

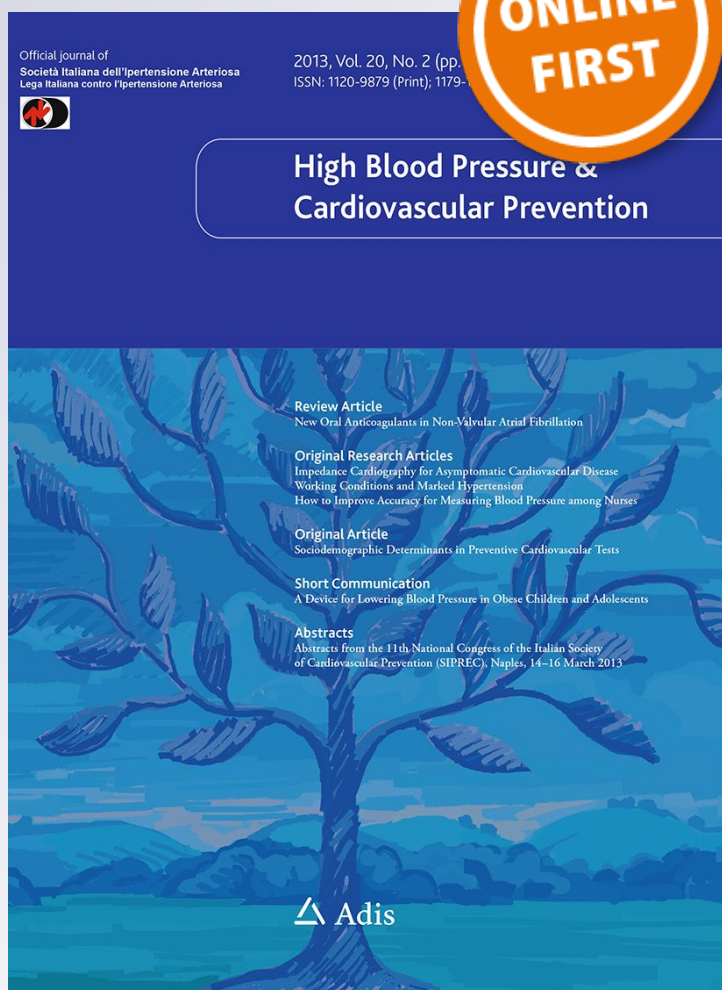
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Comparison of Different Obesity Indices for Predicting Incident Hypertension

Mohsen Janghorbani^{1,2} · Ashraf Aminorroaya¹ · Masoud Amini¹

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Abstract

Introduction Obesity is well recognized to be an important risk factor for hypertension (HTN), but it is not clear which obesity indices have stronger association with HTN.

Aim To evaluate the ability of different obesity indices, including visceral adiposity index (VAI), hypertriglyceridemic-waist (HTGW) phenotype, a body shape index (ABSI), body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR) and waist-to-hip ratio (WHR) as possible hypertension (HTN) predictor in a high-risk population.

Methods Seven years follow-up data in first-degree relatives of consecutive patients with type 2 diabetes aged 30–70 years without diabetes and HTN with at least one follow-up examination (n = 1417) were analysed. Discriminatory capabilities were examined using the receiver operating characteristic (ROC) curve. Logistic regression analysis was performed to determine the strength of association between obesity indices and HTN.

Results Among the indices, the highest quintile compared with the lowest quintile of WHtR and WC was more strongly associated with HTN in age and sex adjusted models [odds ratio (95% CI); WHtR: 4.02 (2.36, 6.85) and WC: 3.26 (2.05, 5.20)]. Those with HTGW phenotype was 2.3 (1.54, 3.35) times more likely to develop HTN than those with normal WC normal triglyceride. On ROC curve

analysis, WHtR (63.1%; 59.6, 66.7) and WC (61.7%, 58.0, 65.4) had the higher area under the ROC.

Conclusions Although higher values of VAI, BMI, WHR and HTGW were associated with the risk of HTN, WHtR and WC was more strongly associated with the development of HTN, while the ABSI showed weaker association.

Keywords Visceral adiposity index · Hypertriglyceridemic-waist · Hypertension · A body shape index · Anthropometry · First-degree relatives · Incidence · Risk factor

1 Introduction

As hypertension (HTN), the most important risk factor for cardiovascular disease, is rapidly increasing in prevalence, it is important to identify high risk individuals early to select persons who need further evaluation. Multiple risk factors are related to HTN, including age, genetic predisposition, unhealthy diet, physical inactivity, and obesity. Obesity is well recognized to be an important risk factor for HTN [1] and increasing in prevalence worldwide. Numerous epidemiological studies have examined the relationship between different indicators of obesity and HTN [1–8]. Nevertheless, because anthropometric measures such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), and a body shaped index (ABSI) [9], a recently proposed index that standardizes WC for BMI and height, cannot fully distinguish visceral fat from subcutaneous fat, and hypertensive risk is thought to be related to visceral fat rather than subcutaneous fat [10], visceral lipid accumulation defined as the visceral adiposity index (VAI) (a mathematical model that combines WC, BMI, triglycerides

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(TG), and high-density lipoprotein cholesterol (HDL) [11], hypertriglyceridemic-waist (HTGW) phenotype (a combination of abdominal obesity and elevated fasting TG [12]) and lipid accumulation product (a combination of WC and TG [13, 14]) has been established to distinguish visceral fat from subcutaneous fat. However, it is not clear which of these obesity indices have stronger association with HTN, despite years of research.

Therefore, the objective of this ongoing longitudinal study was to assess the clinical usefulness of different obesity indices in predicting incidence of HTN in an Iranian high-risk population without HTN and diabetes, and to compare the predictive ability of VAI, HTGW, ABSI, and other easily measureable anthropometric markers.

2 Methods

Data were drawn from the Isfahan Diabetes Prevention Study (IDPS), which was explained in detail before [15]. In brief, IDPS, initiated in 2003, is an ongoing cohort study of subjects with family history of type 2 diabetes (T2D) in central Iran to assess the various potential risk factors for diabetes. At baseline, our sample consist of 3483 (919 men and 2564 women) first-degree relatives (FDR) of consecutive patients with T2D. All patients were attendees at clinics at Isfahan Endocrine and Metabolism Research Center, which is part of Isfahan University of Medical Sciences, Iran. The study was conducted between the years 2003 and 2005. At the time of each examination, they had anthropometric measurements and laboratory tests including a standard 75 g 2-h oral glucose tolerance test (OGTT), and also completed a questionnaire on their health status and on several possible risk factors of diabetes. Participants were followed-up consistent with standard of medical care in diabetes [16] to apprise information on demographic, anthropometric, and lifestyle factors and on newly diagnosed diabetes and HTN. If OGTT was normal at baseline, then repeat testing was carried out at least at 3-year times. Otherwise, repeat testing was usually carried out every year.

2.1 Ethics Statement

This study approved by the Isfahan University of Medical Sciences ethical committee. All participants gave written informed consent.

2.2 Follow-Up and Ascertainment of HTN

Of the 3483 participants who took part at baseline, 2066 were eliminated for one or more of the following reasons at baseline: prevalent T2D ($n = 329$), or prevalent HTN ($n = 632$) and 969 did not attend follow-up examinations;

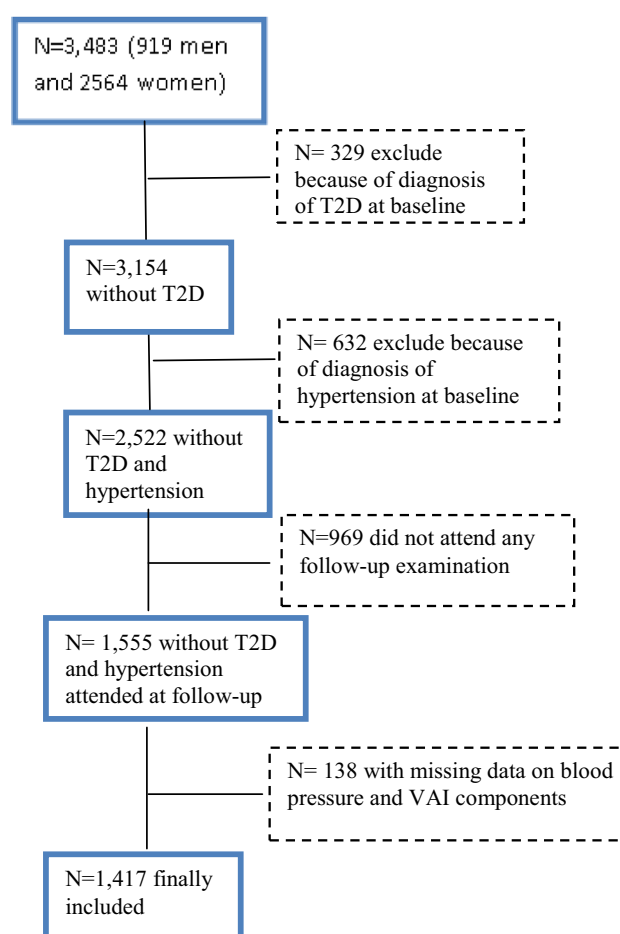


Fig. 1 Flow diagram of inclusion and exclusion criteria in the Isfahan Diabetes Prevention Study. A total of 1417 individuals were finally included

a further 138 participants who accomplished follow-up but had missing data on BP and VAI components were also eliminated, resulting in 1417 participants who completed the study. The mean age [standard deviation (SD)] of participants was 42.6 (6.4) (range 30–70) years and all of them had at least one succeeding review during a mean (SD) follow-up period of 7.3 (2.1) (range 1–10) years. Pregnant women were eliminated (Fig. 1).

2.3 Measurements

At baseline and at follow-ups, data on age, sex, body mass, hemoglobin A1c (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDLC), HDLC, TG, BP, and family and personal medical history was stored. At baseline and at follow-ups, the same methodology was used. The participants were siblings and children of patients with T2D. They were requested to refrain from strong exercise in the evening before and in the morning of their visit when they reported to clinics in the morning after

an overnight fast. Smokers were stimulated to refrain from smoking in the morning of the investigations.

Firstly, on arrival at the clinic, the information provided by the participants in the questionnaire on family history was checked. Then, height, weight, WC and hip circumference (HC) were assessed without shoes and heavy cloths, using standard device and recorded to the nearest 0.1 kg and 0.5 cm. The WC was determined midway between the lower rib margin and the iliac-crest at the end of gentle expiration in the upright position. Hip circumference was determined over the greater trochanters directly over the underwear. BMI was calculated as the weight (kg)/height² (m²). Resting systolic (phase I) and diastolic (phase V) BP were recorded at each examination by a physician with the participants in a sitting position with their legs uncrossed, upon resting in this position for at least 10 min, using a mercury column sphygmomanometer and appropriately sized cuffs. Average BP was calculated from the two consecutive measurements. A blood sample was drawn between 7.00 and 9.00 AM. FPG was assessed by the glucose oxidase method. T2D was defined as FPG ≥ 200 mg/dl, pharmacological treatment, or two FPG was ≥ 126 mg/dl [17]. Those with FPG < 126 mg/dl went through a standard OGTT (75 g glucose 2-h) at baseline and follow-up visits. Venous blood was sampled 0, 30, 60, and 120 min. after oral glucose administration. According to the eight Joint National Committee (JNC-8) guidelines [18], HTN was defined if BP was $\geq 140/90$ mmHg, or using antihypertensive agents.

HbA1c, TC, TG, HDLC, LDLC were recorded. The LDLC levels were calculated with the Friedewald Equation [19]. Non-HDLc was calculated by subtracting HDLC from TC. All the blood analyses were performed at the central laboratory of the Isfahan Endocrine and Metabolism Research Center on the day of blood collection using enzyme-linked method.

2.4 Definitions

VAI was calculated as:

VAI (men) = $[WC/39.68 + (1.88 \times BMI)] \times (TG/1.03) \times (1.31/HDLC)$.

VAI (women) = $[WC/36.58 + (1.89 \times BMI)] \times (TG/0.81) \times (1.52/HDLC)$ [11]. ABSI was defined as: $ABSI = WC/(BMI^{2/3} \times height^{1/2})$ with WC and height in m [9]. The HTGW phenotype was defined as the simultaneous presence of WC $\geq 102/88$ cm in men/women and TG ≥ 150 mg/dl for both sexes [12].

2.5 Analysis

Participants were followed until the occurrence of HTN, the date of the last completed follow-up, death, or end of

follow-up on March 21, 2014, whichever event occurred first. We used the exam visit date that a new case of HTN was recognized as the date of diagnosis. Statistical methods included the following: Student's *t* test or Mann–Whitney U test, one-way analysis of variance (ANOVA) or the Kruskal–Wallis test for continuous variables, the Chi-squared test, Pearson correlation or Spearman's rank correlation, binary logistic regression and receiver operating characteristic (ROC) curves.

Differences between more than two groups were estimated using one-way ANOVA with Benferroni post hoc test. Pearson correlation analysis or Spearman's rank correlation was used to examine the linear relationships between anthropometric variables after holding the effect of age and sex constant. Univariate and multivariate binary logistic regression equations to identify predictors of new-onset HTN were used. We did not adjust for BMI, WC, TG, and HDLC which are components of the VAI, ABSI and HTGW and therefore not appropriate to be adjusted for prediction models already incorporating VAI, ABSI, or HTGW. The continuous anthropometric indices were re-coded into quintiles and compared the risk of developing HTN in each quintile with the lowest category of risk (reference group). To test the significance of HTGW as a predictor of HTN incidence, the HTN incidence was calculated according to the four phenotype groups and compared the risk of developing HTN in each group with the normal waist normal TG group (reference group). The ability of VAI, ABSI, WC, BMI, WHtR, and WHR to predict the HTN incidence was examined with 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, ABSI, WC, BMI, WHtR, and WHR is higher in an individual developing than in an individual not developing HTN. The area under the ROC curve was used as an index of global test performance of VAI, ABSI, WC, BMI, WHtR, and WHR for identification of HTN 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 regarded as good, between 0.70 and 0.80 indicate of fair test performance, and values between 0.50 and 0.70 viewed as poor. Areas under the ROC curves was calculated and compared by a non-parametric test [20]. The general linear model was used to compare age-adjusted means. The SPSS software version 18 for Windows [SPSS Inc., Chicago, IL, USA] were used for data analysis. Reported P values are two-tailed, and $P < 0.05$ were considered to be statistically significant.

Table 1 Age, age-adjusted mean (SE) and proportion characteristics of selected baseline characteristics in 281 first-degree relatives of patients with type 2 diabetes who did and 1136 who did not develop hypertension

Variables	Progressed to hypertension Mean (SE)	Did not progress to hypertension Mean (SE)
Age (year)	44.8 (0.38)	42.0 (0.19)***
Height (cm)	159.3 (0.50)	159.7 (0.24)
Weight (kg)	75.5 (0.69)	72.1 (0.34)***
Body mass index (kg/m ²)	29.7 (0.24)	28.3 (0.12)***
Waist circumference (cm)	90.8 (0.55)	87.5 (0.27)***
Waist-to-hip ratio	0.83 (0.004)	0.82 (0.002)*
Hip circumferences (cm)	109.2 (0.52)	106.4 (0.26)***
Waist-to-stature ratio	0.57 (0.003)	0.55 (0.002)***
A body shape index	0.075 (0.00)	0.075 (0.00)
Follow-up duration (year)	7.9 (0.13)	7.2 (0.06)***
Systolic BP (mmHg)	115.0 (0.66)	109.5 (0.32)***
Diastolic BP (mmHg)	74.2 (0.54)	71.4 (0.26)***
Fasting plasma glucose (mg/dl)	95.7 (0.71)	95.0 (0.35)
Plasma glucose 30 min (mg/dl)	147.6 (1.92)	141.5 (0.95)**
Plasma glucose 60 min (mg/dl)	151.6 (2.61)	146.5 (1.28)
Plasma glucose 120 min (mg/dl)	121.2 (1.98)	118.3 (0.98)
HbA1c (%)	5.0 (0.05)	5.0 (0.02)
Triglyceride (mg/dl)	174.3 (5.44)	155.3 (2.67)**
Cholesterol (mg/dl)	196.1 (2.32)	193.8 (1.14)
HDL cholesterol (mg/dl)	45.0 (0.74)	45.6 (0.36)
LDL cholesterol (mg/dl)	116.9 (2.10)	118.3 (1.01)
Non-HDLc (mg/dl)	150.6 (2.24)	148.3 (1.08)
Visceral adiposity index	3.1 (0.12)	2.7 (0.06)**
	%	%
Women	75.2	75.6
Normal weight (BMI <25 kg/m ²)	11.1	19.6***
Overweight (BMI 25–29.9 kg/m ²)	47.3	50.0***
Obese (BMI ≥30 kg/m ²)	41.6	30.4***
Abdominal obesity, no. (%)	46.4	32.4***
Normal waist normal triglyceride	26.7	44.1***
Normal waist high triglyceride	27.4	24.0***
Enlarged waist normal triglyceride	23.8	17.4***
Hypertriglyceridemic-waist	22.1	14.6***

Data are expressed as mean (SE) or %. Age-adjusted means were calculated using general linear models. Differences in the mean or percentage values of variables between hypertensive and non-hypertensive *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *BP* blood pressure, *Non-HDLc* non-high-density lipoprotein cholesterol

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

3 Results

3.1 Characteristics

Most of the baseline characteristics of individuals who did not return for the follow-up visit (non-respondents), 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 (data not shown). However, non-respondents had slightly lower FPG (95.4 mg/dl vs.

107.5 mg/dl; $P < 0.001$), plasma glucose (PG) at 30 min. (143.0 mg/dl vs. 155.9, $P < 0.001$), 60 min. (148.0 mg/dl vs. 165.1, ($P < 0.001$), and 120 min. (119.2 mg/dl vs. 136.1, $P < 0.001$), levels of HbA1c (5.0 vs. 5.3%, $P < 0.001$), diastolic BP (72.0 mmHg vs. 74.7, $P < 0.001$), and higher HDLc (46.4 mg/dl vs. 45.4, $P < 0.05$) than respondents.

A total of 281 (19.8%) incident cases of HTN occurred during 10,675 person-years of follow-up. Participants on average were overweight with a mean (SD) BMI of 28.6 (4.1) kg/m². Baseline characteristics of the 281 (19.8%)

Table 2 Age- and sex-adjusted correlation coefficients among adiposity parameters

	VAI	WC	BMI	WHtR	WHR	ABSI
VAI	1.00	0.211*	0.141*	0.210*	0.207*	0.156*
WC		1.00	0.851*	0.936*	0.603*	0.353*
BMI			1.00	0.860*	0.263*	-0.149*
WHtR				1.00	0.582*	0.340*
WHR					1.00	0.692*

VAI visceral adiposity index, WC waist circumference, BMI body mass index, WHtR waist-to-height ratio, WHR waist-to-hip ratio, ABSI a body shape index

* $P < 0.001$

participants who did and 1136 (80.2%) who did not progress to HTN are shown in Table 1. As expected, participants who progressed to HTN were older and had higher age-adjusted mean weight, BMI, WC, WHtR, WHR, HC, follow-up duration, systolic and diastolic BP, PG at 30 min, higher TG, and VAI at baseline and a higher proportion of obesity and HTGW.

The mean (SD) age was 44.8 (6.9) years for those progress to HTN and 42.0 (6.2) years for those who did not progress to HTN. The 22.1% of those progressed to HTN and 14.6% of those did not progress to HTN were HTGW at baseline.

The correlation coefficients between various obesity indices are shown in Table 2. All obesity indices showed positive correlation with each other ($P < 0.001$). The strongest correlation coefficients were found between WHtR and WC and the weakest ones were between BMI and VAI.

3.2 Association with HTN

The risk of HTN increased with increasing quintiles of WHtR, WC, BMI, VAI, WHR, and ABSI (Table 3). The highest quintile of WHtR, WC, BMI, WHR, VAI, and ABSI compared with the lowest quintile was associated with HTN in age and sex adjusted models [OR (95% CI); WHtR: 4.02 (2.36, 6.85), WC: 3.26 (2.05, 5.20), BMI: 2.79 (1.79, 4.35), WHR: 2.61 (1.46, 4.67), VAI: 1.65 (1.07, 2.55), and ABSI: 1.37 (0.81, 2.31)]. WHtR and WC had the strongest association with HTN. ABSI had the smallest OR in age- and sex-adjusted models. Controlling for sex did not alter the OR compared to the unadjusted model. Further controlling for age and FPG did not appreciably alter the associations.

The ROC curves for the HTN incidence for WHtR, WC, BMI, VAI, WHR, and ABSI are shown in Fig. 2. The areas under the ROC curves (95% CI) were 0.631 (0.596, 0.667) for WHtR, 0.617 (0.580, 0.654) for WC, 0.594 (0.555, 0.632) for BMI, 0.569 (0.532, 0.607) for WHR, 0.560

(0.521, 0.600) for VAI, and 0.556 (0.517, 0.594) for ABSI. All parameters were significant predictors for future risk of HTN ($P < 0.001$). The global null hypothesis of all indices having the same area under the curve was not rejected ($P > 0.05$). WHtR and WC had the largest areas under the curve, although differences were small with overlapping 95% CI.

4 Discussion

This study revealed that although VAI, ABSI, BMI, WHR and HTGW could be alternative indices to predict HTN; WHtR and WC appeared to be stronger predictors and further emphasizing the usefulness of WHtR and WC in predicting HTN. This observation was confirmed by the results from logistic regression and ROC curve analysis. The area under the ROC curve for all of the obesity indices were close to 0.5, which means the relatively lower predictive discriminatory power. The ABSI, VAI, and WHR had lower areas under the curve values than WHtR, WC, and BMI, although the difference were small, with overlapping 95% CI. To the best of our knowledge, this is the first cohort study to comparing the association between different indicators of obesity including visceral and subcutaneous lipid accumulation and risk of HTN. The results of epidemiological studies that reported the ability of anthropometric indices are inconsistent. Similar to our findings, in systematic review and meta-analysis studies of the association of anthropometric measures and incidence of HTN reported that the ability of WHtR and WC in identifying HTN risk was superior to other anthropometric indices in both sexes in various nationalities and ethnic groups [21–25]. Several studies also provided inconsistent results about the best discriminators for the diagnosis of HTN among obesity indices. For example, Yusuf et al. found WHR more predictive of myocardial infarction than BMI in a case control study of participants from 52 countries [26]. Another cross-sectional study of American adults [27] found WC was associated with HTN after adjusting for BMI. In Chinese cross-sectional [3, 28] studies the BMI, WC and WHR was similarly associated with increased risk of HTN. A longitudinal study of Mauritians also found BMI and indicators of abdominal obesity equally predictive of incident HTN [29]. In a study of Portuguese adolescents, BMI showed the expected positive association with BP but the ABSI showed a negative association with BP [30]. Our findings are also consistent with the Cheung study showing that the ABSI was associated with development of HTN [31], although the predictive power was no better than other anthropometric indices. Fujita et al. [32] found elevated BMI and WC, but not higher ABSI, also increased the risk of HTN. Our

Table 3 Incidence rates and odds ratio (OR)^a of hypertension by visceral adiposity index quintile and four hypertriglyceridemic-waist phenotype groups, The Isfahan Diabetes Prevention Study

	1st quintile	2nd quintile	3rd quintile	4th quintile	5th quintile
Visceral adiposity index at baseline					
Incidence/1000 person-year (95% CI)	20.8 (15.0, 28.0)	22.9 (16.8, 30.3)	22.2 (16.2, 29.7)	28.7 (21.8, 37.0)	33.8 (26.3, 42.9)
Odds ratio (95% CI)					
Unadjusted	1.00	1.10 (0.69, 1.73)	1.06 (0.67, 1.68)	1.45 (0.93, 2.25)	1.75 (1.14, 2.70)*
Sex adjusted	1.00	1.10 (0.69, 1.73)	1.06 (0.67, 1.68)	1.45 (0.93, 2.25)	1.75 (1.14, 2.69)*
Age and sex adjusted	1.00	1.08 (0.68, 1.71)	1.01 (0.63, 1.61)	1.33 (0.85, 2.08)	1.65 (1.07, 2.55)*
Age, sex, and FPG adjusted	1.00	1.07 (0.68, 1.70)	1.00 (0.63, 1.60)	1.32 (0.85, 2.07)	1.65 (1.06, 2.55)*
A body shape index at baseline					
Incidence/1000 person-year (95% CI)	21.4 (15.7, 28.6)	21.9 (16.2, 29.0)	25.1 (18.9, 32.7)	28.7 (21.8, 37.0)	33.9 (26.3, 42.9)
Odds ratio (95% CI)					
Unadjusted	1.00	0.98 (0.63, 1.54)	1.17 (0.76, 1.82)	1.31 (0.85, 2.02)	1.56 (1.02, 2.38)*
Sex adjusted	1.00	0.99 (0.63, 1.55)	1.21 (0.78, 1.88)	1.45 (0.92, 2.27)	1.93 (1.17, 3.18)*
Age and sex adjusted	1.00	0.94 (0.60, 1.47)	1.10 (0.71, 1.72)	1.21 (0.76, 1.92)	1.37 (0.81, 2.31)
Age, sex, and FPG adjusted	1.00	0.93 (0.59, 1.46)	1.09 (0.70, 1.71)	1.20 (0.76, 1.90)	1.34 (0.80, 2.26)
Body mass index at baseline					
Incidence/1000 person-year (95% CI)	18.1 (12.9, 24.8)	22.7 (16.9, 29.8)	25.5 (19.2, 33.0)	26.5 (20.2, 34.2)	38.2 (30.5, 47.2)
Odds ratio (95% CI)					
Unadjusted	1.00	1.32 (0.84, 2.09)	1.54 (0.98, 2.42)	1.64 (1.05, 2.57)*	2.62 (1.71, 4.02)***
Sex adjusted	1.00	1.32 (0.83, 2.09)	1.56 (1.00, 2.46)	1.67 (1.06, 2.62)*	2.72 (1.76, 4.20)***
Age and sex adjusted	1.00	1.28 (0.80, 2.04)	1.48 (0.93, 2.34)	1.66 (1.05, 2.63)*	2.79 (1.79, 4.35)***
Age, sex, and FPG adjusted	1.00	1.28 (0.80, 2.04)	1.47 (0.93, 2.33)	1.66 (1.05, 2.63)*	2.81 (1.79, 4.40)***
Waist circumference at baseline					
Incidence/1000 person-year (95% CI)	15.4 (10.7, 21.4)	20.6 (15.1, 27.4)	22.9 (17.0, 30.0)	34.1 (26.6, 43.0)	40.5 (32.3, 50.2)
Odds ratio (95% CI)					
Unadjusted	1.00	1.38 (0.86, 2.23)	1.58 (0.99, 2.52)	2.61 (1.66, 4.10)***	3.15 (2.03, 4.91)***
Sex adjusted	1.00	1.41 (0.87, 2.27)	1.64 (1.03, 2.62)*	2.87 (1.81, 4.56)***	3.62 (2.28, 5.74)***
Age and sex adjusted	1.00	1.33 (0.82, 2.16)	1.53 (0.95, 2.45)	2.64 (1.66, 4.21)***	3.26 (2.05, 5.20)***
Age, sex, and FPG adjusted	1.00	1.33 (0.82, 2.16)	1.53 (0.95, 2.46)	2.64 (1.65, 4.22)***	3.29 (2.05, 5.27)***
Waist-to-hip ratio at baseline					
Incidence/1000 person-year (95% CI)	17.0 (12.0, 23.3)	23.5 (17.6, 30.7)	31.0 (24.0, 39.5)	24.9 (18.6, 32.8)	35.6 (27.8, 44.7)
Odds ratio (95% CI)					
Unadjusted	1.00	1.43 (0.91, 2.26)	1.98 (1.27, 3.08)**	1.39 (0.87, 2.18)	2.14 (1.39, 3.32)**
Sex adjusted	1.00	1.45 (0.92, 2.28)	1.99 (1.28, 3.10)**	1.57 (0.98, 2.52)	3.33 (1.89, 5.87)***
Age and sex adjusted	1.00	1.30 (0.82, 2.06)	1.70 (1.09, 2.67)*	1.27 (0.78, 2.05)	2.61 (1.46, 4.67)**
Age, sex, and FPG adjusted	1.00	1.29 (0.82, 2.05)	1.69 (1.08, 2.65)*	1.25 (0.77, 2.02)	2.55 (1.42, 4.56)**

Table 3 continued

	1st quintile	2nd quintile	3rd quintile	4th quintile	5th quintile
Waist-to-height ratio at baseline					
Incidence/1000 person-year (95% CI)	9.2 (5.7, 14.1)	23.3 (17.3, 30.6)	26.3 (19.8, 34.1)	36.5 (28.9, 45.3)	35.7 (28.1, 44.7)
Odds ratio (95% CI)					
Unadjusted	1.00	2.79 (1.61, 4.82)***	3.16 (1.83, 5.44)***	4.98 (2.94, 8.41)***	4.60 (2.72, 7.80)***
Sex adjusted	1.00	2.81 (1.62, 4.86)***	3.17 (1.84, 5.46)***	4.99 (2.95, 8.44)***	4.60 (2.72, 7.80)***
Age and sex adjusted	1.00	2.65 (1.52, 4.60)**	3.07 (1.77, 5.30)***	4.53 (2.66, 7.69)***	4.02 (2.36, 6.85)***
Age, sex, and FPG adjusted	1.00	2.64 (1.52, 4.59)**	3.06 (1.77, 5.29)***	4.51 (2.65, 7.67)***	4.03 (2.36, 6.90)***
	NWNT	NWHT	EWNT	HTGW	
Hypertriglyceridemic-waist phenotype groups at baseline					
Incidence/1000 person-year (95% CI)	17.0 (13.2, 20.8)	29.5 (23.4, 36.7)	33.6 (26.1, 42.4)	36.5 (28.1, 46.6)	
Odds ratio (95% CI)					
Unadjusted	1.00	1.89 (1.33, 2.68)***	2.27 (1.57, 3.28)***	2.50 (1.71, 3.65)***	
Sex adjusted	1.00	1.85 (1.30, 2.64)**	2.30 (1.59, 3.34)***	2.52 (1.72, 3.69)***	
Age and sex adjusted	1.00	1.75 (1.22, 2.51)**	2.33 (1.59, 3.40)***	2.27 (1.54, 3.35)***	
Age, sex, and FPG adjusted	1.00	1.75 (1.22, 2.50)**	2.32 (1.58, 3.40)***	2.29 (1.55, 3.38)***	

CI confidence interval, *NWNT* normal waist normal triglyceride, *NWHT* normal waist high triglyceride, *EWNT* enlarge waist normal triglyceride, *HTGW* hypertriglyceridemic-waist, *FPG* fasting plasma glucose

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

^a Odds ratio (with 95% CI) calculated by multiple logistic regression

results were consistent with those studies that reported the ability of WHtR and WC in identifying HTN risk was superior to other anthropometric indices, even though the precise reasons for the discrepancy were unable to be ascertained. Only limited studies have examined the association between visceral adiposity measured by computer tomography and risk of HTN [10, 33–38] and the results were inconclusive. Some of these studies showed a significant or borderline significant association [33, 35, 37–39], whereas others reported no association [40] or an association among women but not men [36]. No longitudinal study has examined the association between VAI and HTGW phenotype and risk of HTN and the clinical usefulness of VAI and HTGW phenotype in predicting HTN have not been explored. In fact, greater ABSI poorly predicted HTN and the ability of VAI and HTGW in identifying HTN risk was not superior to other anthropometric indices reflecting from 95% CI of OR and area under the ROC curve.

WC has been proposed to be the best among subcutaneous measures of fat distribution [29]. However, WC does not account for differences in height, therefore, potentially over- and under-evaluating risk for tall and short individuals respectively [21]. Consequently, researchers proposed

the WHtR as an alternative to WC [21, 25]. This ratio has been shown to be a good indicator of abdominal obesity, similar to WC [41]. However, some have argued against use of WHR or WHtR as a measure of obesity because of its ambiguous biologic interpretation, their lesser sensitivity to weight gain, its greater variability across age, sex, and ethnic groups, and its greater computational complexity and interpretation in public health context [41].

On the basis of our overall findings, both WC and WHtR have the approximately same predictive discrimination. Because WC is strongly correlated with WHtR, they are unlikely to yield different answers and the two measures yield similar information, with the correlation coefficient above 0.93. In addition, a simple WC measurement is a better predictor of progression to HTN than the BMI or WHtR due to the easy to measure, reliability and conveniences, although it does require some training and standardization. Both BMI and WHtR require measurement of height. Whereas accurate weighing requires removal of shoes and most clothing, and correction for occasional appliances or casts, and the use of a high-quality scale that is periodically recalibrated. But, WC requires only the removal (or loosening) of clothing around the waist and an inexpensive tape measure made of non-stretchable

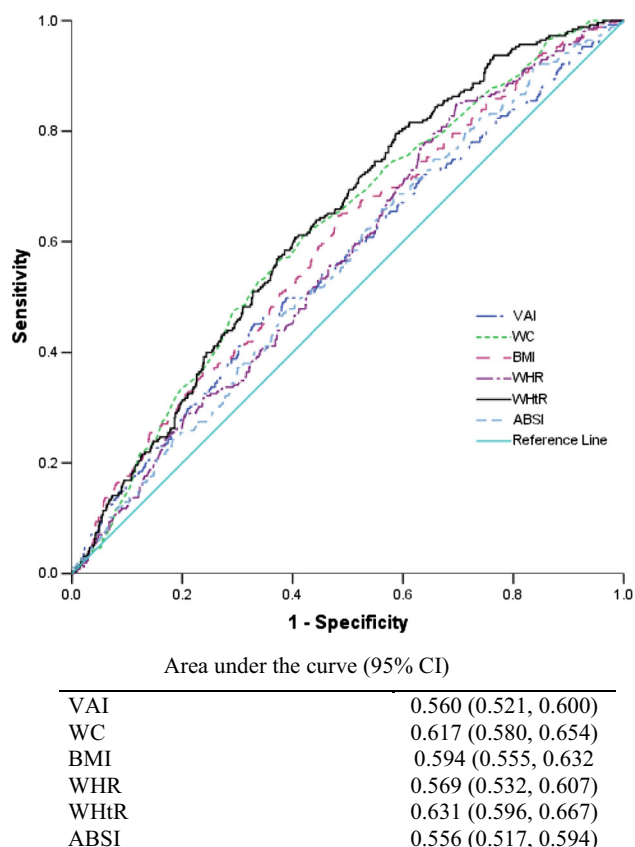


Fig. 2 Receiver operating characteristic curves for visceral adiposity index (VAI), waist circumference (WC), body mass index (BMI), waist-to-hip ratio (WHT), waist-to-height ratio (WHtR) and a body shape index (ABSI) to predict hypertension in first-degree relatives of patients with type 2 diabetes without diabetes and hypertension. Sensitivity represents true positive results and 1-specificity, the false-positive results. The estimates of the area under the ROC curves and their 95% confidence intervals (CI) are shown

material. The standardized landmark for waist measurement is usually simple to identify after a short training period, and WC measurement can be highly reproducible. However, ratios are more difficult to interpret biologically, are less sensitive to weight gain, and have statistical limitations [41].

There are limitations related to this study. At follow-up, non-attendees in the entire population did not differ from attendees according to major risk factors for progression to HTN, although a difference too small to explain the high progression rate to HTN in our study was seen in the mean levels of PG. In term of our definition of incidence HTN, some selection bias may be present as participants who attend for screening may have been more likely to be tested and consequently diagnosed as having HTN. Thus, participants with HTN who had lower risk may have been missed through lack of testing. We did not conduct sex-specific analyses because there were too few events in some subgroups to

calculate stable risk estimates and we used sex as an adjustment factor in all analyses. The current findings were drawn from an Iranian population with FDR of patients with T2D and, therefore, the results might not be generalized to all populations. BP was measured only during follow-up visits and was not monitored. We could not include several possible confounding variables that are known HTN risk factors, such as family history of HTN, estimated glomerular filtration rate, serum uric acid, creatinine, physical activity, diet, stress, and socioeconomic status. These variables could be relevant for explaining the relationship between obesity indices and incidence of HTN. However, it is necessary to validate the association of VAI, HTGW, ABSI and HTN in other populations. However, this study is meaningful as a first study to clarify the relationship between obesity indices including visceral and subcutaneous lipid accumulation and incident HTN among an Iranian population of FDR of patients with T2D.

The high risk of developing HTN in FDR of patients with T2D with high WHtR or WC underlines the importance of prevention of HTN in these individuals.

5 Conclusion

These data provides further evidence that although higher values of VAI, BMI, WHR and HTGW were associated with the risk of HTN, WC and WHtR were more strongly associated with the development of HTN, while the ABSI showed weaker association. WHtR and WC are very highly correlated and likely to behave similarly in HTN prediction. WHtR and WC showed almost the same discriminating ability.

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Authors contributions MJ designed the study, performed statistical analyses and interpreted the data and drafted the manuscript; AA and MA, recruited samples, contributed to interpretation of results and revised the manuscript. All authors approved the final version submitted for publication.

Compliance with Ethical Standards

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

Statement of human and animal rights This study has been approved by the Isfahan University of Medical Sciences ethical committee.

Informed consent Informed consent was obtained from all participants for being included in the study.

References

- Pereira M, Lunet N, Paulo C, Severo M, Azevedo A, Barros H. Incidence of hypertension in a prospective cohort study of adults from Porto, Portugal. *BMC Cardiovasc Disord.* 2012;12:114.
- Ishikawa-Takata K, Ohta T, Moritaki K, Gotou T, Inoue S. Obesity, weight change and risks for hypertension, diabetes and hypercholesterolemia in Japanese men. *Eur J Clin Nutr.* 2002;56:601–7.
- Deng WW, Wang J, Liu MM, Wang D, Zhao Y, Liu YQ, Wang H, Dong GH. Body mass index compared with abdominal obesity indicators in relation to prehypertension and hypertension in adults: the CHPSNE study. *Am J Hypertens.* 2013;26:58–67.
- Gillum RF, Mussolino ME, Madans JH. Body fat distribution and hypertension incidence in women and men. The NHANES I Epidemiologic Follow-up Study. *Int J Obes Relat Metab Disord.* 1998;22:127–34.
- Harris MM, Stevens J, Thomas N, Schreiner P, Folsom AR. Associations of fat distribution and obesity with hypertension in a bi-ethnic population: the ARIC study. *Atherosclerosis Risk in Communities Study. Obes Res.* 2000;8:516–24.
- Folsom AR, Prineas RJ, Kaye SA, Munger RG. Incidence of hypertension and stroke in relation to body fat distribution and other risk factors in older women. *Stroke.* 1990;21:701–6.
- Cassano PA, Segal MR, Vokonas PS, Weiss ST. Body fat distribution, blood pressure, and hypertension. A prospective cohort study of men in the normative aging study. *Ann Epidemiol.* 1990;1:33–48.
- Troisi RJ, Weiss ST, Segal MR, Cassano PA, Vokonas PS, Landsberg L. The relationship of body fat distribution to blood pressure in normotensive men: the normative aging study. *Int J Obes.* 1990;14:515–25.
- Krakauer NY, Krakauer JC. A new body shape index predicts mortality hazard independently of body mass index. *PLoS One.* 2012;7:e39504.
- Koh H, Hayashi T, Sato KK, Harita N, Maeda I, Nishizawa Y, Endo G, Fujimoto WY, Boyko EJ, Hikita Y. Visceral adiposity, not abdominal subcutaneous fat area, is associated with high blood pressure in Japanese men: the Ohtori study. *Hypertens Res.* 2011;34:565–72.
- Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, Galluzzo A, AlkaMeSy Study Group. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care.* 2010;33:920–2.
- Lemieux I, Poirier P, Bergeron J, Alméras N, Lamarche B, Cantin B, Dagenais GR, Després JP. Hypertriglyceridemic waist: a useful screening phenotype in preventive cardiology? *Can J Cardiol.* 2007;23(Suppl B):23B–31B.
- Kahn HS. The “lipid accumulation product” performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. *BMC Cardiovasc Disord.* 2005;5:26.
- Bozorgmanesh M, Hadaegh F, Azizi F. Diabetes prediction, lipid accumulation product, and adiposity measures; 6-year follow-up: Tehran lipid and glucose study. *Lipids Health Dis.* 2010;9:45.
- Amini M, Janghorbani M. Diabetes and impaired glucose regulation in first degree relatives of patients with type 2 diabetes in Isfahan, Iran: prevalence and risk factors. *Rev Diabet Stud.* 2007;4:169–76.
- Anonymous. Executive summary: standard of medical care in diabetes-2013. *Diabetes Care.* 2013;36:S4–10.
- James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Oggedegbe O, Smith SC Jr, Svetkey LP, Taler SJ, Townsend RR, Wright JT Jr, Narva AS, Ortiz E. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA.* 2014;311:507–20.
- Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2003;(suppl 1):S5–20.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18:499–502.
- DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics.* 1988;44:837–45.
- Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev.* 2010;23:247–69.
- Park SH, Choi SJ, Lee KS, Park HY. Waist circumference and waist-to-height ratio as predictors of cardiovascular disease risk in Korean adults. *Circ J.* 2009;73:1643–50.
- Lee CM, Huxley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol.* 2008;61:646–53.
- Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev.* 2012;13:275.
- XiaoZhen Lv, Hang Y, Zhan S. The predictive value of waist-height ratio to discriminate adult hypertension: a meta-analysis. *Chin J Prev Control Chronic Dis.* 2009;17:254–7.
- Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS, INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet.* 2005;366:1640–9.
- Ostchega Y, Hughes JP, Terry A, Fakhouri TH, Miller I. Abdominal obesity, body mass index, and hypertension in US adults: NHANES 2007–2010. *Am J Hypertens.* 2012;25:1271–8.
- Lin S, Cheng TO, Liu X, Mai J, Rao X, Gao X, Deng H, Shi M. Impact of dysglycemia, body mass index, and waist-to-hip ratio on the prevalence of systemic hypertension in a lean Chinese population. *Am J Cardiol.* 2006;97:839–42.
- Nyamdorj R, Qiao Q, Söderberg S, Pitkäniemi J, Zimmet P, Shaw J, Alberti G, Nan H, Uusitalo U, Pauvaday V, Chitson P, Tuomilehto J. Comparison of body mass index with waist circumference, waist-to-hip ratio, and waist-to-stature ratio as a predictor of hypertension incidence in Mauritius. *J Hypertens.* 2008;26:866–70.
- Duncan MJ, Mota J, Vale S, Santos MP, Ribeiro JC. Associations between body mass index, waist circumference and body shape index with resting blood pressure in Portuguese adolescents. *Ann Hum Biol.* 2013;40:163–7.
- Cheung YB. “A Body Shape Index” in middle-age and older Indonesian population: scaling exponents and association with incident hypertension. *PLoS One.* 2014;9:e85421.
- Fujita M, Sato Y, Nagashima K, Takahashi S, Hata A. Predictive power of a body shape index for development of diabetes, hypertension, and dyslipidemia in Japanese adults: a retrospective cohort study. *PLoS One.* 2015;10:e0128972.
- Hayashi T, Boyko EJ, Leonetti DL, McNeely MJ, Newell-Morris L, Kahn SE, Fujimoto WY. Visceral adiposity is an independent predictor of incident hypertension in Japanese Americans. *Ann Intern Med.* 2004;140:992–1000.

34. Hayashi T, Boyko EJ, Leonetti DL, McNeely MJ, Newell-Morris L, Kahn SE, Fujimoto WY. Visceral adiposity and the prevalence of hypertension in Japanese Americans. *Circulation*. 2003;108:1718–23.
35. Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, Vasan RS, Murabito JM, Meigs JB, Cupples LA, D'Agostino RB Sr, O'Donnell CJ. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation*. 2007;116:39–48.
36. Foy CG, Hsu FC, Haffner SM, Norris JM, Rotter JI, Henkin LF, Bryer-Ash M, Chen YD, Wagenknecht LE. Visceral fat and prevalence of hypertension among African Americans and Hispanic Americans: findings from the IRAS family study. *Am J Hypertens*. 2008;21:910–6.
37. Oka R, Miura K, Sakurai M, Nakamura K, Yagi K, Miyamoto S, Moriuchi T, Mabuchi H, Koizumi J, Nomura H, Takeda Y, Inazu A, Nohara A, Kawashiri MA, Nagasawa S, Kobayashi J, Yamagishi M. Impacts of visceral adipose tissue and subcutaneous adipose tissue on metabolic risk factors in middle-aged Japanese. *Obesity (Silver Spring)*. 2010;18:153–60.
38. Boyko EJ, Leonetti DL, Bergstrom RW, Newell-Morris L, Fujimoto WY. Visceral adiposity, fasting plasma insulin, and blood pressure in Japanese-Americans. *Diabetes Care*. 1995;18:174–81.
39. Kanai H, Matsuzawa Y, Kotani K, Keno Y, Kobatake T, Nagai Y, Fujioka S, Tokunaga K, Tarui S. Close correlation of intra-abdominal fat accumulation to hypertension in obese women. *Hypertension*. 1990;16:484–90.
40. Johnson D, Prud'homme D, Després JP, Nadeau A, Tremblay A, Bouchard C. Relation of abdominal obesity to hyperinsulinemia and high blood pressure in men. *Int J Obes Relat Metab Disord*. 1992;16:881–90.
41. Molarius A, Seidell JC. Selection of anthropometric indicators for classification of abdominal fatness—a critical review. *Int J Obes Relat Metab Disord*. 1998;22:719–27.