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Smoking inhibits visceral fat accumulation in Turkish women Relation of visceral fat and body fat mass to atherogenic dyslipidemia, inflammatory markers, insulin resistance, and blood pressure

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Abstract

We investigated among sexes the associations of visceral adipose tissue area (VAT) and body fat mass with smoking status, atherogenic dyslipidemia, inflammatory markers, insulin resistance, and blood pressure (BP). A random sample of the Turkish adult population consisting of 157 middle-aged men and women was evaluated cross-sectionally and partly prospectively. Although men were not influenced significantly, smoking vs never-smoking women had 4 years later a lower VAT (by 31 cm^2, $P = .005$). Fat mass was significantly correlated with homeostasis model, C-reactive protein, and BP in both sexes, although not with atherogenic dyslipidemia as was VAT. Compared with men, women had lower VAT ($P < .01$) and, because of interaction of sex and smoking ($P = .06$), tended to be less susceptible to accumulation of VAT per kilogram body fat mass. In linear regression models comprising 7 variables, VAT was associated in men with systolic BP, apolipoprotein B, and C-reactive protein (each $P = .04$) and was associated in women with age, smoking status, and high-density lipoprotein cholesterol (each $P \leq .01$). Significant positive correlations of VAT were obtained with future systolic BP in either sex ($P < .03$). Body fat mass and visceral fat accumulation are inhibited by cigarette smoking in women. Markers of insulin resistance and inflammation are independently associated with visceral fat marginally in women but significantly in men. Visceral fat is better associated than fat mass with atherogenic dyslipidemia and, in men, with apolipoprotein B. Thus, sex interacts with the dynamics of cardiometabolic risk.

1. Introduction

It has been emphasized that the conceptual definition of metabolic syndrome (MetS) is wider than the 5 components recommended by the National Cholesterol Education Program–Adult Treatment Panel III for clinical use as screening tools and that further data are needed to evaluate the added value in global risk assessment of markers of inflammation, insulin resistance, atherogenic dyslipidemia, adipokines, etc [1]. Visceral adipose tissue area (VAT) or mass, a major driver of cardiometabolic risk, needs to be studied by computerized tomography (CT) or magnetic resonance imaging. Important ethnic differences exist in susceptibility to visceral adiposity and related metabolic abnormalities [2].

The notion has been expressed that individuals with an excess of visceral adipose tissue are not only at increased risk of standard components of MetS, but are more likely to have the expanded features of this syndrome (elevated apolipoprotein [apo] B, small dense low-density lipoprotein [LDL], prothrombotic profile, elevated C-reactive protein [CRP], and reduced adiponectin) [3]. Data are needed to corroborate this notion in diverse ethnicities. Furthermore, although cigarette smoking has been shown to be generally associated adversely with abdominal obesity [4] or MetS [5], reports on

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the associations of smoking with visceral adiposity have been, to our knowledge, very scarce. Only 1 study reported that the number of Brinkman index for smoking status was positively related to visceral fat area [6]. Finally, the relative contributions of subcutaneous and visceral fat to cardiovascular disease remain controversial [7].

Turks have a high and rapidly increasing prevalence of MetS [8]. We had previously reported the covariates of VAT as concerned anthropometric indices and serum lipoproteins in a subsample of the Turkish Adult Risk Factor Study [9] in whom CT-assessed variables were performed [10]. However, associations with inflammatory markers or adipokines (CRP, apo B, adiponectin) and other variables that are relevant (homeostasis model [HOMA], fibrinogen, etc) were not sufficiently sought; nor were the associations with blood pressure (BP) or the influence of smoking status. In addition, a follow-up of up to 5 years is currently available. Therefore, we aim in this study, using the same initial study sample with the baseline CT-assessed variables, to investigate separately in the sexes the (*a*) associations of smoking status with VAT and body fat mass and (*b*) associations of VAT with atherogenic dyslipidemia (triglyceride/high-density lipoprotein [HDL] cholesterol), inflammatory markers (CRP, apo B), insulin resistance (by HOMA), and BP.

2. Methods

2.1. Subjects

The study sample comprising 157 residents of the city of Istanbul within the cohort of the Turkish Adult Risk Factor Study [9] was identical with that in whom abdominal fat areas had been assessed by CT at the end of 2002, details of which were previously reported [10]. Consent was obtained in all those enrolled.

2.2. Measurement of anthropometry and total body fatness at baseline

Waist circumference was measured using a spring scale (O Haus, Florham Park, NJ), with the subject standing and wearing only underwear, at the end of gentle expiration at the level midway between the lower rib margin and the iliac crest. Body mass index (BMI) was calculated as weight divided by height squared (kilograms per square meter). Body composition was measured by the hydrostatic weighing technique with a body composition analyzer (Tanita TBF 300, Tokyo, Japan). Body fat mass was computed from percentage body fat with the value of body weight.

Computed tomography was performed on a Siemens Somatom AR SP 40 (Erlangen, Germany) spiral scanner according to the procedure of Sjöström et al [11] and as described by Ferland et al [12]. A single axial scan was made at the abdominal level, between the fourth and fifth lumbar vertebrae, using an abdominal topogram. The sagittal diameter of the abdomen was determined from the abdominal image generated by the computer by connecting the anterior and posterior midline points.

Total adipose tissue areas were calculated by delineating the abdomen with a graph pen and then computing the adipose tissue surface using an attenuation range of −190 to −30 Hounsfield units [12]. By subtracting the abdominal VAT from the total adipose tissue area, the abdominal subcutaneous area was obtained.

2.3. Measurement of other risk factors

Blood pressure was measured in the sitting position on the right arm using an aneroid sphygmomanometer (Erka, Bad Tölz, Germany) after at least 5 minutes of rest. Readings were recorded to the nearest even number, and the mean of 2 recordings 3 minutes apart was computed. Self-reported cigarette smoking was categorized into never smokers, former smokers (discontinuance of 3 months or more), and current smokers (regularly 1 or more cigarettes daily), as elicited in interview during examination. 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 worker, sewing/knitting, walking less than or equal to 1 km daily; grade 2—repair worker, house work, walking 1 to 2 km daily; grade 3—mason, carpenter, truck driver, cleaning floors and windows, walking 4 km daily; grade 4—heavy labor, farming, regular sports activity [9].

Blood samples were collected while the participant was seated and in abstinence from smoking for at least one-half hour. Serum concentrations of cholesterol, HDL cholesterol, fasting triglycerides, and glucose were determined by the enzymatic dry chemistry method using a Reflotron apparatus (Roche Diagnostics, Mannheim, Germany). Plasma concentrations of CRP were measured by means of particle-enhanced immunonephelometry with the Behring nephelometer method using N Latex CRP mono reagent (Behring Diagnostics, Westwood, MA). Plasma apo B and A-I levels were measured by immunoturbidimetric method (Turbitimer, Behring Diagnostics). Concentrations of insulin were determined by the chemiluminescent immunometric method using Diagnostic Products (Los Angeles, CA) kits and the autoimmune analyzer Immulite (Diagnostic Products). Serum concentration of total adiponectin was assayed by a sandwich enzyme-linked immunosorbent assay system (Adiponectin ELISA BioVendor; BioVendor Laboratory Medicine, Brno, Czech Republic) at the Acibadem Labnet, Istanbul. External quality control was performed with a reference laboratory in a random selection of 5% to 6% of participants. Homeostasis model assessment was calculated with the following formula [13]: insulin (in micro–international units per liter) ∗ glucose (in millimoles per liter)/22.5.

2.4. Follow-up and study design

Participants were tracked from the fall of 2002 when CT examinations were performed until September 2007 over a

maximum of 5 years (mean, 3.5 years). Although a large part of current analyses is cross-sectional pertaining to year 2002, 2 sets of analyses are prospective in design: (*a*) VAT and body fat mass were related to the smoking status in 1998, and (*b*) VAT values were correlated with the smoking status and certain clinical and biochemical variables at the final examination in 2007.

2.5. Data analysis

Descriptive parameters were shown as mean ± SD or as age-adjusted mean estimate and in percentages. Log-transformed values were used for CRP, insulin, HOMA, and VAT because of their skewed distribution. Spearman correlations were performed with categorical or log-transformed variables. Two-sided *t* tests and Pearson χ^2 tests served to analyze the differences in means and proportions between groups. Analysis of variance comparisons and pairwise comparisons with Bonferroni adjustment were made to detect significance between groups of estimated means. Among men and women, 1 SD of VAT corresponded to 50 and 45 cm^2, respectively. A value of *P* less than .05 on the 2-sided test was considered statistically significant. Statistical analyses were performed using SPSS 10 for Windows (SPSS, Chicago, IL, No. 9026510).

3. Results

The study sample consisted of 79 men and 78 women. Mean ± SD age of the sample was 49 ± 9 years at baseline examination. Sex prevalence, BP, glucose, lipid, apo, and CRP values were similar in this sample to the entire cohort of the Turkish Adult Risk Factor Study. Because subjects at least 70 years of age were excluded, this study sample at baseline was 4 years younger ($P < .001$). They were representative of the middle-aged residents of the metropolis, having (biologically little meaningful) narrower waist circumference (0.6 cm, $P < .03$) and lower BMIs (0.5 kg/m^2, $P < .036$) and with the women being more frequent current smokers (35% vs 17.4%, $P < .001$), but not significantly different with respect to physical activity compared with the entire cohort. Forty-two women were postmenopausal; none was a user of hormone replacement.

Visceral adipose tissue area ranged between 25 and 331 cm^2. Age-adjusted geometric mean VAT was 132.4 ±1.05 cm^2 in men and 107.2 ±1.06 cm^2 in women ($P = .003$). Age-adjusted means for abdominal subcutaneous fat area were larger in women ($P < .001$); sagittal abdominal diameter was similar in the sexes (Table 1). Age-adjusted means of BMI, systolic BP, LDL cholesterol, and fibrinogen were significantly higher, but fasting triglycerides and glucose levels were lower, among women than men.

Table 1
Age-adjusted (48.8 years) characteristics of the study sample (N = 157) at baseline, by sex

	Men	n = 79	Women	n = 78
	Mean	SE	Mean	SE
Unadjusted age, y (SD)	49	9	49	9
Sagittal diameter, cm	22.5	0.36	22.3	0.37
Visceral abdominal fat area,[a] cm^2	132.4[†]	1.05	107.2	1.05
Subcutaneous abdominal fat area, cm^2	220.3[‡]	10.6	335.7	10.7
Percentage body fat	27.5[‡]	0.76	36.5	0.77
Fat mass, kg	22.7[†]	1.00	26.8	1.01
HOMA index[a] (n = 119)	2.10	1.09	1.87	1.09
Waist circumference, cm	91.6	1.17	92.1	1.17
BMI, kg/m^2	27.2*	0.49	28.8	0.5
Systolic BP, mm Hg	126.2[†]	2.42	135.1	2.44
Diastolic BP, mm Hg	80.6	1.44	84.1	1.45
Apo B, g/L (n = 136)	1.15	0.05	1.19	0.05
Fasting insulin,[a] mIU/L (n = 120)	8.91	1.07	7.82	1.07
Total cholesterol, mmol/L	4.68*	0.11	5.03	0.11
HDL cholesterol, mmol/L	0.91[‡]	0.03	1.18	0.03
LDL cholesterol, mmol/L (n = 115)	2.98*	0.11	3.34	0.11
Fasting triglyceride,[a] mmol/L (n = 115)	1.61[†]	1.07	1.24	1.07
Fasting glucose, mmol/L (n = 139)	5.75*	0.15	5.44	0.14
CRP,[a] mg/L (n = 136)	1.81	1.14	1.77	1.17
Apo A-I, g/L (n = 134)	1.29[†]	0.04	1.40	0.04
Fibrinogen,[a] g/L (n = 118)	2.46[†]	0.14	3.06	0.15
Physical activity grade, 1-4	2.41[‡]	0.07	2.05	0.06
Current/former smokers, %	45.6/20.3[‡]		32.1/6.4	

*P less than .05, [†]less than .01, and [‡]less than .001 between men and women.
[a] Geometric means.

3.1. Smoking and other correlates of VAT and body fat mass

Table 2 shows Spearman correlations between VAT and body fat mass with certain inflammatory markers and other risk factors. Both HOMA index and fasting insulin were significantly correlated with VAT as well as with fat mass in men, whereas in women, only HOMA and fat mass, not VAT, were so with each other. Both adiposity variables disclosed significant correlations with CRP in both sexes. Diastolic BP was correlated in women in a much weaker fashion with both adiposity variables than in men. Serum triglyceride and apo B levels were significantly correlated only with VAT in both sexes. Serum adiponectin levels measured 4 years later in 30 men and 40 women were significantly correlated neither with VAT ($P > .6$) nor with fat mass ($r = -0.13$, $P = .51$ in men; $r = +0.25$, $P = .12$ in women). Body mass index, controlled for age, was highly correlated with body fat mass in men ($r = 0.87$) and women ($r = 0.85$).

To focus on the influence of smoking on body fat distribution, data of smoking in 1998 (which had been available in the study participants) and in 2002 were each compared with VAT and fat mass of 2002. When simultaneous 2002 data were analyzed, current-smoking men had similar age-adjusted VAT and fat mass compared with never-smoking men (gray bars in Fig. 1). In contrast, smoking women revealed 21% lower fat mass and 30%

Table 2
Spearman correlation coefficients of visceral adipose tissue[a] and body fat mass with certain risk factors, at baseline

	Visceral adipose tissue, cm^2						Fat mass, kg			
	Men			Women			Men		Women	
	n	*r*	*P*	n	*r*	*P*	*r*	*P*	*r*	*P*
Age, y	79	**0.28**	.012	78	**0.48**	<.001	0.11	.93	0.14	.24
Body fat mass, kg	79	**0.62**	<.001	78	**0.52**	<.001				
HOMA index[a]	57	**0.48**	<.001	62	0.16	.20	**0.48**	<.001	**0.34**	.006
Fasting insulin,[a] mIU/L	58	**0.41**	.001	62	0.15	.25	**0.48**	<.001	0.23	.07
CRP,[a] mg/L	67	**0.37**	.002	69	**0.27**	.023	**0.34**	.005	**0.30**	.013
Systolic BP, mm Hg	79	**0.37**	.001	78	**0.27**	.019	**0.29**	.009	**0.24**	.035
Diastolic BP, mm Hg	79	**0.45**	<.001	78	0.19	.09	**0.50**	<.001	**0.23**	.039
HDL cholesterol, mg/dL	79	−0.21	.07	78	**−0.30**	.008	−0.21	.068	−0.17	.13
Fasting triglyceride,[a] mg/dL	61	**0.32**	.012	55	**0.42**	.001	0.24	.065	0.24	.077
Apo B, mg/dL	70	**0.39**	.001	69	**0.25**	.035	0.15	.23	0.10	.43
Smoking status (0-2)	79	−0.04	.71	78	**−0.40**	<.001	−0.11	.34	**−0.35**	.002
Physical activity grade I-IV	79	**−0.29**	.009	78	−0.12	.28	−0.19	.096	−0.16	.17

Fibrinogen not significant. Bold fonts highlight significant values.
[a] Log transformed.

lower VAT than never-smoking women (6.2 kg, $P = .026$ and 37 cm^2, $P = .002$, respectively). Similar relations were found when smoking data of 1998 were considered (black bars in Fig. 1); namely, female current smokers subsequently displayed mean VAT that was 26% lower than that of female never smokers ($P = .005$). This indicates that current smoking in women preceded by 4 years the recorded lower visceral fat area than in never-smoking women.

3.2. Visceral adipose tissue area per unit body fat

As an index of VAT accumulation, the ratio of VAT per unit fat mass was calculated in consideration that this is preferable to the ratio per unit BMI when both values are available because, especially in women, BMI was less well correlated with VAT ($r = 0.62$) than body fat mass ($r = 0.82$) [10]. The VAT per fat mass ratio was correlated with age in men ($r = 0.41$, $P < .001$) and women ($r = 0.36$, $P = .001$). For 1 kg of total body fat mass, age-adjusted men and women had geometric mean VAT to fat mass ratio (5.74 vs 3.99 cm^2/kg, $P < .001$) indicating a 1.44-fold higher susceptibility of men to visceral fat accumulation than women (Table 3). Female sex and current smoking interacted to yield a lower age-controlled geometric mean VAT to fat mass ratio of 22.1% ($P = .06$) in this simple model that explained 37% of the variance of this ratio ($P < .001$).

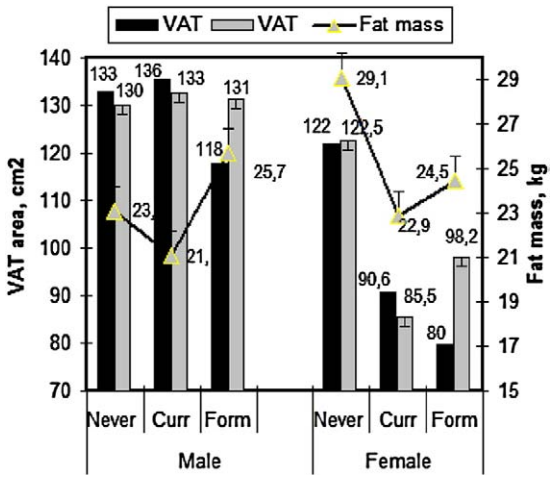

Fig. 1. Visceral adiposity tissue and total fat mass in categories of cigarette smoking, by sex. Age-adjusted VAT values are provided for both the smoking status 4 years preceding (black bars) the tomographic examination and the simultaneous status (gray bars). Differences in men were not significant. Significantly lower (by 6.2 kg) fat mass and 26% ($P = .005$) and 30% ($P = .002$) lower VAT area among current- vs never-smoking women were noted.

3.3. Independent covariates of VAT

The association between HOMA and VAT, when adjusted for age and physical activity, was highly significant in men, but not in women (Supplementary Table 1). When smoking status was added to the model, no change was observed among men, although the explained variance in VAT nearly doubled in women in whom current smoking was significantly associated, whereas HOMA's association with VAT was attenuated further.

Table 4 demonstrates findings of a multiple linear regression analysis in seeking best covariates between VAT

Table 3
Age-adjusted visceral adipose tissue to fat mass ratio among men and women, by smoking status at baseline examination

	Women			Men		
	n	Mean[a]	SE	n	Mean[a]	SE
Never smokers	48	4.44	1.05	27	6.07	1.05
Former smokers	5	4.24	1.18	16	5.31	1.07
Current smokers	25	3.94*	1.08	36	6.87*	1.05
P value (current vs never)	.65			.26		

[a] Geometric mean.
* Interaction between sex and smoking, −22%, $P = .06$.

Table 4
Multiple linear regression analysis* between visceral adipose tissue (square centimeters)[a] as dependent variable and certain covariates at baseline

Model 1	β coefficient	P value	β coefficient	P value	β coefficient	P value
	Total, n = 130		Men, n = 63		Women, n = 67	
HDL cholesterol, mg/dL	0.985	<.001	0.994	.37	0.982	.001
Smoking status (2-0)	0.912	.029	0.97	.66	0.858	.009
Apo B, mg/dL	1.001	.19	1.003	.048	1.000	.96
CRP,[a] mg/L	1.11	.19	1.27	.042	0.94	.62
Systolic BP, mm Hg	1.002	.15	1.006	.041	1.001	.54
Variance explained (r^2)	.32	<.001	.23	.009	.46	<.001
Model 2	Total, n = 108*		Men, n = 50		Women, n = 58	
HDL cholesterol, mg/dL	0.981	<.001	0.992	.26	0.977	<.001
HOMA index[a]	1.46	.010	1.33	.22	1.37	.18
Smoking status (2-0)	0.903	.025	0.94	.40	0.867	.026
Apo B, mg/dL	1.001	.32	1.002	.25	1.000	.77
CRP,[a] mg/L	1.07	.41	1.28	.075	0.92	.42
Systolic BP, mm Hg	1.001	.77	1.004	.36	1.000	.88
Variance explained (r^2)	.39	<.001	.29	.011	.48	<.001

[a] Log transformed.
* Adjusted also for sex (β = 0.89, P = .20 in model 1), age (significant only in women, +29% per decade, P < .001), and physical activity grade (not significant).

and baseline risk variables related to inflammation/insulin resistance. In both models, more than a third of the variance of VAT was explained. In the model not including HOMA, VAT was associated significantly in men with systolic BP, apo B, and CRP (each $P < .05$), in contrast to being associated in women with age, smoking status, and HDL cholesterol (each $P \leq .01$). Current smoking was associated with 25% lower VAT than never smoking in women. In the model comprising HOMA that itself proved a significant covariate ($P = .01$), no more than minimal modifications occurred in women; but in men, BP and apo B attenuated, whereas CRP was only marginally changed (significance reduced likely because of smaller sample size).

3.4. Visceral fat vs future BP, smoking, and physical activity

Certain variables of a later survey, at a mean 3.5 years from baseline examination, were also correlated with baseline VAT measures with the purpose of evaluating long-term relationships. Table 5 shows significant positive correlations of VAT with subsequent systolic BP in either sex ($P < .03$) and inverse ones in women with smoking status ($P = .001$) and physical activity grade ($P = .007$).

Table 5
Spearman correlation coefficients of visceral adipose tissue[a] at baseline with BP, smoking status, and other risk factors, at final survey

	Men			Women		
	n	r	P	n	r	P
Systolic BP, mm Hg	78	0.25	.029	78	0.37	.001
Diastolic BP, mm Hg	78	0.19	.095	78	0.23	.046
Smoking status (0-2)	79	−0.03	.80	78	−0.37	.001
Physical activity grade, I-IV	74	−0.19	.11	76	−0.31	.007
Fibrinogen, g/L	61	−0.02	.87	56	−0.03	.80

[a] Log transformed.

4. Discussion

In this study on a sample of residents of the metropolis of Istanbul, Turkey, age independently determined VAT only in women; and sex interacted with cigarette smoking to significantly inhibit body fat mass and visceral fat accumulation, important novel findings. A sex difference existed also regarding the significant associations with visceral fat of HOMA and proinflammatory (apo B and CRP) markers primarily in men and the anti-inflammatory particle HDL mainly in women. Men accumulated VAT per unit of fat mass at a rate of more than 1.4-fold as women. Implications of these findings may include sex-modulated contribution of visceral and overall fatness to the dynamics of cardiometabolic disorders such as diabetes, MetS, and coronary heart disease for which we currently have evidence (scope of another manuscript).

4.1. Cigarette smoking inhibits visceral fat accumulation

The inverse association of smoking status and VAT selectively in women is the most striking finding of the present study, although it is not surprising to the authors because previous prospective analyses had shown that smoking protected men [14] and women from abdominal obesity [15] as well as women from the development of MetS and type 2 diabetes mellitus [16]. The current study first documents though that the observed favorable effect of smoking in Turkish women is partly mediated via VAT accumulation. The stated relationship to VAT in women was consistently significant on analyses with preceding, simulta-

neous, and subsequent smoking status. To our knowledge, no study reported analyses of smoking status with VAT in women; and only one study has been conducted in men in whom positive but nonsignificant relation to VAT was observed [6]. In contrast, smoking is considered to aggravate abdominal obesity in most populations. Of particular interest was the current finding of a reduced visceral fat accumulation in female smokers beyond an effect of reduced overall fatness because adverse cardiometabolic consequences of visceral fat are greater than overall fatness.

4.2. Sex, inflammatory markers, dyslipidemia, and visceral fat

The lack of an independent association between CRP and VAT (and absent correlation with fat mass) among women is in line with our previous prospective analysis of determinants of elevated CRP [17]. Baseline CRP level, presumably reflecting mainly genetic determinants, was overwhelming as a determinant in women in whom levels were not independently associated with waist circumference (CRP tended to be associated with fasting insulin rather than waist girth, and risk of developing an elevated CRP was not increased in women [17]). In contrast, in men, apart from the major role of baseline CRP and significant roles of such environmental factors as cigarette smoking, low family income, and serum apo B levels, CRP tended to be associated with waist circumference, being in agreement with the significantly correlated VAT in the current study.

Findings on the relationship between body fat composition and inflammatory markers, dyslipidemia, and visceral fat have not been consistent [18-21]. A cross-sectional analysis of the Framingham study on 1250 elderly participants found visceral adiposity to be associated independently with CRP, interleukin-6, and monocyte chemoattractant protein–1, without major difference across sexes [18]. Likewise, interleukin-6 levels were significantly higher among 189 men with high visceral fat and were found to contribute independently to the variation of fasting insulin, whereas tumor necrosis factor–α was associated rather with BMI [19]. In contrast, in studying 1934 black and white men and women, Vega et al [7] found that intraperitoneal fat did not contribute independently to the association of percentage total fat with CRP in white women, but did so in men; intraperitoneal fat explained most of the variance in insulin levels in all race and sex groups. Increased insulin resistance was predicted prospectively also by greater visceral adiposity at baseline among 306 Japanese Americans independently of abdominal adipose tissues [20]. Results obtained by Garg [21], however, supported a role for excess subcutaneous truncal fat rather than intraperitoneal or visceral fat in causing insulin resistance in nondiabetic or diabetic subjects. These observations, along with a demonstrated insignificant reduction of incident coronary heart disease risk in female current smokers in prospective multiadjusted evaluations [17], should not be interpreted that an overall health benefit may be obtained from active smoking in Turkish women, given the potential hazards on cancer and obstructive pulmonary disease.

As regards the lipoprotein profile, whereas subcutaneous adipose tissue was not independently related in 382 subjects with type 2 diabetes mellitus, higher visceral fat independent of BMI was associated with higher very low-density lipoprotein and LDL particle number, larger very low-density lipoprotein particles, and smaller LDL and HDL particles [22]. A deterioration of lipoprotein lipids observed in the study by Pascot et al [23] in women with impaired glucose tolerance was largely related to increased visceral fat depot found in obese women, but overall fatness was not specifically evaluated. In 55 early postmenopausal women, the intraabdominal fat was found to strongly influence insulin sensitivity and plasma triglyceride levels, whereas plasma free fatty acids were closely related to the amount of subcutaneous fat [24]. Some investigators [2,25] propose that abdominal subcutaneous fat carries as much or more pathogenic significance for the MetS as visceral fat.

Related findings in the present study may be summarily interpreted as follows. Visceral fat is the determining compartment in men in each mentioned aspect except for insulin resistance in which total fat mass is equally associated as well. Among women, fat mass and visceral fat seem to contribute equally to inflammatory markers and BP, whereas visceral fat is primarily associated with atherogenic dyslipidemia. This suggests that sex is an important modulator of the relationships between body fat compartments and risk components. Of note is an interrelationship alike Turkish women in 30 overweight prepubertal children, namely, that insulin sensitivity was independently and negatively associated with subcutaneous abdominal rather than visceral adipose tissue, which was correlated with CRP [26].

4.3. Correlation of visceral fat with BP and physical activity

In men with essential hypertension, fat was found to be preferentially accumulated intraabdominally and intrathoracically; and visceral adiposity was quantitatively related to both level of BP and severity of insulin resistance [27]. Our findings on a population at large are consistent with this observation inasmuch as systolic BP was significantly and linearly associated with simultaneous VAT among men (partly mediated by HOMA), as was VAT correlated in both sexes with subsequent systolic pressure in the prospective analysis.

4.3.1. Clinical implications

Present findings are consistent, particularly among men, with the notion that visceral rather than subcutaneous fat deposition seems to be generally contributing more to the pathogenesis of cardiometabolic risk. Subcutaneous fat (due to its large mass) may be a contributor equally or to a greater extent among Turkish women (confirmed by us in an outcome study). Thus, the 2 hypotheses on the pathogenic

significance of visceral and subcutaneous fat for cardiometabolic risk apply to both Turkish men and women at varying extent. This sex differential in relation to central obesity/overall fatness may have potential clinical implications in terms of prevention and therapeutically.

4.3.2. Limitations and strengths

The studied sample size may be considered limited but is larger than most published ones in which abdominal imaging techniques were used. Conclusions reached may not be fully applicable to a population in which the effect of smoking on abdominal obesity is unfavorable or the prevalence of MetS is far lower than in the present one. As strengths of this study, the following may be cited: the inclusion of both sexes; its being representative of a middle-aged general population; the concomitant availability of data on body fat distribution, anthropometric indices, and related diverse biochemical determinations; and the partly prospective nature of the study.

We conclude that sex is a determinant of the dynamics of cardiometabolic risk by way of modulating the biologic activity of visceral and overall adiposity in Turkish adults. Body fat mass and accumulation of visceral fat are significantly inhibited by cigarette smoking only in women. Atherogenic dyslipidemia in both sexes and inflammatory markers in men are independently associated primarily with visceral fat rather than fat mass. In women, insulin resistance and visceral fat seem to be poorly associated.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.metabol.2009.02.029.

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