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Predictors of abdominal obesity and high susceptibility of cardiometabolic risk to its increments among Turkish women: a prospective population-based study

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Abstract

To investigate determinants of abdominal obesity and its metabolic and clinical consequences relative to its degree in women, a prospective evaluation of 1682 female participants (aged 28-79 years at baseline), representative of Turkey's women, was performed. For components of metabolic syndrome (MS), criteria of National Cholesterol Education Program guidelines were adopted, modified for cut point of 91 cm or greater for abdominal obesity and less than 45 mg/dL for low high-density lipoprotein (HDL) cholesterol. Fasting insulin and C-reactive protein concentrations and (inversely) smoking more than 10 cigarettes daily were significant predictors of newly developed abdominal obesity at a follow-up of mean 5.9 years. In the prediction of high triglyceride–low HDL dyslipidemia, elevated blood pressure (BP) or MS and doubling of baseline fasting insulin level contributed approximately 25% to the hazard ratio (HR), whereas waist circumference exhibited independent HRs of 1.30, 1.62, and 2.22, respectively. Waist girth (or body mass index) quartiles was the major predictor (HR, 1.72) of diabetes mellitus (DM), followed by physical inactivity and total cholesterol and insulin levels, all independent of each other. Waist girth quartiles in women conferred excess risk of incident coronary heart disease from quartile II onward, independent of age, DM, and elevated BP. Fasting insulin and C-reactive protein levels and (inversely) heavy smoking are main predictors in Turkish women of abdominal obesity. Across waist girth quartiles, multiadjusted relative risks for dyslipidemia, elevated BP, MS, and coronary heart disease rise sharply and asymptotically from quartile II (≥ 83 cm) onward, whereas risk of DM emerges in the top quartile. A waist girth of 83 cm or greater should be regarded as abdominal obesity among Turkish women.

1. Introduction

In a recent conference, obesity and disorders of the adipose tissue (particularly visceral adiposity) were identified as one of 3 potential etiologic categories of the metabolic syndrome (MS) [1]. In the new International Diabetes Federation definition of MS, central (abdominal) obesity and insulin resistance are acknowledged as causative factors for MS [2]. Cut points for "action level" are needed not only because of their usefulness for practicing physicians and the public, but also for studying the interrelation between abdominal obesity and various metabolic abnormalities. The appropriateness of such cut points is recognized to be ethnicity specific and one set of cut points is not necessarily applicable to different ethnic groups [2]. Among women, a cut point of greater than 88 cm, which has been used to define abdominal obesity as a central component of MS, was adopted for Western populations [3]. Nonetheless, indices of visceral adiposity vary by ethnic group in their distribution in and relationship to metabolic abnormalities, and non-European ethnic groups display significantly higher levels of fasting glucose or metabolic abnormalities for a

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given body mass index (BMI) than Europeans [4]. The International Diabetes Federation recommended thresholds for South Asians, Chinese, and Japanese and acknowledged that better data will be needed to link these pragmatic cut points to risk. For East Mediterranean populations, it was recommended that European data be used until more specific data become available [2].

To reach an appropriate cut point of waist circumference, one must determine more accurately the relationship between the degree of abdominal obesity and the various metabolic consequences (or outcomes), notably high triglyceride–low high-density lipoprotein (HDL) dyslipidemia, elevated blood pressure (BP), MS, type 2 diabetes mellitus (DM), and coronary heart disease (CHD). Such information might assist in planning strategies for the prevention and management of abdominal obesity. Data in Turkish adults have not been reported in this area as yet. Because sex-specific features exist in visceral adiposity, we have focused on women in this article and evaluated prospectively relevant data of the Turkish Adult Risk Factor Study. A more suitable modification of the Adult Treatment Panel III definition of MS for this population, taking into account the prevailing low plasma levels of HDL cholesterol (HDL-C) [5,6], might improve the recognition of the various interrelationships of abdominal obesity.

The purpose of the present prospective study was to elucidate the determinants as well as the clinical impact of abdominal obesity, delineating more accurately the relation between the extent of the latter and the metabolic and cardiovascular consequences in the cohort comprising 1682 women of the Turkish Adult Risk Factor Study. This cohort is representative of Turkish middle-aged and elderly women in whom MS is highly prevalent [7]. The study aimed at the following specific points: (1) to assess the main determinants of abdominal obesity; (2) to examine the interrelation between abdominal obesity and high triglyceride–low HDL dyslipidemia, elevated BP, DM, and MS, controlled for smoking and sedentary lifestyle; (3) to delineate the independent risk abdominal obesity confers prospectively to CHD; and (4) to ascertain its most appropriate cut point with regard to several risks in women.

2. Methods

2.1. Population sample

Participants of the nationwide 1997-1998 survey of the Turkish Adult Risk Factor Study and followed up thereafter till 2004-2005, numbered 3388, among whom 1714 were women. This is a prospective survey on the prevalence of cardiac disease and risk factors in a representative sample of adults in Turkey that has been carried out periodically almost biennially since 1990 in 59 communities scattered throughout all geographical regions of the country [6]. Details of sampling were described previously [8]. Because combined measurements of waist circumference, HDL-C, and apolipoprotein (apo) B were first performed at the follow-up visit in 1997-1998, the latter examination formed the baseline. Participants were aged 28 years or older at baseline examination. Of the survivors, 8% were examined up to the 2001-2002 survey, 14% up to 2003, and the remainder in the 2004-2005 survey. Exclusion of 32 women aged 80 years or older limited the study sample to 1682 women. The survey conformed to the principles embodied in the Declaration of Helsinki and was approved by the Istanbul University ethics committee. Individuals of the cohort signed consent for participation after having read an explanatory note. Data were obtained from the individual's history via a questionnaire, physical examination of the cardiovascular system, sampling of blood, and recording of a resting electrocardiogram (ECG).

2.2. Measurements of risk variables

Blood pressure was measured on the right arm after 5 minutes of rest, with the subject in the sitting position, and the mean of 2 recordings 3 minutes apart was recorded. Weight was measured by using scales, with the subject in light indoor clothes and without shoes. Waist circumference was measured with a tape (Roche LI95 63B 00), with the subject standing and wearing only underwear, at the level midway between the lower rib margin and the iliac crest. BMI was calculated as weight (in kilograms) divided by height (in meters) squared. Physical activity was graded by the participant himself into 4 categories of increasing order with the aid of the following scheme: grade 1, white-collar job, sewing-knitting, walking 1 km or less daily; grade 2: repair work, house work, walking 1 to 2 km daily; grade 3, masonry, carpentry, truck driving, floor and window cleaning, walking 4 km daily; grade 4, heavy labor, farming, regular sports activity [8].

Plasma concentrations of cholesterol, fasting triglycerides, HDL-C, and glucose were determined at baseline examination by the enzymatic dry chemistry method using a Reflotron apparatus (Roche Diagnostics, Mannheim, Germany). Low-density lipoprotein cholesterol (LDL-C) values were computed according to the Friedewald formula. In the final 3 surveys, the stated parameters, as well as apo B, insulin, and C-reactive protein (CRP) values were assayed in a central laboratory. Blood samples were spun at 1000*g* for 10 minutes and shipped within a few hours on cooled gel packs at 2°C to 5°C to Istanbul to be stored in deep-freeze at −75°C until analyzed at a central laboratory in the same city. Concentrations of insulin were determined by the chemiluminescent immunometric method using Roche kits and an Elecsys 1010 immunoautoanalyzer (Roche Diagnostics). Concentrations of CRP were measured by Behring nephelometry using an N Latex CRP mono reagent (Behring Diagnostics, Marburg, Germany), as were serum apo B values. External quality control was performed with a reference laboratory in a random selection of 5% to 6% of participants. Data on CRP and insulin were available from the 2000-2001 survey onward.

2.3. Definitions and outcomes

Never smokers, past smokers, and current smokers formed the categories in cigarette smoking. Current smokers of more than 10 cigarettes daily were designated as heavy smokers. Anyone consuming alcohol once a week or more was considered as an alcohol user. Elevated blood pressure was defined, in agreement with National Cholesterol Education Program (NCEP) guidelines [3], as receiving antihypertensive treatment or having a systolic BP of 130 mm Hg or greater and/or a diastolic pressure of 85 mm Hg or greater. Individuals with diabetes and prediabetes were diagnosed with criteria of the American Diabetes Association [9], namely, by self-report or when plasma fasting glucose was 126 mg/dL or greater or 2-hour postprandial glucose was greater than 200 mg/dL. Impaired fasting glucose denoted fasting glucose values of 100 to 125 mg/dL. Abdominal obesity was defined in this study in terms of waist circumference in agreement with this anthropometric measure emerging as the most appropriate one to reflect visceral adiposity among Turks [10]; a cut point was not set because it constituted an aim of the study. Results of receiver operating characteristics (ROCs) related to CHD, DM, MS, and a surrogate of subclinical inflammation were used for this purpose to detect an optimal cut point. MS was defined with criteria of the NCEP [3] modified for prediabetes (fasting glucose $\geq$100 mg/dL) [1,9]; these criteria were further modified for abdominal obesity to be determined in this study and HDL-C as less than 45 mg/dL. The latter threshold for low HDL-C rather than less than 50 mg/dL was chosen because (*a*) the 45-mg/dL cut point still comprises more than half of women who have low HDL-C because of a genetic predisposition of Turks to low HDL-C levels [5] and (*b*) this cut point was more in agreement with both the mean gender difference and the gender difference in multiple adjusted linear regression models [11], and (*c*) in partial agreement with the Genetic Epidemiology of Metabolic Syndrome Project [12] in which a mean gender difference of 4.9 mg/dL was found between HDL-C concentrations affected by MS. Missing data on fasting triglycerides in one sixth of the sample did not preclude the identification of MS because availability of no more than 3 criteria was required, and the MS status of the subsequent survey was taken into account in 42 women presenting 2 positive criteria. Values of the baseline examination were used to evaluate prospective developments.

Information on the mode of death was obtained from first-degree relatives and/or health personnel of the local health office. Diagnosis of nonfatal CHD was based on the presence of angina pectoris, on a history of myocardial infarction with or without accompanying Minnesota codes of the ECG [13], or on a history of myocardial revascularization. Typical angina and age older than 45 years were prerequisite for a diagnosis in women when angina was isolated. ECG changes of the "ischemic type" greater than minor degree (codes 1.1-2, 4.1-2, 5.1-2, and 7.1) were considered as myocardial infarct sequelae or myocardial ischemia, respectively.

2.4. Data analysis

Four quartiles of waist circumference were formed, delineated by cut points of 83, 90.5, and 100 cm, which were composed of the following number of women in increasing quartiles: 433, 414, 413, and 422. Analysis to discriminate with an 80% power between first and second waist quartiles for incident CHD and MS disclosed the requirement of 381 and 64 women, respectively, and of 288 women to discriminate between first and third waist quartiles for incident DM. BMI quartiles were formed by cut points of 24.9, 28.4, and 32.0 kg/m^2. Because of the skewed distribution of concentrations of insulin and CRP, these were log transformed for calculations. Descriptive parameters were shown as age-adjusted mean estimate ± SE and as percentages. Two-sided *t* tests and Pearson's χ^2 tests were used to analyze the differences in means and proportions between groups. In multivariate prediction of the incidence of a dependent variable, the cohort in whom that particular variable existed at baseline examination was excluded from multivariate analysis. Estimates (and 95% confidence intervals [CIs]) for relative risk (RR) of a dependent variable were obtained by use of logistic regression analysis in models that controlled for potential confounders. Hazard ratio (HR) estimates were obtained when needed for comparing the effect of multiple independent parameters by taking into account that the gradient across the waist circumference quartiles represented 2.54 SDs. The RR of a log-transformed independent variable was assessed in terms of doubling and calculated by multiplying the log of the RR value by 0.2 and then taking its antilog. A value of $P < .05$ on the two-sided test was considered statistically significant. Statistical analyses

Table 1
Sensitivity and specificity of selected thresholds of waist girth for future metabolic and cardiovascular abnormalities

Waist at baseline (cm)	Incident CHD (n = 153)		Incident DM (n = 105)		Incident MS (n = 255)		Developing CRP $\geq$3 mg/L	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
$\geq$92	0.65	0.57	0.69	0.57	0.44	0.81	0.47	0.66
$\geq$91	0.69	0.54	0.75	0.55	0.46	0.80	0.48	0.63
>88	0.77	0.44	0.81	0.46	0.58	0.71	0.63	0.44
$\geq$84	0.88	0.32	0.89	0.32	0.81	0.51	0.76	0.38
Area under the curve	0.64, $P < .001$		0.68, $P < .001$		0.72, $P < .001$		0.62, $P = .001$	

Table 2
Age-adjusted mean estimates of baseline cardiovascular risk parameters in 1682 women by waist girth quartiles

	<83 cm (n = 433)		83-90.5 cm (n = 414)		91-99.5 cm (n = 413)		>100 cm (n = 422)		*P*
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	
Crude age (y)	42.8	10.6	46.6	11.9	50.5	11.6	53.1	10.7	
Waist circumference (cm)	75.4	0.23	86.6[a]	0.23	94.7[a]	0.23	107.4[a]	0.23	[b]
BMI (kg/m^2)	23.4	0.2	27.5[a]	0.2	30.3[a]	0.2	34.5[a]	0.2	[b]
Apo B (mg/dL), n = 1057	104.1	2.3	111.7[a]	2.1	116.1[b]	2.2	118.9[b]	2.1	[b]
Fasting triglycerides (mg/dL), n = 1383	104.5	4.7	134.1[a]	4.6	140.7	4.7	162.4[a]	4.6	[b]
HDL-C (mg/dL)	48.8[a]	0.7	45.0[a]	0.7	43.0	0.7	42.9	0.7	[b]
LDL-C (mg/dL), n = 1461	115	1.8	119.2[a]	1.7	125.7[a]	1.8	120[b]	1.8	[b]
Total cholesterol (mg/dL)	180.2	1.9	188.1[a]	1.9	192.6	1.9	194.1[b]	1.9	[b]
Fasting log insulin (mIU/L)[c], n = 972	5.6	1.0	7.46[a]	1.0	8.53[a]	1.0	10.4[a]	1.0	[b]
Log CRP (mg/L),[c] n= 1368	1.35	1.06	2.21[a]	1.6	2.74[a]	1.06	3.43[a]	1.1	[b]
Systolic BP (mm Hg)	123.8	1.1	131[a]	1.1	135.3[a]	1.1	140.3[a]	1.1	[b]
Diastolic BP (mm Hg)	77.0	0.6	81.9[a]	0.6	84.4[a]	0.6	88.1[a]	0.6	[b]
Alcohol use (%)	2.3		1		0.5				<.004
Current smoker (%)	31.4		16.4		14.1		10.5		<.001
Diabetes at baseline (%)	2.1		4.6		7.7		9.3		<.001
MS (%)	9.9		18.1		60.3		72		<.001
Incident CHD (%)	3.3		8.3		11.9		14.9		<.001

[a] Significantly higher than the category with next lower mean value, hence categories with still higher values are automatically significantly different as well. For example, total cholesterol in quartiles II and III are significantly higher than the lower categories but quartile IV is significantly higher than quartile II only.
[b] Significantly higher than the 2 next lower categories.
[c] Log-transformed values.

were performed using SPSS-10 for Windows (SPSS, Chicago, IL, No. 9026510).

3. Results

Mean age of the study sample was 48.2 ± 11.9 years at baseline. Over a mean follow-up of 5.9 years (total, 9925 person-years), 73 deaths occurred, 32 of which were identified as resulting from CHD. Incident fatal (19 women) or nonfatal CHD (9.7%) was diagnosed in a total of 153 female participants, incident type 2 DM in 105 (6.5%) women, and new MS in 252 (24.9%) women.

3.1. Ascertainment of the most appropriate cut point

Analyses of the ROC curves between waist circumference and new cases of CHD, MS, or DM or of a CRP level of 3.0 mg/L or greater (a surrogate of subclinical inflammation [3]) revealed ratios of sensitivity and specificity for selected waist girths provided in Table 1. The areas under the ROC curves for incident CHD, DM, and MS had ratios of 0.64, 0.68, and 0.72, respectively (each $P < .001$). Although 84 cm or greater appeared to be optimal for MS as outcome, for prediction of CHD and DM as well as for that of the high CRP level, it was deduced that a cutoff of 91 cm or greater for waist circumference was most appropriate, inasmuch as it had a sensitivity of 69% and a specificity of 54% for incident CHD, and a slightly higher sensitivity for incident DM. This threshold allowed the obtaining of a substantially higher specificity as opposed to a slight loss in sensitivity compared with a cut point of greater than 88 cm. Thus, 91 cm or greater was defined as abdominal obesity for Turkish women, which prevailed in 835 (49.6%) women at baseline examination. Abdominal obesity appeared marginally superior to BMI by the assessment of areas under the ROC curves related to CHD (0.642 vs 0.628) or DM (0.680 vs 0.676).

Table 3
Predictors of incident abdominal obesity in women

	Model 1 (n = 661)		Model 2 (n = 443)		Model 3 (n = 396)	
	RR	95% CI	RR	95% CI	RR	95% CI
Log CRP	2.24	1.54-3.25	1.96	1.26-3.07	1.84	1.15-2.94
Age (y)	1.004	NS	1.007	NS	1.01	NS
Heavy smoking	0.37	0.17-0.80	0.34	0.13-0.89	0.31	0.11-0.90
Alcohol use	0.65	NS	1.55	NS	1.14	NS
Total cholesterol (mg/dL)	1.002	NS	1.00	NS	1.006	.999-1.013
Physical activity grade I-IV	0.99	NS	1.04	NS	0.91	NS
Log fasting insulin			2.62	1.08-6.34		
HDL-C (mg/dL)					0.997	NS
Fasting glucose (mg/dL)					1.002	NS

Models comprised 170, 116, and 102 women (26%) with newly developed abdominal obesity. Light smoking and past smoking (RR <0.65) not significant. NS indicates not significant.

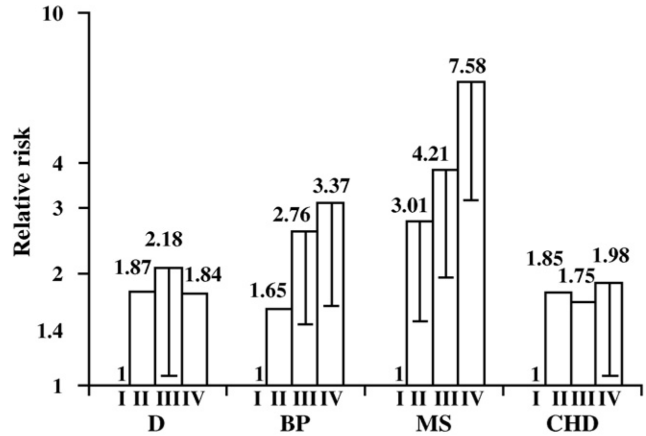

Fig. 1. Relative risks (expressed in logarithmic scale) of waist girth quartiles for incident dyslipidemia (D, n = 711), elevated BP (n = 425), and MS (n = 491) in regression models including fasting insulin level, and for incident CHD (n = 1559) in women. Bars for lower limits of 95% CI are provided; others were of borderline significance. Note the asymptotic shape of the risk curve across the quartiles.

3.2. Prevalences and baseline characteristics by waist girth quartiles

The difference in waist circumference across the bottom and top quartiles amounted to 32 cm, equivalent to 2.54 SD. Risk characteristics differing significantly by quartiles of waist circumferences are presented as age adjusted in Table 2 because age differed by a full decade across the quartiles. The following parameters did not differ significantly across the quartiles: apo A-I, fasting glucose, fibrinogen, and physical activity grade. Compared with the "lean" quartile, significant differences in most of the risk parameters emerged in the next category: lower HDL-C and prevalence of smokers, higher concentrations of triglyceride, apo B, total and LDL cholesterol, fasting insulin, and CRP, and blood pressure. With rising waist quartiles, it was anticipated that the prevalence of type 2 DM and of MS would be increasingly higher, as was the more than 4-fold crude incidence of subsequent CHD with 25.3 vs 5.6 per 1000 person-years.

3.3. Predictors of abdominal obesity

Results of logistic regression analysis for predictors at baseline of newly developed abdominal obesity during the follow-up period in 170 of 661 women free of abdominal obesity at baseline are shown in model 1, Table 3. Whereas age, physical activity grade, total cholesterol, and alcohol use were not significant predictors, heavy cigarette smoking (inversely) and log CRP level proved to be so. When fasting insulinemia was included (model 2), it revealed a significant but moderate 2.62-fold RR (corresponds to an RR of 1.21 for a doubling of insulin values), attenuating the RR of CRP slightly to 1.96 (95 % CI, 1.26-3.07), corresponding to an RR of 1.14 for a doubling of CRP values, without modifying the independent protective role of heavy smoking (RR, 0.34; 95 % CI, 0.13-0.89). Baseline HDL-C and fasting glucose levels were not independent predictors of subsequent abdominal obesity (model 3).

3.4. Multiadjusted prediction of elevated BP, dyslipidemia, and MS by abdominal obesity

Incident (new) cases of elevated BP, atherogenic (high triglyceride–low HDL-C) dyslipidemia, and MS in the course of the follow-up were tested as dependent variables in separate logistic regression analyses in which cases with the respective abnormalities existent at baseline were excluded. In each regression analysis, a basic model with waist girth quartiles and 5 other variables (age, total cholesterol, smoking status, alcohol use, and physical activity grade) were included as independent parameters to which fasting insulin was added in a second model. The number of participants in the basic models varied between 965 and 1140, whereas the models with insulin encoded only 425 to 711 women because fasting insulin was measured in just more than one half of the women. In each basic model, compared with the bottom quartile, quartile II significantly predicted the outcome (dyslipidemia: RR, 2.21 [95% CI, 1.31-3.74]; elevated BP: RR, 1.51 [95% CI, 1.04-2.20]; MS: RR, 3.64 [95% CI, 2.35-5.65]).

In models using fasting insulin as well (Fig. 1), log fasting insulin significantly predicted dyslipidemia (RR,

Table 4
Prediction in women by waist girth or BMI quartiles of incident diabetes

	Waist circumference				BMI			
	Model 1 (n = 1472)		Model 2 (n = 864)		Model 1 (n = 1483)		Model 2 (n = 865)	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Waist circumference (cm)								
83-90.5	1.04	NS	1.24	NS	3.08	1.22-7.8	3.1	1.009-9.5
91-99.5	1.83	0.83-4.02	1.81	0.66-5.01	3.88	1.57-9.6	2.22	0.70-7.0
≥100	3.99	1.91-8.31	4.50	1.70-12.0	5.64	2.32-13.7	4.37	1.45-13.2
Age (y)	1.02	0.999-1.042	1.00	NS	1.025	1.004-1.047	1.00	NS
Heavy smoking	0.16	0.02-1.18	0.21	0.03-1.56	0.38	NS	0.35	NS
Alcohol use	0.09	NS	0.04	NS	0.03	NS	0.02	NS
Total cholesterol (mg/dL)	1.006	1.000-1.011	1.008	1.001-1.015	1.005	0.999-1.010	1.006	0.999-1.013
Physical activity grade IV	0.72	0.51-1.002	0.49	0.32-0.75	0.86	NS	0.59	0.39-0.89
Log fasting insulin			3.59	1.30-9.97			5.51	1.98-15.3

Models comprised 89 and 64 women with newly developed diabetes. Light smoking and past smoking not significant. NS indicates not significant.

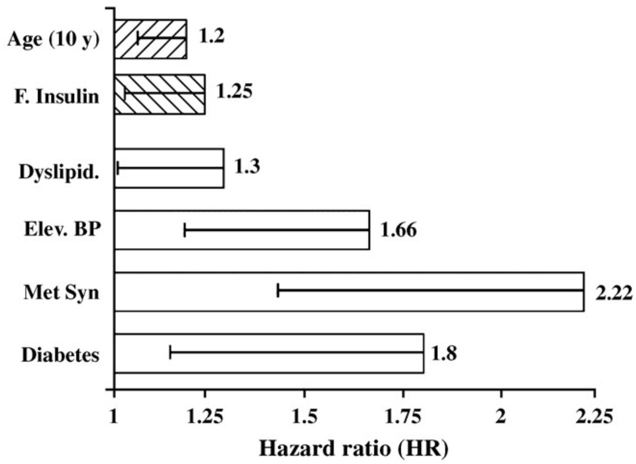

Fig. 2. Multiple adjusted HRs of waist girth quartiles as independent predictors of dyslipidemia (n = 711), elevated BP (n = 425), MS (n = 491), and diabetes (n = 864) in regression models including fasting insulin level in women. Hazard ratios of a decade of age and relative risk of doubling of fasting insulin are provided additionally to compare the magnitudes. Bars for lower limits of 95% CI are provided.

2.71; 95% CI, 1.15-6.41). Regarding elevated BP, other than total cholesterol at borderline significance and the significant covariates age and fasting insulin (RR, 1.27, for a doubling of value), waist circumference proved most powerful (HR, 1.62). With regard to MS, waist quartiles were the main predictor with an HR of 2.22, and more than half the risk conferred by the top quartile was significantly contained in quartile II. Further significant predictors were log fasting insulin (RR, 2.81; 95% CI; 1.10-7.20), heavy smoking (inverse), age, and total cholesterol level.

3.5. Prediction of DM

In a logistic regression model comprising waist quartiles and 5 other variables, prediction of 89 incident cases of type 2 DM is summarized in Table 4. Waist quartile IV was the only significant variable. Addition of log fasting insulin displayed the latter to be a modest but significant predictor (RR, 3.59) with an HR of 1.29, followed by physical inactivity and total cholesterol. HRs (and SDs) of waist quartiles calculated from RRs in the prediction of 4 outcomes, namely, atherogenic dyslipidemia and elevated BP, MS, and DM are illustrated in Fig. 2, comparing the magnitudes with the HR of a decade of age and doubling of fasting insulin.

Diabetes was better predicted in the same model by BMI quartiles when substituted for waist quartiles: even quartile I revealed a RR of 3.08 (Table 4). Yet, the model with insulin indicated that, as opposed to waist quartiles, the improved prediction by BMI was mediated more by insulin levels.

3.6. Prediction of subsequent CHD risk

In a logistic regression comprising 1559 women (free of CHD at baseline), waist girth quartiles and further standard risk factors (age, elevated BP, smoking status, total cholesterol, and physical activity grade) were analyzed in the prediction of 151 incident cases of CHD (Table 5). Apart from age, 3 top waist girth quartiles proved to be significant independent predictors of future CHD risk, with RR reaching 2-fold in quartile II. Even when DM and elevated BP, to which waist girth contributed substantially, were added in model 2; RRs of quartiles II and III (of around 1.8) attenuated to borderline significance, but that of the top quartile persisted to be significant (1.98). Development of CHD was not as well predicted in the same model by BMI quartiles (replacing waist quartiles): although top BMI quartile was slightly better predictive, RRs in quartiles II and III did not reach significance, as contrasted to that of waist girth (Table 5).

4. Discussion

In a representative sample of middle-aged and elderly Turkish women, we found a cut point of 91 cm or greater waist circumference for abdominal obesity, which was used in analyses of this prospective study. Serum fasting insulin and CRP concentrations and (inversely) heavy smoking were significant independent predictors of abdominal obesity. Although only the top quartile of waist girth strongly predicted risk of incident type 2 DM, the novel

Table 5
Prediction in women of incident coronary heart disease by waist girth or BMI quartiles

	Waist circumference				BMI			
	Model 1 (n = 1559)		Model 2 (n = 1559)		Model 1 (n = 1559)		Model 2 (n = 1559)	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Waist circumference (cm)								
83-90.5	2.05	1.04-4.02	1.85	0.94-3.66	1.70	0.90-3.21	1.54	0.94-3.66
91-99.5	2.10	1.09-4.04	1.75	0.90-3.41	1.59	0.84-3.01	1.42	0.90-3.41
≥100	2.42	1.28-4.59	1.98	1.03-3.80	2.95	1.62-5.36	2.35	1.27-4.34
Presence of diabetes			1.98	1.13-3.48			1.89	1.08-3.33
Elevated BP (>130/85 mm Hg)			1.87	1.15-3.03			1.75	1.06-2.88
Age (y)	1.084	1.065-1.104	1.078	1.058-1.098	1.089	1.069-1.11	1.082	1.061-1.10
Total cholesterol (mg/dL)	1.004	0.999-1.008	1.003	NS	1.003	NS	1.003	NS
Heavy smoking	0.74	NS	0.74	NS	0.82	NS	0.82	NS
Physical activity grade I-IV	0.92	NS	0.96	NS	0.91	NS	0.94	NS

Models comprised 151 incident cases of CHD. Light and past smoking and alcohol use are not significant. NS indicates not significant.

findings were that quartile II (83-90.5 cm) emerged to be a significant predictor of atherogenic dyslipidemia, elevated BP, and MS independent of age, fasting insulin, total cholesterol, and smoking status (all significant covariates), and sedentary lifestyle. Hence, 2 action levels should be instituted. CHD risk also emerged significantly from quartile II onward, and a borderline significance persisted when controlled for DM and elevated BP.

4.1. Two levels of waist circumference cut points

The selected cutoff of 91 cm or greater waist circumference to define abdominal obesity appears appropriate in view of ROC curves displaying higher positive predictive values, notably substantially higher specificities, than a cutoff of greater than 88 cm, not only with respect to crude incident CHD, but also to diabetes, or a surrogate of proinflammatory state. Attainment of borderline significant levels of prediction in quartile III and of significant levels in the adjusted model of DM and more completely adjusted model of CHD in the top quartile supports this contention. This cut point of 91 cm or greater should be a criterion for action level 2 and constitutes the highest threshold of female abdominal obesity among the populations studied [2]. The gender difference in waist cut points is low (4 cm) among Turks compared with 14 cm in Western populations and 10 cm in South Asians and Chinese, and also different from that of Japanese individuals in whom it is −5 cm [2]. This study confirms that waist circumference is a continuum in terms of risk for various important metabolic and cardiovascular diseases. As assessed by significantly raised risk appearing in quartile II, it may be asserted that in this population sample, with respect to dyslipidemia, BP elevation, and MS, 83 cm or greater should be regarded as action level 1. For female Asian Indians, waist circumference action levels 1 and 2 were proposed newly as 72 and 80 cm or greater, respectively, based on the association of at least one cardiovascular risk factor or presence of a high odds ratio for risk factors [14]. Because our study sample has been regarded as representative of Turkish middle-aged and elderly women [6], conclusions arrived at in this study are expected to be applicable for the Turkish female population at large.

4.2. CRP and smoking as determinants of abdominal obesity

Cigarette smoking (inversely) and fasting insulin and CRP levels were significant independent predictors of abdominal obesity. Our observations parallel the findings of McLaughlin et al [15] in 38 insulin-sensitive and insulin-resistant obese women who concluded that the relation between CRP concentrations and insulin resistance was independent of obesity. Raised CRP concentrations have been found associated with obesity and DM cross-sectionally [16], and CRP levels found more elevated in healthy Indian Asians than in European whites were accounted for by greater central obesity and insulin resistance in Indian Asians [17]. However, this is the first demonstration, to our knowledge, that baseline levels of CRP predicted abdominal obesity prospectively. Noteworthy is that the contribution of insulin levels was not as high as might be anticipated.

Smoking more than 10 cigarettes daily was clearly an inverse determinant of abdominal obesity in women and independent of waist quartiles. This finding is consistent with an inverse correlation of cigarette use and obesity in a recent cross-sectional study of Turkish adults of the Black Sea region [18], in which the crude odds ratio for obesity of current adult smokers was reported to be significantly lower (0.71; 95% CI, 0.58-0.89) than that of nonsmokers. An interaction between diminished appetite and raised metabolic rate among smokers [19], diminished risk for elevated CRP specifically in women (unpublished observation), and the lack of effect of smoking on insulin sensitivity [20] may underlie our observation, and the issue is currently under study. The protective effect of heavy smoking in Turkish women against abdominal obesity demonstrated here and the lack of adverse effect on insulin sensitivity [20] stand in contrast to several other populations: for example, starting to smoke during the study increased 1.5-fold the risk of progressing to incident hyperinsulinemia in the Atherosclerosis Risk in Communities Study [21]. Cigarette smoking was found to be associated with high plasma insulin levels [22] and is also a risk factor, with an approximately 2-fold odds ratio, for MS among Japanese men and women [23]. In multivariate analyses, current smoking was positively related to waist-hip ratio in 6705 French men and women [24].

4.3. Susceptibility of dyslipidemia, BP elevation, and MS to abdominal obesity

We confirmed that waist circumference as a surrogate of visceral adiposity independently predicts dyslipidemia, raised BP, and MS even after adjustment for age, fasting insulin, smoking, and other confounders. However, the finding less anticipated was that all 3 outcomes were extremely susceptible to abdominal obesity in Turkish women, being significantly predicted in quartile II (waist circumference, 83-90.5 cm). The roughly asymptotic shape—rather than parabolic shape as existed in diabetes risk—of the relationship between these consequences and the relative risk in waist quartiles confirms this susceptibility in general. This observation illustrates the variability in expression of these risk factors that are subject to regulation through genetic and acquired factors [1]. Because reports on the relation of these consequences to the degree of abdominal obesity are scarce at best, we are unable to make comparisons. But we may point out that as compared with 75% of Turkish women exhibiting this susceptibility, less than a quarter of a random sample of Dutch women were classified to have a waist circumference greater than 88 cm and designated to be in action level 2 [25]. Cross-sectional data from a limited number of Singaporean women indicated that absolute risks for having at least one component of MS was high at waist girths 75 to 80 cm, and RRs were significantly higher compared with the reference category [26].

The multiadjusted HRs of waist circumference in regard to risk of 4 outcomes (Fig. 2) indicate that the greatest involves MS, followed by DM and elevated BP, and the least atherogenic dyslipidemia. This generally reflects the estimated prevalence of these conditions among Turkish compared with Western women.

4.4. Comparative roles of insulin resistance and adiposity

Insulin resistance and disorders of adipose tissue within the context of abdominal obesity have been implicated by the National Heart, Lung, and Blood Institute/American Heart Association Conference as 2 of the 3 potential etiologic categories in the pathogenesis of MS [1]. Our findings with respect to HRs of fasting insulin and waist girth suggest that the role of insulin resistance in MS, although independently important, is not as great as that of abdominal adiposity in Turkish women.

4.5. Risk prediction for diabetes and CHD

In agreement with the knowledge that (abdominal) obesity and physical inactivity are the main nongenetic modifiable determinants of diabetes, the disease was predicted with a 4.5-fold RR in Turkish women by the top vs the bottom waist quartile when controlled for fasting insulin, total cholesterol, and physical activity grade, among other covariates. Physical activity was also confirmed to be protective against the development of DM in the general population. Previous studies provided evidence that lifestyle changes are effective in preventing diabetes in persons at high risk for the disease [27,28]. In a large prospective study in US middle-aged women, those engaged in vigorous exercise at least once per week had a significantly reduced RR (0.84) for the development of diabetes [29].

Body mass index and waist circumference are highly correlated in women, more so than in Turkish men [10], but although cardiometabolic risk of BMI was more extensively mediated by insulin levels, waist circumference and insulin seemed to be more independent. Moreover, the susceptibility of waist girth to (dyslipidemia and) CHD was greater than that of BMI, inasmuch as quartiles II and III of waist girth alone significantly predicted CHD. Abdominal obesity in female Turks likely exerted its adverse effects on CHD not only through the intermediary of its effects on BP and diabetes, but also by conferring substantial independent risk, presumably via subclinical inflammation, procoagulant state, elevated serum nonesterified fatty acids, and action of various cytokines. In the Danish study [30], a 10% larger waist circumference corresponded to a 1.33 times higher all-cause mortality over the whole range of waist measurements after adjustment for sex, BMI, and smoking.

A possible limitation of the study is that serum insulin values of about 2 years later have been substituted for baseline, but because these preceded by 4 years the end of the follow-up, this issue should not substantially alter the result of the relevant analyses, as can be judged by only a modest alteration of similar findings obtained in regression models without using insulin levels. Another limitation pertains to the applicability of these results only for populations of the East Mediterranean area and the Middle East, which have a fairly similar risk profile, but these may not be generalized for other populations because abdominal obesity is largely ethnicity specific.

We conclude that serum concentrations of fasting insulin and CRP and (inversely) heavy smoking are significant independent predictors of abdominal obesity in Turkish women in whom waist girths of 83 and 91 cm or greater constitute 2 action levels. This is based on finding a high susceptibility to increments in waist girth of atherogenic dyslipidemia, elevated BP, and MS, all of which were predicted in quartile II (83-90.5 cm), but also on prediction of CHD risk. Our findings, furthermore, suggest that the role of insulin resistance, although independently important in Turkish women, is not as great as that of intrinsic abdominal obesity.

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