Identification of Sex-Specific Thresholds for Accumulation of Visceral Adipose Tissue in Adults

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Objective: The purpose of this study was to measure the linearity of visceral adipose tissue (VAT) accumulation with measures of total body adiposity to determine whether a threshold exists and to explore the association with cardiometabolic risk factors in adults.

Methods: Using a cross-sectional design, data were obtained from 723 adults (324 females) age 19-47 years. Body mass index ranged from 15 to 52 kg/m². Segmented linear regression was used to identify sex-specific percent body fat thresholds at which VAT slope changes. Linear regression measured the association of VAT mass, total fat mass, and subcutaneous fat with cardiometabolic risk factors above and below each threshold.

Results: Adiposity thresholds were identified at 23.4% body fat in males and 38.3% body fat in females beyond which the slope of VAT per unit of percent body fat increased to strongly positive. Males and females above these adiposity thresholds had significant dyslipidemia (P < 0.001), increased insulin resistance (P < 0.001), and higher fat mass across all depots.

Conclusions: From these cross-sectional data, the following were inferred: the accumulation of VAT mass is not linear with increasing adiposity; increases in visceral accumulation above threshold are associated with decreased insulin sensitivity and cardiovascular risk in males and females independent of total body fat.

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Introduction

Over a third of United States adults are obese (1). While the prevalence of obesity has stabilized recently (1), the overall number of obese individuals is alarming considering both the financial and the health consequences of obesity (2). The accumulation of total body fat occurring with obesity results in excess fat in several subcutaneous and ectopic depots located around the body. The body preferentially stores excess fat subcutaneously (3,4). However, at some point fat is also stored in ectopic depots, such as the visceral region. Visceral adipose tissue (VAT) surrounds the internal organs in the abdominal region and has a significant association with cardiometabolic risk factors (5-12), independent of total fat mass. Thus, measurement of VAT has become an important marker for identifying cardiometabolic risk.

Recently, dual energy x-ray absorptiometry (DXA) was validated against CT as an accurate and reliable method for estimating VAT within the entire abdominal region and as a reliable marker of cardiometabolic risk (12-14). In addition to VAT, DXA provides measurement of regional fat, lean body mass, and bone mass. This new method allows for measurement of total VAT mass along with other regional composition measurements. Using this novel method in professional football players, we observed an adiposity threshold at 22 percent body fat, after which the slope of visceral fat with change in percent body fat increased significantly with increasing adiposity (15).

Professional football players are a unique population. As such, we hypothesized that a similar threshold existed in a community based population of adults. Our secondary hypothesis was that being above
threshold would be associated with a worsened cardiometabolic profile.

Methods

The subjects in this study were participants in two population based longitudinal studies (16,17) assessing cardiovascular (CV) and metabolic changes associated with CV risk between childhood and adulthood. Data were obtained from the most recent follow-up visits (2004-2011) when participants were mean age 23.1 ± 2.4 (16) and mean age 39.0 ± 2.1 (17). A total of 723 (324 females and 399 males) participants included in this study completed a full body DXA scan, blood draw, and hyperinsulinemic euglycemic clamp to measure insulin sensitivity. Participants were excluded if they were missing data or VAT mass could not be determined by DXA. The respective protocols were approved by the University of Minnesota Institutional Review Board, and consent was obtained from each participant.

Anthropometric and blood pressure measurements

Testing was conducted at the University of Minnesota Clinical Translation Science Institute after an overnight fast for a minimum of 8 h. Height and weight were measured on a calibrated stadiometer and electronic scale, respectively, while participants were wearing light clothes and without shoes. Body mass index (BMI) was calculated as kg/m². Waist circumference was measured to the nearest 0.5 cm, taken in duplicate and the mean value reported. Blood pressure was measured in duplicate on the right arm after participants were sitting in a quiet room for at least 5 min using a digital blood pressure cuff; the average of the two values was reported.

Body composition and visceral adipose quantification

Total body composition was measured using DXA (Lunar Prodigy, General Electric Medical Systems, Madison, WI) and analyzed using its enCore™ software (platform version 13.6). Participants were scanned using standard imaging and positioning protocols while fasted and hydrated. Subcutaneous fat (total, android [abdominal] and gynoid [hip/gluteal]) and VAT were estimated using a method described previously for adults (13). The android region was defined with a caudal limit placed at the top of the iliac crest and its height set to 20% of the distance from the top of the iliac crest to the base of the skull (18). The gynoid region is located mid-pelvis to mid-thigh, with the upper limit set below the iliac crest a distance 1.5 times the height of the android region and the lower limit set a distance of two times the height of the android region (18). A single technician reviewed each scan to assure accurate placement of the android region of interest.

Metabolic measurements

Insulin sensitivity was measured by the hyperinsulinemic euglycemic clamp as previously described (19). Insulin was infused at a constant rate of 1 mU/kg/min for 3 h, and glucose was infused at a variable rate to maintain euglycemia. Insulin sensitivity ($M_{LBM}$) was expressed as the glucose infusion rate (mg/kg/min of glucose) during the last 40 min of the clamp, with adjustment for lean body mass (LBM). Fasting blood samples were collected prior to beginning the clamp for glucose, insulin and lipid levels including total cholesterol (Chol), triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). All assays were conducted with standard procedures at the Fairview Diagnostic Laboratories, Fairview-University Medical Center (Minneapolis, MN), Centers for Disease Control and Prevention-certified laboratory.

Statistical analysis

Unpaired t-tests compared males and females for demographic, body composition, and cardiometabolic characteristics. Data are presented as means ± standard deviation (SD). Normality of data that were right skewed was tested using the Anderson-Darling test. If significantly skewed, data were log transformed for comparisons and data were presented as geometric means and 95% confidence intervals (CI). Body composition data were log transformed to measure if non-normality affected the comparison and all comparisons resulted in the same sex differences whether data was log transformed or not. Segmented linear regression (segmented package in R) was used to evaluate potential break-points (thresholds) in the relationship between VAT mass and total percent body fat in both males and females. This method has been detailed previously (15,20,21). We used a segmented linear regression model with a single break-point (VAT = total percent body fat + Study); using the scatterplot we initialized the break-point (“estimate numeric vector” parameter in R) at 25% body fat for males and 40% body fat for females. The segmented analysis uses the linear regression and estimates a new model having a non-continuous linear relationship (break-point) with the specified variables. The break-point is determined at the point where the slope of the linear relationship changes using the least squares method to minimize the sum of squared differences.

We tested whether the slopes of VAT with total percent body fat were significantly different above and below the threshold. The study from which the data arose was a covariate within the analyses because of the age difference between the populations. If study was significantly associated with the dependent variable, subgroup analysis (linear regression) of each study was completed to determine if it affected the relationship between VAT, TFM and the dependent variable. Unpaired t-tests compared males and females above and below the threshold for anthropometric, cardiometabolic and body composition measurements. Tukey honest significant difference was used to compare the means of males and females both above and below threshold.

Linear regression measured the association of cardiometabolic risk factors with various fat depots above and below threshold, and analyses were completed separately for males and females. VAT, subcutaneous android fat and total body fat were identified as independent variables. Based on previous studies, possible covariates were identified as age, study, race, cigarette status and birth control status (females only). Covariates were removed from the model if they were not significantly associated with the dependent variable and the model was reassessed. Criteria for removal was conservatively set at $P > 0.3$ for the first analysis and $P > 0.1$ for subsequent analyses. Variance inflation factor was calculated with each model to measure multicollinearity of independent variables. Conservative estimates were used (2.5 for independent variables and 5.0 for covariates). If multicollinearity was observed, the variables were
TABLE 1 Demographic, body composition, and clinical measurements [mean (±sd)]

|                | Female (n = 324) | Male (n = 399) | P-value |
|----------------|------------------|----------------|---------|
| Age (yr)       | 34 (7)           | 33 (8)         | 0.04    |
| Race (%)       | Caucasian (70)   | Caucasian (71) | 0.89    |
|                | African-American (21) | African-American (21) | 0.95    |
|                | Other (9)        | Other (8)      | 0.85    |
| Height (cm)    | 164.3 (9.0)      | 177.6 (7.8)    | <0.001  |
| Weight (kg)    | 79.1 (19.8)      | 87.2 (19.5)    | <0.001  |
| Body mass (%)  | 41.4 (8.9)       | 26.8 (10.0)    | <0.001  |
| BMI (kg/m²)    | 29.5 (8.7)       | 27.6 (5.7)     | <0.001  |
| Waist (cm)     | 94.8 (17.9)      | 96.8 (15.9)    | 0.001   |
| Total fat mass (kg) | 31.5 (13.9)   | 23.9 (12.7)    | <0.001  |
| Total lean mass (kg) | 46.2 (14.5)   | 48.4 (15.3)    | 0.05    |
| Android fat (kg) | 2.6 (1.6)    | 2.2 (1.7)      | 0.001   |
| Subcutaneous abdominal fat (kg) | 2.0 (1.1)    | 1.3 (0.9)      | <0.001  |
| Visceral fat (kg) | 0.6 (0.6)     | 0.9 (0.9)      | <0.001  |
| Gynoid fat (kg) | 5.7 (2.3)      | 3.8 (2.0)      | <0.001  |
| SV ratio a     | 4.7 (4.3, 5.2)  | 2.4 (2.1, 2.8) | <0.001  |
| Triglycerides a (mmol/L) | 0.99 (0.94, 1.03) | 1.27 (1.20, 1.36) | <0.001  |
| HDL-C (mmol/L) | 1.4 (0.4)       | 1.1 (0.3)      | <0.001  |
| LDL-C (mmol/L) | 2.7 (0.7)       | 3.2 (0.4)      | 0.03    |
| SBP (mmHg)     | 118 (17)        | 122 (16)       | 0.002   |
| DBP (mmHg)     | 68 (11)         | 71 (10)        | <0.001  |
| Glucose a (mmol/L) | 5.4 (5.2, 5.5) | 5.7 (5.5, 5.8) | <0.001  |
| Insulin a (pmol/L) | 36 (33,40)   | 36 (33,40)     | 0.8992  |
| Insulin sensitivity (M LBM) (mg/kg LBM) | 11.9 (5.1) | 9.5 (4.1) | <0.001  |

*aIndicates log transformed data presented as the geometric mean and 95% confidence interval.

BMI, body mass index; SV ratio, subcutaneous/visceral fat ratio; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Android ROI, region from the top of the iliac crest to 20% of the height from the base of the skull (just below the rib cage). Gynoid ROI, region 1.5 times the height of the android ROI below the top of the iliac crest to a lower limit of 2 times the height of the android ROI.

Results

Table 1 presents the demographic, body composition and clinical characteristics of males and females from the sample population. All the following differences were statistically significant. As expected, males were taller and heavier than females and had greater lean body mass and waist circumferences, but lower percent fat and BMI. Females had a higher level of abdominal fat mass than males, but males had a higher VAT mass. Females had higher total fat mass, subcutaneous fat mass, hip-gluteal fat mass, and subcutaneous-visceral ratio. Males had adverse CV profiles compared to females, with higher LDL-C, triglycerides, and blood pressure, lower HDL-C, higher fasting glucose, and lower insulin sensitivity. Fasting insulin was not significantly different between males and female.

Because study participation did not significantly affect the results of the relation between VAT and percent body fat, the participants from the two longitudinal studies were combined for the analyses. VAT mass displayed a nonlinear relationship with percent body fat. VAT mass displayed a nonlinear relationship with percent body fat (Figure 1a,b) for both males and females. Segmented linear regression was used to determine if there was a threshold at which point a significant increase in the slope of the relation between VAT and percent body fat [VAT = β0 + β1 (%Fat) + ε] could be identified. In males, a threshold was identified at 23.4% body fat with a 95% confidence interval of 19.2% and 27.6%. The slope below the threshold point was not significant, that is, β = 16.9 (SE = 13.3, P = 0.204, 95%CI = -9.251, 43.13), while a significant slope was identified above the threshold, that is, β = 77.2 (SE = 5.8, P = <0.001, 95%CI = 65.7, 88.6). In females, a higher threshold was identified at 38.3% body fat with a 95% confidence interval of 33.4 and 43.2%. As
found in the males, below the threshold the slope was not significant, 
\( b = 10.7 \) (SE = 10.9, \( P = 0.328, \) 95%CI = –10.8, 32.2), while above the 
threshold the slope increased significantly to \( b = 49.7 \) (SE = 4.5, 
\( P < 0.001, \) 95%CI = 40.8, 58.5). Similar results were found in males 
when BMI was used instead of percent body fat. In sensitivity analysis 
using BMI in place of percent body fat, a threshold was identified at a 
BMI of 23.5 kg/m\(^2\) (95%CI = 22.1, 24.9), with an insignificant slope 
below the threshold, that is, \( -3.7 \) (SE = 24.3, \( P = 0.878, \) 95%CI = 
–51.4, 44.0) and a significant positive slope above the threshold, that 
is, 120.6 (SE = 5.9, \( P < 0.001, \) 95%CI = 109.0, 132.1). A significant 
change in slope relative to BMI was not identifiable in women.

Table 2 presents the comparisons between individuals above and 
below their identified adiposity threshold, as grouped by gender. 
Within males, significantly adverse differences in body fatness, 
lipids, fasting insulin and glucose, blood pressure, and decreased 
insulin sensitivity were observed above the adiposity threshold. 
Similarly, females above threshold demonstrated significantly increased 
body fatness, lipids, fasting insulin and glucose, blood pressure, and 
decreased insulin sensitivity.

A comparison of males and females above their respective thresh-
holds indicated that males had higher VAT mass and adverse levels 
of the CV risk factors, including insulin sensitivity, than females. 
However, males had higher fat mass in all regions other than VAT. 
Males and females below the adiposity threshold were much 
more similar. Few differences were found between males and 
females below the adiposity threshold, with females having higher 
subcutaneous fat measurements and higher insulin sensitivity 
(\( M_{LBMI} \)) compared with males.

Table 3 presents the linear regression analyses above and below the 
adiposity threshold. Subcutaneous android fat was removed from all 
final models for lack of significance or multicollinearity with total fat mass. In the case of multicollinearity, removal of subcutaneous 
android fat resulted in a lower AIC than removal of total body fat. 
Total body fat is presented even when it did not remain significantly 
associated within the final model to demonstrate the relative importance of VAT compared to total fat mass. In addition to considering the possibility of multicollinearity consistently through all the models, 
Q-Q plots and residual plots suggested normality and constant 
variance. With few exceptions, the standardized coefficients were 
significantly higher in males above threshold compared to males 
below threshold. The study from which the data arose was a significant 
factor, which resulted in a significantly higher intercept for the 
PHBPC study (17), which had an older average age (HDL-C = 0.16 
mmol/l; Chol = 0.57 mmol/l; LDL-C = 0.30 mmol/l; SBP = 17 
mmHg; DBP = 6 mmHg; Glucose = 0.32 mmol/l). However, with few exceptions, it only accounted for minimal variability within the 
final model. A separate analysis was completed on each study to 
determine if the results held across both studies. For each study pop-
ulation VAT remained significantly associated with each dependent 
variable with similar standardized coefficients (\( P > 0.05 \)). Study par-
ticipation was a significant factor below threshold, which resulted in 
a significantly higher intercept for the PHBPC study (17), (HDL-
C = 0.24 mmol/l; Chol = 0.55 mmol/l; LDL-C = 0.39; SBP = 16 
mmHg).

Table 4 presents the linear regression analyses above and below the 
female adiposity threshold for cardiometabolic risk factors. Similar 
to males, subcutaneous android fat was removed from all final mod-
els, except for insulin. Subcutaneous android fat provided a stronger 
marker than total body fat in the insulin model. Fat depots are pre-
seated even when it did not remain significantly associated within 
the final model to demonstrate the relative importance of each fat 
depot. In addition to multicollinearity, consistently through all the 
models, QQ plots and residual plots suggested normality and constant 
variance. Above threshold, VAT was significantly associated with 
triglycerides, HDL, M/Lbm and fasting insulin, however, no signifi-
cant association was observed for cholesterol, LDL-C, SBP, DBP,
TABLE 2 Body composition and cardiometabolic variables above and below percent body fat thresholds [mean (±SD)]

|                  | Males < 23.4% (n = 158) | Males ≥ 23.4% (n = 241) | Females < 38.3% (n = 133) | Females ≥ 38.3% (n = 191) |
|------------------|-------------------------|--------------------------|---------------------------|---------------------------|
| Age (yr)         | 30.5 (9)                | 35.6 (7)                 | 34.6 (8)                  | 35.6 (7)                  |
| Height (cm)      | 177.2 (8.2)             | 177.8 (7.6)              | 164.9 (8.4)               | 164.7 (6.2)               |
| Weight (kg)      | 73.3 (12.2)             | 96.3 (17.8)              | 64.9 (11.1)               | 89.3 (18.2)               |
| BMI (kg/m²)      | 23.3 (8.1)              | 30.4 (5.2)               | 24.0 (4.0)                | 33.0 (6.5)                |
| Waist (cm)       | 82.9 (7.0)              | 105.9 (13.1)             | 81.9 (12.5)               | 104.0 (15.3)              |
| Body fat (%)     | 16.4 (6.4)              | 33.7 (5.3)               | 32.8 (5.6)                | 47.5 (4.7)                |
| Total fat mass (kg) | 13.4 (4.8)          | 30.9 (11.2)              | 20.5 (5.8)                | 39.4 (12.6)               |
| Total lean mass (kg) | 50.1 (14.2)       | 47.3 (16.0)              | 45.7 (14.6)               | 46.4 (14.4)               |
| Android fat (kg) | 0.8 (0.5)               | 3.1 (1.5)                | 1.4 (0.7)                 | 3.5 (1.4)                 |
| Subcutaneous fat (kg) | 0.6 (0.4)           | 1.8 (0.9)                | 1.1 (0.5)                 | 2.6 (1.0)                 |
| Visceral fat (kg) | 0.3 (0.2)               | 1.4 (0.8)                | 0.3 (0.3)                 | 0.9 (0.6)                 |
| Gynoid fat (kg)  | 2.2 (0.9)               | 4.8 (1.7)                | 4.0 (1.1)                 | 6.9 (2.2)                 |
| SV ratio         | 3.6 (3.0, 4.4)          | 1.8 (1.6, 2.2)           | 7.2 (6.0, 8.6)            | 3.6 (3.1, 4.4)            |
| Triglycerides (mmol/L) | 0.9 (0.8, 1.2)    | 1.6 (1.4, 2.1)           | 0.9 (0.6, 1.0)            | 1.1 (0.8, 1.2)            |
| Total cholesterol (mmol/L) | 4.3 (0.8)          | 4.9 (0.9)                | 4.5 (0.8)                 | 4.6 (0.8)                 |
| HDL-C (mmol/L)   | 1.3 (0.3)               | 1.1 (0.3)                | 1.5 (0.4)                 | 1.3 (0.3)                 |
| LDL-C (mmol/L)   | 2.5 (0.7)               | 3.0 (0.7)                | 2.6 (0.7)                 | 2.6 (0.7)                 |
| SBP (mmHg)       | 116 (13)                | 126 (17)                 | 114 (13)                  | 121 (18)                  |
| DBP (mmHg)       | 68 (10)                 | 74 (10)                  | 67 (11)                   | 69 (11)                   |
| Glucose (mmol/L) | 5.4 (5.1, 5.8)          | 5.8 (5.3, 6.1)           | 5.2 (4.9, 5.6)            | 5.5 (5.2, 5.9)            |
| Insulin (pmol/L) | 22 (18, 25)             | 50 (45.57)               | 25 (22, 29)               | 47 (41.55)                |
| Insulin sensitivity (M/LBM) (mg/kgLBM) | 12.5 (4.5)          | 10.0 (4.1)               | 13.8 (4.7)                | 12.1 (4.9)                |

*aIndicates log transformed data presented as the geometric mean and 95% confidence interval.

BMI, body mass index; SV ratio, subcutaneous/visceral ratio; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Discussion

The present cross-sectional study shows that there is a percent body fat threshold at which a steep increase in VAT slope (presumably representing rate of accumulation) occurs in both male and female adults. While we have previously shown this relation exists in National Football League players, this study expands those findings by showing that the threshold is significantly higher in females than males and that the threshold was similar in this average group of adult males to the threshold found in the significantly larger football players. Moreover, in both males and females, individuals above the threshold had significantly worse levels of metabolic risk factors, apparently related to VAT, since, after accounting for VAT mass, the association between total fat mass and cardiometabolic risk was greatly reduced.

BMI is the generally accepted standard used to assess CV risk. However, BMI has been shown in some studies to be inferior to body fat measurements as an indicator of elevated cardiometabolic risk factors, particularly in thin individuals (22,23). In this study, BMI was related to VAT in men but not women. While waist circumferences are used as a surrogate measure of visceral adiposity, it also is an indirect measurement. The recent documentation of DXA as a valid estimate of VAT in adults (13) now offers a reliable alternative for assessment of visceral adiposity. In this study, DXA was able to clearly show increased levels of VAT relative to percent body fat, and VAT is an established marker of cardiometabolic risk. Thus, DXA may yield a more reliable method for the clinical evaluation of cardiometabolic disease risk.

Females were found to have a higher percent body fat threshold for accumulation of VAT than males. This seems most likely to be a result of the well-known differences between males and females in the pattern of fat accumulation, related to hormonal differences. Estrogen promotes distribution of fat to peripheral subcutaneous adipose tissue, whereas testosterone shifts fat to abdominal and visceral regions (24). The higher female threshold also may be related to differences in adipocyte characteristics. Despite having greater stores...
of subcutaneous fat, females generally have smaller adipocytes until reaching morbid obesity (25,26). Increased fat depot volume tends to occur through adipocyte hyperplasia (creation of new adipocytes). In contrast, increased fat volume in males tends to occur via adipocyte hypertrophy (growth of existing adipocytes), resulting in fewer but larger adipocytes (27). Since adipocyte size is related to dysfunction, which is a signal for redistribution to more distant storage depots (28), this also could influence the lower percent fat threshold associated with increased VAT in males. However, regardless of the different thresholds observed in this study between males and females, the increasing slope of VAT accumulation results in a similar adverse effect on the cardiometabolic risk factors.

Consistent with previous reports (5-12) VAT mass in this study was shown to be significantly related to cardiometabolic risk, and this relation was stronger than with total fat mass or subcutaneous fat mass, noting that the latter was significantly greater above and below the threshold in females. Although below the percent fat threshold both VAT mass and cardiometabolic risk factors were similar in males and females, in individuals with percent fat above the threshold males had more VAT and a worse cardiometabolic profile. Previous work demonstrated that VAT, as opposed to subcutaneous fat, is associated with insulin sensitivity (29). While total fat mass also was positively associated (Tables 3 and 4) with insulin sensitivity, it accounted for only a small, but significant, percent of the variance (4%).

There are some limitations to this study. First, although the results were significant, PHPBC study (17) had a higher intercept than the insulin study (16). For all models where study was significant, PHPBC study had a higher intercept than the insulin study. Second, physical activity was not included (each study measured physical activity differently); however, separate analyses within each study demonstrated

### TABLE 3 Linear regression analyses above and below threshold in males

| Variable | Standard coeff. | SE | P-value |
|----------|-----------------|----|---------|
| logTG (Model $R^2 = 0.034$) | VAT | 0.14 | 0.10 | 0.17 |
| | TFM | −0.19 | 0.10 | 0.06 |
| HDL-C (Model $R^2 = 0.124$) | VAT | −0.13 | 0.10 | 0.184 |
| | TFM | 0.02 | 0.09 | 0.806 |
| Insulin sensitivity ($M_{BM}$) (Model $R^2 = 0.040$) | VAT | −0.05 | 0.11 | 0.675 |
| | TFM | 0.20 | 0.11 | 0.058 |
| Total cholesterol (Model $R^2 = 0.135$) | VAT | 0.03 | 0.10 | 0.776 |
| | TFM | −0.03 | 0.10 | 0.738 |
| LDL-C (Model $R^2 = 0.095$) | VAT | 0.03 | 0.10 | 0.757 |
| | TFM | 0.04 | 0.10 | 0.703 |
| SBP (Model $R^2 = 0.331$) | VAT | −0.06 | 0.09 | 0.466 |
| | TFM | 0.03 | 0.09 | 0.764 |
| DBP (Model $R^2 = 0.102$) | VAT | 0.16 | 0.11 | 0.141 |
| | TFM | −0.07 | 0.10 | 0.492 |
| Glucose (Model $R^2 = 0.014$) | VAT | 0.13 | 0.10 | 0.218 |
| | TFM | −0.07 | 0.10 | 0.467 |
| Insulin (Model $R^2 = 0.011$) | VAT | −0.09 | 0.10 | 0.376 |
| | TFM | 0.11 | 0.10 | 0.271 |

VAT, visceral adipose tissue; TFM, total fat mass; TG, triglycerides.

$^a$Indicates if coefficients are significantly different between models above and below threshold ($P < 0.01$).

$^b$Indicates covariate factors with a significant association (indicated as dependent variable – significant independent variable).

For all models where study was significant, PHPBC study had a higher intercept than the insulin study. PHPBC study (17) had a higher intercept than the insulin study (16).

Models for males above >23.4% percent fat: TG, cigarette use-status-current smoker > never = cessation; HDL-C – study; Chol – Study; LDL-C Study; SBP – Study; DBP – Study; Glucose – Study.

Models for males below <23.4% percent fat: HDL-C – Study, current smoker > Chol – Study; LDL-C Study; SBP – Study; DBP – Race AA > Caucasian.
TABLE 4 Linear regression analyses above and below threshold in females

| Variable               | Standard Coeff. | SE    | P-value | Variable               | Standard Coeff. | SE    | P-value |
|------------------------|-----------------|-------|---------|------------------------|-----------------|-------|---------|
| logTG (Model^b R^2 = 0.085) |                 |       |         | logTG (Model^b R^2 = 0.179) |                 |       |         |
| VAT                    | 0.19            | 0.12  | 0.113   | VAT                    | 0.54^a          | 0.10  | <0.001  |
| TFM                    | -0.02           | 0.12  | 0.885   | TFM                    | -0.28^a         | 0.10  | 0.005   |
| HDL-C (Model^b R^2 = 0.195) |               |       |         | HDL-C (Model^b R^2 = 0.176) |               |       |         |
| VAT                    | -0.14           | 0.11  | 0.214   | VAT                    | -0.35^a         | 0.10  | <0.001  |
| TFM                    | -0.05           | 0.11  | 0.634   | TFM                    | 0.01            | 0.10  | 0.883   |
| Insulin sensitivity (M\_{BMI}) (Model^b R^2 = 0.096) |               |       |         | Insulin sensitivity (M\_{BMI}) (Model^b R^2 = 0.243) |               |       |         |
| VAT                    | -0.14           | 0.11  | 0.251   | VAT                    | -0.54^a         | 0.11  | <0.001  |
| TFM                    | 0.27            | 0.13  | 0.04    | TFM                    | 0.20            | 0.10  | 0.05    |
| Cholesterol (Model^b R^2 = 0.162) |               |       |         | Cholesterol (Model^b R^2 = 0.049) |               |       |         |
| VAT                    | 0.25            | 0.12  | 0.035   | VAT                    | 0.10            | 0.10  | 0.306   |
| TFM                    | -0.11           | 0.12  | 0.344   | TFM                    | -0.08           | 0.10  | 0.419   |
| LDL-C (Model^b R^2 = 0.107) |               |       |         | LDL-C (Model^b R^2 = 0.013) |               |       |         |
| VAT                    | 0.37            | 0.11  | 0.001   | VAT                    | 0.13^a          | 0.10  | 0.209   |
| TFM                    | -0.13           | 0.11  | 0.248   | TFM                    | -0.03           | 0.11  | 0.805   |
| SBP (Model^b R^2 = 0.117) |               |       |         | SBP (Model^b R^2 = 0.308) |               |       |         |
| VAT                    | 0.08            | 0.13  | 0.541   | VAT                    | -0.03           | 0.10  | 0.761   |
| TFM                    | 0.03            | 0.13  | 0.813   | TFM                    | 0.31^a          | 0.09  | <0.001  |
| DBP (Model^b R^2 = 0.010) |               |       |         | DBP (Model^b R^2 = 0.133) |               |       |         |
| VAT                    | 0.11            | 0.13  | 0.382   | VAT                    | -0.03           | 0.11  | 0.774   |
| TFM                    | -0.08           | 0.12  | 0.526   | TFM                    | 0.23^a          | 0.11  | 0.033   |
| Glucose (Model^b R^2 = 0.007) |               |       |         | Glucose (Model^b R^2 = 0.057) |               |       |         |
| VAT                    | 0.07            | 0.12  | 0.531   | VAT                    | 0.11            | 0.11  | 0.306   |
| TFM                    | 0.02            | 0.12  | 0.898   | TFM                    | 0.06            | 0.11  | 0.567   |
| Insulin (Model^b R^2 = 0.130) |               |       |         | Insulin (Model^b R^2 = 0.263) |               |       |         |
| VAT                    | 0.03            | 0.11  | 0.678   | VAT                    | 0.11            | 0.11  | 0.306   |
| Subcutaneous Fat        | 0.33            | 0.11  | 0.003   | TFM                    | 0.06^a          | 0.11  | 0.567   |

VAT: Visceral Adipose tissue; TFM, Total Fat Mass; TG, triglycerides; subcutaneous fat, subcutaneous abdominal fat.

^bIndicates if coefficients are significantly different between models above and below threshold (P < 0.01).

^aIndicates other covariate factors were significantly associated in the model.

For all models where study was significant PHPBC study (17) had a higher intercept than the insulin study (16). Models for females above >38.3%: TG – being on birth control ≠ no birth control; HDL – Study and being a current smoker > quit > never smoked; (M\_{BMI}) – being on birth control > no birth control and Study; Chol – Study; SBP – Study; DBP – Study; Glucose – Race (other)>AA = Caucasian). Models for females below <38.3%: TG – Study; HDL – Study; M/lbm – Study; Chol – Study; SBP – Study.

that it did not provide additional information to the models after we controlled for other variables. Third, the study was restricted to Caucasian and African-American subjects and these data may not be applicable to other ethnic/racial groups. Additionally, it is noteworthy in Figure 1 that there were a group of males and females above threshold with high percent body fat but low visceral mass. This group of “nonresponders” warrants further study to determine why their visceral accumulation remains low at increased adiposity.

In summary, VAT increased to a significantly greater degree above specific percent fat thresholds in men and women. Thus, increases in adiposity below the percent body fat threshold are likely to be distributed subcutaneously rather than to VAT. VAT mass is a stronger marker for CV risk and insulin resistance compared with total fat mass or subcutaneous android mass, as such, being above the percent body fat threshold could increase the risk of cardiometabolic complications. These results suggest that percent body fat may be an important clinical measurement because of its relationship with VAT mass.

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