUICKI[8], ISIMatsuda[10], IAI, AUC_{Glu}/AUC_{Ins}[12] and HOMA-IR[11] were calculated as simple indices to evaluate insulin resistance.

Hyperinsulinemic euglycemic clamp technique

Three days before the test, the subject was asked to take a normal calorie balanced diet (1806kcal/day, carbohydrate accounted for 55%, protein accounted for 15% and fat accounted for 30% of the total calories). The day before the clamp test, the subject should avoid severe activities after dinner, not drink alcohol and take drugs, and start fasting at 20:00pm. At 8:00am on the day of the clamp test, the subject took a supine position with one cubital vein set with a double channel trocar, one channel was connected with an injection pump, insulin was continuously infused at the speed of 40 mIU · m⁻² · min⁻¹ to obtain a certain concentration of serum insulin platform and to inhibit the output of hepatic glucose and gluconeogenesis; the other channel was connected with a three-way pipe. Among them, two infusion pumps were connected at each end with one pump was used to infuse 20% glucose injection intravenously, the other was infused with potassium chloride (1.5g) plus saline (0.9% 500ml) at a constant rate. A trocar was placed in the vein of the forearm on the opposite side of the infusion side and sealed with heparin for blood sampling. The arm for collecting blood samples was placed in a constant temperature device to maintain the temperature around 55 ° C, so as to achieve the arterialization of venous blood.

Fasting blood glucose was set as the target normal blood glucose level (5±0.5mmol/ L). During the clamp test, the arterialized venous blood was measured every 5 minutes, and the glucose infusion rate was adjusted according to the equation described by Defronzoto to maintain the blood glucose in a satisfactory range, that was target blood glucose value±10%, so as to inhibit the secretion of endogenous insulin.

The classical Defronzo equation: $S_i = [(G_d - G_i) \times 10 \times (0.25 \times \text{body weight}) \times PF] / (\text{glucose concentration} \times 15) + [SM_{i-2} - (G_d / G_i)] \times FM_{i-1}$ ($SM_i = SM_{i-2} \times FM_i \times FM_{i-2}$, $FM_i = (G_d / G_i)$). (S_i is the drop rate of glucose to

be adjusted at any time; G_d is the target blood glucose level; PF is the adjustment coefficient of different infusion pumps.)

The blood samples were taken every 20 minutes in 2 hours for the measurements of serum insulin and C-peptide, all those blood samples were sent to the laboratory on the same day. ADVIA Centaur XP immunoassay system was used to analyze insulin and C peptide concentrations. The unit of glucose disposal rate value (M value) was $\text{mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, the calculation formula was the glucose infusion per kilogram of body weight per minute in the last 40 minutes of clamp test + $(G_{80}-G_{120}) \times 0.0625$ (where G_{80} and G_{120} were the blood glucose values at the time of 80 and 120 minutes respectively, the unit is g/L).

Standardized questionnaire

Detailed in-person interviews were administered using a standardized questionnaire to collect information on demographic characteristics, past medical history, family history, alcohol intake, smoking and exercise habits. Drinking habits were classified as never drinking and currently drinking. Smoking habits were classified as never, former or currently smoking. Regular exercise was evaluated as any kind of physical activity except for walking for work or daily life performed at least 30 minutes for no less than 3 days per week.

Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation and percentages were as categorical variables. Differences between continuous variables were analyzed by the ANCOVA analysis, and the variables that failed the normality test were logarithmically transformed before analysis. Differences between categorical variables were analyzed by the chi-square test. Pearson linear regression analysis was performed to evaluate correlations between SUA and other clinical parameters. A stepwise multiple linear regression analysis was carried out to evaluate the independent associations of variables and SUA. P-value less than 0.05 was considered significant. All statistical analyses were carried out using the statistical program SPSS (version 25, SPSS, Chicago, IL).

Results

Characteristics of the subjects by serum uric acid categories

We recruited 19 euglycemic Chinese subjects, the ratio of male to female was 11:8, and the mean age was 33.2 ± 6.8 years old. General characteristics and laboratory tests of these subjects were summarized in **Table 1**.

Based on the SUA levels, we grouped these subjects by the median value (SUA=288 $\mu\text{mol/L}$). SUA levels were significantly higher in the male group than in female group. With an increased level of SUA, the level of systolic blood pressure (SBP) ($P=0.035$), waist circumference ($P=0.009$), waist-to-hip ratio ($P=0.004$), weight ($P=0.01$), CVAI ($P=0.028$), Cr ($P=0.05$) and the percentage of drinking habits ($P=0.03$) were all

increased significantly. The level of M value and HDL-c significantly decreased (M value, $P=0.041$ and HDL-c, $P=0.09$, respectively) in hyperuricemia group. There was no significant difference between simple indices evaluated insulin resistance and SUA.

Association between serum uric acid and insulin resistance

In simple linear regression analysis (**Table 2**), the SUA levels inversely correlated with M value ($r=-0.666$, $P=0.002$; **Figure 1**) and HDL-c ($r=-0.619$, $P=0.005$), positively correlated with waist circumference ($r=0.615$, $P=0.005$), CVAI ($r=0.630$, $P=0.004$), SBP ($r=0.521$, $P=0.022$) and Cr ($r=0.550$, $P=0.015$) levels.

To further examine the relationship between SUA and the anthropometric and laboratory parameters, stepwise multiple regression was performed with SUA as the independent variable after grouping by gender. The results showed the independent association between SUA and M value in both female and male (**Table 3** and **Table 4**). In women, the results showed an independent association of M value ($P=0.002$), HDL-c ($P=0.044$) and SUV level after adjusting for potential confounding factors. In men, only M value ($P=0.001$) was selected as a result of stepwise regression analysis.

Table 1. Characteristics of the subjects grouped by median of uric acid

	Uric acid		P value	Total
Median of uric acid concentration ($\mu\text{mol/L}$)	≤ 288	> 288		
Number of subjects	10	9		19
age (year)	34.4 ± 7.5	31.8 ± 6.1	0.418	33.2 ± 6.8
Male (%)	10.0%	77.8%	0.003*	42.1%
M value (mg/kg/min)	8.0 ± 2.8	5.4 ± 2.3	0.041*	6.8 ± 2.8
HOMA-IR	2.7 ± 1.4	3.2 ± 1.4	0.47	2.9 ± 1.4
ISIMatsuda	88.6 ± 60.5	64.0 ± 28.5	0.28	77.0 ± 48.5
QUICKI	0.34 ± 0.02	0.33 ± 0.02	0.47	0.33 ± 0.02
IAI	0.020 ± 0.009	0.017 ± 0.009	0.47	0.019 ± 0.009
$\text{AUC}_{\text{Glu}}/\text{AUC}_{\text{Ins}}$	0.12 ± 0.10	0.09 ± 0.06	0.43	0.11 ± 0.08
SBP (mmHg)	105.9 ± 7.4	118.4 ± 15.6	0.035*	111.8 ± 13.3
DBP (mmHg)	64.1 ± 10.7	72.0 ± 12.4	0.15	67.8 ± 11.9
Waist circumference (cm)	79.9 ± 5.3	95.6 ± 16.0	0.009*	87.3 ± 13.9
Waist-to-hip ratio	0.82 ± 0.03	0.90 ± 0.07	0.004*	0.86 ± 0.06
Thigh circumference (cm)	47.2 ± 2.7	50.3 ± 6.4	0.18	48.7 ± 5.0
Weight (kg)	63.6 ± 6.1	80.6 ± 17.4	0.01*	71.6 ± 15.2
BMI (kg/m^2)	23.6 ± 2.1	27.2 ± 6.4	0.11	25.3 ± 4.9
CVAI	51.09 ± 20.86	114.50 ± 66.34	0.028*	81.13 ± 57.58
Drinking habits (%)				
Never drinking	90.0%	44.4%		68.40%
Currently drinking	10.0%	55.6%	0.03*	31.60%
Smoking habits (%)				
Never smoking	80.0%	66.7%		73.70%
Former smoking	0	0		0
Currently smoking	20.0%	33.3%	0.51	26.30%
Exercise habits (%)				
None	70.0%	55.6%		63.20%

Regular exercise	30.0%	44.4%	0.52	36.80%
Fasting blood glucose (mmol/L)	5.11±0.39	5.29±0.36	0.31	5.19±0.38
2-hour blood glucose (mmol/L)	6.13±0.81	6.38±1.56	0.66	6.25±1.20
Fasting serum insulin (μIU/mL)	12.18±6.56	13.47±6.06	0.66	12.79±6.18
HbA1c (mmol/mol)	33.33±2.54	33.82±3.18	0.73	33.56±2.87
TC (mmol/L)	4.74±0.74	4.60±1.00	0.72	4.67±0.85
TG (mmol/L)	1.34±0.58	1.29±0.52	0.85	1.32±0.54
HDL-c (mmol/L)	1.28±0.19	1.10±0.22	0.09*	1.19±0.22
LDL-c (mmol/L)	2.89±0.65	3.08±0.91	0.60	2.98±0.77
Cr (μmol/L)	64.10±10.39	75.33±13.22	0.05*	69.42±12.84
hsCRP (mg/L)	1.34±1.22	2.29±2.36	0.28	1.79±1.86

Abbreviations: M value, glucose disposal rate value; HOMA-IR, homeostasis model assessment of insulin resistance; ISIMatsuda, insulin sensitivity index proposed by Matsuda et al.; QUICKI, quantitative insulin sensitivity check index; IAI, insulin action index; AUC, area under curve; Glu, glucose; Ins, insulin; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; CAVI, Chinese visceral adiposity index; HbA1c, glycosylated hemoglobin A1c; TC, total cholesterol; TG, triglyceride; LDL-c, low density lipoprotein-cholesterol; HDL-c, high density lipoprotein-cholesterol; Cr, serum creatinine; hsCRP, hypersensitive C-reactive protein.

* represents statistical significance.

Table 2. Simple linear regression analysis of SUA and other variables

	Pearson's correlation coefficient (r)	P value
SBP (mmHg)	0.521	0.022*
age (year)	-0.408	0.083
Wrist circumference (cm)	0.615	0.005*
CVAI	0.630	0.004*
BMI (kg/m ²)	0.419	0.074
TG (mmol/L)	0.261	0.281
HDL-c (mmol/L)	-0.619	0.005*
Cr (μmol/L)	0.550	0.015*
Fasting blood glucose (mmol/L)	0.192	0.431
M value (mg/kg/min)	-0.666	0.002*

Abbreviations: SBP, systolic blood pressure; CVAI, Chinese visceral adiposity index; BMI, body mass index; TG, triglyceride; HDL-c, high density lipoprotein-cholesterol; Cr, serum creatinine; M value, glucose disposal rate value.

* represents statistical significant.

Table 3. Multiple linear regression analysis of SUA and other variables

Variable	Male			Female		
	Standardized β	t	P value	Standardized β	t	P value
M value (mg/kg/min)	-0.875	-4.422	0.004*	-0.860	-4.400	0.002*
SBP (mmHg)	0.400	-1.009	0.359	0.133	0.544	0.603
age (year)	-0.369	-2.501	0.054	-0.034	-0.099	0.924
Waist circumference (cm)	-0.458	-1.591	0.611	0.102	0.447	0.668
CVAI	-0.448	-1.574	0.176	0.049	0.246	0.813
BMI (kg/m ²)	-0.308	-0.994	0.366	0.160	0.670	0.524
Fasting blood glucose (mmol/L)	-0.040	-0.115	0.913	-0.042	-0.207	0.842
TG (mmol/L)	-0.023	-0.995	0.365	-0.135	-0.638	0.544
HDL-c (mmol/L)	-0.211	-1.112	0.317	-0.468	-2.392	0.044*
Cr (μ mol/L)	0.325	1.582	0.174	-0.373	-2.181	0.066

Abbreviations: M value, glucose disposal rate value; SBP, systolic blood pressure; CVAI, Chinese visceral adiposity index; BMI, body mass index; TG, triglyceride; HDL-c, high density lipoprotein-cholesterol; Cr, serum creatinine.

* represents statistical significance.

Table 4. Model summary of multiple linear regression analysis

	Male			Female		
	R ²	F	P value	R ²	F	P value
Model 1	0.765	19.555	0.004	0.521	9.799	0.012
Model 2				0.721	10.33	0.006

Model 1: M value
Model 2: M value, HDL-c

Abbreviations: M value, glucose disposal rate value; HDL-c, high density lipoprotein-cholesterol.

Discussion

In this study, we evaluated correlations between SUA levels and anthropometric measurements and insulin resistance parameters in 19 euglycemic Chinese subjects. We found significant differences in M

values between subjects with low and high SUA levels, and SUA levels inversely correlated to M values independently in both male and female, which indicated even in subjects without DM or IGT, the level of SUA also increased with the aggravation of insulin resistance.

Recently, a large body of studies have proved the underlying mechanisms of correlations between insulin resistance and SUA levels. On the one hand, hyperuricemia could induce increased level of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and reactive oxygen species (ROS) and then result in the oxidative stress in adipose tissue, which showed low sensitivity to insulin subsequently[14, 18]. Also, increased SUA levels could cause inactivity of nitric oxide (NO) and reduce endothelial NO supply which was associated with insulin resistance[19]. On the other hand, insulin resistance could lead to the decreased secretion of SUA and result in further hyperuricemia[20]. It is noteworthy that, simple indices evaluated insulin resistance including HOMA-IR, QUICKI, ISIMatsuda, IAI and AUC_{Glu}/AUC_{Ins} were all of no significant differences between two groups in our study. These indices derived from OGTT or fasting blood glucose and insulin, have been proved to correlate well with hyperinsulinemic euglycemic clamp technique, however, there are other biological processes could confound the results other than insulin resistance. For those derived from OGTT, the variability of glucose absorption and differences in incretin action on insulin secretion among different populations should be taken into consideration. And fasting-derived indices have been shown to be weaker in healthy populations considering healthy subjects may exhibit a large range of insulin sensitivity levels while fasting blood glucose and insulin values are maintained within narrow ranges[12, 21]. The application of those indirect indices are limited by specific applicable population and sample size. For our cohort of a relative small sample size and normal glucose metabolism subjects, M value was much more exact comparing with those simple surrogate indices.

Metabolic syndrome is characterized by a cluster of abnormal physiological and anthropometric signs, including abdominal fat distribution, low HDL-c level, hypertriglyceridemia, hypertension and abnormal glucose metabolism[22]. The level of SUA is currently believed to be a strong risk factor for metabolic syndrome[2, 23]. In our study, we found significant increases in CVAI, waist circumference, waist-to-hip ratio, weight and SBP in higher SUA group, while significantly decreased M value and HDL-c were observed in the same group. In Pearson linear regression analysis, the higher SUA levels were positively correlated with increased CVAI, waist circumference, SBP, Cr concentration and decreased M value and HDL-c concentration. Those results were coincided with previous studies that have confirmed the correlations between components of metabolic syndrome and SUA levels in patients have already diagnosed of metabolic syndrome. Our results suggested even in subjects who have not yet met the diagnostic criteria, the close correlations between SUA levels and parameters related to fat mass, hyperlipidemia, hypertension and insulin resistance have existed.

Furthermore, we found SUA levels positively correlated with CVAI, but not with BMI. The role of body fat distribution in UA metabolism is still ambiguity[24], of traditional parameters related to fat distribution, BMI is used as an index of general obesity, unable to differentiate from central to peripheral fat, subcutaneous to visceral fat, lean mass to fat mass, and waist circumference usually used to present central obesity without accounting for differences in height. CVAI is proposed as a simple and more

suitable clinical index for Chinese people to evaluate the distribution of visceral fat[17] that is derived from VAI[25], it is characterized by a combination of sex, BMI, waist circumference, TG and HDL-c levels. Our finding indicated the rather important role of visceral fat mass in SUA levels than general adiposity.

Up to now, there have been an increasing number of reports on the independent relationship between SUA levels and insulin resistance mostly evaluated by HOMA-IR in patients with IGT or T2DM. In a 6-year follow-up Japanese research, Koshi Nakamura et al. [26] included 2071 Japanese men without hyperuricemia and DM and reported increased HOMA-IR was positively related to the risk of development of hyperuricemia after adjustment for age, baseline SUA, creatinine, BMI, lifestyle and other metabolic diseases. Wu Y et al.[27] reported SUA levels significantly correlated with HOMA-IR among 2886 subjects of impaired glucose regulation after adjusting for multiple confounding risk factors. Abreu E et al. [28] proved that both genders in the upper quartile of UA levels were positively associated with HOMA-IR. However, just a few studies discovered the relationship between SUA levels and insulin resistance in the population of normal glucose metabolism, for example, in a study involved Jewish healthy populations done by Modan et al. [29], they observed that SUA levels showed a positive linear association with plasma insulin response (sum of 1- and 2-hour post glucose load levels) in both genders, and this association remained statistically significant after analyzed by multiple regression analysis for age and major correlates of SUA. In our study, after adjusted for various confounding factors, we found a correlation between SUA levels and insulin sensitivity (M value) in both genders in euglycemic Chinese subjects, which was in agreement with previous researches.

There were only several previous studies have evaluated the relationship between SUA levels and the degree of insulin resistance demonstrated by hyperinsulinemic euglycemic clamp technique in Western populations. Höiegggen et al. [30] studied the relationship between SUA and insulin resistance in untreated borderline hypertensive young men, and they found no relationship. Other two studies conducted by Vuorinen-markkola et al. [31] and Fiorentino et al. [32] reported SUA was independently associated with insulin sensitivity in non-diabetic subjects, which were accorded with our results. Fiorentino et al. [32] also found high SUA levels correlated with reduced insulin clearance.

Although we got the relationship between insulin sensitivity (M-value) and SUA levels in euglycemic Chinese subjects by hyperinsulinemic euglycemic clamp technique. The present study still had several limitations. First, the sample size was quite small and further study of larger population was needed. Secondly, we did not have the data of other confounding factors affecting SUA levels such as a detailed diet habitual and medications which might influence the level of SUA.

Conclusions

We described the association of insulin resistance evaluated by hyperinsulinemic euglycemic clamp technique with SUA levels in euglycemic Chinese subjects. We found significant correlation between SUA levels and glucose disposal rate value in euglycemic Chinese subjects, which suggested that UA played an important role on insulin resistance even in those non-diabetic subjects.

Declarations

Ethics approval and Consent to participate: This study was approved by the PUMCH Ethics Committee and followed the ethical standards of the responsible committee on human experimentation (institution and national) and with the Helsinki Declaration of 1964, as revised in 2013. All participants signed written informed consent.

Consent to publication: The authors affirm that all individual participants provided informed consent for publication of the data. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Availability of data and material: The data generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Authors' Contributions

Conceptualization: Tao Yuan and Shixuan Liu; Investigation: Yingyue Dong and Yong Fu; Methodology: Yan Tang, Yingyue Dong and Weigang Zhao; Writing - original draft: Tao Yuan and Shixuan Liu; Writing - review editing: Tao Yuan and Weigang Zhao; Supervision: Weigang Zhao.

Acknowledgments

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Abbreviations

SUA (serum uric acid), T2DM (type 2 diabetes mellitus), M value (glucose disposal rate), OGTT (oral glucose tolerance test), HDL-c (high-density lipoprotein cholesterol), UA (uric acid), IGT (impaired glucose tolerance), NGT (normal glucose tolerance), QUICKI (quantitative insulin sensitivity check index), HOMA-IR (homeostasis model assessment of insulin resistance), IAI (insulin action index), AUC (area under curve), Glu (glucose), Ins (insulin), ISIMatsuda (insulin sensitivity index proposed by Matsuda et al.), PUMCH

(Peking Union Medical College Hospital), BMI (Body mass index), CAVI (Chinese visceral adiposity index), Cr (serum creatinine), TC (total serum cholesterol), LDL-c (low-density lipoprotein cholesterol), TG (triglyceride), HbA1c (glycosylated hemoglobin A1c), SD (standard deviation), SBP (systolic blood pressure), DBP (diastolic blood pressure), ISI(Comp) (composite whole-body insulin sensitivity index), hsCRP (hypersensitive C-reactive protein), NADPH (nicotinamide adenine dinucleotide phosphate), ROS (reactive oxygen species), NO (nitric oxide).

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Figures

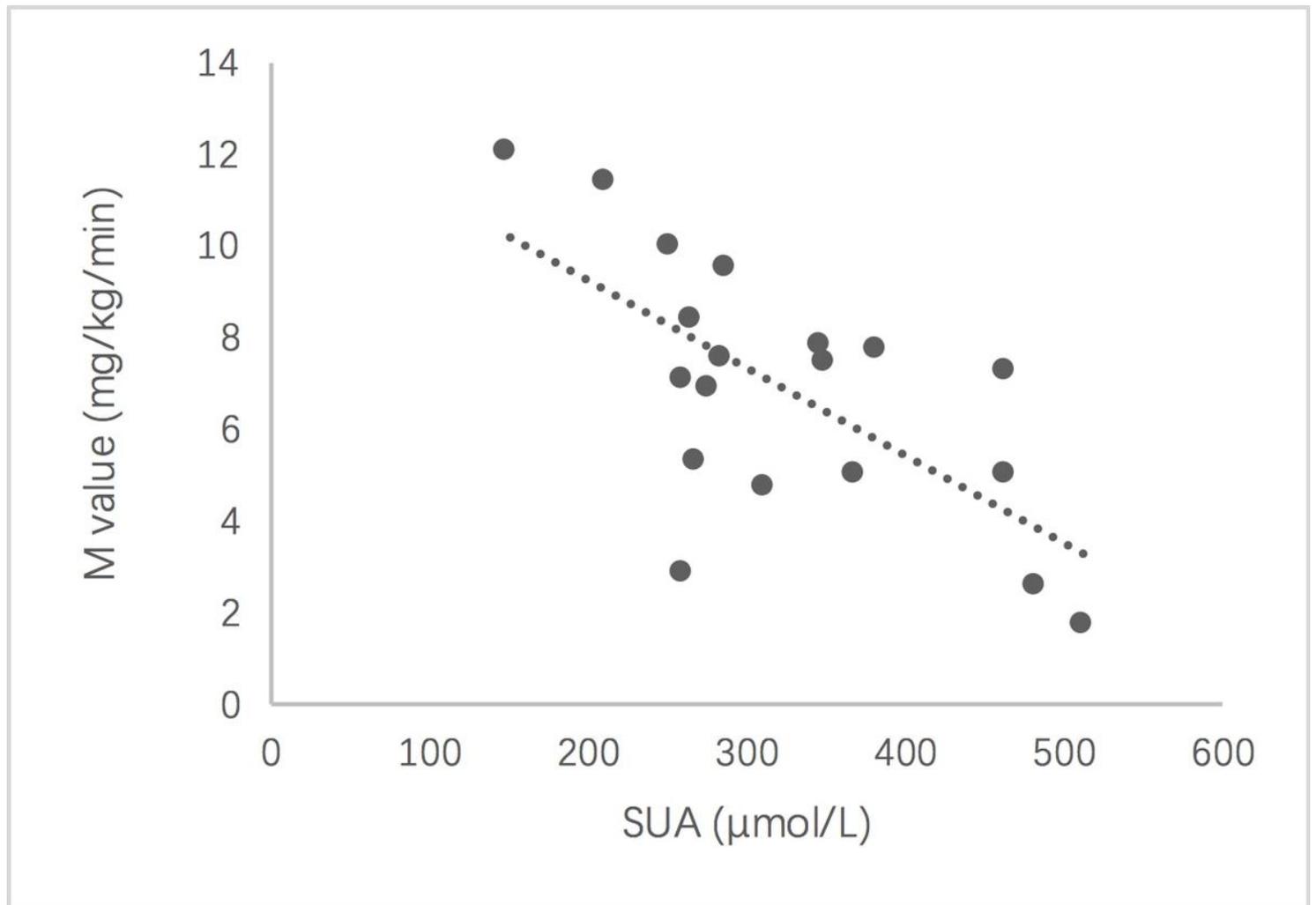


Figure 1

The relationship between SUA and M value Abbreviations: SUA, serum uric acid; M value, glucose disposal rate value. Dotted line represented linear prediction line.