



Metabolic Score for Visceral Fat: a novel predictor for the risk of type 2 diabetes mellitus

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Abstract

To investigate the association between the Metabolic Score for Visceral Fat (METS-VF) and risk of type 2 diabetes mellitus (T2DM) and compare the predictive value of the METS-VF for T2DM incidence with other obesity indices in Chinese people. A total of 12 237 non-T2DM participants aged over 18 years from the Rural Chinese Cohort Study of 2007–2008 were included at baseline and followed up during 2013–2014. The cox proportional hazards regression was used to calculate hazard ratios (HR) and 95 % CI for the association between baseline METS-VF and T2DM risk. Restricted cubic splines were used to model the association between METS-VF and T2DM risk. Area under the receiver operating characteristic curve (AUC) analysis was used to evaluate the ability of METS-VF to predict T2DM incidence. During a median follow-up of 6.01 (95 % CI 5.09, 6.06) years, 837 cases developed T2DM. After adjusting for potential confounding factors, the adjusted HR for the highest *v.* lowest METS-VF quartile was 5.97 (95 % CI 4.28, 8.32), with a per 1-SD increase in METS-VF positively associated with T2DM risk. Positive associations were also found in the sensitivity and subgroup analyses, respectively. A significant nonlinear dose–response association was observed between METS-VF and T2DM risk for all participants ($P_{\text{nonlinearity}} = 0.0347$). Finally, the AUC value of METS-VF for predicting T2DM was largest among six indices. The METS-VF may be a reliable and applicable predictor of T2DM incidence in Chinese people regardless of sex, age or BMI.

Key words: Metabolic Score for Visceral Fat: Type 2 diabetes mellitus: Dose–response association: Receiver operating characteristic curve: Cohort study

Diabetes is one of the fastest growing health challenges of the twenty-first century with the number of adults living with diabetes more than tripling over the past 20 years⁽¹⁾. In 2019, the International Diabetes Federation estimated that 463 million adults had diabetes globally. In China, the number of people with diabetes reached 116 million in 2019 and is expected to reach 147.2 million in 2045⁽²⁾. Type 2 diabetes mellitus (T2DM), which is characterised by insulin resistance, accounts for 90 % of all diabetes⁽³⁾ and is becoming one of the world's

leading disease burdens, especially in China^(4,5). 55.9% of people with diabetes in China are still undiagnosed, however⁽²⁾; therefore, early and accurate identification of T2DM-related risk factors is urgently needed to effectively reduce the incidence and disease burden of T2DM into the future.

The Metabolic Score for Visceral Fat (METS-VF) is a novel estimator which combines measures of fasting plasma glucose (FPG), TAG, BMI, HDL-cholesterol, waist to height ratio (WHtR), age and sex to estimate visceral adipose tissue (VAT)

Abbreviations: ABSI, a body shape index; AUC, area under the receiver operating characteristic curve; FPG, fasting blood glucose; METS-VF, Metabolic Score for Visceral Fat; T2DM, type 2 diabetes mellitus; VAI, visceral adiposity index; VAT, visceral adipose tissue; WC, waist circumference; WHtR, waist to height ratio.

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and predict the incidence of cardiometabolic complications⁽⁶⁾. In a Mexican urban population, METS-VF was validated as a better performing predictor of T2DM incidence compared with other surrogate VAT indexes, including visceral adiposity index (VAI) and lipid accumulation product⁽⁶⁾. One study to date, in southern Indian individuals with morbid obesity⁽⁷⁾, has validated the utility of METS-VF as a surrogate measure of visceral adiposity, while another retrospective cohort study from China indicated that METS-VF could be a useful tool for the hierarchical prevention and management of hyperuricaemia among non-obese women⁽⁸⁾. So far, however, no published studies have explored the relationship between METS-VF and T2DM risk in the Chinese population.

This study therefore aimed to evaluate the association of the METS-VF with incidence of T2DM and to compare the predictive value of the METS-VF for T2DM incidence with that of other obesity indices (VAI, a body shape index (ABSI), WHtR, waist circumference (WC) and BMI) in the Chinese population.

Subjects and methods

Participants and study setting

This was a prospective cohort study with 20 194 participants aged ≥ 18 years, who were recruited during July to August 2007 and July to August 2008 from a rural area in Henan Province in China⁽⁹⁾. All participants were investigated using an interview questionnaire, anthropometric measurements and laboratory measurements. All participants were free of severe psychological disorders, physical disabilities, Alzheimer disease, dementia, tuberculosis, AIDS or other infectious diseases at the time of enrolment. Follow-up examination of 17 265 participants was performed between July and August 2013 and from July to October 2014 (response rate was 85.5%). All individuals signed an informed consent form, approved by the Ethics Committee of Zhengzhou University.

During follow-up, the same interview questionnaire was administered again and the same measurements taken as for the baseline examination, including questionnaire interview, anthropometric measurements and laboratory measurements.

In the current analysis, we have excluded participants with diabetes (T2DM, T1DM, gestational diabetes and other special types of diabetes) at baseline (n 1512), those whose diabetes status was unknown at baseline or follow-up (n 3477) and those with missing data for baseline age, weight, height, WC, FPG, TAG or HDL-cholesterol (n 39). Finally, a total of 12 237 individuals were included in the study.

Data collection

Interview questionnaire. Well-trained research staff collected demographic information (age, sex and education level), lifestyle data (smoking, alcohol drinking and physical activity) and medical history (family history of disease and personal history of disease) during face-to-face interviews, using a standard questionnaire. The definition of smoker, alcohol drinking and physical activity level were in accordance with the international standards, which has been described in detail in the previous studies^(10,11).

Anthropometric measurements. All participants were asked to wear light clothing and no shoes for anthropometric measurement. Height was measured to the nearest 0.1 cm. Weight was measured to the nearest 0.5 kg. WC was measured at the mid-point between the lowest rib and the iliac crest to the nearest 0.1 cm. All measurements were taken twice and recorded as the average of the two. Before blood pressure measurement, participants were instructed to refrain from smoking and from drinking alcohol, coffee and tea. Blood pressure was measured three times using an electronic sphygmomanometer device (HEM-770AFuzzy; Omron) on the unclothed right upper arm, at intervals of 30 s, with the three measurements recorded, according to the American Heart Association's standardised protocol⁽¹²⁾.

Laboratory measurements. Fasting blood samples were obtained after an overnight fast of at least 8 h. Levels of FPG, TAG, total cholesterol and HDL-cholesterol were measured using a HITACHI automatic clinical analyser (Model 7060). The Friedewald formula was used to calculate serum concentrations of LDL-cholesterol⁽¹³⁾. METS-VF⁽⁶⁾, VAI⁽¹⁴⁾, ABSI⁽¹⁵⁾, WHtR and BMI were calculated as follows:

$$\text{METS - VF(men)} = 4.466 + 0.011$$

$$\times ((\ln((\ln(2 * \text{FPG}) + \text{TG}) * \text{BMI}) / (\ln(\text{HDL} - \text{C})))) * *3)$$

$$+ 3.239 * ((\ln(\text{WHtR})) * *3) + 0.319 * 1 + 0.594 * (\ln(\text{age}))$$

$$\text{METS - VF(women)} = 4.466 + 0.011$$

$$\times ((\ln((\ln(2 * \text{FPG}) + \text{TG}) * \text{BMI}) / (\ln(\text{HDL} - \text{C})))) * *3)$$

$$+ 3.239 * ((\ln(\text{WHtR})) * *3) + 0.319 * 0 + 0.594$$

$$* (\ln(\text{age}))$$

$$\text{VAI(men)} = (\text{WC} / (39.68 + (1.88 * \text{BMI}))) * (\text{TG} / 1.03) * (1.31 / \text{HDL} - \text{C})$$

$$\text{VAI(women)} = (\text{WC} / (36.58 + (1.89 * \text{BMI}))) * (\text{TG} / 0.81) * (1.52 / \text{HDL} - \text{C})$$

$$\text{ABSI} = \text{WC} / ((\text{BMI} * * (2/3)) * (\text{height} * * (1/2)))$$

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

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

Type 2 diabetes definition. T2DM was considered FPG ≥ 7.0 mmol/l and/or use of insulin or oral hypoglycaemic medication and/or a self-reported history of T2DM after excluding gestational diabetes, T1DM and other special types of diabetes⁽¹⁶⁾.

Statistical analyses

Baseline demographic characteristics were described with continuous data summarised as median (interquartile range) for the skewed distribution, and for categorical variables as frequency (%). χ^2 or Kruskal–Wallis tests were used to compare differences among groups. The cox proportional hazards regression was



Table 1. Baseline characteristics of the included participants (Numbers and percentages; median and interquartile ranges)

Characteristics	Total		T2DM		Non-T2DM		P
	n	%	n	%	n	%	
Men	4646	37.97	314	37.51	4332	38.00	0.780
Age (years)							
Median	51		53		50		<0.001
Interquartile range	41–59		44–60		41–59		
Married/cohabitation	11 247	91.91	773	92.35	10 474	91.88	0.626
High school or higher	1224	10.00	73	8.72	1151	10.10	0.201
Smoking	3256	26.61	207	24.73	3049	26.75	0.203
Drinking	1365	11.15	97	11.59	1268	11.12	0.679
Physical activity							0.609
Low	3524	28.80	253	30.23	3271	28.69	
Moderate	2620	21.41	179	21.39	2441	21.41	
High	6093	49.79	405	48.39	5688	49.89	
	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	
SBP (mmHg)	122.00	111.33–136.00	129.33	117.67–142.67	121.67	111.00–135.67	<0.001
DBP (mmHg)	77.33	70.67–85.67	81.67	74.33–89.67	77.00	70.33–85.33	<0.001
FPG (mmol/l)	5.31	4.98–5.67	5.92	5.39–6.37	5.28	4.96–5.63	<0.001
TC (mmol/l)	4.37	3.82–5.01	4.61	4.05–5.21	4.36	3.81–4.99	<0.001
TAG (mmol/l)	1.35	0.96–1.95	1.80	1.23–2.63	1.33	0.95–1.90	<0.001
LDL-cholesterol (mmol/l)	2.50	2.10–3.00	2.60	2.10–3.10	2.50	2.10–3.00	<0.001
HDL-cholesterol (mmol/l)	1.14	0.99–1.32	1.09	0.95–1.25	1.15	0.99–1.33	<0.001
VAI	1.88	1.20–3.03	2.78	1.75–4.45	1.83	1.17–2.93	<0.001
ABSI	0.78	0.75–0.81	0.80	0.77–0.83	0.78	0.75–0.81	<0.001
WHtR	0.52	0.47–0.56	0.56	0.52–0.60	0.51	0.47–0.56	<0.001
WC (cm)	81.75	74.90–89.25	88.75	81.25–95.50	81.30	74.50–88.60	<0.001
BMI (kg/m ²)	24.06	21.73–26.54	26.09	23.65–28.58	23.93	21.64–26.37	<0.001
METS-VF	6.48	5.98–6.88	6.85	6.48–7.12	6.45	5.95–6.85	<0.001

SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting blood glucose; TC, total cholesterol; METS-VF, Metabolic Score for Visceral Fat; VAI, visceral adiposity index; ABSI, a body shape index; WHtR, waist-to-height ratio; WC, waist circumference.

used to estimate the risk of T2DM by calculating the hazard ratios and 95% CI, with the lowest quartile of METS-VF as the reference. We also estimated the risk of T2DM with a per 1-sd increase in METS-VF. Model 1 was unadjusted; model 2 was adjusted for age and sex; model 3 was adjusted for model 2 plus education level, marital status, physical activity, tobacco, alcohol and family history of T2DM; and model 4 was adjusted for model 3 plus systolic blood pressure, diastolic blood pressure, total cholesterol and LDL-cholesterol at baseline. A sensitivity analysis was also performed to verify the robustness of our results by excluding participants with cancer, kidney disease, stroke, myocardial infarction or heart failure at baseline. We also performed subgroup analyses stratified by sex (men and women), age (< 45 and ≥ 45 years) and BMI (BMI < 24 and ≥ 24 kg/m²) at baseline after adjusting for the potential confounding factors in model 4. We used restricted cubic splines with four knots at the 5th, 25th, 75th and 95th centiles to flexibly model the association between METS-VF and T2DM risk, with the knot at the 25th percentile of the distribution as the reference.

Finally, the area under the receiver operating characteristic curve (AUC) was used to test the ability of baseline METS-VF, VAI, ABSI, WHtR, WC and BMI to predicting T2DM incidence at follow-up. The Z statistic was used to test differences between the AUC.

The receiver operating characteristics were calculated using Medcalc V9.3, and restricted cubic splines were performed with R.3.6.3 (R Foundation), while other analyses involved using SAS V9.4 for Windows (SAS Inst.). All statistical analyses were considered statistically significant, with two-sided $P < 0.05$.

Results

Demographic characteristics of the study population

Table 1 shows the baseline characteristics of the study participants with and without T2DM during follow-up. A total of 12 237 participants (4646 or 37.97% men) were included in this study. Participants who developed T2DM were older, with a median age (interquartile range) of 53 (44–60) for T2DM and 50 (41–59) for non-T2DM, respectively. Values for systolic blood pressure, diastolic blood pressure, FPG, total cholesterol, TAG, LDL-cholesterol, METS-VF, VAI, ABSI, WHtR, WC and BMI were higher, while HDL-cholesterol levels were lower for those with T2DM than for those without ($P < 0.001$).

Association of baseline Metabolic Score for Visceral Fat and type 2 diabetes mellitus risk

During a median follow-up of 6.01 (5.09–6.06) years, T2DM developed in 837 cases among the 12 237 participants. The incidence densities of T2DM were 3.55, 8.07, 12.42 and 22.63 per 1000 person-years for quartiles 1, 2, 3 and 4 of METS-VF, respectively (Table 2). In unadjusted model 1, with METS-VF quartile 1 as the reference, the hazard ratios for T2DM were 2.42 (95% CI 1.81, 3.24), 3.96 (95% CI 3.01, 5.22) and 7.74 (95% CI 5.95, 10.07) for quartiles 2, 3 and 4, respectively. After adjusting for potential confounding factors, the positive association between METS-VF and T2DM risk persisted. In model 4, the hazard ratios for T2DM with quartiles 2, 3 and 4 of METS-VF were 2.18 (95% CI 1.56, 3.07), 3.16 (95% CI 2.27, 4.40) and 5.97 (95% CI 4.28, 8.32),

Table 2. Cox proportional hazard regression analysis of the association of baseline metabolic score for visceral fat and risk of type 2 diabetes mellitus (Hazard ratios and 95 % confidence intervals)

	Quartile 1	Quartile 2		Quartile 3		Quartile 4		P_{trend}	Per 1-sd	
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI		HR	95 % CI
Range	< 5.98	5.98–6.48		6.48–6.88		≥ 6.88				
No. of cases	65	147		229		396				
No. of person-years	18 320.77	18 217.62		18 437.54		17 497.55				
Incidence density*	3.55	8.07		12.42		22.63				
Model 1	1 (ref)	2.42	1.81, 3.24	3.96	3.01, 5.22	7.74	5.95, 10.07	<0.001	2.34	2.14, 2.56
Model 2	1 (ref)	2.33	1.73, 3.12	3.69	2.79, 4.89	7.09	5.37, 9.34	<0.001	2.32	2.10, 2.56
Model 3	1 (ref)	2.46	1.76, 3.44	3.89	2.82, 5.37	7.89	5.75, 10.84	<0.001	2.38	2.12, 2.66
Model 4	1 (ref)	2.18	1.56, 3.07	3.16	2.27, 4.40	5.97	4.28, 8.32	<0.001	2.15	1.90, 2.44
Sensitivity analysis	1 (ref)	2.17	1.54, 3.07	3.17	2.26, 4.45	6.06	4.31, 8.51	<0.001	2.18	1.92, 2.47

* Per 1000 person-years. Model 1: Unadjusted.

Model 2: Adjusted for age and sex at baseline.

Model 3: Adjusted for age, sex, physical activity, tobacco, alcohol, education level, marital status and family history of type 2 diabetes mellitus at baseline.

Model 4: Adjusted for age, sex, physical activity, tobacco, alcohol, education level, marital status, family history of type 2 diabetes mellitus at baseline as well as systolic blood pressure, diastolic blood pressure, total cholesterol, LDL-cholesterol at baseline.

Sensitivity analysis: Adjusted for model 4 and further excluded participants with cancer, kidney disease, stroke, myocardial infarction or heart failure at baseline.

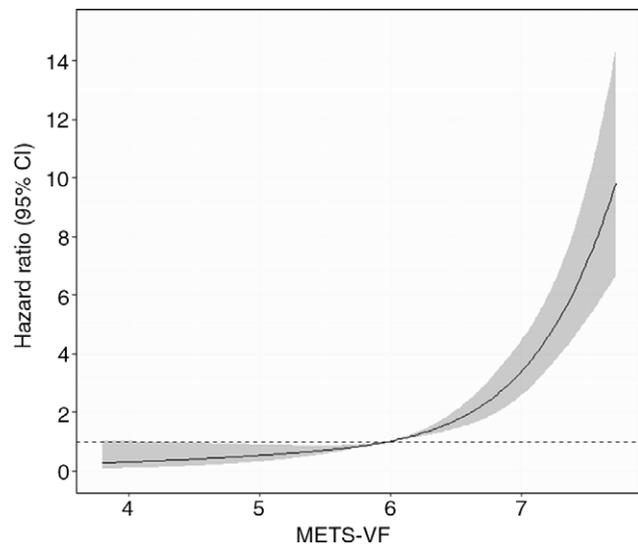


Fig. 1. Dose–response association between Metabolic Score for Visceral Fat (METS-VF) and risk of type 2 diabetes mellitus ($P_{\text{nonlinearity}} = 0.0347$).

respectively, with quartile 1 as reference. T2DM risk significantly increased with higher quartiles of METS-VF ($P_{\text{trend}} < 0.001$).

Risk of T2DM was increased with a per 1-sd increase in METS-VF for all participants. The adjusted hazard ratio was 2.15 (95 % CI 1.90, 2.44) in model 4. Restricted cubic splines indicated a significant nonlinear dose–response association between METS-VF and T2DM risk for all participants ($P_{\text{nonlinearity}} = 0.0347$, Fig. 1)

Sensitivity analysis and subgroup analyses for the association of Metabolic Score for Visceral Fat and type 2 diabetes mellitus risk

In sensitivity analysis, the positive association between METS-VF and T2DM risk was essentially robust after excluding participants with cancers, kidney disease, stroke, myocardial infarction or heart failure at baseline, respectively (Table 2). In the subgroup analyses stratified by sex, age and BMI, after adjusting potential

confounding factors in model 4 and with quartile 1 as reference, the risk of T2DM in the highest quartile still remained significant (Fig. 2).

Comparison of the association of Metabolic Score for Visceral Fat, visceral adiposity index, a body shape index, waist to height ratio, waist circumference and BMI with type 2 diabetes mellitus risk

Table 3 shows AUC (95 % CI), the optimal cut-offs and corresponding sensitivity, specificity, positive likelihood ratio (+LR), negative likelihood ratio (–LR), positive predictive value (+PV), negative predictive value (–PV) and Youden index for each index predicting T2DM risk. The receiver operating characteristic curve analyses for METS-VF, VAI, ABSI, WHtR, WC and BMI for predicting T2DM incidence are shown in online Supplementary Fig. S1. The AUC for METS-VF, VAI, ABSI, WHtR, WC and BMI were 0.690 (95 % CI 0.682, 0.698), 0.657 (95 % CI 0.649, 0.666), 0.621 (95 % CI 0.613, 0.630), 0.681 (95 % CI 0.672, 0.689), 0.680 (95 % CI 0.672, 0.689) and 0.661 (95 % CI 0.652, 0.669), respectively. METS-VF had the largest AUC for predicting T2DM incidence, significantly different from VAI, ABSI and BMI ($P < 0.05$) but not WHtR or WC ($P = 0.058$). Compared with VAI (0.25), ABSI (0.19), WHtR (0.28), WC (0.27) and BMI (0.25), the Youden index for METS-VF was the highest for all participants (0.29).

Discussion

In this large prospective cohort study, we explored the association between METS-VF and the risk of T2DM in a rural Chinese population. Our results showed a positive association of METS-VF with T2DM and a significant increase in T2DM incidence across quartiles of METS-VF after adjusting for potential risk factors. Similar results were observed in the sensitivity analysis. This positive association was also found in subgroup analyses by sex, age and BMI. Additionally, we found a nonlinear association between METS-VF and T2DM. Moreover, among the five indices (METS-VF, VAI, ABSI, WHtR, WC and BMI), METS-VF showed

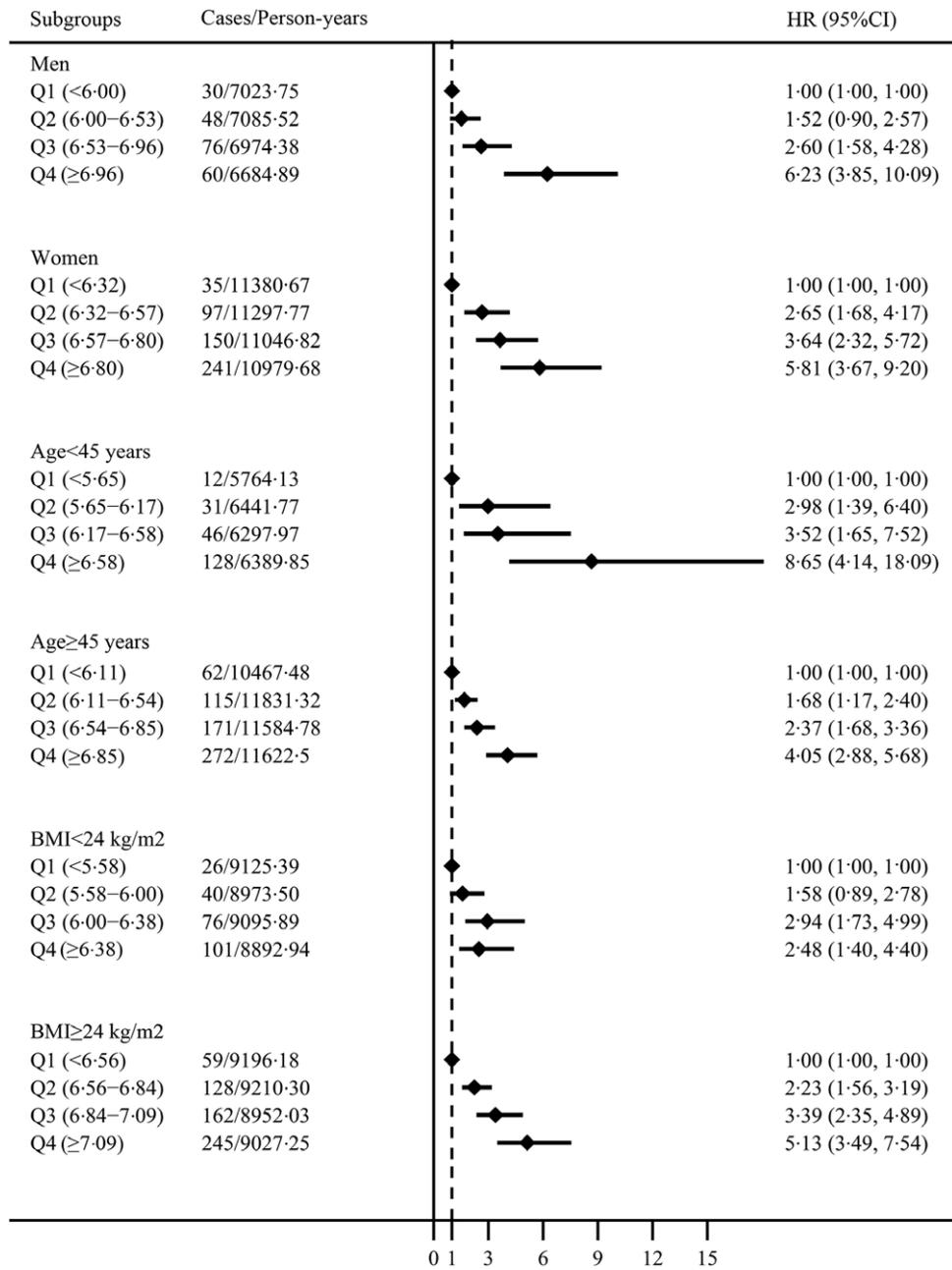


Fig. 2. Subgroup analyses of the association between metabolic score for visceral fat and risk of type 2 diabetes mellitus. HR, hazard ratio; Q, quartile.

Table 3. Comparison of areas under the receiver operating characteristic curves for METS-VF, VAI, ABSI, WC and BMI with type 2 diabetes mellitus risk (95 % confidence intervals)

Index	AUC	95 % CI	Cut-off	Sensitivity%	Specificity%	+LR	-LR	+PV	-PV	Youden index	P
METS-VF	0.690	0.682, 0.698	6.66	65.59	63.40	1.80	0.54	11.70	96.20	0.29	ref
VAI	0.657	0.649, 0.666	2.27	62.84	62.32	1.67	0.60	10.90	95.80	0.25	0.007
ABSI	0.621	0.613, 0.630	0.79	54.36	64.22	1.52	0.71	10.00	95.00	0.19	<0.001
WHtR	0.681	0.672, 0.689	0.52	72.28	55.49	1.62	0.50	10.70	96.50	0.28	0.058
WC	0.680	0.672, 0.689	85.70	61.53	65.97	1.81	0.58	11.70	95.90	0.27	0.058
BMI	0.661	0.652, 0.669	25.09	61.77	62.98	1.67	0.61	10.90	95.70	0.25	<0.001

METS-VF, Metabolic Score for Visceral Fat; METS-IR, Metabolic Score for IR; VAI, visceral adiposity index; ABSI, a body shape index; WHtR, waist-to-height ratio; WC, waist circumference; +LR, positive likelihood ratio; -LR, negative likelihood ratio; +PV, positive predictive value; -PV, negative predictive value.

the largest AUC and the highest Youden index in predicting the risk of T2DM.

An increase in fat mass is considered to be an important risk factor for the incidence of T2DM worldwide^(17–20), especially VAT mass which has been shown to be more harmful than fat stored elsewhere in the body^(1,21,22). Previous studies have also shown that the risk factors associated with diabetes were more related to visceral fat than to the accumulation of systemic fat, especially in East Asian populations who are generally less obese than people in Western countries^(23,24). These reports suggested the importance of measuring visceral fat accumulation. Clinical standards for assessing VAT include MRI, computerised tomography and dual X-ray absorptiometry, but they are expensive, need to be performed and interpreted by a specialist, and are often limited by equipment and technical difficulties^(6,25). A cheap and convenient indicator to measure the VAT is therefore needed.

Routinely applicable anthropometrical indicators of VAT content include WC, BMI and WHtR, but these indicators are of limited value because subcutaneous adipose tissue and VAT cannot be clearly distinguished^(26–31). VAI, based on BMI, WC, TAG and HDL-cholesterol, was established to estimate VAT accumulation predicting cardiometabolic risk in Italians⁽¹⁴⁾, but was not superior to simple obesity indices (BMI and WC) in predicting incidence of T2DM in Chinese people^(32–35). Our study adopted METS-VF, as a novel estimator of VAT, including the main predictors of VAT (insulin resistance, WHtR, age and sex^(14,36,37)), to predict T2DM incidence. Our results showed that METS-VF has the strongest association with the risk of T2DM and had the largest AUC and the highest Youden index in predicting T2DM incidence compared with other indices (VAI, ABSI, WHtR, WC and BMI).

Our analysis showed that a per 1-SD gain in METS-VF was positively associated with the risk of T2DM for all participants after adjusting for potential confounders. Consistent with our findings, Neeland *et al.* found visceral fat mass was independently associated with T2DM among obese individuals (OR 2.40; 95% CI 1.60, 3.70)⁽³⁸⁾. Similarly, a prospective study conducted among Japanese Americans found that intra-abdominal fat was a significant predictor of T2DM risk (OR 1.60; 95% CI 1.10, 2.30)⁽³⁹⁾. In addition, previous studies have suggested that visceral fat was associated with T2DM independent of BMI^(40,41). Our subgroup analyses showed that participants in the highest quartile of METS-VF had a significantly increased risk of T2DM both with normal weight (BMI < 24 kg/m²) and if overweight/obese (BMI ≥ 24 kg/m²), compared with the lowest quartile. Consistent with our findings, a cross-sectional study from Shanghai in China that included 4126 individuals found that visceral fat significantly increased the risk of diabetes in the normal weight and overweight/obese groups⁽⁴²⁾. In addition, our results showed that the positive associations occurred in both sexes, though Lv *et al.* found visceral fat was independently associated with T2DM only among women⁽⁴²⁾. This difference may be due to the cross-sectional study design and the different target population. Further research in other populations may be needed to test the stability of METS-VF in predicting the incidence of T2DM.

The exact mechanism underlying the association of VAT and T2DM incidence is unknown, yet. Several possible mechanisms have been proposed, however. One is that VAT is an active endocrine organ in which excess visceral fat deposition causes disrupted endocrine function and dysregulation of proinflammatory factors, both of which may contribute to insulin resistance and the development of T2DM^(43–45). Another mechanism suggests that excess VAT may result in increased risk for T2DM through overstimulation of hepatic gluconeogenesis by chronic delivery of glycerol arising from mesenteric TAG turnover directly into the portal circulation and the liver⁽⁴⁶⁾.

The strengths of this present study include longitudinal follow-up in a prospective cohort, large sample size and standardised questionnaire and laboratory procedures. We also conducted the sensitivity analysis and subgroup analyses and examined the dose–response association between baseline METS-VF and risk of T2DM. Moreover, the study first explored the association of baseline METS-VF and risk of T2DM, testing the predictive performance of T2DM among various indices (METS-VF, VAI, ABSI, WHtR, WC and BMI) in Chinese people. The AUC further confirmed the robust ability of baseline METS-VF to predict T2DM incidence at follow-up. Several limitations should be noted, however. First, we did not examine 2-h postprandial glucose, which may have led to underestimation of T2DM. Second, all the participants were rural Chinese people in this study, such that generalisation of our findings may be limited. It is yet to be determined whether METS-VF could predict the risk of T2DM in populations other than Chinese. We did not compare the results of METS-VF with actual physical measurements of visceral adiposity using MRI, computerised tomography or dual X-ray absorptiometry scans because we did not collect the relevant data. Finally, although we did adjust for known covariates, there is potential for confounding factors to affect our results given the observational design.

Conclusions

Our results show that a higher baseline METS-VF is positively associated with increased risk of T2DM in Chinese adults regardless of sex, age or BMI. Compared with other indices, METS-VF is a more effective and convenient surrogate marker for VAT measurement; it could be used in identifying the risk of T2DM in large-scale epidemiological studies.

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Y.F. and D.H. designed and conducted the research; F.Y. analyzed the data and wrote the paper; X.Y., Y.L., Y.W., M.H., R.Q., S.H., X.W., Y.Z., J.Z., H.H., L.Y., T.L., D.L., F.H., M.Z., Y.Z., X.L., J.L., L.S., D.H., and Y.Z. provided constructive suggestions; and Y.F. had primary responsibility for the final content.

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The authors declare that they have no conflict of interest.

Supplementary material

For supplementary material referred to in this article, please visit <https://doi.org/10.1017/S0007114521004116>

References

1. Fox CS, Massaro JM, Hoffmann U, *et al.* (2007) Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation* **116**, 39–48.
2. International Diabetic Federation (2019) IDF Diabetes Atlas, 9th ed. <https://diabetesatlas.org/en/> (accessed November 2019).
3. Festa A, Williams K, D'Agostino R, *et al.* (2006) The natural course of beta-cell function in nondiabetic and diabetic individuals: the insulin resistance atherosclerosis study. *Diabetes* **55**, 1114–1120.
4. Vos T, Flaxman AD, Naghavi M, *et al.* (2012) Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**, 2163–2196.
5. World Health Organization (2014) Global Status Report on Noncommunicable Diseases. <http://www.who.int/nmh/publications/ncd-status-report-2014/en/> (accessed December 2017).
6. Bello-Chavolla OY, Antonio-Villa NE, Vargas-Vázquez A, *et al.* (2020) Metabolic Score for Visceral Fat (METS-VF), a novel estimator of intra-abdominal fat content and cardio-metabolic health. *Clin Nutr* **39**, 1613–1621.
7. Kapoor N, Jiwanmull SA, Nandyal MB, *et al.* (2020) Metabolic Score for Visceral Fat (METS-VF) estimation: a novel cost-effective obesity indicator for visceral adipose tissue estimation. *Diabetes Metab Syndrome Obes. Target Ther* **13**, 3261–3267.
8. Liu XZ, Chen DS, Xu X, *et al.* (2020) Longitudinal associations between metabolic score for visceral fat and hyperuricemia in non-obese adults. *Nutr Metab Cardiovasc Dis* **30**, 1751–1757.
9. Zhang M, Zhao Y, Sun L, *et al.* (2020) Cohort profile: the rural Chinese cohort study. *Int J Epidemiol* **50**, 723–724.
10. Han C, Liu Y, Sun X, *et al.* (2017) Prediction of a new body shape index and body adiposity estimator for development of type 2 diabetes mellitus: the Rural Chinese Cohort Study. *Br J Nutr* **118**, 771–776.
11. Craig CL, Marshall AL, Sjöström M, *et al.* (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* **35**, 1381–1395.
12. Perloff D, Grim C, Flack J, *et al.* (1993) Human blood pressure determination by sphygmomanometry. *Circulation* **88**, 2460–2470.
13. Bairaktari E, Hatzidimou K, Tzallas C, *et al.* (2000) Estimation of LDL cholesterol based on the Friedewald formula and on apo B levels. *Clin Biochem* **33**, 549–555.
14. Amato MC, Giordano C, Galia M, *et al.* (2010) Visceral adiposity index: a reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* **33**, 920–922.
15. Krakauer NY & Krakauer JC (2012) A new body shape index predicts mortality hazard independently of body mass index. *PLOS ONE* **7**, e39504.
16. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (2003) Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* **26**, S5–S20.
17. Stefan N (2020) Causes, consequences, and treatment of metabolically unhealthy fat distribution. *Lancet Diabetes Endocrinol* **8**, 616–627.
18. Liu J, Fan D, Wang X, *et al.* (2020) Association of two novel adiposity indicators with visceral fat area in type 2 diabetic patients: novel adiposity indexes for type 2 diabetes. *Medicine* **99**, e20046.
19. Omura-Ohata Y, Son C, Makino H, *et al.* (2019) Efficacy of visceral fat estimation by dual bioelectrical impedance analysis in detecting cardiovascular risk factors in patients with type 2 diabetes. *Cardiovasc Diabetol* **18**, 137.
20. Chen P, Hou X, Hu G, *et al.* (2018) Abdominal subcutaneous adipose tissue: a favorable adipose depot for diabetes? *Cardiovasc Diabetol* **17**, 93.
21. Vega GL, Adams-Huet B, Peshock R, *et al.* (2006) Influence of body fat content and distribution on variation in metabolic risk. *J Clin Endocrinol Metab* **91**, 4459–4466.
22. Yuan S & Larsson SC (2020) An atlas on risk factors for type 2 diabetes: a wide-angled Mendelian randomisation study. *Diabetologia* **63**, 2359–2371.
23. Yoon KH, Lee JH, Kim JW, *et al.* (2006) Epidemic obesity and type 2 diabetes in Asia. *Lancet* **368**, 1681–1688.
24. Sjöström LV (1992) Morbidity of severely obese subjects. *Am J Clin Nutr* **55**, 508s–515s.
25. Shuster A, Patlas M, Pinthus JH, *et al.* (2012) The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis. *Br J Radiol* **85**, 1–10.
26. Ashwell M, Cole TJ & Dixon AK (1985) Obesity: new insight into the anthropometric classification of fat distribution shown by computed tomography. *Br Med J* **290**, 1692–1694.
27. Okorodudu DO, Jumeau MF, Montori VM, *et al.* (2010) Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. *Int J Obes* **34**, 791–799.
28. Nevill AM, Stewart AD, Olds T, *et al.* (2006) Relationship between adiposity and body size reveals limitations of BMI. *Am J Phys Anthropol* **129**, 151–156.
29. Neeland IJ, McGuire DK, Eliasson B, *et al.* (2015) Comparison of adipose distribution indices with gold standard body composition assessments in the EMPA-REG H2H SU Trial: a body composition sub-study. *Diabetes Ther: Res Treat Educ Diabetes Relat Disord* **6**, 635–642.
30. Pou KM, Massaro JM, Hoffmann U, *et al.* (2009) Patterns of abdominal fat distribution: the Framingham Heart Study. *Diabetes Care* **32**, 481–485.
31. Chen C, Xu Y, Guo ZR, *et al.* (2014) The application of visceral adiposity index in identifying type 2 diabetes risks based on a prospective cohort in China. *Lipids Health Dis* **13**, 108.
32. Deurenberg P, Deurenberg-Yap M & Guricci S (2002) Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. *Obes Rev* **3**, 141–146.
33. Wang B, Zhang M, Liu Y, *et al.* (2018) Utility of three novel insulin resistance-related lipid indices for predicting type 2 diabetes mellitus among people with normal fasting glucose in rural China. *J Diabetes* **10**, 641–652.
34. Lim U, Ernst T, Buchthal SD, *et al.* (2011) Asian women have greater abdominal and visceral adiposity than Caucasian women with similar body mass index. *Nutr Diabetes* **1**, e6.
35. Zhang M, Zheng L, Li P, *et al.* (2016) 4-year trajectory of visceral adiposity index in the development of type 2 diabetes: a prospective cohort study. *Ann Nutr Metab* **69**, 142–149.

36. Brundavani V, Murthy SR & Kurpad AV (2006) Estimation of deep-abdominal-adipose-tissue (DAAT) accumulation from simple anthropometric measurements in Indian men and women. *Eur J Clin Nutr* **60**, 658–666.
37. Lee CG, Carr MC, Murdoch SJ, *et al.* (2009) Adipokines, inflammation, and visceral adiposity across the menopausal transition: a prospective study. *J Clin Endocrinol Metab* **94**, 1104–1110.
38. Neeland IJ, Turer AT, Ayers CR, *et al.* (2012) Dysfunctional adiposity and the risk of prediabetes and type 2 diabetes in obese adults. *JAMA* **308**, 1150–1159.
39. Boyko EJ, Fujimoto WY, Leonetti DL, *et al.* (2000) Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. *Diabetes Care* **23**, 465–471.
40. Wei M, Gaskill SP, Haffner SM, *et al.* (1997) Waist circumference as the best predictor of noninsulin dependent diabetes mellitus (NIDDM) compared to body mass index, waist/hip ratio and other anthropometric measurements in Mexican Americans – a 7-year prospective study. *Obes Res* **5**, 16–23.
41. Ohlson LO, Larsson B, Svärdsudd K, *et al.* (1985) The influence of body fat distribution on the incidence of diabetes mellitus. 13.5 years of follow-up of the participants in the study of men born in 1913. *Diabetes* **34**, 1055–1058.
42. Lv X, Zhou W, Sun J, *et al.* (2017) Visceral adiposity is significantly associated with type 2 diabetes in middle-aged and elderly Chinese women: a cross-sectional study. *J Diabetes* **9**, 920–928.
43. Bays HE (2011) Adiposopathy is ‘sick fat’ a cardiovascular disease? *J Am Coll Cardiol* **57**, 2461–2473.
44. Han SJ, Boyko EJ, Fujimoto WY, *et al.* (2017) Low plasma adiponectin concentrations predict increases in visceral adiposity and insulin resistance. *J Clin Endocrinol Metab* **102**, 4626–4633.
45. Karlsson T, Rask-Andersen M, Pan G, *et al.* (2019) Contribution of genetics to visceral adiposity and its relation to cardiovascular and metabolic disease. *Nat Med* **25**, 1390–1395.
46. Neeland IJ, Hughes C, Ayers CR, *et al.* (2017) Effects of visceral adiposity on glycerol pathways in gluconeogenesis. *Metab Clin Exp* **67**, 80–89.