

# Metabolism Score for Visceral Fat (METS-VF): A New Predictive Surrogate for CKD Risk

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**Purpose:** Metabolic disorders are closely related to the occurrence and development of chronic kidney disease (CKD). We explored the prospective association between the Metabolic Score for Visceral Fat (METS-VF) and CKD in a 5-year follow-up study.

**Patients and Methods:** In this cohort study, 631 adults not suffering from CKD from Wanzhai Town, in China in 2012 were included at baseline and followed up in 2017 and 2018. Multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between METS-VF and CKD risk. Area under the receiver operating characteristic curve (AUC) analyses were used to evaluate the ability of METS-VF, waist-to-height ratio (WhtR), visceral adiposity index (VAI), homeostatic model assessment of insulin resistance (HOMA-IR), body mass index (BMI) to predict CKD risk.

**Results:** We identified 103 CKD cases during follow-up. After adjustment for confounding factors, comparing the lowest quartile of METS-VF, the OR (95% CI) of CKD risk in the highest quartile was 3.04 (1.39–6.64). The per Standard deviation (SD) increase in METS-VF was positively correlated with CKD risk. The AUC of METS-VF for predicting CKD risk was, in general, higher than that for WhtR, VAI, HOMA-IR, and BMI.

**Conclusion:** METS-VF may be an indicator for predicting CKD risk.

**Keywords:** CKD, METS-VF, visceral obesity

## Introduction

It is estimated that by 2040, the number of deaths worldwide due to chronic kidney disease (CKD) will reach 3.1 million. Between 1990 and 2017, fasting plasma glucose (FPG), body mass index (BMI) and systolic blood pressure (SBP) were the main metabolic factors used to measure CKD risk. Further analyses of the summary-exposure value of CKD risk showed that BMI and a high FPG level increased significantly by 70% and 38%, respectively, whereas high SBP decreased by 2%.<sup>1,2</sup> A study of 2.7 million participants in China found that more than one in seven met criteria for overall obesity and one third met criteria for abdominal obesity.<sup>3</sup> In a large, retrospective, 10-year study in central China involving 34,630 hospitalized patients who underwent renal biopsy, the prevalence of obesity-related renal disease increased from 0.62% in 2009 to 2.25% in 2018.<sup>4</sup> Increasing numbers of studies have shown that metabolic disorders based on visceral adipose tissue (VAT) are associated with the risk of cardiovascular disease and neurological disease.<sup>5,6</sup> Furthermore, perirenal adipose tissue has been shown to be closely related to kidney disease in obese individuals.<sup>7</sup> Therefore, there is an urgent need for an accurate evaluation index to link the metabolic status of VAT with CKD risk.

Magnetic resonance imaging (MRI) is the “gold standard” for VAT but its application is limited due to the high operating costs and need for highly trained personnel.<sup>8</sup> Metabolic Score for Visceral Fat (METS-VF) combines age, sex, waist-to-height ratio (WhtR), metabolic score for insulin resistance (METS-IR), as well as levels of FPG and

triglycerides (TG). METS-VF has been used to predict intra-abdominal fat volume and cardiometabolic health in the Mexican population.<sup>9</sup> In this study, we explored if METS-VF can also be used as a predictor of CKD.

## Methods

### Ethical Approval of the Study Protocol

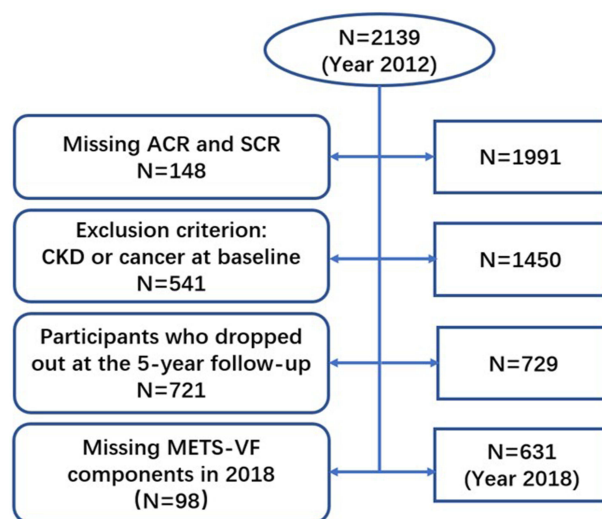
The study protocol was approved (201708011) by the Ethics Committee of the Third Affiliated Hospital of Southern Medical University (Guangdong, China). The study was conducted in accordance with the Declaration of Helsinki 1964 and its later amendments. All participants provided written informed consent.

### Study Population

Participants were recruited from a population-based cohort study in six communities in Wanzhai Town (Zhuhai City, Southern China). Random sampling of clusters at multiple stages was used. Adults (age  $\geq 18$  years) living in these six communities were invited to participate in the survey. We excluded people with CKD or cancer, and 1450 adults not suffering from CKD between June to October 2012 were included at baseline. After 5-year follow-up, 721 dropped out of the study, and 98 people who had missing data for all components of METS-VF were excluded. Finally, 631 participants were followed up from December 2017 to April 2018. A detailed Flowchart of our study is shown as Figure 1.

### Data Collection

Medical staff and medical students helping to carry out this study received standardized training. Basic information regarding age, sex, tobacco smoking, alcohol consumption, education level, physical activity, and disease history was obtained through a questionnaire. A mercury sphygmomanometer was used to measure the blood pressure of each participant after resting for  $\geq 5$  min, and then the mean value of three measurements was calculated. Participants were requested to wear light clothes as well as to stand and breathe naturally. The waist circumference (WC) between the lower costal margin of the midline of the axilla and iliac crest was measured. A blood test was carried out after an overnight fast  $\geq 10$  h. Blood samples were cryopreserved and sent for assay to the central laboratory of the Third Affiliated Hospital of Southern Medical University. To measure the indicators of glucose metabolism, a standard enzymatic method was used to measure the FPG level and an electrochemiluminescence method was employed to measure the fasting insulin (FINS) level. To measure blood lipid levels, a colorimetric method was employed to determine levels of TG, total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C). To measure biochemical indicators, the improved Jaffe method was used to determine the serum creatinine (SCr) level using a Cobas 6000 system (Roche, Basel, Switzerland). To measure the indicators



**Figure 1** Flowchart for the selection of study subjects.

**Abbreviations:** ACR, urinary microalbumin to creatinine ratio; SCR, serum creatinine; CKD, chronic kidney disease; METS-VF, Metabolism Score for Visceral Fat.

of oxidative stress and inflammation risk, enzyme-linked immunosorbent assays were used to measure the superoxide dismutase (SOD) level and immunoturbidimetry was employed to measure the high-sensitivity C-reactive protein (hs-CRP) concentration. In addition, we measured the albumin and creatinine concentrations (ACR) of random urine samples.

## Definition and Calculations

BMI was calculated as  $BMI = \text{weight}(\text{kg}) / \text{height}^2(\text{m}^2)$ .

WhtR was calculated as  $\text{WhtR} = \text{waist}(\text{cm}) / \text{height}(\text{cm})$ .

The estimated glomerular filtration rate (eGFR) was determined using the Modification of Diet in Renal Disease equation:

$$eGFR(\text{mL}/\text{min}/1.73 \text{ m}^2) = 175 \times (\text{SCr})^{-1.234} \times (\text{age})^{-0.179} \times (\text{if female}, \times 0.79).$$

CKD was defined as  $ACR \geq 3$  (mg/g) and/or  $eGFR < 60$  (mL/min/1.73 m<sup>2</sup>).

The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated as:

$$\text{HOMA-IR} = \text{FPG}(\text{mmol/L}) \times \text{FINS}(\text{mU/L}) / 22.5. \text{ Insulin resistance was defined as } \text{HOMA-IR} > 2.69.^{10}$$

Obesity was defined as  $BMI \geq 28.0$  kg/m<sup>2</sup>, or WC (male)  $\geq 90$ cm, or WC (female)  $\geq 85$ cm.<sup>11</sup>

METS-IR,<sup>12</sup> METS-VF,<sup>9</sup> and VAI<sup>13</sup> were calculated as shown below.

$$\text{METS-IR} = \text{Ln}\{[(2 \times \text{GLU}) + \text{TG}] \times [\text{BMI}/\text{Ln}(\text{HDL} - \text{C})]\}$$

$$\text{METS-VF}(\text{man}) = 4.466 + 0.011 \times \{[\text{Ln}(\text{METS-IR})]^3\} + 3.239 \times \{[\text{Ln}(\text{WhtR})]^3\} + 0.319 \times 1 + 0.594 \times \text{Ln}(\text{age})$$

$$\text{METS-VF}(\text{woman}) = 4.466 + 0.011 \times \{[\text{Ln}(\text{METS-IR})]^3\} + 3.239 \times \{[\text{Ln}(\text{WhtR})]^3\} + 0.319 \times 0 + 0.594 \times \text{Ln}(\text{age})$$

$$\text{VAI}(\text{man}) = \{\text{Waist}/[39.68 + (1.88 \times \text{BMI})]\} \times (\text{TG}/1.03) \times (1.31/\text{HDL} - \text{C})$$

$$\text{VAI}(\text{woman}) = \{\text{Waist}/[36.58 + (1.89 \times \text{BMI})]\} \times (\text{TG}/0.81) \times (1.52/\text{HDL} - \text{C})$$

## Statistical Analyses

SPSS 20 (IBM, Armonk, NY, USA) and MedCalc ([www.medcalc.org](http://www.medcalc.org)) were used to analyze data. Continuous variables with a normal distribution are displayed as mean±SD, and the independent sample *t*-test was used for comparison of differences. Continuous variables with a non-normal distribution are presented as median (25th–75th percentile), and the Mann–Whitney *U*-test and Kruskal–Wallis test were used for a comparison of differences. Count data are expressed as percentages, and the chi-square test was employed for comparison of differences. Participants were classified into quartiles, with the lowest quartile as the reference. We also estimated CKD risk with per-SD increase in METS-VF. The specific quartiles of METS-VF were grouped, with Quartile 1(Q1) being  $\text{METS-VF} \leq 5.75$ , Quartile 2(Q2) being  $5.57 < \text{METS-VF} \leq 6.23$ , Quartile 3(Q3) being  $6.23 < \text{METS-VF} \leq 6.56$ , and Quartile 4(Q4) being  $\text{METS-VF} > 6.56$ . We use multivariable logistic regression to assess whether METS-VF could be used to predict the potential risk of CKD.

We established three models. Model 1 was unadjusted. Model 2 was adjusted for tobacco smoking, alcohol consumption, education level, physical activity. Model 3 was adjusted for tobacco smoking, alcohol consumption, education level, physical activity, SBP, diastolic blood pressure (DBP), hs-CRP level, SOD level. Results are presented as odds ratio (ORs) and 95% confidence intervals (CIs). A receiver operating characteristic curve (ROC) was employed to analyze the efficacy of METS-VF, WhtR, VAI, HOMA-IR, and BMI for diagnosing CKD.  $p < 0.05$  (two-tailed) was considered significant.

## Results

### Clinical and Demographic Characteristics in the Non-CKD and CKD Group

Table 1 shows the demographic characteristics of the 631 eligible participants who had or did not have CKD, as well as 103 CKD cases identified during a mean follow-up of 5.4 years. Participants with CKD were older, and had higher BMI, WC, WhtR, SBP, DBP, HOMA-IR, METS-IR, VAI, METS-VF, as well as higher levels of SCr, ACR, TG, FPG, and FINS. In participants with CKD, a higher prevalence of diabetes mellitus, obesity and hypertension, as well as a lower

**Table 1** Clinical and Demographic Characteristics of Participants

| Variable                         | Non-CKD (N=528)    | CKD (N=103)        | P value |
|----------------------------------|--------------------|--------------------|---------|
| Age (years)                      | 52.65±11.39        | 64.74±11.07        | P<0.001 |
| Male, n (%)                      | 256(84.49)         | 47(15.51)          | 0.596   |
| High school or higherer (%)      | 235(90.04)         | 26(9.96)           | P<0.001 |
| Current smoking, n (%)           | 73(90.12)          | 8(9.88)            | 0.093   |
| Current alcohol use, n (%)       | 39(92.86)          | 3(7.14)            | 0.096   |
| Physical activity, n (%)         | 286(80.11)         | 71(19.89)          | 0.006   |
| Obesity, n (%)                   | 202(38.26)         | 54(52.43)          | 0.007   |
| Diabetes, n (%)                  | 38(7.20)           | 16(15.53)          | 0.006   |
| Hypertension, n(%)               | 222(42.05)         | 76(73.39)          | P<0.001 |
| SBP(mmHg)                        | 129.65±17.63       | 145.91±19.68       | P<0.001 |
| DBP(mmHg)                        | 82.24±10.82        | 86.4±9.99          | P<0.001 |
| FPG(mmol/L)                      | 4.91(4.6–5.33)     | 5.12(4.78–5.67)    | 0.001   |
| FINS(mU/l)                       | 8.86(6.56–12.1)    | 9.57(7.25–14.4)    | 0.025   |
| TG(mmol/L)                       | 1.24(0.91–1.77)    | 1.53(1.09–2.34)    | P<0.001 |
| TC(mmol/L)                       | 5.4±1.01           | 5.57±1.03          | 0.137   |
| LDL-C(mmol/L)                    | 3.22±0.87          | 3.28±0.92          | 0.565   |
| HDL-C (mmol/L)                   | 1.53±0.33          | 1.47±0.35          | 0.083   |
| SCR (umol/L)                     | 78(69–90)          | 89(78–110)         | P<0.001 |
| eGFR(mL/min/1.73m <sup>2</sup> ) | 84.11(75.26–94.18) | 59.33(54.09–81.39) | P<0.001 |
| ACR (mg/g)                       | 0.99(0.67–1.48)    | 4.07(1.6–6.41)     | P<0.001 |
| hs-CRP(mg/L)                     | 2.2±5.18           | 3.1±6.19           | 0.117   |
| SOD(U/L)                         | 153.78±15.59       | 151.11±14.87       | 0.109   |
| BMI(kg/m <sup>2</sup> )          | 24.05±3.35         | 25.06±3.39         | 0.005   |
| WC(cm)                           | 84.54±9.84         | 87.93±9.95         | 0.001   |
| WHtR                             | 0.52±0.06          | 0.56±0.06          | P<0.001 |
| HOMA-IR                          | 1.98(1.39–2.84)    | 2.35(1.57–3.72)    | 0.004   |
| METS-IR                          | 6.71±0.8           | 7.04±0.97          | P<0.001 |
| VAI                              | 1.3(0.87–2.04)     | 1.76(1.08–2.94)    | P<0.001 |
| METS-VF                          | 6.15(5.7–6.51)     | 6.51(6.22–6.77)    | P<0.001 |

**Abbreviations:** CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; FINS, fasting insulin; TG, triglycerides; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SCR, serum creatinine; eGFR, estimated glomerular filtration rate; ACR, urinary microalbumin to creatinine ratio; hs-CRP, high-sensitivity C-reactive protein; SOD, superoxide dismutase; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio; HOMA-IR, homeostatic model assessment of insulin resistance; METS-IR, Metabolic Score for Insulin Resistance; VAI, Visceral Adiposity Index; METS-VF, Metabolism Score for Visceral Fat.

**Table 2** Multivariable Logistic Regression to Analyze the Correlation Between Metabolic Score for Visceral and CKD Risk

|                      | Quartile 1       | Quartile 2        | Quartile 3         | Quartile 4         | P Trend | Per 1-SD        |
|----------------------|------------------|-------------------|--------------------|--------------------|---------|-----------------|
| Range                | ≤5.75            | 5.75–6.23         | 6.23–6.56          | >6.56              |         |                 |
| Incidence rate (%)   | 6.37(2.51–10.23) | 10.06(5.34–14.79) | 19.48(13.15–25.81) | 29.19(22.09–36.29) |         |                 |
| Model 1 <sup>a</sup> | 1 (Ref)          | 1.64(0.72–3.75)   | 3.56(1.67–7.56)    | 6.06(2.94–12.51)   | P<0.001 | 2(1.58–2.54)    |
| Model 2 <sup>b</sup> | 1 (Ref)          | 1.52(0.66–3.49)   | 3.29(1.53–7.07)    | 5.81(2.78–12.14)   | P<0.001 | 2(1.56–2.55)    |
| Model 3 <sup>c</sup> | 1 (Ref)          | 1.19(0.5–2.79)    | 1.91(0.85–4.27)    | 3.04(1.39–6.64)    | 0.001   | 1.58(1.21–2.06) |

**Notes:** <sup>a</sup>Unadjusted. <sup>b</sup>Adjusted for education level, tobacco and alcohol consumption, physical activity. <sup>c</sup>Adjusted for education level, tobacco and alcohol consumption, physical activity level, SBP, DBP, hs-CRP, SOD.

**Abbreviations:** Ref, reference; SBP, systolic blood pressure; DBP, diastolic blood pressure; hs-CRP, high-sensitivity C-reactive protein; SOD, superoxide dismutase.

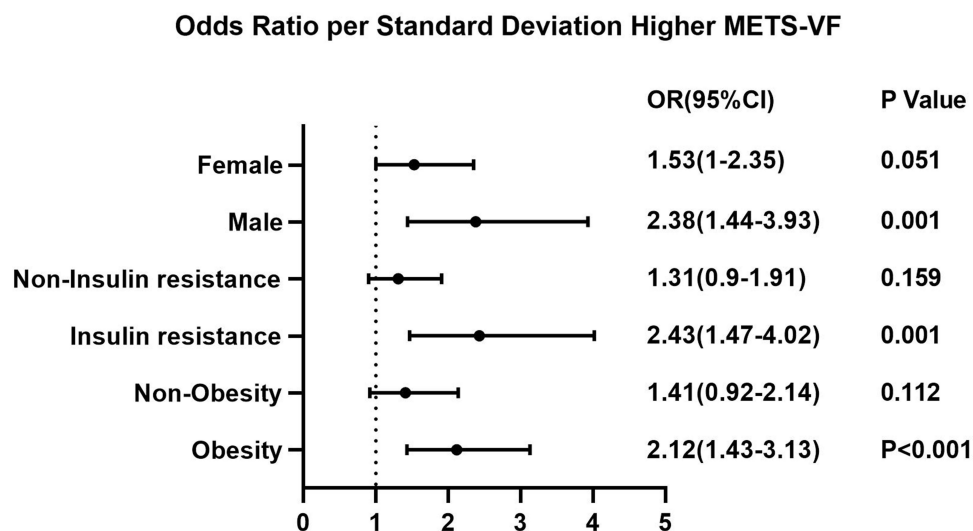
prevalence of high school or higher education and physical activity, were noted. However, the prevalence of tobacco smoking, alcohol consumption as well as levels of TC, HDL-C, LDL-C, hs-CRP, and SOD did not differ in those suffering from CKD or not suffering from CKD.

## Correlation Analysis Between METS-VF and CKD Risk

The ability of METS-VF to predict the CKD risk is shown in Table 2. The CKD prevalence increased with increasing quartiles of METS-VF. The prevalence (95% CI) of CKD for Q1, Q2, Q3, and Q4 was 6.37 (2.51–10.23), 10.06 (5.34–14.79), 19.48 (13.15–25.81), and 29.19 (22.09–36.29), respectively. A positive association between METS-VF and CKD risk was observed among the three models. After adjustment for the education level, tobacco smoking, alcohol consumption, physical activity, SBP, DBP, hs-CRP level, and SOD level, the OR (95% CI) of CKD for Q2, Q3, and Q4 was 1.19 (0.5–2.79), 1.91 (0.85–4.27), and 3.04 (1.39–6.64), respectively. For each increase in SD in METS-VF among three models, the adjusted OR (95% CI) of CKD was 2 (1.58–2.54), 2 (1.56–2.55), and 1.58 (1.21–2.06), respectively.

## Subgroups Analysis of the Association Between METS-VF and CKD Risk

We undertook subgroup analyses of the association between METS-VF and CKD risk. The positive association between METS-VF and CKD risk was still observed in male, insulin resistance, and obesity subgroups. After adjustment for the education level, tobacco smoking, and alcohol consumption, physical activity, SBP, DBP, hs-CRP, SOD, the OR (95% CI) of CKD was 2.38 (1.44–3.93), 2.43 (1.47–4.02), 2.12 (1.43–3.13), respectively (Figure 2).



**Figure 2** Subgroup analyses of the association between metabolic score for visceral fat and CKD risk.

**Abbreviations:** OR, odd ratios; CI, confidence interval; METS-VF, Metabolism Score for Visceral Fat.

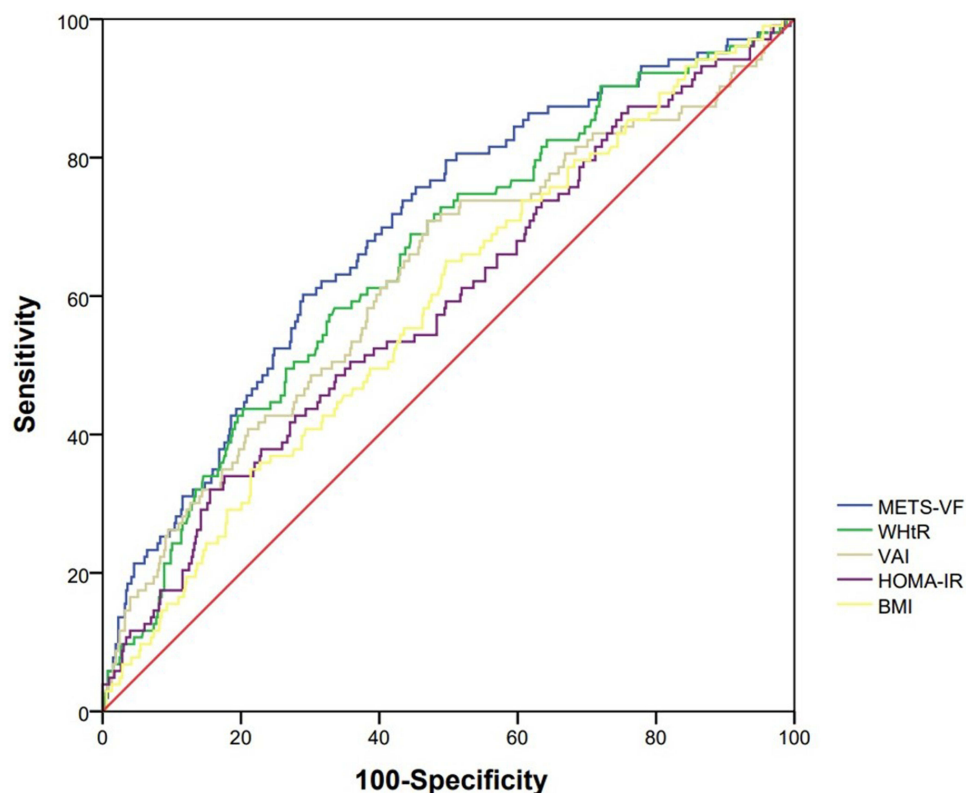
**Table 3** Comparison of Values for Area Under the Receiver Operating Characteristic Curve for METS-VF, WHtR, VAI, HOMA-IR, and BMI with CKD Risk

|         | AUC (95% CI)       | Cutoff value | Sensitivity% | Specificity% | Youden Index | P-value |
|---------|--------------------|--------------|--------------|--------------|--------------|---------|
| METS-VF | 0.692(0.654–0.728) | 6.432        | 60.19        | 71.02        | 0.3122       | <0.001  |
| WHtR    | 0.652(0.613–0.689) | 0.545        | 58.25        | 66.48        | 0.2473       | <0.001  |
| VAI     | 0.626(0.587–0.664) | 1.371        | 70.87        | 53.03        | 0.2390       | <0.001  |
| HOMA-IR | 0.589(0.549–0.628) | 3.491        | 32.04        | 84.47        | 0.1651       | 0.005   |
| BMI     | 0.585(0.545–0.623) | 23.833       | 65.05        | 50.38        | 0.1543       | 0.005   |

**Abbreviations:** METS-VF, Metabolism Score for Visceral Fat; WHtR, waist-to-height ratio; VAI, Visceral Adiposity Index; HOMA-IR, homeostatic model assessment of insulin resistance; BMI, body mass index.

## Comparative Analysis of ROC Curves of METS-VF, WHtR, VAI, HOMA-IR and BMI in Predicting CKD Risk

Table 3 shows the area under the ROC curve (AUC) value (95% CI), optimal cutoff, sensitivity, specificity, and Youden index for each parameter used to predict CKD risk. METS-VF, WHtR, VAI, HOMA-IR, and BMI were used as detection variables. CKD was used as the outcome variable for analyses of ROC curves. The AUC (95% CI) of METS-VF, WHtR, VAI, HOMA-IR, and BMI was 0.692 (0.654–0.728), 0.652 (0.613–0.689), 0.626 (0.587–0.664), 0.589 (0.549–0.628), 0.585 (0.545–0.623), respectively. METS-VF had the largest AUC (95% CI) among METS-VF, WHtR, VAI, HOMA-IR, and BMI, and the difference was significant. Compared with WHtR, VAI, HOMA-IR, and BMI, the Youden index of METS-VF was 0.3122, which was the highest value of all indices tested. Analyses of the ROC curves of the association between METS-VF, WHtR, VAI, HOMA-IR, and BMI, and CKD are shown in Figure 3.

**Figure 3** Comparison of the correlation between METS-VF, WHtR, VAI, HOMA-IR, and BMI and CKD risk.

**Abbreviations:** METS-VF, Metabolism Score for Visceral Fat; WHtR, waist-to-height ratio; VAI, Visceral Adiposity Index; HOMA-IR, homeostatic model assessment of insulin resistance; BMI, body mass index.

## Discussion

We showed that METS-VF was positively associated with CKD risk. For Q1, Q2, Q3, and Q4 of METS-VF, the CKD prevalence was 6.37%, 10.06%, 19.48% and 29.19%, respectively. After adjustment for confounders, the CKD risk at Q2, Q3, and Q4 of METS-VF increased by 1.19-, 1.91- and 3.04-times, respectively, compared with Q1. METS-VF had the largest AUC and Youden index for prediction of CKD risk compared with that of WHtR, VAI, HOMA-IR, and BMI. The optimal value of METS-VF for predicting CKD was 6.432, with a sensitivity of 60.19% and specificity of 71.02%.

Visceral obesity increases the risk of kidney disease. Under normal physiological conditions, adipose tissue coordinates the balance between systemic nutritional status and energy metabolism through adipokines. Under pathological conditions, excessive expansion and accumulation of adipose tissue leads to biological abnormalities and dysfunction of adipose tissue. These actions are accompanied by accumulation of ectopic fat, which leads to impairment of organ functions.<sup>14</sup> Analyses of the potential causal effects of obesity on kidney health from the United Kingdom showed that blood pressure was responsible for approximately 13–16% of cases and type 2 diabetes mellitus was responsible for 21–26% of cases; in enrichment analyses, 61 signaling pathways were found to be correlated with obesity measures.<sup>15</sup> In an obese population not suffering from hypertension or diabetes mellitus and with normal renal function, the thickness of visceral fat (measured using ultrasound) was found to inversely correlated with eGFR, and the latter decreased as visceral fat increases.<sup>16</sup> In our study, METS-VF was higher in the CKD group than in the control group. In a study of the obese subgroup, we found that, for each SD increase in METS-VF, the CKD risk increased by 2.12-times.

Disorders in the metabolism of glucose and lipids metabolism and insulin resistance increase the risk of kidney disease. The balance between glucose metabolism and lipid metabolism helps to maintain the normal function of the kidneys. However, under pathological conditions, excessive fatty acids form TG droplets in renal tubular epithelial cells, excessive accumulation of cholesterol in podocytes ruptures the integrity of the cleft septum, and high glucose can induce upregulation expression of lipogenic gene and reduce  $\beta$ -oxidation of fatty acids. All of these abnormalities in glycolipid metabolism leads to damage to cellular architecture and an inflammatory response in the kidneys.<sup>17–19</sup> In addition, if excessive accumulation of visceral fat leads to the impairment of insulin clearance and transmission of signaling pathways in pancreatic islets, it affects the energy supply of the kidneys which, eventually, leads to kidney damage.<sup>20–22</sup> In our study, levels of TG, FPG, and HOMA-IR were increased in the CKD group, and the differences were significant. In the HOMA-IR subgroup, the CKD risk increased by 2.43-times for each SD increase in METS-VF.

Studies have shown that aging and overnutrition can lead to accumulation of senescent adipocytes in adipose tissue. Simultaneously, this action is accompanied by damage to adipose progenitor cells, which results in disorders of glucose metabolism, lipid metabolism, endocrine dysfunction, and immune dysregulation in adipose tissue.<sup>23,24</sup> There are differences in the metabolic rate in men and women. In men, there may be significant accumulation of intra-abdominal fat due to more glucocorticoid receptors being present in intra-abdominal fat than that in women. In women, especially after the age of 60 years, due to a decline in estrogen levels, blood pressure and adipose-tissue redistribution is affected.<sup>25,26</sup> BMI can better define overweight and obesity, whereas WC can better define abdominal obesity. Impairment of insulin clearance in obese individuals, and the accompanying insulin resistance and disorders of glucose metabolism in tissues and organs, promote morbidly obesity.<sup>20,27</sup> Increased circulating levels of TGs, decreased clearance of LDL-C, and long-term maintenance of lower levels of HDL-C are involved in obesity development.<sup>28,29</sup> METS-VF integrates the above parameters stated above to assess the metabolic status of visceral fat, which can reflect the risk of human disease to a certain extent.<sup>9</sup>

The gold standard for VAT evaluation is MRI, and the other detection methods are computed tomography, dual X-ray absorptiometry (DXA), and bioelectrical impedance analysis (BIA).<sup>30</sup> However, application of these detection methods in daily clinical practice is limited by the requirement of equipment and specialist training. METS-VF is a surrogate index for estimating intra-abdominal adipose tissue and VAT based on DXA, but also has good consistency when compared with visceral-fat parameters measured by DXA, MRI, and BIA to some extent. Moreover, METS-VF can also reflect an unfavorable adipokine profile in people suffering from obesity.<sup>9</sup>

In a study of non-obese individuals, METS-VF was significantly associated with hyperuricemia risk and had the highest predictive ability in women.<sup>31</sup> A cohort study from Henan (China), revealed METS-VF to be positively

correlated with the risk of hypertension and type-2 diabetes mellitus.<sup>32,33</sup> In our study, with an increase in METS-VF quartile, CKD risk increased gradually, reaching 29.19% in Q4. Compared with Q1, the CKD risk increased by 3.04-times in Q4.

Due to the unfavorable changes in diets, the prevalence of obesity and metabolic abnormalities has increased year-by-year in China,<sup>34</sup> and the prevalence of metabolic abnormalities-related kidney diseases has also increased gradually. Studies have shown that increasing age,<sup>23</sup> overnutrition,<sup>24</sup> sex differences in the number of lipid glucocorticoid receptors and estrogen secretion,<sup>25,26</sup> abnormal lipid levels,<sup>28,29</sup> and insulin resistance<sup>20,27</sup> are involved in the development of morbid obesity. We attempted to predict CKD risk using the anthropometric indicators BMI, WHtR,<sup>35,36</sup> visceral fat index,<sup>37</sup> and insulin resistance.<sup>38,39</sup> Although these indices had a certain value, they had certain limitations. In our study, METS-VF had the largest AUC and Youden index for predicting CKD risk compared with that using WHtR, VAI, HOMA-IR, and BMI.

The main advantage of the present study was that it was the first time to investigate the longitudinal association between METS-VF and CKD risk, and we compared it with other metabolic indices (WHtR, VAI, HOMA-IR, BMI) that assess CKD risk. However, our study had three main limitations. First, we adjusted only for the confounding factors of education level, physical activity, tobacco smoking, alcohol consumption, lipid levels in blood, SBP, DBP, hs-CRP levels, SOD levels. Other unknown or unmeasured confounding variables may affect the predictive value of METS-VF for CKD risk. Secondly we lacked validated data on assessment of visceral fat using MRI or computed tomography. Third, we studied the population in Wanzhai Town, but whether METS-VF can be used to predict CKD risk in other parts of China is not known.

## Conclusion

The performance of METS-VF in predicting CKD was higher than that of other indicators (WHtR, VAI, HOMA-IR, BMI). METS-VF could be a useful indicator for predicting CKD.

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## Disclosure

The authors report no conflicts of interest in this work.

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