Eur J Nutr (2013) 52:489–495
DOI 10.1007/s00394-012-0350-4

ORIGINAL CONTRIBUTION

Leg fat might be more protective than arm fat in relation to lipid profile

M. Sánchez-López · F. B. Ortega · P. Moya-Martínez · S. López-Martínez · I. Ortiz-Galeano · M. A. Gómez-Marcos · M. Sjöström · V. Martínez-Vizcaíno

Received: 16 November 2011 / Accepted: 20 March 2012 / Published online: 7 April 2012

Abstract
Purpose The objective of this study was to determine the independent relationships of trunk fat, leg fat and arm fat to cardiovascular (CVD) risk factors, after controlling for relevant confounders such as fat mass index, cardiorespiratory fitness and objectively measured physical activity.
Methods This is a cross-sectional study involving 683 university students, aged 18–30 years. Total and regional body fat distribution was measured using dual-energy X-ray absorptiometry. The associations of trunk, leg and arm fat with CVD risk factors (triglycerides-TG-, high-density lipoprotein cholesterol-HDL-c-, TG/HDL-c ratio, $HOMA_{IR}$, mean arterial pressure, C-reactive protein) were examined using regression linear models, controlling for age, sex, fat mass index [total body fat(kg)/height(m^2)], maximal oxygen consumption and physical activity by accelerometer.
Results After controlling for fat mass index, and other confounders, higher levels of trunk fat were found to be associated with a poorer lipid profile, while higher levels of leg fat were found to be associated with a better lipid profile. We did not find any association between arm fat and lipid profile after controlling for total fatness and other confounders. Neither trunk, leg or arm fat was found to be related to insulin resistance, blood pressure or inflammation markers.
Conclusions Our data suggest that the region where fat is accumulated might have a differential effect on lipid profile: trunk fat has an adverse effect, leg fat has a protective effect, and arm fat has no effect. The differences observed between upper- and lower-body peripheral fat depots should be further explored.

Keywords Cardiovascular risk factors · Fat distribution · Cardiorespiratory fitness and physical activity

M. Sánchez-López · P. Moya-Martínez · I. Ortiz-Galeano · V. Martínez-Vizcaíno
Social and Health Care Research Center, University of Castilla-La Mancha, Cuenca, Spain

M. Sánchez-López
School of Education, University of Castilla-La Mancha, Ciudad Real, Spain

M. Sánchez-López (✉)
Centro de Estudios Sociosanitarios, Universidad de Castilla-La Mancha, 16071 Cuenca, Spain
e-mail: Mairena.Sanchez@uclm.es

F. B. Ortega · M. Sjöström
Unit for Preventive Nutrition, Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge, Sweden

F. B. Ortega
Department of Physiology, School of Medicine, University of Granada, Granada, Spain

S. López-Martínez
Clinical Analysis Laboratory, Hospital Virgen de la Luz, Cuenca, Spain

M. A. Gómez-Marcos
Primary Care Research Unit, La Alamedilla Health Center, Salamanca, Spain

M. A. Gómez-Marcos · V. Martínez-Vizcaíno
Research Network in Preventive and Health Promotion Activities (RedIAP), Instituto de Salud Carlos III, Madrid, Spain

Introduction

Adipose tissue and its distribution are important determinants of metabolic and cardiovascular disease (CVD) risk [1]. There is consistent evidence indicating that not all fat stores contribute equally to the risk of disease, with abdominal fat, and particularly visceral fat, being the main predictor of CVD risk factors in both men and women [2].

While the links between abdominal fat and trunk fat with CVD are well understood, there is limited information addressing the specific role of peripheral fat mass. Some studies support that gluteofemoral fat reduces cardiometabolic risk factors after adjusting for potential confounders such as total or abdominal fat mass [3]. Few studies have examined the independent associations of trunk, leg and arm fat with inflammatory markers [4, 5]. Furthermore, whether different peripheral fat depots (i.e., leg fat vs. arm fat) have similar relationships with CVD risk is also unknown. Some studies showed that arm circumference is negatively associated with mortality [6–8]. Other studies have highlighted the opposite association between trunk and peripheral fat (sum of leg fat and arm fat) in relation to several cardiovascular risk factors [9–11], but few have analyzed leg fat and arm fat separately [12, 13].

Both cross-sectional and intervention studies have shown that high cardiorespiratory fitness (as defined by maximal oxygen consumption, VO_{2max}.) has a beneficial effect on both adiposity and CVD risk [14, 15]. Physical activity (especially highly intense physical activity) has been associated with adiposity and other CDV risk [16, 17, 18]. Because of the established relationship of fitness and physical activity to both adiposity and other CVD risk factors, these factors should be considered possible confounders.

The purpose of this study was to determine the independent relationships of trunk fat, leg fat and arm fat to blood lipids, insulin resistance, blood pressure and inflammation (as measured by C-reactive protein), after controlling for relevant confounders such as fat mass index (FMI), cardiorespiratory fitness and objectively measured physical activity.

Methods

Design and subjects

This is a cross-sectional study involving first-year Caucasian university students, aged 18–30 years, from the University of Castilla-La Mancha, Cuenca Campus, Spain. Of the 770 students invited, a total of 683 (88.7 %) agreed to participate, 178 men and 504 women (73.79 % women), percentages in accordance with the sex ratio of the University Campus of Cuenca, Spain (70 %). Data collection was performed during the academic year 2009–2010. The study was approved by the Cuenca Clinical Research Ethics Committee, and all participants gave their written consent to participate in the study after they were duly informed about the purposes and procedures of the study.

Anthropometrics

Participants in light clothing were weighted twice to the nearest 0.1 kg using a portable electronic scale (Seca 770). Height was measured twice to the nearest 0.1 cm without shoes using a wall-mounted stadiometer (Seca 222). Using the mean of these measurements, body mass index (BMI) was calculated as weight in kilograms divided by height in square meters (kg/m^2).

Body composition: dual-energy X-ray absorptiometry (DXA)

Total body fat and regional fat (trunk, leg and arm fat) were measured by a whole-body DXA scanning, using a total body scan mode: Lunar iDXA (GE Medical Systems Lunar, Madison, WI 53718 USA). The analyses were performed using enCoreTM 2008 software version 12.30.008 (General Electric Company). FMI was calculated as total body fat (kg)/height (m^2). The reasons why we used the ratio body fat by height instead of weight (as it is the case for body fat %) are in detail discussed in the following letter by Cole [19]. By using specific anatomic landmarks, as previously described by Gallagher et al. [20], fat mass in the trunk, legs and arm was measured. The machine's calibration was checked and passed on a daily basis before each scanning session, using the GE Lunar calibration phantom. Participants were instructed to wear clothing containing no metal. Participants were laid down on the scanning table within the scanning area and were asked to relax and to not move until the full scan was finished. Participants' feet were loosely fastened together to keep the lower body in a stable position. Scan time for a total body scan was approximately 6 min. All DXA scans were performed by an X-ray technician.

Cardiovascular disease risk factors

Biochemical variables: the blood samples were taken by puncturing the cubital vein under standardized conditions between 08.15 and 09.00 h, after at least 12 h of fasting. The samples were processed in a system of Roche Diagnostics COBAS C711. The following variables were determined following biochemical parameters: triglycerides (GPO-PAP enzymatic method), c-direct plus HDL

(2nd generation method without deproteinization). The blood concentration of insulin was determined by chemiluminescent microparticle immunoassay (CMIA) in a processing step and a platform composed of two systems i2000SR ARCHITECT, Abbott Laboratories. The insulin sensitivity index was determined by $HOMA_{IR}$ (homeostasis model assessment): fasting glucose (mmol/l) × fasting insulin (μU/ml)/22.516. Higher values indicate a higher insulin resistance. High sensitive C-reactive protein was determined by immunoturbidimetric assay (COBAS C501, 6000 COBAS platform from Roche Diagnostics).

Systolic and diastolic blood pressure: average of two measurements obtained with an interval of 5 min between measurements, and after a rest period of at least 5 min before the first determination. Participants were sitting in a relaxed position, with the right arm semi-flexed at heart level. Blood pressure was obtained by an automated procedure by OMRON M5-I monitor (Omron Healthcare Europe BV, Hoofddorp, Netherlands). We calculated mean arterial pressure (MAP): diastolic blood pressure + [0.333 × (systolic blood pressure − diastolic blood pressure)]. All the measurements were performed by experienced nurses.

Cardiorespiratory fitness

Cardiorespiratory fitness was determined by an incremental submaximal exercise test on a cycle ergometer (Ergoline Variobike 550; Ergometrix, Barcelona, Spain), as previously described [21]. The VO_2 consumption was measured using the gas analyzer Fitmate Pro (COSMED, Rome, Italy), with data being collected every 15 s. The estimation of VO_{2max} (ml/kg/min) was recorded automatically by Fitmate Pro software [21, 22]. The gas analyzer was calibrated automatically before every test. The Cosmed Fitmate Pro predicts VO_{2max} by extrapolating the regression line relating heart rate with measured VO_2 to the age-predicted maximum heart rate (HR = 220-age).

Physical activity assessment

Physical activity was measured using the MTI accelerometer, model 7164 (Actigraph, Shalimar, FL, USA) in a random subsample of 236 participants. The students wore the accelerometer on the right hip for seven consecutive days. All subjects were verbally instructed on how to use the accelerometer. The accelerometer was set to record physical activity data every minute (60 s epoch). The MAHUFFE software (http://www.mrc-epid.cam.ac.uk/Research/PA/Downloads.html) was used to analyze the data. Sequences of 10 or more consecutive zero counts were considered non-wearing time and excluded from the analyses. Inclusion criteria was a minimum of 4 days of registration, including at least 1 weekend day and at least 600 registered minutes per day. Overall physical activity, expressed as mean counts per minute, and minutes of physical activity at vigorous and moderately vigorous intensity, according to cut-offs by Freedson and cols [23], were used as confounders in the analyses.

Statistical analysis

All statistical analyses were performed with SPSS-IBM (SoftWare, v.19.0 SPSS Inc., Chicago, IL, USA), and the level of significance was set at $\alpha = 0.05$. Descriptive characteristics are expressed as mean ± standard deviation. Triglycerides, $HOMA_{IR}$, C-reactive protein and vigorous physical activity outcome variables were logarithmically transformed to obtain a normal distribution. The associations among CVD risk factors (triglycerides, HDL-c, triglycerides/HDL-c ratio, $HOMA_{IR}$, mean arterial pressure and C-reactive protein) and trunk, leg and arm fat were examined using a regression linear model, controlling for potential confounders including sex, age and fat mass index. Additional analysis adjustments were performed including overall physical activity (count/min), logarithms of vigorous physical activity, moderately vigorous physical activity (min/day) and VO_{2max} (ml/kg/min) as confounding variables to test whether the independent associations of cardiovascular risk factor on trunk, leg and arm fat were kept. Previously, association between fat mass index and CVD risk factors, adjusting for age and sex, was examined.

Because of the close correlation among some predicting variables (i.e., FMI ratio with trunk, leg and arm fat), we tested the models for multicollinearity problems according to Tabachnick BG and Fidell LS (2001), to use more restrictive criteria than that which is used by most statistical programs (FIV ≥10 or tolerance ≤0.010) [24].

Results

The characteristics of the study sample are presented in Table 1. Table 2 shows a significant positive association between FMI and $HOMA_{IR}$, and C-reactive protein, after adjusting for age and sex ($p < 0.001$). No relationship was found between FMI and other CVD risk factors examined.

The relationships of trunk fat, leg fat and arm fat to CVD risk factors are shown in Table 3. After adjusting for age and sex, trunk fat levels were positively associated with all the CVD risk factors studied, except for HDL-c, with which trunk fat showed a negative association ($p = 0.03$). When FMI was included in the models, only lipid profile variables (triglycerides, HDL-c and triglycerides/HDL-c ratio) showed a significant association, while no association was found with $HOMA_{IR}$, mean arterial pressure or C-reactive protein. Higher leg fat was not

Table 1 Characteristics of the study sample

	Men ($n = 178$)	Women ($n = 505$)	p
Age (yr)	19.94 (2.90)	20.13 (4.47)	0.535
Height (m)	1.76 (0.07)	1.62 (0.05)	<0.001
Weight (kg)	73.55 (11.85)	58.75 (10.23)	<0.001
BMI (kg/m^2)	23.73 (3.42)	22.20 (3.63)	<0.001
Percentage body fat	23.04 (6.46)	34.17 (5.62)	<0.001
Fat mass index (kg/m^2)	5.28 (2.08)	6.10 (2.09)	0.001
Total body fat (kg)	18.40 (7.23)	19.63 (6.56)	0.091
Trunk fat (kg)	8.24 (4.00)	8.76 (3.60)	0.564
Leg fat (kg)	7.17 (2.75)	8.03 (2.43)	0.002
Arm fat (kg)	1.87 (0.81)	2.04 (0.82)	0.063
Triglycerides (mg/dl)	84.53 (48.26)	75.41 (34.59)	0.050
HDL-c (mg/dl)	50.16 (10.27)	61.72 (12.61)	0.221
Triglycerides/HDL-c ratio	1.82 (1.34)	1.29 (0.72)	<0.001
Glucose (mmol/l)	4.95 (0.44)	4.79 (0.87)	0.060
Insulin (μU/ml)	8.54 (7.89)	8.33 (3.69)	0.680
$HOMA_{IR}$	1.98 (2.95)	1.81 (1.31)	0.371
Systolic blood pressure (mm Hg)	127.32 (11.42)	108.92 (9.31)	<0.001
Diastolic blood pressure (mm Hg)	70.87 (7.25)	68.58 (7.00)	<0.001
MAP (mm Hg)	89.68 (7.48)	82.03 (7.19)	<0.001
C-reactive protein (mg/l)	3.09 (10.22)	2.05 (4.20)	0.268
$VO_{2\ max}$ (ml/kg/min)	38.13 (8.28)	29.46 (4.78)	<0.001
Overall physical activity (counts/min)	354.28 (120.15)	314.58 (83.90)	0.013
Moderate–vigorous physical activity (min/day)	42.76 (22.22)	38.29 (17.73)	0.131
Vigorous physical activity (min/day)	6.17 (7.67)	3.04 (7.51)	0.004

Values are means (standard deviation)

Fat mass index was calculated as total body fat/height (kg/m^2)

BMI body mass index, *HDL-c* high-density lipoprotein cholesterol, *$HOMA_{IR}$* homeostasis model assessment: insulin resistance, *MAP* mean arterial pressure, *VO_{2max}* maximum oxygen consumption

Table 2 Associations of fat mass index with cardiovascular risk factors, adjusting for age and sex

	β	(95 % CI)	p value	R^2
LogTG	0.006	−0.002; 0.014	0.169	0.012
HDL-c (mg/dl)	−0.481	−1.05; 0.093	0.100	0.146
Log TG/HDL-c	0.008	−0.001; 0.018	0.087	0.085
Log $HOMA_{IR}$	0.019	0.010; 0.029	**<0.001**	0.197
MAP (mm Hg)	0.331	−0.003; 0.665	0.052	0.209
Log C-reactive protein	0.029	0.005; 0.053	**0.017**	0.060

Fat mass index was calculated as total body fat/height (kg/m^2)

Bold values are statistically significant ($p \leq 0.05$)

associated with most of the CVD risk factors studied, except for $HOMA_{IR}$, with which higher leg fat showed a positive association ($p < 0.001$). When FMI was included in the models, higher levels of leg fat were associated only with better lipid profile (triglycerides, HDL-c and triglycerides/HDL-c ratio). Higher arm fat was positively associated with $HOMA_{IR}$, mean arterial pressure and C-reactive protein ($p < 0.05$), but not with lipid profile. When FMI was included in the models, arm fat was not associated with any of the CVD risk factors studied.

Additional adjustments for overall physical activity (counts/min), logarithm of vigorous physical activity, moderately vigorous physical activity (min/day) or cardiorespiratory fitness (VO_{2max}) did not affect the results (data not shown). Overall, the results were consistent when the analyses were conducted separately with men and women (data not shown).

Discussion

Our data support that higher levels of trunk fat are associated with a poor lipid profile, while higher levels of leg fat are associated with a better lipid profile, regardless of several confounders including fat mass index, cardiorespiratory fitness or physical activity. We did not observe any association between arm fat and lipid profile after controlling for total fatness and other confounders. Neither trunk, leg or arm fat was related to insulin resistance, blood pressure or inflammation markers, once total fat was accounted for.

Unadjusted models (Table 3) showed positive coefficients that the fatter the worse cardio-metabolic profile. Models adjusted for total adiposity, inform about how the relative accumulation of fat in different parts of the body might be differently related to cardio-metabolic profile.

Previous studies have also reported opposite associations of trunk fat and leg fat with lipid profile [12, 13, 25–28]. The possible mechanisms that may contribute to the protective role of gluteofemoral depot are elucidated in a recent review [3]. It has been suggested that fat in the gluteofemoral area acts as a 'metabolic sink' for the circulating ectopic fat. The protective properties of gluteofemoral fat could derive from a differential local handling of fatty acid uptake and release. Isolated adipocytes in the femoral region are relatively insensitive to lipolytic stimuli, and the femoral fat depot has a correspondingly lipoprotein lipase activity. Another potential mechanism is that gluteofemoral adipose tissue could contribute to a protective adipokine profile by secreting more 'beneficial' adipokines and less pro-inflammatory molecules than those secreted by abdominal fat.

Table 3 Independent associations of trunk fat, leg fat and arm fat with cardiovascular risk factors

	Model 1			Model 2		
	β (95 % CI)	p value	R^2	β (95 % CI)	p value	R^2
Trunk fat						
LogTG	0.005 (0.001; 0.010)	**0.026**	0.027	0.026 (0.010; 0.042)	**0.001**	0.044
HDL-c (mg/dl)	−0.365 (−0.685; −0.0459)	**0.026**	0.151	−1.350 (−2.489; −0.217)	**0.020**	0.158
Log TG/HDL−c	0.007 (0.002; 0.007)	**0.007**	0.095	0.037 (0.018; 0.056)	**<0.001**	0.117
Log $HOMA_{IR}$	0.011 (0.006; 0.016)	**<0.001**	0.199	0.009 (−0.001; 0.028)	0.344	0.165
MAP (mm Hg)	0.194 (0.007; 0.381)	**0.043**	0.209	0.197 (−0.465; 0.859)	0.560	0.209
Log C-reactive protein	0.018 (0.004; 0.031)	**0.010**	0.062	0.026 (−0.021; 0.074)	0.279	0.062
Leg fat						
LogTG	0.001 (−0.006; 0.007)	0.970	0.015	−0.024 (−0.040; −0.008)	**0.003**	0.040
HDL-c (mg/dl)	−0.114 (−0.582; −0.355)	0.634	0.141	1.418 (0.296; 2.539)	**0.013**	0.159
Log TG/HDL-c	0.001 (−0.008; 0.008)	0.956	0.079	−0.035 (−0.054; −0.017)	**<0.001**	0.115
Log $HOMA_{IR}$	0.015 (0.007; 0.023)	**<0.001**	0.049	0.006 (−0.013; 0.024)	0.536	0.051
MAP (mm Hg)	0.261 (−0.008; 0.530)	0.058	0.208	0.106 (−0.541; 0.753)	0.748	0.209
Log C-reactive protein	0.019 (0.001; 0.039)	0.054	0.055	−0.014 (−0.062; 0.033)	0.553	0.060
Arm fat						
LogTG	0.013 (−0.007; 0.033)	0.210	0.019	−0.005 (−0.068; 0.058)	0.882	0.020
HDL-c (mg/dl)	−1.253 (−2.694; −0.188)	0.088	0.147	−1.046 (−5.497; 3.405)	0.644	0.147
Log TG/HDL-c	0.019 (−0.005; 0.044)	0.120	0.084s	−0.008 (−0.083; 0.067)	0.834	0.085
Log $HOMA_{IR}$	0.052 (0.028; 0.076)	**<0.001**	0.057	0.063 (−0.010; 0.137)	0.089	0.057
MAP (mm Hg)	1.001 (0.165; 1.838)	**0.019**	0.212	2.020 (−0.535; 4.575)	0.121	0.213
Log C-reactive protein	0.070 (0.010; 0.130)	**0.023**	0.004	0.026 (−0.182; 0.190)	0.963	0.060

Model 1 was adjusted for age and sex; model 2 was further adjusted for fat mass index as total body fat/height (kg/m^2)

Bold values are statistically significant ($p \leq 0.05$)

There is inconclusive evidence about the relation between leg fat and $HOMA_{IR}$, mean arterial pressure and C-reactive protein. While several studies have reported an inverse association between lower-body fat and insulin resistance markers [4, 5, 13, 27, 29], others have observed no association [10, 25, 30] in agreement with our findings. Similarly, some studies observed an inverse association between leg fat and blood pressure [4, 9, 27], while others did not [5, 12, 26], also in line with our results. To our knowledge, only two studies have assessed the association between leg fat and C-reactive protein, and none between arm fat and C-reactive protein. Vega et al. [4] showed that lower-body fat was negatively related to C-reactive protein after controlling for percent total body fat. Contrarily, Rocha et al. did not observe association between thigh fat and C-reactive protein in obese women [5]. The limited number of studies makes it difficult to draw striking conclusions.

Our data do not support a protective role of arm fat for CDV risk. Previous studies have found a positive relationship between peripheral fat, which includes the sum of leg fat and arm fat, and CVD risk factors [9–11, 26]. Few studies have been conducted to examine the separate effect of leg and arm fat depots on CVD risk. Some of them have shown a lower risk of mortality associated with a higher arm circumference [6–8], though they do not distinguish to what extent this positive effect was due to fat mass or lean mass located in arms [31]. Williams et al. [12], using DXA, observed a negative relationship between arm fat and total cholesterol, and a positive relationship between arm fat and systolic blood pressure. Okura et al. investigated how changes in regional body composition, also measured by DXA, were associated with CVD risk factors in overweight and obese woman after a 14-week intervention for weight reduction through diet and exercise. The authors observed that reductions in arm fat were associated with high LDL-c levels and lower diastolic blood pressure [13], according to the findings reported by Williams et al. [12]. The aforementioned studies did not observe consistent associations between arm fat and other CVD risk factors.

Independent and inverse relationships of trunk fat and leg fat to CVD risk factors seem to remain after adjusting for age, sex, race, total body fat or visceral fat [3] and genetics [27]. Some studies included fitness [11, 27, 32] or self-reported physical activity [11, 26, 32, 33] as potential

confounders in their models, while no study included an objective measurement of physical activity. In the present study, as well as in previous studies [11, 26, 27, 32, 33], additional adjustment for physical activity or fitness did not modify the results.

The current study has several limitations that should be acknowledged. First, its cross-sectional design does not allow one to derive conclusions in terms of causality. Second, because we did not measure thigh fat by computed tomography, we do not know whether the favorable association of lower-body adiposity with blood lipids is specifically related to subcutaneous or intermuscular fat depots. Likewise, we were not able to determine whether the association between trunk fat and metabolic risk was attributable specifically to visceral fat, since trunk fat includes not only visceral fat but also subcutaneous fat. Third, our results were obtained in a young (university students), Caucasian and healthy population, and therefore, generalizations about different age or ethnic groups should be made with caution. Fourth, body fat distribution is potentially influenced by dietary intake, alcohol and tobacco, and such information is lacking in the present study. Nevertheless, studies including these confounders in the regression analyses have shown consistent results before and after adjustment [11, 29], suggesting that the associations studied are independent of these factors. Data on prevalence of smoking in students from Spanish universities (both men and women) seem to be similar to that reported by surveys in students from other countries [34]. Finally, similarly to most of the association studies, data from tables of this study are not free of multiple hypothesis test bias. Readers must be aware of this bias, especially when significance levels are close to 0.05.

In conclusion, our data suggest that depending on the body region where the fat is accumulated its effect on lipid profile might be different, with trunk fat independently related to a worsened blood lipid profile while leg fat is independently related to improved blood lipid profile. Arm fat seems to have a neutral effect. The association between trunk, leg and arm fat and insulin resistance, blood pressure or C-reactive protein is not supported by our results.

Acknowledgments We thank all participants of the study. This study was funded mainly by the Foundation for Health Research of Castilla-La Mancha (Fiscam-grant AN-2008/31). Additional funding was obtained from the Spanish Ministry of Education (EX-2008-0641), the Swedish Heart–Lung Foundation (20090635), and Research Network in Preventive and Health Promotion Activities (Red de Investigación en Actividades Preventivas y de Promoción de Salud-RedIAP) (grant RD06/0018/0038).

Conflict of interest The authors declare that they have not conflict of interest.

References

1. Kannel WB, Cupples LA, Ramaswami R, Stokes J III, Kreger BE, Higgins M (1991) Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 44:183–190
2. Arsenault BJ, Lachance D, Lemieux I, Almeras N, Tremblay A, Bouchard C et al (2007) Visceral adipose tissue accumulation, cardiorespiratory fitness, and features of the metabolic syndrome. Arch Intern Med 167:1518–1525
3. Manolopoulos KN, Karpe F, Frayn KN (2010) Gluteofemoral body fat as a determinant of metabolic health. Int J Obes (Lond) 34:949–959
4. Vega GL, Adams-Huet B, Peshock R, Willett D, Shah B, Grundy SM (2006) Influence of body fat content and distribution on variation in metabolic risk. J Clin Endocrinol Metab 91:4459–4466
5. Rocha PM, Barata JT, Teixeira PJ, Ross R, Sardinha LB (2008) Independent and opposite associations of hip and waist circumference with metabolic syndrome components and with inflammatory and atherothrombotic risk factors in overweight and obese women. Metabolism 57:1315–1322
6. Mason C, Craig CL, Katzmarzyk PT (2008) Influence of central and extremity circumferences on all-cause mortality in men and women. Obesity (Silver Spring) 16:2690–2695
7. Allison DB, Zhu SK, Plankey M, Faith MS, Heo M (2002) Differential associations of body mass index and adiposity with all-cause mortality among men in the first and second National Health and Nutrition Examination Surveys (NHANES I and NHANES II) follow-up studies. Int J Obes Relat Metab Disord 26:410–416
8. Zhu S, Heo M, Plankey M, Faith MS, Allison DB (2003) Associations of body mass index and anthropometric indicators of fat mass and fat free mass with all-cause mortality among women in the first and second National Health and Nutrition Examination Surveys follow-up studies. Ann Epidemiol 13:286–293
9. Tanko LB, Bagger YZ, Alexandersen P, Larsen PJ, Christiansen C (2003) Central and peripheral fat mass have contrasting effect on the progression of aortic calcification in postmenopausal women. Eur Heart J 24:1531–1537
10. Tanko LB, Bagger YZ, Alexandersen P, Larsen PJ, Christiansen C (2003) Peripheral adiposity exhibits an independent dominant antiatherogenic effect in elderly women. Circulation 107:1626–1631
11. Ferreira I, Snijder MB, Twisk JW, van Mechelen W, Kemper HC, Seidell JC et al (2004) Central fat mass versus peripheral fat and lean mass: opposite (adverse versus favorable) associations with arterial stiffness? The Amsterdam Growth and Health Longitudinal Study. J Clin Endocrinol Metab 89:2632–2639
12. Williams MJ, Hunter GR, Kekes-Szabo T, Snyder S, Treuth MS (1997) Regional fat distribution in women and risk of cardiovascular disease. Am J Clin Nutr 65:855–860
13. Okura T, Nakata Y, Yamabuki K, Tanaka K (2004) Regional body composition changes exhibit opposing effects on coronary heart disease risk factors. Arterioscler Thromb Vasc Biol 24:923–929
14. Young DR, Steinhardt MA (1993) The importance of physical fitness versus physical activity for coronary artery disease risk factors: a cross-sectional analysis. Res Q Exerc Sport 64:377–384
15. McMurray RG, Ainsworth BE, Harrell JS, Griggs TR, Williams OD (1998) Is physical activity or aerobic power more influential on reducing cardiovascular disease risk factors? Med Sci Sports Exerc 30:1521–1529
16. Duncan JJ, Gordon NF, Scott CB (1991) Women walking for health and fitness. How much is enough? JAMA 266:3295–3299

17. Rizzo NS, Ruiz JR, Hurtig-Wennlof A, Ortega FB, Sjostrom M (2007) Relationship of physical activity, fitness, and fatness with clustered metabolic risk in children and adolescents: the European youth heart study. J Pediatr 150:388–394
18. Lee DC, Sui X, Ortega FB, Kim YS, Church TS, Winett RA et al (2011) Comparisons of leisure-time physical activity and cardiorespiratory fitness as predictors of all-cause mortality in men and women. Br J Sports Med 45:504–510
19. Cole TJ, Fewtrell MS, Prentice A (2008) The fallacy of using percentage body fat as a measure of adiposity. Am J Clin Nutr 87(6):1959; author reply 1959–1960
20. Gallagher D, Ruts E, Visser M, Heshka S, Baumgartner RN, Wang J et al (2000) Weight stability masks sarcopenia in elderly men and women. Am J Physiol Endocrinol Metab 279:E366–E375
21. Nieman DC, Lasasso H, Austin MD, Pearce S, McInnis T, Unick J (2007) Validation of Cosmed's FitMate in measuring exercise metabolism. Res Sports Med 15:67–75
22. Lee J, Bassett DF, Thompson DF, Fitzhugh E (2009) Validation of the Cosmed Fitmate for predicting maximal oxygen consumption: 2185: Board #73 May 28 2:00 PM–3:30 PM. Med Sci Sports Exerc 41:260
23. Freedson PS, Melanson E, Sirard J (1998) Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc 30:777–781
24. Tabachnick L, Fidell L (2001) Using multivariate statistic, 4th edn. Allyn and Bacon, Boston
25. Van Pelt RE, Jankowski CM, Gozansky WS, Schwartz RS, Kohrt WM (2005) Lower-body adiposity and metabolic protection in postmenopausal women. J Clin Endocrinol Metab 90:4573–4578
26. Hunter GR, Kekes-Szabo T, Snyder SW, Nicholson C, Nyikos I, Berland L (1997) Fat distribution, physical activity, and cardiovascular risk factors. Med Sci Sports Exerc 29:362–369
27. Hunter GR, Chandler-Laney PC, Brock DW, Lara-Castro C, Fernandez JR, Gower BA (2010) Fat distribution, aerobic fitness, blood lipids, and insulin sensitivity in African-American and European-American women. Obesity (Silver Spring) 18:274–281
28. Terry RB, Stefanick ML, Haskell WL, Wood PD (1991) Contributions of regional adipose tissue depots to plasma lipoprotein concentrations in overweight men and women: possible protective effects of thigh fat. Metabolism 40:733–740
29. Snijder MB, Dekker JM, Visser M, Bouter LM, Stehouwer CD, Yudkin JS et al (2004) Trunk fat and leg fat have independent and opposite associations with fasting and postload glucose levels: the Hoorn study. Diabetes Care 27:372–377
30. Yim JE, Heshka S, Albu JB, Heymsfield S, Gallagher D (2008) Femoral-gluteal subcutaneous and intermuscular adipose tissues have independent and opposing relationships with CVD risk. J Appl Physiol 104:700–707
31. Wannamethee SG, Shaper AG, Lennon L, Whincup PH (2007) Decreased muscle mass and increased central adiposity are independently related to mortality in older men. Am J Clin Nutr 86:1339–1346
32. Buemann B, Astrup A, Pedersen O, Black E, Holst C, Toubro S et al (2006) Possible role of adiponectin and insulin sensitivity in mediating the favorable effects of lower body fat mass on blood lipids. J Clin Endocrinol Metab 91:1698–1704
33. Snijder MB, Henry RM, Visser M, Dekker JM, Seidell JC, Ferreira I et al (2004) Regional body composition as a determinant of arterial stiffness in the elderly: the Hoorn study. J Hypertens 22:2339–2347
34. Nerin I, Crucelaegui A, Novella P, Ramon y Cajal P, Sobradiel N, Gerico R (2004) A survey on the relationship between tobacco use and physical exercise among university students. Arch Bronconeumol 40:5–9