Visceral Adipose Tissue Cutoffs Associated With Metabolic Risk Factors for Coronary Heart Disease in Women

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OBJECTIVE — This study determined whether there is a critical level of visceral adipose tissue (VAT) associated with elevated coronary heart disease (CHD) risk factors in a cohort of women >45 years of age.

RESEARCH DESIGN AND METHODS — Measurements of body composition (dual-energy X-ray absorptiometry), body fat distribution (computed tomography), fasting and 2-h postprandial (75-g) glucose concentrations, and fasting lipoprotein lipid and insulin concentrations were performed in 233 perimenopausal (9%) and postmenopausal women (age 59 ± 6 years, 79% Caucasian, 16% on hormone replacement therapy).

RESULTS — Women in the lowest VAT quintile (≤105 cm^2) had higher concentrations of HDL and HDL_2 cholesterol, lower LDL/HDL cholesterol ratios and triglyceride concentrations, and lower fasting glucose and insulin concentrations than women in the remaining four quintiles (P values <0.05–0.001). Women in the second lowest VAT quintile (106–139 cm^2) had higher HDL and HDL_2 cholesterol and lower LDL/HDL ratios than women with a VAT ≥163 cm^2 ($P <$ 0.05). Logistic regression analyses showed that women with a VAT of 106–162 cm^2 are 2.5 times more likely to have a low HDL cholesterol ($P < 0.05$), while women with a VAT ≥163 cm^2 are 5.5 times more likely to have a low HDL cholesterol ($P < 0.01$) and ~4.0 times more likely to have a high LDL/HDL ratio ($P < 0.05$) compared with women with a VAT ≤105 cm^2. Women with a VAT ≥163 cm^2 are at a higher risk of having impaired glucose tolerance ($P < 0.01$).

CONCLUSIONS — A VAT ≥106 cm^2 is associated with an elevated risk, and a VAT ≥163 cm^2 with an even greater risk, for these metabolic CHD risk factors compared with women with a VAT ≤105 cm^2. These values may prove useful for defining "visceral obesity" and for identifying women most likely to benefit from preventative interventions.

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Obesity is a significant health problem, with nearly one-half of U.S. women and men over 20 years of age considered to be overweight (1). The current criterion used for characterizing individuals as overweight (BMI 25–29.9 kg/m^2) or obese (>30 kg/m^2) were derived from epidemiological evidence showing that the presence of adiposity-related comorbidities increases abruptly beyond these cut points (2,3). However, obesity is a heterogeneous disorder in that the storage depot for excess calories differs widely between individuals, and these differences in fat distribution confer differential health risks. An excess of fat in the abdominal region is a better predictor of coronary heart disease (CHD) and type 2 diabetes, as well as their risk factors (dyslipidemia, glucose intolerance, and hyperinsulinemia), than the total amount of adipose tissue (4–7).

Most studies designed to assess the health risks of body fat distribution have used anthropometric measures such as waist circumference or waist-to-hip ratio (WHR) to estimate the amount of abdominal adipose tissue. Both of these measures are known independent predictors of metabolic risk factors for CHD in men and women, and it is likely that this association is due to an enlargement of visceral fat stores. In fact, the associations between risk factors and visceral adipose tissue (VAT), measured directly with computed tomography (CT) or magnetic imaging resonance, are stronger than the associations observed with WHR or waist circumference (8–12). In addition, visceral fat accumulation also contributes to CHD risk factors in healthy, nonobese individuals (10,13–15). Thus, the amount of VAT may be the best predictor of obesity-related metabolic complications and could be more clinically relevant than the quantity of total body fat for assessment of risk status.

There are well-known and physically obvious sex differences in the propensity to store fat in the abdominal region. On average, men have twice as much visceral fat as premenopausal women when matched for total body fat (16,17). However, the accumulation of visceral fat may be more detrimental to health in women than in men. This is evident from studies showing that the relative risk of death from cardiovascular disease is increased eight times in women with the highest WHR (7) but only two times in men with the highest WHR (18). These sex differences suggest that it may be important to assess the relationship of elevated health

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Abbreviations: CHD, coronary heart disease; CT, computed tomography; HRT, hormone replacement therapy; VAT, visceral adipose tissue; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

risk to VAT in women independently of men.

Although the association between VAT and risk and incidence of disease is well established, the specific amount of VAT that confers a health risk in women is not definitely known. To our knowledge, there are data from only three studies that attempted to define a "critical" cut point of VAT (19–21). For the most part, these studies were performed in young and middle-aged men and premenopausal women. Our hypothesis is that there is a critical level of VAT that defines postmenopausal women at heightened risk for CHD. Thus, the purpose of this study was to determine whether there is a critical level of VAT associated with elevated CHD risk factors in a cohort of older women. In addition, because of the cost and radiation exposure associated with direct measurement of VAT, we assessed whether the waist circumference of these women provided an accurate estimate of this VAT cut point.

RESEARCH DESIGN AND METHODS

— The subjects for this study included peri- and postmenopausal women (at least 45 years of age) who were originally recruited for various weight loss and exercise training studies at the University of Maryland in Baltimore. Women were initially screened via telephone and excluded from participation if they were pregnant, were premenopausal (i.e., regular menstrual cycles), had smoked in the past 5 years, were regular exercisers (>15 min twice a week), had significant weight change (±5%) in the past year, or were taking antidepressants or medications affecting lipid or glucose metabolism. Perimenopausal women were those with irregular menstrual cycles not associated with pathology, such as polycystic ovarian disease, in the 6 months before the study. Postmenopausal women had no menses for at least 1 year before the study and follicle-stimulating hormone values >20 mIU/ml.

Written informed consent was obtained on the first clinic visit from each woman according to the guidelines of the University of Maryland Institutional Review Board for Human Research. Initial screening evaluations, including a medical history, physical examination, 12-lead resting electrocardiogram, fasting blood profile (complete blood count and Chem 18), and graded exercise stress test (22) were performed to exclude women with evidence of ischemia, hypertriglyceridemia (>400 mg/dl), untreated hypertension (blood pressure >160/90 mmHg), cancer, liver, renal, or hematological disease, or other medical disorders. A total of 233 women met these criteria, and their baseline data were used in the cross-sectional secondary analysis for this study.

Procedures

Measurements of body composition, body fat distribution, fasting and 2-h postprandial (75-g) glucose concentrations (23), and fasting lipoprotein lipid and insulin concentrations were conducted over the course of 2 days. A fasting blood sample was drawn on both days to provide a duplicate measurement of lipoprotein lipids, and the values reported are the average of these 2 days. If the total cholesterol and triglyceride values differed by >5%, or the HDL cholesterol values differed by >10%, a third sample was drawn, and the values reported are the average of these measurements.

Body composition. Height and weight were measured and BMI calculated as weight in kilograms divided by the square of height in meters. WHR was calculated from the duplicate measurement of the minimal waist circumference to the circumference of the maximal gluteal protuberance. Waist (minimal circumference) and hip (maximal gluteal protuberance) circumferences were measured in duplicate. Percent body fat, fat-free (bone and muscle) mass, and adipose tissue mass were measured using dual-energy X-ray absorptiometry (DPX-L; Lunar Radiation, Madison, WI). A single-slice CT scan taken midway between L4 and L5 was performed using a GE Hi-Light CT scanner to measure abdominal VAT and subcutaneous adipose tissue areas, as previously described (24).

Lipoprotein lipids and glucose and insulin values. Venous blood samples for the measurement of lipoprotein lipids, glucose, and insulin were collected in chilled tubes containing 1 mg EDTA per milliliter of blood. Plasma was separated by centrifugation at 4°C, and lipoprotein lipids were measured as previously described (25). In our laboratory, the inter- and intra-assay coefficients of variation were 6.2 and 1.5%, respectively, for the measurement of total cholesterol, 7.6 and 2.6% for triglycerides, 9.2 and 2.7% for HDL cholesterol, and 7.6 and 2.8% for LDL cholesterol. Glucose was measured using the glucose oxidase method (Beckman Glucose Analyzer; Beckman, Fullerton, CA), and insulin was measured by radioimmunoassay with an insulin-specific antibody (cross-reactivity with proinsulin <0.2%) (Linco, St. Louis, MO). The lower limit of detection of this assay in our laboratory is 12 pmol/l. Intra- and interassay coefficients of variation of pooled control sera average 5 and 9%, respectively.

Statistics. Statistical analyses were performed using SPSS version 10.1. Data were first tested for a normal distribution using the Shapiro-Wilk test for normality. Triglyceride and HDL_2 cholesterol concentrations were not normally distributed. Log transformation normalized the distribution of both variables so the logarithm of these data were used for parametric statistical analyses. Partial correlation coefficients adjusted for age and race were computed to identify statistically significant correlations between VAT and disease risk factors. The level of VAT associated with elevated CHD risk factors was determined in two ways. First, women were divided into quintiles based on their level of VAT (n = 46–47 per group) and risk factors were compared between these groups using ANCOVA with calculation of simple contrasts and controlling for age and race. Next, logistic regression analyses, adjusted for age and race, was used to calculate the relative risks for having a low HDL cholesterol (<1.0 mmol/l or 40 mg/dl) (26), hypertriglyceridemia (≥1.7 mmol/l or 150 mg/dl) (26), high LDL/HDL cholesterol ratio (≥3.0), and impaired glucose tolerance (2-h glucose >7.8 mmol/l or 140 mg/dl [23]). The level of significance was set at $P < 0.05$, and all data are reported as mean ± SD.

RESULTS

Descriptive statistics

The women in this study ranged in age from 45 to 73 years (59 ± 6 years). Of the 233 subjects, 22 were perimenopausal (9%) and 211 postmenopausal (91%) and 50 were African American (21%) and 183 Caucasian (79%). Although no women were on lipid-lowering medications, some did use hormone replacement therapy (HRT), nonsteroidal anti-inflammatory drugs, and antihypertensive medi-

Table 1—*Body composition, body fat distribution, and risk factors in African-American and Caucasian women*

	Caucasian	African American
n	183	50
Body composition		
Weight (kg)	84 ± 13 (52–118)	94 ± 14 (69–130)
Height (cm)	163 ± 6 (143–178)	164 ± 6 (151–181)
BMI (kg/m^2)	31 ± 6 (20–43)	35 ± 4 (27–43)
Percent body fat	46 ± 8 (21–59)	46 ± 9 (28–55)
Fat mass (kg)	39 ± 9 (11–69)	44 ± 9 (30–64)
Lean mass (kg)	41 ± 7 (32–54)	44 ± 9 (35–63)
VAT (cm^2)	158 ± 58 (26–386)	138 ± 47 (71–274)
SAT (cm^2)	439 ± 117 (87–801)	523 ± 117 (275–800)
Waist (cm)	94 ± 11 (63–134)	99 ± 10 (77–117)
Medication use		
HRT	17%	10%
NSAID	9%	8%
Antihypertensives	5%	11%
Risk factors		
Total cholesterol (mmol/l)	5.15 ± 1.13 (1.71–7.91)	4.85 ± 0.85 (2.43–7.06)
LDL cholesterol (mmol/l)	3.38 ± 0.82 (1.27–6.05)	3.08 ± 0.66 (1.81–4.45)
HDL cholesterol (mmol/l)	1.32 ± 0.34 (0.72–2.33)	1.33 ± 0.30 (0.75–2.09)
HDL_2 cholesterol (mmol/l)	0.18 (0.05–0.27)	0.19* (0.06–0.26)
LDL/HDL cholesterol	2.72 ± 0.92 (0.61–6.32)	2.44 ± 0.73 (1.03–3.92)
Triglyceride (mmol/l)	1.47 (0.44–4.06)	1.13* (0.58–2.74)
Fasting insulin (pmol/l)	62 ± 33 (14–186)	100 ± 38 (44–208)
Fasting glucose (mmol/l)	5.27* (4.39–7.36)	5.38* (4.11–6.94)
2-h glucose (mmol/l)	6.77* (3.08–16.49)	7.11* (4.60–13.49)
Systolic blood pressure (mmHg)	128 ± 20 (90–203)	132 ± 16 (102–168)
Diastolic blood pressure (mmHg)	78 ± 8 (59–109)	82 ± 11 (50–100)

Data are mean ± SD (range) or median (range), unless otherwise specified. NSAID, nonsteroidal anti-inflammatory drug; SAT, subcutaneous abdominal adipose tissue.

cations (Table 1). A total of eight women were diagnosed with diabetes based on a 2-h postprandial glucose >200 mg/dl. As shown in Table 1, although the majority of women were overweight/obese, there was a wide range in body weight, body fatness, abdominal fat distribution, and metabolic risk factors among both African-American and Caucasian women.

Associations between VAT area, age, HRT use, and race

VAT was significantly related to total fat mass ($r = 0.43$, $P < 0.001$) and age ($r = 0.33$, $P < 0.001$). Independent of age, there were no differences in VAT between peri- and postmenopausal women. Likewise, VAT did not differ between women on and off HRT. However, African-American women had less VAT than Caucasian women ($P < 0.05$) (Table 1) despite having a higher fat mass ($P < 0.05$) and no differences in age or HRT use.

Associations between metabolic CHD risk factors and VAT

Partial correlation coefficients were calculated to determine whether there was a linear relationship between metabolic CHD risk factors and VAT. This analysis was adjusted for age and race, but not for total fat mass, since we were interested in assessing the association between risk factors and the absolute amount of VAT. Concentrations of total and LDL cholesterol and systolic and diastolic blood pressure did not correlate with VAT in these women; however, all other risk factors were related to VAT (Table 2).

We also assessed whether there were racial differences in the relationships between metabolic CHD risk factors and VAT or waist by including a race times VAT or race times waist interaction term in the regression model. None of the interactions were significant for any of the dependent variables tested, indicating that in our sample of women, the relationships between these CHD risk factors and VAT or waist are similar in Caucasian and African-American women. Thus, data were combined for further analyses.

Table 2—*Partial correlation coefficients between metabolic CHD risk factors and VAT area and waist circumference*

	VAT area	Waist circumference
Total cholesterol	0.04	0.12
LDL cholesterol	0.04	0.10
HDL cholesterol	−0.39*	−0.37*
Log HDL_2 cholesterol	−0.28*	−0.2†
LDL/HDL cholesterol	0.20†	0.13
Log triglyceride	0.25*	0.21†
Fasting insulin	0.42*	0.42*
Fasting glucose	0.28*	0.24†
2-h glucose	0.24*	0.23†

Analysis adjusted for age and race. *$P < 0.001$; †$P < 0.01$.

Figure 1 shows the average lipoprotein lipid concentrations by quintile of VAT. Women in the lowest VAT quintile (≤105 cm^2) had significantly higher concentrations of HDL and HDL_2 cholesterol and lower LDL/HDL cholesterol ratios and triglyceride concentrations than women in the remaining four quintiles (P values <0.05–0.001). Women in the second lowest VAT quintile (106–139 cm^2) had higher HDL and HDL_2 cholesterol concentrations and lower LDL/HDL cholesterol ratios than women with a VAT ≥163 cm^2 ($P < 0.05$), as well as had lower triglyceride concentrations than women with a VAT ≥193 cm^2 ($P < 0.05$).

The glucose and insulin risk factors are shown by VAT quintile in Fig. 2. Women in the lowest VAT quintile (≤105 cm^2) had lower fasting glucose concentrations than women in the remaining four quintiles (P values <0.01–0.001) and had lower 2-h glucose concentrations than women in the two highest VAT quintiles (≥163 cm^2, $P < 0.05$). Women in the lowest VAT quintile had lower fasting insulin concentrations than women in the remaining quintiles (P values <0.05–0.001), and women in the three lowest VAT quintiles had lower insulin concentrations than women in the two highest VAT quintiles (≥163 cm^2, $P < 0.05$).

Relative risks

Table 3 shows the age- and race-adjusted relative risks for having a defined CHD risk factor in women with a VAT greater

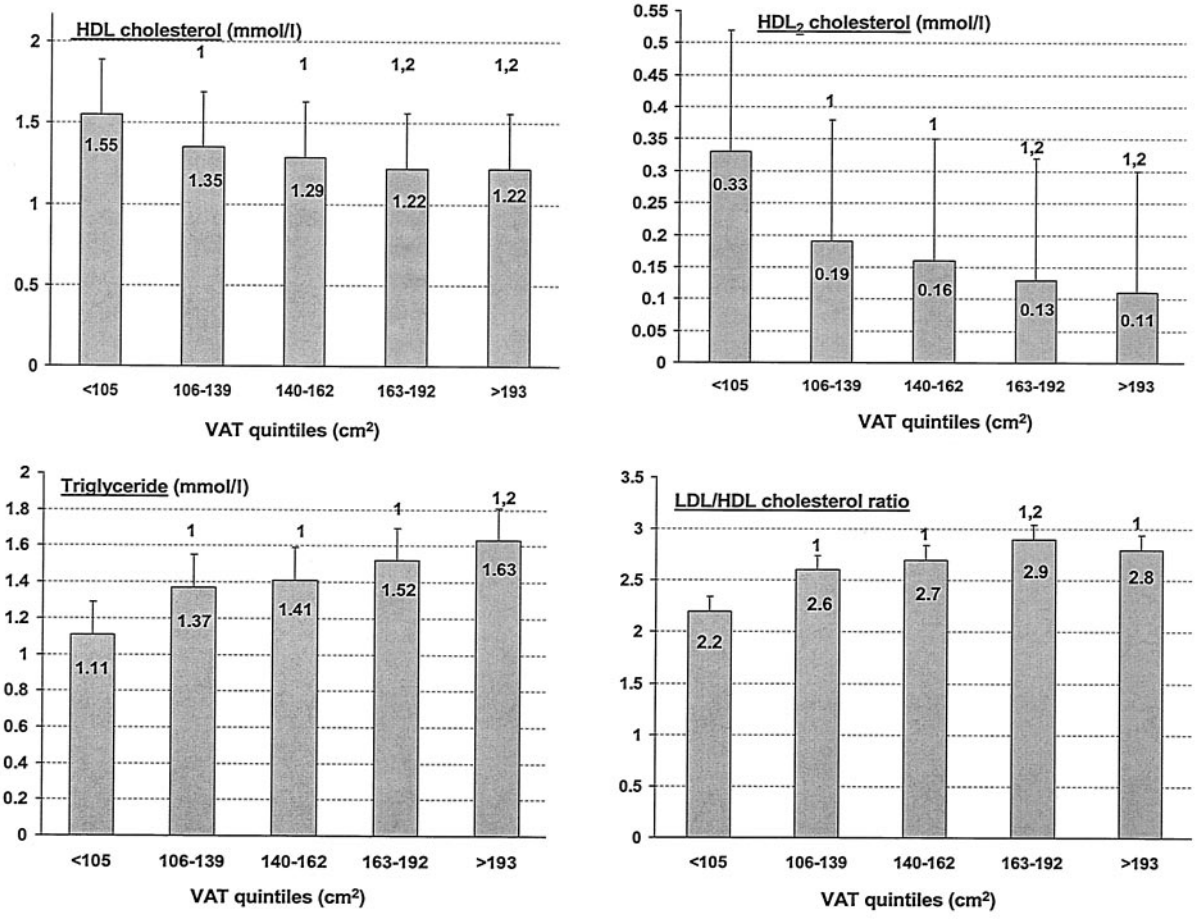

Figure 1—*Associations between lipoprotein lipid concentrations and VAT. VAT groups were derived from the quintile distribution of this sample. Numbers signify* $P < 0.05$ *from quintiles 1 and 2, respectively. Analyses adjusted for age and race.*

than the first quintile (i.e., ≥106 cm^2). We did not include HDL_2 cholesterol or fasting glucose and insulin in this analysis because there are no established criteria for HDL_2 cholesterol and insulin, and there were only 19 women with impaired fasting glucose (≥110 mg/dl). Women with a VAT level of 106–162 cm^2 are ~2.5 times more likely to have a low

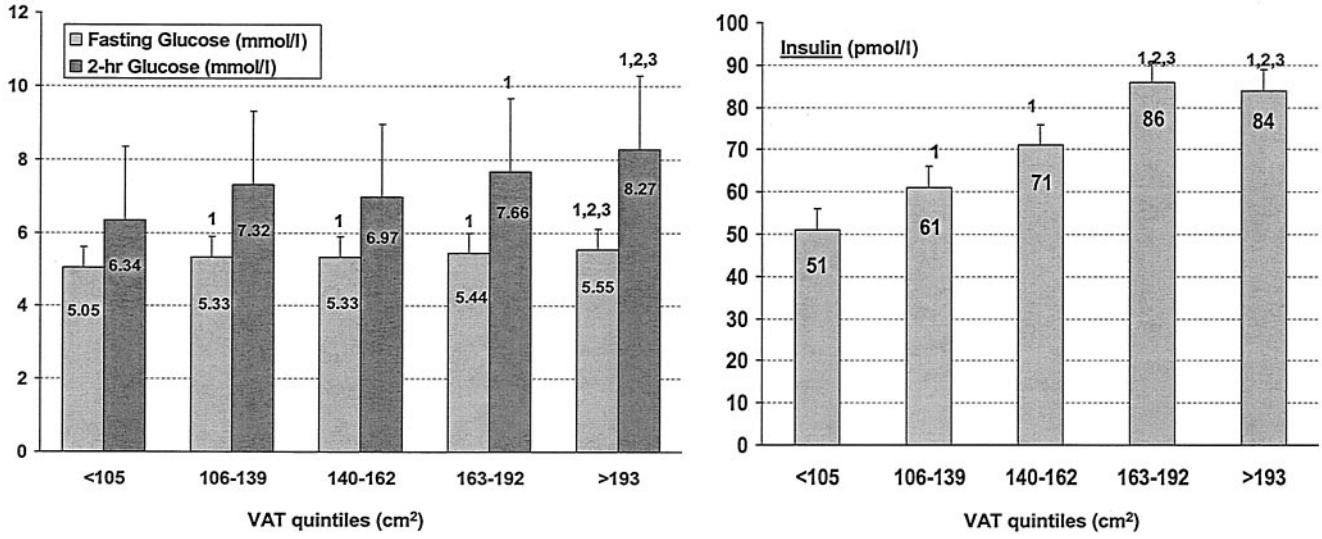

Figure 2—*Associations between fasting glucose, 2-h glucose, and insulin concentrations and VAT. VAT groups were derived from the quintile distribution of this sample. Numbers signify* $P < 0.05$ *from quintiles 1, 2, and 3, respectively. Analyses adjusted for age and race.*

Table 3—*Relative risks (95% CI) for risk factors by level of VAT*

	HDL cholesterol <1.0 mmol/l (40 mg/dl)	Triglyceride >1.7 mmol/l (150 mg/dl)	LDL/HDL cholesterol ratio >3.0	2-h glucose >7.8 mmol/l (140 mg/dl)
n	117	80	78	72
VAT				
≤105 cm^2	1.0	1.0	1.0	1.0
106–139 cm^2	2.5 (1.1–6.0)*	1.7 (0.6–4.5)	2.5 (0.9–6.9)	2.1 (0.8–6.2)
140–162 cm^2	2.3 (1.0–5.9)*	1.7 (0.6–4.5)	1.8 (0.6–5.1)	2.0 (0.7–5.8)
163–192 cm^2	5.5 (2.2–13.7)†	1.7 (0.6–4.5)	4.2 (1.5–11.4)†	4.2 (1.5–12.2)†
≥193 cm^2	5.5 (2.1–14.0)†	3.3 (1.2–8.6)*	3.6 (1.3–10.1)*	9.5 (3.2–27.9)†
Waist circumference				
<88 cm	1.0	1.0	1.0	1.0
89–95 cm	2.3 (1.1–4.9)*	0.6 (0.2–2.5)	2.0 (1.0–4.3)*	1.7 (0.4–6.6)
≥96 cm	2.1 (1.1–3.9)*	1.4 (0.9–3.1)	0.7 (0.6–1.3)	3.2 (1.5–5.3)*

VAT groups are determined by the quintile distribution of the sample (n = 46–47 per group). Waist circumference groups are those corresponding to a VAT level of 106 cm^2 (89 cm) and 163 cm^2 (96 cm) (n = 63, 52, and 111, respectively). *$P < 0.05$; †$P < 0.01$ (analyses adjusted for age and race).

HDL cholesterol ($P < 0.05$), while women with a VAT ≥163 cm^2 are ~5.5 times more likely to have a low HDL cholesterol ($P < 0.01$) and ~4.0 times more likely to have a high LDL/HDL cholesterol ratio ($P < 0.05$) compared with women with a VAT ≤105 cm^2. In addition, women with a VAT level >193 cm^2 are 3.3 times more likely to be hypertriglyceridemic ($P < 0.05$). Women with a VAT level ≥163 cm^2 are at a higher risk of having impaired glucose tolerance ($P < 0.01$). Thus, a VAT ≥106 cm^2 is associated with a significantly elevated risk and a VAT ≥163 cm^2 with an even greater risk for these metabolic CHD risk factors.

Relationship of waist circumference to VAT

Waist circumference correlated positively with VAT ($r = 0.60$, $P < 0.001$), although, as seen in Fig. 3, there is a great deal of variability in waist circumference for a given VAT level. All risk factors, except total and LDL cholesterol and the ratio of LDL/HDL cholesterol, were related to waist circumference (Table 2).

We were interested in determining whether waist circumference provided an accurate estimate of these high-risk (≥106 cm^2) and very high-risk (≥163 cm^2) VAT cut points. We used the equation of the regression line of the waist circumference–to–VAT relationship to determine the corresponding high-risk (89 cm) and very high-risk (96 cm) waist circumferences and then tested whether women with waist circumference >89 cm were at a heightened risk of having adverse CHD risk factors (Table 3). This analysis showed that a waist circumference of 89–95 cm was associated with low HDL cholesterol and high LDL/HDL cholesterol ratio ($P < 0.05$), although the relative risks for these conditions did not increase with increasing waist circumference. In addition, a high waist circumference (i.e., >89 cm) was not associated with a high triglyceride concentration. However, women with a waist circumference ≥96 cm did have a 3.2-fold increased risk for impaired glucose tolerance ($P < 0.05$).

CONCLUSIONS— The results of this study show that in middle-aged and older women, a VAT area ≥106 cm^2 is associated with elevated risk for having low HDL cholesterol concentrations, hypertriglyceridemia, high LDL/HDL cholesterol ratio, impaired glucose tolerance, and hyperinsulinemia compared with those with a VAT ≤105 cm^2. A VAT ≥163 cm^2 is predictive of an even greater risk for these metabolic risk factors for CHD, relative to lower VAT levels. These analyses were adjusted for age and race because of the effects of these factors on

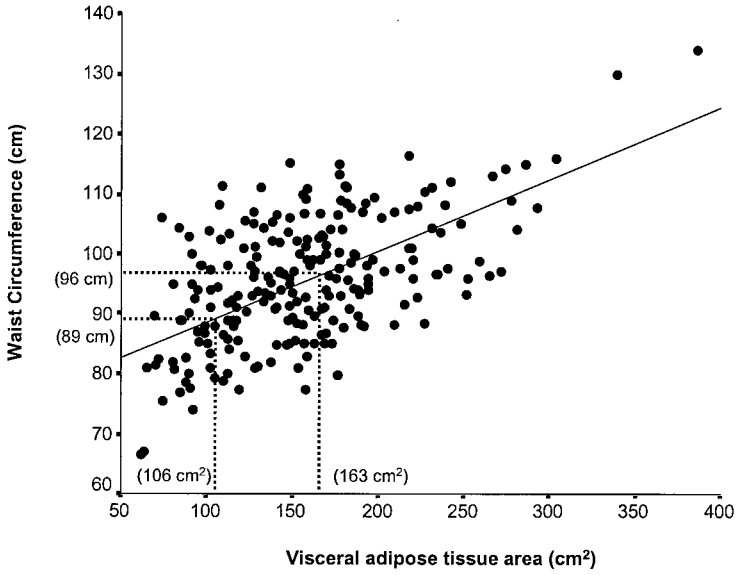

Figure 3—*Relationship between waist circumference and VAT (r = 0.60, P < 0.0001) [waist circumference = 0.119 (VAT) + 76.75].*

the selective accumulation of visceral fat. Although visceral fat mass is, in part, affected by total body fat mass, we chose not to adjust our analyses for total fat mass since we were more interested in determining an absolute level of VAT associated with CHD risk factors. This decision was based on evidence showing that there are large interindividual differences in the amount of visceral fat at any level of body fat content (27,28).

This critical VAT cutoff of 106 cm^2 is similar to the value of 110 cm^2, which was shown by Williams et al. (21) to be associated with elevated risk factors for CHD, including high total cholesterol and triglycerides, low HDL cholesterol, and elevated blood pressure in women. In addition, this value matches that of the critical value of 100 cm^2 shown by Despres and Lamarche (19) to be associated with metabolic risk factors for type 2 diabetes and CHD in younger women. These results are comparable despite the fact that we studied an overall older and more obese sample of women. Moreover, it is important to point out that in the few studies to date that have attempted to identify cut points for VAT, some have used receiver-operating characteristic curve analyses, while others used a similar approach (logistical regression analyses) to ours. We chose the latter approach because, from a clinical standpoint, the degree of relative risk may be more meaningful than a likelihood ratio of sensitivity or specificity. The fact that the 100- to 110-cm^2 value is consistent across studies suggests that the different analyses produce similar results. Thus, our data confirm the finding that a VAT of ~100–110 cm^2 is predictive of adverse lipid (HDL cholesterol and triglyceride) and glucose risk factors in women. However, unlike these other studies (19,21), total and LDL cholesterol were not related to VAT in the sample of women we studied. Instead, age was the only independent predictor of total and LDL cholesterol in our women (data not shown). This finding may be due to the older age or much higher degree of total obesity in our sample, as evidenced by their average age (59 years) and percentage body fat (46%).

The association between an abdominal fat distribution and a greater incidence of metabolic health problems was reported as early as the 1950s (29). Subsequently, it was discovered that the associations observed between anthropometric measures of abdominal fat and higher risk for CHD likely resulted from the excess accumulation of VAT (8–12). Furthermore, while the amount of visceral fat correlates with the amount of total body fat, visceral obesity and its associated metabolic complications are not only evident in obese subjects. Studies show that visceral fat accumulation also contributes to metabolic risk factors in healthy, nonobese individuals (10,13–15). In addition, obese individuals who are "metabolically healthy" have very little visceral fat accumulation (30). Thus, the majority of evidence to date suggests that assessment of visceral fat may be more clinically relevant than assessment of total body fat for the prediction of subsequent CHD onset.

Despite the clinically significant information gained from assessment of VAT, its measurement is costly, it involves radiation exposure, and it is not a practical screening tool for the general population. Therefore, anthropometric or other surrogate measures of VAT need to be defined. For example, waist circumference, which has been shown to be the best predictor of VAT in several studies (31–34), has been proposed as a screening tool for assessment of disease risk (3). In the present study, there was only a modest correlation between waist circumference and VAT, as well as a large degree of variation in waist circumferences for a given VAT level. In addition, the waist circumference cut points that corresponded to the high-risk and very high-risk VAT cut points in these women were predictive of an increased risk for low HDL cholesterol and glucose intolerance, although the relative risks were not as high as those for the VAT cut points.

Recently, Despres and colleagues (4,35) have proposed a novel screening approach for identifying viscerally obese men at risk for CHD that utilizes waist circumference and fasting triglyceride concentrations. As noted by this group, the cut points they propose as useful in young and middle-aged men (waist circumference >90 cm and triglyceride concentration >2 mmol/l) may not be useful in individuals of a different sex, age, or race. For example, this group reports a much higher correlation between waist circumference and VAT (up to 0.87) in their study populations of young Caucasian men and women (32). In addition, they have shown that this relationship is age specific in that values of waist circumference that corresponded to "critical" levels of VAT were lower in subjects >40 than in those <40 years of age (33). Because of the preferential accumulation of VAT with age (16,36), a specific waist circumference may not correspond to a similar VAT level in younger and older individuals. This relationship may be even more complex in postmenopausal women, who are also predisposed to selective fat storage in the visceral region (37). Thus, further research is needed to define visceral obesity and identify simple markers of VAT that accurately predict risk factors and incidence of CHD in older women.

Some discussion is necessary regarding the limitations of this study. First, the women in this study were not randomly selected but were recruited for ongoing weight loss and exercise studies at the University of Maryland. In addition, we did not include women with frank CHD and/or diabetes and our sample was relatively healthy with respect to the risk factors studied. This could potentially limit the generalizability of our findings and/or may change the VAT cut points found by our analyses. Moreover, our sample included Caucasian and a small number of African-American women. Although there were no significant interactions between race and VAT for the risk factors tested, larger sample sizes are needed to definitely test whether there are ethnic differences in the degree of metabolic abnormalities for a given VAT level. In addition, adipose tissue or body weight cut points are a guide that can be used for defining associations with risk or incidence of disease. Like the BMI cut points, a critical level of VAT does not establish causality for an elevated disease risk. However, these values can be used as a guide for defining "visceral obesity" and may prove useful for identifying women most likely to benefit from preventative interventions. Further research is needed to confirm and/or refine these cut points for assessment of incidence of CHD (and to determine whether they differ by sex, ethnicity, or age-group), as well as to determine the percent of individuals in the population with this amount of VAT, i.e., prevalence of visceral obesity.

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References

1. Kuczmarksi R, Carroll M, Flegal K, Troiano R: Varying body mass index cutoff points to describe overweight prevalence among U.S. adults: NHANES III (1988–1994). *Obes Res* 5:542–548, 1997
2. World Health Organization: *Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation on Obesity*. Geneva, World Health Org., 1998
3. National Institutes of Health: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. *Obes Res* (6 Suppl. 2):51S–209S, 1998
4. Despres JP, Lemieux I, Prud'homme D: Treatment of obesity: need to focus on high risk abdominally obese patients. *BMJ* 322:716–720, 2001
5. Fujimoto WY, Bergstrom RW, Boyko EJ, Chen KW, Leonetti DL, Newell-Morris L, Shofer JB, Wahl PW: Visceral adiposity and incident coronary heart disease in Japanese-American men: the 10-year follow-up results of the Seattle Japanese-American Community Diabetes Study. *Diabetes Care* 22:1808–1812, 1999
6. Rexrode K, Carey V, Hennekens C, Walters E, Colditz G, Stampfer M, Willett W, Manson J: Abdominal adiposity and coronary heart disease in women. *JAMA* 280:1843–1848, 1998
7. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjostrom L: Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden. *BMJ* 289:1257–1260, 1984
8. Lemieux S: Contribution of visceral obesity to the insulin resistance syndrome. *Can J Appl Physiol* 26:273–290, 2001
9. Brochu M, Starling RD, Tchernof A, Matthews DE, Garcia-Rubi E, Poehlman ET: Visceral adipose tissue is an independent correlate of glucose disposal in older obese postmenopausal women. *J Clin Endocrinol Metab* 85:2378–2384, 2000
10. Carey D, Jenkins A, Campbell L, Freund J, Chisholm D: Abdominal fat and insulin resistance in normal and overweight women–direct measurements reveal a strong relationship in subjects at both low and high risk of NIDDM. *Diabetes* 45: 633–638, 1996
11. Ross R, Fortier L, Hudson R: Separate associations between visceral and subcutaneous adipose tissue distribution, insulin and glucose levels in obese women. *Diabetes Care* 19:1404–1411, 1996
12. Despres J, Nadeau A, Tremblay A, Ferland M, Moorjani S, Lupien P, Theriault G, Pinault S, Bouchard C: Role of deep abdominal fat in the association between regional adipose tissue distribution and glucose tolerance in obese women. *Diabetes* 38:304–309, 1989
13. DeNino WF, Tchernof A, Dionne IJ, Toth MJ, Ades PA, Sites CK, Poehlman ET: Contribution of abdominal adiposity to age-related differences in insulin sensitivity and plasma lipids in healthy nonobese women. *Diabetes Care* 24:925–932, 2001
14. DiPietro L, Katz L, Nadel E: Excess abdominal adiposity remains correlated with altered lipid concentrations in healthy older women. *Int J Obes* 23:432–436, 1999
15. Park KS, Rhee BD, Lee KU, Kim SY, Lee HK, Koh CS, Min HK: Intra-abdominal fat is associated with decreased insulin sensitivity in healthy young men. *Metabolism* 40:600–603, 1991
16. Enzi G, Gasparo M, Biondetti P, Fiore D, Semisa M, Zurlo F: Subcutaneous and visceral fat distribution according to sex, age and overweight, evaluated by computed tomography. *Am J Clin Nutr* 44:739–746, 1986
17. Lemieux S, Prud'homme D, Bouchard C, Tremblay A, Despres J: Sex differences in the relation of visceral adipose tissue accumulation to total body fatness. *Am J Clin Nutr* 58:463–467, 1993
18. Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G: Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *BMJ* 288:1401–1404, 1984
19. Despres J, Lamarche B: Effects of diet and physical activity on adiposity and body fat distribution: implications for the prevention of cardiovascular disease. *Nutr Res Rev* 6:137–159, 1993
20. Hunter GR, Snyder SW, Kekes-Szabo T, Nicholson C, Berland L: Intra-abdominal adipose tissue values associated with risk of possessing elevated blood lipids and blood pressure. *Obes Res* 2:563–568, 1994
21. Williams MJ, Hunter GR, Kekes-Szabo T, Trueth MS, Snyder S, Berland L, Blaudeau T: Intra-abdominal adipose tissue cutpoints related to elevated cardiovascular risk in women. *Int J Obes Relat Metab Disord* 20:613–617, 1996
22. Bruce RA, Horstein TR: Exercise stress testing in evaluation of patients with ischemic heart disease. *Prog Cardiovasc Dis* 11: 371–390, 1969
23. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 25:S5–S20, 2002
24. Nicklas B, Rogus E, Colman E, Goldberg A: Visceral adiposity, increased adipocyte lipolysis and metabolic dysfunction in obese, postmenopausal women. *Am J Physiol* 270:E72–E78, 1996
25. Nicklas BJ, Katzel LI, Bunyard LB, Dennis KE, Goldberg AP: Effects of an American Heart Association diet and weight loss on lipoprotein lipids in obese, postmenopausal women. *Am J Clin Nutr* 66:853–859, 1997
26. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 285:2486–2497, 2001
27. Bouchard C, Despres JP, Mauriege P: Genetic and nongenetic determinants of regional fat distribution. *Endocr Rev* 14:72–93, 1993
28. Kamel E, McNeill G, Han T, Smith F, Avenell A, Davidson L, Tothill P: Measurement of abdominal fat by magnetic resonance imaging, dual-energy x-ray absorptiometry and anthropometry in nonobese men and women. *Int J Obes* 23: 686–692, 1999
29. Vague J: The degree of masculine differentiation of obesities: a factor determining predisposition to diabetes, atherosclerosis, gout and uric-calculous disease. *Am J Clin Nutr* 4:20–34, 1956
30. Brochu M, Tchernof A, Dionne IJ, Sites CK, Eltabbakh GH, Sims EA, Poehlman ET: What are the physical characteristics associated with a normal metabolic profile despite a high level of obesity in postmenopausal women? *J Clin Endocrinol Metab* 86:1020–1025, 2001
31. Koester RS, Hunter GR, Snyder S, Khaled MA, Berland LL: Estimation of computerized tomography derived abdominal fat distribution. *Int J Obes Relat Metab Disord* 16:543–554, 1992
32. Pouliot MC, Despres JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, Nadeau A, Lupien PJ: Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. *Am J Cardiol* 73:460–468, 1994
33. Lemieux S, Prud'homme D, Bouchard C, Tremblay A, Despres JP: A single threshold value of waist girth identifies normal-weight and overweight subjects with excess visceral adipose tissue. *Am J Clin*

Nutr 64:685–693, 1996
34. Despres JP, Prud'homme D, Pouliot MC, Tremblay A, Bouchard C: Estimation of deep abdominal adipose-tissue accumulation from simple anthropometric measurements in men. *Am J Clin Nutr* 54:471–477, 1991
35. Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Almeras N, Bergeron J, Gaudet D, Tremblay G, Prud'homme D, Nadeau A, Despres JP: Hypertriglyceridemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? *Circulation* 102:179–184, 2000
36. Seidell J, Oosterlee A, Deurenberg P, Hautvast J, Ruijs J: Abdominal fat depots measured with computed tomography: effects of degree of obesity, sex, and age. *Eur J Clin Nutr* 42:805–815, 1988
37. Toth MJ, Tchernof A, Sites CK, Poehlman ET: Menopause-related changes in body fat distribution. *Ann N Y Acad Sci* 904: 502–506, 2000