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Identification of sex-specific thresholds for accumulation of visceral adipose tissue in adults

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Abstract

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 if a threshold exists, and to explore the association with cardiometabolic risk factors in adults.

Design and Methods—Using a cross1sectional design, data were obtained from 723 adults (324 females) age 19-47 years. Body mass index ranged from 15-52 kg/m^2. 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 %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.

Conclusion—We infer from these cross-sectional data that 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.

Keywords

Body composition; metabolic syndrome; insulin resistance; obesity; cardiometabolic risk

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Conflict of Interest

The authors have nothing to report.

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 x1ray 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 and Procedures

The subjects in the present study were participants in two population based longitudinal studies (16, 17) assessing cardiovascular and metabolic changes associated with cardiovascular (CV) risk between childhood and adulthood. Data were obtained from the most recent follow1up 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 the current 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 eight hours. 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/m^2. 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 five minutes 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, USA) and analyzed using its enCore^{TM} 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 2 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 hours, and glucose was infused at a variable rate to maintain euglycemia. Insulin sensitivity (M) was expressed as the glucose infusion rate (mg/kg/min of glucose) during the last 40 minutes of the clamp, with adjustment for lean body mass ($M_{/LBM}$). 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), a 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 mean and 95% confidence intervals. 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 breakpoint (VAT= total percent body fat + Study); using the scatterplot we initialized the breakpoint (’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 t1tests 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 mulitcollinearity was observed, the variables were removed individually and Akaike information criterion (AIC) was compared between the models. The variable that maintained the lowest AIC was kept within the final model. AIC was calculated for each model to determine if removal of covariate variables resulted in the best fit. It addition we measured the normality and variance of the models.

The results are presented as R^2 for the whole model, standardized coefficient (that is, per standard deviation of the predictor), standard error and the p value for each independent variable (fat depots (mass in grams)) that remained in the final model. The individual variance for each independent variable within the model was calculated to compare relative strengths of predictors. All analyses were completed using R (R Foundation for Statistical Computing, www.R-project.org).

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 cardiovascular 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 non-linear relationship with percent body fat (Figure 1a1b) 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= $\beta_0+\beta_1$(%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, i.e., β=16.9 (SE=13.3, p=0.204 95%CI= 19.251, 43.13), while a significant slope was identified above the threshold, i.e., 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, β=10.7(SE=10.91, p=0.328, 95%CI = 110.8, 32.2), while above the threshold the slope increased significantly to β=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/m2 (95%CI = 22.1, 24.9)., with an insignificant slope below the threshold, i.e., −3.7 (SE = 24.3, p=0.878, 95%CI = −51.4, 44.0) and a significant positive slope above the threshold, i.e., 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 thresholds indicated that males had higher VAT mass and adverse levels of the cardiovascular risk factors, including insulin sensitivity, than females. However, females 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_{lbm}) compared to 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, QQplots

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; LDL1C= 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 population VAT remained significantly associated with each dependent variable with similar standardized coefficients ($p>0.05$). Study participation 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 models, except for insulin. Subcutaneous android fat provided a stronger marker than total body fat in the insulin model. Fat depots are presented 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, QQplots and residual plots suggested normality and constant variance. Above threshold, VAT was significantly associated with TG, HDL, M/lbm and fasting insulin, however, no significant association was observed for cholesterol, LDL-C, SBP, DBP, and glucose. Study participation was a significant factor, which resulted in a significantly higher intercept for the PHBPC study (17) (HDL = 0.18 mmol/l; Chol = 0.36 mmol/l; SBP= 17 mmHg; DBP = 7 mmHg). With few exceptions, VAT was not significantly associated with cardiometabolic risk factors below threshold. Birth control status was a significant covariate for triglycerides and insulin sensitivity in females above threshold, but was not significant in females below threshold. Study participation was a significant factor, which resulted in a significantly higher intercept for the PHBPC study (17) (TG= 0.009 mmol/l; HDL1C = 0.34 mmol/l; M/lbm = 2.8 $_{mg/kg/lbm/min}$; Chol= 0.41 mmol/l; SBP = 9 mmHg)

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, the present 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 cardiovascular 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 the present 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 distal 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 (Table 3 and 4) with insulin sensitivity in both males and females below threshold, it accounted for only a small, but significant, percent of the variance (~4%).

There are some limitations to this study. First, although the results show the threshold effect appears to be unique to VAT (all subcutaneous depots displayed a linear relationship with total fat mass), this is a cross-sectional observation and longitudinal data would provide a picture of potentially different fat depot relations. Second, physical activity was not included (each study measured physical activity differently); however, separate analyses within each study demonstrated 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 “non-

responders" 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 cardiovascular risk and insulin resistance compared to 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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JS, AS, AM, and DJ designed the studies, acquired funding, and collected the data. TB performed the analysis and created the manuscript. DD, AK, JS, AS, AM, and DJ edited the manuscript and contributed to the intellectual content.

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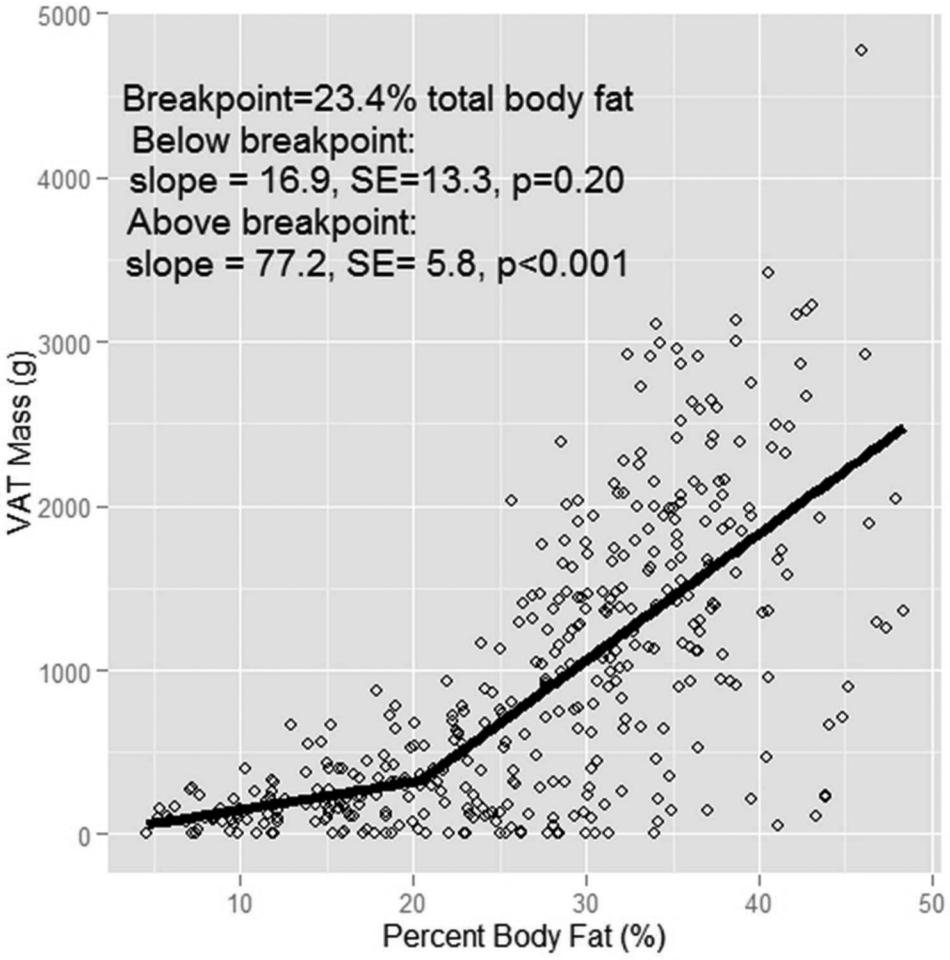
What is known about this subject:

- Visceral fat is an independent marker of cardiometabolic risk factors.
- Males generally distribute fat to the abdominal region where females generally distribute fat the hip-gluteal region.

What this study adds:

- Identification of sex-specific adiposity thresholds at which visceral fat accumulation significantly increases.
- Above threshold, visceral fat has a stronger association with insulin sensitivity and lipids, compared to total body fat.



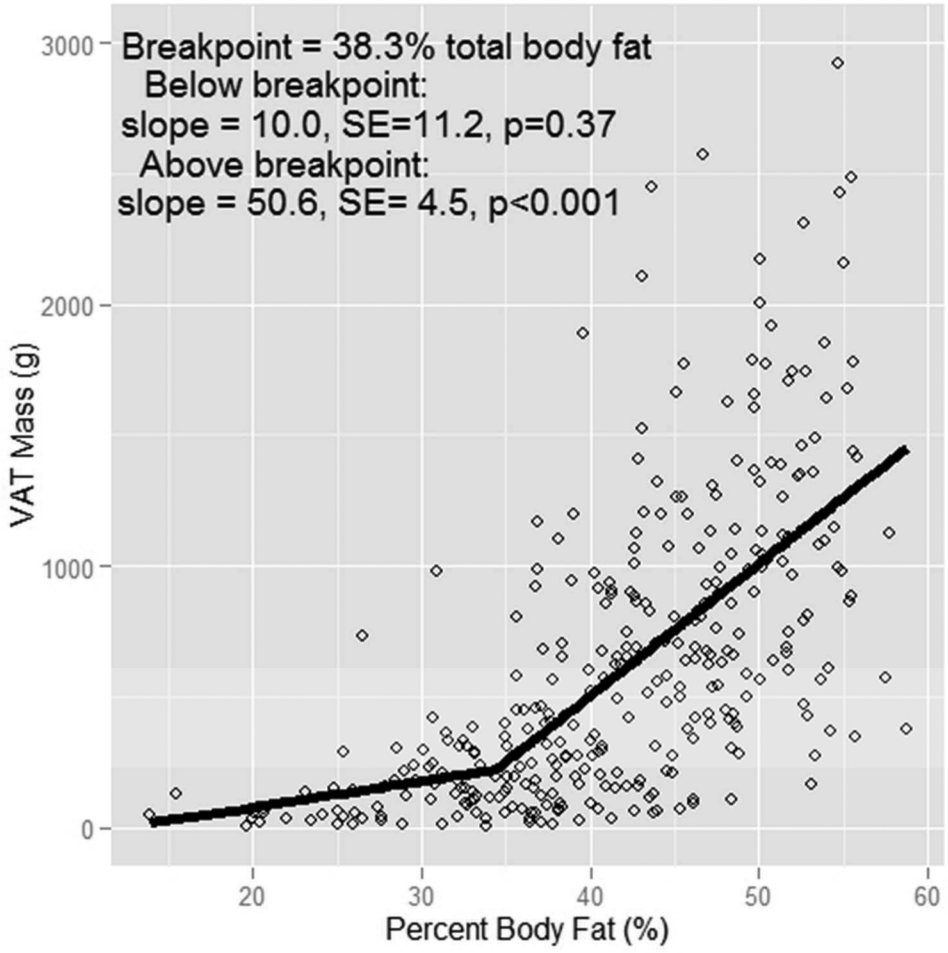


Figure 1.

Scatter plots of visceral adipose tissue (VAT) mass relative to percent body fat, demonstrating the sex-specific thresholds for visceral accumulation. (A) men (B) women

Table 1

Demographic body composition and clinical measurements mean(sd)

	Female (n=324)	Male (n=399)	p-value
Age (yrs)	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 Fat (%)	41.4(8.9)	26.8(10.0)	<0.001
BMI (kg/m^2)	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*	4.7(4.3, 5.2)	2.4(2.1, 2.8)	<0.001
Triglycerides* (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* (mmol/L)	5.4(5.2,5.5)	5.7(5.5,5.8)	<0.001
Insulin* (pmol/L)	36(33,40)	36(33,40)	0.8992
Insulin Sensitivity (mg/kglbm/min)	11.9(5.1)	9.5(4.1)	<0.001

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

* Indicates log transformed data presented as the geometric mean and 95% confidence interval BMI = body mass index, SV = subcutaneous/visceral fat ratio, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, SBP = systolic blood pressure, DBP = diastolic blood pressure

Table 2

Body composition and cardiometabolic variables above and below thresholds mean(±SD)

	Males <23.4% (n=158)	Males >=23.4% (n=241)	Females <38.3% (n=133)	Females>=38.3% (n=191)
Age (yrs)	30^{A}(9)	35^{B}(7)	34^{B}(8)	35^{B}(7)
Height (cm)	177.2^{A}(8.2)	177.8^{A}(7.6)	164^{B}(8.4)	164.7^{B}(6.2)
Weight (kg)	73.3^{A}(12.2)	96.3^{B}(17.8)	64.9^{C}(11.1)	89.3^{D}(18.2)
BMI (kg/m^2)	23.3^{A}(3.1)	30.4^{B}(5.2)	24^{A}(4.0)	33^{C}(6.5)
Waist (cm)	82.9^{A}(7.0)	105.9^{B}(13.1)	81.9^{A}(12.5)	104.0^{B}(15.3)
Body Fat (%)	16.4^{A}(5.4)	33.7^{B}(5.3)	32.8^{B}(5.6)	47.5^{C}(4.7)
Total Fat mass (kg)	13.4^{A}(4.8)	30.9^{B}(11.2)	20.5^{C}(5.8)	39.4^{D}(12.6)
Total Lean mass (kg)	50.1^{A}(14.2)	47.3^{B}(16.0)	45.7^{B}(14.6)	46.4^{B}(14.4)
Android fat (kg)	0.8^{A}(0.5)	3.1^{B}(1.5)	1.4^{C}(0.7)	3.5^{D}(1.4)
Subcutaneous fat (kg)	0.6^{A}(0.4)	1.8^{B}(0.9)	1.1^{C}(0.5)	2.6^{D}(1.0)
Visceral fat (kg)	0.3^{A}(0.2)	1.4^{B}(0.8)	0.3^{A}(0.3)	0.9^{C}(0.6)
Gynoid fat (kg)	2.2^{A}(0.9)	4.8^{B}(1.7)	4.0^{C}(1.1)	6.9^{D}(2.2)
*SV ratio	3.6^{A}(3.0,4.4)	1.8^{B}(1.6,2.2)	7.2^{C}(6.0,8.6)	3.6^{A}(3.1,4.4)
*Triglycerides (mmol/L)	0.9^{A}(0.8,1.2)	1.6^{B}(1.4,2.1)	0.9^{A}(0.6,1.0)	1.1^{C}(0.8,1.2)
Total Cholesterol (mmol/L)	4.3^{A}(0.8)	4.9^{B}(0.9)	4.5^{A}(0.8)	4.6^{A}(0.8)
HDL-C (mmol/L)	1.3^{A}(0.3)	1.1^{B}(0.3)	1.5^{C}(0.4)	1.3^{A}(0.3)
LDL-C (mmol/L)	2.5^{A}(0.7)	3.0^{B}(0.7)	2.6^{A}(0.7)	2.8^{C}(0.7)
SBP (mmHg)	116^{A}(13)	126^{B}(17)	114^{A}(13)	121^{C}(18)
DBP (mmHg)	68^{A}(10)	74^{B}(10)	67^{A}(11)	69^{A}(11)
*Glucose (mmol/L)	5.4^{A}(5.1,5.8)	5.8^{B}(5.3,6.1)	5.2^{C}(4.9,5.6)	5.5^{A}(5.2,5.9)
*Insulin (pmol/L)	22^{A}(18, 25)	50^{B}(45,57)	25^{A}(22,29)	47^{B}(41,55)
Mlbm (mg/kglbm/min)	12.5^{A}(4.5)	10.0^{B}(4.1)	13.8^{C}(4.7)	12.1^{D}(4.9)

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

*Indicates log transformed data presented as the geometric mean and 95% confidence interval If groups do not share a letter in the same row they are significantly different $p<0.025$

Table 3

Linear regression analysis above and below threshold in males.

Males < 23.4% body fat				Males >=23.4% body fat			
Variable	**Standard coeff.**	**SE**	**p-value**	**Variable**	**Standard coeff.**	**SE**	**p-value**
logTG (Model R^2 = 0.034)				logTG (Model* R^2= 0.238)			
VAT	0.14	0.10	0.17	VAT	0.57†	0.08	<0.001
TFM	−0.19	0.10	0.06	TFM	−0.22	0.08	0.008
HDL-C (Model* R^2= 0.124)				HDL-C (Model* R^2 = 0.132)			
VAT	−0.13	0.10	0.184	VAT	−0.47†	0.11	<0.001
TFM	0.02	0.09	0.806	TFM	0.07	0.09	0.430
Insulin Sensitivity M/lbm (Model R^2=0.040)				Insulin Sensitivity M/lbm (Model R^2= 0.162)			
VAT	−0.05	0.11	0.675	VAT	−0.45†	0.08	<0.001
TFM	0.20	0.11	0.058	TFM	0.07†	0.09	0.423
Total Cholesterol (Model* R^2 =0.135)				Total Cholesterol (Model* R^2 =0.139)			
VAT	0.03	0.10	0.776	VAT	0.15†	0.10	0.13
TFM	−0.03	0.10	0.738	TFM	−0.03	0.09	0.738
LDL-C (Model* R^2= 0.095)				LDL-C (Model* R^2=0.072)			
VAT	0.03	0.10	0.757	VAT	0.07	0.11	0.509
TFM	0.04	0.10	0.703	TFM	0.06	0.09	0.489
SBP (Model* R^2=0.331)				SBP (Model* R^2=0.362)			
VAT	−0.06	0.09	0.466	VAT	0.26†	0.09	0.03
TFM	0.03	0.09	0.764	TFM	−0.04	0.08	0.748
DBP (Model* R^2=0.102)				DBP (Model* R2 = 0.217)			
VAT	0.16	0.11	0.141	VAT	0.28†	0.11	0.012
TFM	−0.07	0.10	0.492	TFM	−0.02	0.09	0.839
Glucose (Model R^2=0.014)				Glucose (Model* R^2= 0.121)			
VAT	0.13	0.10	0.218	VAT	0.19	0.11	0.069
TFM	−0.07	0.10	0.467	TFM	0.06	0.09	0.488
Insulin (Model R^2 = 0.011)				Insulin (Model R^2= 0.148)			
VAT	−0.09	0.10	0.376	VAT	0.17†	0.08	0.04
TFM	0.11	0.10	0.271	TFM	0.24	0.08	0.003

VAT = Visceral Adipose tissue, TFM = Total Fat Mass

For all models where Study was significant, 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-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

† Indicates if coefficients are significantly different between models above and below threshold ($p<0.01$)

* Indicates covariates factors with a significant association (indicated as dependent variable – significant independent variable)

Table 4

Linear regression analyses above and below threshold in females

Females <38.3% Body Fat				Females >=38.3% Body Fat			
Variable	**Standard Coeff.**	**SE**	**p-value**	**Variable**	**Standard Coeff.**	**SE**	**p-value**
logTG (Model* R^2= 0.085)					logTG (Model* R^2=0.179)		
VAT	0.19	0.12	0.113	VAT	0.54†	0.10	<0.001
TFM	−0.02	0.12	0.885	TFM	−0.28†	0.10	0.005
HDL-C (Model* R^2=0.195)					HDL-C (Model* R^2=0.176)		
VAT	−0.14	0.11	0.214	VAT	−0.35†	0.10	<0.001
TFM	−0.05	0.11	0.634	TFM	0.01	0.10	0.883
Insulin Sensitivity M/lbm (Model* R^2= 0.096)					Insulin Sensitivity M/lbm (Model* R^2= 0.243)		
VAT	−0.14	0.13	0.251	VAT	−0.54†	0.11	<0.001
TFM	0.27	0.13	0.04	TFM	0.20	0.10	0.05
Cholesterol (Model* R^2= 0.162)					Cholesterol (Model* 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 R^2= 0.107)					LDL-C (Model R^2= 0.013)		
VAT	0.37	0.11	0.001	VAT	0.13†	0.10	0.209
TFM	−0.13	0.11	0.248	TFM	−0.03	0.11	0.805
SBP (Model* R^2= 0.117)					SBP (Model* 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†	0.09	<0.001
DBP (Model R^2= 0.010)					DBP (Model* 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†	0.11	0.033
Glucose (Model R^2=0.007)					Glucose (Model* 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 R^2= 0.130)					Insulin (Model 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†	0.11	0.567

VAT = Visceral Adipose tissue, TFM = Total Fat Mass, subcutaneous fat = subcutaneous abdominal fat

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/LBM – 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%i TG – Study; HDL – Study; M/lbm – Study; Chol – Study; SBP – Study

† Indicates if coefficients are significantly different between models above and below threshold ($p<0.01$)

* indicates other covariates factors were significantly associated in the model