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Association between Chinese visceral adiposity index and lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH): a national cohort study

Kunhui Chang¹, Bo Li¹, Gang Wang¹, Hao Zhou¹, Yonghao Chen^{2*} and Hongbing Gu^{1*}

Abstract

Background Benign prostatic hyperplasia (BPH) and its related lower urinary tract symptoms (LUTS) are commonly observed among aging males and have a substantial effect on quality of life. Metabolic syndrome, with a specific focus on obesity, is believed to play a role in the development of BPH. This study intends to explore the relationship between several obesity-related metrics, including the Chinese Visceral Adiposity Index (CVAI), and LUTS/BPH within a national cohort of Chinese men.

Methods Data from the China Health and Retirement Longitudinal Study (CHARLS) 2015 were analyzed, encompassing a sample of 5,735 male participants aged 45 and older. Eight obesity-related indices—namely Body mass index (BMI), Waist-height ratio (WHtR), Triglyceride-glucose.BMI (TyG.BMI), TyG, Waist circumference (TyG.WC), TyG.WHtR, CVAI, Visceral adiposity index (VAI), and A body shape index (ABSI)—were examined. Logistic regression models, adjusted for potential confounders, were utilized to evaluate the associations between these indices and LUTS or BPH. The predictive capabilities of these indices were further assessed using receiver operating curves (ROC).

Results Among the participants, 718 (12.5%) were diagnosed with LUTS/BPH. All obesity-related indices were significantly higher in the LUTS/BPH group compared to the healthy group. CVAI demonstrated the highest predictive ability for LUTS/BPH, with an area under the curve (AUC) of 0.58. The study highlighted a nonlinear relationship between LUTS/BPH and several obesity-related indices, including CVAI.

Conclusions This study underscores the significant association between visceral fat, as measured by CVAI, and the risk of LUTS/BPH in Chinese men. CVAI emerged as the most effective predictor among the indices evaluated, suggesting its potential utility in identifying individuals at risk for LUTS/BPH. Further prospective studies are needed to confirm these findings and elucidate the underlying mechanisms.

Keywords Benign prostatic hyperplasia, Lower urinary tract symptoms, Obesity, Visceral adiposity index, Chinese Visceral Adiposity Index, Metabolic syndrome

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Introduction

Benign prostatic hyperplasia (BPH), characterized by uncontrolled enlargement of the prostate gland, is becoming more common as the population ages. In China, the prevalence of BPH is at least 11.9% among individuals aged 45 and increases to 22.7% by age 70 [1]. BPH can lead to bladder outlet obstruction (BOO) and lower urinary tract symptoms (LUTS), significantly impacting patients' quality of life. Moreover, BPH is associated with an increased risk of falls [2, 3], and a higher likelihood of developing Alzheimer's disease, dementia, and increased mortality rates [4]. Conventional treatments for BPH, such as 5-alpha reductase inhibitors and alpha-blockers, have been connected to a heightened risk of heart failure [5]. For surgical therapies, there remains heterogeneity in transurethral resection, transurethral incision, and novel technical procedures, indicating the lack of standardization in BPH procedures [6–8]. Therefore, comprehensive risk assessment and preventive measures for LUTS/BPH in the aging male population are urgently needed.

Although the precise etiology of BPH remains unclear, recent research has highlighted the significant role of metabolic syndrome, with a particular focus on obesity as a crucial factor [9, 10]. The prevalence of overweight conditions has emerged as a significant public health concern, adversely affecting individual well-being. This issue largely arises from shifts in lifestyle and dietary habits, revealing a pressing need for awareness and intervention [11]. Studies have established a compelling correlation between visceral fat and the development of BPH [12]. Furthermore, an excessive accumulation of visceral fat can lead to disruptions in lipid metabolism, which may play a critical role in both the initiation and advancement of BPH [13]. This connection underscores the importance of addressing visceral fat accumulation as a potential factor in managing and preventing BPH [14, 15]. Research findings suggest that obesity contributes to metabolic imbalances that elevate the concentrations of circulating pro-inflammatory agents and promote systemic oxidative stress. This cascade of events facilitates the invasion of immune cells, resulting in considerable prostatic enlargement and exacerbation of LUTS [16]. Currently, some obesity and lipid-related indicators can be used to describe the body's fat accumulation and lipid metabolite content: waist circumference (WC), body mass index (BMI), waist-height ratio (WHtR), visceral adiposity index (VAI), a body shape index (ABSI), triglyceride-glucose (TyG) index and its correlation index (TyG-BMI, TyG-WC, TyG-WHtR), and Chinese visceral adiposity index (CVAI). Numerous investigations that concentrate on these metrics mainly analyze cardiovascular conditions and diabetes. For example, Zhang et al.

[17], conducted a systematic evaluation of the predictive significance of 13 quantitative measures related to obesity and fat accumulation concerning type 2 diabetes in middle-aged and older Chinese adults, and they confirmed the predictive value of the 13 measures, where TyG was the best indices.

Nevertheless, there is a lack of comprehensive studies exploring the connection between BPH and these metrics, as well as their predictive effectiveness for BPH. Most of the research that currently exists has primarily focused on Caucasian groups, although anthropometric measurements can differ notably among various racial demographics. To enhance the understanding of visceral fat accumulation within the Chinese population, Xia et al. created the CAVI, a pivotal topic that is also addressed in this article [18]. We comprehensively analyzed the association between LUTS/BPH and eight quantitative measures related to obesity and fat accumulation (BMI, WHtR, TyG.BMI, TyG.WC, TyG.WHtR, VAI, and ABSI) and compared their predictive abilities based on data from a national cohort.

Method and materials

Participants collection

Participants were selected from the China Health and Retirement Longitudinal Study (CHARLS), which gathers high-quality data from individuals aged 45 and above nationwide using standardized questionnaires [19]. This survey includes demographic traits, family dynamics, health conditions, medical service usage, employment and retirement situations, income, and spending, thus offering essential data support for examining the health and economic circumstances of middle-aged and older adults in China. In this study, we enrolled data from 2015 (Fig. 1) with the criteria as follows: Male individuals had data of LUTS/BPH in CHARLS 2015, Had data of waist, height, weight, and assessment of blood. Patients diagnosed with prostate cancer, those lacking information such as LDL or HDL, and extreme values were excluded.

Definition and measures

BPH/LUTS patients were identified based on responses to the question, "Have you ever been diagnosed with a prostate illness, such as prostate hyperplasia, excluding prostate cancer?" [20]. Smoking was defined as smoking ≥ 100 cigarettes in their lifetime, and drinking was defined as consuming alcohol ≥ 12 times in the last year. BMI was calculated as weight (kg) divided by height(m) squared. TyG index, a reliable indicator assessing insulin resistance, was calculated as $\ln(TG \times 88.55 \times FPG \times 18/2)$ (both TG and FPG units in mmol/L). In addition, we enrolled WHtR, TyG.BMI, TyG.WC, TyG.WHtR, CVAI, VAI, and ABSI as indices to quantify the fatty and lipid

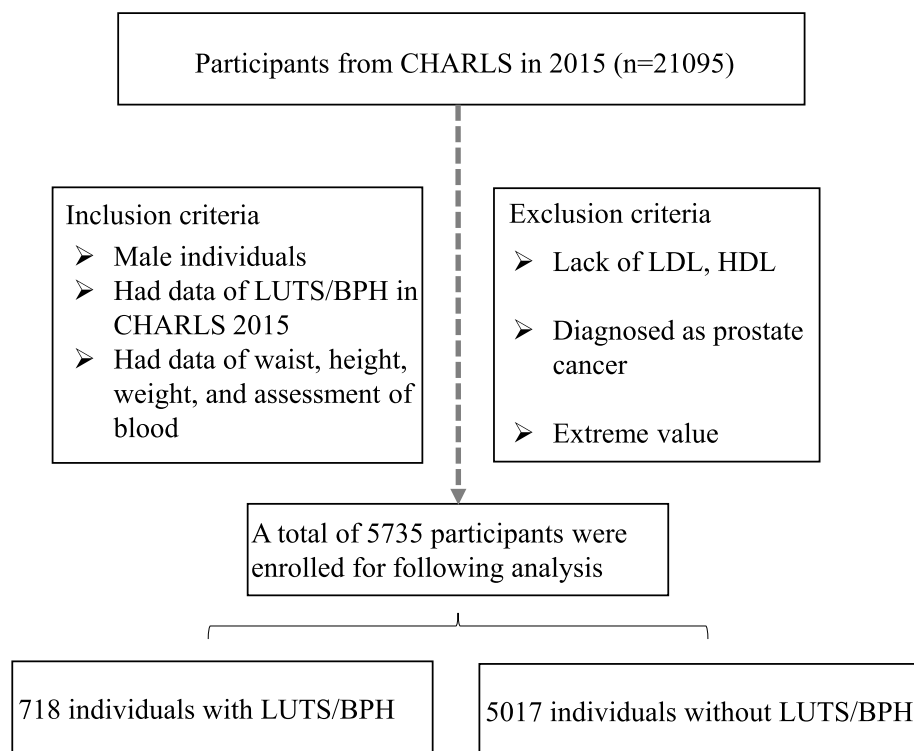


Fig. 1 Participants selection from the China Health and Retirement Longitudinal Study (CHARLS)

deposits, and the detailed calculation could be found in published studies [17, 21–25].

$$\text{WHtR} = \text{WC (cm)} / \text{height (cm)}$$

$$\text{BMI} = \text{Weight (kg)} / \text{height (m)}^2$$

$$\text{TyG index} = \ln(\text{Triglycerides (mg/dL)} \times \text{Fasting Glucose (mg/dL)})$$

$$\text{TyG.BMI} = \text{TyG index} \times \text{BMI}$$

$$\text{TyG.WC} = \text{TyG index} \times \text{Waist Circumference (cm)}$$

$$\text{TyG index} = \ln(\text{Triglycerides (mg/dL)} \times \text{Fasting Glucose (mg/dL)})$$

$$\text{TyG.WHtR} = \text{TyG index} \times \text{WHtR}$$

$$\text{CVAI} = 267.93 + 0.68 * \text{age} + 0.03 * \text{bmi} + 4 * \text{waist} + 22 * \log_{10}(\text{TG}) - 16.32 * \text{HDL}$$

$$\text{VAI} = \text{waist} / (39.68 + (1.88 * \text{bmi})) * (\text{TG} / 1.03) * (1.31 / \text{HDL})$$

$$\text{ABSI} = \text{waist} / (\text{height}^{1/2} * \text{bmi}^{2/3})$$

Covariates

Based on previous reports, risk factors associated with the incidence of LUTS/BPH include age, education level, nighttime sleep duration, and chronic comorbidities. Additional variables included in this study were age, residential area, marital status, education level, BMI, smoking status, alcohol consumption, hypertension, diabetes, and depression [26, 27].

Statistical methods

All statistical analyses were performed using R software. Categorical variables were expressed as frequencies and percentages. Binary logistic regression analysis was used to assess the unadjusted and adjusted associations between obesity- and lipid-related indices and LUTS/BPH, and the multivariate logistic regression analysis was performed to obtain the exact impact of the confounders on BPH/LUTS. The odds ratio (OR) and 95% confidence interval (95%CI) of each obesity- and lipid-related indices with LUTS/BPH were calculated after adjusting for age, education level, marital status, current smoking, alcohol consumption, depression, and diabetes. The area under the curve (AUC) of each index was calculated as a predictor of type 2 diabetes using receiver operating curves (ROC). The indices with the highest AUC were considered the most accurate, and the closer the AUC was to 1,

the more accurate the prediction was, with $P < 0.05$ considered statistically significant.

Results

Baseline information of participants

The study included 5,735 individuals, with 718 (12.5%) diagnosed with BPH/LUTS (Fig. 1, Table 1). The mean age of all participants was 60.8 years, with the BPH/LUTS group having a higher mean age of 64.7 years compared to 60.2 years in the healthy group ($P < 0.001$). Significant variations were observed in demographic and health-related traits, such as educational attainment, marital status, drinking behaviors, obesity rates, depression levels, and the prevalence of chronic illnesses like hypertension and diabetes. Notably, obesity was more prevalent in the BPH/LUTS group (48.1%) compared to the healthy group (40.4%) ($P < 0.001$). Additionally, the BPH/LUTS group exhibited a higher depression rate (32.4%) compared to the healthy group (24.8%) ($P < 0.001$).

Associations between LUTS/BPH and features of obesity

We compared eight fatty-relevant indices between LUTS/BPH and normal participants. The results showed that all of the indices are higher in LUTS/BPH compared to normal (Table 2). In addition, we demonstrated the nonlinear relation between LUTS/BPH and WHtR (P for overall < 0.0001 ; P for non-linear = 0.0037), BMI (P for overall < 0.0001 ; P for non-linear < 0.0001), WHtR (P for overall < 0.0001 ; P for non-linear = 0.0037), TyG.BMI (P for overall < 0.0001 ; P for non-linear < 0.0001), TyG.WC (P for overall < 0.0001 ; P for non-linear = 0.019), TyG.WHtR (P for overall < 0.0001 ; P for non-linear = 0.0064), ABSI (P for overall < 0.0001 ; P for non-linear = 0.011), and CVAI (P for overall < 0.0001 ; P for non-linear = 0.012) (Fig. 2). Age: OR = 1.05 (95% CI, 1.03–1.06, $P < 0.001$), Diabetes: OR = 1.31 (95% CI, 1.03–1.65, $P = 0.03$), and CVAI: OR = 1.01 (95% CI, 1.00–1.03, $P = 0.05$) were associated with LUTS/BPH in the multivariate logistic regression analysis (Table 3).

CVAI exhibited better performance in predicting LUTS/BPH

Considering many exit indices of fatty features and lipid deposits, we compared their discrimination efficiency in distinguishing the risk of LUTS/BPH. As shown in Fig. 3, we found that CVAI might be the best predictor of LUTS/BPH, with an AUC value of 0.58. These results suggested visceral adiposity could reflect the fatty features better.

Table 1 Baseline information of participants

N	Overall 5735	BPH.LUTS 718	Normal 5017	P value
Age (mean (SD))	60.8 (9.8)	64.7 (9.8)	60.2 (9.7)	< 0.001
Education (%)				
College	4446 (77.5)	589 (82.0)	3857 (76.9)	0.006
Second/high school	483 (8.4)	44 (6.1)	439 (8.8)	
Primary	625 (10.9)	72 (10.0)	553 (11.0)	
Illiterate	181 (3.2)	13 (1.8)	168 (3.3)	
Marriage (%)				
Married	5170 (90.1)	635 (88.4)	4535 (90.4)	0.012
Divorced	82 (1.4)	6 (0.8)	76 (1.5)	
Widowed	408 (7.1)	70 (9.7)	338 (6.7)	
Unmarried	75 (1.3)	7 (1.0)	68 (1.4)	
Drinking (%)				
Yes	3346 (58.4)	358 (49.9)	2988 (59.6)	< 0.001
No	2385 (41.6)	359 (50.1)	2026 (40.4)	
Obesity (%)				
Yes	2372 (41.4)	345 (48.1)	2027 (40.4)	< 0.001
No	3363 (58.6)	373 (51.9)	2990 (59.6)	
Depression (%)				
Yes	1396 (25.8)	222 (32.4)	1174 (24.8)	< 0.001
No	4021 (74.2)	464 (67.6)	3557 (75.2)	
CES-D (mean (SD))	6.8 (5.8)	8.0 (6.6)	6.7 (5.6)	< 0.001
Hypertension (%)				
Yes	1796 (31.6)	257 (35.9)	1539 (31.0)	0.009
No	3879 (68.4)	458 (64.1)	3421 (69.0)	
Diabetes (%)				
Yes	699 (12.2)	118 (16.4)	581 (11.6)	< 0.001
No	5033 (87.8)	600 (83.6)	4433 (88.4)	
Dyslipidemia (%)				
Yes	1142 (19.9)	141 (19.6)	1001 (20.0)	0.883
No	4593 (80.1)	577 (80.4)	4016 (80.0)	
Smoking (%)				
Non-smoker	1019 (56.6)	149 (65.4)	870 (55.3)	< 0.001
Ex-smoker	303 (16.8)	43 (18.9)	260 (16.5)	
Smoker	79 (26.6)	36 (15.8)	443 (28.2)	
LDL (mean (SD))	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	0.524
HDL (mean (SD))	1.3 (0.3)	1.3 (0.3)	1.3 (0.3)	0.002
TG (mean (SD))	1.5 (1.0)	1.5 (1.0)	1.5 (1.0)	0.894
Waist (mean (SD))	85.3 (13.3)	87.4 (12.9)	85.0 (13.4)	< 0.001
Weight (mean (SD))	63.5 (11.4)	64.9 (11.4)	63.3 (11.4)	< 0.001
Glucose (mean (SD))	103.3 (34.7)	105.8 (39.2)	102.9 (33.9)	0.037

The boldface represents statistical significance ($P < 0.05$)

SD standard deviation, CES-D Center for Epidemiologic Studies Depression, LDL Low-density lipoprotein, HDL High-density, TG Triglyceride, BPH Benign prostatic hyperplasia, LUTS Lower urinary tract symptoms

Table 2 Comparison eight fatty-relevant indices between LUTS/BPH and normal participants. The boldface represents statistical significance ($P < 0.05$)

	BPH/LUTS	Normal	P value
BMI (mean (SD))	24.0 (3.5)	23.4 (3.5)	<0.001
WHtR (mean (SD))	0.6 (0.1)	0.5 (0.1)	<0.001
TyG.WHtR (mean (SD))	2.2 (0.5)	2.2 (0.6)	0.001
TyG.BMI (mean (SD))	101.1 (25.3)	98.2 (25.7)	0.004
TyG.WC (mean (SD))	368.2 (91.0)	356.4 (93.3)	0.001
CVAI (mean (SD))	108.2 (55.1)	94.7 (56.9)	<0.001
VAI (mean (SD))	1.8 (1.5)	1.7 (1.6)	0.371
ABSI (mean (SD))	0.9 (0.1)	0.8 (0.1)	0.014

SD standard deviation, BMI Body mass index, WHtR Waist-height ratio, VAI Visceral adiposity index, ABSI A body shape index, TyG: Triglyceride-glucose, CVAI Chinese visceral adiposity index, BPH Benign prostatic hyperplasia, LUTS Lower urinary tract symptoms

Discussion

LUTS/BPH is one of the most common conditions among older men, affecting 12.5% of patients in this study. This high incidence not only significantly affects patients' quality of life, but also places a huge burden on the public health system [28]. Currently, many studies described that fatty might promote LUTS/BPH based on many ways, indicating fatty indices might be potential indicator in predicting LUTS/BPH.

In this study, we evaluated eight fat assessment indicators, including BMI, WHtR, TyG.BMI, TyG.WC, TyG.WHtR, CVAI, VAI, and ABSI. These indicators reflect different characteristics of body obesity. For instance, WHtR, TyG.BMI, TyG.WC, and TyG.WHtR represented Central obesity and metabolic obesity, where CVAI and VAI related to visceral obesity. BMI, WHtR, TyG.BMI, TyG.WC, TyG.WHtR, CVAI, VAI, and ABSI exhibited nonlinear correlations with BPH, a finding that aligns with previous research. For instance, numerous studies have demonstrated a positive relationship between prostate size, LUTS, and BMI [29]. However, BMI has certain limitations, particularly its inability to distinguish between fat and non-fat body composition. Kristal et al. investigated BPH risk factors in 5,667 men from the placebo group of the Prostate Cancer Prevention Trial and discovered that for every 0.05 increase in waist-to-hip ratio, the risk of BPH escalated by 10%, which is also associated with an increased likelihood of surgery [30, 31]. One study noted that a higher VAI essentially indicates a larger waist circumference, a well-established risk factor for insulin resistance. This disorder is linked to elevated levels of IGF-1, a proliferative factor for prostate growth. Their study revealed that patients with higher VAI scores had larger prostate sizes, suggesting a static component of VAI related to BPH/LUTS.

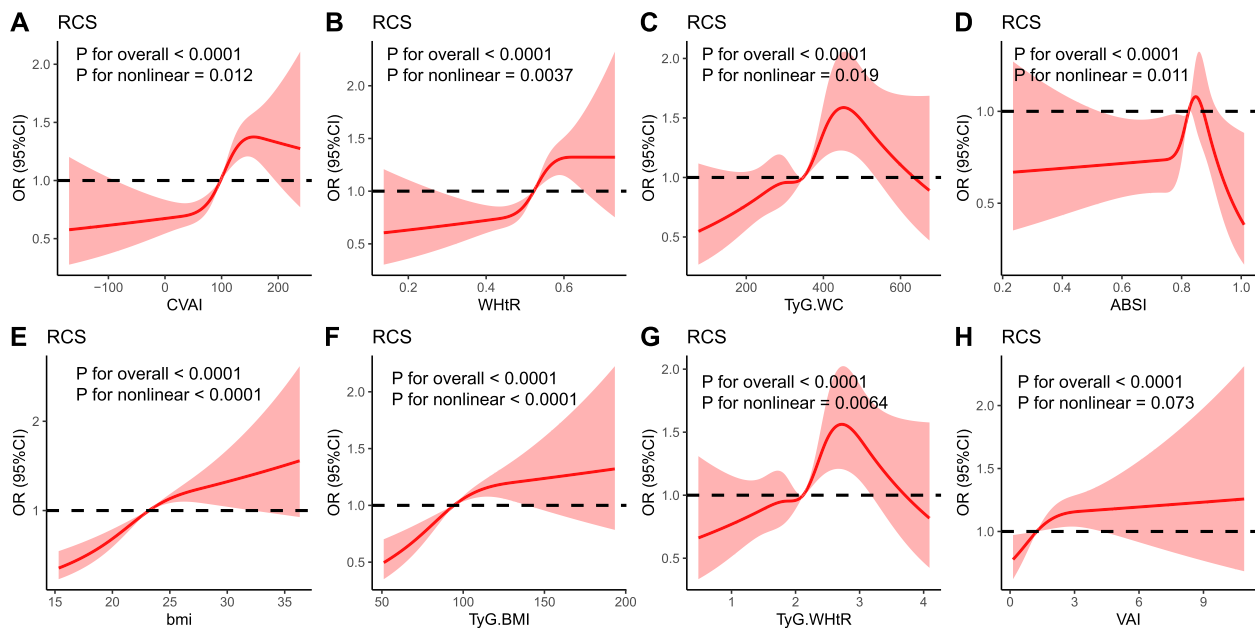


Fig. 2 Overall and nonlinear associations between LUTS/BPH and features of obesity. A. Restricted cubic spline (RCS) for Chinese visceral adiposity index (CVAI). B. RCS for Waist-height ratio (WHtR). C. RCS for Triglyceride-glucose. Waist circumference (TyG.WC). D. RCS for A body shape index (ABSI). E. RCS for Body mass index (BMI). F. RCS for TyG.BMI. G. RCS for TyG.WHtR. H. RCS for Visceral adiposity index (VAI). BPH: Benign prostatic hyperplasia, LUTS: Lower urinary tract symptoms

Table 3 Multivariate logistic regression analysis between indices and LUTS/BPH

	OR (95%CI)	P value
Age	1.05 (1.03–1.06)	<0.001
Hypertension	0.99 (0.84–1.18)	0.93
Diabetes	1.31 (1.03–1.65)	0.03
BMI	1.08 (1.77–1.52)	0.65
WHtR	0.00 (0.00–1191.00)	0.57
TyG.BMI	0.97 (0.92–1.02)	0.30
TyG.WC	1.00 (0.92–1.02)	0.91
TyG.WHtR	2.77 (0.08–97.3)	0.57
CVAI	1.01 (1.00–1.03)	0.05
ABSI	0.02 (0.00–118.50)	0.38

BMI Body mass index, WHtR Waist-height ratio, ABSI A body shape index, TyG Triglyceride-glucose, CVAI Chinese visceral adiposity index, BPH Benign prostatic hyperplasia, LUTS Lower urinary tract symptoms, OR odds ratio

Anthropometric data concerning visceral fat have been shown to be more effective predictors for metabolic disorders than subcutaneous fat [32–34]. These measurements improve the predictive capabilities of current chronic disease models, including those related to diabetes, cardiovascular diseases, hyperuricemia, and metabolic syndrome MetS. The CVAI was created to evaluate visceral adiposity specifically among the Chinese population, analogous to the VAI used in Western

demographics. Extensive research suggests that CVAI is more accurate than other obesity indices in forecasting hypertension, diabetes, and related comorbidities [35, 36]. Since CVAI and VAI are essentially the same indicator, our study corroborates these findings.

We further evaluated the discrimination ability of the eight indices. Although the predictive ability of several indicators for BPH is not high, CVAI is the best indicator among them. This evidence suggests that CVAI is more suitable for the Chinese population compared to VAI. Studies [37] have long revealed a substantial link between visceral fat and BPH. Therefore, it is fair to encourage weight loss, exercise, and a balanced diet as part of routine BPH treatment. A prospective randomized study with an appropriate follow-up period is needed to confirm the link between central obesity and BPH treatment.

This article presents evidence of a nonlinear connection between metabolic disorders linked to the accumulation of visceral fat and BPH. Of the eight indicators related to obesity that were investigated, the CVAI demonstrated the most significant predictive capability. Nonetheless, the overall effectiveness of obesity as a predictor for BPH is insufficient, underscoring that BPH is influenced by multiple factors where obesity is a notable contributor, particularly concerning visceral fat accumulation. Additionally, a cross-sectional analysis involving 400 males hospitalized for BPH/ LUTS identified a positive association between the VAI and

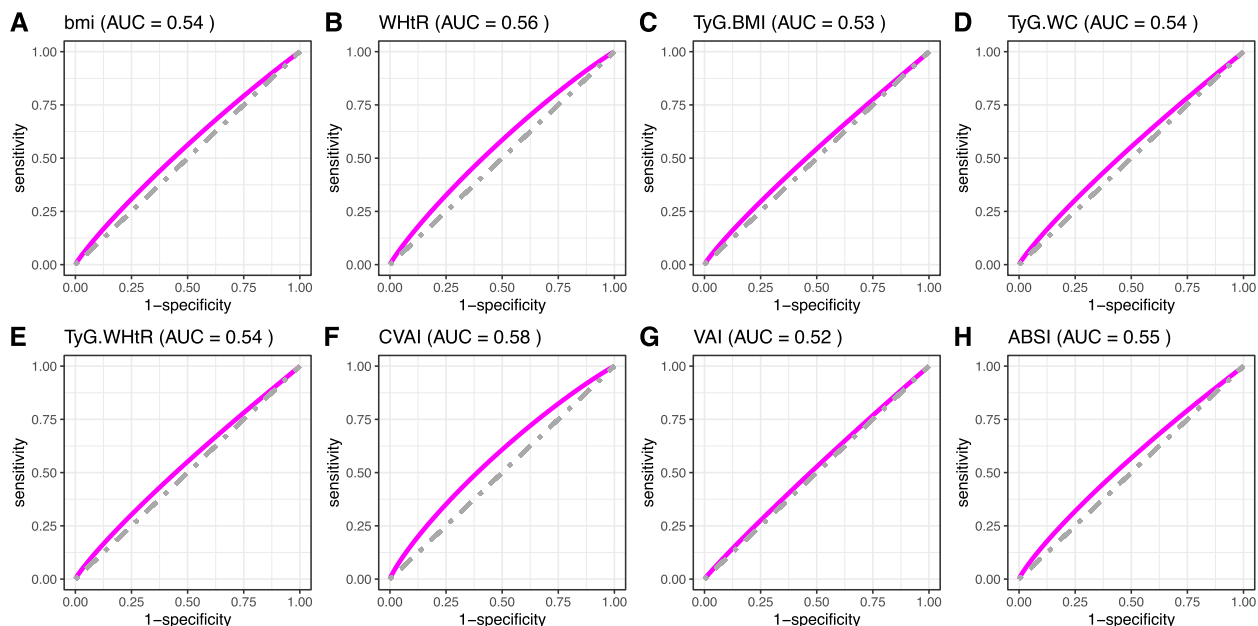


Fig. 3 Discrimination efficiency in distinguishing the risk of LUTS/BPH. A. Area under curve (AUC) for body mass index (BMI). B. AUC for Waist-height ratio (WHtR). C. AUC for Triglyceride-glucose.BMI (TyG.BMI). D. AUC for TyG. Waist circumference (TyG.WC). E. AUC for TyG.WHtR. F. AUC for Chinese visceral adiposity index (CVAI). G. AUC for Visceral adiposity index (VAI). H. AUC for A body shape index (ABSI). BPH: Benign prostatic hyperplasia, LUTS: Lower urinary tract symptoms

prostate volume ($r=0.29$, $p=0.00001$) [38]. This result indicates that the accumulation of visceral fat not only affects the prevalence of BPH/LUTS but also correlates with the size of the prostate.

In this study, we found that the CVAI was significantly associated with LUTS/BPH and demonstrated the highest predictive ability among eight obesity-related indices evaluated. However, we acknowledge that the AUC of 0.58 reflects only modest discriminatory power, indicating that CVAI alone may not be sufficient as a standalone predictor for LUTS/BPH in clinical practice. The modest AUC of CVAI could stem from several factors, such as complex interactions between contributing factors among genetic, hormonal, metabolic, and environmental factors. Our findings underscore the need to interpret obesity-related indices like CVAI within a broader predictive framework. Combining CVAI with other established risk factors for LUTS/BPH—such as age, prostate volume, and serum hormone levels—may yield a more comprehensive risk stratification model. The relatively low AUC values observed across all indices highlight a critical gap in current predictive tools for LUTS/BPH. This underscores the importance of prospective studies designed to validate our findings and explore novel biomarkers or composite indices that better capture the metabolic and systemic processes underlying LUTS/BPH. Additionally, longitudinal studies could clarify the causal relationships between visceral adiposity and LUTS/BPH, offering insights into potential preventive or therapeutic interventions. Regrettably, this cohort did not include data on prostate size, which limited further exploration. Since this is a cross-sectional study, temporal associations cannot be determined, and more prospective studies are needed. Cross-sectional studies can only reflect individual cases and cannot establish causal relationships. Since differences in gender and age distribution, socioeconomic and cultural factors, living environment, and dietary habits may limit the generalizability of these findings to other populations, large-sample, multicenter prospective observational studies are still needed for verification. What is more, small statistical differences in better-performed AUC in CVAI compared to other indices may not always translate to meaningful clinical advantages, which needs further validation of CVAI's predictive value in real-world clinical settings.

Conclusion

This study comprehensively analyzed the association between eight obesity-related anthropometric factors and LUTS/BPH. CVAI exhibited favorable performance in predicting LUTS/BPH, indicating that visceral fat significantly impacts LUTS/BPH.

Abbreviations

BPH	Benign prostatic hyperplasia
LUTS	Lower urinary tract symptoms
CVAI	Chinese Visceral Adiposity Index
CHARLS	China Health and Retirement Longitudinal Study
ROC	Receiver operating curve
AUC	Area under the curve
BOO	Bladder outlet obstruction
WC	Waist circumference
BMI	Body mass index
WHR	Waist-height ratio
VAI	Visceral adiposity index
ABSI	A body shape index
TyG	Triglyceride-glucose
CI	Confidence interval

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Authors' contributions

KHC: Conceptualization, Formal Analysis, Methodology, Software, Writing – original draft. BL: Formal Analysis, Methodology, Writing – original draft. GW: Methodology, Validation, Writing – review & editing. HZ: Validation, Writing – review & editing. YHC: Conceptualization, Methodology, Software, Supervision, Writing – review & editing. HBG: Conceptualization, Supervision, Writing – review & editing, Project administration.

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Data availability

The data that support the findings of this study are available from CHARLS, <http://charls.pku.edu.cn/>, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from requests to access the datasets should be directed to <http://charls.pku.edu.cn/>.

Declarations

Ethics approval and consent to participate

The studies involving humans were approved by Biomedical Ethics Review Committee of Peking University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Competing interests

The authors declare no competing interests.

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