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Sex differences in the associations of visceral adiposity, HOMA-IR, and BMI with lipoprotein subclass analysis in obese adolescents

Jacquelyn A Hatch-Stein, MD^a, Andrea Kelly, MD MSCE^a, Samuel S Gidding, MD^b, Babette S Zemel, PhD^c, and Sheela N Magge, MD MSCE^{a,d}

^aDivision of Endocrinology and Diabetes, The Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard, Philadelphia, PA 19104

^bNemours Cardiac Center, A. I. DuPont Hospital for Children, 1600 Rockland Road, Wilmington, DE 19803

^cDivision of Gastroenterology, Hepatology, and Nutrition, The Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard, Philadelphia, PA 19104

^dDivision of Endocrinology and Diabetes, Center for Translational Science, Children's National Health System, 111 Michigan Ave NW, Washington, DC 20010

Abstract

Background—The relationship of lipoprotein particle subclasses to visceral adipose tissue area (VAT-area) in obese children has not been examined previously.

Objectives—The study aims were to compare the relationships of VAT-area, homeostatic model assessment of insulin resistance (HOMA-IR), and body mass index (BMI) with lipids and lipoprotein subclasses in obese adolescents, and to determine if these relationships vary by sex.

Methods—This cross-sectional study of obese adolescents (BMI 95th percentile), ages 12-18y, measured VAT-area by dual energy x-ray absorptiometry (DXA), BMI, fasting lipids, lipoprotein subclasses, and HOMA-IR. Linear regression models evaluated the associations of VAT-area, HOMA-IR, and BMI with lipid cardiometabolic risk factors. Sex-stratified analyses further explored these associations.

Results—Included were 127 adolescents (age=14.4±1.5 years; 53.5% female; 88.2% African-American), mean BMI=34.0±5.1 kg/m². VAT-area was negatively associated with LDL particle (–P) size (β =–0.28, p =0.0001), HDL-P size (β =–0.33, p <0.0001) and large HDL-P concentration

Address for Correspondence: Jacquelyn Hatch-Stein, MD, The Children's Hospital of Philadelphia, 11NW - Division of Endocrinology and Diabetes, 34th Street and Civic Center Boulevard, Philadelphia, PA 19104-4399, 215-590-3174 (fax 3053), hatchsteinj@email.chop.edu, kellya@email.chop.edu, Samuel.gidding@nemours.org, Zemel@email.chop.edu, shmagge@childrensnational.org

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CONFLICTS OF INTEREST

None.

($\beta=-0.29$, $p<0.0001$), and positively associated with small LDL-P concentration ($\beta=0.23$, $p=0.0005$) and small HDL-P concentration ($\beta=0.25$, $p=0.05$). When VAT-area, HOMA-IR, and BMI associations were compared, VAT-area had the strongest associations with most of the lipoprotein subclasses. After sex-stratification, the associations of VAT-area with HDL cholesterol, LDL-P size, and large LDL-P concentration were significant only for females (all $p<0.05$).

Conclusions—In a cohort of largely African-American obese adolescents, VAT-area was associated with a more atherogenic lipoprotein subclass profile. When compared to HOMA-IR and BMI, VAT-area had the strongest associations with most lipoprotein subclasses. The relationships between VAT-area and certain lipoprotein subclasses are significantly different in males versus females.

Keywords

lipoprotein subclasses; visceral fat; obesity; pediatric; sex differences

INTRODUCTION

Specific depots of adipose tissue, rather than total body fat mass, may be more strongly associated with dyslipidemia, metabolic dysregulation, future diabetes, and cardiovascular disease.(1-3) Recent studies in adults have found a significant association between VAT-area and standard cardiometabolic risk factors, even after adjustment for age, BMI, and waist circumference.(4, 5) Racial, ethnic, and sex differences in VAT-area are apparent, with men and Caucasians having higher VAT-area than women and African-Americans, respectively. (3, 5, 6)

VAT-area has also been associated with various lipoprotein subclasses, which provide additional risk information beyond the standard lipid panel. In obese adults, VAT-area is associated with smaller LDL and HDL particle size, larger VLDL particle size, and increased LDL and VLDL particle number, as well as decreased insulin sensitivity - all characteristics of an atherogenic phenotype.(7, 8) Although women typically have an overall lower-risk subclass profile, including larger LDL and HDL particles,(9, 10) no significant differences by sex or race have been reported in the relationship between VAT-area and lipoprotein subclasses.(7)

As with adults, African-American children have less VAT-area compared to Caucasians and Hispanics,(11) but sex differences have yet to be established.(11, 12) Early findings suggest VAT-area may be associated with greater cardiometabolic risk in females versus males,(13) but the sex-specific relationship of VAT-area with lipoprotein subclasses has not been examined. The association of more standard measures of cardiometabolic risk, such as BMI or HOMA-IR, with lipoprotein subclasses has received limited attention in children.(14, 15) The primary aims of this study were to compare the independent relationships of VAT-area, HOMA-IR, and BMI with standard lipid measures and lipoprotein subclasses in obese adolescents, and to examine the sex-specific relationships of VAT-area, HOMA-IR, and BMI with lipids and lipoprotein subclass particles.

METHODS

Sample

We performed secondary analyses of cross-sectional data derived from two study cohorts, one consisted of baseline data from a cholecalciferol supplementation study in obese pubertal African-American adolescents; the other included obese adolescents from a study of cardiometabolic risk factors in pubertal adolescents. Subjects, ages 12-18 years, were included in the current study if they were obese (BMI ≥ 95th percentile for age and sex) and had a whole-body DXA scan. Exclusion criteria for these studies included genetic syndromes or conditions known to affect glucose tolerance and/or insulin resistance (such as cystic fibrosis, Prader Willi syndrome, and congenital lipodystrophies) and treatment with medications known to affect lipid profiles or high dose inhaled steroids (>1000 mcg/day). Original data were collected from 10/2007 to 6/2012. Both protocols were approved by the Children's Hospital of Philadelphia Institutional Review Board and consent/assent was obtained from parents and participants, respectively.

Anthropometric measures

Anthropometry was performed in The Children's Hospital of Philadelphia (CHOP) Clinical and Translational Research Center (CTRC) Nutrition Core Laboratory by trained research anthropometrists. Weight was measured on an electronic scale (Scaletronix), calibrated daily, with the participant in a light gown without shoes. Height was measured using a wall-mounted Harpenden stadiometer (Holtain). Measurements were repeated three times, and average values utilized. BMI z-scores were calculated using the CDC 2000 growth charts. (16) Pubertal staging (determined by breast stage for girls and testicular volume for boys) was performed by a pediatric endocrinologist. (17, 18) Pubertal staging data was missing in 3 subjects.

Body composition

Whole Body DXA scans were acquired to measure body composition using a Hologic (Bedford, MA) Discovery system and analyzed using the Enhanced Whole Body Version 13.5 software to provide a measure of visceral adiposity (VAT-area). Standard positioning techniques were used. Adolescents weighing greater than 300 pounds could not undergo DXA, because of the weight limit of the scanner.

Laboratory measurements

After subjects fasted for 12 hours, a blood sample was obtained for measurement of lipids (triglycerides, total cholesterol and HDL-C), lipoprotein subclass analysis, glucose, and insulin. Lipid analyses were performed on a Hitachi 912 using Roche reagents. LDL-C was calculated using the Friedewald equation ($LDL-C = TC - HDL-C - (TG/5)$) for $TG < 400$ mg/dL. Lipoprotein subclass analysis was measured by LipoScience, Inc. (Raleigh, NC), using NMR spectroscopy. Insulin was measured by enzyme-linked immunosorbent assay, using a kit from ALPCO Diagnostics (Salem, New Hampshire). HOMA-IR was calculated using the equation $[fasting\ insulin\ (uIU/mL) \times fasting\ glycemia\ (mmol/L)]/22.5$.

Statistical analysis

Baseline descriptive measures were compared between males and females using t-tests for normal or normalized continuous variables, Mann-Whitney rank sum tests for continuous variables that could not be normalized, and Chi squared analyses for categorical variables. Non-HDL cholesterol was categorized as normal (<120 ng/dl), borderline high (120 and <145 ng/dl), or high (≥145 ng/dl).⁽¹⁹⁾ Lipid and lipoprotein particle outcome variables were either log or square root transformed as needed to normalize. Descriptive measures were also compared between African Americans and non-African Americans.

We initially examined the association of VAT-area with lipid and lipoprotein particle outcomes using linear regression analysis adjusting all models for sex, age, Tanner stage, and BMI. BMI was included in this initial analysis as a covariate to see if VAT-area relationships persisted even after accounting for BMI. A sensitivity analysis with non-African Americans excluded was performed which showed similar results to analyses with non-African Americans included; therefore we presented data on all eligible subjects.

In order to investigate and compare the independent relationships of VAT-area, HOMA-IR, and BMI with standard lipid measures and lipoprotein subclasses, these relationships were first inspected graphically and then linear regression models were developed with VAT-area, HOMA-IR, and BMI as predictor variables and lipid measures and lipoprotein subclasses as outcome variables. In this case, BMI was not included in models since VAT-area and HOMA-IR were specifically being compared to BMI. Also, since best possible models were desired for comparisons, sex, pubertal staging, and age were only included as covariates in a model if they significantly contributed to a model, defined as p-value ≤ 0.05 for each of the variables' semipartial R² value. To compare the final models, standardized beta coefficients were examined. Standardized beta coefficient 95% confidence intervals were calculated using the methods of Cohen, et al.^(20, 21) The model with standardized beta coefficient of greatest magnitude (either negative or positive) without significant overlap of 95% confidence intervals with the standardized beta coefficients of the other models was then considered to represent the strongest model.

In order to then examine the sex-specific relationships of VAT-area with lipids and lipoprotein subclass particles, sex-specific relationships were examined graphically and sex interaction terms (sex by VAT-area, sex by HOMA-IR, and sex by BMI) were added to the models. Analyses with significant sex interaction terms p ≤ 0.05 or marginally significant 0.05 ≤ p ≤ 0.10 (to capture the greatest amount of sex-specific relationships that appeared graphically significant) were then stratified by sex to further explore the independent associations of the cardiometabolic outcomes with VAT-area, HOMA-IR, and BMI. Pubertal staging and age were included in all final models.

STATA software (version 13.1; Stata Corp., College Station, Texas) was used for all statistical analysis.

RESULTS

Of the 141 eligible participants in the original two studies, 127 had DXA performed and were included in this study (Table 1). Mean age was 14.4 ± 1.5 years and African-Americans comprised 112/127 (88%) of the group. All participants were pubertal with 77/127 (61%) being Tanner stage 5. Mean BMI was 34.0 kg/m^2 and did not significantly differ between males and females, but BMI was positively associated with age ($p=0.004$). VAT-area did not significantly differ between sexes or by age (Figure 1). VAT-area did increase with increasing BMI ($p<0.0001$).

Lipid and lipoprotein subclass values by sex are also reported in Table 1. In the entire group, 24.4% had borderline high levels of non-HDL cholesterol, and 13.4% had high levels, with similar rates between sexes. None of these values differed by race category.

VAT-area associations with lipids and lipoprotein subclasses

VAT-area was negatively associated with HDL cholesterol and positively associated with triglycerides and TG/HDL ratio (Table 2). VAT-area was positively associated with total LDL particle number and inversely associated with LDL-P size. Other VAT-area associations with lipoprotein subclasses are shown in Table 2.

Comparisons between VAT-area, HOMA-IR, and BMI models

Standardized beta coefficients were compared between models of VAT-area, HOMA-IR, and BMI as predictor variables and each of the standard lipid panel measurements as outcome variables (Table 3). VAT-area had the strongest negative association with HDL cholesterol, while HOMA-IR had the strongest positive associations with triglycerides and TG/HDL ratio. HOMA-IR and BMI had similar positive standardized beta coefficients in associations with non-HDL cholesterol, which were both greater than that of the VAT-area model.

Similarly, standardized beta coefficients of linear regression models with VAT-area, HOMA-IR, and BMI as predictor variables and lipoprotein subclasses as outcome variables were compared (Table 3). The VAT-area models had the strongest negative standardized beta coefficients compared to HOMA-IR and BMI models when predicting LDL-P size, large LDL-P concentration, HDL-P size, and large HDL-P concentration. Each of the VAT-area, HOMA-IR, and BMI models had similar positive standardized beta coefficients in the models that included total LDL-P and small LDL-P concentration as outcome variables. HOMA-IR models had the largest positive standardized beta coefficients in association with large VLDL-P concentration. VAT-area and HOMA-IR had similar positive standardized beta coefficients in their associations with small HDL-P concentration. Neither VAT, BMI, nor HOMA-IR were predictive of VLDL size.

Sex specific analyses

Analyses with significant sex interaction terms (Table 4) were then stratified by sex to further explore sex specific independent associations of the lipid and lipoprotein subclass outcomes with VAT-area, HOMA-IR, and BMI.

Once stratified, the associations between VAT-area and HDL cholesterol, average LDL particle size (Figure 2), and large LDL-P concentration persisted in females, but not in males. Similarly, the association of VAT-area with small HDL particle concentration persisted only in males.

All of the relationships between BMI and average LDL particle size, total LDL particle number, small LDLP concentration and HDL-P size were significant only in females.

There were no significant sex interaction terms in our HOMA-IR models. However, when analyses included the 14 participants that were too obese to undergo a full-body DXA (total n=141), sex interaction terms in the HOMA-IR models were significant for non-HDL cholesterol, total LDL-P, and large VLDL concentration. When stratified by sex, the relationships between each of these measures and HOMA-IR proved to be significant only in males.

DISCUSSION

The relationship between VAT-area and lipids and lipoprotein particle subclasses in obese adolescents has not been previously reported. In our cohort of obese, mostly African American adolescents, we compared VAT-area, BMI, and HOMA-IR as predictor variables of lipids and lipoprotein particle subclasses, and identified important sex differences in these associations.

Overall, the lipoprotein subclasses in our sample reflected a more atherogenic profile, as would be expected in obese adolescents, when compared to a large cohort of middle school children described by Mietus-Snyder et al, the only available normative data for these measures in children.(22) VAT-area in our group was higher than non-obese children.(23) In contrast to studies in adults in which higher VAT-area is reported in males,(12) we did not detect sex differences in VAT-area. Reported sex differences of VAT-area in children and adolescents have been mixed, with some studies showing males with more VAT-area, and others showing no sex differences.(11, 12) Sex differences in VAT-area found in non-obese populations may disappear when the population becomes increasingly more obese, and VAT-area becomes a significantly greater proportion of the total body size, such as in our subjects. Of note, the males in this study were less advanced in puberty than the females. Our analyses included pubertal staging to account for maturational differences in males and females, but this statistical adjustment might not sufficiently account for the possibility of visceral fat accumulation during puberty that was not fully achieved by the less mature males in our sample.

VAT-area in the pediatric population has been associated with standard measures of cardiometabolic risk, such as a positive relationship between VAT-area and triglycerides and HOMA-IR, and an inverse association with HDL cholesterol, as well as an overall positive association with the metabolic syndrome.(13-15) In our cohort, VAT-area was associated with most of the obesity-related components of the standard lipid panel and lipoprotein subclasses; these associations are considered atherogenic and related to cardiometabolic risk. These associations persisted when analyses controlled for BMI, indicating that VAT-area

provides additional independent information about these outcomes beyond the level of traditional definitions of obesity. Both total body fat and fat distribution play a contributing role to cardiometabolic risk.

Pediatric studies have shown a relationship between insulin resistance and lipoprotein subclasses, with the most insulin resistant children having more dyslipidemia.(24) We compared the VAT-area vs. lipid and lipoprotein subclass relationships to those of HOMA-IR and BMI vs. lipids and lipoprotein subclasses, hypothesizing that VAT-area provides information about cardiometabolic risk in addition to HOMA-IR and BMI. We found that HOMA-IR best predicted many of the standard lipid panel outcomes, but that VAT-area was a stronger predictor of most of the lipoprotein subclasses. The Insulin Resistance Atherosclerosis Study showed that in adults both insulin resistance and adiposity influence LDL-P size, leading to greater concentrations of small LDL particles and lower concentrations of large LDL particles, but that this adverse particle redistribution could *not* be recognized when measuring *only* LDL-C.(25) In addition, a longitudinal study of middle school children found that, just as in adults, there can be discordances in LDL-P and LDL-C percentiles, and that children with LDL-P percentiles greater than LDL-C percentiles have higher BMI, HOMA-IR, and TG levels. This study concluded that at least in obese and/or insulin resistant children, cardiometabolic risk may be underestimated by examining only standard lipid panels.(26) From this, as well as our own data, it appears that in obese adolescents, VAT-area may more fully capture the true spectrum of cardiometabolic risk than HOMA-IR or BMI alone due to its association with lipoprotein particle number, size, and subclasses.

When associations were stratified by sex, higher VAT-area appeared to be associated with more components of an atherogenic lipoprotein subclass profile in females compared to males. In fact, in males some of these associations disappeared completely. Rothney et al. showed that VAT-area in adults predicted standard lipid panel measures in women with higher effect size and odds ratios than men.(4) In the only pediatric study to investigate these relationships, Kelly et al. found that girls, but not boys, had an inverse association of VAT-area with HDL cholesterol and a positive association with fasting glucose, fasting insulin, HOMA-IR, and triglycerides.(13) Our data suggested a similar pattern, with both increased VAT-area and BMI being associated with a more atherogenic lipoprotein profile among girls. In addition, sex-stratified analyses of HOMA-IR associations including subjects too obese to undergo a DXA found that higher HOMA-IR was associated worsening of some lipoprotein subclasses in males but not females.

These associations and sex differences suggest that in females an atherogenic lipoprotein subclass profile is driven primarily by excess body weight, especially excess visceral fat, while in males it may be driven more so by insulin resistance. There are certainly overlapping features, as visceral fat is known to contribute to insulin resistance,(27) but this finding still has important implications as we look towards interventions that aim to improve cardiometabolic risk factors in obese youths. These findings suggest that in females decreasing excess body weight, specifically visceral fat, should be targeted, whereas in males, targeting insulin resistance, such as through exercise without specifically aiming for weight loss, may be more effective to improve cardiometabolic risk. Intervention studies in

adults have shown that a decrease in visceral fat over a one year period correlates with a decrease in metabolic risk factors and cardiovascular events, but these results have not been closely examined by sex.(1) VAT-area increases throughout childhood and adolescence,(11) and compared to adults, adolescents appear to have a worse pattern of insulin resistance.(28) Juonala et al. have shown though that moving from obesity in youth to normal weight in adulthood eliminates the cardiometabolic risk present in youth.(29) Collectively, these data argue for early intervention, perhaps in a sex-specific manner, to correct obesity and its metabolic consequences.

Sex differences in regional fatty acid metabolism, a key precursor to cholesterol metabolism, have been described,(30) and are likely involved in the sex differences that we have uncovered. Females are more sensitive to the antilipolytic effects of insulin than males,(31) which leads to more insulin-induced free fatty acid release from VAT in females than in males.(30) In addition to similar total VAT-area, our males and females had similar levels of insulin resistance as quantified by HOMA-IR. With similar VAT-area and levels of insulin resistance, females may have more free fatty acid release, providing more substrate for triglyceride production and cholesterol metabolism. This mechanism may explain the greater atherogenic impact that VAT-area has in our females as compared to males.

Both a strength and limitation of this cross-sectional study is that the majority of our adolescent participants were African American. We were unable to uncover significant racial differences between groups, likely due to the small numbers of non-African Americans. It would be important to know if our results can be generalized to other racial groups. When attempting to uncover racial differences in this and other areas of body composition, future studies should also consider not only racial heritage but also other differences not quantified by race such as country of origin. Significant intra-ethnic group variation in body composition has been uncovered in a number of studies, such as by Meyer et al., who found that for a given BMI z-score East African immigrant girls had a higher fat mass index and percent body fat than African American girls.(32) Given the genetic heterogeneity from different parts of Africa, it is also possible that the racial differences may be related to lifestyle differences of communities within the U.S.

Another strength and a limitation of our study is that the cohort was exclusively obese. Our results are most relevant to our most at-risk (obese) patients. It also would be important to know if these relationships remain as strong across the spectrum of weight status. The results cannot be generalized to children less than 12 years of age. Although DXA-derived measures of VAT-area are easier, less-expensive to obtain, and validated in adults,(2, 33) CT- and MRI- derived measures of VAT-area are considered the gold standards. DXA-derived VAT-area measurements have some limitations, such as increased precision error in the most obese populations ($\text{BMI} > 40 \text{ kg/m}^2$).(34) In pediatrics, a significant correlation between DXA-derived and CT derived VAT-area measurements has been shown, and is especially strong in overweight and obese children.(14)

In conclusion, our data indicate that in a cohort of obese, mostly African-American adolescents, VAT-area is highly associated with a more atherogenic lipid panel and lipoprotein subclass profile. These associations were independent of BMI and often

appeared stronger than associations with BMI or HOMA-IR alone. As lipoprotein subclasses are thought to provide data on CMR above and beyond standard lipid measures, our results indicate that VAT-area may also provide information on CMR not described by HOMA-IR or BMI. In addition, some of the relationships between VAT-area and outcome measures varied greatly between sexes. This suggests that in our most at-risk youth, and perhaps especially in obese females, VAT-area measurements may be a useful clinical tool to describe true CMR. Overall, more research is needed into how sex influences the relationship between obesity and CMR, and most importantly how we can improve interventions to target the sex-specific risks.

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Table of Abbreviations

BMI	Body mass index
CHOP	The Children's Hospital of Philadelphia
CMR	Cardiometabolic risk
CT	Computed tomography
CTRC	Clinical and Translational Research Center
DXA	Dual energy x-ray absorptiometry
HDL-C	High-density lipoprotein cholesterol
HDL-P	High-density lipoprotein particle
HOMA-IR	Homeostatic model assessment of insulin resistance
LDL-C	Low-density lipoprotein cholesterol
LDL-P	Low-density lipoprotein particle
MRI	Magnetic resonance imaging
TG	Triglycerides
VAT-area	Visceral adipose tissue area

VLDL Very low-density lipoprotein

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Highlights

- Visceral adipose tissue area is associated with atherogenic lipoprotein subclasses
- VAT-area provides information on CMR not described by HOMA-IR or BMI
- The relationship between VAT-area and LDL particle size differs by sex

Figure 1.
Visceral fat area measures by age, stratified by sex.
(Figure to be printed in black and white)

Figure 2.
LDL particle size by visceral fat area, stratified by sex.
(Figure to be printed in black and white)

Table 1

Descriptive statistics of the participants by sex, summarized with frequencies (percentages) or means (SD).

	Male (n=59)	Female (n=68)	p values
Age (years)	14.5 (1.4)	14.4 (1.6)	0.4
African-American	54/59 (91.5%)	58/68 (85.3%)	0.3
Tanner stage			<0.0001
Tanner 2	5/57 (8.8%)	1/67 (1.5%)	
Tanner 3	14/57 (24.6%)	3/67 (4.5%)	
Tanner 4	20/57 (35.1%)	4/67 (6.0%)	
Tanner 5	18/57 (31.6%)	59/67 (88.1%)	
BMI (kg/m ²)	34.0 (5.1)	33.9 (5.1)	0.9
BMI-z	2.3 (0.4)	2.2 (0.3)	0.01
Visceral fat area (cm ²)	77.8 (20.1)	79.0 (27.3)	0.9
HOMA-IR	4.7 (2.9)	4.6 (2.7)	0.7
Total cholesterol (mg/dL)	153.5 (32.9)	159.9 (30.4)	0.3
LDL cholesterol (mg/dL)	96.6 (28.9)	98.5 (26.3)	0.6
HDL cholesterol (mg/dL)	41.7 (9.6)	46.0 (11.4)	0.03
Non-HDL cholesterol (mg/dL)	111.7 (32.7)	113.9 (27.5)	0.5
Triglycerides (mg/dL)	80.0 (34.6)	76.7 (29.5)	0.8
TG/HDL	2.1 (1.2)	1.8 (1.0)	0.3
LDL-P size (nm)	20.9 (0.5)	21.2 (0.7)	0.006
Total LDL-P (nmol/L)	942.4 (288.2)	933.7 (258.4)	0.9
Small LDL-P (nmol/L)	611.2 (248.5)	522.8 (294.4)	0.05
Large LDL-P (nmol/L)	311.9 (128.2)	367.3 (170.8)	0.07
HDL-P size (nm)	8.8 (0.3)	9.1 (0.4)	0.0001
Small HDL-P (umol/L)	18.0 (4.3)	16.8 (3.7)	0.1
Large HDL-P (umol/L)	5.3 (2.3)	7.2 (2.9)	0.0002
VLDL-P size (nm)	47.8 (4.7)	46.9 (7.4)	0.4
Large VLDL-P (nmol/L)	1.2 (1.5)	0.71 (1.1)	0.04

T-tests used for normal or normalized continuous variables. Mann Whitney rank sum tests used if unable to normalize continuous variables. Chi squared tests used for categorical variables.

Table 2

Linear regression model outcomes with VAT-area as the predictor variable, with age, sex, Tanner stage, and BMI included in each model.

	Standardized beta coefficient	Adjusted R ²	p value
HDL cholesterol	−0.2	0.19	<0.0001
LDL cholesterol	0.04	−0.02	0.7
Non-HDL cholesterol	0.05	0.01	0.3
Triglycerides	0.18	0.13	0.002
TG/HDL ratio	0.22	0.18	0.0001
LDL-P size	−0.28	0.17	0.0001
Small LDL-P concentration	0.23	0.15	0.0005
Large LDL-P concentration	−0.21	0.05	0.06
Total LDL-P	0.17	0.05	0.08
HDL-P size	−0.33	0.28	<0.0001
Small HDL-P concentration	0.25	0.06	0.05
Large HDL-P concentration	−0.29	0.27	<0.0001
VLDL-P size	−0.02	−0.03	0.9
Large VLDL-P concentration	0.16	0.15	0.0004

Table 3

Linear regression model outcomes with VAT-area, HOMA-IR, and BMI as a predictor variables and standard lipid panel and lipoprotein subclass particle measures as dependent variables.

		Standardized beta coefficient	Calculated standardized beta coefficient 95% confidence interval	p value
HDL cholesterol	VAT ^{2,3}	−0.3	−0.30 β −0.30	0.0001
	HOMA-IR ²	−0.24	−0.25 β −0.23	0.002
	BMI ²	−0.22	−0.23 β −0.21	0.003
LDL cholesterol	VAT	0.07	0.07 β 0.07	0.5
	HOMA-IR	0.1	0.08 β 0.12	0.3
	BMI	0.11	0.10 β 0.12	0.2
Non-HDL cholesterol	VAT	0.1	0.10 β 0.10	0.2
	HOMA-IR	0.18	0.16 β 0.20	0.05
	BMI ¹	0.18	0.17 β 0.19	0.05
Triglycerides	VAT	0.26	0.26 β 0.26	0.004
	HOMA-IR	0.33	0.31 β 0.35	0.0002
	BMI	0.19	0.18 β 0.20	0.03
TG/HDL ratio	VAT	0.31	0.31 β 0.31	0.0005
	HOMA-IR	0.35	0.32 β 0.38	0.0001
	BMI	0.24	0.22 β 0.26	0.007
LDL-P size	VAT	−0.33	−0.33 β −0.33	0.0001
	HOMA-IR ¹	−0.21	−0.25 β −0.17	0.01
	BMI	−0.24	−0.26 β −0.22	0.007
Total LDL-P	VAT	0.24	0.24 β 0.24	0.006
	HOMA-IR	0.24	0.22 β 0.26	0.006
	BMI	0.25	0.24 β 0.26	0.004
Small LDL-P concentration	VAT	0.34	0.30 β 0.38	0.0001
	HOMA-IR ¹	0.29	−0.09 β 0.67	0.001
	BMI	0.32	0.12 β 0.52	0.0003
Large LDL-P concentration	VAT	−0.2	−0.23 β −0.17	0.03
	HOMA-IR ¹	−0.03	−0.30 β 0.24	0.3
	BMI	−0.07	−0.22 β 0.08	0.4
HDL-P size	VAT ²	−0.4	−0.40 β −0.40	<0.0001
	HOMA-IR ²	−0.33	−0.33 β −0.33	<0.0001
	BMI ²	−0.27	−0.27 β −0.27	<0.0001
Small HDL-P concentration	VAT	0.23	0.20 β 0.26	0.009
	HOMA-IR ³	0.21	−0.04 β 0.46	0.01
	BMI ³	0.09	−0.05 β 0.23	0.07

		Standardized beta coefficient	Calculated standardized beta coefficient 95% confidence interval	p value
Large HDL-P concentration	VAT ²	-0.36	-0.36 β -0.36	<0.0001
	HOMA-IR ²	-0.29	-0.32 β -0.26	<0.0001
	BMI ²	-0.24	-0.26 β -0.22	<0.0001
VLDL-P size	VAT	-0.007	-0.05 β 0.04	0.9
	HOMA-IR	0.12	-0.28 β 0.52	0.2
	BMI	0.04	-0.18 β 0.26	0.6
Large VLDL-P concentration	VAT ²	0.25	0.25 β 0.25	0.002
	HOMA-IR	0.39	0.36 β 0.42	<0.0001
	BMI ²	0.22	0.20 β 0.24	0.005

¹ Adjusted for age,

² Adjusted for sex,

³ Adjusted for tanner stage

Table 4

Stratification of linear regression models by sex, with VAT-area and BMI as predictor variables, all adjusted for age and pubertal stage.

		Male subjects standardized beta coefficient	Male adjusted R ²	Male p value	Female subjects standardized beta coefficient	Female adjusted R ²	Female p value
VAT	HDL cholesterol	−0.1	0.1	0.06	−0.45	0.15	0.01
	LDL-P size	−0.13	0.03	0.2	−0.39	0.28	0.0001
	Large LDL-P concentration	0.04	−0.04	0.7	−0.28	0.11	0.03
	Small HDL-P concentration	0.38	0.19	0.007	0.13	−0.02	0.6
BMI	LDL-P size	−0.06	0.02	0.3	−0.43	0.29	0.0001
	Total LDL-P	0.16	0.08	0.5	0.38	0.09	0.06
	Small LDL-P concentration	0.09	−0.005	0.5	0.51	0.34	<0.0001
	HDL-P size	−0.26	0.08	0.09	−0.52	0.2	0.002