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Original Research

# The Visceral Adiposity Index in Comparison with Easily Measurable Anthropometric Markers Did Not Improve Prediction of Diabetes

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ABSTRACT

*Objectives:* We evaluated the ability of the visceral adiposity index (VAI) compared to hypertriglyceridemic-waist (HTGW) phenotype, body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR) and waist-to-hip ratio (WHR) as a possible predictor of diabetes in a nondiabetic high-risk population.
*Methods:* We analyzed 7-year follow-up data in nondiabetic first-degree relatives of consecutive patients 30 to 70 years of age with type 2 diabetes and with at least 1 follow-up examination (N=1720). The primary outcome was the diagnosis of type 2 diabetes based on repeated oral glucose tolerance tests. We examined the incidence of type 2 diabetes across quintiles of the VAI and plotted a receiver operating characteristic (ROC) curve to compare the abilities of predicting type 2 diabetes of the VAI, BMI, WC, WHR and WHtR.
*Results:* The highest quintile of VAI compared with the lowest quintile was associated with type 2 diabetes in age- and gender-adjusted models (OR 2.45; 95% CI 1.56, 3.86). Those with the HTGW phenotype were 2.36 times (OR 2.36; 95% CI: 161, 3.44) more likely to develop type 2 diabetes than those with normal WCs and normal triglyceride levels. On ROC curve analysis, almost similar areas under the ROC were found for BMIs (60.9%; 95% CI: 57.1, 64.6); WC (61.0%, 95% CI 57.4, 64.5); WHtR (62.6%; 95% CI: 59.1, 66.2); WHR (55.7%; 95% CI 52.2, 59.3) and VAI (58.3%; 95% CI: 54.5, 62.1).
*Conclusions:* These data provide further evidence that VAI and HTGW are robust predictors of type 2 diabetes, but the predictive power was similar to that of BMI, WC, WHtR and WHR in our study population.


*Mots clés :*
parents de premier degré
taille hypertriglycéridémiante
facteur de risque
incidence du diabète de type 2
indice d'adiposité viscérale

RÉSUMÉ

*Objectifs :* Nous avons évalué la capacité potentielle de l'indice d'adiposité viscérale (IAV) par rapport au phénotype de taille hypertriglycéridémiante (THTG), à l'indice de masse corporelle (IMC), au tour de taille (TT), au rapport tour de taille/taille (RTTT) et au rapport taille/hanches (RTH) à prédire le diabète chez la population non diabétique exposée à un risque élevé.
*Méthodes :* Nous avons analysé les données du suivi de 7 ans de parents non diabétiques de premier degré de patients consécutifs de 30 à 70 ans souffrant du diabète de type 2 et ayant eu au moins 1 examen de suivi (N=1720). Le critère de jugement principal était le diagnostic du diabète de type 2 fondé sur les épreuves répétées d'hyperglycémie provoquée par voie orale. Nous avons examiné l'incidence du diabète de type 2 dans tous les quintiles de l'IAV et tracé une courbe caractéristique d'efficacité du récepteur (ROC) pour comparer les capacités de l'IAV, de l'IMC, du TT, du RTH et du RTTT à prédire le diabète de type 2.
*Résultats :* Le quintile le plus élevé comparativement au quintile le plus bas de l'IAV était associé au diabète de type 2 dans les modèles ajustés selon l'âge et le sexe (RIA 2,45; IC à 95% : 1,56, 3,86). Ceux du phénotype de THTG étaient 2,36 fois (RIA 2,36; IC à 95% : 161, 3,44) plus susceptibles de développer le diabète de type 2 que ceux ayant des TT normaux et des concentrations normales de triglycérides. À l'analyse de la courbe ROC, des surfaces sous la courbe ROC presque similaires étaient observées pour les IMC (60,9%; IC à 95% : 57,1, 64,6); le TT (61,0%, IC à 95% : 57,4, 64,5); le RTTT (62,6%; IC à 95% : 59,1, 66,2); le RTH (55,7%; IC à 95% : 52,2, 59,3) et l'IAV (58,3%; IC à 95% : 54,5, 62,1).

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*Conclusions :* Ces données fournissent une preuve supplémentaire que l'IAV et la THTG sont des prédicteurs fiables du diabète de type 2, qui ont un pouvoir prédictif similaire à celui de l'IMC, le TT, le RTTT et le RTH de notre population faisant l'objet de l'étude.



## Introduction

It is well established that obesity, particularly abdominal obesity, is a strong risk factor for type 2 diabetes, and measuring waist circumference (WC) is an effective tool for screening individuals at high-risk for type 2 diabetes (1,2). Excess abdominal fat may lead to insulin resistance and abnormal glucose metabolism (3,4). However, obesity is remarkably heterogeneous; some obese individuals never develop type 2 diabetes (5). Nevertheless, because WC cannot fully discriminate between visceral and subcutaneous fat, visceral lipid accumulation, which is defined as the visceral adiposity index (VAI), a mathematic model that combines WC, body mass index (BMI), triglyceride levels (TG) and high-density lipoprotein cholesterol (HDLC) levels (6), hypertriglyceridemic-waist (HTGW) phenotype (a combination of abdominal obesity and elevated fasting TG (7)) and lipid accumulation product (a combination of WC and TG (8,9)) has been established to distinguish visceral fat from subcutaneous fat. Although magnetic resonance imaging and computed tomography are the gold standards for measuring visceral fat, they are not suitable for epidemiologic studies and daily practice for practical, ethical and economic reasons. The clinical utility of the VAI to identify individuals with both cardiovascular and cerebrovascular disease was first reported by Amato et al (6). Their results have been replicated for predicting insulin sensitivity (10), glycemic disturbances (11) and type 2 diabetes (12). The VAI was associated with visceral fat tissue but not with subcutaneous fat tissue in obese and overweight postmenopausal women (13). The VAI is also a reliable marker of visceral fat function associated with cardiometabolic risk (6) and metabolic syndrome (13). Only a few studies have examined the association between the VAI and the risk for type 2 diabetes and compared it to various body fatness indexes, and they came to inconsistent conclusions (12,14–17); its discriminatory power was not better than other anthropometric indexes in identifying the risk for type 2 diabetes in some (14–16) but not all (12,17) studies. In Chinese cross-sectional (12,16) and cohort (15,17) studies and in the Tehran Lipid and Glucose cohort (14) study, the VAI was associated with increased risk for type 2 diabetes. However, the ability of VAI to identify type 2 diabetes risk was not found to be superior to easily measurable anthropometric markers, such as BMI, WC, waist-to-height ratio (WHtR) (14–16). The clinical usefulness of the VAI in predicting type 2 diabetes has not been explored among Iranian first-degree relatives (FDRs) of patients with type 2 diabetes, who are known to have a high prevalence of prediabetes and type 2 diabetes (18).

The objective of this ongoing longitudinal study, therefore, was to explore the clinical usefulness of the VAI in predicting the incidence of type 2 diabetes in an Iranian nondiabetic high-risk population and to compare the predictive ability of the VAI, HTGW and other anthropometric indexes. We hypothesized that the VAI would predict type 2 diabetes better than the HTGW and the other anthropometric markers in a high-risk population.

## Methods

### *Data collection*

This study was conducted within the framework of the Isfahan Diabetes Prevention Study (IDPS), which has been described in detail elsewhere (19). In brief, IDPS, initiated in 2003, is an ongoing cohort in central Iran established to assess the various potential risk factors for diabetes in subjects with family histories of type 2 diabetes (1 of the main risk factors for diabetes). Our study sample at baseline comprised 3483 (919 men and 2564 women) FDRs of consecutive patients with type 2 diabetes. All patients were attendees at clinics at Isfahan Endocrine and Metabolism Research Center, which is affiliated with Isfahan University of Medical Sciences, Iran. The study was conducted between the years 2003 and 2005. All participants were from Isfahan city and adjoining areas. They completed laboratory tests, including standard 75 g 2-hour oral glucose tolerance tests (OGTTs), fasting serum lipid profiles and questionnaires concerning their health statuses and various potential risk factors for diabetes. Participants received follow-up tests according to Standard of Medical Care in Diabetes (20) to update information on demographic, anthropometric and lifestyle factors and on newly diagnosed diabetes. Accordingly, if OGTTs at baseline were normal, repeat testing was carried out at least at 3-year intervals. Otherwise, repeat testing was usually carried out annually.

### *Ethics statement*

This study approved by the Isfahan University of Medical Sciences ethical committee, and an informed consent form was signed by each participant.

### *Follow up and ascertainment of type 2 diabetes*

Of the 3483 persons who participated at baseline, 329 subjects were excluded because of diagnosis of type 2 diabetes at baseline, 1285 did not attend any follow-up examinations and 149 had missing data on TG and/or HDLC at baseline, leaving 1720 participants with a mean age of 43.0 (6.5) (range 30 to 70) years for this analysis, all of whom had at least 1 subsequent review during a mean (SD) follow-up period of 7.3 (2.2) (range, 1 to 10) years. Pregnant women were excluded.

### *Clinical and laboratory measurements*

Information about ages, gender, body sizes, glycated hemoglobin (A1C), total cholesterol (TC), low-density lipoprotein cholesterol (LDLC), HDLC, TG and blood pressure (BP) levels and family and personal medical histories was collected at baseline and throughout follow ups. The same methodology was used for baseline and follow-up studies. The participants included siblings and children of patients with type 2 diabetes. Participants reported to clinics in the morning after an overnight fast. They were asked to abstain from vigorous exercise in the evening and in the morning of their visit. Smokers were encouraged to abstain from smoking in the morning of the investigations. First, on arrival at the clinic, the information provided by the participants in the questionnaire on family history was verified. Then, with the subjects in light clothing and without shoes, height, weight, WC and hip circumference (HC) were measured using standard apparatus and recorded to the nearest 0.1 kg and 0.5 cm, respectively. The WC was measured midway between the lower rib margin and the iliac crest at the end of gentle expiration in the standing position. Hip circumference was measured over the greater trochanters directly over the underwear. The BMIs were calculated as the weight in kg divided by square of the height in meters. Resting BP was measured at each examination by physicians, with the participants in a sitting position after

having been been seated for 10 minutes, by a mercury column sphygmomanometer and appropriately sized cuffs by using standard techniques. A blood sample was drawn between 7 am and 9 am. Fasting plasma glucose (FPG) levels were measured using an enzymatic colorimetric method with glucose oxidase. Participants with FPG ≥11.1 mmol/L or pharmacologic treatment were considered to be persons with diabetes. If FPG levels were ≥7 mmol/L or <11.1 mmol/L, second FPG levels were measured on another day. If the second FPGs were also ≥7 mmol/L, participants were considered to be persons with diabetes (21). Those with FPG levels <7 mmol/L underwent standard OGTTs (75 g glucose, 2 hours) at baseline and at the follow-up visits. Venous blood was sampled 0, 30, 60 and 120 minutes after oral glucose administration.

A1C (measured by ion-exchange chromatography), TC, TG, HDLC and LDLC levels were recorded. The LDLC levels were calculated using the Friedewald equation (22) provided total TG levels did not exceed 400 mg/dL. Non-HDLC was calculated by subtracting HDLC from TC levels. All the blood analyses were performed at the central laboratory of the Isfahan Endocrine and Metabolism Research Center on the day of blood collection by using the enzyme-linked method.

*Definitions*

VAI was calculated as:

$$\text{VAI (men)} = (\text{WC}/39.68 + (1.88 \times \text{BMI})) \times (\text{TG}/1.03) \times (1.31/\text{HDLC})$$

VAI (women)=(WC/36.58+(1.89×BMI))×(TG/0.81)×(1.52/HDLC), assuming a VAI=1 in healthy, nonobese individuals with normal fat distribution and normal TG and HDLC levels (6). The HTGW phenotype was defined as the simultaneous presence of WC ≥102/88 cm in men/women and TG ≥1.7 mmol/L for both genders.

*Analysis*

Incidence was expressed as the number of cases of type 2 diabetes per 1000 person-years of follow up beginning on the date of completion of the baseline examination in 2003 to 2005 and continuing until the occurrence of type 2 diabetes, the date of the last completed follow up, death or end of follow up on March 21, 2014, whichever came first.

Statistical methods included the Student t test or Mann-Whitney U test, the 1-way analysis of variance (ANOVA) or the Kruskal-Wallis test for continuous variables, the chi-squared test, the Pearson correlation or Spearman rank correlation and binary logistic regression. Differences among more than 2 groups were estimated using 1-way ANOVA with the Benferroni post hoc test. Pearson correlation analysis or Spearman rank correlation was used to examine the linear relationships between the VAI and other anthropometric variables after holding the effect of age and gender constant. Univariate and multivariate binary logistic regression equations were fitted to identify predictors of new-onset diabetes. We did not adjust for WC, TG or HDLC levels, which are components of the VAI and, therefore, not appropriate to be adjusted for prediction models already incorporating the VAI. The VAI was recoded into quintiles so as to compare the risk for developing diabetes in each quintile with the lowest category of risk (reference group). Cox proportional hazards models were used as alternative analyses; the results were essentially identical to the logistic models, so only logistic regression results are presented. The ability of VAI, WC, BMI, WHtR and waist-to-hip ratio (WHR) to predict the incidence diabetes was examined with receiver operating characteristic (ROC) curves and their respective areas under the curve, in which sensitivity was plotted as a function of 1-specificity. The area under the ROC curve is a global summary statistic of the discriminative value of a model, describing the probability that the VAI, WC, BMI, WHtR and WHR are higher in an individual developing than in an individual not developing type 2 diabetes. The area under the ROC curve was used as an index of global test performance of VAI, WC, BMI, WHtR and WHR for identification of type 2 diabetes across the entire range of values, with an area under the curve of 0.5 indicating no discrimination ability. Conventionally, an area under the curve of 0.90 or more is considered excellent, values between 0.80 and 0.90 are regarded as good, values between 0.70 and 0.80 indicate fair test performance and values between 0.50 and 0.70 are viewed as poor. Areas under the ROC curves were compared by the algorithm developed by DeLong et al (23). The general linear model was used to examine the significance of trends in potential predictors of diabetes across the VAI quintile and compared age-adjusted means. The SPSS software v. 18 for Windows (SPSS, Chicago, Illinois, USA) was used for data analysis. All tests for statistical significance were 2-tailed, and all were done assuming a type I error probability of <0.05.

## Results

*Characteristics*

Most baseline characteristics of individuals who did not return for follow-up visits, such as age, height, weight, BMI, WC, HC, WHR, WHtR, LDLC, TC, TG, systolic BP and obesity were similar to those who attended the follow-up visits. However, those who did not return for follow up, when compared with respondents, had slightly lower levels of FPG (5.26 mmol/L vs. 5.31; p<0.05); plasma glucose (PG) at 30 minutes (7.75 mmol/L vs. 8.01; p<0.001); 60 minutes (7.82 mmol/L vs. 8.32; p<0.001); and 120 minutes (6.14 mmol/L vs. 6.63; p<0.001); levels of A1C (5.0% vs. 5.1; p<0.05); diastolic BP (73.4 mm Hg vs. 75.7 mm Hg; p<0.001); and higher levels of HDLC (1.20 mmol/L vs. 1.15; p<0.001).

A total of 256 (14.9%) cases of type 2 diabetes occurred during 12,395 person-years of follow up. The mean (SD) VAI was 2.9 (2.1). Baseline characteristics of the 256 (14.9%) participants who did and 1464 (85.1%) who did not progress to type 2 diabetes are shown in Table 1. As expected, participants who progressed to type 2 diabetes were older and had higher age-adjusted mean weights, BMIs, WCs, WHRs, WHtRs, HCs, follow-up durations, FPG levels and PG levels at 30, 60 and 120 minutes, higher A1C, TG, TC and non-HDLC levels at baseline and higher proportions of obesity and HTGW.

The mean (SD) age was 44.4 (6.8) years for those who progressed to type 2 diabetes and 42.7 (6.4) years for those who did not progress to type 2 diabetes. The mean (SD) VAI was 3.5 (2.8) for those who progressed to type 2 diabetes and 2.8 (2.0) for those who did not progress to type 2 diabetes. The 24.6% of those who progressed to type 2 diabetes and the 18.1% of those who did not progress to type 2 diabetes were HTGW at baseline.

The baseline characteristics of the study participants by VAI quintile are shown in Table 2. In comparisons of variables at baseline, all variables were more likely to increase. HDLC was more likely to decrease across all 5 subject groups.

The VAI showed significant positive correlations (p<0.001) with WC (r=0.213), BMI (r=0.146), WHtR (r=0.208) and WHR (r=0.222) (Table 3).

*Incidence of diabetes*

The overall incidence of subsequent diabetes was 20.7 (95% CI: 18.1, 23.2) per 1000 person-years. Incidence rates were similar in women (20.8, 95% CI: 18.0, 23.5 per 1000 person-years) and men (20.8, 95% CI: 16.3, 26.2).

The incidence of type 2 diabetes was 13.0 per 1000 person-years (95% CI: 8.9, 18.4) for participants in the lowest quintile and 29.3 per 1000 person-years (95% CI: 23.0, 36.8) in the highest

**Table 1**
Age, age-adjusted mean (SE) and proportion characteristics of selected baseline characteristics in 256 first-degree relatives of patients with type 2 diabetes who did and 1464 who did not develop type 2 diabetes

| Variables | Progressed to type 2 diabetes | Did not progress to type 2 diabetes |
|---|---|---|
| | Mean (SE) | Mean (SE) |
| Age (years) | 44.4 (0.39) | 42.7 (0.16)** |
| Height (cm) | 159.3 (0.50) | 159.9 (0.21) |
| Weight (kg) | 76.8 (0.72) | 73.3 (0.30)** |
| Body mass index (kg/m$^2$) | 30.3 (0.25) | 28.7 (0.10)** |
| Waist circumference (cm) | 92.1 (0.57) | 88.7 (0.24)** |
| Waist-to-hip ratio | 0.84 (0.004) | 0.83 (0.002)* |
| Hip circumference (cm) | 110.0 (0.53) | 107.0 (0.22)** |
| Waist-to-height ratio | 0.58 (0.003) | 0.56 (0.001)** |
| Follow-up duration (years) | 7.8 (0.13) | 7.2 (0.05)** |
| Systolic BP (mm Hg) | 117.4 (0.95) | 115.5 (0.40) |
| Diastolic BP (mm Hg) | 77.0 (0.72) | 75.5 (0.30) |
| Fasting plasma glucose (mmol/L) | 5.8 (0.04) | 5.2 (0.02)** |
| Plasma glucose 30 min (mmol/L) | 9.1 (0.10) | 7.8 (0.04)** |
| Plasma glucose 60 min (mmol/L) | 10.4 (0.13) | 7.9 (0.06)** |
| Plasma glucose 120 min (mmol/L) | 8.1 (0.11) | 6.4 (0.04)** |
| A1C (%) | 5.4 (0.05) | 5.0 (0.02)** |
| Triglyceride (mmol/L) | 2.2 (0.07) | 1.8 (0.03)** |
| Cholesterol (mmol/L) | 5.2 (0.06) | 5.1 (0.03)* |
| HDL cholesterol (mmol/L) | 1.1 (0.02) | 1.2 (0.008) |
| LDL cholesterol (mmol/L) | 3.1 (0.06) | 3.1 (0.02) |
| Non-HDLC (mmol/L) | 4.0 (0.06) | 3.9 (0.03)* |
| Visceral adiposity index | 3.5 (0.13) | 2.8 (0.06)** |
| | % | % |
| Women | 74.5 | 73.8 |
| Normal weight (BMI <25 kg/m$^2$) | 9.4 | 17.1** |
| Overweight (BMI 25–29.9 kg/m$^2$) | 43.5 | 48.3** |
| Obese (BMI≥30 kg/m$^2$) | 47.1 | 34.6** |
| Abdominal obesity | 53.3 | 36.7** |
| Normal waist normal triglyceride | 21.4 | 39.9** |
| Normal waist high triglyceride | 26.1 | 24.3 |
| Enlarged waist normal triglyceride | 27.9 | 17.7** |
| Hypertriglyceridemic-waist | 24.6 | 18.1** |

*BP*, blood pressure; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *Non-HDLC*, non-high-density lipoprotein cholesterol.
*Notes:* Data are expressed as mean (SE) or percentage. Age-adjusted means were calculated using general linear models. Differences in the mean or percentage values of variables between type 2 diabetes and no type 2 diabetes.
* p<0.05.
** p<0.001.

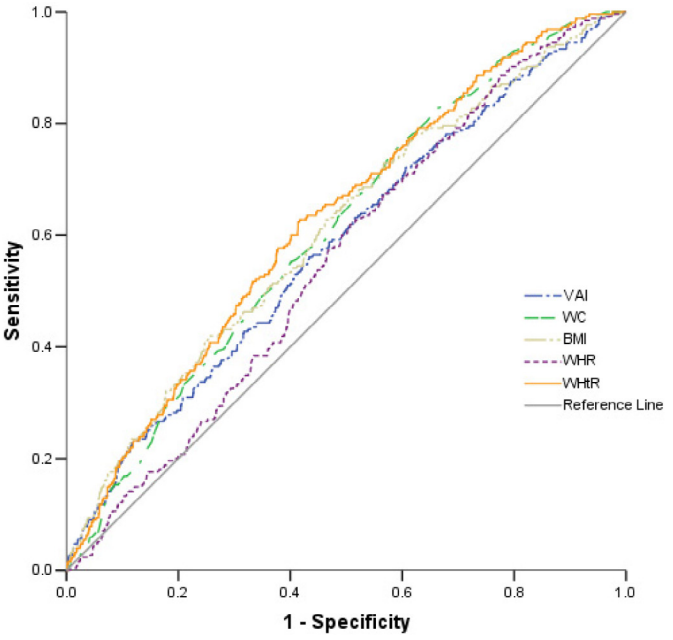


**Figure 1.** Receiver operating characteristic curves for visceral adiposity index (VAI), waist circumference (WC), body mass index (BMI), waist-to-hip ratio (WHT) and waist-to-height ratio (WHtR) to predict type 2 diabetes in nondiabetic first-degree relatives of patients with type 2 diabetes. Sensitivity represents the true-positive results, and 1-specificity represents the false-positive results. The estimates of the area under the ROC curves and their 95% confidence intervals (CI) are shown. Area under the curve (95% CI): 0.583 (0.545, 0.621) VAI, 0.610 (0.574, 0.645) WC, 0.609 (0.571, 0.646) BMI, 0.557 (0.522, 0.593) WHR, 0.626 (0.591, 0.662) WHtR.

quintile. The risk for type 2 diabetes increased with increasing quintiles of the VAI. Compared with participants in the lowest quintile, the risk for type 2 diabetes was 2.5 times higher in those in the highest quintile at baseline (odds ratio [OR] 2.45; 95% CI: 1.56, 3.85); 1.9 times higher in those in the fourth quintile (OR 1.85; 95% CI: 1.16, 2.95); 1.6 times higher in those in the third quintile (OR 1.58; 95% CI: 0.98, 2.53) and 1.5 times higher in those in the second quintile (OR 1.47; 95% CI: 0.91, 2.39) in unadjusted models. Controlling for gender did not appreciably alter the OR compared to the unadjusted model. Further controlling for age, FPG and cholesterol attenuated associations (Table 4).

The incidence of type 2 diabetes was 11.7 per 1000 person-years (95% CI: 8.8, 14.7) in participants in the normal weight, normal TG group and 27.2 per 1000 person-years (95% CI: 21.2, 34.4) in the HTGW group. Compared with participants in the normal-weight, normal TGs group, the risk for type 2 diabetes was 2.4 times higher in those in the HTGW group (OR 2.36; 95% CI: 1.61, 4.44) in age- and gender-adjusted models.

The ROC curves for the incidence of type 2 diabetes for VAI, WC, BMI, WHtR and WHR are shown in the Figure 1. The areas under the ROC curves (95% CI) were 0.583 (0.545, 0.621) for VAI; 0.610 (0.574, 0.645) for WC; 0.609 (0.571, 0.646) for BMI; 0.557 (0.522, 0.593) for WHR and 0.626 (0.591, 0.662) for WHtR. All parameters were significant predictors for future risk of type 2 diabetes (p<0.001). The areas under the curve were almost similar for VAI, WC, BMI, WHR and WHtR. However, it is apparent that in this population of FDRs of patients with type 2 diabetes, the VAI was similar to HTGW and simple anthropometric indexes in predicting future risk for type 2 diabetes.

## Discussion

Current studies show that both VAI and HTGW are similarly predictors of incidence of type 2 diabetes in a large cohort of FDRs of patients with type 2 diabetes in Iran. Although the VAI and HTGW could be alternative indexes to predict type 2 diabetes, BMI, WC, WHtR and WHR appeared to be almost similar to those observed with the VAI. This observation was confirmed by the results of ROC curve analysis. The area under the ROC curve for the VAI and all of the body fatness indexes were close to 0.5, which means relatively lower predictive discriminatory power. Easily measurable anthropometric markers, such as BMI, WC, WHtR and WHR, have been advocated in the literature as being valuable type 2 diabetes prediction tools also (1,24,25). Our findings are consistent with the limited studies showing that the VAI is an independent predictor of type 2 diabetes (12,14–17). In Chinese cross-sectional (12,16) and cohort (15,17) studies and the Tehran Lipid and Glucose cohort study (14) the VAI was associated with increased risk for type 2 diabetes. However, the ability of the VAI to identify diabetes risk was not found to be superior to easily measurable anthropometric markers, such as BMI, WC, WHtR, in previous studies (14–16). In a Chinese cohort study of 3461 individuals free of diabetes followed for 5 years, Chen et al (17) reported that the ability of the VAI to identify risk for type 2 diabetes was superior to other anthropometric indexes. In fact, the ability of the VAI to identify risk for type 2 diabetes was not superior to other anthropometric indexes, reflecting 95% CI of area under the ROC curve.

**Table 2**
Age and age-adjusted mean (SE) and proportion baseline characteristics of first-degree relatives of patients with type 2 diabetes by visceral adiposity index quintile, The Isfahan Diabetes Prevention Study

| Characteristic | Total | Visceral adiposity index at baseline | | | | |
|---|---|---|---|---|---|---|
| | | 1st quintile (≤1.39) | 2nd quintile (1.40–1.98) | 3rd quintile (1.99–2.74) | 4th quintile (2.75–3.93) | 5th quintile (≥3.94) |
| Participants, no. (%) | 1720 (100) | 325 (18.9) | 342 (19.9) | 358 (20.8) | 349 (20.3) | 346 (20.1) |
| Age (years) | 43.0 (0.15) | 41.7 (0.35) | 42.6 (0.35) | 43.1 (0.34) | 43.8 (0.34) | 43.6 (0.34)*** |
| Height (cm) | 159.8 (0.20) | 159.2 (0.47) | 160.0 (0.45) | 159.9 (0.44) | 160.0 (0.45) | 159.7 (0.45) |
| Weight (kg) | 73.9 (0.28) | 70.4 (0.65) | 73.0 (0.64) | 74.3 (0.62) | 74.8 (0.63) | 76.5 (0.63)*** |
| Waist circumference (cm) | 89.2 (0.23) | 85.4 (0.51) | 87.7 (0.50) | 89.7 (0.48) | 90.3 (0.49) | 92.7 (0.49)*** |
| Hip circumference (cm) | 107.5 (0.21) | 105.6 (0.48) | 106.9 (0.47) | 107.6 (0.46) | 108.3 (0.47) | 108.8 (0.47)*** |
| Waist-to-hip ratio | 0.83 (0.002) | 0.81 (0.004) | 0.82 (0.004) | 0.83 (0.004) | 0.83 (0.004) | 0.85 (0.004)*** |
| Body mass index (kg/m$^2$) | 28.9 (0.10) | 27.8 (0.23) | 28.5 (0.22) | 29.1 (0.22) | 29.2 (0.22) | 30.0 (0.22)*** |
| Waist-to-height ratio | 0.56 (0.001) | 0.54 (0.003) | 0.55 (0.003) | 0.56 (0.003) | 0.57 (0.003) | 0.58 (0.003)*** |
| FPG (mg/dL) | 5.3 (0.02) | 5.3 (0.04) | 5.3 (0.04) | 5.3 (0.04) | 5.3 (0.04) | 5.4 (0.04)* |
| PG 30 min (mmol/L) | 8.0 (0.04) | 7.8 (0.10) | 7.9 (0.10) | 8.1 (0.09) | 7.9 (0.09) | 8.3 (0.10)** |
| PG 60 min (mmol/L) | 8.3 (0.02) | 7.8 (0.13) | 8.1 (0.13) | 8.3 (0.13) | 8.4 (0.13) | 9.0 (0.13)*** |
| PG 120 min (mmol/L) | 6.7 (0.05) | 6.3 (0.10) | 6.5 (0.10) | 6.6 (0.10) | 6.7 (0.10) | 7.1 (0.10)*** |
| A1C (%) | 5.1 (0.02) | 5.0 (0.05) | 5.0 (0.05) | 5.1 (0.05) | 5.1 (0.05) | 5.1 (0.05) |
| Cholesterol (mmol/L) | 5.1 (0.03) | 4.8 (0.06) | 5.1 (0.06) | 5.1 (0.05) | 5.2 (0.05) | 5.3 (0.06)*** |
| LDL (mmol/L) | 3.1 (0.02) | 3.0 (0.05) | 3.2 (0.05) | 3.2 (0.05) | 3.2 (0.05) | 2.9 (0.05)*** |
| HDL (mmol/L) | 1.2 (0.007) | 1.4 (0.01) | 1.3 (0.01) | 1.2 (0.01) | 1.1 (0.01) | 0.9 (0.01)*** |
| Triglyceride (mmol/L) | 1.9 (0.03) | 0.93 (0.04) | 1.3 (0.04) | 1.6 (0.04) | 2.1 (0.04) | 3.4 (0.04)*** |
| Non-HDLC (mmol/L) | 3.9 (0.02) | 3.4 (0.05) | 3.8 (0.05) | 4.0 (0.05) | 4.1 (0.05) | 4.3 (0.05)*** |
| Systolic BP (mm Hg) | 115.6 (0.39) | 111.8 (0.86) | 114.2 (0.84) | 116.0 (0.81) | 116.9 (0.83) | 118.9 (0.83)*** |
| Diastolic BP (mm Hg) | 75.7 (0.29) | 73.1 (0.65) | 74.0 (0.64) | 76.3 (0.62) | 76.3 (0.63) | 78.4 (0.63)*** |
| Visceral adiposity index | 2.9 (0.05) | 1.0 (0.07) | 1.7 (0.07) | 2.3 (0.06) | 3.3 (0.06) | 6.1 (0.06)*** |
| Women, no. (%) | 1283 (74.6) | 246 (75.7) | 254 (74.3) | 264 (73.7) | 266 (76.2) | 253 (73.1) |
| Overweight, no. (BMI ≥25) | 1444 (84.2) | 241 (74.2) | 277 (81.5) | 304 (85.2) | 306 (87.9) | 316 (91.9)*** |
| Abdominal obesity, no. (%) | 676 (39.3) | 85(26.2) | 113 (33.0} | 133 (37.2) | 165 (47.3) | 180 (52.0)*** |
| Hypertriglyceridemic-waist, no. (%) | 347 (20.2) | 0.0 (0.0) | 7 (2.0) | 39 (10.9) | 127 (36.4) | 174 (50.3)*** |

*BP*, blood pressure; *FPG*, fasting plasma glucose; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *non-HDLC*, non-high-density lipoprotein cholesterol; *PG*, plasma glucose.
*Notes:* Data are expressed as mean (SE) or number (%). Age-adjusted means were calculated using general linear models.
* p<0.05; ** p<0.01; *** p<0.001 comparison across all 5 groups.

**Table 3**
Age- and gender-adjusted correlation coefficients in adiposity parameters

| | VAI | WC | BMI | WHtR | WHR |
|---|---|---|---|---|---|
| VAI | 1.00 | 0.213* | 0.146* | 0.208* | 0.222* |
| WC | | 1.00 | 0.847* | 0.940* | 0.610 |
| BMI | | | 1.00 | 0.851* | 0.258* |
| WHtR | | | | 1.00 | 0.596* |

*BMI*, body mass index; *VAI*, visceral adiposity index; *WC*, waist circumference; *WHR*, waist-to-hip ratio; *WHtR*, waist-to-height ratio.
* p<0.001.

Our study has several strengths and limitations. The strengths include the use of a sample consisting of men and women, the performance on standard OGTTs, information about potential determinants of type 2 diabetes and the use of direct measurements of the anthropometric indexes rather than self-reported data. At follow up, nonattendees in the entire population did not differ from attendees in terms of major risk factors for progression to type 2 diabetes, although a difference too small to explain the high progression rate to type 2 diabetes in our study was seen in the mean levels of PG. Our database is 1 of the few that has followed FDRs of patients with type 2 diabetes, thereby enabling us simultaneously to control the genetic factors that may predict type 2 diabetes. In terms of our definition of the incidence of type 2 diabetes, some selection bias may be present because participants who attended screenings may have been more likely to be tested and, consequently, diagnosed as having type 2 diabetes. Thus, participants with type 2 diabetes who had lower risk may have been missed through lack of testing. We did not conduct gender-specific analyses because there were too few events in some subgroups to calculate stable

**Table 4**
Incidence rates and odds ratio (OR)[a] of type 2 diabetes by visceral adiposity index quintile, the Isfahan Diabetes Prevention Study

| | Visceral adiposity index at baseline | | | | |
|---|---|---|---|---|---|
| | 1st quintile (≤1.39) | 2nd quintile (1.40–1.98) | 3rd quintile (1.99–2.74) | 4th quintile (2.75–3.93) | 5th quintile (≥3.94) |
| Number of cases (%.) | 31 (12.1) | 46 (18.0) | 51 (19.9) | 57 (22.3) | 71 (27.7) |
| Person-years | 2392 | 2475 | 2565 | 2543 | 2420 |
| Incidence/1000 person-years (95% CI) | 13.0 (8.9, 18.4) | 18.6 (13.6, 24.7) | 19.9 (14.8, 26.1) | 22.4 (17.0, 29.0) | 29.3 (23.0, 36.8) |
| Odds ratio (95% CI) | | | | | |
| Unadjusted | 1.00 | 1.47 (0.91, 2.39) | 1.58 (0.98, 2.53) | 1.85 (1.16, 2.95)* | 2.45 (1.56, 3.85)*** |
| Gender adjusted | 1.00 | 1.48 (0.91, 2.39) | 1.58 (0.98, 2.53) | 1.85 (1.16, 2.95)* | 2.45 (1.56, 3.86)*** |
| Age and gender adjusted | 1.00 | 1.41 (0.87, 2.29) | 1.46 (0.90, 2.35) | 1.71 (1.07, 2.74)* | 2.26 (1.43, 3.56)*** |
| Age, gender and FPG adjusted | 1.00 | 1.35 (0.81, 2.27) | 1.48 (0.90, 2.46) | 1.84 (1.11, 3.03)* | 1.98 (1.22, 3.21)** |
| Age, gender, FPG and cholesterol adjusted | 1.00 | 1.37 (0.82, 2.30) | 1.50 (0.90, 2.49) | 1.86 (1.13, 3.08)* | 1.99 (1.22, 3.25)** |

*CI*, confidence interval; *FPG*, fasting plasma glucose levels.
[a] Odds ratio (with 95% CI) calculated by multiple logistic regression.
* p<0.05; ** p<0.01; *** p<0.001.

risk estimates, and we used gender as an adjustment factor in all analyses. The current findings were drawn from a study population with FDRs of patients with type 2 diabetes and, therefore, the results might not be generalizable to all populations. Residual confounders could not be eliminated, so they may increase the possibility that uncontrolled or inadequately measured confounders affected our results. However, it is necessary to validate the association of the VAI with type 2 diabetes in other populations. This study is meaningful as a first study to clarify the relationship between the VAI and HTGW and incident type 2 diabetes in an Iranian population of FDRs of patients with type 2 diabetes.

In conclusion, these data provide further evidence that the VAI and HTGW are robust predictors of type 2 diabetes in high-risk individuals in Iran and that BMI, WC, WHtR and WHR show similar discriminating abilities.

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## Author Contributions

MJ conceived and designed the study, analyzed and interpreted the data and drafted the manuscript; MA recruited samples and contributed to the discussion and revision of the manuscript and obtained funding for the IDPS.

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