Abdominal visceral and subcutaneous adipose tissues in association with cardiometabolic risk in children and adolescents: the China Child and Adolescent Cardiovascular Health (CCACH) study

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ABSTRACT

Objective To investigate the association of abdominal visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) with cardiometabolic risk factors in children and adolescents.

Research design and methods This cross-sectional study consisted of 8460 children and adolescents aged 6–18 years from Chinese urban areas who underwent dual-energy X-ray absorptiometry scan and had metabolic risk factors measured.

Results In multivariate analysis adjusted for region, family income, age, puberty development, physical activity, and smoking, VAT and SAT were significantly associated with all metabolic risk factors for both sexes (all p<0.01). After additional adjustment for fat mass index, most of these associations remain significantly positive. In boys, SAT had greater magnitude of associations compared with VAT, whereas VAT had greater ORs for all risk factors compared with SAT. In girls, however, SAT had greater odds for high triglycerides, and similar odds for other risk factors compared with VAT. In addition, boys had greater magnitude of associations of SAT with high total cholesterol, high low-density lipid cholesterol, and low high-density lipid cholesterol compared with girls; no sex differences for VAT were observed.

Conclusions Both abdominal VAT and SAT have adverse impacts on most of the cardiometabolic risk factors in youth. However, their relative contributions differ between sexes.

INTRODUCTION

Childhood obesity is a significant public health problem because of its increasing prevalence and association with adult cardiovascular disease.1,3 Childhood obesity is correlated with multiple cardiometabolic disorders, including hypertension, dyslipidemia, type 2 diabetes, and insulin resistance.4 Studies have shown that obesity is a heterogeneous condition with some obese individuals being metabolically healthy,5 which may be explained by the variation of regional fat distribution within individuals. Thus, research on the association between regional fat distribution and cardiometabolic risk will help better understand the obesity heterogeneity.

Abdominal visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT), two distinct abdominal adipose compartments, have been shown to confer different metabolic risk.6–8 Despite strong tracking of obesity from youth to adulthood, there are significant differences in the fat distribution between youth and adults. Also, regional fat
compartments, including VAT and SAT, vary with age during childhood. Studies in adults have demonstrated that VAT is more strongly associated with cardiometabolic risk factors than total fat and SAT.6,7 Several pediatric studies examining the association between abdominal fat compartments and cardiometabolic risk have reported inconsistent results.9–14 Given that body mass index (BMI) is the most commonly used measure for screening obesity and obesity-related complications in childhood, it would be important to determine whether VAT and SAT provide more information of cardiometabolic risk in addition to BMI.

Using large-scale cross-sectional data from the China Child and Adolescent Cardiovascular Health (CCACH) study, we aimed to examine the relative influences of VAT and SAT measured by dual-energy X-ray absorptiometry (DXA) on multiple cardiometabolic risk factors in children and adolescents and to determine whether these associations are independent of total fat and BMI.

**RESEARCH DESIGN AND METHODS**

**Study population**

The CCACH study is a large-scale population-based cross-sectional study conducted during 2013–2015, which was designed to select a representative sample of children and adolescents aged 6–18 years living in urban areas of China. In brief, we first stratified China into northern and southern regions by Qinling-Huaihe line according to characteristics of climate, economic development, and the residents’ life habits. Then, we chose four cities from the northern region (ie, Beijing, Changchun, Jinan, and Yinchuan) and two cities from southern region (ie, Shanghai and Chongqing). Next, several schools were randomly selected from each city to ensure the representativeness of sex, age, and socioeconomic status. All students (n=9757) from the selected schools were invited to participate in a clinical examination, including a questionnaire survey, anthropometric measurements, blood sample collection, and DXA scan. We excluded 1297 participants who were aged <6 years or >18 years or had missing data on DXA measures and metabolic risk factors. Finally, a total of 8460 children and adolescents (4267 boys and 4193 girls) were available for analysis.

The study protocol was approved by the Institution Review Board of each center, and the written informed consents were obtained from all participants or their parents.

**General information**

Data collection was conducted at each selected school by trained staffs according to a standard protocol. Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, in lightweight clothing without shoes in a calibrated digital scale (Jianmin II, China Institute of Sport Science, Beijing, China). Weight and height were measured twice, and the mean values were used to calculate BMI (calculated as weight in kilograms divided by height in meters squared). Overweight and obesity were defined using the sex-specific and age-specific BMI cutoffs recommended by the International Obesity Task Force for children aged 6–18 years.15

Blood pressure (BP) was measured by trained examiners using a calibrated automatic electronic sphygmomanometer (OMRON HEM-7012, Omron Co., Kyoto, Japan), which has been clinically validated according to a standardized protocol.16 Systolic blood pressure and diastolic blood pressure were measured three times with 1–2 min intervals, and the mean values of last two readings were used for analysis. If a difference of more than 10 mm Hg was obtained between the two adjacent BP readings, an additional measurement was obtained. Elevated BP was defined according to the US Fourth Report of National High Blood Pressure Education Program Working Group on HBP in Children and Adolescents and the updated US references by sex, age, and height.17

Information on demographic characteristics (sex and age), socioeconomic data (annual family income), and lifestyle factors (including smoking and physical activity) was collected by a self-administered questionnaire survey. Physical activity was assessed by asking questions about the frequency and duration of specific activities according to intensity over the past 12 months. All subjects were asked whether they had experienced menarche (first menstruation)/spermarche (first ejaculation), and a dichotomous response (yes/no) was obtained for their pubertal development status.

**Laboratory measurements**

After an overnight fast of at least 12 hours, blood samples were collected from the antecubital vein in the morning and then were transfused into vacuum tubes containing EDTA. Total cholesterol (TC) and triglyceride (TG) were measured by the enzymatic method, and high-density lipid cholesterol (HDL-C) and low-density lipid cholesterol (LDL-C) were measured by the direct method (Sekisui Medical, Tokyo, Japan). These biochemical variables were measured using an autoanalyzer (Hitachi 7080; Hitachi, Tokyo, Japan). The interassay coefficient of variation was <10%. Abnormal lipid concentrations were defined according to National Heart, Lung, and Blood Institute expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents:18 high TC: TC≥200 mg/dL; high TG: TG≥130 mg/dL; high LDL-C: LDL-C ≥130 mg/dL; low HDL-C: HDL-C≤40 mg/dL.

**VAT and SAT measurements**

The whole-body DXA scans were performed using Hologic Discovery (A, W, and Wi) fan-beam densitometers according to standard procedures in the user guide (Hologic, Bedford, Massachusetts, USA). DXA measurements were analyzed using Hologic APEX software (V.4.0). Daily quality control scans were conducted during the study period for each center. Subjects were scanned using standard imaging and positioning protocols. DXA...
is capable of measuring total body and regional fat mass. Fat mass index (FMI) was calculated as total fat mass in kilograms divided by height in meters squared.

Abdominal VAT and SAT can be estimated based on DXA scan using appropriate modeling, which has been described previously. In brief, the abdominal cavity is automatically defined whose caudal limit is identified in a 5 cm wide region just above the iliac crest at a level that approximately coincides with the fourth lumbar vertebrae. The software measures the total fat mass within the abdominal cavity, a region that contains both subcutaneous and visceral fat. The software then automatically locates the outer and inner margins of the abdominal wall on both sides of projected DXA image based on fat and lean mass profiles across the abdomen at the level of the fourth lumbar vertebra. The amount of SAT above and below the visceral region is estimated by measuring the subcutaneous fat between the skin line and outer abdominal wall on both sides of the image, and this estimate is subtracted from the total abdominal fat mass measured within the abdominal cavity to yield VAT. The APEX software provided the values of mass (g), area(cm²), and volume (cm³) of VAT and SAT. In this study, the area values (cm²) of VAT and SAT were used for analysis.

Statistical analysis

Values for TG were log-transformed before analyses because of their skewed distributions. Continuous variables were expressed as mean with SD, and categorical variables were expressed as frequency with percentage. The comparisons between boys and girls were performed using t-tests for continuous variables and χ² tests for categorical variables. To compare the relative importance of VAT and SAT on metabolic risk factors, both VAT and SAT were standardized to a mean of 0 and a SD of 1 specific for sex and age before all analysis. All analyses were performed in boys and girls separately because of sex difference in abdominal fat distributions.

Covariate-adjusted Pearson correlations of VAT and SAT with BMI, FMI, and each metabolic risk factor were performed. Multivariate logistical regression models were performed with VAT or SAT as the independent variables and metabolic risk factor as the dependent variables. The basic adjustment model included region, family income, age, puberty development, physical activity, and smoking; additional models included FMI or BMI to basic model to examine whether the impact of VAT and SAT on metabolic risk factors is independent of FMI and BMI. The ORs and their 95% CIs for each risk factor per 1-SD increase in VAT and SAT were estimated. The interaction effects of VAT and SAT with sex were examined using interaction terms (sex×VAT or sex×SAT) in the models. To assess the incremental utility of adding VAT and SAT on BMI for the identification of cardiometabolic risk, we compared the area under the receiver operator characteristic curves (AUC) between the model that included BMI and abdominal adipose variables (VAT alone, SAT alone, or both) and the model that included BMI.

All analyses were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA); a 2-tailed p<0.05 was considered statistically significant.

RESULTS

A total of 4267 boys and 4193 girls were included for analysis. Boys were more physically active but more likely to smoke than girls. About half of girls had menarche but only 14.9% of boys had spermatarche. Boys had lower SAT (119.7±93.3 cm² vs 189.1±74.7 cm², p<0.001), but greater VAT (49.7±39.0 cm² vs 36.6±29.2 cm², p<0.001) compared with girls. For other adiposity measures, boys had higher BMI, but lower FMI and fat mass percentage compared with girls (all p<0.001). Boys had higher prevalence of elevated blood pressure, high TG, and low HDL-C but lower prevalence of high TC and high LDL-C than girls (table 1).

Table 2 presents covariate-adjusted Pearson correlations of VAT and SAT with metabolic risk factors by sex. VAT and SAT strongly correlated (correlation coefficients [r]=0.85 for boys and 0.84 girls). BMI and FMI strongly correlated with VAT and SAT for both sexes (all p<0.001). In addition, both VAT and SAT were significantly correlated with all continuous metabolic risk factors (all p<0.05), with correlation coefficients varying by sex and specific risk factors.

Results of sex-specific logistic regression analyses for SAT and VAT with dichotomous metabolic risk factors are shown in table 3. In multivariate model adjusted for region, family income, age, puberty development, physical activity, and smoking, both VAT and SAT were significantly associated with elevated blood pressure and all lipid disorders for both sexes (model 1). After additional adjustment for FMI, all these associations remain significant (except for low HDL-C in girls) (model 2). In boys, SAT had greater ORs for all factors compared with VAT; in girls, however, SAT had greater odds for high TGs, smaller odds for high LDL-C, and similar odds for other risk factors compared with VAT. Boys had greater magnitude of associations of SAT with high TC, high LDL-C, and low HDL-C compared with girls; no sex differences for VAT were observed. In addition, both VAT and SAT were positively associated with elevated blood pressure and all lipid disorders (except for low HDL-C in girls) after further adjustment for BMI (model 3). We also performed sex-specific regression analyses of SAT and VAT for continuous metabolic risk factors with similar results (online supplementary table S1). Individuals aged 6–11 years had greater ORs of low HDL-C for both VAT and SAT compared with individuals aged 12–18 years; no significant difference in ORs between these two age groups for other risk factors (online supplementary table S2).

Table 4 presents the ROC analyses for improvement of VAT alone, SAT alone, or both on BMI for the identification of cardiometabolic risk factors by sex. In boys, compared with basic model including BMI, region,
Table 1  Clinical characteristics of the study participants (n=8460)

| Variables                      | Boys (n=4267) | Girls (n=4193) | P value |
|--------------------------------|---------------|---------------|---------|
| Age, years                     | 12.6±3.7      | 12.8±3.7      | <0.001  |
| Physical inactivity, n (%)     | 3501 (82.0)   | 3746 (89.3)   | <0.001  |
| Smoking, n (%)                 | 533 (12.5)    | 202 (4.8)     | <0.001  |
| Menarche/Spermarche, n (%)     | 637 (14.9)    | 2127 (50.7)   | <0.001  |
| Family income, $/year          | 10413±7939    | 10376±7817    | 0.432   |
| BMI, kg/m²                     | 20.1±4.4      | 19.4±3.7      | <0.001  |
| DXA-measured variables         |               |               |         |
| FMI, kg/m²                     | 5.58±2.6      | 6.41±2.23     | <0.001  |
| FMP, %                         | 26.8±7.7      | 32.3±5.6      | <0.001  |
| SAT, cm²                       | 119.7±93.3    | 189.1±74.7    | <0.001  |
| VAT, cm²                       | 49.7±33.0     | 36.6±23.2     | <0.001  |
| SBP, mm Hg                     | 113.2±12.6    | 108.5±10.5    | <0.001  |
| DBP, mm Hg                     | 66.5±8.4      | 66.8±8.24     | 0.051   |
| TC, mg/dL                      | 146.8±28.9    | 150.6±29.4    | <0.001  |
| TG, mg/dL                      | 55.8 (39.0–80.6) | 59.3 (43.4–82.4) | 0.043  |
| LDL-C, mg/dL                   | 82.8±23.9     | 84.9±24.5     | <0.001  |
| HDL-C, mg/dL                   | 53.3±11.1     | 55.4±11.2     | <0.001  |
| Weight status, n (%)           |               |               |         |
| Normal weight                  | 2820 (66.1)   | 3290 (78.5)   | <0.001  |
| Overweight                     | 755 (17.7)    | 547 (13.1)    |         |
| Obesity                        | 692 (16.2)    | 356 (8.5)     |         |
| Elevated BP, n (%)             | 487 (11.4)    | 362 (8.6)     | <0.001  |
| High TC, n (%)                 | 189 (4.4)     | 226 (5.4)     | 0.041   |
| High TG, n (%)                 | 297 (7.0)     | 248 (5.9)     | 0.049   |
| High LDL-C, n (%)              | 145 (3.4)     | 189 (4.5)     | 0.009   |
| Low HDL-C, n (%)               | 450 (10.6)    | 302 (7.2)     | <0.001  |

Data are mean±SD, median (25–75 percentile) or n (%).
BMI, body mass index; DBP, diastolic blood pressure; DXA, dual-energy X-ray absorptiometry; FMI, fat mass index; FMP, fat mass percentage; HDL-C, high-density lipid cholesterol; LDL-C, low-density lipid cholesterol; SAT, subcutaneous adipose tissue; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; VAT, visceral adipose tissue.

family income, age, puberty development, physical activity, smoking, models that adding VAT and/or SAT had greater AUC values for high TC and high LDL-C but not for other risk factors; in girls, however, adding VAT and SAT alone or both into the BMI model did not improve the AUC for all risk factors.

Trends in distributions of risk factors across tertiles of VAT and SAT within BMI categories (normal weight, overweight, and obesity) by sex are shown in online supplementary figures S1 and S2. The prevalence of elevated blood pressure and lipid disorders showed increasing trends across tertiles of VAT and SAT within normal weight, overweight, and obesity, though statistical significances were only observed for several groups. For example, a significantly increasing trend in the prevalence elevated BP across VAT was found only in obesity group but not in normal-weight and overweight groups in both boys and girls.

DISCUSSION

This large-scale population-based study of Chinese children and adolescents provides a unique opportunity to examine the associations between abdominal adipose compartments quantified by DXA and cardiometabolic risk profiles. We found that both high SAT and VAT were positively associated with elevated blood pressure and lipid disorders for both sexes (except for low HDL-C in girls) independent of FMI or BMI. However, their relative contributions differ between sexes. In addition, boys had a stronger association between SAT and most of metabolic risk factors compared with girls, but no sex differences for VAT were observed.

It is well documented that visceral fat accumulation bears adverse effects on cardiometabolic health in adults.6–8 20 21 Several longitudinal studies have indicated that visceral adiposity has been shown to be associated with incident cardiovascular disease after adjustment for
clinical risk factors and general adiposity. However, several cross-sectional studies of children and adolescents have demonstrated inconsistent results, with some showing the adverse effect of VAT on metabolic disorders but not for others. These inconsistencies may be due to small sample size, focusing only on obese subjects or without adjustment of body fat mass. Our results extended prior findings within the context of a large population-based sample of Chinese children and adolescents. In agreement with findings from studies of adults, we found significant associations of VAT with most of metabolic risk factors, including elevated blood pressure and high-risk lipid profiles, independent of total fat mass in boys and girls. All these findings suggest that VAT plays a pathological role in the development of metabolic disorders in both adults and children.

The majority of studies in adults have shown that SAT is positively associated with obesity-related complications, but the association is weaker than that for VAT. In several studies, however, SAT is not associated with cardiometabolic risk and even exerts a protective effect after accounting for total fat mass. In contrast, we demonstrated adverse effects of high SAT on all risk factors after adjustment for body fat. In addition, the associations of SAT were even stronger than those for VAT for most risk factors, especially in boys. Similar results have been reported in several prior small studies. A recent study of 94 Mexican school children showed magnetic resonance-measured SAT rather than VAT was associated with higher cardiometabolic risk. Another small cross-sectional study of 30 overweight and obese prepubertal children reported that insulin sensitivity was negatively correlated with DXA-measured SAT but not with VAT. A study consisting of 999 individuals aged 6–90 years compared the association of abdominal fat depots with cardiometabolic traits between youth and adults, showing that abdominal SAT was the most significant predictor of metabolic traits in children and adolescents, whereas VAT was the most significant predictor in adults. The difference in the contribution of SAT on cardiometabolic health between youth and adults suggests that abdominal fat depots may differ in their pathogenic significance at different life stages. In the present study, we also found that the SAT area was much greater than VAT area in both girls and boys, suggesting that SAT may contribute to more absolute cardiometabolic risk than VAT in early life.

It should be noted that abdominal SAT can be further divided into superficial and deep compartments. Prior studies have shown that abdominal deep and superficial SATs have different metabolic function and activity and deep SAT has been more strongly associated with metabolic risk factors superficial compared with superficial SAT. However, we did not differentiate these two distinct fat deposits in the current study, and further studies are required to explore the impacts of these two specific depots of SAT on metabolic health in youth.

Interestingly, we found a sex difference in the association of SAT with lipid risk factors, with boys exhibiting greater association. In line with our findings, a cross-sectional study of 1223 Hispanic/Latino youth aged 8–16 years indicated that the associations between multiple measures (BMI, waist circumference, waist-to-hip ratio, and fat mass percentage) and insulin resistance were stronger in boys than in girls. These results were inconsistent with several prior studies of adults demonstrating that SAT and VAT were more strongly associated with adverse risk factors levels in women than in men. However, we did not find sex differences in the associations of VAT with metabolic risk factors. The underlying mechanism for this sex-difference for SAT is not clear and remains to be elucidated in future studies.

### Table 2

|   | Boys |          |          |          |          |          |          |          |          |          |          |          |
|---|------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|   | SAT  | VAT      | SAT      | FMI      | BMI      | SAT      | VAT      | SAT      | FMI      | BMI      | SAT      | VAT      |
| SAT | 0.85** | –        | –        | –        | –        | 0.84**   | –        | –        | –        | –        | –        |
| FMI | 0.78** | 0.85**   | 0.80**   | –        | –        | 0.63**   | 0.68**   | –        | –        | –        | –        |
| BMI | 0.76** | 0.84**   | 0.74**   | 0.81**   | 0.68**   | 0.76**   | 0.84**   | 0.80**   | –        | –        | 0.63**   | 0.68**   |
| SBP | 0.33** | 0.34**   | 0.47**   | 0.40**   | 0.35**   | 0.33**   | 0.34**   | 0.47**   | 0.40**   | 0.35**   | 0.33**   | 0.34**   |
| DBP | 0.20** | 0.20**   | 0.27**   | 0.19**   | 0.20**   | 0.20**   | 0.20**   | 0.27**   | 0.19**   | 0.20**   | 0.20**   | 0.20**   |
| TC  | 0.23** | 0.23**   | 0.13**   | 0.15**   | 0.22**   | 0.23**   | 0.23**   | 0.13**   | 0.15**   | 0.22**   | 0.23**   | 0.23**   |
| TG  | 0.36** | 0.39**   | 0.41**   | 0.35**   | 0.22**   | 0.36**   | 0.39**   | 0.41**   | 0.35**   | 0.22**   | 0.36**   | 0.39**   |
| LDL-C| 0.32** | 0.33**   | 0.27**   | 0.26**   | 0.18**   | 0.32**   | 0.33**   | 0.27**   | 0.26**   | 0.18**   | 0.32**   | 0.33**   |
| HDL-C| –0.22**| –0.25**  | –0.30**  | –0.27**  | –0.18**  | –0.22**  | –0.25**  | –0.30**  | –0.27**  | –0.18**  | –0.22**  | –0.25**  |

Covariates included region, family income, age, puberty development, physical activity, and smoking.

*P<0.05.

**P<0.001.

BMI, body mass index; DBP, diastolic blood pressure; FMI, fat mass index; HDL-C, high-density lipid cholesterol; LDL-C, low-density lipid cholesterol; SAT, subcutaneous adipose tissue; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; VAT, visceral adipose tissue.
|                    | Boys                        |                     |          | Girls                       |                     |          | P value for sex interaction† |
|--------------------|-----------------------------|---------------------|----------|-----------------------------|---------------------|----------|----------------------------|
|                    | Model 1                     | Model 2             | Model 3  |                             | Model 1             | Model 2             | Model 3  |                             |
| Elevated BP        |                             |                     |          |                             |                     |          |                             |
| VAT                | 1.57 (1.45 to 1.70)         | 1.20 (1.04 to 1.39) | 1.15 (1.02 to 1.29) | 1.53 (1.40 to 1.67)     | 1.24 (1.06 to 1.45) | 1.26 (1.11 to 1.44)     | 0.680     |
| SAT                | 1.66 (1.53 to 1.80)         | 1.39 (1.13 to 1.72)*| 1.15 (1.01 to 1.33) | 1.56 (1.42 to 1.71)     | 1.21 (1.01 to 1.48) | 1.24 (1.06 to 1.44)     | 0.181     |
| High TC            |                             |                     |          |                             |                     |          |                             |
| VAT                | 1.64 (1.46 to 1.83)         | 1.44 (1.15 to 1.81) | 1.79 (1.52 to 2.10) | 1.28 (1.15 to 1.42)     | 1.52 (1.24 to 1.86) | 1.42 (1.21 to 1.67)     | 0.646     |
| SAT                | 1.77 (1.56 to 2.01)         | 2.11 (1.51 to 2.95)*| 2.56 (2.06 to 3.18) | 1.25 (1.11 to 1.41)     | 1.49 (1.16 to 1.92) | 1.41 (1.16 to 1.71)     | 0.022     |
| High TG            |                             |                     |          |                             |                     |          |                             |
| VAT                | 2.01 (1.83 to 2.20)         | 1.25 (1.06 to 1.47) | 1.46 (1.28 to 1.66) | 1.51 (1.38 to 1.67)     | 1.27 (1.06 to 1.52) | 1.22 (1.06 to 1.42)     | 0.851     |
| SAT                | 2.33 (2.11 to 2.58)         | 1.72 (1.33 to 2.21)*| 1.78 (1.50 to 2.12) | 1.59 (1.43 to 1.76)     | 1.47 (1.16 to 1.85)*| 1.30 (1.09 to 1.55)     | 0.201     |
| High LDL-C         |                             |                     |          |                             |                     |          |                             |
| VAT                | 1.74 (1.55 to 1.95)         | 1.53 (1.22 to 1.93) | 1.70 (1.45 to 2.00) | 1.50 (1.35 to 1.66)     | 1.67 (1.36 to 2.05) | 1.48 (1.26 to 1.74)     | 0.434     |
| SAT                | 1.96 (1.72 to 2.24)         | 2.62 (1.84 to 3.74)*| 2.40 (1.92 to 3.00) | 1.44 (1.28 to 1.62)     | 1.30 (1.00 to 1.69)*| 1.26 (1.03 to 1.54)     | <0.001    |
| Low HDL-C          |                             |                     |          |                             |                     |          |                             |
| VAT                | 1.50 (1.39 to 1.62)         | 1.16 (1.01 to 1.35) | 1.19 (1.06 to 1.34) | 1.48 (1.35 to 1.62)     | 1.17 (0.98 to 1.39) | 1.12 (0.97 to 1.29)     | 0.967     |
| SAT                | 1.59 (1.46 to 1.72)         | 1.38 (1.12 to 1.71)*| 1.27 (1.10 to 1.47) | 1.52 (1.38 to 1.68)     | 1.12 (0.91 to 1.39) | 1.05 (0.89 to 1.25)     | 0.043     |

Model 1, adjusted for region, family income, age, puberty development, physical activity, and smoking; Model 2, model 1+ adjusted for fat mass index; Model 3, model 1+ adjusted for body mass index.

*P<0.05 for difference in the magnitude of effect sizes between VAT and SAT in model 2.
†P for sex-interaction for model 2.

BP, blood pressure; HDL-C, high-density lipid cholesterol; LDL-C, low-density lipid cholesterol; SAT, subcutaneous adipose tissue; TC, total cholesterol; TG, triglycerides; VAT, visceral adipose tissue.
Table 4  Receiver operating characteristic curve analyses for improvement of VAT alone, SAT alone or both on BMI for Identification of cardiometabolic risk factors by sex

|                | Boys (AUC (95% CI)) | P value | Girls (AUC (95% CI)) | P value |
|----------------|--------------------|---------|----------------------|---------|
| Elevated BP    |                    |         |                      |         |
| BMI model*     | 0.678 (0.653 to 0.704) | –       | 0.642 (0.611 to 0.673) | –       |
| +VAT           | 0.681 (0.656 to 0.706) | 0.890   | 0.646 (0.615 to 0.676) | 0.860   |
| +SAT           | 0.681 (0.656 to 0.706) | 0.895   | 0.642 (0.611 to 0.672) | 0.996   |
| +VAT+SAT       | 0.681 (0.656 to 0.706) | 0.880   | 0.644 (0.614 to 0.675) | 0.903   |
| High TC        |                    |         |                      |         |
| BMI model*     | 0.638 (0.597 to 0.678) | –       | 0.550 (0.510 to 0.590) | –       |
| +VAT           | 0.696 (0.659 to 0.733) | 0.038   | 0.584 (0.545 to 0.624) | 0.235   |
| +SAT           | 0.714 (0.678 to 0.750) | 0.006   | 0.585 (0.546 to 0.625) | 0.221   |
| +VAT+SAT       | 0.718 (0.682 to 0.754) | 0.004   | 0.590 (0.550 to 0.629) | 0.167   |
| High TG        |                    |         |                      |         |
| BMI model*     | 0.773 (0.747 to 0.800) | –       | 0.657 (0.621 to 0.693) | –       |
| +VAT           | 0.792 (0.766 to 0.818) | 0.329   | 0.658 (0.622 to 0.695) | 0.958   |
| +SAT           | 0.794 (0.768 to 0.820) | 0.285   | 0.659 (0.622 to 0.696) | 0.940   |
| +VAT+SAT       | 0.796 (0.769 to 0.822) | 0.246   | 0.659 (0.623 to 0.696) | 0.936   |
| High LDL-C     |                    |         |                      |         |
| BMI model*     | 0.663 (0.617 to 0.710) | –       | 0.580 (0.533 to 0.626) | –       |
| +VAT           | 0.727 (0.684 to 0.770) | 0.048   | 0.626 (0.582 to 0.669) | 0.155   |
| +SAT           | 0.733 (0.691 to 0.775) | 0.028   | 0.604 (0.559 to 0.649) | 0.455   |
| +VAT+SAT       | 0.739 (0.697 to 0.780) | 0.018   | 0.622 (0.578 to 0.666) | 0.196   |
| Low HDL-C      |                    |         |                      |         |
| BMI model*     | 0.680 (0.654 to 0.707) | –       | 0.657 (0.623 to 0.690) | –       |
| +VAT           | 0.683 (0.656 to 0.709) | 0.904   | 0.658 (0.625 to 0.691) | 0.958   |
| +SAT           | 0.683 (0.656 to 0.710) | 0.887   | 0.656 (0.623 to 0.689) | 0.973   |
| +VAT+SAT       | 0.683 (0.656 to 0.710) | 0.888   | 0.659 (0.626 to 0.692) | 0.934   |

*The model included BMI, region, family income, age, puberty development, physical activity, and smoking.

BMI is the widely used method to assess overall adiposity and identify individuals for further assessment of cardiometabolic risk. In adults, VAT but not SAT can improve the identification of cardiometabolic risk.6 However, a recent study from the National Health and Nutrition Examination Survey showed that the use of fat mass does not improve on BMI for the identification of metabolic syndrome in US adolescents.35 In the current study, although the associations of VAT and SAT with multiple cardiometabolic risk factors were independent of BMI, adding VAT or SAT or both on BMI did not improve the identification of most outcome factors. Given that measuring BMI had great convenience and low-cost, BMI remains an appropriate measure for screening obesity in children and adolescents in public health settings. However, we found that the prevalence of elevated blood pressure and lipid disorders showed increasing trends across tertiles of VAT and SAT among individuals with overweight and obesity. Thus, VAT and SAT may be useful to identify those with higher cardiovascular risk among overweight and obese children and adolescents.

The strengths of our study include a large sample size and estimating abdominal fat compartments using DXA. This study also has several limitations. First, our study is cross-sectional and thus causal relationship of VAT and SAT with metabolic risk factors cannot be inferred. Longitudinal studies are required to examine their long-term health impact. Second, we measured abdominal VAT and SAT using DXA rather than MRI and CT. However, studies have shown that DXA-derived VAT performed as well as a clinical read of VAT from a CT scan.19 Third, we cannot distinguish superficial and deep SAT compartments using DXA, and their relative contributions on cardiometabolic risk need to be elucidated in future studies. Fourth, hyperglycemia has been considered as one important cardiometabolic risk factor; however, we did not assess the influence of VAT and...
CONCLUSION
This cross-sectional study showed that both abdominal SAT and VAT are positively associated with cardiometabolic risk factors in a Chinese pediatric population, but their relative contributions differ between sexes. Longitudinal and interventional studies are warranted to investigate the impact of reduction in VAT and SAT on metabolic health in children and adolescents.

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Contributors
YY and JM designed and conceived the study. All authors performed the analysis and interpretation of data. YY and JM drafted the article. JM was responsible for administrative, technical, and financial support to the study. All authors revised the manuscript critically and approved the final version to be published.

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REFERENCES
1 Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the global burden of disease study 2013. The Lancet 2014;384:766–81.
2 Liang Y-J, Xi B, Song A-Q, et al. Trends in general and abdominal obesity among Chinese children and adolescents 1993–2009. Pediatr Obes 2012;7:355–64.
3 Twigg G, Yaniv G, Levine H, et al. Body-Mass index in 2.3 million adolescents and cardiovascular death in adulthood. N Engl J Med 2016;374:2430–40.
4 Weiss R, Dziura J, Burgert TS, et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 2004;350:2362–74.
5 Wildman RP, Munter P, Reynolds K, et al. The obese without cardiometabolic risk factor clustering and the normal-weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). Arch Intern Med 2008;168:1617–24.
6 Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham heart study. Circulation 2007;116:39–48.
7 Abraham TM, Pedley A, Massaro JM, et al. Association between visceral and subcutaneous adipose depots and incident cardiovascular disease risk factors. Circulation 2015;132:1639–47.
8 Liu J, Fox CS, Hickson DA, et al. Impact of abdominal visceral and subcutaneous adipose tissue on cardiometabolic risk factors: the Jackson heart study. The Journal of Clinical Endocrinology & Metabolism 2010;95:5419–26.
9 Bosch TA, Dengel DR, Kelly AS, et al. Visceral adipose tissue measured by DXA correlates with measurement by CT and is associated with cardiometabolic risk factors in children. Pediatr Obes 2015;10:172–9.
10 Kelly AS, Dengel DR, Hodges J, et al. The relative contributions of the abdominal visceral and subcutaneous fat depots to cardiometabolic risk in youth. Clin Obes 2014;4:101–7.
11 González-Alvárez C, Ramos-Ibáñez N, Azpriz-Leehan J, et al. Intra-Abdominal and subcutaneous abdominal fat as predictors of cardiometabolic risk in a sample of Mexican children. Eur J Clin Nutr 2017;71:1069–73.
12 Ali O, Cerjak D, Kent JW, et al. Obesity, central adiposity and cardiometabolic risk factors in children and adolescents: a family-based study. Pediatr Obes 2014;9:658–62.
13 Gishi O, Gaillard R, Durnus B, et al. BMI, total and abdominal fat distribution, and cardiometabolic risk factors in school-age children. Pediatr Res 2015;77:710–8.
14 Pausova Z, Mahboubi A, Abrahamowicz M, et al. Sex differences in the contributions of visceral and total body fat to blood pressure in adolescence. Hypertension 2012;59:579–85.
15 Ji C-Y, Working Group on Obesity in China. Report on childhood obesity in China (1)–body mass index reference for screening overweight and obesity in Chinese school-age children. Biomed Environ Sci 2005;18:390–400.
16 Meng L, Hou D, Shan X, et al. Accuracy evaluation of Omron HEM-7012 electronic sphygmomanometers in measuring blood pressure of children and adolescents. Chinese Journal of Hypertension 2012;18:1518–62.
17 National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555–76.
18 Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics 2011;128 Suppl 5:S213–56.
19 Micklefield LK, Goedecke JH, Punyanitya M, et al. Dual-Energy X-ray performs as well as clinical computed tomography for the measurement of visceral fat. Obesity 2012;20:1109–14.
20 Chandra A, Neeland IJ, Berry JD, et al. The relationship of body mass and fat distribution with incident hypertension: observations from the Dallas heart study. J Am Coll Cardiol 2014;64:997–1002.
21 Oka R, Miura K, Sakurai M, et al. Impacts of visceral adipose tissue and subcutaneous adipose tissue on metabolic high risk factors in middle-aged Japanese. Obesity 2010;18:153–60.
22 Neeland IJ, Turer AT, Ayers CR, et al. Body fat distribution and incident cardiovascular disease in obese adults. J Am Coll Cardiol 2015;65:2150–7.
23 Britton KA, Massaro JM, Murabito JM, et al. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. J Am Coll Cardiol 2013;62:921–5.
24 Kwon H, Kim D, Kim JS. Body fat distribution and the risk of incident metabolic syndrome: a longitudinal cohort study. Sci Rep 2017;7:10955.
25 Tu AW, Humphries KH, Lear SA. Longitudinal changes in visceral and subcutaneous adipose tissue and metabolic syndrome: results from the multicultural community health assessment trial (M-CHAT). Diabetes Metab Syndr Obes 2011;4 Suppl 1:S153–61.
26 Maffess C, Manfredi R, Trombetta M, et al. Insulin sensitivity is correlated with subcutaneous but not visceral body fat in
overweight and obese prepubertal children. *The Journal of Clinical Endocrinology & Metabolism* 2008;93:2122–8.

27 Frederiksen L, Nielsen TL, Wraae K, et al. Subcutaneous rather than visceral adipose tissue is associated with adiponectin levels and insulin resistance in young men. *J Clin Endocrinol Metab* 2009;94:4010–5.

28 Monzon JR, Basile R, Heneghan S, et al. Lipolysis in adipocytes isolated from deep and superficial subcutaneous adipose tissue. *Obes Res* 2002;10:266–9.

29 Lundbom J, Haikkarainen A, Lundbom N, et al. Deep subcutaneous adipose tissue is more saturated than superficial subcutaneous adipose tissue. *Int J Obes* 2013;37:620–2.

30 Walker GE, Verti B, Marzullo P, et al. Deep subcutaneous adipose tissue: a distinct abdominal adipose depot*. *Obesity* 2007;15:1933–43.

31 Kim S-H, Chung J-hye, Song S-W, et al. Relationship between deep subcutaneous abdominal adipose tissue and metabolic syndrome: a case control study. *Diabetol Metab Syndr* 2016;8.

32 Marinou K, Hodson L, Vasan SK, et al. Structural and functional properties of deep abdominal subcutaneous adipose tissue explain its association with insulin resistance and cardiovascular risk in men. *Diabetes Care* 2014;37:821–9.

33 Qi Q, Hua S, Perreira KM, et al. Sex differences in associations of adiposity measures and insulin resistance in US Hispanic/Latino youth: the Hispanic community children’s health Study/Study of Latino youth (sol youth). *J Clin Endocrinol Metab* 2017;102:185–94.

34 Tanaka S, Togashi K, Rankinen T, et al. Sex differences in the relationships of abdominal fat to cardiovascular disease risk among normal-weight white subjects. *Int J Obes* 2004;28:320–3.

35 Weber DR, Leonard MB, Shults J, et al. A comparison of fat and lean body mass index to BMI for the identification of metabolic syndrome in children and adolescents. *J Clin Endocrinol Metab* 2014;99:3208–16.