# Clinical utility of visceral adipose tissue for the identification of cardiometabolic risk in white and African American adults $1-3$

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# ABSTRACT

Background: Visceral adipose tissue (VAT) has been identified as a harmful fat depot, and sex and race differences in VAT have been reported in white and African Americans.

Objectives: We determined the clinical utility of VAT in the identification of individuals at elevated cardiometabolic risk in white and African American adults and compared the clinical utility with measures obtained by using dual-energy X-ray absorptiometry (DXA) and anthropometric measures.

Design: The sample included 429 white women, 311 African American women, 406 white men, and 100 African American men who were 18–74 y of age. VAT was measured by using computed tomography, fat mass (FM) and percentage of body fat were measured by using DXA, and waist circumference (WC) and BMI were assessed. Receiver operating characteristic curves were used to compare the utility of measures in the identification of participants in the upper quintile of a continuous score derived from principal components analysis of fasting glucose, HDL cholesterol, triglycerides, and blood pressure.

Results: The clinical utility of measures varied across sex-by-race groups. In the overall sample, the areas under the curve were significantly higher for VAT and WC in comparison with the other indicators. Identified VAT thresholds were higher in white men  $(140 \text{ cm}^2)$ and women  $(141 \text{ cm}^2)$  than in African American men  $(82 \text{ cm}^2)$  and women  $(97 \text{ cm}^2)$ .

Conclusions: VAT and WC showed greater clinical utility than did other obesity measures. Because of the complexity of measuring VAT, the use of WC is recommended for the identification of adults with elevated cardiometabolic risk factors. The Pennington Center Longitudinal Study was registered at clinicaltrials.gov as NCT00959270. Am J Clin Nutr 2013;97:480–6.

# INTRODUCTION

There is considerable scientific evidence that excess adiposity is associated with significant health risks, especially at high amounts (1). Abdominal obesity, in particular visceral adipose tissue  $(VAT)^4$ , has been identified as a particularly harmful fat depot (2–4). Although the mechanisms are not yet fully understood, high amounts of VAT are predictive of insulin resistance and other metabolic abnormalities (3). Several studies have identified thresholds of VAT that are related to elevated cardiometabolic risk factors and metabolic syndrome (MetS) in white men and women (5–9). Limited studies have also identified optimal thresholds of VAT in other ethnic groups such as

Indians (10), Chinese (11), Koreans (12, 13), Japanese (14, 15), and Japanese Americans (16).

Sex and race differences in VAT have been consistently shown in samples of white and African Americans. Men have higher amounts of VAT than women do, and white Americans have higher amounts of VAT than African Americans do (17–21). These ethnic differences in VAT persist even after statistical control for amounts of total body fat (19, 21). The relation between VAT and cardiometabolic risk factors has not been studied extensively across different ethnic groups; however, significant associations have been shown in both white and African American adults (22). One study has reported VAT thresholds in a combined sample of white and African American women (23); however, to our knowledge, differences in VAT thresholds among white and African Americans have not been studied. Thus, the purpose of this study was to determine the clinical utility of the use of VAT to identify individuals at elevated cardiometabolic risk in white and African American men and women and to compare the clinical utility to other common obesity measures obtained by using dual-energy X-ray absorptiometry (DXA) and anthropometric measures.

# SUBJECTS AND METHODS

# Sample

Participants were drawn from the baseline assessment for the Pennington Center Longitudinal Study (www.clinicaltrials.gov; NCT00959270), which is an ongoing investigation of the effects

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<sup>&</sup>lt;sup>4</sup> Abbreviations used: DXA, dual-energy X-ray absorptiometry; FM, fat mass; MetS, metabolic syndrome; ROC, receiver operating characteristic; VAT, visceral adipose tissue; WC, waist circumference.

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#### TABLE 1

Descriptive characteristics of the analysis sample from the Pennington Center Longitudinal Study



<sup>1</sup> Mean  $\pm$  SD (all such values). <sup>2</sup> Significant difference between white and African Americans, within sex, based on independent samples t test or chi-square test. <sup>3</sup> Or self-reported hypertension.

<sup>4</sup> Or self-reported diabetes.

of obesity and lifestyle factors on the development of chronic diseases. The sample is composed of volunteers who have participated in a variety of clinical studies conducted at the Pennington Biomedical Research Center in Baton Rouge, LA, between 1992 and 2012. Participants were recruited from the greater Baton Rouge area through the local media and Web-based advertisements. The current cross-sectional study included 1246 participants (429 white women, 311 African American women, 406

#### TABLE 2

Age-adjusted partial correlations in measures of adiposity and cardiometabolic risk factors<sup>1</sup>



<sup>1</sup> DBP, diastolic blood pressure; MetS Score, metabolic syndrome score derived from principal components analysis; SBP, systolic blood pressure.

<sup>2</sup> All correlations were significant ( $P < 0.05$ ) with the exception of those indicated.

white men, and 100 African American men) who were 18–74 y of age. Each participant provided their written informed consent, and all Pennington Center Longitudinal Study procedures were approved by the Pennington Biomedical Research Center Institutional Review Board.

#### VAT

Abdominal VAT cross-sectional areas  $\text{(cm}^2\text{)}$  at the L4–L5 anatomic landmark were measured by using computed tomography on a scanner (General Electric) as previously described (21, 24). Commercially available software (Analyze; Analyze Direct) was used to electronically measure areas of adipose tissue by selecting regions of interest defined by using attenuation values  $(-30$  to  $-190$  Hounsfield units for adipose tissue).

#### Anthropometric measures and total body fat

Height and weight were measured by using a wall-mounted stadiometer and a digital scale, respectively, after the volunteer removed outer clothing, heavy pocket items, and shoes. BMI (in  $\text{kg/m}^2$ ) was calculated as weight divided by the square of height.

Waist circumference (WC) was measured at the midpoint between the inferior border of the ribcage and the superior aspect of the iliac crest by using an inelastic measuring tape. Total-body fat mass (FM; in kg) and percentage of body fat were estimated by using DXA with a whole-body scanner (Hologic) as previously described (21).

#### Cardiometabolic risk factors

Resting blood pressure measurements were taken manually by using a stethoscope and standard sphygmomanometer or, in some cases, a validated automatic measuring device (Omron). Serum triglycerides, HDL cholesterol, and glucose were obtained from a 12-h fasting blood draw. Participants were asked to refrain from consuming alcohol or engaging in vigorous exercise  $\geq$  24 h before blood withdrawal.

# **Covariates**

Participant age was computed from birth and observation dates. Smoking status was self-reported during the screening process, and participants were classified as nonsmokers, current

#### TABLE 3

Results of logistic regression analysis for visceral adipose tissue, BMI, waist circumference, fat mass, and percentage of body fat in the prediction of abnormal risk factor levels and the upper quintile  $(20%)$  of the continuous MetS score<sup>1</sup>



 $<sup>I</sup>$  All values are ORs; 95% CIs in parentheses. ORs are expressed per SD of the explanatory variable from logistic regression analysis. All models included age,</sup> smoking, and menopausal status (women only) as covariates. Abnormal levels of risk factors were defined according to current recommendations as follows: high blood pressure:  $\geq 140/90$  mm Hg or self-reported hypertension; high glucose concentration:  $\geq 126$  mg/dL or self-reported diabetes; high triglycerides:  $\geq 200$  mg/dL; and low HDL-cholesterol concentration:  $\leq 40$  mg/dL. MetS score, metabolic syndrome score derived from principal components analysis.

smokers, or former smokers. Menopausal status (premenopausal compared with postmenopausal) was determined in women from their ages and responses to questions regarding their reproductive histories  $(21)$ .

#### Statistical analysis

Abnormal levels of risk factors were defined according to current recommendations as follows: high blood pressure  $(\geq 140/$ 90 mm Hg or reported hypertension) (25), high triglyceride concentrations ( $\geq$ 200 mg/dL) (26), high glucose concentrations  $(\geq 126 \text{ mg/dL} \text{ or reported diabetes})$  (27), and low HDL-cholesterol concentrations  $(\leq 40 \text{ mg/dL})$  (26). A continuous MetS risk-factor score was derived by using a principal components analysis of MetS risk factors (ie, systolic and diastolic blood pressures, triglycerides, glucose, and HDL cholesterol) (28) with the exception of WC. Individuals at high risk were defined as those in the upper quintile (20%) of the risk factor score.

Logistic regression was used to determine the odds of having abnormal risk-factor levels and of being in the upper quintile of the continuous MetS score in each sex-by-ethnicity group. ORs are expressed per SD of the explanatory variable (VAT, BMI, WC, FM, and percentage of body fat). Age, smoking status, and menopausal status (in women) were included as covariates in logistic regression models. Receiver operating characteristic

(ROC) curves were used to select thresholds that identified individuals in the upper quintile of the continuous MetS score in each sex-by-ethnicity group. Because the AUC is considered a measure of the utility of the predictor variable and represents the tradeoff between the correct identification of high-risk individuals (sensitivity) and the correct identification of lowrisk individuals (specificity), the threshold was determined from the Youden index, which is the maximum value of  $J(16, 29, 30)$ , whereby

$$
J = sensitivity + specificity - 1 \tag{1}
$$

Significant differences in AUCs in adiposity indicators were determined by using the nonparametric approach of DeLong et al (31). SAS software (version 9.3; SAS Institute Inc) was used for data management and preliminary analyses and MedCalc software (version 12.3) was used to perform ROC analyses. The level of significance was set at  $P \leq 0.05$ .

### **RESULTS**

Descriptive characteristics of the sample are presented in Table 1. The average age of the sample was 44.5 y (range: 18– 74 y). Average BMI was 29.7, with a range from 17.3 to 48.7.

#### TABLE 4

Results of receiver operating characteristic curve analyses for the utility of visceral adipose tissue  $(cm^2)$ , BMI (kg/m<sup>2</sup>), waist circumference (cm), total fat mass (kg), and percentage of body fat in the prediction of the upper quintile of the continuous metabolic syndrome score<sup>1</sup>



 $<sup>I</sup>$  Groups with different superscript letters were significantly different from each other within sex-by-race groups on the basis of pairwise comparisons by</sup> using the method of DeLong et al (31).

The first principal component from the analysis of MetS risk factors was retained for additional analysis as a continuous MetS score. The component explained 37% of the variance in original risk-factor variables and was characterized by positive loadings for systolic blood pressure (0.62), diastolic blood pressure (0.64), glucose (0.50), and triglycerides (0.65) and a negative loading for HDL cholesterol  $(-0.62)$ .

Partial correlations between adiposity variables and the risk factors, adjusted for age, are shown in Table 2. Correlations were consistently negative for HDL cholesterol and positive for the other risk factors. In addition, with few exceptions, correlations were significant.

The odds of having abnormal levels of risk factors and of being in the upper quintile of the continuous MetS score associated with each SD of obesity variables are presented in Table 3. With few exceptions, there are significantly higher odds of being in the upper quintile of the continuous MetS score associated with each SD of all obesity variables in all subgroups. ORs for all risk factors ranged from 1.7 to 6.2 for VAT, 1.5 to 4.5 for BMI, 1.6 to 5.0 for WC, 1.5 to 3.5 for FM, and 1.2 to 4.0 for percentage of body fat across the 4 sex-by-ethnicity groups.

Identified thresholds of VAT, BMI, WC, and FM in this sample, along with the AUC and sensitivity and specificity of the optimal threshold at predicting individuals in the upper quintile of the continuous MetS score, are presented in Table 4. ROC curves for VAT, BMI, WC, FM, and percentage of body fat in the overall sample are presented in Figure 1. In the overall sample, the AUC was significantly higher for VAT and WC compared with the other indicators of obesity; whereas BMI, FM and percentage of body fat did not differ from one another. Optimal VAT thresholds were higher in white men  $(140 \text{ cm}^2)$  and women  $(141 \text{ cm}^2)$ than in African American men  $(82 \text{ cm}^2)$  and women  $(97 \text{ cm}^2)$ .

Optimal WC thresholds were higher in African American men (102 cm) than in white men (96 cm); however, thresholds were similar in African American (96 cm) and white (95 cm) women.

### DISCUSSION

Results of this study indicated that VAT and WC have more utility as a marker of cardiometabolic risk than do BMI, FM, and percentage of body fat, although the results differed by ethnicity and sex. VAT thresholds were higher in white men and women than in African American women and men. Identified thresholds for VAT in white men  $(140 \text{ cm}^2)$  and women  $(141 \text{ cm}^2)$  in this study were somewhat higher but within the range of those identified in previous studies. For example, in a sample of white adults, Després et al  $(5)$  identified a threshold of 130 cm<sup>2</sup> as indicative of metabolic disturbances. In addition, thresholds of 131 and 110  $\text{cm}^2$  have been identified in samples of white men (6) and women (9), respectively, in the identification of elevated metabolic risk factors. von Eyben et al (8) reported a threshold of VAT of 144  $\text{cm}^2$  (at L2–L3) in a small sample of Danish men and women to identify subjects with  $\geq 2$  cardiometabolic risk factors, and a recent study by Pickhardt et al (7) identified 125 and 70 cm<sup>2</sup> (at the level of the umbilicus) as the best thresholds for the prediction of MetS in men and women, respectively. Differences in identified thresholds in these studies were likely due to differences in measurement protocols for VAT, outcomes used to assess metabolic risk, and analytic approaches used to determine the thresholds.

To our knowledge, the current study is the first to identify VAT thresholds associated with metabolic risk factors in African American adults; however, one previous study identified 106 and  $163 \text{ cm}^2$  as thresholds for elevated and significantly elevated



FIGURE 1. Receiver operating characteristic curves for VAT, BMI, WC, FM, and %Body Fat for the prediction of the upper quintile of a continuous metabolic syndrome score in 1246 white and African American adults in the Pennington Center Longitudinal Study. FM, fat mass; VAT, visceral adipose tissue; WC, waist circumference; %Body Fat, percentage of body fat.

cardiometabolic risk, respectively, in a combined sample of white and African American women (23). Ethnic differences in VAT thresholds observed in this study  $(58 \text{ cm}^2 \text{ in men and}$  $44 \text{ cm}^2$  in women) were greater than the ethnic differences in thresholds for the other obesity measures. VAT thresholds associated with risk were at or above the mean amount of VAT (Table 1) in all sex-by-race groups except African American men, where the identified threshold  $(81.9 \text{ cm}^2)$  was below the mean  $(90.3 \text{ cm}^2)$ . Additional research is required to determine whether the ethnic differences in VAT thresholds in the current study are present in other samples and whether this risk is independent of risk associated with general adiposity. The degree to which differences in the VAT thresholds are due to true differences in risk associated with the visceral compartment compared with confounding as a result of the association between VAT and total adiposity has yet to be determined. This study addressed the clinical utility of absolute amounts of VAT; future studies should determine whether the use of a relative measure of VAT in relation to total adiposity might produce different results.

A recent study by Sumner et al (30) identified BMI thresholds of 30 and 32 in African American men and women, respectively, for the prediction of insulin resistance (30). These thresholds are similar to those obtained in the current study for African American men (31) and women (30) (Table 4). Corresponding WC thresholds in the study by Sumner et al (30) were 102 cm in men and 98 cm in women compared with 102 cm in men and 96 cm in women in the current study. The comparability of these results support the face validity of the results reported in the current study. More research is required to determine whether ethnic-specific BMI and WC thresholds are clinically more useful than single thresholds proposed by the NIH (32).

Body-composition estimates obtained by using DXA are becoming more common. For example, reference curves for body fat and bone mineral density have been produced from DXA data collected in the US NHANES (33). In the current study, FM and percentage of body fat had a somewhat lower utility than VAT, WC, and BMI (Table 4). A recent study in white and African Americans showed that DXA-derived estimates of FM were also inferior to WC in the prediction of MetS (34), which also supported earlier work that showed that the percentage of body fat from air-displacement plesthysmography was not superior to BMI and WC in the prediction of risk factors (35). Taken together, these results do not support the routine use of DXA in the assessment of obesityrelated cardiometabolic risk when anthropometric measures such as BMI and WC are available; thus, the need for ethnic- and sex-specific thresholds of FM or percentage of body fat is not clear.

This study had several strengths and limitations. A marked strength was the large biethnic sample of men and women, with a wide range of age and BMI, and the availability of measured VAT, FM, percentage of body fat, and cardiometabolic risk factors. However, because the sample represented volunteers who have attended screening visits for clinical research studies, the results may not be generalizable to the wider population. Unfortunately, information on the use of lipid- or cholesterol-lowering medications was not available, and thus, we were unable to incorporate this information into the analysis. These results should be replicated in representative population samples as VAT data become more widely available. The current study uses a cross-sectional design, and as such, cause-and-effect conclusions could not be made.

Future studies should focus on studying the association between VAT and cardiometabolic risk by using prospective research designs.

In conclusion, results of this study show that VAT is a useful clinical marker of cardiometabolic risk; however, its utility in this study was not any better than that of WC. Although VAT is currently measured most commonly by using computed tomography or magnetic resonance imaging, technological advances have allowed for more precise estimation by using DXA (36, 37), and it is likely that VATwill be assessed more readily in clinical settings in the near future. This study presents some preliminary thresholds for VAT that can be used clinically in white and African Americans until they can be verified or adapted by using data from representative population samples. In cases in which VAT cannot be directly assessed, it is recommended that WC should be measured.

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The authors' responsibilities were as follows—PTK: designed and conducted the research, analyzed data, and had primary responsibility for the final content of the manuscript; and all authors: wrote the manuscript and read and approved the final manuscript. None of the authors had a conflict of interest.

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