Lipids in Health and Disease

RESEARCH

Open Access

Identifying reliable obesity indices for hyperuricemia among middle-aged and elderly populations: a longitudinal study

Yuntong Liu[1,2†], Wei Zhao[2†], Xuhan Liu[2], Haodong Jiang[3], Yixia Wu[2], Lan Luo[2*] and Zhengnan Gao[2*]

Abstract

Background Given the established link between obesity and hyperuricemia (HUA), the research want to investigate the relationship between different obesity indices and HUA, and further analyze which obesity index can better predict HUA.

Methods The data were obtained from a longitudinal study involving middle-aged and elderly populations in Dalian, China. The research encompassed individuals who exhibited typical uric acid levels initially and tracked their progress over a three-year period. 8 obesity indices were evaluated retrospectively. Subgroup analyses were conducted to identify susceptible populations. Restricted cubic splines (RCS) were utilized to model the dose-response relationships between obesity indices and HUA. Receiver operating characteristic (ROC) curves were applied to visualize and compare the predictive value of both traditional and new obesity indices for HUA.

Results Among 4,112 individuals with normal baseline uric acid levels, 950 developed HUA. Significant associations with HUA were observed for body mass index (BMI), waist circumference (WC), body roundness index (BRI), cardiometabolic index (CMI), visceral adiposity index (VAI), Chinese visceral adiposity index (CVAI), lipid accumulation product (LAP), and abdominal volume index (AVI). Subgroup analysis indicated that all obesity indices proved more effective in assessing the onset of HUA in women without Metabolic Syndrome (MetS). Further analysis using RCS revealed non-linear dose-response relationships between LAP, CMI, VAI, and HUA in males, with similar non-linear relationships observed for all indices in females. The results from the ROC curves indicate that LAP may serve as a better predictor of HUA in males, and CVAI may serve as a better predictor in females.

Conclusion HUA is closely associated with obesity indices. Among females, CVAI emerges as the preferred predictive index for HUA. In males, LAP emerges as the preferred predictive index for HUA.

Keywords Obesity indices, Hyperuricemia, Metabolic syndrome, Longitudinal study

†Yuntong Liu and Wei Zhao contributed equally to this work.

*Correspondence:
Lan Luo
rolland_304224@sohu.com
Zhengnan Gao
gao2008@dlut.edu.cn

[1]Dalian municipal Central Hospital, China Medical University, Shenyang, China
[2]Department of Endocrinology, Dalian Municipal Central Hospital, Dalian, China
[3]Department of Cardiovascular, the Second Hospital of Jilin University, Changchun, China

Background

Hyperuricemia (HUA) is defined by elevated serum uric acid (SUA) levels, which occur when uric acid production exceeds excretion. The condition is characterized by serum uric acid levels exceeding 420 μmol/L in men and 360 μmol/L in women [1]. Literature indicates that HUA elevates the risk of multiple conditions, including gout, hypertension, diabetes, stroke, chronic kidney disease, metabolic syndrome (MetS), and non-alcoholic fatty liver disease [2–5], significantly impacting quality of life. Recent changes in dietary habits, particularly increased consumption of high-purine and sugary foods [6], have increased the prevalence of HUA. The prevalence among Chinese adults rose from 11.1% in 2015-16 to 14.0% in 2018-19, with a higher occurrence in males [7]. In the United States, the incidence rate was reported as 21% according to the 2007–2008 NHANES survey [8]. Given the significant impact of HUA on health, managing and mitigating HUA and its associated complications is now a pivotal public health priority.

Obesity can be categorized into general and central obesity. BMI is typically used to evaluate general obesity, while WC is employed to assess central obesity. However, these measurements do not identify the differences between subcutaneous and visceral fat [9]. Visceral fat, which is stored within or between internal organs such as the liver and intestines [10], is influenced by factors including epigenetics, race, aging, and hormonal changes [11–13]. Increased visceral fat is more strongly linked to metabolic disorders (including disturbances in glucose, lipid, and uric acid metabolism) and a higher incidence of cardiovascular diseases [14]. Obesity, particularly increased visceral adipose tissue, significantly increases the risk of HUA. Traditional obesity indices have limitations in accurately measuring and distributing body fat, which has resulted in the creation of new indices for improved identification of central and visceral fat [15, 16]. Recent obesity indices include the AVI [17], BRI [18], VAI [19], CVAI [20], LAP [21], and CMI [22]. Compared to traditional indices, these new obesity-related indices provide a better reflection of body fat content, especially visceral fat.

Numerous longitudinal studies have examined the relationship between obesity indicators and HUA, yet the findings remain inconsistent. Additionally, significant debate persists over the merits and limitations of various obesity indicators, particularly concerning their applicability across different genders. Current research is inadequate in addressing the associations between both traditional and innovative obesity indicators and HUA. Consequently, this study seeks to explore these relationships further and evaluate their potential to predict HUA in community-dwelling individuals. Due to gender differences in fat distribution [23], gender-specific analyses were conducted to develop more accurate predictive tools that can enhance the early detection and prevention of HUA within the community.

Methods

Research subject

The REACTION (Risk Evaluation of Cancers in Chinese Diabetic Individuals: A Longitudinal Study) was a multicenter, population-based prospective cohort study conducted from 2011 to 2012. It involved 259,657 individuals aged 40 and older from 25 centers across various geographical regions of China, the follow-up period spanned from 2014 to 2016 [24, 25]. This study is part of the Dalian center of the REACTION study. The research at the Dalian branch involved 10,207 participants who were recruited in 2011 from six communities through cluster random sampling, with follow-up conducted in 2014. Given that follow-up occurred at the same two time points for all participants, the median follow-up time is consistently three years. The inclusion criteria were individuals with normal baseline SUA levels. The exclusion criteria included incomplete data collection, a history of gout, age under 40, and loss to follow-up. The study encompassed a total of 4,112 participants. The screening process is depicted in Fig. 1. The research protocol conformed to the Declaration of Helsinki. All participants provided written informed consent, and the protocol was approved by the Ethical Review Committee of Ruijin Hospital (RUIJIN-2011-14).

Initial data gathering

The personnel assisting with the survey consisted of medical and nursing staff from the Endocrinology Department at the Central Hospital of Dalian. All personnel underwent training at Ruijin Hospital in Shanghai prior to initiating this epidemiological survey. Personal information was collected through questionnaires, including gender, age, marital status, smoking and alcohol consumption history, medication history, educational background, and history of coronary heart disease (CHD). Alcohol consumption was categorized into three groups: never drinkers, occasional drinkers (less than once weekly) and regular drinkers (at least once weekly for over six months). Similarly, smoking status was defined in three categories: never smokers, occasional smokers (less than one cigarette daily or fewer than seven weekly), and regular smokers (at least one cigarette daily). Participants were required to fast from 10 PM the night before the survey and maintain an overnight fast of over 12 h before collecting venous blood from the right arm to measure fast plasma glucose (FPG), lipid profile, liver and kidney function and SUA. Heights and weights were measured using an RGZ-120 body scale. Blood pressure and heart rate were also measured. The people have been

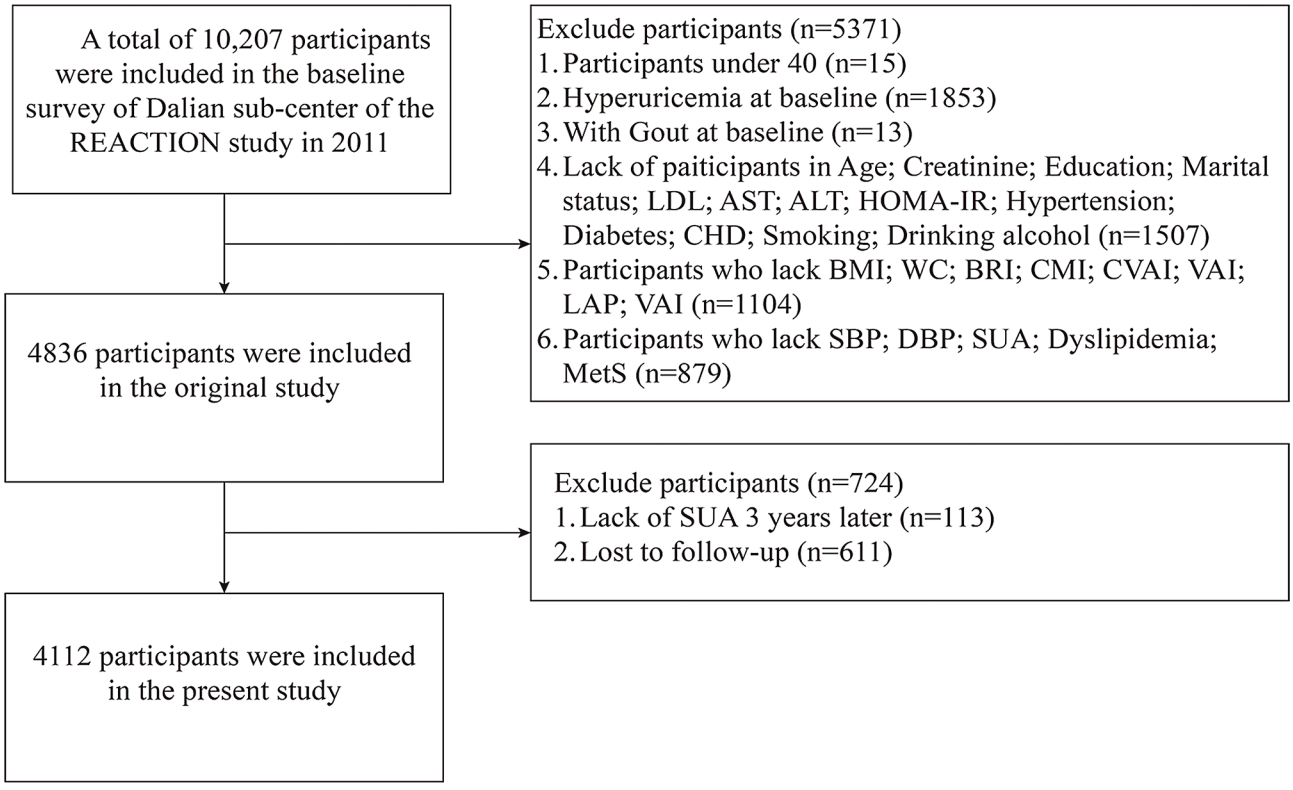

Fig. 1 Screening flowchart

$$BMI = Weight\ (kg) / Height\ (m)^2$$
$$BRI = 364.2 - 365.5 \times [1 - WC^2\ (m) / (\pi^2 \times Height^2\ (m))]^{1/2}$$
$$LAP\ for\ males = [WC\ (cm) - 65] \times TG$$
$$LAP\ for\ females = [WC\ (cm) - 58] \times TG$$
$$VAI\ for\ males = WC\ (cm) / (39.68 + 1.88 \times BMI) \times TG / 1.03 \times 1.31 / HDL\text{-}C$$
$$VAI\ for\ females = WC\ (cm) / (36.58 + 1.89 \times BMI) \times TG / 0.81 \times 1.52 / HDL\text{-}C$$
$$CMI = TG/\ HDL\text{-}C \times Waist\text{-}to\text{-}Height\ Ratio\ (WHtR)$$
$$CVAI\ for\ males = -267.93 + 0.68 \times Age + 0.03 \times BMI + 4.00 \times WC + 22 \times \log10(TG) - 16.32 \times HDL\text{-}C$$
$$CVAI\ for\ females = -187.32 + 1.71 \times Age + 4.23 \times BMI + 1.12 \times WC + 39.76 \times \log10\ (TG) - 11.66 \times HDL\text{-}C$$
$$AVI = [WC^2\ (cm) + 0.7 \times (WC - HC)^2\ (cm)] / 1000$$

Fig. 2 Obesity indices calculation formulas

seated and resting for at least five minutes, using the same model Omron blood pressure monitor on the right arm, with an average of three measurements taken.

Grouping standards and related definitions

Hypertension diagnostic criteria: meeting one of the following: Taking antihypertensive drugs or having a blood pressure above current norms (140/90mmHg).

Diabetes diagnostic criteria: meeting one of the following: Taking hypoglycemic drugs, FPG, 2-hour postprandial glucose, and glycation above current standards [26].

MetS diagnostic criteria: meeting this criteria.

Homeostatic Model Assessment for Insulin Resistance (HOMA-IR): FPG(mmol/L) × Insulin(μU/mL) / 22.5.

Obesity indices calculation formulas

Figure 2 displays the methods used to calculate obesity indices.

Statistical analysis

Categorical data was presented with frequency and percentage (n%), and group comparisons were done using the chi-square test. The Kolmogorov-Smirnov test was employed to assess the normality of the data. For comparing two groups, t-tests were employed with normally distributed data. Using the median (P25, P75) and U-tests for data not following a normal distribution. Binary logistic regression examined the link between obesity indices and HUA. The newly introduced obesity indices lack established cutoff points. Consequently, the independent variables were categorized into quartiles for analysis. All obesity indices were normalized using the Z-score method, with the relative risk increase reported per standard deviation and statistical significance assessed through score tests when the associations are linear. A multivariate logistic regression model was employed for trend testing, coding categorical variables as numerical variables and including them as predictors in the regression model. Three models were constructed: Model 1 was unadjusted; Model 2 accounted for age, marital status, and educational level; Model 3 included further adjustments for a history of hypertension, diabetes, CHD, smoking status, drinking status, creatinine, LDL, ALT, AST, and HOMA-IR. Interaction terms were used to assess subgroup heterogeneity, a P-value < 0.05 indicated statistically significant interactions. Subgroup analysis was additionally used to pinpoint vulnerable groups. Curve fitting was performed using 3-knots restricted cubic spline (RCS) methods. Lastly, receiver operating characteristic (ROC) curves were employed to develop a foundational model using a stepwise approach. Eight obesity indices were progressively incorporated into the model. The enhancement in predictive power for HUA was evaluated and compared using the area under the curve (AUC). All analyses used EmpowerStats (version 4.2), and R software (version 4.3.3). Significance set at $P < 0.05$, two-tailed.

Results

Baseline characteristics

As indicated in Table 1; Fig. 3, among the male group, individuals who developed to HUA exhibited increased baseline levels of SUA, weight, WC, BMI, BRI, CMI, VAI, CVAI, LAP, AVI, Creatinine, TG, ALT, Insulin, and HOMA-IR. Their levels of HDL were notably lower. Additionally, increases in baseline hypertension, CHD, dyslipidemia, MetS, and regular alcohol consumption were observed in the HUA group, whereas fewer exhibited baseline diabetes. In the female group, individuals with HUA exhibited higher baseline age, SUA, weight, WC, BMI, BRI, CMI, ABSI, VAI, CVAI, LAP, AVI, Creatinine, LDL, TG, ALT, AST, FPG, Insulin, and HOMA-IR. Their levels of HDL were significantly lower. Additionally, there was a higher likelihood of baseline hypertension, diabetes, CHD, dyslipidemia, and MetS in patients with HUA.

Relationship between obesity indices and HUA based on sex

The associations between eight obesity indices and HUA after adjusting for potential covariates are shown in Tables 2 and 3. All obesity indices were normalized using the Z-score method, reporting the relative risk increase per standard deviation and assessing statistical significance through score tests when the associations are linear. In the fully adjusted model for males, the odds ratio (OR) increased by 1.42 (95% CI: 1.20, 1.67) for each standard deviation increase in BMI, by 1.45 (95% CI: 1.23, 1.71) for WC, by 1.45 (95% CI: 1.24, 1.70) for BRI, by 1.36 (95% CI: 1.17, 1.58) for CMI, by 1.53 (95% CI: 1.30, 1.81) for CVAI, by 1.33 (95% CI: 1.14, 1.54) for VAI, by 1.41 (95% CI: 1.20, 1.64) for LAP, and by 1.43 (95% CI: 1.22, 1.67) for AVI. In females, in the fully adjusted model, the OR increased by 1.67 (95% CI: 1.52, 1.83) for each standard deviation increase in BMI, by 1.61 (95% CI: 1.46, 1.78) for WC, by 1.58 (95% CI: 1.44, 1.73) for BRI, by 1.41 (95% CI: 1.29, 1.55) for CMI, by 2.05 (95% CI: 1.84, 2.29) for CVAI, by 1.34 (95% CI: 1.23, 1.47) for VAI, by 1.55 (95% CI: 1.41, 1.70) for LAP, and by 1.57 (95% CI: 1.43, 1.73) for AVI. Assessing statistical significance through score tests, all obesity indices showed significant associations with HUA in both males and females ($P < 0.05$). In males, compared to the first quartile, the OR for the highest quartile of BMI was 2.22, 95% CI: (1.41, 3.49); for WC was 2.71, 95% CI: (1.71, 4.30); for CMI was 2.83, 95% CI: (1.78, 4.49); for BRI was 2.58, 95% CI: (1.63, 4.07); for CVAI was 3.09, 95% CI: (1.95, 4.89); for VAI was 2.82, 95% CI: (1.78, 4.48); for LAP was 3.01, 95% CI: (1.86, 4.87); for AVI was 2.55, 95% CI: (1.62, 4.00). In females, the OR for the highest quartile of BMI was 3.68, 95% CI: (2.75, 4.91); for WC was 3.55, 95% CI: (2.66, 4.74); for BRI was 4.00, 95% CI: (2.97, 5.40); for CMI was 4.65, 95% CI: (3.37, 6.41); for CVAI was 8.20, 95% CI: (5.72, 11.75); for VAI was 3.41, 95% CI: (2.52, 4.61); for LAP was 7.21, 95% CI: (5.04, 10.32); for AVI was 3.87, 95% CI: (2.88, 5.20). All obesity indices showed a positive correlation with HUA that increased progressively across quartiles, maintaining a positive trend (P-trend < 0.001). All obesity indices were demonstrated to have a causal relationship with HUA.

Subgroup analysis

To further explore the relationship between obesity indices and HUA across different subgroups, this study conducted subgroup analyses based on age, hypertension, diabetes, and MetS. According to Fig. 4, among male subgroups stratified by age, hypertension, diabetes, and

Table 1 Baseline characteristics for 4112 subjects

Characteristics	Male (*N* = 1010)			Female (*N* = 3102)		
	HUA (*N* = 269)	Control (*N* = 741)	*P*-value	HUA (*N* = 681)	Control (*N* = 2421)	*P*-value
Age (years)	59.95 (55.30, 64.97)	59.97 (54.95, 66.05)	0.643	57.60 (52.99, 62.88)	55.45 (51.26, 60.33)	< 0.001
Hypertension (%)	192 (71.7)	420 (56.7)	< 0.001	463 (68.0)	1140 (47.1)	< 0.001
Diabetes (%)	71 (26.4)	273 (36.8)	0.002	165 (24.2)	459 (19.0)	0.002
CHD (%)	24 (8.9)	38 (5.1)	0.026	39 (5.7)	83 (3.4)	0.006
Dyslipidemia (%)	129 (48.0)	301 (40.6)	0.037	352 (51.7)	940 (39.8)	< 0.001
MetS (%)	129 (48.0)	238 (32.1)	< 0.001	319 (46.8)	609 (25.2)	< 0.001
Smoking (%)			0.339			0.475
No	146 (54.3)	439 (59.2)		672 (98.7)	2383 (98.4)	
occasionally	13 (4.8)	36 (4.9)		4 (0.6)	25 (1.0)	
frequently	110 (40.9)	266 (35.9)		5 (0.7)	13 (0.5)	
Drinking (%)			0.010			0.664
No	98 (36.4) a	320 (43,2) a		597 (87.7)	2118 (87.5)	
occasionally	78 (29.0) a	236 (31.8) a		80 (11.7)	280 (11.6)	
frequently	93 (34.6) a	185 (25.0) b		5 (0.7)	23 (1.0)	
Education (%)			0.062			0.286
Primary school and lower	219 (81.4)	562 (75.8)		601 (88.3)	2099 (86.7)	
middle and high school	50 (18.6)	179 (24.2)		80 (11.7)	322 (13.3)	
Marriage (%)			0.220			0.582
Married	260 (96.7)	706 (95.3)		598 (87.8)	2166 (89.5)	
Single	0 (0)	3 (0.4)		2 (0.3)	10 (0.4)	
Divorced or widowed	3 (1.1)	3 (0.4)		2 (0.3)	6 (0.2)	
Other	6 (2.2)	29 (3.9)		79 (11.6)	239 (9.9)	
SUA (μmol/L)	370.00 (342.00, 394.00)	319.00 (286.00, 354.00)	< 0.001	310.00 (282.00, 332.00)	267.00 (235.00, 296.00)	< 0.001
Height (cm)	169.00 (165.00, 173.50)	169.00 (165.00, 174.00)	0.623	158.50 (155.00, 162.00)	159.00 (155.00, 162.00)	0.225
Weight (Kg)	75.00 (68.00, 82.00)	72.50 (65.00, 80.00)	< 0.001	66.00 (60.00, 73.00)	62.00 (56.00, 68.00)	< 0.001
BMI (Kg/m2)	26.49 (24.33, 28.26)	25.20 (23.25, 27.35)	< 0.001	26.49 (24.44, 28.72)	24.65 (22.66, 26.77)	< 0.001
WC (cm)	96.00 (90.00, 100.00)	93.00 (86.00, 98.50)	< 0.001	92.00 (85.00, 98.00)	87.00 (80.00, 93.00)	< 0.001
BRI	4.66 (4.00, 5.27)	4.26(3.54, 5.04)	< 0.001	4.98(4.16, 5.83)	4.29(3.48, 5.15)	< 0.001
CMI	0.69 (0.42, 1.00)	0.50 (0.33, 0.76)	< 0.001	0.63 (0.44, 0.90)	0.44 (0.29, 0.69)	< 0.001
VAI	1.66 (1.03, 2.41)	1.26 (0.81, 1.86)	< 0.001	2.17 (1.50, 3.03)	1.57 (1.04, 2.38)	< 0.001
CVAI	139.03 (114.77, 160.88)	123.59 (98.15, 149.52)	< 0.001	118.51 (99.47, 138.25)	95.72 (73.43, 118.46)	< 0.001
LAP	41.70 (28.30, 64.43)	31.32 (20.77, 48.81)	< 0.001	48.64 (34.15, 68.31)	33.60 (21.28, 51.48)	< 0.001
AVI	9.23 (8.17, 10.04)	8.66 (7.53, 9.75)	< 0.001	8.47 (7.48, 9.63)	7.61 (6.61, 8.75)	< 0.001
Creatinine (μmol/L)	72.70 (68.00, 82.65)	72.40 (67.00, 81.10)	0.096	61.50 (56.60, 66.25)	60.40 (56.30, 65.20)	0.001
HDL (mmol/L)	1.20 (1.08, 1.38)	1.26 (1.10, 1.48)	0.002	1.35 (1.18, 1.54)	1.46 (1.28, 1.67)	< 0.001
LDL (mmol/L)	3.19 (2.69, 3.78)	3.12 (2.64, 3.64)	0.112	3.38 (2.86, 3.95)	3.27 (2.73, 3.85)	0.013
TG (mmol/L)	1.43 (1.01, 1.97)	1.16 (0.88, 1.62)	< 0.001	1.47 (1.12, 1.98)	1.16 (0.86, 1.65)	< 0.001
ALT (U/L)	19.00 (15.00, 25.50)	17.00 (13.00, 22.50)	< 0.001	17.00 (13.00, 23.00)	15.00 (12.00, 20.00)	< 0.001
AST (U/L)	22.00 (18.00, 26.00)	21.00 (18.00, 25.00)	0.105	21.00 (18.00, 25.00)	21.00 (18.00, 24.00)	0.003
FPG (mmol/L)	5.89 (5.40, 6.56)	5.94 (5.42, 7.20)	0.219	5.73 (5.35, 6.27)	5.54 (5.20, 6.09)	< 0.001
Insulin	8.00 (5.90, 10.20)	6.50 (4.70, 9.50)	< 0.001	9.00 (6.70, 12.15)	7.20 (5.30, 9.90)	< 0.001
HOMA-IR	2.12 (1.53, 3.11)	1.87 (1.24, 2.90)	0.008	2.37 (1.68, 3.32)	1.84 (1.30, 2.67)	< 0.001

Data are expressed as mean (P25, P75) or number (percent). Abbreviation: HUA, hyperuricemia; CHD, coronary heart disease; MetS, metabolic syndrome; SUA, serum uric acid; BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FPG, fast plasma glucose; HOMA-IR, Homeostatic model assessment for insulin resistance

MetS, there was a similar relationship between all obesity indices and HUA (P for interaction > 0.05). BMI, WC, CMI, CVAI, and AVI showed significant interactions with the age subgroups in females (P for interaction < 0.05), with a more pronounced OR for HUA in those under 60 years of age. BMI, WC, BRI, CVAI, and AVI exhibited interactions with the diabetes subgroups (P for interaction < 0.05), showing a more significant OR for HUA in the non-diabetes population. WC, CMI, CVAI, VAI, AVI, and LAP also had interactions with the

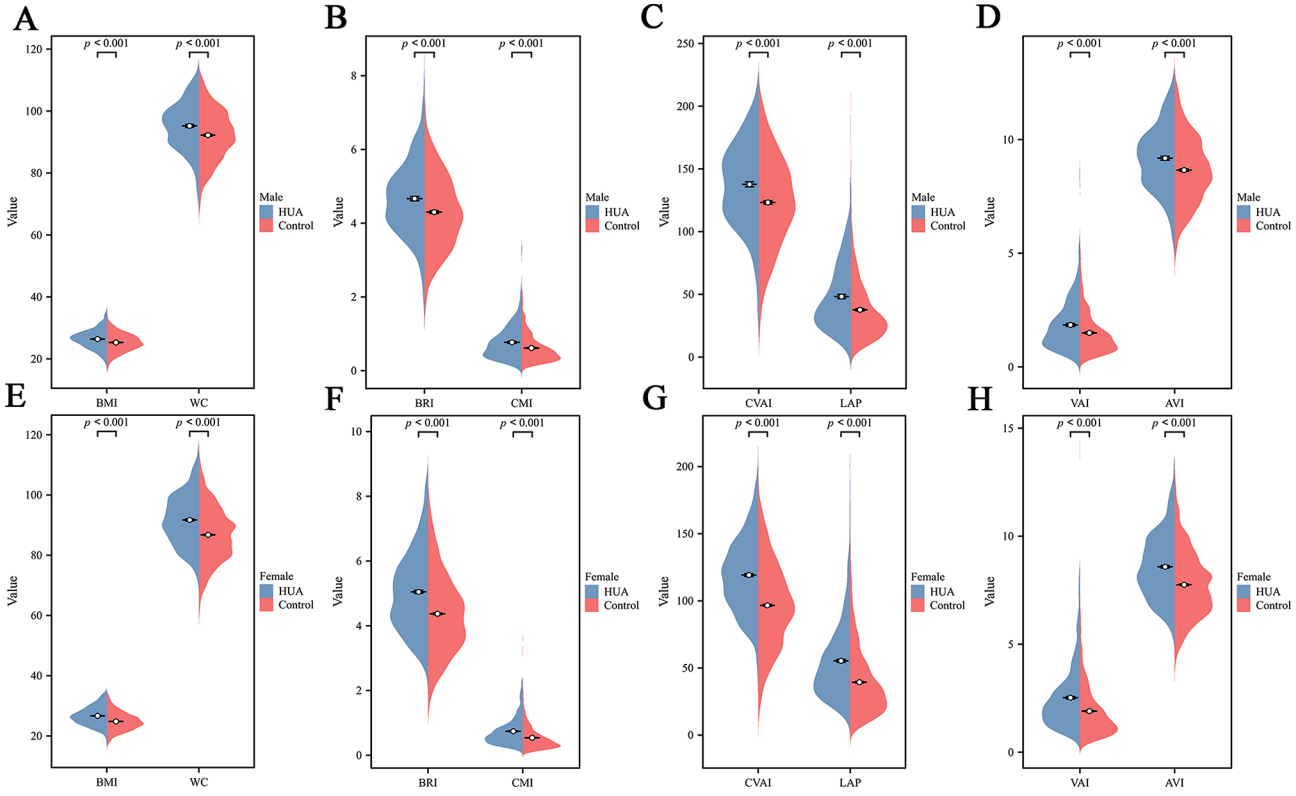

Fig. 3 The comparison of different obesity indices between the HUA group and the Control group the comparison of WC and BMI (**A**), BRI and CMI (**B**), CVAI and LAP (**C**), VAI and AVI (**D**) between the HUA group and the Control group in male, and comparison of WC and BMI (**E**), BRI and CMI (**F**), CVAI and LAP (**G**), VAI and AVI (**H**) between the HUA group and the Control group in female. Abbreviation: BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index

hypertension subgroups (P for interaction < 0.05), indicating a higher OR for HUA in those without hypertension. Furthermore, all obesity indices in females showed interactions with the MetS subgroups (P for interaction < 0.05), being stronger in those without MetS. Subgroup RCS analyses were subsequently conducted, with the results shown in Supplementary Material 1.

Dose-response relationship between obesity indices and HUA

Figure 5 depicts the dose-response associations between various obesity indices and HUA, utilizing RCS for visualization and analysis. Following adjustments for multiple covariates, an escalation in obesity indices was linked with an elevated risk of HUA. In males, non-linear dose-response patterns were evident for CMI, VAI, and LAP (non-linear P < 0.05), exhibiting threshold values at 0.85, 2.04, and 53.08, respectively. Conversely, a linear correlation with HUA risk was observed as WC, BMI, BRI, CVAI, and AVI increased (non-linear P = 0.630, 0.997, 0.295, 0.511, and 0.478, respectively), with threshold values at 100.00, 27.68, 5.10, 152.94, and 10.00. For females, non-linear dose-response relationships were apparent across WC, BMI, BRI, CMI, CVAI, VAI, LAP, and AVI with HUA (non-linear P < 0.05), with respective threshold values of 94, 27.24, 5.33, 0.75, 124.11, 2.60, 55.74, and 8.99.

Validation of HUA diagnoses using ROC curves analysis

A stepwise approach was employed to develop a baseline model that incorporates various non-obesity metrics, including age, hypertension, diabetes, CHD, smoking status, drinking status, creatinine, LDL, ALT, AST, and HOMA-IR. 8 obesity indices were then separately integrated into the model, segmented by gender, as depicted in Fig. 6; Table 4, assessing their impact on the model's AUC. In this study, the initial baseline AUC for males was 0.668 (95% CI: 0.631, 0.704). It increased to 0.683 (95% CI: 0.648, 0.719) with the inclusion of BMI, to 0.688 (95% CI: 0.653, 0.724) with WC, to 0.693 (95% CI: 0.658, 0.728) with BRI, to 0.693 (95% CI: 0.658, 0.729) with CMI, to 0.697 (95% CI: 0.662, 0.732) with CVAI, to 0.691 (95% CI: 0.655, 0.727) with VAI, to 0.697 (95% CI: 0.662, 0.732) with LAP, and to 0.688 (95% CI: 0.652, 0.723) with AVI. In males, all indicators, except for BMI, significantly enhanced the model's predictive accuracy (P < 0.05), with LAP yielding the highest incremental predictive value. This was followed by CVAI, CMI, BRI, VAI, WC, AVI,

Table 2 The relationship between different obesity indices and HUA in male

		Model 1		Model 2		Model 3	
		OR (95% CI)	***P*-value**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
BMI		1.45 (1.25, 1.67)	< 0.001	1.44 (1.25, 1.67)	< 0.001	1.42 (1.20, 1.67)	< 0.001
BMI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.29 (0.84, 2.00)	0.249	1.31 (0.85, 2.03)	0.226	1.26 (0.80, 1.98)	0.325
	Q3	2.08 (1.37, 3.15)	< 0.001	2.03 (1.34, 3.09)	< 0.001	1.88 (1.20, 2.94)	0.006
	Q4	2.36 (1.56, 3.55)	< 0.001	2.33 (1.54, 3.52)	< 0.001	2.22 (1.41, 3.49)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
WC		1.47 (1.27, 1.70)	< 0.001	1.45 (1.25, 1.69)	< 0.001	1.45 (1.23, 1.71)	< 0.001
WC	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.98 (1.25, 3.14)	0.004	1.94 (1.22, 3.08)	0.005	1.63 (1.01, 2.64)	0.046
	Q3	2.32 (1.51, 3.56)	< 0.001	2.30 (1.50, 3.53)	< 0.001	2.02 (1.28, 3.17)	0.002
	Q4	2.91 (1.89, 4.48)	< 0.001	2.86 (1.85, 4.40)	< 0.001	2.71 (1.71, 4.30)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
BRI		1.45 (1.25, 1.67)	< 0.001	1.46 (1.26, 1.69)	< 0.001	1.45 (1.24, 1.70)	D
BRI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.22 (1.43, 3.45)	< 0.001	2.18 (1.40, 3.39)	< 0.001	1.86 (1.18, 2.93)	0.008
	Q3	2.52 (1.63, 3.90)	< 0.001	2.46 (1.58, 3.82)	< 0.001	2.07 (1,31, 3.27)	0.002
	Q4	2.73 (1.77, 4.21)	< 0.001	2.74 (1.77, 4.25)	< 0.001	2.58 (1.63, 4.07)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
CMI		1.42 (1.24, 1.62)	< 0.001	1.41 (1.23, 1.62)	< 0.001	1.36 (1.17, 1.58)	< 0.001
CMI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.40 (0.90, 2.19)	0.137	1.42 (0.90, 2.22)	0.129	1.33 (0.83, 2.11)	0.238
	Q3	2.25 (1.47, 3.45)	< 0.001	2.23 (1.46, 3.42)	< 0.001	2.30 (1.46, 3.63)	< 0.001
	Q4	2.97 (1.96, 4.51)	< 0.001	2.93 (1.92, 4.46)	< 0.001	2.83 (1.78, 4.49)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
CVAI		1.53 (1.31, 1.77)	< 0.001	1.55 (1.33, 1.80)	< 0.001	1.53 (1.30, 1.81)	< 0.001
CVAI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.13 (1.37, 3.32)	< 0.001	2.10 (1.35, 3.28)	0.001	1.74 (1.10, 2.76)	0.019
	Q3	2.09 (1.34, 3.26)	0.001	2.11 (1.35, 3.30)	0.001	1.77 (1.11, 2.81)	0.017
	Q4	3.35 (2.18, 5.14)	< 0.001	3.42 (2.21, 5.29)	< 0.001	3.09 (1.95, 4.89)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
VAI		1.39 (1.21, 1.59)	< 0.001	1.39 (1.21, 1.59)	< 0.001	1.33 (1.14, 1.54)	< 0.001
VAI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.84 (1.19, 2.84)	0.006	1.83 (1.18, 2.84)	0.007	1.64 (1.04, 2.60)	0.033
	Q3	1.87 (1.21, 2.90)	0.005	1.86 (1.20, 2.88)	0.005	1.90 (1.20, 3.01)	0.006
	Q4	3.11 (2.04, 4.73)	< 0.001	3.05 (2.00, 4.66)	< 0.001	2.82 (1.78, 4.48)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
LAP		1.47 (1.28, 1.69)	< 0.001	1.46 (1.27, 1.68)	< 0.001	1.41 (1.20, 1.64)	< 0.001
LAP	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.81 (1.15, 2.83)	0.01	1.82 (1.16, 2.85)	0.01	1.58 (0.99, 2.53)	0.055
	Q3	2.35 (1.52, 3.65)	< 0.001	2.35 (1.51, 3.65)	< 0.001	2.15 (1.35, 3.42)	0.001
	Q4	3.46 (2.25, 5.31)	< 0.001	3.39 (2.20, 5.22)	< 0.001	3.01 (1.86, 4.87)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
AVI		1.44 (1.25, 1.66)	< 0.001	1.43 (1.24, 1.65)	< 0.001	1.43 (1.22, 1.67)	< 0.001
AVI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.69 (1.08, 2.62)	0.02	1.65 (1.06, 2.58)	0.027	1.40 (0.88, 2.22)	0.16
	Q3	2.33 (1.52, 3.58)	< 0.001	2.31 (1.51, 3.55)	< 0.001	2.04 (1.30, 3.21)	0.001
	Q4	2.73 (1.79, 4.16)	< 0.001	2.67 (1.75, 4.08)	< 0.001	2.55 (1.62, 4.00)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	

Model 1: unadjusted. Model 2: further adjusted for age, education, marriage. Model3: further adjusted for hypertension, diabetes, CHD, smoking history, drinking history, creatinine, LDL, AST, ALT, HOMA-IR. Abbreviation: Ref, reference; CHD, coronary heart disease; LDL, low-density lipoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HOMA-IR, Homeostatic model assessment for insulin resistance; BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index; Q, quartile; OR, odds ratio; CI, confidence interval

Table 3 The relationship between different obesity indices and HUA in female

		Model 1		Model 2		Model 3	
		OR (95% CI)	***P*-value**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
BMI		1.81 (1.66, 1.98)	< 0.001	1.77 (1.62, 1.94)	< 0.001	1.67 (1.52, 1.83)	< 0.001
BMI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	1.93 (1.44, 2.60)	< 0.001	1.91 (1.42, 2.58)	< 0.001	1.76 (1.30, 2.38)	< 0.001
	Q3	3.05 (2.30, 4.06)	< 0.001	2.93 (2.20, 3.90)	< 0.001	2.59 (1.93, 3.46)	< 0.001
	Q4	4.70 (3.56, 6.19)	< 0.001	4.42 (3.34, 5.85)	< 0.001	3.68 (2.75, 4.91)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
WC		1.75 (1.60, 1.92)	< 0.001	1.69 (1.54, 1.85)	< 0.001	1.61 (1.46, 1.78)	< 0.001
WC	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.23 (1.66, 3.01)	< 0.001	2.13 (1.58, 2.88)	< 0.001	2.01 (1.48, 2.73)	< 0.001
	Q3	2.79 (2.08, 3.73)	< 0.001	2.61 (1.94, 3.51)	< 0.001	2.39 (1.77, 3.23)	< 0.001
	Q4	4.46 (3.38, 5.88)	< 0.001	4.00 (3.01, 5.31)	< 0.001	3.55 (2.66, 4.74)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
BRI		1.70 (1.56, 1.86)	< 0.001	1.63 (1.49, 1.79)	< 0.001	1.58 (1.44, 1.73)	< 0.001
BRI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.71 (2.01, 3.64)	< 0.001	2.62 (1.94, 3.53)	< 0.001	2.44 (1.80, 2.31)	< 0.001
	Q3	2.84 (2.11, 3.82)	< 0.001	2.67 (1.98, 3.60)	< 0.001	2.46 (1,82, 3.34)	< 0.001
	Q4	5.07 (3.81, 6.75)	< 0.001	4.49 (3.34, 6.03)	< 0.001	4.00 (2.97, 5.40)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
CMI		1.59 (1.47, 1.73)	< 0.001	1.54 (1.42, 1.68)	< 0.001	1.41 (1.29, 1.55)	< 0.001
CMI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.82 (2.05, 3.87)	< 0.001	2.66 (1.93, 3.67)	< 0.001	2.56 (1.85, 3.54)	< 0.001
	Q3	4.32 (3.18, 5.88)	< 0.001	4.01 (2.94, 5,47)	< 0.001	3.73 (2.71, 5.12)	< 0.001
	Q4	6.26 (4.63, 8.47)	< 0.001	5.68 (4.18, 7.71)	< 0.001	4.65 (3.37, 6.41)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
CVAI		2.14 (1.94, 2.36)	< 0.001	2.49 (2.20, 2.81)	< 0.001	2.05 (1.84, 2.29)	< 0.001
CVAI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	3.64 (2.55, 5.19)	< 0.001	2.10 (1.35, 3.28)	0.001	1.74 (1.10, 2.76)	< 0.001
	Q3	6.10 (4.33, 8.60)	< 0.001	2.11 (1.35, 3.30)	0.001	1.77 (1.11, 2.81)	< 0.001
	Q4	9.93 (7.09, 13.91)	< 0.001	11.96 (8.23, 17.40)	< 0.001	8.20 (5.72, 11.75)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
VAI		1.53 (1.41, 1.65)	< 0.001	1.48 (1.37, 1.61)	< 0.001	1.34 (1.23, 1.47)	< 0.001
VAI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.25 (1.67, 3.04)	< 0.001	2.16 (1.60, 2.92)	< 0.001	2.05 (1.51, 2.78)	< 0.001
	Q3	3.51 (2.63, 4.69)	< 0.001	3.26 (2.44, 4.36)	< 0.001	2.97 (2.20, 4.01)	< 0.001
	Q4	4.69 (3.53, 6.22)	< 0.001	4.27 (3.21, 5.69)	< 0.001	3.41 (2.52, 4.61)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
LAP		1.73 (1.59, 1.87)	< 0.001	1.67 (1.53, 1.82)	< 0.001	1.55 (1.41, 1.70)	< 0.001
LAP	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	4.05 (2.86, 5.74)	< 0.001	3.87 (2.73, 5.50)	< 0.001	3.82 (2.69, 5.44)	< 0.001
	Q3	5.53 (3.93, 7.79)	< 0.001	5.18 (3.67, 7.31)	< 0.001	4.91 (3.45, 6.99)	< 0.001
	Q4	9.22 (6.60, 12.89)	< 0.001	8.40 (5.98, 11.81)	< 0.001	7.21 (5.04, 10.32)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	
AVI		1.71 (1.56, 1.86)	< 0.001	1.64 (1.50, 1.80)	< 0.001	1.57 (1.43, 1.73)	< 0.001
AVI	Q1	1 (Ref)		1 (Ref)		1 (Ref)	
	Q2	2.50 (1.86, 3.36)	< 0.001	2.38 (1.76, 3.21)	< 0.001	2.27 (1.68, 3.07)	< 0.001
	Q3	2.85 (2.13, 3.81)	< 0.001	2.67 (1.99, 3.58)	< 0.001	2.43 (1.80, 3.27)	< 0.001
	Q4	4.87 (3.67, 6.46)	< 0.001	4.37 (3.27, 5.82)	< 0.001	3.87 (2.88, 5.20)	< 0.001
P-trend		< 0.001		< 0.001		< 0.001	

Model 1: unadjusted. Model 2: further adjusted for age, education, marriage. Model3: further adjusted for hypertension, diabetes, CHD, smoking history, drinking history, creatinine, LDL, AST, ALT, HOMA-IR. Abbreviation: Ref, reference; CHD, coronary heart disease; LDL, low-density lipoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HOMA-IR, Homeostatic model assessment for insulin resistance; BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index; Q, quartile; OR, odds ratio; CI, confidence interval

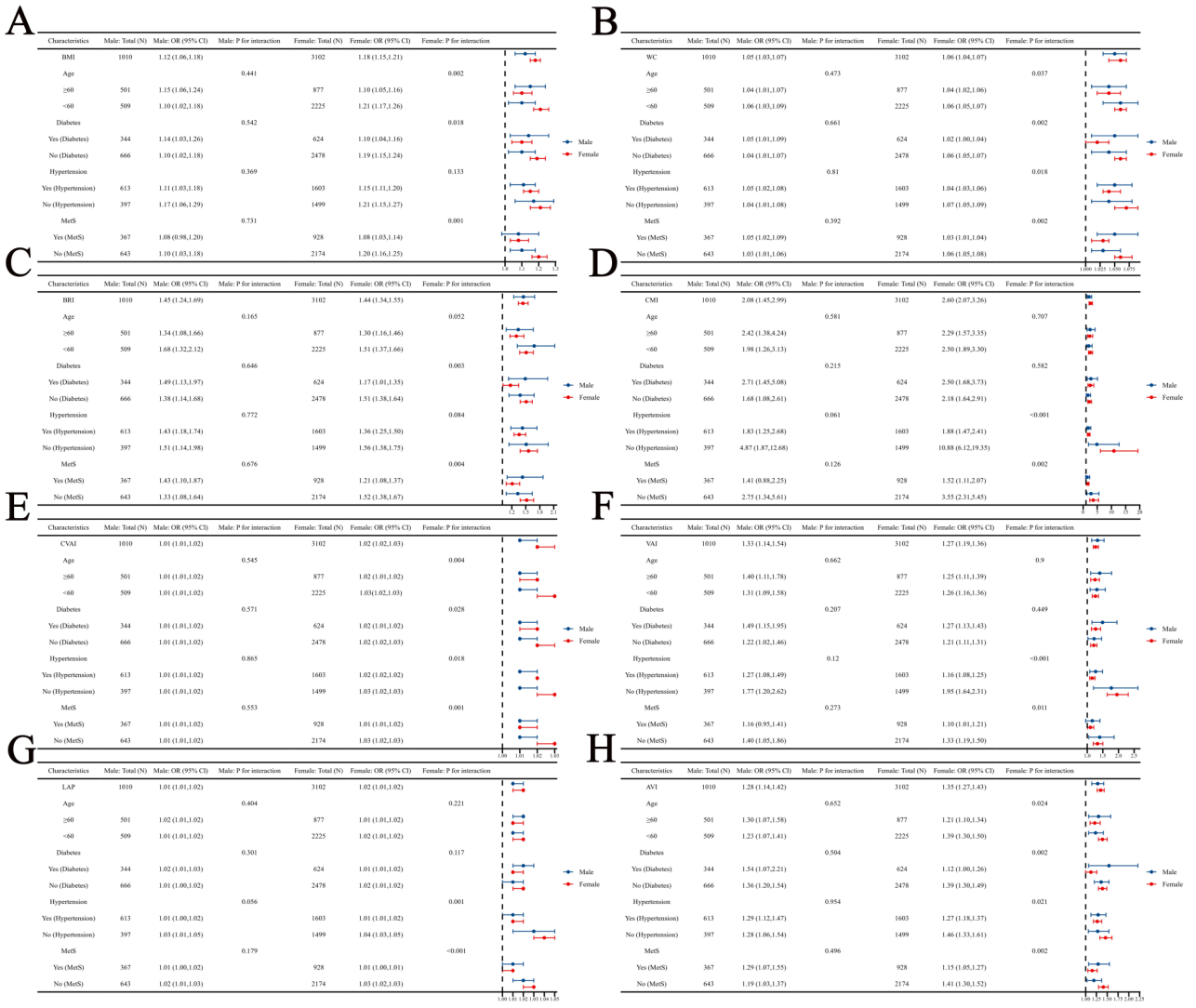

Fig. 4 Subgroup analysis of the association between obesity indices and HUA. Subgroup analysis of the association between BMI (**A**), WC (**B**), BRI (**C**), CMI (**D**), CVAI (**E**), VAI (**F**), LAP (**G**), AVI (**H**) and HUA, stratified by age, hypertension, diabetes, and MetS. Red represents females, while blue represents males. Abbreviation: MetS, metabolic syndrome; BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index; OR, odds ratio

and finally BMI. Conversely, BMI did not significantly enhance the model's accuracy ($P>0.05$). The initial baseline AUC for females was 0.650 (95% CI: 0.628, 0.673). It increased to 0.694 (95% CI: 0.673, 0.716) with the inclusion of BMI, to 0.684 (95% CI: 0.663, 0.706) with WC, to 0.683 (95% CI: 0.661, 0.704) with BRI, to 0.678 (95% CI: 0.657, 0.700) with CMI, to 0.713 (95% CI: 0.693, 0.733) with CVAI, to 0.672 (95% CI: 0.650, 0.693) with VAI, to 0.689 (95% CI: 0.668, 0.710) with LAP, and to 0.684 (95% CI: 0.663, 0.706) with AVI. In females, all obesity indices significantly enhanced the model's predictive accuracy ($P<0.05$), with CVAI delivering the highest incremental predictive value. It was followed by BMI, LAP, AVI, WC, BRI, CMI, and VAI. According to the results of the ROC curves, LAP was identified as a better predictor of HUA in males, while CVAI was found to be a better predictor in females.

Discussion

In the longitudinal study, this research explored the relationship between traditional and novel obesity indices and HUA based on gender. This research found that WC, BMI, BRI, CMI, CVAI, VAI, LAP, and AVI were associated with HUA in both male and female populations. Additionally, in females without MetS, the association between obesity indices and HUA was stronger. The results from the ROC curves indicate that LAP provided the highest incremental predictive value in the male group, while CVAI provided the highest incremental predictive value in the female group.

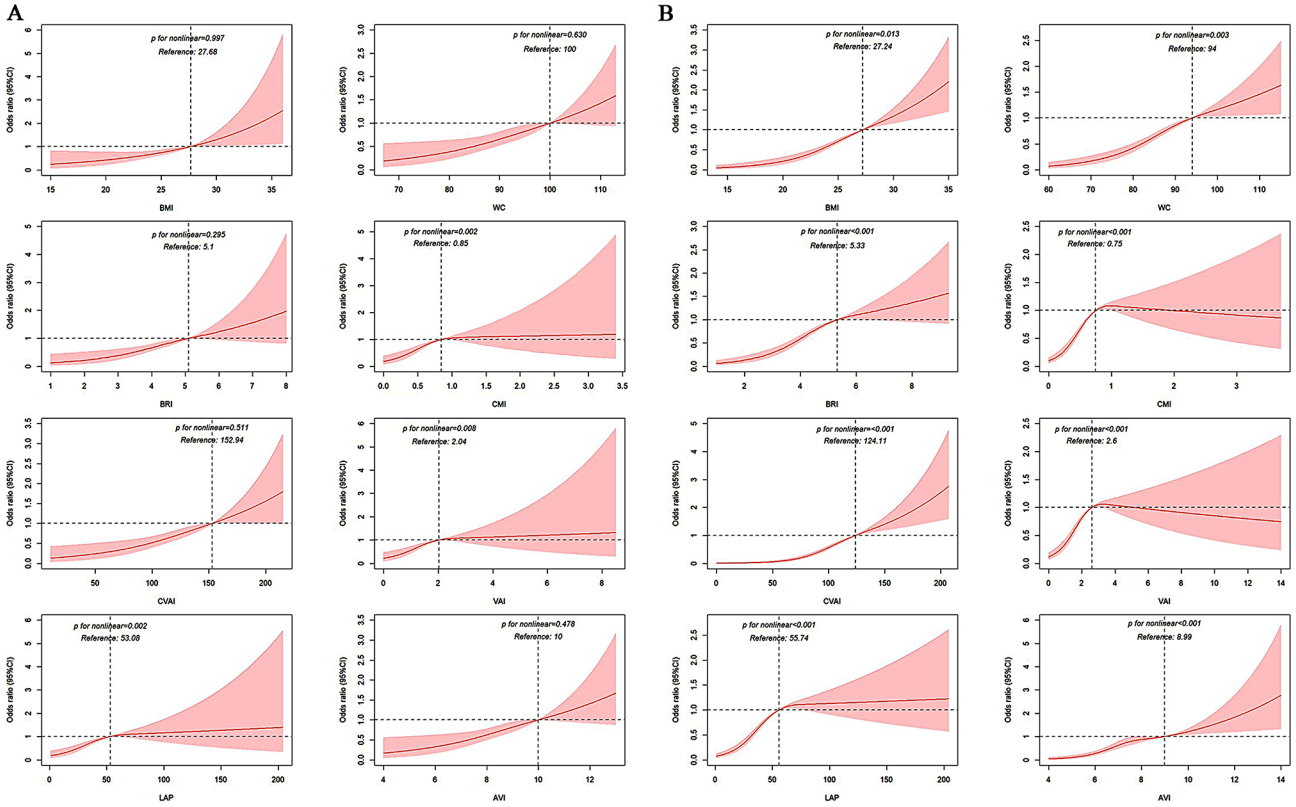

Fig. 5 The dose-response relationship between obesity Indices and HUA. (**A**). The dose-response relationship between obesity indices and HUA in males. (**B**). The dose-response relationship between obesity Indices and HUA in females. Abbreviation: BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index

However, A cross-sectional study across 31 provinces and cities in China found in both males and females, BMI, WC, BRI, LAP, VAI, ABSI, WTI, and WWI significantly correlated with HUA. Notably, LAP exhibited the highest predictive value, while ABSI showed the lowest [27]. Another cross-sectional study from the Xinjiang region of China found no significant correlation between BMI and HUA, and WC and WHtR showed no significant correlation with HUA in males [28]. A cross-sectional study from Spain found significant associations between BMI, ABSI, AVI, BRI, and HUA [29]. In a rural Chinese cross-sectional study, BRI was found to have a greater predictive value for HUA in females in comparison to BMI but not in males. Su et al. found significant correlations between BMI, BRI, ABSI, AVI, LAP, VAI, and HUA. Notably, the obesity indices for females demonstrated stronger predictive abilities for HUA compared to those for males [30].

Explanation of the findings: Firstly, visceral fat build-up leads to increased free fatty acids (FFAs) entering the portal vein, stimulating the liver to produce more TG, thereby activating the de novo purine synthesis pathway and resulting in elevated SUA levels [31, 32]. Secondly, the blood lipid index TG is associated with visceral fat distribution. Obesity measures like LAP, CVAI, and CMI are determined using the blood lipid levels of TG and HDL. A lipidomics study on HUA indicated that, compared to normal individuals, patients with HUA exhibit significant increases in substances such as TG and lysophosphatidylinositol. This suggests that disorders in lipid metabolism increase the risk of HUA [33]. Thirdly, the accumulation of visceral fat leads to the secretion or activation of specific pro-inflammatory molecules, such as interleukin-6, interleukin-8, and leptin, this, in turn, results in insulin resistance. Furthermore, visceral fat cells enhance the release and reduce the absorption of FFAs. Circulating FFAs at high concentrations can cause insulin resistance. Insulin resistance and hyperinsulinemia may mediate the activity of SLC2A9, which encodes GLUT9, to promote renal tubular reabsorption of uric acid. This action reduces the clearance rate of SUA and increases SUA levels [34–37]. Fourthly, an increase in visceral fat can lead to increased activity of xanthine oxidoreductase, thereby promoting uric acid synthesis [38]. Fifthly, the NADPH oxidase subunit p22 can generate reactive oxygen species. A gene expression profiling of peripheral blood cells indicated a correlation between higher visceral fat and elevated p22 mRNA

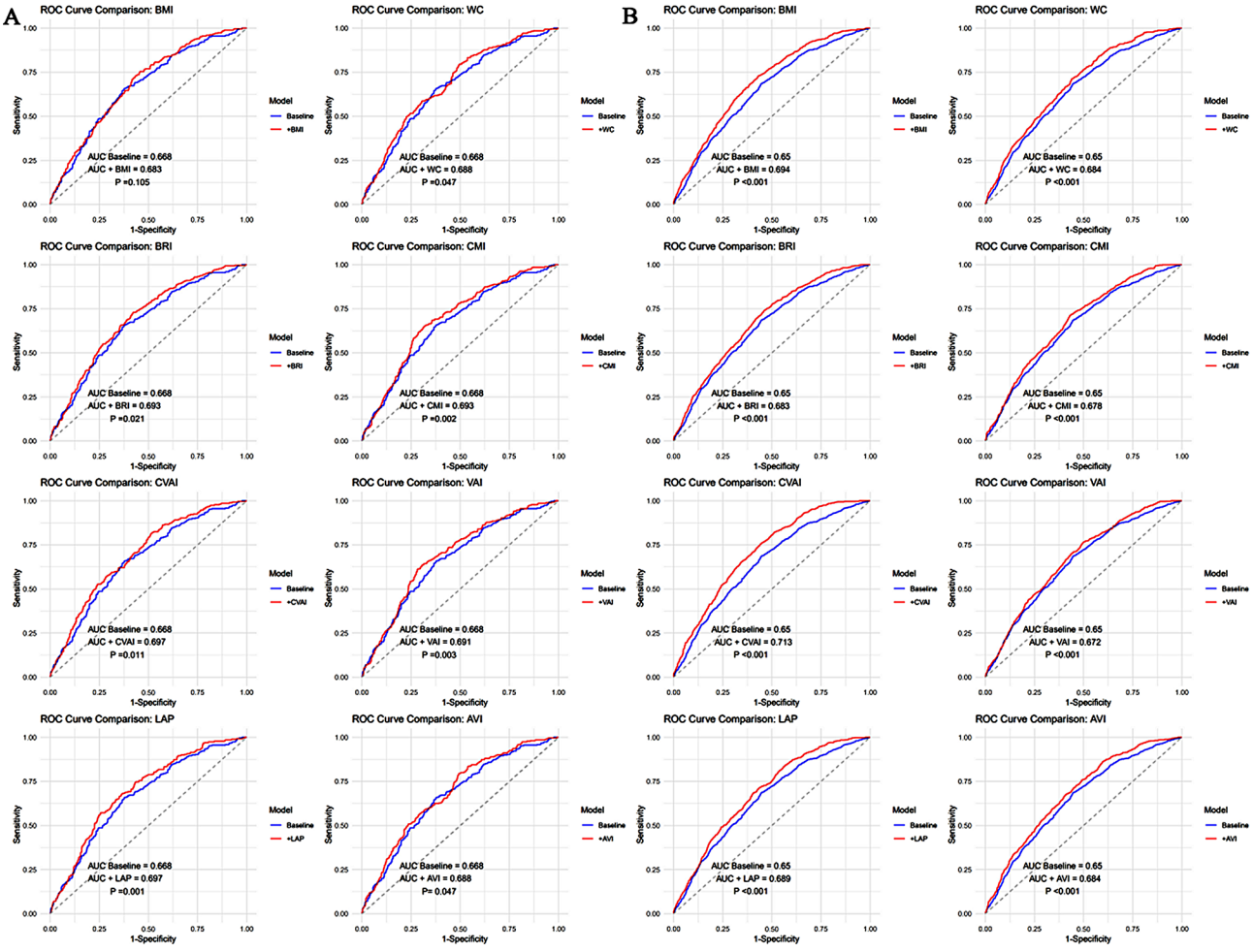

Fig. 6 ROC curves stratified by gender (**A**). The ROC curves between obesity indices and HUA in males. (**B**). The ROC curves between obesity Indices and HUA in females. Abbreviation: BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index

expression. This upregulation causes local inflammatory changes, metabolic abnormalities, and increased SUA levels [39]. Lastly, adiponectin is a biologically active protein secreted by adipose tissue, which can downregulate the expression of transcription factors and cytokines associated with inflammation. Additionally, it can inhibit gluconeogenesis and the expression of the GLUT4 gene, thereby enhancing insulin sensitivity [40, 41]. Deposition of visceral fat can lead to hypoadiponectinemia, which can affect the body's inflammatory response and insulin resistance. This in turn can result in elevated SUA levels, thereby causing HUA [42, 43].

Regarding gender differences, potential reasons for the analysis are as follows: Firstly, during perimenopause, females experience a decrease in estrogen levels, leading to reduced urate clearance rates and a higher prevalence of HUA [44]. Secondly, dysregulation of inflammatory mechanisms differs between obese males and females, indicating gender-specific pathways in obesity-associated inflammation. In females, this primarily results from lower levels of the anti-inflammatory agent adiponectin. In males, it primarily results from higher levels of pro-inflammatory mediators like leptin and IL-6. Therefore, this may affect the regulation of inflammation in women, thereby increasing susceptibility to HUA [45]. Thirdly, adipocytes in visceral fat contain α2-adrenergic receptors, α2-adrenergic receptor interaction, and hormone-sensitive lipase dysfunction impedes catecholamine lipolysis in subcutaneous adipocytes. In females, the affinity of α-2 adrenergic receptors is reduced, promoting lipolysis in visceral fat cells. FFAs released from visceral fat cells are transported to the liver via the portal vein system, thereby raising uric acid levels in the body [46].

Additionally, through subgroup analysis, this research discovered a strong connection between eight obesity indices and HUA in females without MetS, which was statistically significant compared to those with MetS. This particular finding has not been reported before. This

Table 4 AUC for different obesity indices in identifying HUA

Variable	AUC	95% CI	*P*- Value	Sensitivity	Specificity	Youden index
Male						
Basic model	0.668	0.631, 0.704	ref	0.658	0.623	0.281
+WC	0.688	0.653, 0.724	0.047	0.796	0.505	0.301
+BMI	0.683	0.648, 0.719	0.105	0.755	0.543	0.298
+BRI	0.693	0.658, 0.728	0.021	0.729	0.579	0.308
+CMI	0.693	0.658, 0.729	0.002	0.651	0.683	0.334
+CVAI	0.697	0.662, 0.732	0.011	0.814	0.489	0.303
+VAI	0.691	0.655, 0.727	0.003	0.636	0.695	0.331
+LAP	0.697	0.662, 0.732	0.001	0.572	0.744	0.316
+AVI	0.688	0.652, 0.723	0.047	0.796	0.506	0.302
Female						
Basic model	0.650	0.628, 0.673	ref	0.687	0.553	0.24
+WC	0.684	0.663, 0.706	< 0.001	0.712	0.561	0.273
+BMI	0.694	0.673, 0.716	< 0.001	0.727	0.572	0.299
+BRI	0.683	0.661, 0.704	< 0.001	0.742	0.539	0.281
+CMI	0.678	0.657, 0.700	< 0.001	0.714	0.568	0.282
+CVAI	0.713	0.693, 0.733	< 0.001	0.762	0.552	0.314
+VAI	0.672	0.650, 0.693	< 0.001	0.767	0.500	0.267
+LAP	0.689	0.668, 0.710	< 0.001	0.684	0.595	0.279
+AVI	0.684	0.663, 0.706	< 0.001	0.678	0.590	0.268

Abbreviation: BMI, body mass index; WC, waist circumference; BRI, body roundness index; CMI, cardiometabolic index; VAI, visceral adiposity index; CVAI, Chinese visceral adiposity index; LAP, lipid accumulation product; AVI, abdominal volume index

research speculate that in females without MetS, obesity may become the predominant factor influencing uric acid levels. Furthermore, MetS comprises components such as hypertension, hyperglycemia, and hyperlipidemia. The combined effects of these factors may obscure the individual influence of obesity on uric acid levels. In subgroups without these coexisting conditions, the influence of obesity on uric acid levels may be more pronounced. Moreover, the stronger association between obesity and HUA may be attributed to other related components such as insulin resistance, which partially "explains" changes in uric acid levels in subgroups with MetS. Future research is needed to confirm these observations through more extensive and in-depth studies.

According to cubic splines some obesity surrogate indicated no significant response beyond the deflection point. The potential reasons for the analysis are as follows: Firstly, surrogate markers of obesity may reach a threshold at which their impact on uric acid metabolism saturates. This indicates that beyond a certain level of body fat, the influence on uric acid production or excretion likely reaches its peak, rendering further increases in these markers ineffective at significantly elevating HUA risk. This saturation effect may result from adipose tissue's regulatory mechanisms on uric acid metabolism reaching a physiological limit, which slows or halts the risk escalation. Secondly, scarcity at higher value ranges may result in insufficient statistical power to detect significant associations. In the upper ranges of BMI or other obesity surrogate markers, limited sample sizes may compromise statistical models' ability to accurately estimate effects, decreasing the precision of these estimates. Additionally, a small sample size can undermine the outcomes of significance tests, complicating the detection of associations in these ranges. In addition, certain confounding factors might distort the relationship between obesity indicators and HUA at higher values. For example, other metabolic or health conditions that are more prevalent in these higher ranges could obscure the direct association between the markers and HUA. Despite adjustments for multiple covariates in the models, unaccounted confounders may still affect the results.

Advantages and drawbacks of the research

This research possesses multiple strengths. Initially, it is a large-scale longitudinal study conducted among middle-aged and elderly residents in Dalian, China, focusing on individuals with normal baseline uric acid levels who were followed up for 3 years to identify those who developed HUA. This method enabled us to investigate the causal link between traditional and novel obesity indices and HUA, offering benefits compared to cross-sectional studies. Secondly, the study population consisted exclusively of residents from Dalian, China, minimizing sample bias from different regions and enabling a better understanding of the incidence of HUA and its contributing elements in the Dalian area. Additionally, this research employed rigorous selection criteria and investigated the relationship between a total of 8 obesity indices and HUA among both males and females. This research

conducted subgroup interaction analyses and used RCS curves to fit the non-linear connection between obesity indices and HUA in different genders and subgroups. Furthermore, this research investigated how well different obesity indices could predict HUA. Considering the differences in predictive value between traditional and novel obesity indices, this research also identified the preferred screening indices for predicting HUA in middle-aged and elderly populations of both genders. Therefore, HUA can be accurately predicted and it is applicable to Chinese community residents. In females without MetS, a notable correlation between obesity and HUA has been identified, indicating that weight reduction could be a critical strategy for preventing HUA in middle-aged and elderly females who do not have concurrent conditions such as hypertension and hyperglycemia. However, the study also has limitations. Firstly, this research did not include lifestyle and exercise factors that may affect uric acid levels, potentially influencing the study results. Secondly, this research focused on community residents in Dalian, China, a coastal city where residents consume a diet rich in purine-containing foods. This dietary pattern leads to a higher prevalence of HUA compared to other regions. Therefore, dietary interference cannot be ruled out, and further analysis of the correlation between diet and HUA is warranted. Lastly, this findings may not be universally applicable to other countries and regions, as this study group consisted solely of middle-aged and elderly individuals. This demographic focus restricts the relevance of the results to children and young adults.

Conclusions

This study unveiled the causal link between obesity indices and HUA, delving into both the linear and non-linear relationships between them and identifying the preferred obesity index for HUA based on gender. This approach facilitates the early prevention of HUA, thereby improving the management of HUA and its associated complications among community residents, and further promoting community health development.

Abbreviations

HUA	Hyperuricemia
CHD	Coronary heart disease
MetS	Metabolic syndrome
SUA	Serum uric acid
BMI	Body mass index
WC	Waist circumference
BRI	Body roundness index
CMI	Cardiometabolic index
VAI	Visceral adiposity index
CVAI	Chinese visceral adiposity index
LAP	Lipid accumulation product
AVI	Abdominal volume index
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
TG	Triglycerides
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
FPG	Fast plasma glucose
HOMA-IR	Homeostatic model assessment for insulin resistance
eGFR	Estimated glomerular filtration rate
RCS	Restricted cubic splines
ROC	Receiver operating characteristic
AUC	Area under the curve
CI	Confidence interval
OR	Odds ratio
FFAs	Free fatty acids

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02296-6.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

We would like to express our gratitude to all participants in the longitudinal study, We would also like to express our gratitude to the editors and reviewers for their valuable suggestions, which have enriched our article and made it more understandable.

Author contributions

Study design: ZN-G and YT-L. Data collection and analysis: WZ, and XH-L. Drafting and revising the manuscript: L-L, HD-J and YX-W. All authors have read and agreed to the final manuscript.

Funding

The study was supported by grants from the National Key R&D Program of China (2017YFC1310700) and the Dalian Science and Technology Bureau (project 2022RG11).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The protocol was approved by the Ethical Review Committee of Ruijin Hospital (RUIJIN-2011-14), and all participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 20 June 2024 / Accepted: 13 September 2024
Published online: 26 September 2024

References

1. Piao W, Zhao L, Yang Y, Fang H, Ju L, Cai S, Yu D. The prevalence of Hyperuricemia and its correlates among adults in China: results from CNHS 2015–2017. Nutrients. 2022;14(19):4095.
2. Vareldzis R, Perez A, Reisin E. Hyperuricemia: an intriguing connection to metabolic syndrome, diabetes, kidney disease, and hypertension. Curr Hypertens Rep; 2024.
3. Lin Z, Wu S, Chen Z, Luo W, Lin Z, Su H, Guo D. Poor serum uric acid control increases risk for developing hypertension: a retrospective cohort study in China. Front Endocrinol (Lausanne). 2024;15:1343998.

4. Zheng J, Li X, Zhang Y, Miao Y, Zhang Q. Hyperuricemia as an effect modifier of the association between metabolic phenotypes and nonalcoholic fatty liver disease in Chinese population. J Transl Med. 2023;21:39.
5. Weir CJ, Muir SW, Walters MR, Lees KR. Serum urate as an independent predictor of poor outcome and future vascular events after acute stroke. Stroke. 2003;34:1951–6.
6. Zhou M, Huang X, Li R, Zhang Z, Zhang L, Gao X, Yang H, Ma Y. Association of dietary patterns with blood uric acid concentration and hyperuricemia in northern Chinese adults. Nutr J. 2022;21:42.
7. Zhang M, Zhu X, Wu J, Huang Z, Zhao Z, Zhang X, Xue Y, Wan W, Li C, Zhang W, et al. Prevalence of Hyperuricemia among Chinese adults: findings from two nationally Representative cross-sectional surveys in 2015-16 and 2018-19. Front Immunol. 2021;12:791983.
8. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. Arthritis Rheum. 2011;63:3136–41.
9. Tang L, Zeng L. Comparative efficacy of anthropometric indices in predicting 10-year ASCVD risk: insights from NHANES data. Front Cardiovasc Med. 2024;11:1341476.
10. Chait A, den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including Diabetes and Cardiovascular Disease. Front Cardiovasc Med. 2020;7:22.
11. Hilton C, Neville MJ, Wittemans LBL, Todorcevic M, Pinnick KE, Pulit SL, Luan J, Kulyté A, Dahlman I, Wareham NJ, et al. MicroRNA-196a links human body fat distribution to adipose tissue extracellular matrix composition. EBioMedicine. 2019;44:467–75.
12. Sun C, Kovacs P, Guiu-Jurado E. Genetics of Body Fat distribution: comparative analyses in populations with European, Asian and African ancestries. Genes (Basel). 2021;12(6):841.
13. Frank AP, de Souza Santos R, Palmer BF, Clegg DJ. Determinants of body fat distribution in humans may provide insight about obesity-related health risks. J Lipid Res. 2019;60:1710–9.
14. Powell-Wiley TM, Poirier P, Burke LE, Després JP, Gordon-Larsen P, Lavie CJ, Lear SA, Ndumele CE, Neeland IJ, Sanders P, St-Onge MP. Obesity and Cardiovascular Disease: A Scientific Statement from the American Heart Association. Circulation. 2021;143:e984–1010.
15. Zhang N, Chang Y, Guo X, Chen Y, Ye N, Sun Y. A body shape index and body roundness index: two new body indices for detecting association between obesity and hyperuricemia in rural area of China. Eur J Intern Med. 2016;29:32–6.
16. Tatsumi Y. Sex and age difference in associations between anthropometric indices and hypertension. Hypertens Res. 2024;47:1429–30.
17. Guerrero-Romero F, Rodríguez-Morán M. Abdominal volume index. An anthropometry-based index for estimation of obesity is strongly related to impaired glucose tolerance and type 2 diabetes mellitus. Arch Med Res. 2003;34:428–32.
18. Thomas DM, Bredlau C, Bosy-Westphal A, Mueller M, Shen W, Gallagher D, Maeda Y, McDougall A, Peterson CM, Ravussin E, Heymsfield SB. Relationships between body roundness with body fat and visceral adipose tissue emerging from a new geometrical model. Obes (Silver Spring). 2013;21:2264–71.
19. Petta S, Amato M, Cabibi D, Cammà C, Di Marco V, Giordano C, Galluzzo A, Craxì A. Visceral adiposity index is associated with histological findings and high viral load in patients with chronic hepatitis C due to genotype 1. Hepatology. 2010;52:1543–52.
20. Xia MF, Chen Y, Lin HD, Ma H, Li XM, Aleteng Q, Li Q, Wang D, Hu Y, Pan BS, et al. A indicator of visceral adipose dysfunction to evaluate metabolic health in adult Chinese. Sci Rep. 2016;6:38214.
21. Kahn HS. The lipid accumulation product performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. BMC Cardiovasc Disord. 2005;5:26.
22. Wakabayashi I, Sotoda Y, Hirooka S, Orita H. Association between cardiometabolic index and atherosclerotic progression in patients with peripheral arterial disease. Clin Chim Acta. 2015;446:231–6.
23. Link JC, Reue K. Genetic basis for sex differences in obesity and lipid metabolism. Annu Rev Nutr. 2017;37:225–45.
24. Ning G. Risk evaluation of cAncers in Chinese diabeTic individuals: a lONgitudinal (REACTION) study. J Diabetes. 2012;4:172–3.
25. Bi Y, Lu J, Wang W, Mu Y, Zhao J, Liu C, Chen L, Shi L, Li Q, Wan Q, et al. Cohort profile: risk evaluation of cancers in Chinese diabetic individuals: a longitudinal (REACTION) study. J Diabetes. 2014;6:147–57.
26. 2. Classification and diagnosis of diabetes: standards of Medical Care in Diabetes-2021. Diabetes Care. 2021;44:S15–33.
27. Chen D, Lu C, Chen K, Liu T, Li Y, Shan Z, Teng W. Association between anthropometric indices and hyperuricemia: a nationwide study in China. Clin Rheumatol. 2024;43:907–20.
28. Kahaer M, Zhang B, Chen W, Liang M, He Y, Chen M, Li R, Tian T, Hu C, Sun Y. Triglyceride glucose index is more closely related to Hyperuricemia Than obesity indices in the Medical Checkup Population in Xinjiang, China. Front Endocrinol (Lausanne). 2022;13:861760.
30. Sánchez-Bacaicoa C, Santano-Mogena E, Rico-Martín S, Rey-Sánchez P, Juárez-Vela R, Sánchez Muñoz-Torrero JF, López-Espuela F. Calderón-García JF: Association between Asymptomatic Hyperuricemia with Adiposity indices: a cross-sectional study in a Spanish Population. Nutrients. 2023;15(22):4798.
31. Su SY, Lin TH, Liu YH, Wu PY, Huang JC, Su HM, Chen SC. Sex difference in the associations among obesity-related indices with hyperuricemia in a large Taiwanese Population Study. Nutrients. 2023;15(15):3419.
31. Fabregat I, Revilla E, Machado A. Short-term control of the pentose phosphate cycle by insulin could be modulated by the NADPH/NADP ratio in rat adipocytes and hepatocytes. Biochem Biophys Res Commun. 1987;146:920–5.
32. Nakanishi N, Yoshida H, Nakamura K, Suzuki K, Tatara K. Predictors for development of hyperuricemia: an 8-year longitudinal study in middle-aged Japanese men. Metabolism. 2001;50:621–6.
33. Ma L, Wang J, Ma L, Ge Y, Wang XM. The effect of lipid metabolism disorder on patients with hyperuricemia using Multi-omics analysis. Sci Rep. 2023;13:18211.
34. Wang HP, Xu YY, Xu BL, Lu J, Xia J, Shen T, Fang J, Lei T. Correlation between abdominal Fat distribution and serum uric acid in patients recently diagnosed with type 2 diabetes. Diabetes Metab Syndr Obes. 2023;16:3751–62.
36. Yanai H, Adachi H, Hakoshima M, Iida S, Katsuyama H. A possible therapeutic application of the selective inhibitor of Urate Transporter 1, Dotinurad, for metabolic syndrome, chronic kidney Disease, and Cardiovascular Disease. Cells. 2024;13(5):450.
37. Dhokte S, Czaja K. Visceral adipose tissue: the hidden culprit for type 2 diabetes. Nutrients. 2024;16(7):1015.
38. Perez-Ruiz F, Aniel-Quiroga MA, Herrero-Beites AM, Chinchilla SP, Erauskin GG, Merriman T. Renal clearance of uric acid is linked to insulin resistance and lower excretion of sodium in gout patients. Rheumatol Int. 2015;35:1519–24.
39. Bai R, Ying X, Shen J, Wu T, Lai X, Wang L, Yu M, Qi X, Mei Y. The visceral and liver fat are significantly associated with the prevalence of hyperuricemia among middle age and elderly people: a cross-sectional study in Chongqing, China. Front Nutr. 2022;9:961792.
39. Obata Y, Maeda N, Yamada Y, Yamamoto K, Nakamura S, Yamaoka M, Tanaka Y, Masuda S, Nagao H, Fukuda S, et al. Impact of visceral fat on gene expression profile in peripheral blood cells in obese Japanese subjects. Cardiovasc Diabetol. 2016;15:159.
40. Pandey GK, Vadivel S, Raghavan S, Mohan V, Balasubramanyam M, Gokulakrishnan K. High molecular weight adiponectin reduces glucolipotoxicity-induced inflammation and improves lipid metabolism and insulin sensitivity via APPL1-AMPK-GLUT4 regulation in 3T3-L1 adipocytes. Atherosclerosis. 2019;288:67–75.
41. Berg AH, Combs TP, Du X, Brownlee M, Scherer PE. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. Nat Med. 2001;7:947–53.
42. Hossain MM, Mukheem A, Kamarul T. The prevention and treatment of hypoadiponectinemia-associated human diseases by up-regulation of plasma adiponectin. Life Sci. 2015;135:55–67.
43. Luo L, Liu M. Adiponectin: friend or foe in obesity and inflammation. Med Rev (2021). 2022;2:349–62.
44. Liu Z, Zhou Q, Tang Y, Li J, Chen Q, Yang H, Zhou S. Sex-specific differences in the associations between adiposity indices and incident hyperuricemia among middle-aged and older adults: a nationwide longitudinal study. Front Endocrinol (Lausanne). 2024;15:1336471.
45. Ter Horst R, van den Munckhof ICL, Schraa K, Aguirre-Gamboa R, Jaeger M, Smeekens SP, Brand T, Lemmers H, Dijkstra H, Galesloot TE, et al. Sex-specific regulation of inflammation and metabolic syndrome in obesity. Arterioscler Thromb Vasc Biol. 2020;40:1787–800.
46. Alser M, Naja K, Elrayess MA. Mechanisms of body fat distribution and gluteal-femoral fat protection against metabolic disorders. Front Nutr. 2024;11:1368966.

Publisher's note