Visceral Fat Area to Leg Muscle Mass Ratio Are Significantly Associated With the Risk of Hyperuricemia Among Women: A Cross-sectional Study

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Research

Keywords: Body composition, Visceral fat area, Skeletal muscle mass, Metabolic diseases, Hyperuricemia, Chinese adults

Posted Date: May 28th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-28417/v1

Abstract

Background: Previous studies have found a significant positive association between obesity, visceral fat accumulation and hyperuricemia. The purpose of the study was to explore the association between the ratio of visceral fat area to leg muscle mass(VFA-to-LMM) and hyperuricemia, and verify the role of sex differences in the association.

Methods: In this cross-sectional study, a total of 3393 (43.3% for men) participants from Tianjin Union Medical Center-Health Management Center were recruited. Body composition were measured by multielectrode bioelectrical impedance analyzer. The VFA-to-LMM ratio was used as independent variable. Hyperuricemia, defined as a serum uric acid level ≥ 416 μmol/L in men and menopausal women, and ≥ 357 μmol/L in premenopausal women, was used as the dependent variable. Multiple logistic regression analysis was used to estimate the odds ratio and 95% confidence interval between VFA-to-LMM ratio and hyperuricemia.

Results: The overall prevalence of hyperuricemia was 14.8%, and the prevalence of hyperuricemia in women (8.9%) was significantly lower than that in men (22.5%). After adjustment for age, smoking status (for males), menopause status (for females), drinking status, exercise frequency, blood pressure, alanine aminotransferase, fasting plasma glucose, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, and history of diseases, a strong positive association was observed between VFA-to-LMM ratio and hyperuricemiain bothmen (4th vs. 1st quartile 1.60, 95%CI: 1.03-2.49) and women (4th vs. 1st quartile 5.22, 95%CI: 2.44-12.56).After additionally adjustment for BMI, there was still a significant positive association in women (4th vs. 1st quartile 2.57, 95%CI: 1.06-6.77), while the association disappeared in men(4th vs. 1st quartile 0.97, 95%CI: 0.55-1.70).

Conclusions: The VFA-to-LMM ratio was positively associated with the risk of hyperuricemia in women after adjustments for confounders. In addition, the highest risk of hyperuricemia was observed when both VFA and LMM were at the highest quartile. However, well-controlled prospective studies are needed to further confirm the causality between VFA-to-LMM ratio and hyperuricemia.

Introduction

According to the National Health and Nutrition Examination Survey (1), the prevalence rates of hyperuricemia were 20.2% for men and 20.0% for women during 2007–2016, and the rates has not shown any decline in the decade. Although the prevalence of hyperuricemia was relatively low in the Chinese population (2), it was still rising according to the latest data (3). Hyperuricemia, as a metabolic disease, is closely related to the inflammatory response and the disorder of glucose and lipid metabolism (4). Moreover, hyperuricemia has also been shown to be significantly associated with lifestyle-related chronic diseases, such as hypertension, diabetes (5), metabolic syndrome (6), non-alcoholic fatty liver disease (NAFLD) (7), and cancer. Besides, a meta-analysis based on cohort studies also confirmed that hyperuricemia was associated with higher cancer incidence and mortality (8).

Considering the serious health outcomes caused by hyperuricemia, a large number of studies on its risk factors are accumulating. A large population-based study confirmed that four modifiable risk factors, such as body mass index (BMI), alcohol use, diuretic use and Dietary Approaches to Stop Hypertension diet, are

independently associated with the development of hyperuricemia (9). Among these modifiable risk factors, BMI is a comprehensive indicator that could indirectly reflect the overall condition of diet, physical activity, and metabolism. However, it fails to reflect metabolic differences between men and women, such as fat distribution and skeletal muscle mass (SMM). In fact, studies have found that there was a positive association between visceral fat and hyperuricemia (10–12), and a significant inverse association between serum uric acid (SUA) levels and SMM (13, 14). In addition, studies have shown that the composition of leg was associated with some metabolic diseases (15, 16). The thigh circumference which can indirectly reflect leg composition has also been confirmed to be associated with various metabolic diseases, such as insulin resistance (IR), carotid atherosclerosis (17) and type 2 diabetes (18). One explanation is that decreased SMM and fat mass in the lower limbs may be associated with disorders of glucose and lipid metabolism (19), which is closely related to hyperuricemia (20, 21).

Based on the previous studies, we speculated that the visceral fat area (VFA) and the leg muscle mass (LMM) seemed to play a key role in the pathogenesis of hyperuricemia, and assumed that the combination of the two indicators would be a potential predictor of hyperuricemia. Therefore, we designed a cross-sectional study to explore the association between the VFA-to-LMM ratio and hyperuricemia, and to verify the role of sex differences in the association, so as to find a clinically feasible and sex-sensitive predictor for the risk of hyperuricemia.

Materials And Methods

Participants

A total of 4 084 adults who visited the Tianjin Union Medical Center-Health Management Center for an annual physical examination and concurrently measured body composition were enrolled in the study during Sep 2019 to Dec 2019. Those who did not provide complete information, including physical examinations, biochemical analysis, questionnaires, and body composition were excluded (n = 602). Subjects with a history of cancer (n = 9) and aged above 85 (n = 52) also be excluded, as the association between body composition and hyperuricemia due to stability of physiological indicators or serious declination of health status might be affected. Besides, we excluded the participants (n = 28) who have extreme values in the measurement indicators. Finally, 3 393 (83% of those eligible) subjects had valid body composition data and covariate information required for the study.

This study was approved by the Institutional Review Board of Tianjin Union Medical Center, Nankai University affiliated hospital. All participants were informed about the study objectives and examination procedures in detailed, and were asked to sign the informed consent form before enrolled.

Measurement Of Body Composition

Body composition were measured by multielectrode bioelectrical impedance analyzer (Inbody 770, Biospace Inc., Korea). According to the manufacturer’s guidelines, subjects were required to fast overnight, and wiped the bottom of their feet with clean water before taking measurements. Participants were instructed to stand barefoot on the base components with light clothing and grasp the handles of the instrument to ensure full

contact with a total of 8 electrodes. The participant was asked to slightly abduct his or her arms and maintained the posture during the assessment. The entire measurement process took about 3–4 minutes, and the data were automatically saved in the computer after the measurement was completed. Based on the purpose of this study, we selected the VFA-to-LMM ratio as the independent variable.

Covariables

Weight and height were measured by an automatic height and weight instrument (DST-600, DONGHUAYUAN, China), and participants were required to be on barefoot and light clothing during the measurement. BMI was calculated as weight in kilograms divided by the square of height in meters. All measurements are carried out in strict accordance with the national standards.

Blood pressure was measured using an automatic electronic blood pressure monitor (AC-05C, Ling Qian, China) after a 10-minute rest, and measured three per person and averaged. Hypertension is defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg or the subjects who had a history of hypertension. The diagnosis of non-alcoholic fatty liver diseases was performed by ultrasound diagnosis system (Phoenix, Philips and Neusoft Medical Systems Co., Ltd., China). Blood biochemical analysis was performed using an automatic biochemical analyzer (TBA-120FR, Toshiba, Japan), and participants were required to fast overnight (only water can be taken), and the venous blood was collected in a fasting state. The main indicators of blood biochemical analysis include alanine aminotransferase (ALT), fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C) and high-density lipoprotein (HDL-C) cholesterol, and serum uric acid. Diabetes was defined as FPG ≥ 7.0 or the subjects with a history of diabetes. Dyslipidemia were defined as TC ≥ 6.2 mmol/L or TG ≥ 2.3 mmol/L or LDL-C ≥ 4.1 mmol/L or HDL-C < 1.0 mmol/L according to the Chinese guidelines for the management of dyslipidemia in adults (2016) (22). Hyperuricemia is defined as a serum uric acid level ≥ 416 μmol/L in men and menopausal women, and ≥ 357 μmol/L in premenopausal women.

The socio-demographic variables, such as sex, age, and menopause status, were collected through questionnaires. Information on lifestyles, including exercise frequency (‘never’, ‘occasional’, and ‘regularly’), smoking status (‘smoker’, ‘Ex-smoker’, and ‘Non-smoker’), drinking status (‘drinker’, and ‘ex-drinker’, and ‘non-drinker’), and sedentary status (> 6 h/day), was also obtained through questionnaires. The participant's history of diseases (including diabetes, hypertension, coronary heart disease, and cancer) were assessed by answering “yes” or “no”.

Statistical analysis

The characteristics of participants were presented as the means ± standard deviation or the median (interquartile range) for continuous variables and percentages for categorical variables. Statistical differences between groups were examined using analysis of variance for continuous variables and Chi-square test for categorical variables. Multiple logistic regression analysis was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) between the VFA-to-LMM ratio and hyperuricemia. For further analysis, we fitted four models and performed a quartile conversion of the independent variables. Model 1 was adjusted for age and Model 2 was adjusted for age, smoking status (for males), menopause status (for females), drinking status,

exercise frequency and history of diseases. Model 3 was additionally adjusted for SBP, DBP, ALT, FPG, TC, TG, LDL-C, HDL-C, and creatinine. Model 4 was additionally adjusted for BMI based on Model 3. All statistical analyses were performed with SAS 9.4 for Windows (SAS Institute, Cary, NC, USA). *P* values were two-tailed, and the differences were considered to be significant when $P < 0.05$.

Results

Characteristics of participants

The characteristics of participants according to sex and hyperuricemia status are presented in Table 1. It showed that the overall prevalence of hyperuricemia was 14.8% (22.5% in men and 8.9% in women), and the average age of participants was 45.9 years. Analysis of the differences between hyperuricemia group and non-hyperuricemia group showed that there were significant differences in almost all indicators in both men and women, except for smoking, drinking, exercise, and history of diseases. Indicators such as SBP, FPG, hypertension and diabetes were observed to have significant differences only in women, and indicators such as LMM and regular exercise were observed to have significant differences only in men. Besides, the differences in VFA-to-LMM ratio between hyperuricemia and non-hyperuricemia was showed in Fig. 1. The figure showed that there were significant differences in VFA-to-LMM ratio not only between hyperuricemia and non-hyperuricemia, but also between men and women ($P < .0001$).

Table 1

Characteristics of the study population according to sex and hyperuricemia status [a]

Characteristics	Men (n = 1 469)		*P* [b]	Women (n = 1 924)		*P*
	Non-Hyperuricemia (n = 1 139)	Hyperuricemia (n = 330)		Non-Hyperuricemia (n = 1 753)	Hyperuricemia (n = 171)	
Age, y	47.9 ± 15.7	44.4 ± 14.6	0.0002	44.0 ± 14.5	54.4 ± 16.1	< .0001
BMI, kg/m^2	25.4 ± 3.2	27.0 ± 3.5	< .0001	22.8 ± 3.2	26.0 ± 3.9	< .0001
SBP, mmHg	127.0 ± 16.8	127.8 ± 15.4	0.4377	117.3 ± 18.1	129.8 ± 19.3	< .0001
DBP, mmHg	80.2 ± 10.0	83.4 ± 10.0	< .0001	75.4 ± 9.7	79.1 ± 11.5	< .0001
VFA, cm^2	90.7 ± 32.8	104.9 ± 36.6	< .0001	95.1 ± 35.4	129.1 ± 41.0	< .0001
LMM, kg	17.4 ± 2.2	18.0 ± 2.2	< .0001	12.3 ± 1.6	12.5 ± 1.8	0.1409
ALT, units/L	21.6 (15.3, 31.6) [c]	27.3 (18.8, 45.5)	< .0001	13.8 (10.0, 19.6)	18.3 (13.6, 26.0)	< .0001
FPG, mmol/L	5.3 (4.9, 5.9)	5.2 (5.0, 5.7)	0.3329	5.1 (4.8, 5.4)	5.6 (5.1, 6.5)	< .0001
TC, mmol/L	5.0 ± 0.9	5.2 ± 0.9	< .0001	5.1 ± 1.0	5.8 ± 1.2	< .0001
TG, mmol/L	1.3 (0.9, 1.8)	1.7 (1.2, 2.3)	< .0001	1.0 (0.7, 1.4)	1.6 (1.1, 2.2)	< .0001
LDL-C, mmol/L	2.6 ± 0.5	2.8 ± 0.5	< .0001	2.7 ± 0.6	3.1 ± 0.7	< .0001
HDL-C, mmol/L	1.3 ± 0.2	1.3 ± 0.2	< .0001	1.6 ± 0.3	1.5 ± 0.3	< .0001
SUA, umol/L	336.0 ± 50.3	468.7 ± 47.1	< .0001	260.4 ± 45.8	395.3 ± 38.0	< .0001
Creatinine, umol/L	74.7 ± 10.0	79.8 ± 11.7	< .0001	55.6 ± 7.7	61.5 ± 11.6	< .0001
Smoking, n (%)	247 (21.7)	69 (20.9)	0.7624	13 (0.7)	0 (0.0)	0.6208
Drinking, n (%)	459 (40.3)	129 (39.1)	0.6934	107 (6.1)	5 (2.9)	0.1275
Exercise, n (%)						
Never	285 (25.0)	95 (28.8)	0.1689	461 (26.3)	50 (29.2)	0.4057
Occasional	380 (33.4)	124 (37.6)	0.1557	733 (41.8)	63 (36.8)	0.2076
Regular	474 (41.6)	111 (33.6)	0.0091	559 (31.9)	58 (33.9)	0.5872
Menopause, n (%)	-	-	-	559 (31.9)	113 (66.1)	< .0001
Hypertension, n (%)	355 (31.2)	114 (34.6)	0.2465	288 (16.4)	71 (41.5)	< .0001

Characteristics	Men (n = 1 469)		*P*[b]	Women (n = 1 924)		*P*
	Non-Hyperuricemia (n = 1 139)	Hyperuricemia (n = 330)		Non-Hyperuricemia (n = 1 753)	Hyperuricemia (n = 171)	
Diabetes, n (%)	124 (10.9)	28 (8.5)	0.2071	69 (3.9)	26 (15.2)	< .0001
Dyslipidemia, n (%)	258 (22.7)	131 (39.7)	< .0001	316 (18.0)	76 (44.4)	< .0001
NAFLD, n (%)	473 (41.5)	211 (63.9)	< .0001	405 (23.1)	116 (67.8)	< .0001
Obesity, n (%)	232 (20.4)	122 (37.0)	< .0001	123 (7.0)	36 (21.1)	< .0001
History of diseases, n (%)						
Hypertension	367 (32.2)	111 (33.6)	0.6290	317 (18.1)	75 (43.9)	< .0001
Diabetes	116 (10.2)	23 (7.0)	0.0789	84 (4.8)	25 (14.6)	< .0001
CHD	68 (6.0)	18 (5.5)	0.7254	53 (3.0)	19 (11.1)	< .0001
Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; VFA, visceral fat area; LMM, leg muscle mass; ALT, alanine aminotransferase; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SUA, serum uric acid; NAFLD, non-alcoholic fatty liver diseases; CHD, coronary heart disease.						
[a] Continuous variables are expressed as means ± standard deviation (SD) and categorical variables are expressed as percentages unless otherwise indicated.						
[b] Analysis of variance or chi-square test where appropriate.						
[c] Data are expressed as medians (interquartile range).						

Furthermore, we divided the subjects into four groups based on the quartiles of VFA-to-LMM ratio, and analyzed the linear trend of each indicators (Fig. 2). As the VFA-to-LMM ratio increased, most of the indicators (BMI, FPG, TG, LDL-C, SUA) have a significant linear upward trend in both men and women, while a downward trend was observed in HDL-C.

Vfa-to-lmm Ratio And Risk Of Hyperuricemia

The associations between the VFA-to-LMM ratio and hyperuricemia was explored through the multiple logistic regression models, which results were presented in Table 2. After adjustment for age in Model 1, strong positive associations were observed between VFA-to-LMM ratio and hyperuricemia in both men (4th vs. 1st quartile OR: 2.73; 95% CI: 1.89–3.95) and women (4th vs. 1st quartile OR: 8.25; 95% CI: 4.05–19.14), and significant linear trends were observed in both men ($P < 0.0001$) and women ($P < 0.0001$). After additionally adjustment for smoking status (for men), menopause status (for women), drinking status, exercise frequency, SBP, DBP, ALT, FPG, TC, TG, LDL-C, HDL-C, creatinine, and history of diseases in Model 3, there were still significant positive associations between VFA-to-LMM ratio and hyperuricemia in both men (4th vs. 1st quartile OR: 1.60; 95% CI:

1.03–2.49) and women (4th vs. 1st quartile OR: 5.22; 95% CI: 2.44–12.56). To further analyze whether the association was independent of general obesity, we added BMI as an adjustment factor in model 3. The results showed that there was still a significant positive association between VFA-to-LMM ratio and hyperuricemia in women (4th vs. 1st quartile OR: 2.57; 95% CI: 1.06–6.77), while the association was disappeared in men (4th vs. 1st quartile OR: 0.97; 95% CI: 0.55–1.70).

Table 2
Odds ratio with 95% confidence interval for the association between VFA-to-LMM ratio and hyperuricemia according to sex [a]

Quartiles of VFA-to-LMM ratio	Model 1 [b]	Model 2	Model 3	Model 4
Male				
Quartile 1	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Quartile 2	1.25 (0.86, 1.82)	1.21 (0.83, 1.77)	0.91 (0.60, 1.36)	0.75 (0.49, 1.15)
Quartile 3	1.58 (1.09, 2.31)	1.51 (1.03, 2.21)	1.03 (0.67, 1.57)	0.79 (0.50, 1.25)
Quartile 4	2.73 (1.89, 3.95)	2.49 (1.70, 3.65)	1.60 (1.03, 2.49)	0.97 (0.55, 1.70)
P for trend [c]	< .0001	< .0001	0.0180	0.9563
Female				
Quartile 1	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Quartile 2	2.66 (1.23, 6.42)	2.58 (1.19, 6.23)	2.13 (0.96, 5.21)	1.68 (0.75, 4.17)
Quartile 3	5.20 (2.55, 12.10)	4.95 (2.41, 11.54)	3.74 (1.75, 8.95)	2.42 (1.09, 6.01)
Quartile 4	8.25 (4.05, 19.14)	7.37 (3.59, 17.24)	5.22 (2.44, 12.56)	2.57 (1.06, 6.77)
P for trend	< .0001	< .0001	< .0001	0.0454

[a] Values are ORs (95% CIs) unless otherwise indicated. VFA, visceral fat area; LMM, leg muscle mass.

[b] Model 1: adjusted for age; Model 2: adjusted for age, smoking status (for men), menopause status (for women), drinking status, exercise frequency, and history of diseases (hypertension and diabetes); Model 3: additionally adjusted for systolic blood pressure, diastolic blood pressure, alanine aminotransferase, fasting plasma glucose, total cholesterol, triglycerides, low-density lipoprotein and high-density lipoprotein cholesterol, and creatinine. Model 4: adjusted for Model 3 + BMI.

[c] P values for linear trends were calculated using the median value of quartiles of VFA-to-LMM ratio.

In addition, we compared the prevalence of hyperuricemia and the odds ratios of hyperuricemia between men and women according to the quartiles of VFA-to-LMM ratio. As showed in Fig. 3, the prevalence of

hyperuricemia in women is significantly lower than that in men, but the risk of hyperuricemia in women is much higher than in men as the VFA-to-LMM ratio increasing.

The interaction of VFA and LMM on the risk of hyperuricemia

In the further analysis, we divided the subjects into 16 groups according to the quartiles of visceral fat area and leg muscle mass (the lowest quartile of VFA and the lowest quartile of LMM as the reference), and investigated the risk of hyperuricemia in each group after adjusting age and sex (Fig. 4). The figure showed that the risk of hyperuricemia raised with increasing VFA regardless of LMM, while the risk of hyperuricemia was relatively low when the LMM was in the second quantile at the same level of VFA. The highest risk of hyperuricemia was observed when VFA and LMM were both in the highest quantile (OR: 11.50; 95% CI: 4.86–31.98). The results suggested that there was an interaction between VFA and LMM, and the rising of the two would lead to a rapid increase of the risk of hyperuricemia.

Discussion

In the present study, we explored the association of VFA-to-LMM ratio with hyperuricemia. The results showed that the VFA-to-LMM ratio was positively associated with the risk of hyperuricemia in women after adjustments for age, BMI, smoking status (for males), menopause status (for females), drinking status, exercise frequency, SBP, DBP, ALT, FPG, TC, TG, LDL-C, HDL-C, creatinine, and history of diseases. In addition, the highest risk of hyperuricemia was observed when both VFA and LMM were at the highest quartile.

At present, the association between visceral fat mass and hyperuricemia has been confirmed by several studies. A study conducted by Huang et al. (23) found that visceral adipose accumulation was closely associated with hyperuricemia in Chinese adults. Similarly, a study from Takahashi et al. (24) also confirmed the important role of visceral fat accumulation in elevated blood uric acid levels of male obese subjects. Both studies have confirmed a significant association between increased visceral fat mass and hyperuricemia, and further compared the contribution of visceral and subcutaneous fat to the association. Consistent with previous studies, our results also showed a significant positive association between VFA and hyperuricemia. However, studies on the association between skeletal muscle mass of lower limbs and hyperuricemia are still limited. A cross-sectional study based on 7 544 adults revealed that serum uric acid negatively associated with skeletal muscle mass index (13). Similarly, Tanaka et al. (25) also found that a higher SUA level was associated with reduced muscle mass in men with diabetes. Conversely, several studies have found that higher serum uric acid level was a protective factor of muscle function (26–28), which can counteract the excessive production of free radicals that cause muscle protein damage and eventually lead to the decline of muscle mass and strength (29).

In the current study, we found that the increase of skeletal muscle mass (or VFA-to-SMM ratio) was not associated with hyperuricemia after adjusting BMI, but the VFA-to-LMM ratio was independently associated with the risk of hyperuricemia. The results indicated that the relative increase in skeletal muscle mass of the lower limbs has a greater contribution to the formation of hyperuricemia. There are several indirect evidences that can provide partial support. For example, a previous study had found that thigh circumference, a comprehensive indicator of leg muscle mass, was strongly associated with diabetes and could be used as a

good predictor (30). Another study conducted by Min et al. found that there was a negative association between thigh circumference and peripheral arterial disease when thigh circumference was less than 55 cm (31). The above evidence showed that the changes of leg composition are closely related to the body metabolism and health status, which may promote the formation of hyperuricemia.

The underlying mechanism of the association between body composition and hyperuricemia has not been clearly elucidated. There are several possible explanations for our results: Firstly, previous studies have confirmed that both visceral fat accumulation and skeletal muscle mass are significantly associated with insulin resistance (32, 33), which can lead to hyperuricemia in the following three ways: 1) IR can directly affect the reabsorption of uric acid by renal tubules and ultimately lead to the formation of hyperuricemia (34, 35); 2) IR can indirectly cause hyperinsulinemia, which in turn provoke hyperuricemia in a similar way; 3) IR could indirectly increase the production of NADPH by promoting the lipolysis pathway, which is an important source of serum uric acid and eventually leads to hyperuricemia (36, 37). Our results showed that the increase of VFA-to-LMM ratio had a higher risk of hyperuricemia than the increase of VFA alone, indicating that increased LMM may play a protective role in the association, which was consistent with previous studies. Secondly, as far as we know, visceral fat accumulation is significantly associated with metabolic syndrome, while relative skeletal muscle mass was confirmed to be inversely associated with the development of metabolic syndrome (38). Similarly, some studies have confirmed that SUA was closely related to the metabolic syndrome and may play a dual role as cause and consequence in it (39, 40). It is worth noting that Kim et al. also confirmed that women with metabolic syndrome had a higher risk of hyperuricemia when compared to men, which was consistent with our results. Besides, some studies have shown that the disorder of glucose and lipid metabolism is related to the abnormal secretion of leptin, which can further lead to the increase of serum uric acid (41). Finally, as we all know, there are considerable differences in both the distribution and mass of body fat and skeletal muscle between men and women due to the differences of sex hormone levels (42, 43). Compared with women, men have a higher SMM (or LMM), which may play a protective role, thereby reducing the risk of hyperuricemia in men. However, unlike women, visceral obesity in men is more closely related to BMI. Therefore, after adjustment for BMI, the association between VFA-to-LMM ratio and hyperuricemia was disappears in men. This could be an explanation for the significant sex differences in our results, and why women are at a higher risk.

There are three advantages in the present study. First of all, as far as we know, this is the first study on the association between VFA-to-LMM ratio and hyperuricemia. We conducted a comprehensive analysis of body composition, including VFA, LMM and their interactions. Secondly, all measurements and statistical analysis are performed in strict accordance with the standard procedures to ensure the accuracy of the data. Thirdly, given the significant sex differences in body composition, we stratified men and women in the analysis to ensure the reliability of the results. However, several limitations also need to be mentioned. Firstly, based on the cross-sectional data, we could not obtain the causality of VFA-to-LMM ratio and hyperuricemia, and could not further analyze its potential mechanism. Secondly, although we had adjusted as many confounding factors as possible, there were still factors that were not included. However, we adjusted as many confounders as possible to ensure the robustness of the results.

Conclusions

The results showed that the VFA-to-LMM ratio was positively associated with the risk of hyperuricemia in women after adjustments for confounding factors, and women were more sensitive than men to the risk of hyperuricemia caused by changes in body composition. In addition, the highest risk of hyperuricemia was observed when both VFA and LMM were at the highest quartile, suggesting that there was an interaction between VFA and LMM. However, well-controlled prospective studies are needed to further confirm the causality between VFA-to-LMM ratio and hyperuricemia.

List Of Abbreviations

ALT, Alanine aminotransferase; BMI, Body mass index; CI, Confidence interval; DBP, Diastolic blood pressure; FPG, Fasting plasma glucose; HDL-C, High-density lipoprotein cholesterol; IR, Insulin resistance; LDL-C, Low-density lipoprotein cholesterol; LMM, Leg muscle mass; NAFLD, Non-alcoholic fatty liver disease; OR, Odds ratio; SMM, Skeletal muscle mass; SUA, Serum uric acid; SBP, Systolic blood pressure; TC, Total cholesterol; TG, Triglycerides; VFA, visceral fat area.

Declarations

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Tianjin Union Medical Center, Nankai University affiliated hospital. All participants were informed about the study objectives and examination procedures in detailed, and were asked to sign the informed consent form before enrolled.

Consent for publication

All authors have read and approve the submission of the manuscript.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare no competing interests.

Funding

This work was partially supported by Grants from Natural Science Foundation of Tianjin (19JCZDJC36100 to C.J.L and 18ZXDBSY22120 to J.N.L) and National Key R&D Program of China (2016YFC0900600,

2016YFC0900604 to M.Y.Z).

Authorship:

CJL and JNL: contributed to the concept and design of the study;XHW and WRJ: contributed to the design of analysis, statistical analysis, and manuscript preparation; CJL, XHW, WRJ, YPJ, MYZ and YXS: contributed to coordination of the fieldwork, data collection and management, and interpretation of results and revision of manuscript drafts. All authors were involved in the interpretation of the results and the revision of the manuscript and approved the submitted version of the manuscript.

Acknowledgements

We gratefully acknowledge all the participants of the study and Tianjin Union Medical Center-Health Management Department and Nankai University affiliated hospital and for the possibility to perform the study.All data generated during this study can be freely obtained with the permission of corresponding authors.

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Figures

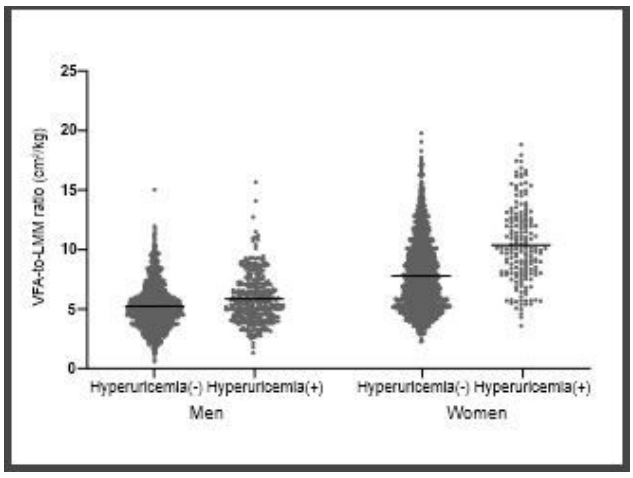

Figure 1

The differences in VFA-to-LMM ratio between hyperuricemia and non-hyperuricemia among men and women. VFA, visceral fat area; LMM, leg muscle mass.

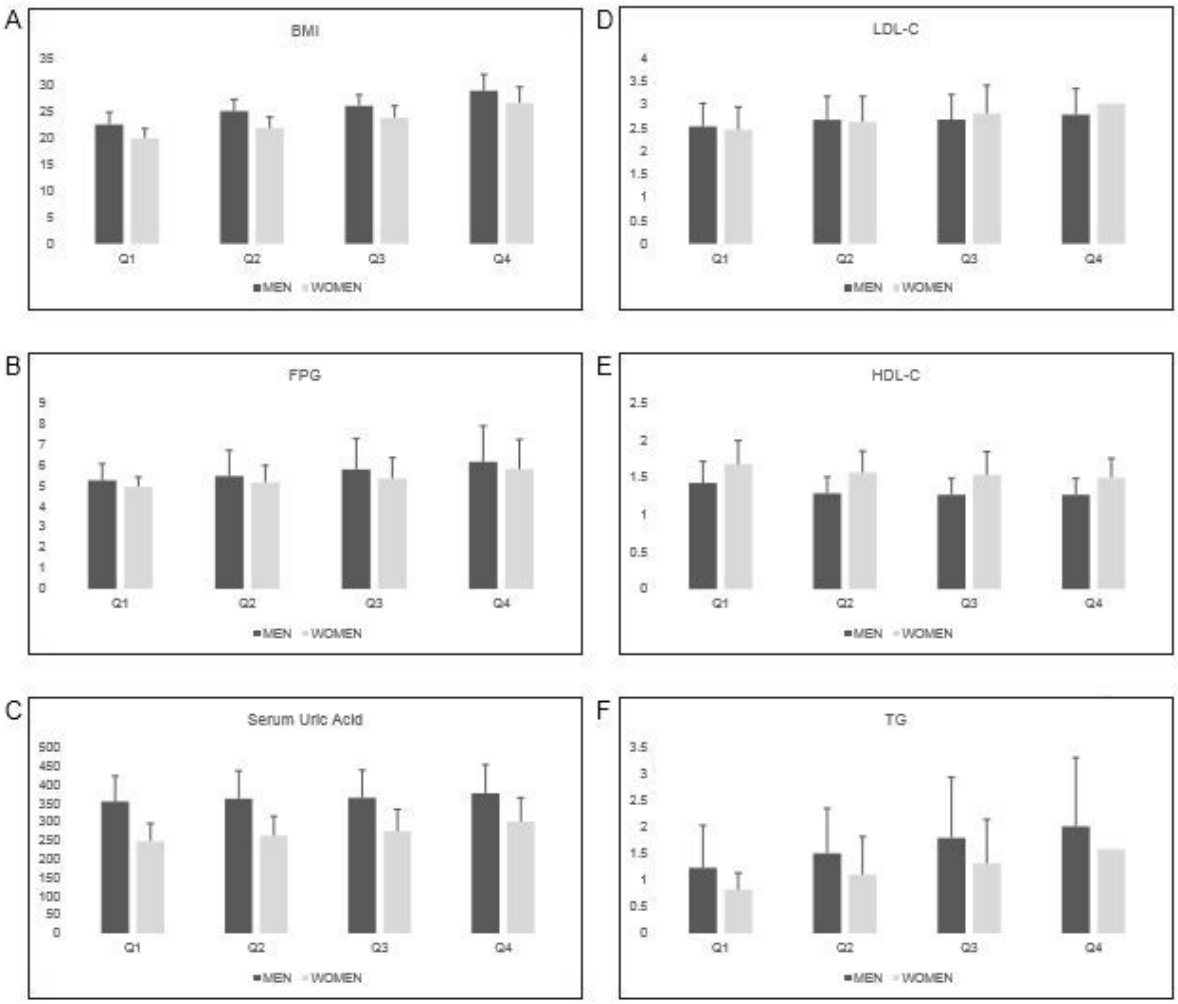

Figure 2

Characteristics of subjects according to quartiles of VFA-to-LMM ratio. (A) BMI, body mass index; (B) FPG, fasting plasma glucose; (C) Serum Uric Acid; (D) LDL-C, low-density lipoprotein cholesterol; (E) HDL-C, high-density lipoprotein cholesterol; (F) TG, triglycerides. VFA, visceral fat area; LMM, leg muscle mass.

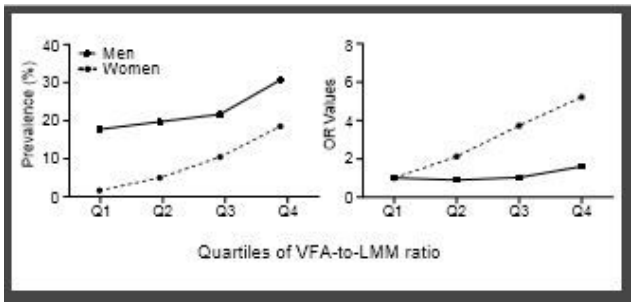

Figure 3

The odds ratio (A) and prevalence (B) for hyperuricemia according to quartiles of the visceral fat area to leg muscle mass ratio among men and women.

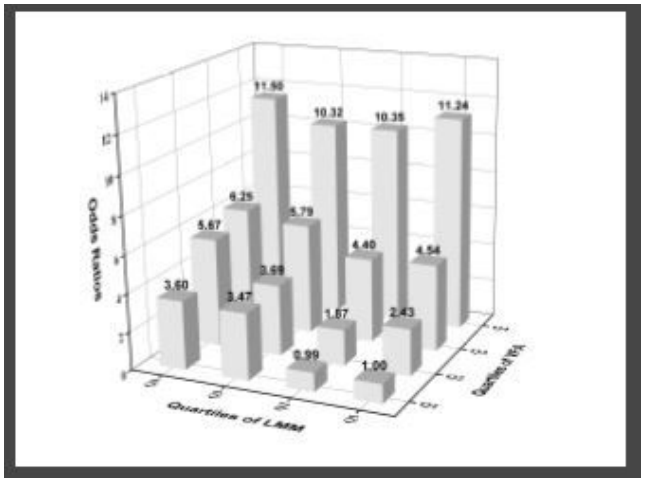

Figure 4

Age- and sex-adjusted odds ratios for hyperuricemia according to the quartiles of visceral fat area and leg muscle mass.