

# Anthropometric indices predicting incident hypertension in an Iranian population: The Isfahan cohort study

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## ABSTRACT

**Objective:** The aim of the present study was to assess different obesity indices, as well as their best cut-off point, to predict the occurrence of hypertension (HTN) in an Iranian population.

**Methods:** In a population-based study, subjects aged 35 years and older were followed for 7 years. Blood pressure was measured at baseline and after the follow-up. Anthropometry indices included body mass index (BMI), body adiposity index (BAI), the waist-to-height ratio (WHtR), the waist-to-hip ratio (WHpR), and waist and hip circumferences (WC and HC). Logistic regression was employed to calculate the odds ratio (OR) and 95% confidence intervals (CI) per standard deviation (SD) increment. The operating characteristic analysis was used to derive the best cut-off value for each index.

**Results:** Among original 6504 participants, 2450 subjects who had no cardiovascular diseases (CVD) and HTN at baseline were revisited, and 542 (22.1%) new cases of HTN were detected. There were minimal differences between most indices in the adjusted models; however, the best HTN predictors were BMI (OR per SD 1.32; 95% CI 1.12–1.56) and almost equally WC (1.35; 1.13–1.60) in men and WC (1.20; 1.04–1.39) in women. As a binary predictor, BMI with a cut-off point of 24.9 kg/m<sup>2</sup> in men (1.91; 1.40–2.62) and WC with a cut-off point of 98 cm in women (1.57; 1.17–2.10) were the best in adjusted models. WC, WHpR, and WHtR were significantly associated with an increased risk of HTN only in participants whose weight was normal (BMI, 18.5–24.9 kg/m<sup>2</sup>).

**Conclusion:** Therefore, BMI in men and WC in women were the best predictors of HTN, both as continuous and binary factors at their appropriate cut-off points. (*Anatol J Cardiol* 2019; 22: 33-43)

**Keywords:** hypertension, adiposity, prediction, incidence

## Introduction

Hypertension (HTN) is one of the most important risk factors that can lead to cardiovascular diseases (CVD) and is thus regarded as a serious public health problem. The prevalence of HTN has been increasing in most areas worldwide, especially in developing countries (1). Studies in Iran have also shown a high incidence of the condition (2). A previous study from this area showed that almost one-third of the CVD events and 27% of mortalities ensued from HTN, indicating the highest attributable risks (3). The presence of other risk factors such as insulin resis-

tance, dyslipidemia, obesity, and metabolic syndrome increases the HTN's harmful impact on target organs and CVD risk (4).

HTN is very complex, and both environmental and genetic factors are involved. Yet, it is linked to overweight and obesity in several ways (5). Several epidemiological studies have revealed a strong relationship between obesity and HTN, but there is still controversy regarding the best obesity indicator for HTN and the most appropriate cut-off point to use (6-9).

Several indirect methods are able to precisely estimate obesity, such as the total amount of body fat, as well as its distribution (10). While using computed tomography, dual-energy X-ray absorptiometry, and magnetic resonance imaging has a

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high sensitivity and specificity to diagnose obesity, using anthropometric indices such as body mass index (BMI), waist-to-hip ratio (WHR), waist circumference (WC), the waist-to-hip ratio (WHpR), and the waist-to-height ratio (WHtR) are the simplest and the most cost-effective methods recommended in clinical practice and in epidemiological studies (10, 11). A relatively large body of data is available regarding cut-off values of obesity indicators to predict HTN among different populations (12-14). Nevertheless, the relationship between obesity indicators and cardiovascular risk factors and HTN in particular, to the best of our knowledge, has not been fully established in an Iranian population. We believe that ethnic and racial differences in our population might require different cut-off points and/or use of different anthropometric parameters to predict HTN.

There is however often a vigorous debate, particularly regarding at which values obesity indices are better predictors of HTN incidence. Therefore, this study was designed to compare different obesity indicators, as well as to determine their best cut-off points regarding the incidence of HTN in an Iranian population.

## Methods

### Study population

The Isfahan Cohort Study (ICS) is a population-based, ongoing longitudinal study of adults aged 35 years old or older, living in urban and rural areas of three counties in central Iran: Isfahan, Najafabad, and Arak (15). The population was divided into urban and rural areas according to a general census conducted in 2008. These three cities were selected due to their consistent populations and a smaller number of migrants compared to the capital and other Iranian cities. Nearly 5%–10% of this population were included in the study. Moreover, Isfahan is the third largest city in Iran with 1,986,542 individuals living in this city and its surrounding villages. In Arak and Najafabad, the population was 555,975 and 282,430 in 2006, respectively (16). The participants were recruited from January 2 to September 28, 2001. Participants were selected by multistage random sampling and were recruited to reflect the age, sex, and urban/rural distribution of the community (17). Patient subgroups <35 years are at times referred to as very young and less likely to suffer from CVD, and hence we considered the cut-off point of 35 years of age to include subjects who are more prone to CVD (18). The Ethics Committee of the Isfahan Cardiovascular Research Center approved the study.

### Follow-up surveys

After the baseline survey in 2001, the follow-up of the participants was carried out every 2 years. Telephone interviews were carried out in 2003 and in 2005–2006. In 2007, full structured interviews and physical and biochemical measurements were repeated in the same way as for the baseline survey. A

fifth telephone interview follow-up was finished in 2011. The patients or their close family members were asked about the patients' health status using a questionnaire with a specific focus on cardiovascular and cerebrovascular events and experiencing any of the following five neurological symptoms (hemiparesis, dysarthria, facial asymmetry, imbalance, and transient monocular blindness). If a patient was hospitalized due to a cardiovascular disease, records of the time in hospital were found and summarized by experienced personnel and were reviewed by cardiac and neurologic panel. If a patient died during the follow-up, the cause of death was asked from family members. The verbal autopsy used a predefined questionnaire, including a medical history and signs and symptoms before death. Expert nurses conducted additional secondary interviews for hospitalized cases where information was incomplete or inconsistent.

### Assessments

After obtaining informed written consent, medical interview and physical examination were conducted. Measurements of blood pressure, anthropometric parameters as well as fasting blood tests were carried out following standard protocols and using calibrated instruments as previously described (19).

For the biochemical analysis, 5 ml blood samples were drawn following 12 h of overnight fasting to measure the lipid profile and fasting blood sugar. Diabetes mellitus was defined as hyperglycemia at more than 126 mg/dL fasting blood sugar (or the use of diabetes medications). All testing of lipids and lipoprotein cholesterol concentrations were performed in the Isfahan Cardiovascular Research Center Laboratory previously described (20).

In brief, using a mercury sphygmomanometer, blood pressure was measured in a sitting position and after a minimum resting period of 10 min. Phases I and V Korotkoff sounds were used to identify systolic blood pressure (SBP) and diastolic blood pressure (DBP), respectively; the SBP and DBP values were taken as the average of three different measurements, separated by 2 minutes from one another.

A range of anthropometric measurements was investigated. Weight was determined with individuals wearing light clothes and no shoes (Sega, Germany) to the nearest 0.1 kg on a calibrated beam scale. Height was also measured while individuals were barefoot using a wall-mounted stadiometer to the nearest 0.1 cm. WC was taken as the smallest circumference at or below the costal margin and the Hip circumference (HC) at the level of greater trochanter. BMI was computed as weight (kg) divided by height<sup>2</sup> (m). Body adiposity index (BAI) was calculated using the equation suggested by Bergman et al.  $BAI = [(hip\ circumference) / (height^{1.5}) - 18]$  (21). The WHpR and WHtR were calculated through dividing WC by HC and height, respectively.

To define central obesity based on WC, we used the recommendation of International Diabetes Federation for Middle East-

erners as WC  $\geq 94$  cm in men and  $\geq 80$  cm in women (12), the local recommendation for Iranian population to predict CVD events by ICS as WC  $\geq 90$  for men and  $\geq 97$  for women (22), as well as the updated Adult Treatment Panel III guideline of the National Cholesterol Education Program as WC  $\geq 102$  cm in men and  $\geq 88$  cm in women (23). According to the World Health Organization definition, a BMI  $\geq 25$  means the individual is overweight, whereas a BMI  $\geq 30$  indicates obesity (24). Subjects who smoked daily were considered as current smokers.

In 2007 (the 7<sup>th</sup> year of the follow-up), participants were invited for repeated laboratory measurements, physical examination, and an interview using the same protocol as the baseline survey. Laboratory measurement methods were similar in 2001 and 2007, but the autoanalyzer was different (Eppendorf, Hamburg, Germany, in 2001 and Hitachi 902, Japan, in 2007). Both instruments have been validated with an external standard laboratory center.

### Statistical analysis

Data entry was carried out using EPI info. Data were analyzed using the STATA software (Stata/IC 11.0, StataCorp LP, College Station, TX, USA). A test of normality for the distribution of variables was performed using the Kolmogorov–Smirnov test. Data were expressed as the mean  $\pm$  standard deviation. For all analyses, statistical significance was assessed at the level of 0.05 (two-tailed). No variable had more than 3% of missing values. Stochastic regression was used to impute missing values (25). Due to skewness, the Mann-Whitney U test was employed to compare triglycerides and the triglycerides/HDL-C ratio between men and women. Remaining comparisons were made using Student's t-test and a chi-squared test.

The associations of adiposity indices as continuous variables with incident diabetes were separately assessed in crude and adjusted logistic regression models, and the models' fit were compared. The linearity of associations in the crude models was then evaluated. The discrimination power of indices was assessed using the receiver operating characteristic (ROC) analysis, and the best cut-off value for each index was derived. The association of adiposity indices as binary variables was subsequently assessed using the plan identical to continuous variables. Finally, the associations of central obesity indices with HTN were adjusted for BMI.

The deviance (a likelihood ratio statistic for comparing each model to the saturated model) and Akaike's 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 indicates a better fit of the model. 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, separately in men and women. The value of the first knot was used as the reference for the estimation of odds ratios in each model (17). The associations were adjusted

for age, smoking, education, and a family history of diabetes, systolic blood pressure, and triglyceride/HDL-C ratio.

### Results

Among 6504 participants at the baseline evaluation in 2001, 6323 had no CVD history, of which 3283 participants were revisited in 2007, and laboratory measurements and physical examination were repeated. Among the population with repeated measurements, 833 (25.4%) participants with HTN at baseline were excluded, resulting in 2450 subjects included in this analysis. The average age of subjects was increased from  $47.3 \pm 9.4$  years in 2001 to  $55.4 \pm 10.3$  years in 2007. While obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) was more than twice higher in women, there was no significant difference in being overweight (BMI  $\geq 25$  kg/m<sup>2</sup>) between men and women (Table 1). All anthropometric indices were correlated with each other, but the strongest correlations were seen for WC with WHtR ( $r=0.91$ ,  $p<0.001$ ) and with HC ( $r=0.80$ ,  $p<0.001$ ), having same patterns in both genders (Supplementary Table 1).

After 7 years of follow-up, 542 (22.1%) new cases of HTN were found indicating cumulative incidence (95% CI) of 22.6% (20.3–24.9) in men and 21.6% (19.3–23.9) in women. In unadjusted models, WHtR was the strongest predictor of HTN with a 60% and 27% increase in the HTN risk for each SD increase in men and women, respectively (Table 2). It had the smallest deviance and AIC, indicating the best fit in the model. However, in adjusted models, the WHtR revealed an almost similar AIC and deviance to WC and BMI, which were similar and had the lowest AIC and deviance in men. In addition, WC had also the lowest AIC and deviance in women, with WHtR being again the closest index to WC.

In men, the adjusted risk of incident HTN for each unit increase in WC (1 cm), HC (1 cm), WHpR (0.01), WHtR (0.01), BMI (0.1 kg/m<sup>2</sup>), and BAI (0.1) was linearly increased as 2.3%, 2.5%, 2.3%, 3.5%, 0.8%, and 0.3%, respectively. In women, for each unit increase in WC (1 cm), HC (1 cm), and BMI (0.1 kg/m<sup>2</sup>), the adjusted risk of incident HTN was linearly increased as 1.4%, 1.7%, and 0.3%, respectively (Supplementary Table 2).

Considering logistic models including restricted cubic splines, the null hypothesis indicating that coefficient of the 2<sup>nd</sup> and 3<sup>rd</sup> splines equaled zero was not rejected ( $p>0.05$ ) for all interested factors in men and women. Accordingly, all associations between continuous indicators were found to be linear.

Table 3 represents what central obesity adds to BMI for incident HTN prediction. In men, except for HC, all central adiposity indices were associated with HTN independent of BMI; moreover, BMI lost its statistically significant association when WC or WHtR were introduced to the models. On the other hand, in women, WHpR and WHtR were independently associated with HTN; however, BMI did not show any significant association with each of the central obesity indices included in the model.

Considering subjects with BMI 18.5–25 kg/m<sup>2</sup> as a reference group, the risk of developing HTN significantly increased in over-

**Table 1. Characteristics of study participants**

	Men n=1242	Women n=1208	Total n=2450	P-value
Age (year)	47.9±9.7	46.7±9.1	47.3±9.4	0.001
Body mass index	25.4±3.8	27.7±4.5	26.6±4.3	<0.001
Obesity (BMI≥30 kg/m <sup>2</sup> )	149 (12.0%)	363 (30.0%)	512 (20.9%)	<0.001
Overweight (BMI≥25 kg/m <sup>2</sup> )	495 (39.9%)	517 (42.8%)	1012 (41.3%)	0.139
Body adiposity index	27.3±4.3	35.4±5.6	31.3±6.4	<0.001
Waist circumference (cm)	91.8±10.9	95.7±12.5	93.7±11.9	<0.001
Central obesity (>90/97 cm)*	728 (58.6%)	583 (48.3%)	1311 (53.5%)	<0.001
Central obesity (>94/80 cm)*	564 (45.4%)	1080 (89.4%)	1644 (67.1%)	<0.001
Waist-to-hip ratio	0.92±0.06	0.92±0.08	0.92±0.07	0.608
Central obesity (>0.85/0.90 cm)**	1063 (85.6%)	763 (63.2%)	1826 (74.5%)	<0.001
Waist-to-height ratio	0.54±0.06	0.61±0.08	0.58±0.08	<0.001
Central obesity (>0.5)	905 (72.9%)	1095 (90.6%)	2000 (81.6%)	<0.001
Triglycerides (mg/dL)	169.0±104.4	155.0±93.0	161.9±99.3	<0.001
Hypertriglyceridemia <sup>†</sup>	741 (59.7%)	635 (52.6%)	1376 (56.2%)	<0.001
LDL cholesterol (mg/dL)	122.6±42.9	130.6±41.4	126.5±42.3	<0.001
High LDL cholesterol <sup>††</sup>	550 (44.3%)	608 (50.3%)	1158 (47.3%)	0.003
HDL cholesterol (mg/dL)	45.2±10.2	48.1±10.1	46.6±10.3	<0.001
Low HDL cholesterol <sup>‡</sup>	438 (35.3%)	718 (59.4%)	1156 (47.2%)	<0.001
Triglycerides/HDL-C ratio	3.8±2.7	3.3±2.2	3.5±2.5	<0.001
Fasting plasma glucose (mg/dL)	85.5±28.6	86.8±29.6	86.1±29.1	0.243
Diabetes <sup>‡‡</sup>	74 (6.0%)	105 (8.7%)	179 (7.3%)	0.009
Family history of hypertension	221 (17.8%)	246 (20.4%)	467 (19.1%)	0.105
Systolic blood pressure (mm Hg)	112.4±11.7	111.7±11.7	112.1±11.7	0.105
Diastolic blood pressure (mm Hg)	73.9±7.8	73.5±7.9	73.7±7.9	0.140
Ever smoking	534 (43.0%)	37 (3.1%)	571 (23.3%)	<0.001

The numerical values are presented as mean±standard deviation and compared using Student's t-test, except for items indicated by § where the Mann-Whitney U test was employed. Categorical data are shown as n (%) and are tested by chi-square.

\*Waist circumference ≥97 cm for women and ≥90 cm for men based on a previous ICS recommendation and ≥80 cm for women and ≥94 cm for men based on an International Diabetes Federation recommendation for Middle East.

\*\*Waist-to-hip ratio ≥0.85 for women and ≥0.90 cm for men (World Health Organization recommendation)

<sup>†</sup>Triglycerides ≥150 mg/dL or on anti-lipid agents

<sup>††</sup>LDL-C ≥130 mg/dL or on anti-lipid agents

<sup>‡</sup>HDL-C <40 mg/dL for men <50 mg/dL for women or on anti-lipid agents

<sup>‡‡</sup>Hyperglycemia at more than 126 mg/dL fasting blood sugar or use of diabetes medications

HDL - high-density lipoprotein; LDL - low-density lipoprotein

weight men [1.73 (1.29–2),  $p=0.001$ ] but not in overweight women [1.33 (0.93–1.89),  $p=0.114$ ]. Obesity was related to an increased risk of incident HTN in men [2.21 (1.48–3.32),  $p<0.001$ ] and women [1.59 (1.10–2.31),  $p=0.014$ ]. On the other hand, WC, WHpR, and WHtR had significant associations with the incidence of HTN in participants who had normal weight, but not in overweight and obese subjects (Table 4). WHtR was marginally associated with an increased risk of HTN in obese men.

Height significantly decreased the HTN risk in crude models in men, but not in adjusted models and in women. No statistically significant interaction was found between height and other fac-

tors (data not shown). HC showed no statistically significant association when it was adjusted for age and WC in men ( $p=0.918$ ) and women ( $p=0.490$ ). The same pattern was seen when more adjusted factors were included.

A ROC curve analysis showed the highest discrimination power [area under the curve (AUC)] in WHtR for men and women closely followed by WC (Table 5). For each anthropometric index, the optimal cut-off point is presented maximizing Youden's index for incident HTN and its corresponding sensitivity and specificity in men and women. The highest positive likelihood ratio was observed in the indices with highest AUC.

**Table 2. Association of adiposity indices with incident hypertension for one standard deviation increase (n=2450)**

Cut-off points	Crude OR* (95% CI)	P-value	Deviance	AIC	Fully adjusted OR** (95% CI)	P-value	Deviance	AIC	C
<b>Men</b>									
WC	1.32 (1.13-1.55)	<0.001	1315	1319	1.35 (1.13-1.60)	0.001	1190	1206	0.7222
HC	1.41 (1.21-1.63)	<0.001	1304	1311	1.28 (1.09-1.50)	0.003	1193	1209	0.7263
Height	0.81 (0.69-0.97)	0.021	1323	1327	1.02 (0.85-1.22)	0.861	1202	1218	0.7167
WHpR	1.41 (1.22-1.62)	<0.001	1305	1309	1.20 (1.03-1.40)	0.020	1196	1212	0.7245
WHtR	1.60 (1.36-1.89)	<0.001	1295	1299	1.35 (1.13-1.62)	0.001	1191	1207	0.7260
BMI	1.35 (1.17-1.57)	<0.001	1311	1315	1.32 (1.12-1.56)	0.001	1190	1206	0.7282
BAI	1.41 (1.16-1.71)	<0.001	1315	1319	1.23 (1.00-1.51)	0.050	1198	1214	0.7204
<b>Women</b>									
WC	1.14 (1.00-1.31)	0.053	1257	1261	1.20 (1.04-1.39)	0.011	1164	1180	0.6976
HC	1.20 (1.05-1.37)	0.006	1253	1257	1.17 (1.01-1.35)	0.031	1166	1182	0.6926
Height	0.88 (0.72-1.07)	0.216	1259	1263	1.08 (0.87-1.33)	0.477	1170	1186	0.6889
WHpR	1.23 (1.08-1.39)	0.002	1251	1255	1.10 (0.96-1.26)	0.174	1168	1184	0.6885
WHtR	1.27 (1.11-1.45)	<0.001	1249	1252	1.18 (1.02-1.36)	0.023	1165	1181	0.6922
BMI	1.14 (1.00-1.30)	0.042	1257	1261	1.13 (0.98-1.29)	0.091	1167	1183	0.6918
BAI	1.18 (1.01-1.38)	0.034	1256	1260	1.14 (0.96-1.34)	0.125	1168	1184	0.6890

\*Per one standard deviation increase for each index. Because of strong correlations among these variables, each one was evaluated in a separate model.

\*\*Adjusted for age, smoking, education, and family history of hypertension, diabetes, triglyceride/HDL-C ratio

OR - odds ratio; CI - confidence interval; BMI - body mass index; HDL - high-density lipoprotein; WC - waist circumference; WHpR - waist-to-hip ratio; WHtR - waist-to-height ratio

**Table 3. Body mass index adjusted associations of one standard deviation increase in central obesity indices with incident hypertension**

	Central obesity indices		Body mass index		Deviance	AIC	C
	OR (95% CI)	P-value	OR (95% CI)	P-value			
<b>Men</b>							
Body mass index	-	-	1.35 (1.17-1.57)	<0.001	1311	1315	0.576
Waist circumference	1.28 (1.06-1.55)	0.011	1.16 (0.96-1.40)	0.133	1310	1304	0.593
Hip circumference	1.15 (0.96-1.39)	0.134	1.26 (1.05-1.50)	0.010	1309	1315	0.586
Waist-to-hip ratio	1.31 (1.13-1.53)	<0.001	1.22 (1.04-1.43)	0.014	1299	1305	0.600
Waist-to-height ratio	1.55 (1.24-1.92)	<0.001	1.05 (0.86-1.27)	0.637	1295	1301	0.606
<b>Women</b>							
Body mass index	-	-	1.14 (1.00-1.30)	0.042	1257	1261	0.538
Waist circumference	1.17 (0.99- 1.39)	0.058	1.03 (0.87-1.22)	0.686	1253	1259	0.557
Hip circumference	1.08 (0.90-1.28)	0.400	1.09 (0.92-1.29)	0.298	1256	1262	0.543
Waist-to-hip ratio	1.20 (1.05-1.37)	0.007	1.09 (0.95-1.25)	0.211	1249	1255	0.569
Waist-to-height ratio	1.30 (1.09-1.56)	0.004	0.96 (0.81-1.14)	0.627	1248	1254	0.570

OR - odds ratio; CI - confidence interval

Table 6 shows the association between central and overall obesity with incident HTN considering different definitions, including those derived from findings in Table 5. In the crude model, a WC $\geq$ 93 cm was the best predictor in men followed by a BMI $\geq$ 24.9 kg/m<sup>2</sup>. However, when the association was adjust-

ed for other risk factors, a BMI $\geq$ 24.9 kg/m<sup>2</sup> was considerably better than other indices for men, resulting in 72.8% right discrimination in the adjusted model. In women, WC $\geq$ 98 cm was the best in both the crude and adjusted model with a 69.8% discrimination.



**Table 4. Association of central obesity indices with incident hypertension in normal weight, overweight, and obese subjects**

	Normal OR (95% CI)	P-value	Overweight OR (95% CI)	P-value	Obese OR (95% CI)	P-value
<b>Men</b>						
<b>n</b>	598		495		149	
Waist circumference	1.58 (1.18-2.11)	0.002	1.05 (0.79-1.39)	0.738	1.10 (0.72-1.66)	0.664
Hip circumference	1.30 (0.97-1.73)	0.075	1.04 (0.79-1.38)	0.743	0.98 (0.63-1.53)	0.935
Waist-to-hip ratio	1.32 (1.06-1.65)	0.014	1.21 (0.95-1.55)	0.117	1.48 (1.00-2.20)	0.050
Waist-to-height ratio	1.90 (1.37-2.63)	<0.001	1.12 (0.81-1.55)	0.473	1.57 (0.92-2.69)	0.095
<b>Women</b>						
<b>n</b>	328		517		363	
Waist circumference	1.81 (1.28-2.56)	0.001	1.04 (0.80-1.35)	0.749	0.93 (0.71-1.22)	0.608
Hip circumference	1.10 (0.79-1.52)	0.575	1.05 (0.80-1.38)	0.727	1.01 (0.76-1.35)	0.929
Waist-to-hip ratio	1.75 (1.31-2.33)	<0.001	1.05 (0.86-1.29)	0.613	1.06 (0.85-1.32)	0.615
Waist-to-height ratio	1.94 (1.32-2.83)	0.001	1.23 (0.94-1.61)	0.133	0.98 (0.75-1.30)	0.914

Normal, BMI 18.5–24.9 kg/m<sup>2</sup>; Overweight, BMI 25–29.9 kg/m<sup>2</sup>; Obese, BMI ≥30 kg/m<sup>2</sup>  
The associations were calculated for one standard deviation increase.  
OR - odds ratio; BMI - Body mass index; CI - confidence interval

**Table 5. Best Cut-off values of adiposity indices maximizing sensitivity plus specificity using receiver operating characteristic analysis for detecting incident hypertension**

	Best cut-off points	Sensitivity	Specificity	Youden index*	LR+	LR-	AUC (95% CI)
<b>Men</b>							
WC	93 cm	0.630	0.552	0.181	1.40	0.67	0.602 (0.565-0.639)
WHpR	0.92	0.587	0.564	0.151	1.35	0.73	0.597 (0.560-0.634) <sup>†</sup>
WHtR	0.45	0.644	0.538	0.182	1.39	0.66	0.612 (0.575-0.648) <sup>†</sup>
BMI	24.9	0.655	0.509	0.164	1.33	0.68	0.591 (0.553-0.628) <sup>†</sup>
BAI	26.2	0.737	0.415	0.145	1.25	0.65	0.585 (0.549-0.622) <sup>†</sup>
<b>Women</b>							
WC	98 cm	0.540	0.572	0.112	1.26	0.80	0.560 (0.521-0.599)
WHpR	0.92	0.663	0.466	0.119	1.22	0.74	0.561 (0.522-0.600)
WHtR	0.59	0.713	0.391	0.103	1.70	0.73	0.563 (0.525-0.602)
BMI	29.0	0.448	0.637	0.085	1.23	0.86	0.549 (0.510-0.588)
BAI	35.3	0.575	0.519	0.093	1.19	0.82	0.542 (0.502-0.580)

\*sensitivity+specificity-1

<sup>†</sup>AUC for WHtR [0.032 (0.026 (0.002–0.050), P=0.032, (0.036 (0.064–0.007), P=0.013, 0.022 (0.008–0.036), P=0.002] was significantly higher than BAI and WHpR and WC respectively; no other significant differences were observed in men.

No significant differences were observed in women.

BMI - Body mass index; WC - waist circumference; WHpR - waist-to-hip ratio; WHtR - waist-to-height ratio;

LR+ - positive likelihood ratio; LR- - negative likelihood ratio; AUC - area under the curve; CI - confidence interval

## Discussion

In this large cohort study that included Iranian adults, we found that BMI in men and WC in both men and women were the best continuous predictors of incident HTN. In addition, a BMI ≥24.9 kg/m<sup>2</sup> in men and WC ≥98 cm in women were the best

fitted binary indices in multivariate adjusted models, while central obesity was independently associated with an increased risk in participants whose weight was normal.

Although many cross-sectional studies have been conducted to indicate the association between anthropometric indicators and HTN, to the best of our knowledge, this is the

**Table 6. Best cut-off values of anthropometric indices maximizing univariate and multivariate model prediction efficacy for incident hypertension**

	Best cut-off points	Crude OR (95% CI)	P-value	Deviance	AIC	Adjusted OR (95% CI)	P-value	Deviance	AIC	AUC <sup>†</sup>
<b>Men</b>										
WC	102	1.66 (1.21-2.28)	0.002	1319	1323	1.42 (1.01-2.00)	0.045	1198	1214	0.721
ATPIII	94	2.08 (1.59-2.73)	<0.001	1299	1303	1.71 (1.27-2.30)	0.001	1189	1205	0.725
IDF	90	1.82 (1.37-2.42)	<0.001	1310	1314	1.47 (1.07-2.01)	0.016	1196	1212	0.720
ICS for CVD	93 cm	2.09 (1.59-2.75)	<0.001	1299	1303	1.70 (1.26-2.29)	0.001	1190	1206	0.723
WHpR	0.90	1.86 (1.37-2.52)	<0.001	1311	1315	1.37 (0.99-1.91)	0.059	1198	1214	0.721
WHO	0.92	1.65 (1.26-2.16)	<0.001	1315	1319	1.20 (0.89-1.62)	0.224	1200	1216	0.719
WHtR	0.45	2.17 (1.17-4.04)	0.014	1321	1325	1.77 (0.92-3.41)	0.088	1198	1214	0.719
BMI	24.9	1.96 (1.48-2.58)	<0.001	1305	1309	1.91 (1.40-2.62)	<0.001	1185	1201	0.728
BAI	26.2	1.88 (1.40-2.52)	<0.001	1309	1313	1.50 (1.10-2.05)	0.011	1195	1211	0.721
<b>Women</b>										
WC	88 cm	1.50 (1.06- 2.12)	0.022	1255	1259	1.40 (0.97-2.02)	0.073	1167	1183	0.692
ATPIII	80 cm	2.22 (1.27-3.88)	0.005	1251	1255	1.85 (1.03-3.30)	0.038	1166	1182	0.692
IDF	97 cm	1.45 (1.10-1.91)	0.008	1254	1258	1.33 (0.99-1.78)	0.055	1167	1183	0.691
ICS for CVD	98 cm	1.69 (1.28-2.23)	<0.001	1247	1251	1.57 (1.17-2.10)	0.003	1161	1177	0.698
WHpR	0.85	1.26 (0.84-1.87)	0.264	1259	1264	1.07 (0.70-1.63)	0.767	1170	1186	0.688
WHO	0.92	1.65 (1.24-2.20)	0.001	1249	1253	1.36 (1.00-1.84)	0.046	1166	1182	0.690
WHtR	0.59	1.59 (1.18-2.14)	0.002	1251	1255	1.39 (1.01-1.91)	0.040	1166	1182	0.691
BMI	29	1.40 (1.06-1.85)	0.017	1255	1259	1.43 (1.06-1.93)	0.018	1164	1181	0.691
BAI	35.3	1.34 (1.02-1.77)	0.034	1256	1260	1.23 (0.92-1.64)	0.162	1168	1184	0.688
Adjusted for age, smoking, education, and family history of hypertension, diabetes, triglyceride/HDL-C ratio										
<sup>†</sup> Area under the curve for multivariate logistic regression models indicating the ability of model for right discrimination										
OR - odds ratio; CI - confidence interval; BMI - body mass index; WC - waist circumference; WHpR - waist-to-hip ratio; WHtR - waist-to-height ratio; DM - diabetes mellitus										

first large-scale cohort study in an Iranian population that compares the obesity indices with regard to the HTN risk. It is well documented that ethnic and racial differences affect determining the optimal anthropometric indicators to predict cardiovascular risk factors (26). In this regard, a study by Tuan et al. (27) demonstrated no superiority in obesity indices to predict the HTN risk among Chinese adults; however, published reports from various parts of the world reported dissimilar indicators as superior indices (28-36).

Adiposity indices could be treated as binary indicators to determine those at risk or as original continuous values. These two approaches can lead to different best indices. While the first approach is inevitably needed to identify those needing clinical interventions, the latter is important for assessing the effect for incremental increases. However, in our study, the two approaches resulted in reporting similar optimal indices.

Some studies believe that WC is a preferable indicator to predict HTN (28). Gus et al. (29) also showed the risk for HTN might be better identified by obesity defined by a higher WC than a higher BMI in Brazilian population. Moreover, some investigators have proposed that WC is a superior indicator be-

cause it only requires one measurement and correlates well with visceral adiposity among South East Asians (30, 31). Ardern et al. (32) revealed that WC is a better predictor for CVD risks than BMI in American (White, Black, and Hispanic) and Canadian participants of different age, body composition, lifestyles, and socioeconomic characteristics. Several mechanisms were suggested to explain this finding. First of all, unlike BMI, WC in crude analysis is an indicator that shows the distribution of body fat in the abdominal region, which is more related to cardiovascular risks than body weight (33). However, BMI as an indicator of general obesity has been shown in some studies to be as strong as central-obesity indices such as WC in predicting cardiovascular risk factors (34, 35). In addition, a study by Li et al. (36) showed that the combination of BMI and WC could increase the predictive efficacy of the HTN incidence. Similarly, our findings showed that BMI and WC are the best continuous predictors in men and women, respectively.

Studies have shown that the percentage of total body fat is higher in shorter individuals than in taller individuals with the same BMI (37); thus, considering the power of WC, a simple measure of central obesity for HTN prediction that does not ac-

Supplementary Table 1. Pairwise correlation between anthropometric indices						
	BMI	WC	WHpR	WHtR	HC	Height
<b>Men</b>						
BMI	1					
WC	r=0.70 P<0.001	1				
WHpR	r=0.43 P<0.001	r=0.64 P<0.001	1			
WHtR	r=0.73 P<0.001	r=0.94 P<0.001	r=0.65 P<0.001	1		
HC	r=0.59 P<0.001	r=0.82 P<0.001	r=0.09 P<0.001	r=0.73 P<0.001	1	
Height	r=-0.15 P<0.001	r=0.13 P<0.001	r=-0.08 P=0.012	r=-0.22 P<0.001	r=0.23 P<0.001	1
<b>Women</b>						
BMI	1					
WC	r=0.67 P<0.001	1				
WHpR	r=0.27 P<0.001	r=0.68 P<0.001	1			
WHtR	r=0.71 P<0.001	r=0.94 P<0.001	r=0.69 P<0.001	1		
HC	r=0.68 P<0.001	r=0.77 P<0.001	r=0.05 P=0.023	r=0.68 P<0.001	1	
Height	r=-0.14 P<0.001	r=0.11 P<0.001	r=-0.07 P=0.037	r=-0.22 P<0.001	r=0.22 P<0.001	1
<b>Total</b>						
BMI	1					
WC	r=0.70 P<0.001	1				
WHpR	r=0.33 P<0.001	r=0.65 P<0.001	1			
WHtR	r=0.74 P<0.001	r=0.91 P<0.001	r=0.61 P<0.001	1		
HC	r=0.66 P<0.001	r=0.80 P<0.001	r=0.07 P<0.001	r=0.71 P<0.001	1	
Height	r=-0.28 P<0.001	r=-0.03 P=0.048	r=-0.06 P<0.001	r=-0.45 P<0.001	r=0.010 P=0.709	1

BMI - body mass index; WC - waist circumference; HC - hip circumference; WHpR - waist-to-hip ratio; WHtR - waist-to-height ratio

count for differences in height, may not be a valid measure for predicting HTN (37). Diabetes and HTN have also been shown to be more prevalent in short-stature subjects compared with taller subjects, even after adjusting for confounders (27, 37). A recent longitudinal study showed that the predictive power of WC for incident HTN was improved when WC was corrected with height

or HC (28, 37). However, in our population, central obesity was more prevalent than overall obesity measured by BMI. Therefore, these further support the use of both BMI and WC as the two best indices for the prediction of incident HTN in both genders.

Azimi-Nezhad et al. (38) in their cross-sectional study on another Iranian population reported that WHtR was the strongest



**Supplementary Table 2. Association of continuous adiposity indices with incident hypertension**

Cut-points	Crude OR* (95% CI)	P-value	Deviance	AIC	Fully Adjusted OR** (95% CI)	P-value	Deviance	AIC
<b>Men</b>								
WC (cm)	1.033 (1.011-1.046)	<0.001	1303	1307	1.023 (1.009-1.038)	0.001	1191	1207
HC (cm)	1.025 (1.008-1.042)	0.003	1319	1323	1.025 (1.007-1.043)	0.007	1194	1210
Height (cm)	0.981 (0.963-1.000)	0.051	1324	1329	1.006 (0.985-1.027)	0.567	1201	1217
WHpR×100	1.048 (1.027-1.069)	<0.001	1307	1311	1.023 (1.001-1.046)	0.042	1198	1214
WHtR×100	1.060 (1.038-1.083)	<0.001	1297	1301	1.035 (1.012-1.060)	0.003	1193	1209
BMI×10	1.008 (1.005-1.017)	<0.001	1307	1311	1.008 (1.004-1.012)	<0.001	1186	1202
BAI×10	1.006 (1.003-1.010)	<0.001	1312	1316	1.003 (1.000-1.007)	0.043	1197	1213
<b>Women</b>								
WC (cm)	1.016 (1.005-1.028)	<0.001	1252	1256	1.014 (1.002-1.027)	0.026	1165	1181
HC (cm)	1.011 (0.997-1.025)	0.129	1258	1262	1.017 (1.001-1.032)	0.031	1166	1182
Height (cm)	0.990 (0.971-1.010)	0.329	1260	1264	1.010 (0.989-1.032)	0.343	1169	1185
WHpR×100	1.027 (1.008-1.045)	0.004	1253	1257	1.010 (0.990-1.029)	0.320	1169	1185
WHtR×100	1.028 (1.010-1.045)	0.002	1251	1255	1.017 (0.999-1.036)	0.060	1167	1183
BMI×10	1.004 (1.001-1.007)	0.017	1255	1259	1.003 (1.000-1.007)	0.037	1166	1182
BAI×10	1.002 (1.000-1.005)	0.039	1256	1260	1.002 (0.999-1.004)	0.159	1168	1184

\*Per unit of measurement for each index. Each variable was evaluated in a separate model.

\*\*Adjusted for age, smoking, education, and family history of hypertension, diabetes, triglyceride/HDL-C ratio

OR - odds ratio; CI - confidence interval; BMI - body mass index; WC - waist circumference; HC - hip circumference; WHpR - waist-to-hip ratio; WHtR - waist-to-height ratio

predictor for HTN, and for practical reasons, the values of 0.5 for men and 0.6 for women may be the most practical measures to be used. This is comparable to our cut-off points for WHtR being 0.45 for men and 0.59 for women. However, considering different definitions of anthropometric cut-off points in our study, BMI and WC seemed to have the best HTN predictor cut-off points for men and women, respectively. In addition, we found that the cut-off points were all higher in women than in men. As previously reported, men in this population showed a higher incidence of CVD (39).

As in line with previous reports from the same studied population determining the best anthropometry indices for predicting diabetes mellitus and CVD (17, 39), our results suggest that separate analyses for males and females may be worthwhile. Significant heterogeneity between the sexes was found for BMI when discriminating the HTN risk and the rankings of the overweight and obesity indices as best cardiovascular risk discriminators varied between males and females.

#### Study limitation

This study had several strengths, including its large sample size from a multicenter setting with a wide-area coverage from urban and rural regions, and to directly measure anthropometric indices. However, the fact that our population was Iranian limits the generalizability of our findings beyond the Middle East region.

## Conclusion

In conclusion, both WC and BMI, and BMI on its own, were the best binary and continuous indicators for men, respectively. In addition, WC found to be the best predictor of HTN as both the continuous and binary factor for women. Furthermore, the best cut-off points for adiposity indices were BMI for men and WC for women.

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