Gender Differential in the Association of Body Mass Index and Abdominal Obesity with Prehypertension and Hypertension in Iranian Adults

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Gender Differential in the Association of Obesity and Blood Pressure

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ABSTRACT

Objective. The aim of this study was to determine the gender differential in the relationship of body mass index (BMI) and abdominal obesity with blood pressure (BP) and prevalence of hypertension (HTN) and prehypertension (Pre-HTN) among the adult population of Iran.

Design. A nationwide cross-sectional survey was conducted from December 2004 to February 2005. The selection was conducted by stratified probability cluster sampling through household family members in Iran.

Subjects and Measurements. Weight, height, waist circumference (WC), and systolic and diastolic BP of 45 082 men and 44 322 women aged 15-65 (mean 39.2) were measured.

Results. The prevalence of HTN was 25.2% in men and 24.8% in women; and 50.1% of men and 39.1% of women were prehypertensive. WC and BMI were strongly associated with BP in both genders. Multivariate analysis revealed that both WC and BMI had the stronger association with HTN and Pre-HTN in men than women. Compared to men and women with normal weight, the multivariate-adjusted odds ratio (OR) (95% confidence interval) of HTN was 5.75 (5.13, 6.44) for men and 4.29 (3.95, 4.66) for women with BMI 30. The multivariate OR of prevalence HTN in men with abdominal obesity compared with men without was 3.76 (3.41, 4.22) and in women, 2.92 (2.73, 3.13).

Conclusion. These data indicate that both BMI and WC had the stronger association with HTN and Pre-HTN in men than women.

Keywords. Adults, abdominal obesity, blood pressure, epidemiology, gender, hypertension, prehypertension, obesity.

INTRODUCTION

Obesity is an established risk factor for hypertension (HTN) and prehypertension (Pre-HTN) (1-5) in both men and women and in diverse racial/ethnic group. Both body mass index (BMI) and abdominal obesity are important predictors of HTN and Pre-HTN (1-5). Several studies have reported that, compared with total body fat, abdominal obesity is more closely related to blood pressure (BP), or HTN (6-10). Furthermore, although patterns of obesity, abdominal obesity (11-13), HTN (14, 15), and Pre-HTN (5) differ between men and women, it is still unclear whether there is a gender difference in the association of obesity and abdominal obesity with Pre-HTN and HTN. Only a few studies have examined the gender differences in the association of obesity with BP (14, 16-18); one study showed the WC in men and BMI in women appeared to be increased the risk of HTN (16), whereas other reported even an inverse relation (17) or a different association for men and women (14).

Given the conflicting results in previous studies, we used a large nationwide cross-sectional study to determine the gender differences in relationship of BMI and abdominal obesity with Pre-HTN and HTN among adults aged 15 to 65 years in Iran.

SUBJECTS AND METHODS

Data source: From December 2004 to February 2005, we conducted a population-based cross-sectional survey among 89 404 Iranian men and women studied for non-communicable disease (NCD) risk factors. The survey was designed to provide information about a wide range of behaviors that affect Iranians' health at a provincial level. So that, provincial health authorities can adjust national policies and programs and respond to their local needs. By accumulating the provincial data, an estimate of the national figures can be obtained. The study protocol is based on the World Health Organization (WHO) STEPwise approach to Surveillance (STEPS) of risk factors for NCD (19). STEPS uses different levels of risk factor assessment, including collecting information using questionnaires (Step 1), taking physical measurements (Step 2), and taking blood samples for biochemical assessment (Step 3). Detailed information of this study population has been reported elsewhere (5, 11).

Subjects: A stratified, multistage probability cluster sample, with a probability in proportion to size procedure, was used to obtain a nationally representative sample of the population. The frame for the selection of the sampling units was based on the Iranian national zip code databank. The postal addresses of the starting points for the survey in each cluster were determined centrally, using Iranian national zip code databank. A counterclockwise movement from this point was used to ensure a representative sample of households. A total of 45 082 men and 44 322 women aged 15-65, free from any physical handicaps, were weighed, and their height, waist circumference (WC) and BP (systolic and diastolic) were measured. In total of 89 404 participants in the study, 1920 (2.1%) participants have missing data on education, 1821 (2.0%) on marital status, 2414 (2.7%) on physical activity, 3336 (3.7%) on systolic or diastolic BP, and 2342 (2.6%) on weight or height. These individuals excluded from subgroup analyses. The subjects had a mean age of 39.0 years. All of the women were post-menarche. Women who reported they were pregnant at the time of the survey, homeless people and subjects living in institutions or in the armed forces were excluded from the analysis.

Data collection: Subjects were contacted to schedule an interview in their home at their convenience. Trained staff members of local medical universities/schools served as interviewers in pairs, and a trained supervisor monitored the process in each district. Before the data collection began, the interviewers thoroughly explained to subjects the purpose and procedure of the study and sought their consent. Interviews, anthropometric and BP measurements were performed at the subjects' home with standard techniques and equipment (20), and subjects 25-64 years were then invited to a referral laboratory for blood testing and 25 511 men and 27 574 women provided blood sample.

BP was measured with a standard mercury sphygmomanometer and a cuff of suitable size to the subject's arm circumference after an adequate rest period of at least 15 min. Korotkoff phase I and V were used for systolic and diastolic BP, respectively. Three measurements were taken for each subject with a 30-second interval between measurements in the sitting position, and mean values were calculated.

Height and weight were measured with subjects in light clothes and without shoes using standard apparatus. Weight was measured to the nearest 0.1 kg on a calibrated beam scale. Height and WC were measured to the nearest 0.5 cm with a measuring tape. To measure height, a measuring tape was fixed to the wall and the subject stood with heels, buttocks, shoulders, and occiput touching the vertical tape. The head was held erect with the external auditory meatus and the lower border of the orbit in one horizontal plane. Waist was measured midway between the lower rib margin and the iliac-crest at the end of a gentle expiration in a standing position.

Overnight fasting blood samples were taken, and plasma was separated and analyzed on the same day. Total cholesterol and fasting blood glucose were assessed by standardized procedures. In addition to measurements, all participants completed a set of interviewer-administered questionnaires on sociodemography, smoking habits, diet, physical activity, diabetes mellitus, hypertension, .and use of antihypertensive medicine. The Medical Ethics Committee of the Ministry of Health and Medical Education approved the study protocol, and all subjects gave their written consent. The study complied with the current version of the Declaration of Helsinki.

Definitions: The criteria for normal blood pressure, Pre-HTN, and HTN used in the present study were consistent with the definitions set forth by the Seventh Report of Joint National Committee (21). Normal BP was defined as not being on antihypertensive medication and having a systolic BP <120 mmHg and diastolic BP <80 mmHg. Pre-HTN was defined as not being on antihypertensive medication and having a systolic BP 120 to 139 mmHg and/or diastolic BP 80 to 89 mmHg. HTN was defined as systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg and/or the current use of antihypertensive medications. BMI is recognized as the measure of overall obesity. The criteria for normal weight, overweight and obesity used in the present study were based on BMI (weight/height^2 [kg/m^2]) defined as normal weight <25.0, overweight 25-29.9, and obesity 30. WC was used as a measure of abdominal obesity, defined as WC 102 cm in men and 88 cm in women to distinguish subjects at increased cardiovascular risk (22, 23). Smoking was estimated from self-report and categorized in current, former, and never smokers. The leisure time physical activity variable was based on a detailed interview about activity at work and leisure time. Interviewers had a codebook that listed an activity level beside common occupations and also probed participants about the nature of their activity outside of working hours. When a participant repeatedly spent at least 30 min/week of their leisure time performing physical activity, this was considered as ‘regular physical exercise’. Diabetes was based on a history of physician-diagnosed report.

Analysis: Data were entered on a computer in each medical university/school, with EPI info software. Datasets were transfer into SPSS-compatible format to calculate means and standard errors (SE), t-test, and chi-square tests. All analyses were stratified by gender. The results are given in the text as mean (SE). Robust SEs were calculated to minimize the effect of cluster sampling on the test statistics. Multivariate logistic regression was performed with the SPSS for Windows computer package (SPSS Inc., Chicago, IL, USA) to assess associations of BMI and WC with Pre-HTN and HTN, with normotensive subjects as reference and with adjustment for age, educational level, leisure time physical activity, smoking habits, and area of residence for men and women separately. All tests for statistical significance were two tailed and performed at $\alpha<0.05$.

RESULTS

Distributions of selected characteristics among 45 082 men and 44 322 women are shown in Table 1. Women had lower educational level, physical activity, Pre-HTN, age-adjusted weight, height, and systolic and diastolic blood pressure and were more likely never to have smoked than men. Men had lower overweight, obesity, abdominal obesity, age-adjusted BMI, and WC than women. Women had higher prevalence of clinical diabetes than men. The age-adjusted mean (SE) BMI was 24.6 (0.02) kg/m^2 in men, and 26.5 (0.02) in women and for WC was 86.6 (0.06) cm in men and 89.6 (0.06) in women. The age-adjusted mean (SE) systolic BP was 123.3 (0.08) mmHg in men, and 121.3 (0.08) in women and for diastolic BP was 78.5 (0.06) mmHg in men and 76.4 (0.06) in women. The mean (SE) age was 39.1 (0.07) years for men, and 39.0 (0.07) years for women, and was not significantly different between men and women. The prevalence of overweight or obesity (BMI 25 kg/m^2) and obesity (BMI 30 kg/m^2) was 42.8% and 10.9% for men, and 56.9% and 24.5% for women, respectively.

Table 2 present the gender-specific prevalence of Pre-HTN and HTN according to age and weight categories. 24.7% of the men and 36.1% of women had normal blood pressure. 44.6% (95% CI 44.3, 44.9) of Iranian adults 15-65 years were prehypertensive. Overall, 50.1% men (95% CI 49.6, 50.6) and 39.1% women (95% CI 38.6, 39.5) were prehypertensive, and 25.2% men (95% CI 24.8, 25.6) and 24.9% women (95% CI 24.4, 25.3) were hypertensive. In all age groups and weight categories Pre-HTN was more common among men, whereas HTN was more common in men before 45 years, after that HTN in women tend to be more common. Among men, WC appears more important in the prediction of HTN whereas among women, BMI is more important

In both genders systolic and diastolic BP was correlated with BMI (r=0.28 men, 0.30 women for SBP and 0.25 men, 0.28 women for DBP) and WC (r=0.32 men, 0.36 women for SBP and 0.28 men, 0.32 women for DBP).

Age-adjusted and multivariate adjusted odds ratio (OR) and 95% CI of Pre-HTN and HTN, as the dependent variables, in relation to overweight, obesity, and abdominal obesity are shown in Table 3. The OR of both Pre-HTN and HTN for abdominal obesity and overweight and obesity was higher in men than women. Compared with men and women with normal weight, the age-adjusted risk of HTN was about six-fold higher in men with BMI 30 kg/m^2 (OR 5.7; 95% CI 5.07, 6.32) and four-fold higher in women with BMI 30 (OR 4.11; 95% CI 3.79, 4.46) in age-adjusted models. The age-adjusted risk of Pre-HTN was 2.36 times higher in men with BMI 30 kg/m^2 (OR 2.36; 95% CI 2.13, 2.62) and 2.21 times higher in women with BMI 30 (OR 2.21; 95% CI 2.07, 2.35) in age-adjusted models. When men and women were divided based on WC, risk of HTN was approximately four-fold (OR 3.91; 95% CI 3.52, 4.37) higher in men with abdominal obesity and three-fold higher in women with abdominal obesity (OR 2.87; 95%CI 2.69, 3.07) than men and women without abdominal obesity. The pattern was similar in Pre-

HTN. In a multivariate model, the additional adjustment for other covariates did not appreciably alter the relationship between either obesity or abdominal obesity and HTN or Pre-HTN risk compared to the model adjusted for age alone. When weight categories and abdominal obesity were included in the same model, in both men and women the relationship between obesity and Pre-HTN and HTN was slightly stronger than WC, whereas the pattern was similar to when weight categories and abdominal obesity were considered separately (data not shown).

The receiver operating characteristic curves for the prevalence of Pre-HTN and HTN in each gender are shown in Figures 1 and 2. The area under the curve for Pre-HTN and HTN was similar for WC and BMI and in men and women.

DISCUSSION

In this nationwide cross-sectional study of 89 404 adults aged 15-65; both BMI and WC were associated with significantly higher risk of HTN and Pre-HTN and were important predictors of systolic and diastolic BP among both men and women. There are no studies on the gender differential in the relationship of BMI and abdominal obesity with Pre-HTN and few studies have assessed the gender differential in the relationship of BMI and abdominal obesity with BP, and the results are inconsistent. A cohort study found that the WC appears more important than BMI in the prediction of BP in men.

Whereas, BMI was more important than WC among women (16). In contrast, in a cross-sectional study, WC in men and BMI in women had the strongest association with BP (17). In another cross-sectional study, however, normal and obese women had similar diastolic BP, as opposed to obese men, who had raised diastolic BP (14). An animal experiment after 10 weeks of cafeteria diet found male and female rats had the same increase in fat pad weight and in plasma leptin levels. However, in contrast to male, female had normal BP (18).

Our results are in accordance with 25 randomized-controlled trials showing that increased body weight is a strong risk factor for hypertension (24). The BP and prevalence of Pre-HTN was higher in men, and support the finding that men have a higher BP than women. Consistent with other studies (14, 15), prevalence of HTN was more common in men before 45 years. After menopause, however, the prevalence of HTN in women tends to be higher than men. Higher BP in men may be related to high testosterone levels, whereas lower BP in women may be related to low estrogen levels (25). In addition, the plasma rennin activity in women is lower than in men regardless of age, menopause state and ethnicity. This contributes to differences in the concentrations of angiotensin II and aldostrone and in sodium reabsorption in the distal nephron.

The mechanisms whereby obesity in general and abdominal obesity in particular exerts negative effects on HTN and Pre-HTN are not entirely clear. As the prevalence of the cardiovascular complications is much higher in obese men than obese women, sex hormones are likely involved in the relative protection against cardiovascular disease in women before menopause (26). It has also postulated that tissue concentration or blood elevation of free fatty acids, caused by the accumulation of visceral fat in the abdomen, could be responsible. Thus, elevated free fatty acids, not only increase vasoconstriction by increasing vascular sensitivity to a-adrenergic stimuli, but also blunt the reflex vasorelaxation by inhibiting nitric oxide production (27). Both these effects lead to HTN. Other mechanisms, like sympathetic nervous system over-activation, excess secretion of angiotensinogen and renal sodium retention secondary to hyperinsulinemia may also be involved in obesity-related HTN (27, 28). Furthermore, the α_2-adrenergic receptors stimulation in the kidney has been shown to increase urine flow rate, osmolar clearance, free water clearance, and sodium excretion (29-31) and responses to a α_2-adrenergic receptors agonist differ according to gender (32).

Our study has several strengths and limitations. The strengths include the large sample consisting of both urban and rural populations, sound representativeness of the national population, and information on potential determinants of BP and obesity. As a cross-sectional study, the present analysis is limited in its ability to elucidate causal relationships between overweight and Pre-HTN and HTN. BMI can overestimate body fat in individuals who are very muscular and underestimate body fat in individuals who have lost muscle mass, such as many elderly (33). However, estimates from these potentially misclassified groups likely had little overall impact on the analysis.

In summary, both BMI and WC are strong independent predictors of Pre-HTN and HTN. The results of this study may indicate that in the relationship between obesity and Pre-HTN and HTN, BMI and abdominal obesity may be of greater importance in men.

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Table 1. Age and age-adjusted means and proportions of selected characteristics among 45,082 men and 44,322 women.

Characteristics	Age- adjusted mean (SE)		Difference (95% CI)
	Men	Women	
Age (yr.)	39.1 (0.07)	39.0 (0.07)	0.1 (-0.05, 0.33)
Weight (Kg)	70.8 (0.06)	64.7 (0.07)	6.1 (5.92, 6.28)*
Height (cm)	169.7 (0.04)	156.5 (0.04)	13.2 (13.1, 13.3)*
Waist circumference (cm)	86.6 (0.06)	89.6 (0.06)	-3.0 (-3.19, -2.81)*
BMI (Kg/m^2)	24.6 (0.02)	26.5 (0.02)	-1.9 (-1.97, -1.83)*
Systolic BP (mmHg)	123.3 (0.08)	121.3 (0.08)	2.0 (1.85, 2.33)*
Diastolic BP (mmHg)	78.5 (0.06)	76.4 (0.06)	2.1 (1.94, 2.26)*
Education (%)			
Primary or below	44.1	59.7	-15.6 (-16.2, -14.9)*
Secondary	44.3	33.0	11.3 (10.6, 11.9)*
Matriculation or above	11.6	7.3	4.3 (3.9, 4.6)*
Marital status (%)			
Married	76.0	73.5	2.5 (1.91, 3.06)*
Single	23.3	19.9	3.4 (2.87, 3.96)*
Others	0.7	6.6	-5.9 (-6.15, -5.65)*
Smoking (%)			
Never-smoker	64.4	91.5	-27.1 (-27.7, -26.6)*
Current-smoker	28.1	5.8	22.3 (21.8, 22.7)*
Ex-smokers	7.5	2.7	4.8 (
Leisure time physical activity (%)			
Yes	35.4	20.3	15.1 (14.4, 15.6)*
No	64.6	79.7	-
Residential area (%)			
Urban	64.7	64.6	0.1 (-0.55, 0.70)
Rural	35.3	35.4	-
Diabetes (%)	3.4	5.6	-2.0 (-2.29, -1.74)*
Prevalence of obesity (%)			
BMI 25 Kg/m^2	42.8	56.9	-14.1 (-14.7, -13.4)*
BMI 30 Kg/m^2	10.9	24.5	-13.6 (-14.1, -13.1)*
Prevalence of abdominal obesity† (%)	12.9	54.5	-41.6 (-42.2, -41.1)*
Prevalence of hypertension‡(%)	25.2	24.9	0.3 (-0.23, 0.93)
Prevalence of prehypertension	50.1	39.1	11.0 (10.4, 11.7)*

Age-adjusted means were calculated using general linear models. †Abdominal obesity was defined as waist circumference 102 cm in men and 88 cm in women (22, 23). ‡Hypertension was defined as a systolic blood pressure of 140 mmHg or over, a diastolic blood pressure of 90 mmHg or over, or taking antihypertensive medications. Pre-HTN was defined as not being on antihypertensive medication and having a SBP 120 to 139 mmHg and/or DBP 80 to 89 mmHg. *P<0.001.

Table 2. Prevalence (%) rate (95% CI) of prehypertension and hypertension by age and weight categories in 45,082 men and 44,322 women, Iran.

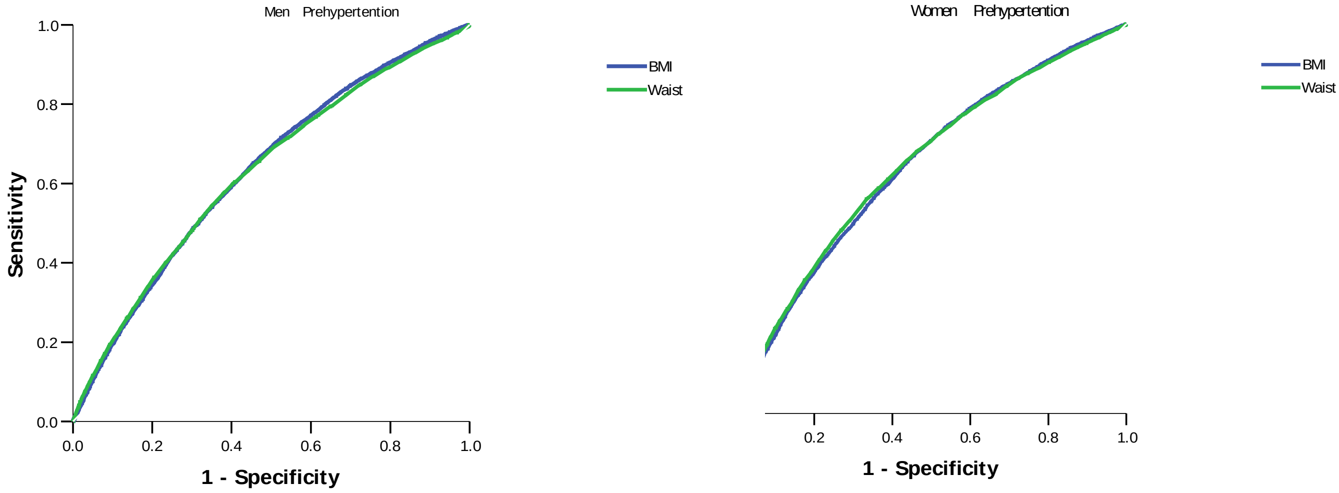
Variables	**Prevalence (95% CI)**		**Men/women rate ratio (95% CI)**
	Men	**Women**	
		Hypertension	
All ages (yr.)	25.2 (24.8, 25.6)	24.9 (24.4, 25.3)	1.01 (0.99, 1.04)
Age (yr.)			
15-24	9.2 (8.6, 9.8)	4.9 (4.5, 5.4)	1.88 (1.67, 2.10)*
25-34	14.5 (13.8, 15.2)	9.2 (8.6, 9.8)	1.58 (1.45, 1.72)*
35-44	21.2 (20.4, 22.1)	19.9 (19.1, 20.7)	1.07 (1.01, 1.13)*
45-54	33.7 (32.7, 34.7)	36.7 (35.7, 37.7)	0.92 (0.88, 0.96)*
55-64	47.0 (46.0, 48.1)	53.8 (52.7, 54.8)	0.87 (0.85, 0.90)*
Weight categories†			
Normal weight	10.9 (10.6, 11.3)	12.5 (12.0, 12.5)	0.87 (0.83, 0.93)*
Overweight	22.0 (21.3, 22.7)	24.7 (23.9, 25.4)	0.89 (0.86, 0.93)*
Obesity	32.1 (30.8, 33.5)	35.8 (34.9, 36.7)	0.90 (0.86, 0.94)*
Abdominal obesity‡			
Absent	14.2 (13.9, 14.6)	10.9 (10.5, 11.3)	1.30 (1.24, 1.37)*
Present	34.2 (32.9, 35.4)	32.0 (31.4, 32.6)	1.07 (1.02, 1.11)*
		Prehypertension	
All ages (yr.)	50.1 (49.6, 50.6)	39.1 (38.6, 39.5)	1.28 (1.26, 1.30)*
Age (yr.)			
15-24	51.0 (49.9, 52.0)	33.4 (32.4, 34.4)	1.53 (1.47, 1.58)*
25-34	54.2 (53.1, 55.2)	39.8 (38.7, 40.8)	1.36 (1.32, 1.41)*
35-44	54.1 (53.1, 55.2)	44.7 (43.6, 45.7)	1.21 (1.18, 1.25)*
45-54	49.8 (48.8, 50.9)	42.9 (41.8, 43.9)	1.16 (1.13, 1.20)*
55-64	41.5 (40.4, 42.5)	34.5 (33.5, 35.5)	1.20 (1.16, 1.25)*
Weight categories†			
Normal weight	57.3 (56.6, 57.9)	38.5 (37.8, 39.2)	1.49 (1.46, 1.52)*
Overweight	62.1 (61.3, 62.9)	45.8 (44.9, 46.6)	1.36 (1.33, 1.39)*
Obesity	57.6 (56.1, 59.0)	45.8 (44.9, 46.8)	1.26 (1.22, 1.30)*
Abdominal obesity‡			
Absent	59.2 (58.7, 59.7)	39.6 (38.9, 40.3)	1.49 (1.47, 1.52)*
Present	56.9 (55.6, 58.2)	45.5 (44.8, 46.1)	1.25 (1.22, 1.29)*

CI= confidence interval. †Normal weight = <25.0, overweight=BMI 25-29.9 kg/m^2, obesity= BMI 30 kg/m^2. ‡Abdominal obesity was defined as waist circumference 102 cm in men and 88 cm in women (22, 23). *P<0.001.

TABLE 3. Age- and multivariate-adjusted odds ratio (95% CI) of the prevalence of hypertension and prehypertension for obesity and abdominal obesity.

Characteristic	**Age-adjusted odds ratio (95% CI)**		**Multivariate-adjusted odds ratio (95% CI)†**	
	Men	**Women**	**Men**	**Women**
		Hypertension		
Weight categories				
Normal weight	1.00	1.00	1.00	1.00
Overweight	2.76 (2.58, 2.96)*	2.10 (1.95, 2.26)*	2.75 (2.56, 2.95)*	2.16 (2.00, 2.33)*
Obesity	5.66 (5.07, 6.32)*	4.11 (3.79, 4.46)*	5.75 (5.13, 6.44)*	4.29 (3.95, 4.66)*
Abdominal obesity				
Absent	1.00	1.00	1.00	1.00
Present	3.91 (3.52, 4.35)*	2.87 (2.69, 3.07)*	3.76 (3.41, 4.22)*	2.92 (2.73, 3.13)*
		Prehypertension		
Weight categories				
Normal weight	1.00	1.00	1.00	1.00
Overweight	1.78 (1.68, 1.88)*	1.54 (1.46, 1.62)*	1.74 (1.64, 1.84)*	1.56 (1.48, 1.65)*
Obesity	2.36 (2.13, 2.62)*	2.21 (2.07, 2.35)*	2.32 (2.09, 2.57)*	2.26 (2.12, 2.41)*
Abdominal obesity				
Absent	1.00	1.00	1.00	1.00
Present	2.07 (1.87, 2.28)*	1.71 (1.63, 1.80)*	2.00 (1.81, 2.21)*	1.71 (1.63,1.80)*

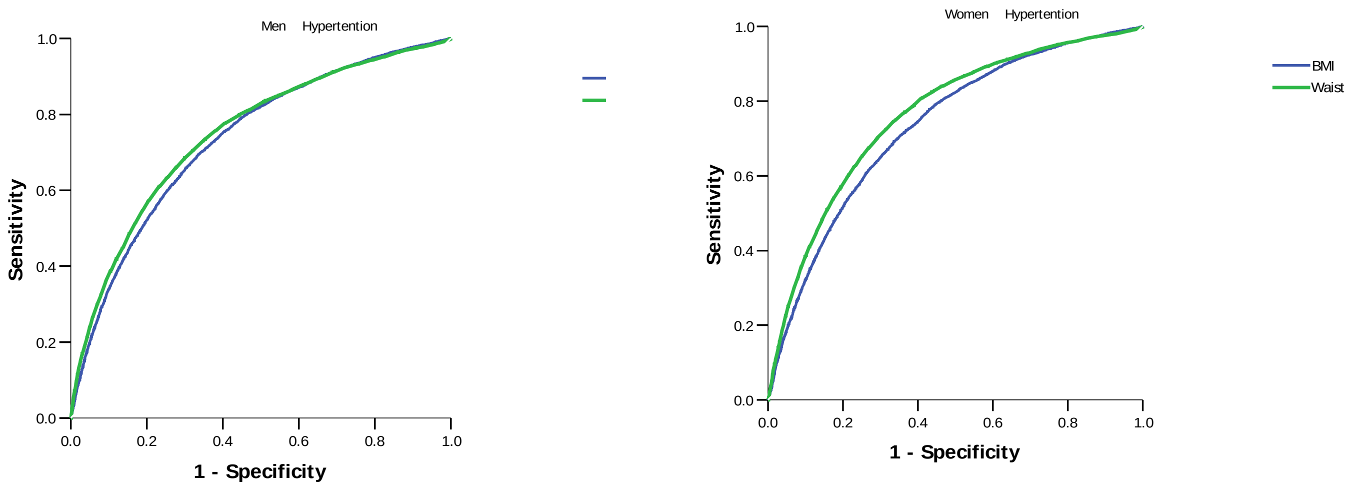
Normal weight =BMI <25. kg/m², overweight=BMI 25-29.9 kg/m², and obese= BMI 30 kg/m². Abdominal obesity was defined as waist circumference 102 cm in men and 88 cm in women (22, 23). †odds ratio (with 95% CI) calculated by binary logistic regression. Adjusted for age, marital status, leisure time physical activity, smoking habits, and area of residence. *p <0.001. CI= Confidence interval.



Area under the curve (95% CI)

	Men	Women
Body mass index	0.630 (0.624, 0.637)	0.637 (0.631, 0.643)
Waist circumference	0.627 (0.620 , 0.633)	0.641 (0.635, 0.647)

Figure 1. Receiver operating characteristic curves for prehypertension in men and women. The estimates of the area under the curves and their 95% confidence intervals are shown.



Area under the curve (95% CI)

	Men	Women
Body mass index	0.733 (0.727, 0.740)	0.734 (0.727, 0.740)
Waist circumference	0.748 (0.741 , 0.754)	0.764 (0.758, 0.770)

Figure 2. Receiver operating characteristic curves for hypertension in men and women. The estimates of the area under the curves and their 95% confidence intervals are shown.