Original article

Anthropometric indices predicting incident type 2 diabetes in an Iranian population: The Isfahan Cohort Study

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Abstract

Background. — The link between adiposity and type 2 diabetes (T2D) is well known. However, it remains controversial as to which index and cutoff point is the best predictor in different populations.

Methods. — A total of 2981 urban and rural Iranian adults over 35 years of age, and free of cardiovascular disease and diabetes were followed for 7 years. Anthropometric indices included body mass index (BMI), body adiposity index [BAI = (hip circumference/height1.5) – 18], waist-to-height ratio (WHtR), waist-to-hip ratio (WHpR), and waist and hip circumferences. T2D was defined as fasting plasma glucose ≥ 126 mg/dL or 2-h post-prandial plasma glucose ≥ 200 mg/dL, or the use of antidiabetic agents. Receiver operating characteristic curve analysis determined the best cutoff point for each adiposity index.

Results. — After 7 years of follow-up, 389 new cases of diabetes were found. Most indices were linearly associated with increased risk of diabetes but the best continuous predictor was WHtR in men [odds ratio: 1.10 (95% confidence interval: 1.07–1.12) for one unit] and BMI in women [1.08 (1.04–1.11) for 0.1 kg/m2], BMI cutoffs of 26 kg/m2 in men and 30 kg/m2 in women were the best binary predictors in adjusted models, and showed increased T2D risks of 2.91 (2.06–4.12) and 1.94 (1.42–2.66) times, respectively. All central-obesity indices in men and WHpR in women were also significantly associated with T2D independent of BMI. BAI was significantly associated with T2D in men but not in women.

Conclusion. — BMI at the appropriate cutoffs in both genders and WHtR in men and BMI in women as continuous factors were the best predictors of incident T2D in this Iranian population.

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Keywords: Type 2 diabetes; Overall obesity; Central obesity; Risk; Body adiposity index

Résumé

Facteurs de risque du diabète de type 2 dans la population iranienne : étude de la cohorte d’Isfahan.

Contexte. — La relation entre l’adiposité et le risque de diabète de type 2 est mal connue dans la population iranienne.

Méthodes. — Un total de 2981 adultes iraniens de plus de 35 ans, exempts de maladies cardiaques et de diabète, a été suivi pendant sept ans. Les indices anthropométriques étudiés comprenaient l’indice de masse corporelle (IMC), l’indice d’adiposité corporelle [BAI = (tour de hanches/taille1.5) – 18], la taille, le ratio tour de taille/taille, le rapport taille-hanches. Les seuils de prédiction des indices anthropométriques ont été déterminés par analyse des courbes ROC.

Résultats. — Après sept ans de suivi, 389 nouveaux cas de diabète ont été trouvés. La plupart des indices étaient associés de manière linéaire au risque de diabète mais le meilleur prédicteur continu était WHtR pour les hommes [odds ratio : 1.10 (intervalle de confiance 95 % : 1.07 à 1.12) pour une unité] et l’IMC pour les femmes [1.08 (1.04 à 1.11) pour 0.1 kg/m2]. Un IMC supérieur à 26 chez les hommes et supérieur à 30 chez les femmes était le facteur prédictif le plus puissant dans les modèles ajustés. Tous les indices d’obésité centrale chez les hommes et WHpR chez les femmes étaient significativement associés au risque de diabète, indépendamment de l’IMC. L’indice d’adiposité corporelle était significativement associé au risque de diabète chez les hommes mais pas chez les femmes.

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Conclusion. — Un IMC supérieur à 26 chez les hommes et supérieur à 30 chez les femmes, et le ratio tour de taille/taille chez les hommes étaient des facteurs prédictifs indépendants de l’incidence du diabète dans cette population iranienne.

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Mots clés : Diabète de type 2 ; Obésité ; Indice d’adiposité corporelle

1. Introduction

The global prevalence of diabetes mellitus is rapidly increasing. Over the past three decades, the number of people with diabetes has doubled [1]. Asia is known as the world’s “diabetes epicenter”, and the Persian Gulf area is a hot spot within Asia [2]. The cause of this epidemic is due to complex genetic and acquired factors, and it is certain that the increase in type 2 diabetes (T2D) is inherently linked to the increase in obesity and overweight [3]. It was reported that Iran was the world’s tenth most obese country in 2005 [body mass index (BMI) > 30 kg/m²] [4], but other countries in the Middle East share this problem as five of the 10 countries with the highest prevalence of obesity and overweight were from this area [4].

As adiposity definitions have been based on different criteria, the World Health Organization (WHO) has recommended BMI as a simple strategy to identify patients at risk of diabetes [5]. However, the distribution of BMI varies across different geographical and ethnic groups, and a large number of different measures of adiposity also contribute differentially to the associated metabolic disturbances [6].

Ashwell et al. [7], in their meta-analysis, have recently suggested that waist-to-height ratio (WHtR) might be better than the traditionally used BMI and waist circumference (WC) to predict cardiovascular disease and its risk factors, including diabetes. However, as they stated, the notion needs to be further investigated. Furthermore, body adiposity index (BAI) has recently been introduced as a new index offering good estimation of percentage body fat, but its association with the risk of diabetes and cardiovascular diseases has still to be assessed in different populations [8].

In response to the insufficiency of evidence from the Middle East described by the WHO Expert Consultation on central obesity [6], the present study aimed to evaluate the predictive ability of various anthropometric indices — BMI, BAI, WHtR, waist-to-hip ratio (WHpR), waist circumference (WC) and hip circumference (HC) — as continuous and binary factors for incident diabetes.

2. Methods

2.1. Study population

The Isfahani Cohort Study (ICS) is an ongoing population-based longitudinal study of adults, aged ≥ 35 years, living in urban and rural areas of three counties in central Iran — namely, Isfahani, Najafabad and Arak [9]. Participants were recruited between January 2 and September 28, 2001. Selected by multistage random sampling, they were recruited to reflect the age, gender and urban/rural distribution of their communities [10]. Ethical approval was obtained from the Ethics Committee of the Isfahani Cardiovascular Research Centre (a WHO collaborating centre).

2.2. Assessments

After their informed written consent had been obtained, medical interviews and physical examinations of all participants were conducted. Measurements of blood pressure and anthropometric parameters as well as fasting blood tests were carried out, following standard protocols and using calibrated instruments as described elsewhere [10]. A range of anthropometric measurements was investigated. WC was taken as the smallest circumference at or below the costal margin, and the HC was taken at the level of the greater trochanter. BMI was computed as weight (kg) divided by height squared (m²). BAI was calculated using the equation suggested by Bergman et al.: BAI = [(HC/height)1.5] – 18 [8]. WHpR and WHtR were calculated by dividing WC by HC and by height, respectively. To define central obesity based on WC, the recommendation of the International Diabetes Federation (IDF) for Middle Easterners was used: ≥ 94 cm in men and ≥ 80 cm in women [11]. The local ICS recommendation for the Iranian population — WC ≥ 90 cm in men and ≥ 97 cm in women [12] — was used to predict cardiovascular disease (CVD) events as were the updated Adult Treatment Panel III (ATP III) guidelines of the US National Cholesterol Education Program (NCEP): WC ≥ 102 cm in men and ≥ 88 cm in women [13].

T2D was defined as fasting plasma glucose (FPG) ≥ 7.0 mmol/L (126 mg/dL) or 2-h post-prandial plasma glucose (PPG) ≥ 11.1 mmol/L (200 mg/dL), or the use of glucose-lowering drugs. Subjects who smoked every day were considered current smokers. In 2007 (the seventh year of follow-up), participants were invited to have repeat laboratory measurements, physical examinations and interviews, using the same protocol as the baseline survey. Laboratory measurement methods were similar in 2001 and 2007, although the auto analyzer used was different (Eppendorf, Hamburg, Germany in 2001 and Hitachi 902, Tokyo, Japan in 2007). An external accredited laboratory, however, validated both instruments.

2.3. Statistical analysis

Data entry was carried out using EPI Info™ software, and data analysis was done using STATA software (Stata/IC 11.0, StataCorp LP, College Station, TX, USA). For all analyses,
statistical significance was assessed at the level of 0.05 (two-tailed). No variable had more than 3% missing values, and stochastic regression was used to impute missing values [14]. Due to skewness, the Mann–Whitney test was employed to compare age, triglycerides and the triglyceride/high-density lipoprotein cholesterol (HDL-C) ratio between men and women. The remaining comparisons were made by the Student’s t-test and chi-square test.

Associations between adiposity indices as continuous variables and incident diabetes were separately assessed in crude and adjusted logistic regression models, and the models’ fits were compared. The linearity of associations in the crude models was then evaluated. The discriminatory power of the indices was assessed using receiver operating characteristic (ROC) analysis, and the best cutoff value for each index derived. The association of adiposity indices as binary variables was also assessed using a plan identical to that for continuous variables. Finally, the associations of central-obesity indices with diabetes were adjusted for BMI.

Deviance (a likelihood ratio statistic for comparing each model with the saturated model) and Akaike information criteria (AIC; a statistical trade-off between the likelihood of a model against its complexity) were used as indicators of the goodness of fit of the model and prediction error. A lower value for both deviance and AIC indicated better model fit. To test non-linearity, all variables were modeled by restricted cubic splines with four knots (at percentiles 5%, 35%, 65% and 95%) in a logistic regression model in men and women separately. The value of the first knot served as the reference group for estimation of the odds ratios (ORs) in each model [15]. Associations were adjusted for age, smoking status, education and family history of diabetes, systolic blood pressure and triglyceride/HDL-C ratio.

ROC analysis and the area under the curve (AUC) were used to identify discriminatory power as well as the sensitivity and specificity of possible cutoff points for each adiposity indicator for detection of incident diabetes. Using bootstrapping, the P value of each pair of AUCs was calculated by the Wald statistic and the 95% confidence interval (CI) of difference between them was derived. The optimal cutoff values were defined as the point at which the value of sensitivity + specificity – 1 was maximum (Youden index). This cutoff value corresponded to the point on the ROC curve with the maximum vertical distance from the curve to the chance line, and has also been defined as an accuracy indicator in clinical epidemiology. This method is superior to the closest-to-(0.1) criterion [16]. Cutoff values were also determined by discriminant analysis. In cases of inconsistency between the two methods, both cutoffs were considered.

Based on these cutoffs for each indicator, the study population was divided into two groups. The corresponding binary variables were evaluated in logistic regression models to predict incident diabetes, and the models were compared based on similar goodness-of-fit statistics. Crude associations were adjusted for factors similar to those in models including continuous variables. In addition, the C statistic (AUC for logistic regression models) as a measure of discrimination [17] was used to determine the general discriminatory ability of adjusted models including each adiposity indicator as a binary factor.

3. Results

Of the 6323 participants free of CVD on baseline evaluation in 2001, laboratory measurements and physical examinations were repeated in 3284 participants in 2007 (1611 were lost to follow-up and 1150 were non-attendees). Of the population with repeat measurements, 303 (9.2%) had diabetes at baseline and were removed from the analysis, resulting in 2981 subjects included in all analyses. The average age of our subjects increased from 48.7 ± 10.2 years in 2001 to 55.4 ± 10.3 years in 2007.

Except for hypertriglyceridaemia and smoking, men overall had a better risk profile than women (Table S1-1, Supplementary data). All anthropometric indices correlated with each other, but a high correlation coefficient (≥ 0.80) was only seen between WC and WHtR (r = 0.91, P < 0.001) and HC (r = 0.80, P < 0.001), with the same pattern in both genders (Table S2-1, Supplementary data).

After 7 years of follow-up, 389 (13.0%) new cases of diabetes were found, including a cumulative incidence (95% CI) of 9.5% (8.0–11.0) in men and 11.3% (9.7–12.9) in women. Of all the anthropometric indices assessed, WHtR was the strongest predictor of diabetes in men, with almost two-fold increase in diabetes risk for each increase in standard deviation (SD; Table 1). This index also had the lowest deviance and AIC, indicating the best fit in the model. BAI performed better than BMI in men in both bivariate and multivariate models. In women, the model that included BMI had a better fit while in adjusted models, WHtR did not reach significance in women. In addition, it was found that in men, the adjusted risk of incident diabetes for each unit increase in WC (1 cm), HC (1 cm), WHtR (0.01), BMI (0.1 kg/m²) and BAI (0.1) was linearly increased by 4.2%, 4.7%, 7.4%, 7.4%, 1.1% and 0.9%, respectively. In women, for each unit increase in WC (1 cm), WHtR (0.01) and BMI (0.1 kg/m²), the adjusted risk of incident diabetes was linearly increased by 1.6%, 2.8% and 0.6%, respectively (Table S2-2, Supplementary data).

Considering the logistic models including restricted cubic splines, the null hypothesis indicating that the coefficient of the second and third splines equaled zero was not rejected (P > 0.05) for all factors of interest in men and women, except for WHtR in men (P = 0.032). Likewise, all associations between continuous indicators were linear (Supplementary data, Fig. S2), except for WHtR in men (Fig. 1). Similar patterns were also observed using z scores (data not shown).

(Table S1–2, Supplementary data) presents what central obesity adds to BMI in the prediction of incident diabetes. In men, although all central-obesity indices were independently associated with diabetes, BMI lost its statistically significant association when WC or WHtR were introduced into the models. WHtR alone had the best model fit (AIC 1014 in Table 1 vs 1016 in Table S1-2, Supplementary data). On the other hand, in women, only WHtR showed a relationship independent of
BMI, and their combination resulted in a substantially better model than BMI or any other index on its own.

Taking subjects with BMI 18.5–25 kg/m² as a reference group, the risk of developing T2D significantly increased in overweight men [1.93 (1.32–2.82), P = 0.001], but not in overweight women [1.15 (0.76–1.74), P = 0.491], whereas obesity was related to an increased risk of incident diabetes in both men [3.69 (2.34–5.81), P < 0.001] and women [2.35 (1.57–3.51), P < 0.001]. However, normal-weight and overweight men were still at increased risk if they had higher WC, WHpR and WHtR, whereas no significant association was observed with these indices in obese men (Table 2). In women, only higher WHpR resulted in increased risk, in both overweight obese and obese subjects but not normal weight women.

Height in women significantly increased diabetes risk when adjusted for other risk factors, but not in crude models or in men. No statistically significant interaction was found between height and other factors (data not shown), and when height was categorized, a significant association was seen only in the last group (n = 11) with height > 176 cm. HC showed no statistically significant association when adjusted for age and WC in both men (P = 0.885) and women (P = 0.153). The same pattern was seen when more adjusted factors were included. However, a protective effect of higher HC was observed in overweight women (Table 2).

ROC curve analysis showed the greatest discriminatory power (AUC) for WHtR in men and for BMI in women (Table 3). For each anthropometric index, the optimal cutoff point was shown to maximize the Youden index for incident diabetes and its corresponding sensitivity and specificity in men and in women. The highest positive likelihood ratio was observed for the indices with the highest AUCs. Cases of substantially different cutoff points by discriminant analysis are also presented in Table 3.

Table S1-3, Supplementary data shows the association between central and overall obesity with incident diabetes using different definitions, including those derived from findings in Table 3. In the crude model, WHtR ≥ 0.56 was the best predictor in men followed by WC ≥ 93 cm. However, when the association was adjusted for other risk factors, BMI ≥ 26.3 kg/m² was considerably better than other indices in men, resulting in 72.2% discrimination in the adjusted model. Of the central-obesity indices, WHtR ≥ 0.56 and WC ≥ 93 cm were similarly good predictors of diabetes. In women, BMI ≥ 30 kg/m² was the best indicator in both crude and adjusted models, with 70.5% discrimination, while WHpR ≥ 0.95 was the best central-obesity indicator of diabetes in women.
Table 2
Association* of central-obesity indices with incident diabetes in normal-weight, overweight and obese subjects.

<table>
<thead>
<tr>
<th></th>
<th>Normal-weightb</th>
<th></th>
<th>Overweightb</th>
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<th>Obeseb</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P value</td>
<td>OR (95% CI)</td>
<td>P value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>642</td>
<td></td>
<td>618</td>
<td></td>
<td>186</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>1.60 (1.08–2.36)</td>
<td><strong>0.017</strong></td>
<td>1.51 (1.07–2.12)</td>
<td><strong>0.018</strong></td>
<td>1.44 (0.89–2.35)</td>
</tr>
<tr>
<td>Hip circumference</td>
<td>1.32 (0.89–1.97)</td>
<td>0.162</td>
<td>1.31 (0.93–1.84)</td>
<td>0.115</td>
<td>1.14 (0.73–1.79)</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>1.57 (1.17–2.11)</td>
<td><strong>0.003</strong></td>
<td>1.39 (1.04–1.85)</td>
<td><strong>0.023</strong></td>
<td>1.19 (0.79–1.80)</td>
</tr>
<tr>
<td>Waist-to-height ratio</td>
<td>2.85 (1.75–4.56)</td>
<td>&lt;0.001</td>
<td>1.65 (1.13–2.43)</td>
<td><strong>0.010</strong></td>
<td>1.25 (0.74–2.10)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>370</td>
<td></td>
<td>633</td>
<td></td>
<td>485</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>1.33 (0.89–2.00)</td>
<td>0.162</td>
<td>1.17 (0.86–1.58)</td>
<td>0.294</td>
<td>1.03 (0.80–1.32)</td>
</tr>
<tr>
<td>Hip circumference</td>
<td>1.39 (0.93–2.08)</td>
<td>0.099</td>
<td>0.71 (0.53–0.95)</td>
<td><strong>0.022</strong></td>
<td>0.82 (0.63–1.06)</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>1.06 (0.80–1.41)</td>
<td>0.659</td>
<td>1.56 (1.20–2.01)</td>
<td><strong>0.001</strong></td>
<td>1.26 (1.03–1.55)</td>
</tr>
<tr>
<td>Waist-to-height ratio</td>
<td>1.59 (0.99–2.54)</td>
<td>0.053</td>
<td>1.20 (0.88–1.64)</td>
<td>0.246</td>
<td>0.95 (0.74–1.21)</td>
</tr>
</tbody>
</table>

Figures in bold indicate statistical significance.

* Body mass index (BMI) 18.5–24.9 kg/m².
b BMI 25–29.9 kg/m².
c BMI ≥ 30 kg/m².
d Calculated for 1 standard deviation increase.

4. Discussion

Our present study found that WHtR in men and BMI in women were the best continuous predictors of incident diabetes. The combination of WHpR and BMI provided the best model for incident diabetes prediction whereas WHtR alone was the best for men. BMI with a cutoff point of 26 kg/m² in men and 30 kg/m² in women was the best binary predictor in adjusted models, while central obesity was independently associated with an increased risk especially in normal-weight and overweight participants.

These findings were partly in contrast with those of Bozorgmanesh et al. [18], who reported no statistically significant associations between any central-obesity indices and incident diabetes in men and WC in women, even though associations were adjusted for similar factors in our study. Previous

Table 3
Best cutoff values of adiposity indices maximizing sensitivity plus specificity using receiver operating characteristic analysis for detecting incident diabetes.

<table>
<thead>
<tr>
<th></th>
<th>Best cutoff points</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Youden index&lt;sup&gt;c&lt;/sup&gt;</th>
<th>LR+</th>
<th>LR–</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>WC</td>
<td>93 cm</td>
<td>0.738</td>
<td>0.668</td>
<td>0.257</td>
<td>1.46</td>
<td>0.51</td>
<td>0.658 (0.633–0.683)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>95 cm</td>
<td>0.651</td>
<td>0.584</td>
<td>0.235</td>
<td>1.54</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>WHpR</td>
<td>0.93</td>
<td>0.616</td>
<td>0.594</td>
<td>0.210</td>
<td>1.52</td>
<td>0.65</td>
<td>0.624 (0.600–0.648)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.57</td>
<td>0.639</td>
<td>0.619</td>
<td>0.258</td>
<td>1.68</td>
<td>0.58</td>
<td>0.673 (0.652–0.693)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>0.56&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.680</td>
<td>0.560</td>
<td>0.241</td>
<td>1.55</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>26.3</td>
<td>0.639</td>
<td>0.606</td>
<td>0.245</td>
<td>1.62</td>
<td>0.59</td>
<td>0.647 (0.613–0.680)</td>
</tr>
<tr>
<td></td>
<td>26.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.633</td>
<td>0.616</td>
<td>0.250</td>
<td>1.65</td>
<td>0.59</td>
<td></td>
</tr>
<tr>
<td>BAI</td>
<td>27.4</td>
<td>0.709</td>
<td>0.505</td>
<td>0.215</td>
<td>1.43</td>
<td>0.57</td>
<td>0.648 (0.606–0.690)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC</td>
<td>94</td>
<td>0.737</td>
<td>0.405</td>
<td>0.142</td>
<td>1.24</td>
<td>0.65</td>
<td>0.589 (0.562–0.615)</td>
</tr>
<tr>
<td></td>
<td>98&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.562</td>
<td>0.531</td>
<td>0.094</td>
<td>1.2</td>
<td>0.82</td>
<td></td>
</tr>
<tr>
<td>WHpR</td>
<td>0.93</td>
<td>0.635</td>
<td>0.536</td>
<td>0.172</td>
<td>1.37</td>
<td>0.68</td>
<td>0.596 (0.575–0.617)</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.95&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.599</td>
<td>0.583</td>
<td>0.178</td>
<td>1.43</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.64&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.553</td>
<td>0.582</td>
<td>0.13</td>
<td>1.27</td>
<td>0.76</td>
<td>0.581 (0.558–0.603)</td>
</tr>
<tr>
<td>BMI</td>
<td>30</td>
<td>0.474</td>
<td>0.703</td>
<td>0.177</td>
<td>1.6</td>
<td>0.75</td>
<td>0.602 (0.569–0.634)</td>
</tr>
<tr>
<td></td>
<td>28.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.514</td>
<td>0.588</td>
<td>0.140</td>
<td>1.33</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>BAI</td>
<td>37.6</td>
<td>0.514</td>
<td>0.651</td>
<td>0.065</td>
<td>1.18</td>
<td>0.89</td>
<td>0.527 (0.484–0.569)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

LR+: LR–: positive/negative likelihood ratios; AUC: area under the curve; CI: confidence interval; WC: waist circumference; WHpR: waist-to-hip ratio; WHtR: waist-to-height ratio; BMI: body mass index; BAI: body adiposity index.

<sup>a</sup> Sensitivity + specificity – 1.
<sup>b</sup> By discriminant analysis.
<sup>c</sup> WC [0.043 (0.013–0.077), P = 0.002] and WHtR [0.050 (0.081–0.107), P = 0.007] significantly higher than WHpR (no other significant differences observed in men).
<sup>d</sup> WC [0.052 (0.014–0.090), P = 0.007], WHtR [0.037 (0.006–0.062), P = 0.010] and BMI [0.071 (0.034–0.106), P < 0.001] significantly higher than BAI; BMI [0.034 (0.003–0.090), P = 0.050] had significantly higher discriminatory capacity than WHtR (no other significant differences observed in women).
studies evaluating anthropometric measurements for incident diabetes have been inconsistent [19,20], although a recent meta-analysis [24] and a prospective study in Iran [21] showed that WHtR might be a better predictor of T2D. This was in agreement with our present findings, but only for men. Although abdominal fat is commonly known to indicate higher risk for diabetes, BMI as an indicator of general obesity is still of value with some studies showing BMI to be as strong as central-obesity indices such as WHtR for predicting diabetes [22,23]. Considering ethnic differences in adipocytes and body composition [24], genetic and geographical variations may also play a role in this regard. In addition, despite the superiority of high BMI scores over central obesity, our study showed that body shape independent of overall obesity is a strong risk factor that should not be ignored.

In their meta-analysis, Ashwell et al. [7] reported that diabetic risk was correctly indicated by WHtR, WC and BMI in 71%, 69% and 66% of men and in 75%, 74% and 69% of women, respectively. However, these indices’ discriminatory power in our present study was slightly lower in men and considerably lower in women. Furthermore, the superiority of WHtR in men and BMI in women over other indices was not statistically significant in most cases when AUC was considered. In fact, the notion of statistical significance on comparing AUCs has not been substantiated in the relevant literature.

In men, no boundary values of WHR were made for a better-adjusted model compared with BMI, and the models’ characteristics were very similar for WHR (cutoff of 0.56) and WC (cutoff of 93 cm) in adjusted models. Our findings also showed that, on the one hand, adiposity indices may demonstrate different characteristics as continuous or binary factors and, on the other hand, the best adiposity indicator based on ROC curve analysis may not be the best in multivariate models as a more comprehensive approach.

The best cutoff points obtained for WC (93 cm and 94 cm in men and women, respectively), WHpR (0.93 and 0.95), WHR (0.56 and 0.63), BMI (26.3 kg/m² and 30 kg/m²) and BAI (27.4 and 37.6) support the idea that the adoption of different cutoffs for different countries is more feasible than one-size-fits-all definitions [6,11,25]. The cutoffs in women were all higher than in men. It has been claimed that as cutoffs derived by ROC analysis are dependent on distribution in the study population, a higher distribution would automatically result in higher cutoff points [26]. Women in this population had a considerably higher incidence of CVD similar to that seen at the same age in men [12]. This suggests that higher cutoffs in women, albeit in line with other reports [27], should be used with caution.

Adiposity indices could be treated as binary indicators to determine those at risk or as original continuous values. As shown in men, these two approaches can lead to different best indices. While the first approach is inevitably needed to identify those needing clinical interventions at both community and individual levels, the latter is important for assessing the effect of incremental increases. However, most studies used a 1-SD increase or quartiles instead of actual, original values [18,28–30]. Although this may show the linearly increasing effect of adiposity indices, it is difficult to convert the implications into practical applications in the clinical setting. In our present study, the linearity of the association of most indices with diabetes risk was demonstrated, and the corresponding risk for each unit increase was quantified using the original values. This has yielded estimations to precisely measure the risk of small changes in adiposity indices in populations or individuals in terms of future incident diabetes.

The exception for linear association was WHpR in men. The risk of incident diabetes started when WC was about 90% of HC and consistently increased thereafter to peak at the point that these two parameters were almost equal. With further excess WC compared with HC, the risk showed an approximately steady state with only a slight decrease. The non-linearity of such an association was also seen in another study [30] although, in that case, it peaked in the last deciles of WHpR. WC is known to be a good marker of visceral fat that, in turn, has been shown to be associated with circulating free fatty acids, insulin resistance and hyperinsulinemia [28]. Both subcutaneous fat and lean tissue may proportionally make up HC [31], but subcutaneous fat has less potential to release free fatty acids into the bloodstream, and there is evidence that femoral–gluteal fat may act as a sink for circulatory free fatty acids and play a protective role [32]. However, properties unique to adipose and lean components of WHpR cannot be independently evaluated, and evaluation of non-linear associations between the numerator and denominator is prohibited by a ratio [28]. Some studies have found protective effects with larger HC for a given WC against developing diabetes [18,28,33]. In contrast, except in overweight women, such an inverse association was not seen in our population and is in agreement with the findings of a study in first-degree relatives of diabetic patients [34].

Two previous studies in Iranian populations [18,34] found an inverse association between height and risk of diabetes, but that is contrary to our present findings. In our study, a detrimental association of height with diabetes was seen only in a small group of 11 tall women and so is not generalizable. However, diabetes in Chinese women has also shown a positive association with height that emerged after controlling for baseline BMI, birth cohort, education and income [35]. In fact, those authors suggested using the ratio of leg length to sitting height as an alternative to standing height.

In our study, BAI was linearly associated with incident diabetes in men, but not in women. Moreover, while it outperformed BMI in both crude and adjusted models in men, BAI was not better than either WHtR or WC. Although BAI had considerable accuracy for showing body fat in some studies in Brazil [36,37], others failed to demonstrate any substantial superiority over BMI [38,39]. However, a cross-sectional study in the USA showed that BAI was associated with elevated cardiometabolic risk [40]. Thus, it may be necessary to modify the equation for other ethnic groups.

The present study had several strengths, such as its multicentre setting with wide coverage, including rural areas, as well as a relatively large sample size, longitudinal design, direct measurement of anthropometrics, and the use of both FPG and 2-h PPG to ascertain incident diabetes. However, a major limitation was the large number of non-respondents, although the subject has been covered elsewhere and concluded that a substantial bias
was unlikely [41]. Nevertheless, the slightly higher frequency of diabetes and hypertension at baseline in non-attendees suggests that those who were available for both measurements constituted a slightly lower-risk population, which may have resulted in underestimation of the true risk. However, presence of the metabolic syndrome and other CVD risk factors, and gender and urban/rural residency did not differ between non-attendees and attendees.

In conclusion, our study has found that the best adiposity index in men differed depending on the way it was considered. WHtR, as a numerical factor, was the best predictor of diabetes in men but a high BMI was best compared with other indices as a dichotomous factor. In women, BMI was the best predictor of diabetes as both a continuous and binary factor. Yet, in spite of the superiority of BMI, all central-obesity indices in men and WHpR in women showed an increased risk of incident diabetes independent of BMI. Furthermore, the best cutoff points for adiposity indices differed considerably from the current international recommendations.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.diabet.2013.04.001.

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