Body mass index and hip and thigh circumferences are negatively associated with visceral adipose tissue after control for waist circumference[1–3]

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ABSTRACT

Background: Waist circumference (WC) is positively associated with morbidity and mortality with or without control for hip circumference (HC) or body mass index (BMI; in kg/m^2). This association is thought to be explained by an expanded visceral adipose tissue (VAT) depot. Conversely, HC and BMI are negatively associated with morbidity and mortality after control for WC. Whether this inverse association is explained in part by the ability of HC and BMI to identify subjects with increased subcutaneous adipose tissue (SAT), increased skeletal muscle (SM) mass, or decreased VAT after control for WC is unclear.

Objective: We examined the independent associations between WC, HC, thigh circumference (ThC), and BMI with VAT and total, lower-body, and abdominal SAT and SM.

Design: Total and regional body composition were measured in 256 white men and women with magnetic resonance imaging.

Results: WC, HC, ThC, and BMI were all positively correlated with total, lower-body, and abdominal SAT and SM and with VAT. After statistical control for WC, HC, ThC, and BMI remained positively associated with total, lower-body, and abdominal SAT and SM (men only) but were negatively associated with VAT ($P < 0.05$). HC ($P < 0.05$) but not BMI ($P > 0.10$) or ThC ($P = 0.06$) remained negatively associated with VAT after further control for age.

Conclusions: HC, ThC, and BMI are positively associated with total, lower-body, and abdominal SAT and SM but negatively associated with VAT after control for WC. However, only HC remained negatively associated with VAT after control for age and WC. *Am J Clin Nutr* 2007;85:1540–4.

KEY WORDS Body composition, magnetic resonance, obesity, skeletal muscle

INTRODUCTION

It is established that waist circumference (WC), hip circumference (HC), thigh circumference (ThC) and body mass index (BMI; in kg/m^2) show a positive association with morbidity (1–6) and mortality (7–11). However, after statistical control for WC, BMI and HC are negatively associated with mortality risk, whereas WC remains a positive predictor after control for BMI or HC (7, 8). It is reasoned that the health "protective" effect of a larger BMI, HC, or ThC for a given WC may be explained by a greater accumulation of subcutaneous adipose tissue (SAT), skeletal muscle (SM) in the lower body, or both (12). Indeed, Snijder et al (12, 13) report that, after control for abdominal AT, thigh AT is negatively associated with glucose intolerance and with dyslipidemia (13).

The mechanistic link that explains the attenuation in morbidity and mortality associated with elevations in lower-body adiposity when abdominal obesity is held constant is unclear. It is suggested that the increased capacity to buffer energy and store lipid in the gluteal-femoral subcutaneous adipocytes may protect against excess lipid deposition within tissues ectopic to subcutaneous fat such as the liver, muscle, and visceral AT (VAT) (14). Unlike gluteal-femoral subcutaneous adipocytes, excess lipid accumulation within these ectopic depots is clearly associated with deleterious metabolic consequences (9, 15–17). However, in addition to lower-body adipocytes, subcutaneous adipocytes in the abdomen can also act as a sink for excess energy consumption (18). Thus, a greater HC or ThC for a given WC may in fact represent a phenotype with elevations in both lower-body and abdominal SAT. If this is true, it would suggest that, consequent to greater amounts of abdominal SAT, persons with elevations in HC and ThC for a given WC would have lower VAT. Because VAT is an established marker of morbidity (19) and mortality (9), this notion would provide a plausible alternate mechanism by which elevations in HC and ThC for a given WC attenuate health risk.

In this study we examined the independent associations between WC, HC, ThC, and BMI with total, lower-body, and abdominal SAT and SM and with VAT. We tested the hypothesis that for a given WC, a larger HC, ThC, or BMI represents a phenotype with greater lower-body and abdominal SAT and, thus, reduced VAT.

SUBJECTS AND METHODS

Subjects

Subjects were healthy white men ($n = 113$) and women ($n = 143$) who participated in various body-composition or weight-loss

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TABLE 1
Subject characteristics[1]

	Men (n = 113)	Women (n = 143)
Age (y)	44.5 ± 9.1 (25.0–69.0)	41.2 ± 11.8[2] (19.0–79.0)
BMI (kg/m^2)	31.2 ± 3.5 (22.5–40.8)	30.9 ± 5.6 (18.7–47.8)
Waist circumference (cm)	106.7 ± 9.1 (83.8–127.0)	94.3 ± 13.0[2] (65.1–135.0)
Hip circumference (cm)	109.9 ± 7.0 (92.3–127.7)	113.7 ± 12.6[2] (87.4–156.0)
Thigh circumference (cm)	63.1 ± 5.3 (42.6–78.0)	65.5 ± 9.2[2] (37.5–90.5)
Total AT (kg)	31.4 ± 7.3 (15.8–53.8)	36.3 ± 12.5[2] (7.6–75.5)
Total SAT (kg)	24.0 ± 6.4 (11.8–45.3)	31.4 ± 10.9[2] (6.8–65.8)
Thigh SAT (kg)	4.8 ± 1.5 (2.0–9.7)	6.9 ± 2.4[2] (2.2–15.9)
Abdominal SAT (kg)	4.5 ± 1.5 (1.7–9.6)	5.5 ± 2.3[2] (0.9–13.5)
Abdominal SAT at L4–L5 (cm^2)	295 ± 97 (90–607)	375 ± 161[2] (43–946)
Visceral AT (kg)	3.5 ± 1.3 (0.9–8.3)	1.8 ± 1.0[2] (0.1–5.1)
Visceral AT at L4–L5 (cm^2)	170 ± 66 (33–482)	102 ± 53[2] (4–310)
Total skeletal muscle (kg)	33.9 ± 4.3 (22.0–43.5)	21.7 ± 3.5[2] (14.1–32.6)
Abdominal skeletal muscle (kg)	3.8 ± 0.5 (2.5–5.9)	2.5 ± 0.4[2] (1.6–3.9)
Thigh skeletal muscle (kg)	9.0 ± 1.3 (5.2–12.6)	5.8 ± 1.0[2] (3.6–8.9)

[1] All values are $\bar{x}$ ± SD; range in parentheses. AT, adipose tissue; SAT, subcutaneous adipose tissue.
[2] Significantly different from men, $P < 0.05$ (Student's t test).

studies at Queen's University (Kingston, Canada) (20–25). Subjects were not taking medications that are known to influence the primary outcome measures. All participants gave informed consent for their respective studies before participation in accordance with the ethical guidelines set by Queen's University.

Anthropometric measurements

Body mass was measured to the nearest 0.1 kg on a calibrated balance. Standing height was measured to the nearest 0.1 cm with the use of a wall-mounted stadiometer. WC was taken at the level of the last rib to the nearest 0.1 cm after a normal expiration. HC was taken at the maximum extension of the buttocks as viewed from the side. ThC was measured at the proximal right thigh directly below the gluteal fold.

Measurement of total and regional fat and muscle by magnetic resonance imaging

Whole-body (41–47 equidistant images) magnetic resonance imaging data were obtained with a General Electric (Waukesah, WI) 1.5 Tesla magnet with the use of an established protocol (21). The magnetic resonance imaging data were analyzed with a specially designed image analysis software (Tomovision Inc, Montreal, Canada) using an established protocol (21, 26).

Total AT and SM volumes were determined with the use of all 41–47 images. The image at 5 cm below L4–L5 (image 20 or 23) was used to divide the upper and lower body. VAT and abdominal SAT were calculated from the 5 images extending from 5 cm below to 15 cm above L4–L5. Thigh AT and SM were derived from the 7 images distal to the femoral head. AT and SM volumes (expressed in L) were converted to mass units (expressed in kg) with the use of assumed constant densities (0.92 and 1.04 kg/L, respectively) (27).

Statistical analyses

Pearson's correlation and multiple linear regression analyses were performed to determine the univariate and multivariate relations between WC, HC, ThC, and BMI with VAT and total AT, total lower-body, upper-body, abdominal, and thigh SAT and SM with and without control for age. All analyses were conducted within each sex separately because of the significant sex interactions with WC, HC, ThC, and BMI ($P < 0.05$). All independent variables were normally distributed. All models were undisturbed by multicollinearity with tolerance ≤ 0.20 and variance inflation factor ≤ 5 (28). All statistical procedures were performed with the use of SAS (version 9; SAS Institute, Cary, NC).

RESULTS

Subject characteristics are shown in **Table 1**. WC was positively correlated with BMI, HC, and ThC in both men and women (r = 0.47–0.89; data not shown). WC, BMI, HC, and ThC were positively associated with total AT and with total, lower body, abdominal, and thigh SAT and SM in both men and women (**Table 2**; $P < 0.001$). WC, BMI, and HC were positively associated with VAT in both men and women ($P < 0.001$). ThC was associated with VAT in women ($P < 0.001$) but not men ($P >$ 0.10).

The associations between BMI, HC, and ThC with the measures of total, lower-body, abdominal, and thigh AT and SM after control for WC are shown in **Table 3**. BMI, HC, and ThC were positively associated with total, lower-body, and abdominal SAT in both men and women before and after control for WC (**Figure 1**). Further, BMI, HC, and ThC remained positively associated with total, lower-body, and abdominal SM in men after control for WC. In women, BMI and ThC but not HC were positively associated with total, lower-body, and abdominal SM after control for WC. Control for age did not alter the significance of these observations.

After adjustment for WC, the association between BMI, HC, and ThC with VAT was inversed, such that BMI, HC, and ThC were negatively associated with VAT in both men and women (Table 3; Figure 1). HC ($P < 0.05$), but not BMI ($P > 0.10$) or ThC, (P = 0.06) remained a significant negative correlate of VAT after further control for age. Thus, for a given WC, persons with a higher BMI, HC, or ThC have greater quantities of SAT

TABLE 2
Unadjusted correlation coefficients for the association between waist circumference (WC), hip circumference (HC), thigh circumference (ThC), and BMI with total and regional body composition[1]

	Men				Women			
	WC	HC	ThC	BMI	WC	HC	ThC	BMI
Total AT	0.83	0.79	0.58	0.82	0.90	0.95	0.80	0.96
Visceral AT	0.65	0.29	−0.02[2]	0.43	0.77	0.58	0.38	0.64
Subcutaneous AT								
Total	0.71	0.80	0.64	0.78	0.87	0.95	0.82	0.95
Upper body	0.78	0.74	0.52	0.79	0.92	0.92	0.70	0.92
Lower body	0.54	0.75	0.71	0.66	0.70	0.88	0.85	0.86
Abdominal	0.66	0.75	0.59	0.76	0.85	0.91	0.72	0.90
Thigh	0.47	0.68	0.72	0.60	0.59	0.79	0.81	0.77
Skeletal muscle								
Total	0.43	0.50	0.59	0.56	0.62	0.58	0.62	0.63
Upper body	0.39	0.37	0.50	0.50	0.62	0.58	0.59	0.62
Lower body	0.42	0.57	0.62	0.57	0.59	0.55	0.61	0.60
Abdominal	0.48	0.49	0.50	0.61	0.60	0.59	0.60	0.64
Thigh	0.31	0.43	0.58	0.46	0.46	0.38	0.47	0.44

[1] AT, adipose tissue. All Pearson correlation coefficients are significant at $P < 0.001$ except where marked otherwise.
[2] $P > 0.10$.

and SM and less VAT within the abdomen than do persons with lower BMI, HC, or ThC.

DISCUSSION

The novel finding of this study was that BMI, HC, and ThC, for a given WC, were positively associated with lower-body and abdominal SAT and SM but were negatively associated with VAT independent of sex. The findings support the notion that the negative association commonly observed between BMI, HC, and ThC with morbidity and mortality after control for WC may be explained by an increased deposition of lower-body and abdominal SAT and SM, a decreased accumulation of VAT, or both.

In recent years numerous studies have shown that, after WC is controlled for, the strong positive association commonly observed between BMI and HC with morbidity (1–3, 5) and mortality (7, 8) is inversed. It is reasoned that the health protective effect of a larger BMI, HC, or ThC for a given WC may be explained by greater accumulation of SAT, SM, or both in the lower body (12). Through the clearance of circulating lipid, lower-body subcutaneous adipocytes could decrease metabolic risk by limiting excess lipid deposition within tissues ectopic to lower-body subcutaneous tissues such as the liver, muscle, and VAT, all of which are associated with increased health risk (14). Indeed, clinical examples of SAT excess (ie, multiple

TABLE 3
Partial correlation coefficients for the independent association between WC, HC, ThC, and BMI with total and regional body composition[1]

Dependent variable (y)	Men						Women					
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
	WC	BMI	WC	HC	WC	ThC	WC	BMI	WC	HC	WC	ThC
Total AT	0.45	0.41	0.63	0.49	0.76	0.38	0.36	0.78	0.52	0.79	0.82	0.64
Visceral AT	0.58	−0.27[2]	0.67	−0.35	0.73	−0.47[3]	0.58	−0.17[2]	0.65	−0.28	0.72	−0.23[3]
Subcutaneous AT												
Total	—	0.48	0.34	0.58	0.59	0.50	—	0.77	0.30	0.79	0.75	0.66
Upper body	0.33	0.42	0.54	0.40	0.70	0.27[2]	0.57	0.56	0.64	0.59	0.85	0.31
Lower body	—	0.45	—	0.62	0.32	0.61	−0.30	0.73	−0.22	0.74	0.33	0.37
Abdominal	—	0.50	0.30	0.51	0.53	0.43	0.22	0.61	0.31	0.65	0.70	0.42
Thigh	—	0.42	—	0.55	0.20	0.64	−0.35	0.68	−0.25	0.66	—	0.70
Skeletal muscle												
Total	—	0.41	—	0.33	0.19	0.49	—	0.23	0.26	—	0.37	0.37
Upper body	—	0.33	0.20[4]	—	—	0.40	0.20	0.17[2]	0.29	—	0.38	0.33
Lower body	—	0.43	—	0.44	—	0.53	0.17[4]	0.21	0.26	—	0.31	0.73
Abdominal	—	0.44	0.20[4]	0.25	0.25	0.34	—	0.29	0.19	0.19[3]	0.36	0.34
Thigh	—	0.39	—	0.35	—	0.52	—	—	0.25	—	0.25	0.44

[1] AT, adipose tissue. Listed partial Pearson correlation coefficients are mutually adjusted for the other variable in each model without control for age. Only significant partial correlation coefficients ($P < 0.05$) are listed. These associations remained significant after control for age ($P < 0.05$).
[2,3] Associations after control for age: $^2P > 0.10$, $^3P = 0.06$.
[4] Associations were only significant after control for age ($P < 0.05$).

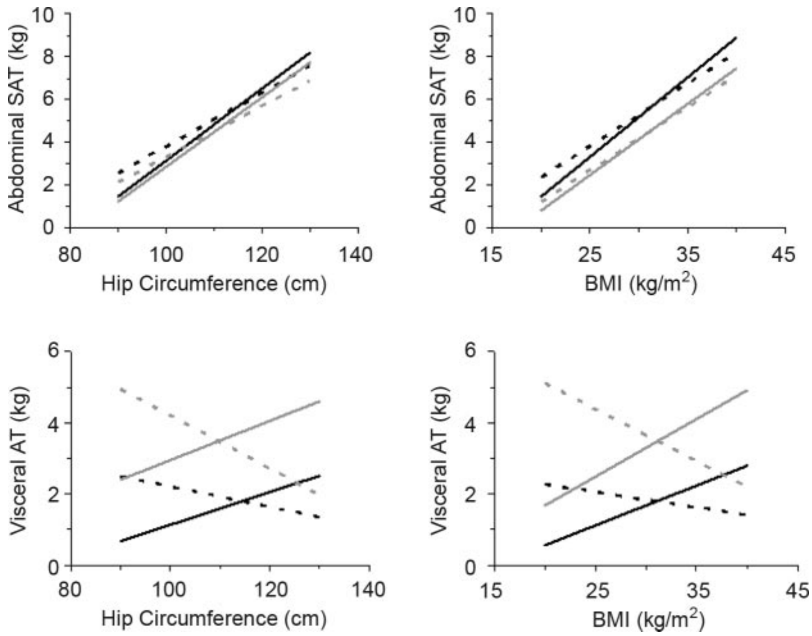

FIGURE 1. Associations of hip circumference and BMI with abdominal subcutaneous adipose tissue (SAT) and visceral AT before and after control for waist circumference in men and women. The associations were determined with the use of simple and multiple linear regressions in 114 men (gray lines) and 143 women (black lines) before (solid lines) and after (dotted lines) adjustment for waist circumference. All associations are significant at $P < 0.05$.

symmetric lipomatosis) are associated with minimal lipid accumulation in the liver, muscle, and VAT and a normal metabolic profile despite a frank obese state (29), whereas SAT deficiency (ie, lipodystrophy) is associated with fat storage in the liver and muscle and an insulin resistant state (30). Further, Snijder et al (12) report that after control for total abdominal AT, greater amounts of thigh AT are associated with improved glucose tolerance.

In this study we observed that when controlled for WC, larger BMI, HC, or ThC values represented a phenotype with elevations in both lower lower-body and abdominal SAT and, consequently, lower VAT values independent of sex. These observations extend those previously reported by Seidell et al (4) wherein HC was inversely associated with VAT after control for WC in men but not in women. Together, these findings suggest that the inverse association observed between BMI and HC with morbidity (1–3, 5) and mortality (7, 8) for a given WC may be mediated through the positive association with SAT and SM or through the negative association with VAT (14), itself a strong independent marker of morbidity (19) and mortality (9).

From a clinical perspective our findings underscore the notion that the simultaneous acquisition of BMI, HC, or ThC in combination with WC may inform the practitioner with respect to obesity phenotype. For example, in situations wherein adults have similar WC values, greater BMI, HC, or ThC values would indicate a greater accumulation of abdominal SAT and thus lower VAT, whereas lower values for BMI, HC, or ThC would represent a phenotype with lower abdominal SAT and, hence, greater VAT. In other words, when WC is held constant, these anthropometric measures act as surrogate markers of SAT deposition and thus inform the practitioner about the relative contribution of SAT and VAT to abdominal adiposity. Unfortunately, threshold values for BMI, HC, and ThC that may be used in conjunction with WC to identify obesity phenotype are unknown.

In this study we also observed that for a given WC, higher BMI, HC, and ThC values were associated with increases in lower-body and abdominal SM. It is possible that the inverse relations observed between BMI and rates of morbidity and mortality, when WC is controlled for, is at least partially explained by the associated increase in SM. This observation is consistent with the notion that the elevated mortality rates associated with low BMI values may be due to insufficient fat-free mass (31). However, Goodpaster et al (32) report that thigh SM is not associated with insulin sensitivity in a group of heterogeneous men and women.

Limitations of this study warrant mention. The study sample consisted of a relatively homogeneous group of sedentary, obese, middle-aged white men and women from the middle-to-upper class. This characteristic may limit the generalizability of the results of our study but should not affect the internal validity. Indeed, the homogeneity of our study group on demographics, socioeconomic factors, and lifestyle characteristics is a benefit because it reduces the likelihood of confounding by these factors. Further, most studies reporting an inverse association between BMI or HC with morbidity or mortality were conducted in older populations with greater ranges of data than reported in this study. Because we show a similar association with VAT, SAT, and SM in our relatively homogeneous younger sample of obese men and women, this association reinforces the importance and strength of our findings. However, the degree to which these multivariate associations are true in leaner or older cohorts is unknown.

In conclusion, our findings show that when obtained in conjunction with WC, elevations in BMI, HC, and ThC describe a phenotype that is characterized by corresponding increases in total and abdominal SAT and SM and decreases in VAT. These findings extend the original hypothesis that the health protective effect of a larger BMI, HC, or ThC for a given WC may be explained by a greater accumulation of SAT, SM, or both in the lower body. Accordingly, the findings set the stage for further study designed to distinguish whether it is the increase in SAT and SM, the decrease in VAT, or both that explains the attenuation in morbidity and mortality observed with increasing BMI, HC, and ThC when WC is held constant.

The author's responsibilities were as follows—JLK and PMJ: data analysis; JLK, PMJ, and RR: interpretation of results and writing of the manuscript. None of the authors declared any conflicts of interest.

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