

Original Article

Truncal and leg fat associations with metabolic risk factors among Chinese adults

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Background and Objectives: To examine the associations of regional body fat distribution with metabolic risk factors among Chinese. **Methods and Study Design:** Truncal fat (TF) and leg fat (LF) were measured by dual-energy X-ray absorptiometry (DXA) among 947 adults, and abdominal visceral fat (VAT) and subcutaneous fat (SAT), upper leg SAT were measured by magnetic resonance image (MRI) among 103 adults during 2008-2013. Metabolic risk factors included fasting blood glucose, total triglyceride, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and metabolic syndrome (MetS). **Results:** TF showed adverse effect while LF showed beneficial effect on metabolic risk factors, and all these effects were independent of body mass index (BMI) (mostly $p < 0.01$). Individuals with higher TF and lower LF experienced the highest risk of MetS compared to other subgroups of combination of TF and LF (all $p < 0.05$). Abdominal VAT was positively associated with risk of MetS (men: odds ratio (OR)=4.45, 95% confidence interval (CI): 1.18, 16.8; women: OR=6.54, 95% CI: 1.08, 39.6) and serum triglyceride (men: beta (β)=0.379, 95% CI: 0.090, 0.667; women: β =0.700, 95% CI: 0.327, 1.07). Upper leg SAT showed an opposite association with most metabolic factors compared to abdominal SAT and VAT, however, the association was not statistically significant. **Conclusion:** TF and LF showed opposite effects on metabolic risk factors among Chinese adults. Abdominal VAT, but not abdominal SAT, was positively associated with serum triglyceride and risk of MetS. Future studies are warranted to examine the potential mechanism of the opposite effects between TF and LF on metabolic risk factors among Chinese.

Key Words: truncal fat, leg fat, metabolic risks, Chinese, adults

INTRODUCTION

Obesity is a primary risk factor of a number of metabolic chronic diseases, such as type 2 diabetes and cardiovascular disease (CVD).^{1,2} Compelling evidences suggested that body fat distribution, e.g. excess fat deposit in the truncal or abdominal region, is a better predictor of metabolic diseases than overall obesity measured by body mass index (BMI).³⁻⁸ Therefore, waist circumference (WC), the anthropometric indicator of regional fat distribution, has been included as an important component of metabolic syndrome (MetS),⁹ which has widely accepted as the metabolic risks cluster including central obesity, insulin resistance, dyslipidemia, and hypertension.

With the development of body composition measurement technologies, the accurate parameters of fat distribution measured by dual-energy X-ray absorptiometry (DXA), magnetic resonance image (MRI) and computed tomography (CT) provided new perspectives regarding the associations between regional body fat and metabolic risk factors.¹⁰ Numerous studies, which were conducted primarily among Caucasians, have consistently shown that truncal fat, especially abdominal visceral adipose tissue (VAT) accumulation was strongly associated with adverse metabolic profiles,^{6,11-13} while the effects of abdominal subcutaneous adipose tissue (SAT) were inconsistent in different studies among different populations.

¹⁴⁻¹⁹ Some other studies have also demonstrated that anthropometric measures such as BMI and WC might underestimate the risks of diabetes and CVD in the population who had higher amounts of VAT at a given value of BMI or WC, such as Chinese and Asian people.²⁰⁻²³

Several studies reported that gluteofemoral or LF mass might have favorable effects on blood pressure, fasting plasma glucose level, lipid profiles, and other metabolic risk factors.²⁴⁻²⁹ Nevertheless, the findings were not consistent.^{27,30,31} In our previous study, we found that gynoid fat (located in the hip and thigh) may have favorable effects on metabolic risks among Chinese women.³² However, evidence is still limited regarding the effect of regional body fat (BF) especially LF on metabolic risks among Chinese.

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The present study aimed to examine the associations of regional body fat accumulation with metabolic risk factors among Chinese adults, and to identify the potential gender disparities with these associations.

MATERIALS AND METHODS

Study population

A total of 1,029 subjects (403 men and 626 women) were voluntarily recruited from an urban and a suburban community in Hangzhou through leaflets and posters, and the data on questionnaire, physical examination, blood sampling and DXA scan were collected from November 2008 to May 2009.³²⁻³⁴ After excluding subjects with age younger than 18 or over 80 years (n=8), missing data from anthropometric measurements, blood test and DXA information (n=21), and the use of medications that may interfere with metabolism and body composition (n=54), a final sample of 947 participants (378 men and 569 women) were included in the DXA analysis.

Between December 2009 and June 2013, 120 subjects (60 men and 60 women) were randomly selected from the above DXA sample with stratification by BMI and age, and finally 71 participants (54 men and 17 women) accepted the invitation and had a whole body MRI scan, as well as a questionnaire survey, physical examination, blood testing and DXA scan in the same day. In addition, 37 volunteers (7 men and 30 women) were recruited from a near community and participated in the survey. After exclusion of subjects with age less than 18 years old (n=1), missing information on MRI scan (n=3), and blood sample (n=1), finally 103 participants (57 men and 46 women) were included in the MRI study.

The study protocols were approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University and Zhejiang University School of Public Health. Written form of consents was obtained from all participating subjects prior to testing. None of the women had ever received hormone replacement therapy in both surveys.

Anthropometric measurements and DXA scan

Anthropometric measurements and DXA scan were conducted at the Obesity and Body Composition Research Center at Zhejiang University School of Public Health, according to a standardized protocol.³² Body weight was measured with only light clothing and barefoot on a balance scale (Detecto, USA) calibrated to 0.1 kg. Height was measured with a hypsometer to the nearest 0.1 cm. BMI was calculated as body weight in kilograms divided by the square of height in meters (kg/m²). Waist circumference, to the nearest 0.1 cm, was measured at the mid-point between the iliac crest and the lower costal margin while standing and at the end of an exhalation. Hip circumference was measured at the widest area between waist and thigh, including buttocks. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured in a sitting position with a mercury sphygmomanometer after at least a 10-minute rest period. All values of anthropometric measurements were recorded based on the average value of three repeated measures and the blood pressure was based on the average value of two repeated measures.

A whole body DXA scan (software version 11.40.004; GE Lunar Prodigy, Madison, WI, USA) was used to measure the total and regional BF in the trunk, arms and legs, from which percent total fat (total fat mass divided by total body mass) and percent regional fat (TF or LF mass divided by total fat mass) were derived. The DXA was operated by training technicians according to a standard protocol.³³ Calibration was performed daily using a phantom provided by the manufacturer and measurements were maintained with the manufacturer's precision standards of $\leq 0.8\%$.

Magnetic resonance imaging (MRI) scan

Whole body MRI scans were performed at two large central hospitals in Hangzhou. The participants from DXA sample (n=71) were scanned at the Second Affiliated Hospital of Zhejiang University (Signa, 3.0 Tesla, GE Healthcare, USA), and the new recruited subjects (n=37) were scanned at the Tongde Hospital of Zhejiang Province (Siemens Verio, 3.0 Tesla, Siemens Healthcare, Germany). Both of the MRI detecting labs followed a standardized imaging acquisition protocol to ensure accuracy and reproducibility.

All participants were required to lie in a supine position with arms extended overhead. The intervertebral space between the fourth and fifth lumbar vertebrae (L4-L5) was used as the point of scanning origin, and the transverse images (10 mm image thickness) were obtained every 50 mm from hand to foot.³⁵ All images were analyzed by a trained technician using SliceOmatic 4.3 software (TomoVision Inc, Montreal, Canada).

The specific anatomical regional fat tissues were delineated using a computer interface semiautomatic method according to a standard protocol. The areas of VAT, SAT and intermuscular adipose tissue (IMAT) were quantified and calculated from each cross-section image. The formula was used to calculate volumes (V) of VAT, SAT and IMAT respectively,

$$V = (t + h) \sum_i^N A_i$$

where t is the thickness (10 mm) of each image, h (40 mm) is the distance between consecutive images and A_i is each image's area.³⁶ Volumes further converted to mass units (Kg) by multiplying the density of 0.92 kg/L for adipose tissue.³⁷ The abdominal VAT, SAT and IMAT were calculated by summing the mass of slices between the top of the kidneys to the top of greater trochanter.³⁸ LF mass were calculated the slices between the top of greater trochanter to the toe, and then further divided it into upper and lower leg at the level of superior margin of patella. Total BF was the sum of VAT, SAT and IMAT. The percentage of BF (%BF) was calculated as the mass of BF divided by the body weight, while the percentage of abdominal fat (%AF) and LF (%LF) were calculated as AF and LF divided by BF respectively. The percentage of upper-leg SAT (%UL SAT) was calculated as the mass of upper leg SAT divided by total LF mass.

Blood testing

After a 12-hour overnight fasting, blood samples were collected to determine the serum levels of fasting blood

glucose (FG), total triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDLC) and high-density lipoprotein cholesterol (HDLC) with a biochemical auto-analyzer (Hitachi 7060, Tokyo, Japan).

Metabolic risk factors definition

Metabolic risk factors were defined according to the criteria of MetS (International Diabetes Federation 2009).³⁹ (1) WC \geq 85 cm in men and WC \geq 80 cm in women; (2) TG \geq 1.7 mmol/L (150 mg/dL) or on treatment for TG; (3) HDLC $<$ 1.0 mmol/L (40 mg/dL) in men and HDLC $<$ 1.3 mmol/L (50 mg/dL) in women or on treatment for HDLC; (4) SBP \geq 130 mmHg and/or DBP \geq 85 mmHg or on treatment for hypertensive therapy; (5) FBG \geq 5.6 mmol/L (100 mg/dL) or on treatment for elevated glucose. Participants were diagnosed as MetS if they satisfied any three or more of the metabolic risk factors. Risk factors \geq 1 and 2 were defined as containing at least one or two above-mentioned metabolic risks excluding elevated waist circumference.

Covariates

Comprehensive questionnaires including information on demographic factors, socioeconomic factors, health behaviours, medical history and menopause were conducted via face to face interview by trained interviewers. Covariates included age (in years), household income ($<$ 30,000, \geq 30,000 RMB per year), smoking (never smoking or current smoked $<$ 100 cigarettes, current smoked \geq 100 cigarettes in total), drinking (never drinking or drank wine, beer, or hard liquor $<$ 1 time/day, drank \geq 1 time/day during the past month),⁴⁰ and physical activity (leisure time physical activity $<$ 150 min/week, \geq 150 min/week). Menopausal status in women was categorized as pre- or post-menopause. Post-menopause was defined if there had been complete cessation of menses for more than 12 months.

Statistical analysis

Because the effect modification was found between gender and fat indicators, all analyses in this study were stratified by gender. Summary statistics were performed to describe the characteristics of study participants. The quantitative data were expressed as means \pm standard deviations (SD) for continuous variables, and as frequencies (percentages) for categorical variables. Normal distribution was evaluated by the Kolmogorov-Smirnov test, and log transformations were performed if the variables were not normal distributed. The *t*-test and chi-square test were used to compare the mean and frequency differences between men and women for continuous and categorical variables, respectively. Multivariate linear regression models were used to examine the associations between regional fat mass, i.e., TF, LF, abdominal VAT and SAT, upper leg SAT with metabolic risk factors including SBP, DBP, TG, HDLC and FG. Multivariate logistic regression models were used to identify the associations of various regional body fat indicators with metabolic risks \geq 1, risks \geq 2 and MetS. Multivariate models were adjusted for the above-mentioned covariates, as well as other regional fat indices. In order to further understand the effects of TF and LF on MetS and its risk factors, a four-level variable

based on the combination of TF (two levels cut off on median) and LF (two levels cut off on median) was developed. Multivariate logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CI) for MetS according to the four-level, adjusted for the same set of covariates. All statistical analyses were performed by SPSS for Windows, version 16.0. A *p*-value $<$ 0.05 (two tails) was considered as the significance level.

RESULTS

DXA analysis

Characteristics of the DXA analysis subjects

The characteristics of the DXA participants are shown in Table 1. There was no significant difference in age, BMI and hip circumference between men and women (all $p>$ 0.05). Women had significantly higher total BF, TF, LF, percent of BF (%BF) and LF (%LF) and lower levels of WC and percent of TF (%TF) than men (all $p<$ 0.001). Compared to women, men had significantly higher TG, SBP, DBP, FG, but lower HDLC (all $p<$ 0.001 except for FG, $p=$ 0.016). The prevalence of MetS was 30.8% (34.1% in men and 28.6% in women) among the study population. Approximately 74.4% subjects had at least one metabolic abnormality in all subjects (75.4% in men and 73.8% in women) and 40.7% subjects had at least two metabolic abnormalities (43.7% in men and 38.7% in women). No significant differences were found for metabolic risks \geq 1, risks \geq 2 and MetS between men and women.

Associations between DXA-derived regional fat indicators with metabolic risk factors

Table 2 shows the results of a series of multivariable regression models identifying the associations of DXA derived TF and LF with metabolic risk factors in men and women. After adjusting for age, socioeconomic status, and health behavior factors (Model 1), both TF and LF were positively associated with TG, SBP, DBP, FG, risk factors \geq 1, risk factors \geq 2 and MetS, and negatively associated with HDLC in men (all $p<$ 0.001). The results for women showed similar direction of associations but weaker significance compared to men. After further adjusting for BMI (Model 2), the associations between TF and metabolic risk factors were attenuated but most associations remained significant in men, including TG, HDLC, DBP, risk factors \geq 1, risk factors \geq 2, and MetS. Whereas in women, the associations between TF and metabolic indicators were only significant for TG and HDLC after BMI was adjusted in the models. In Model 2, LF was only associated with HDLC and FG in men, but it was associated with most of the metabolic risks in women, including TG, HDLC, SBP, FG, risk factors \geq 1, risk factors \geq 2, and MetS. When TF and LF were simultaneously considered in the models (Model 3), the fat tissue in two body regions showed opposite effects on metabolic risk factors (TF showed an adverse effect but LF showed a favorable effect), including TG, DBP, FG, risk factors \geq 1, risk factors \geq 2, and MetS for men and all metabolic risk factors except for the associations of TF with SBP and DBP for women.

Table 3 and Figure 1 show the results of multivariate

Table 1. Characteristics of the DXA analysis participants (n=946): Chinese adults aged 18-79 years, 2008-2009

Characteristics	Men (n=378)	Women (n=569)	p-value
Age (years)	50.1±14.3	49.0±13.2	0.227 [†]
Anthropometric characteristics			
BMI (kg/m ²)	23.6±3.17	23.4±3.15	0.372 [†]
Waist circumference (cm)	85.6±10.1	79.9±8.79	<0.001 [†]
Hip circumference (cm)	92.1±5.82	91.7±5.70	0.281 [†]
Fat measures by DXA			
Body fat mass (Kg)	14.1±6.72	18.4±5.61	<0.001 [†]
%BF	20.5±7.46	31.6±5.88	<0.001 [†]
Truncal fat mass (Kg)	8.94±4.50	10.4±3.58	<0.001 [†]
%TF	61.9±5.79	55.7±5.39	<0.001 [†]
Leg fat mass (Kg)	3.44±1.65	5.39±1.64	<0.001 [†]
%LF	25.4±4.71	29.9±5.49	<0.001 [†]
Metabolic risk factors			
TG (mmol/L) [§]	1.61±1.26	1.33±0.90	<0.001 [†]
HDLC (mmol/L) [§]	1.26±0.28	1.40±0.32	<0.001 [†]
SBP (mmHg) [§]	128±16.9	122±18.5	<0.001 [†]
DBP (mmHg) [§]	80.7±9.80	76.2±9.80	<0.001 [†]
FG (mmol/L) [§]	5.56±0.85	5.44±0.74	0.016 [†]
Risk factors ≥1	285 (75.4)	420 (73.8)	0.595 [‡]
Risk factors ≥2	165 (43.7)	220 (38.7)	0.126 [‡]
Metabolic syndrome	129 (34.1)	163 (28.6)	0.074 [‡]
Lifestyle characteristic, n (%)			
Low income	49 (13.0)	64 (11.2)	0.474 [‡]
Smoker	262 (69.3)	13 (2.3)	<0.001 [‡]
Heavy drinker	165 (43.7)	57 (10.0)	<0.001 [‡]
Low physical activity	287 (75.9)	374 (65.7)	<0.001 [‡]

DXA: dual-energy X-ray absorptiometry; BMI: body mass index; TG: triglyceride; HDLC: high density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure; FG: fasting glucose.

Continuous variables are expressed as mean±SD and categorical variables are expressed as number (percentage).

[†]: independent t-test; [‡]: χ^2 test; [§]: variables have been transformed by the log.

Low income, annual household income <30,000; Smoker, current smoked ≥100 cigarettes in total; Heavy drinkers, drink wine, beer, or hard liquor equal to or great than once per day during the past month; Low physical activity; leisure time physical activity <150 min/week (including 0 min/week).

logistic regression models using T2L1 (more TF and less LF) as the reference group. Compared to individuals with T2L1, those in other combination groups of TF and LF were less likely to experience MetS (all $p<0.05$). The T1L2 (less TF and more LF) group showed the most protective effects on metabolic risks in men (OR=0.198, 95% CI: 0.073, 0.535), while the T1L1 (less TF and less LF) group showed the most protective effects in women (OR=0.044, 95% CI: 0.012, 0.162).

MRI analysis

Characteristics of the MRI study subjects

The characteristics of the 103 MRI scan participants are shown in Table 4. The differences on characteristics between men and women were similar to the results from DXA sample. Compared to women, men had higher waist circumference, abdominal VAT, SBP, DBP, FG, higher prevalence of low income, smoking, alcohol use and low physical activity, lower values on most of fat measures (BF, %BF, AF, abdominal SAT, LF, %LF, upper leg SAT, lower leg SAT, all $p<0.05$).

Associations between MRI-derived regional fat indicators and metabolic risk factors

The results of the associations between MRI derived fat indicators and metabolic risk factors are presented in Table 5. After adjusting for age, socioeconomic status and health behavior factors (Model 1), both abdominal SAT

and VAT were positively associated with TG, SBP, risk factors ≥1, risk factors ≥2, and MetS, and were negatively associated with HDLC in men (all $p<0.05$). In women, abdominal VAT was positively associated with TG and DBP, and upper leg SAT was positively associated with DBP (all $p<0.05$). However, after BMI (Model 2) or upper leg SAT, abdominal VAT and SAT (Model 3) were controlled in the models, only abdominal VAT was positively associated with TG, DBP, risk factors ≥2, and MetS in men and TG, risk factors ≥1, and MetS in women (all $p<0.05$). Abdominal SAT was negatively associated with FG in men but it was not significantly associated with any other metabolic risks. Upper leg SAT did not show significant associations with most metabolic risks in these models (except with DBP in men, β value=-3.79 and 95% CI: -7.27, -0.319), but it showed opposite directions of associations compared to abdominal SAT and VAT in most metabolic indicators especially in men.

DISCUSSION

In the present study, TF showed adverse effects while LF showed favorable effects on metabolic risk factors among the Chinese population. Individuals with higher TF and lower LF experienced the highest risk of MetS compared to other subgroups of combinations of TF and LF. In addition, the effects on MetS seemed to be bigger from TF than from LF in men, but smaller from TF than from LF in women. Abdominal VAT was significantly positively

Table 2. Sex-specific multivariable-adjusted regressions analysis for DXA derived fat mass with metabolic syndrome and its components

		Men			Women		
		Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
TG [†]	LF	0.121 (0.086, 0.156) ^{***}	-0.022 (-0.078, 0.033)	-0.132 (-0.196, -0.068) ^{***}	0.026 (0.000, 0.052) [*]	-0.078 (-0.113, 0.043) ^{***}	-0.100 (-0.136, -0.064) ^{***}
	TF	0.064 (0.052, 0.076) ^{***}	0.058 (0.032, 0.083) ^{***}	0.093 (0.062, 0.123) ^{***}	0.046 (0.034, 0.058) ^{***}	0.032 (0.007, 0.058) [*]	0.053 (0.027, 0.079) ^{***}
HDL [†]	LF	-0.032 (-0.045, -0.019) ^{***}	-0.029 (-0.050, -0.007) ^{**}	-0.021 (-0.047, 0.005)	-0.001 (-0.013, 0.010)	0.041 (0.026, 0.057) ^{***}	0.052 (0.036, 0.068) ^{***}
	TF	-0.012 (-0.016, -0.007) ^{**}	-0.013 (-0.023, -0.002) [*]	-0.007 (-0.019, 0.005)	-0.016 (-0.022, -0.011) ^{**}	-0.016 (-0.027, -0.005) ^{**}	-0.027 (-0.038, -0.015) ^{***}
SBP [†]	LF	0.015 (0.008, 0.022) ^{***}	-0.001 (-0.012, 0.010)	-0.006 (-0.020, 0.007)	0.001 (-0.006, 0.007)	-0.018 (-0.026, -0.009) ^{***}	-0.019 (-0.028, -0.010) ^{***}
	TF	0.007 (0.004, 0.009) ^{***}	0.003 (-0.003, 0.008)	0.005 (-0.002, 0.011)	0.005 (0.002, 0.008) ^{***}	-0.001 (-0.007, 0.006)	0.003 (-0.003, 0.010)
DBP [†]	LF	0.017 (0.010, 0.025) ^{***}	-0.008 (-0.019, 0.004)	-0.025 (-0.039, -0.011) ^{***}	0.008 (0.002, 0.014) ^{**}	-0.008 (-0.016, 0.000)	-0.009 (-0.018, -0.001) [*]
	TF	0.010 (0.007, 0.012) ^{***}	0.008 (0.002, 0.014) ^{**}	0.015 (0.008, 0.021) ^{***}	0.007 (0.004, 0.010) ^{***}	0.001 (-0.005, 0.007)	0.003 (-0.003, 0.009)
FG [†]	LF	0.020 (0.012, 0.028) ^{***}	-0.014 (-0.027, -0.001) [*]	-0.026 (-0.042, -0.010) ^{***}	-0.005 (-0.011, 0.001)	-0.024 (-0.032, -0.016) ^{***}	-0.028 (-0.036, -0.019) ^{***}
	TF	0.011 (0.008, 0.014) ^{***}	0.003 (-0.003, 0.009)	0.010 (0.002, 0.017) ^{**}	0.005 (0.002, 0.008) ^{***}	0.004 (-0.002, 0.010)	0.010 (0.004, 0.016) ^{**}
Risk factors $\geq 1^{\ddagger}$	LF	1.79 (1.45, 2.21) ^{***}	1.02 (0.74, 1.41)	0.567 (0.385, 0.834) ^{**}	0.954 (0.842, 1.08)	0.507 (0.410, 0.627) ^{***}	0.432 (0.341, 0.547) ^{***}
	TF	1.31 (1.22, 1.42) ^{***}	1.26 (1.09, 1.47) ^{**}	1.50 (1.23, 1.82) ^{***}	1.20 (1.12, 1.29) ^{**}	1.12 (0.974, 1.28)	1.36 (1.16, 1.58) ^{***}
Risk factors $\geq 2^{\ddagger}$	LF	1.59 (1.34, 1.87) ^{***}	0.907 (0.704, 1.17)	0.670 (0.500, 0.897) ^{**}	0.925 (0.828, 1.03)	0.551 (0.458, 0.662) ^{***}	0.504 (0.414, 0.613) ^{***}
	TF	1.26 (1.18, 1.34) ^{***}	1.15 (1.03, 1.29) [*]	1.28 (1.11, 1.48) ^{***}	1.14 (1.07, 1.20) ^{***}	1.07 (0.952, 1.20)	1.23 (1.08, 1.40) ^{**}
Metabolic syndrome [‡]	LF	1.92 (1.59, 2.32) ^{***}	0.875 (0.657, 1.17)	0.604 (0.441, 0.829) ^{**}	1.12 (0.999, 1.26)	0.565 (0.462, 0.691) ^{***}	0.49 (0.39, 0.61) ^{***}
	TF	1.40 (1.30, 1.51) ^{***}	1.18 (1.04, 1.34) ^{**}	1.35 (1.16, 1.58) ^{***}	1.32 (1.23, 1.42) ^{***}	1.21 (1.06, 1.38) ^{**}	1.42 (1.23, 1.65) ^{***}

TG: triglyceride; HDLC: high density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure; FG: fasting glucose.

[†]Beta (β) values and 95% confidence interval (95% CI); [‡]Odds ratio and 95% CI; have been expressed as the associations of truncal and leg fat mass with Metabolic syndrome and its single and combined components.

Model 1: adjustment for age, alcohol use, smoking, income, physical activity, and menopause status (only in women).

Model 2: Model 1 added adjustment for BMI.

Model 3: Model 2 added adjustment for truncal and leg fat mass.

* p -value <0.05 ; ** p -value <0.01 ; *** p -value <0.05 .

Table 3. Adjusted odds ratio and 95% confidence intervals of metabolic syndrome for different groups of combination of TF and LF

	Total	n (%)	Odds ratio (95% CI)	<i>p</i> -value [†]
Men				
T1L1	31	5 (16.1)	0.197 (0.054,0.710)	0.013
T1L2	158	16 (10.1)	0.198 (0.073,0.535)	0.001
T2L1	31	20 (64.5)	1	
T2L2	158	88 (55.7)	0.410 (0.170,0.988)	0.047
Women				
T1L1	71	3 (4.2)	0.044 (0.012, 0.162)	<0.001
T1L2	213	26 (12.2)	0.164 (0.078, 0.346)	<0.001
T2L1	71	46 (64.8)	1	
T2L2	214	88 (41.1)	0.251 (0.130, 0.486)	<0.001

T1L1: lower TF and lower LF, T1L2: lower TF and higher LF, T2L1: higher TF and lower LF, T2L2: higher TF and higher LF.

[†]Logistic regression, adjusted for age, BMI, alcohol use, smoking, income, physical activity, and menopause status (only in women).

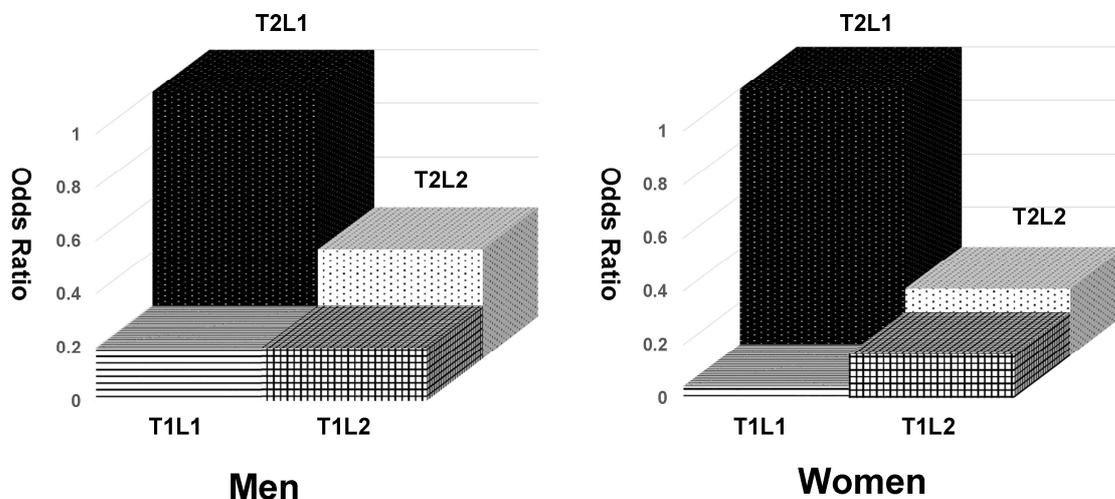


Figure 1. Adjusted odds ratio of metabolic syndrome for different groups of combination of TF and LF in men (left) and women (right). Adjusted odds ratio of metabolic syndrome according to four-level based on combination of TF (two levels cut off on median) and LF (two levels cut off on median). Adjusted covariates including age, BMI, alcohol use, smoking, income, physical activity, and menopause status (only in women). T1L1: lower TF and lower LF; T1L2: lower TF and higher LF; T2L1: higher TF and lower LF; T2L2: higher TF and higher LF.

associated with risk of MetS and serum TG, and upper leg SAT showed the opposite effects on most metabolic risk factors compared to abdominal SAT and VAT, however, the associations were not statistically significant.

Studies on Caucasians showed that truncal or abdominal fat accumulation was strongly associated with increased risk of MetS, type 2 diabetes and CVD.^{5,6,8,41} Chinese and other Asian population had been reported to have greater total body fat and TF than Caucasians for a given BMI,⁴²⁻⁴⁴ and TF could in part account for the higher metabolic risk factors observed in Chinese in both men and women.³⁴ Our present data from DXA analysis confirmed that TF was positively associated with multiple metabolic risk factors among Chinese adults, even after adjustment for BMI, which indicated that individuals with elevated level of TF would suffer from an increased risk of having metabolic disorders independent of their BMIs. On the contrary, body fat depots in lower body regions have revealed a significant protective property in both Chinese men and women. Similar favorable associations have been observed among Caucasians and other ethnic people.^{26,28,29,45-47} In Chinese, Wu et al reported the independent and opposite associations between LF and TF

with MetS in middle-aged and older people.⁴⁸ In the present study, we included the subjects with larger range of age and separated the VAT and SAT through MRI scan, and we found similar results. In addition, our previous study based on the same sample found the opposite associations of android and gynoid fat on the metabolic risks only in women but not in men.³² The difference might be because different regional adipose indices of TF and LF were used to evaluate the associations in this study.

In trunk, abdominal VAT has been found a stronger association with all-cause and cardiovascular morbidity and mortality than abdominal SAT.^{6,11-13,49} However, evidence is also scarce in Asians, especially in Chinese population.⁴⁸ In the current MRI study, we estimated comprehensive fat profiles, such as abdominal VAT and SAT, upper and lower leg SAT, among 103 Chinese participants, and found that abdominal VAT but not SAT was positively associated with MetS and TG independent of BMI. These results corresponded with those of previous findings.^{6,11,13} In addition, upper leg SAT did not show significant associations with most metabolic risks (except for DBP in men), and this conclusion was, however, inconsistent with our DXA study and some previous

Table 4. Characteristics of the MRI analysis participants (n=103): Chinese adults aged 18-79 years, 2009-2013

Characteristics	Men (n=57)	Women (n=46)	p-value
Age (years)	51.3±13.7	53.2±11.0	0.428 [†]
Anthropometric characteristics			
BMI (kg/m ²)	24.1±3.28	23.3±2.57	0.197 [†]
Waist circumference (cm)	86.9±9.94	81.5±8.10	0.004 [†]
Hip circumference (cm)	93.0±5.40	93.2±5.60	0.827 [†]
Fat measures by MRI			
Body fat mass(Kg)	19.1±5.36	21.8±4.96	0.01 [†]
%BF	27.9±4.93	37.7±5.71	<0.001 [†]
Abdominal fat mass (Kg)	7.66±2.48	8.87±2.33	0.013 [†]
%AF	39.7±4.15	40.4±3.48	0.337 [†]
Abdominal VAT (Kg)	3.45±1.31	2.62±0.73	<0.001 [†]
%AVAT	30.3±5.02	21.1±4.74	<0.001 [†]
Abdominal SAT (Kg)	3.84±1.32	5.93±1.78	<0.001 [†]
%ASAT	34.2±5.18	46.5±5.31	<0.001 [†]
Leg fat mass (Kg)	6.18±1.60	7.57±1.69	<0.001 [†]
%LF	32.9±4.00	35.1±3.78	0.006 [†]
Upper-leg SAT (Kg)	3.65±1.07	4.96±1.15	<0.001 [†]
%UL SAT	58.7±3.87	65.5±3.63	<0.001 [†]
Metabolic risk factors			
TG (mmol/L) [§]	1.78±1.53	1.71±1.66	0.511 [†]
HDLC (mmol/L) [§]	1.26±0.35	1.36±0.31	0.151 [†]
SBP (mmHg)	127±12.1	117±14.4	<0.001 [†]
DBP (mmHg)	82.7±7.74	74.5±9.67	<0.001 [†]
FG (mmol/L) [§]	5.84±1.19	5.07±0.62	<0.001 [†]
Risk factors ≥1	46 (80.7)	31 (67.4)	0.171 [‡]
Risk factors ≥2	29 (50.9)	15 (32.6)	0.074 [‡]
Metabolic syndrome	23 (40.4)	12 (26.1)	0.147 [‡]
Lifestyle characteristic, n (%)			
Low Income	21 (36.8)	8 (17.4)	0.046 [‡]
Smoking	31 (54.4)	1 (2.2)	<0.001 [‡]
Alcohol use	42 (73.7)	16 (34.8)	<0.001 [‡]
Low physical activity	34 (59.6)	13 (28.3)	0.001 [‡]

MRI: magnetic resonance imaging; VAT: visceral adipose tissue; SAT: subcutaneous adipose tissue.

Continuous variables are expressed as mean±SD and categorical variables are expressed as number (percentage).

[†]: independent t-test; [‡]: χ^2 test; [§]: variables have been transformed by the log.

research such as the Health, Aging and Body Composition Study (Health ABC), which reported that there was a favourable association of subcutaneous thigh fat (measured by CT) with glucose and lipid levels, independently of abdominal fat, in both genders.⁵⁰ The discordance, in our opinion, might be due to the smaller number of MRI subjects than our DXA study and the Health ABC. We made such speculation because compared to abdominal VAT, the opposite directions of associations with upper leg SAT in most metabolic risks have been observed. As for the single negative association with DBP in men, which was not observed in women group nor in other models, cannot yet be ruled out the possibility of a false positive result. Therefore, MRI or CT studies (gold standard of body fat measurement) with larger samples are still needed to further clarify the associations between SAT and metabolic disorders in the future.

The sex difference of regional body fat distribution has been well described in both DXA and MRI study. Similar to the characteristic of fat depot in Caucasians,⁵¹ Chinese women had more total body fat, abdominal SAT and leg SAT, whereas Chinese men had more abdominal VAT. The reduced risk of cardiovascular diseases in women has been speculated partly due to a reduced abdominal VAT accumulation in women (at least before menopause).^{51,52} In addition, it has also been reported that women were more likely to store fat in the lower body and had a lower

risk of developing MetS, diabetes and CVD compared to men.⁵³ Sex hormones especially estrogen, might be a determinant of body fat distribution pattern, as well as the key media between body fat distribution and metabolic diseases.^{51,54,55} The sex-specific differences in the association between TF and LF with MetS had also been observed in our DXA study. At the same level of TF, the difference of ORs between higher and lower LF group was bigger in women than in men, by contrast, the difference of ORs between higher and lower TF group was bigger in men than in women especially at the higher level of LF. Kirschner et al reported that upper body obesity was associated with greater increases in testosterone and dihydrotestosterone compared to lower body obesity, and lower body obesity was associated with the increased androstenedione on the contrary.⁵⁵ This might partly explain the reason why the effects on MetS seemed to be bigger from TF than from LF in men, but seemed to be smaller in women.

The biological mechanisms of TF (mainly VAT) and LF (mainly SAT) accumulation on metabolic risk factors were not entirely clear. Variations in the capacity of different depots to store, releasing free fatty acids (FAA) and producing adipokines and inflammatory were considered to be important determinants of fat distribution and its metabolic consequences.⁵⁶ Evidence showed that a large amount of SAT located in the trunk and leg act as a

Table 5. Sex-specific multivariable-adjusted regressions analysis for MRI derived fat mass with metabolic syndrome and its components

		Men			Women		
		Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
†TG	UL SAT	0.122 (-0.033, 0.277)	-0.032 (-0.222, 0.158)	-0.193 (-0.439, 0.053)	0.003 (-0.197, 0.204)	0.050 (-0.021, 0.310)	-0.200 (-0.543, 0.143)
	ASAT	0.169 (0.052, 0.286)**	0.082 (-0.096, 0.260)	0.164 (-0.068, 0.397)	-0.015 (-0.140, 0.111)	0.012 (-0.179, 0.203)	-0.048 (-0.275, 0.180)
	AVAT	0.231 (0.115, 0.348)**	0.214 (0.028, 0.401)*	0.217 (0.027, 0.407)*	0.379 (0.090, 0.667)*	0.507 (0.196, 0.818)***	0.700 (0.327, 1.07)***
†HDLC	UL SAT	-0.134 (-0.225, -0.043)	-0.060 (-0.174, 0.054)	0.025 (-0.130, 0.179)	-0.006 (-0.099, 0.087)	0.027 (-0.093, 0.147)	0.079 (-0.103, 0.262)
	ASAT	-0.135 (-0.203, -0.066)***	-0.096 (-0.202, 0.009)	-0.101 (-0.247, 0.045)	-0.010 (-0.068, 0.048)	0.014 (-0.074, 0.102)	0.005 (-0.116, 0.127)
	AVAT	-0.132 (-0.206, -0.058)***	-0.076 (-0.193, 0.041)	-0.059 (-0.178, 0.061)	-0.081 (-0.224, 0.062)	-0.071 (-0.232, 0.091)	-0.136 (-0.336, 0.063)
†SBP	UL SAT	1.64 (-1.59, 4.86)	-1.07 (-5.10, 2.95)	-4.84 (-10.1, 0.461)	3.82 (-0.228, 7.88)	2.84 (-2.42, 8.10)	2.56 (-5.58, 10.7)
	ASAT	2.96 (0.513, 5.41)*	1.86 (-1.92, 5.63)	4.35 (-0.653, 9.36)	1.91 (-0.681, 4.50)	0.767 (-3.14, 4.67)	-1.38 (-6.77, 4.02)
	AVAT	3.67 (1.08, 6.16)**	3.17 (-0.89, 7.24)	3.20 (-0.898, 7.29)	6.07 (-0.281, 12.4)	4.66 (-2.44, 11.8)	3.75 (-5.12, 12.6)
†DBP	UL SAT	0.356 (-1.80, 2.52)	-1.55 (-4.24, 1.13)	-3.79 (-7.27, -0.319)*	3.12 (0.425, 5.81)*	3.39 (-0.120, 6.90)	2.42 (-2.95, 7.79)
	ASAT	1.40 (-0.267, 3.08)	0.43 (-2.14, 2.99)	2.28 (-1.01, 5.56)	1.44 (-0.309, 3.18)	1.44 (-1.21, 4.10)	-0.612 (-4.17, 2.95)
	AVAT	2.44 (0.758, 4.12)**	2.80 (0.110, 5.49)*	3.07 (0.390, 5.76)*	5.26 (1.08, 9.43)*	5.07 (0.355, 9.78)*	3.67 (-2.18, 9.53)
†FG	UL SAT	0.035 (-0.009, 0.079)	0.014 (-0.043, 0.071)	0.065 (-0.011, 0.141)	0.012 (-0.023, 0.046)	0.009 (-0.035, 0.053)	-0.040 (-0.106, 0.025)
	ASAT	0.013 (-0.023, 0.048)	-0.030 (-0.083, 0.023)	-0.075 (-0.147, -0.004)*	0.013 (-0.008, 0.034)	0.019 (-0.013, 0.051)	0.025 (-0.018, 0.068)
	AVAT	0.033 (-0.004, 0.070)	0.014 (-0.044, 0.072)	0.017 (-0.041, 0.076)	0.047 (-0.005, 0.098)	0.050 (-0.008, 0.108)	0.061 (-0.010, 0.133)
‡Risk factors ≥1	UL SAT	1.54 (0.727, 3.26)	0.761 (0.251, 2.31)	0.314 (0.050, 1.96)	1.01 (0.562, 1.80)	0.774 (0.356, 1.68)	0.290 (0.060, 1.39)
	ASAT	2.14 (1.01, 4.55)*	1.23 (0.464, 3.25)	2.97 (0.511, 17.2)	1.02 (0.709, 1.46)	0.784 (0.438, 1.40)	0.579 (0.219, 1.53)
	AVAT	2.18 (1.01, 4.69)*	1.04 (0.361, 2.97)	0.985 (0.306, 3.17)	2.63 (0.909, 7.63)	2.58 (0.795, 8.40)	22.6 (1.56, 327)*
‡Risk factors ≥2	UL SAT	1.58 (0.81, 3.07)	0.468 (0.232, 4.09)	0.114 (0.013, 1.00)	1.13 (0.583, 2.18)	0.795 (0.348, 1.82)	0.294 (0.070, 1.23)
	ASAT	2.23 (1.20, 4.15)*	1.07 (0.439, 2.58)	3.02 (0.580, 15.6)	1.28 (0.845, 1.95)	1.09 (0.600, 1.96)	1.42 (0.590, 3.44)
	AVAT	3.80 (1.70, 8.53)***	2.75 (0.990, 7.66)	3.99 (1.15, 13.8)*	2.44 (0.803, 7.40)	2.05 (0.606, 6.93)	4.31 (0.891, 20.8)
‡Metabolic syndrome	UL SAT	2.48 (1.13, 5.45)	0.958 (0.281, 3.27)	0.420 (0.062, 2.87)	1.19 (0.578, 2.44)	0.815 (0.340, 1.96)	0.268 (0.056, 1.29)
	ASAT	3.23 (1.45, 7.17)**	1.39 (0.458, 4.21)	1.95 (0.329, 11.6)	1.33 (0.843, 2.11)	1.07 (0.561, 2.03)	1.37 (0.528, 3.54)
	AVAT	5.88 (2.05, 16.9)***	4.10 (1.16, 14.5)*	4.45 (1.18, 16.8)*	3.12 (0.902, 10.8)	2.57 (0.660, 9.98)	6.54 (1.08, 39.6)*

†: Beta (β) values and 95% confidence interval (95% CI); ‡: EXB value and 95% CI; have been expressed as the associations of truncal and leg fat mass with Metabolic syndrome and its single and combined components.

Model 1: adjustment for age, alcohol use, smoking, income, physical activity, and menopause status (only in women).

Model 2: Model 1 added adjustment for BMI.

Model 3: Model 2 added adjustment for truncal and leg fat mass.

* p -value<0.05; ** p -value<0.01; *** p -value<0.005.

buffer or sink for circulating FAAs and TGs to prevent their accumulation of ectopic sites, e.g., skeletal muscle, liver and pancreas.⁵⁷ Compare to SAT, VAT adipocytes have a higher rate of lipolysis, which have been postulated to play a critical role in the development of obesity-induced insulin resistance, a major risk factor for diabetes and cardiovascular disease.⁵⁸ Martin et al reported that the major difference in resting FFA metabolism between upper and lower body obese women was because the later had the ability to down-regulate upper body fat lipolysis so as to maintain normal level of FFA.⁵⁹ In addition, there are obviously differences of adipokines and inflammatory produced by different depots of adipose.⁶⁰ Wu et al indicated that LF was associated with a favorable profile of adipokines (higher adiponectin and lower PAI-1 and RBP4 levels), whereas TF was associated with the unfavorable adipokines (lower adiponectin and higher RBP4 and PAI-1 levels) and inflammatory markers (higher CRP and IL-6 levels).⁴⁸ These findings from above mentioned studies provide novel insights regarding the potential molecular mechanisms of fat distribution and metabolic disorders, further research to reveal the related pathophysiological mechanisms in vivo should be great encouraged.

The most strength in our study is, except for DXA, we also used MRI to assess VAT and SAT in different body regions. We hypothesis that the opposite effects of TF and LF mainly contribute to the different characteristics of adipose cells in SAT and VAT, which could only have been accurately distinguished by MRI scan now, and similar studies were also scarce in Chinese population. Although the protective effects of upper leg SAT on most of metabolic risk factors have not been observed as expected, we confirmed that abdominal VAT was significantly positively associated with risk of MetS and serum TG in both men and women. More important to note, the elevated serum TG was the single metabolic risk which consistently associated with both TF and abdominal VAT in the current study. Recently, TG has been demonstrated to be an important cause of leptin resistance, which may ultimately lead to insulin resistance and MetS, meanwhile reducing dietary carbohydrates lower serum TGs may protect against this form of leptin resistance.⁵⁷ Whether TG and leptin resistance played a key medium among the associations of TF and LF with the related metabolic diseases in Chinese people was unclear, and this study provided us with a valuable clue for the future research.

There are several limitations in present study. First, the sample size was limited in the current MRI analysis, and we failed to observe similar protect effects of leg SAT with MetS especially in female population, although the opposite directions of associations compared to abdominal SAT and VAT in most metabolic indicators have been showed. Second, it was a cross-sectional study, which prohibited us from inferring causality in the associations between regional body fat distribution and the metabolic risk factors. Third, all participants in DXA and MRI study were community-based convenience samples in the east of China, which may not be generalized to other areas and other ethnicities.

Conclusions

TF and LF showed opposite associations on metabolic

risk factors among Chinese adults. For TF, abdominal VAT, but not abdominal SAT, was positively associated with risk of MetS and level of TG. For a given BMI, a larger proportion of LF bore protective effect on MetS independent of truncal fat, especially in women. Future studies were warranted to use larger sample size and to examine the potential mechanism of the opposite effects of TF and LF on metabolic risk factors.

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AUTHOR DISCLOSURES

The authors have declared no competing interest exists.

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Original Article

Truncal and leg fat associations with metabolic risk factors among Chinese adults

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中国成年人躯干和腿部脂肪与代谢危险因素相关

背景与目的：检测中国人局部身体脂肪分布与代谢危险因素之间的相关性。**方法与研究设计：**2008-2013年期间，研究者采用双能X线吸收仪检测了947名中国成年人的躯干和腿部脂肪，采用核磁共振检测了103名中国人腹部的内脏脂肪和皮下脂肪，以及大腿的皮下脂肪。检测的代谢危险因素包括空腹血糖、甘油三酯、总胆固醇、低密度脂蛋白胆固醇、高密度脂蛋白胆固醇和代谢综合征。**结果：**躯干脂肪对中国人代谢危险因素具有不利的影响，而腿部脂肪显示出有利的影响，且所有这些影响独立于身体质量指数（BMI）（绝大多数 $p < 0.01$ ）。躯干脂肪较高而腿部脂肪较低的个体，相对于其他亚组个体，具有最高的代谢综合征发病风险（ $p < 0.05$ ）。腹部内脏脂肪与代谢综合征的发病风险（男性：OR=4.45, 95% CI：1.18, 16.8；女性：OR=6.54, 95% CI：1.08, 39.6），以及血清甘油三酯（男性： $\beta=0.379$, 95% CI：0.090, 0.667；女性： $\beta=0.700$, 95% CI：0.327, 1.07）呈正相关。大腿皮下脂肪与大多数代谢危险因素的关系，与腹部皮下脂肪和内脏脂肪相反，但差异无统计学意义。**结论：**本研究表明中国成年人躯干和腿部脂肪对代谢危险因素具有相反的影响。腹部的内脏脂肪而不是皮下脂肪，与血清甘油三酯和代谢综合征风险呈正相关。未来的研究有必要在中国人中探讨躯干和腿部脂肪对代谢危险因素具有作用相反的潜在机制。

关键词：躯干脂肪、腿部脂肪、代谢危险因素、中国人、成人