Body Composition and Age in African-American and Caucasian Women: Relationship to Plasma Leptin Levels

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Leptin is a recently isolated peptide hormone released from adipocytes that has been postulated to play a role in appetite regulation and energy metabolism. Aging affects both food intake and body composition. Body composition is also affected by ethnicity. We have evaluated the relationships between serum leptin levels, age, body composition (by dual-energy x-ray absorptiometry), and hormonal parameters in a cross-sectional study of 94 women, 53 African-American (AAF) and 41 Caucasian (CF). Our hypotheses were as follows: (1) changes in body composition would be related to age in a sinusoidal pattern, (2) changes in serum leptin would parallel changes in body fat, (3) serum leptin levels would be influenced by body fat distribution, and (4) serum leptin would be related to serum concentrations of sex hormones. Serum leptin paralleled changes in body fat and body mass index (BMI) with age. In the entire group, serum leptin correlated closely with measures of body fat, including BMI and total fat mass, and there was no difference in leptin levels between the two ethnic groups. In simple regression analysis, serum leptin was related to both serum estradiol and testosterone. The relationship between serum leptin and trunk fat was linear in both groups, but significantly different in AAF and CF ($P = .014$). Serum leptin was associated with the trunk to lower-extremity fat ratio in CF ($r = .67$, $P = .001$) but not in AAF. Body fat was increased with advancing age until about 65 years and then declined. Measures of lean body mass declined linearly with age in the entire group, as well as both subgroups. In the entire group, total lean body mass and lean body mass corrected for BMI (lean body mass/BMI) were inversely related to age. In subjects aged less than 60 years AAF were stronger ($P < .05$) and had both a larger BMI and fat mass ($P < .05$) than CF. However, the patterns of age-related changes in fat body mass, lean body mass, and BMI were similar in both groups. In the entire group, multiple regression analysis indicated that the age, free thyroxine index (FTI), and leptin concentration were predictors of the body composition and distribution of trunk to lower-body fat. These observations indicate that there is a sinusoidal relationship between body fat and age, with a decline in body fat in extreme old age in both AAF and CF, and that serum leptin concentrations are more closely related to body fat and BMI than to age or ethnicity.

FOOD INTAKE has been reported to decrease with age.[1] This age-related decrease in appetite is associated with a concomitant decrease in dietary intake. Despite this, the body mass index (BMI) and percent body fat have been reported to increase in middle age and in young-old individuals.[2-11] A peptide hormone, leptin, has been isolated from adipose tissue,[12] and studies in genetically obese (ob/ob) mice suggest that this hormone may play a role in appetite regulation and energy metabolism.[13,14] In humans, serum leptin levels may increase in direct proportion to body fat mass.[14-16]

The effect of age-related changes in body composition may be considerable. In particular, decreased lean body mass and strength potentially diminish everyday functional abilities. Protective responses (for example, the righting response after a slip) may also be compromised. Ethnicity also appears to play a role in determining body composition. In African-American women (AAF), both adipose and lean body mass have been reported to be greater than in Caucasian women (CF).[17] There is a paucity of data on body composition in those over the age of 70 years of either ethnicity. In addition, only a few studies have examined the potential effects of alterations in hormonal status on body composition and strength over the life span, and the relationship of serum leptin to these parameters has not been examined. We have previously reported that body fat increases in middle age in CF and that a decline in body fat occurs after age 85.[18] In this latter study,[18] body fat was quantified using biochemical impedance, which may lack precision.

We have now examined the potential role of serum leptin in age- and ethnicity-related changes in appetite and body composition in a cohort of CF and AAF over a broad age spectrum. Body composition was quantified using dual-energy x-ray absorptiometry. The primary aims of the study were to examine the relationships between age, changes in body composition, plasma steroid hormone levels, and leptin concentrations in AAF and CF. The broad hypotheses to be addressed were as follows: (1) changes in body composition would be related to age in a sinusoidal pattern, (2) changes in serum leptin with age and changes in body fat with age would be in parallel, (3) serum leptin levels would be influenced by body fat distribution, and (4) serum leptin levels would be related to serum concentrations of sex hormones.

SUBJECTS AND METHODS

Patients

The study group was a convenience sample of community-dwelling healthy women between the ages of 18 and 89 years. Nonfasting venous blood samples were obtained between 8 and 9 AM. The remainder of the evaluation was then completed. Demographic characteristics of this population and the factors modulating bone density have been described in detail elsewhere.[19] Race was assigned according to the patient's characterization of herself as either AAF or non-Hispanic CF. No woman had been confined to complete bedrest for 3 months or longer at any time. Details of current and past medications were sought. Individuals taking systemic glucocorticoids and postmenopausal women

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receiving sex hormone replacement were excluded. Two subjects had non–insulin-dependent diabetes mellitus for more than 1 year. For some analyses, the population was divided into AAF and CF and into three age groups: less than 40, 41 to 70, and 71 to 87 years.

Body Composition

The BMI was calculated as weight (in kilograms) divided by height (in meters) squared. Body composition was determined by dual-energy x-ray absorptiometry (model DPX; Lunar Radiation, Madison, WI). The coefficient of variation (defined as the standard deviation divided by the mean and then expressed as a percent) determined in duplicate measurements in 10 individuals 1 week apart was 1.6% for total body lean mass and 1.9% for total body fat mass. Besides total fat and lean body mass, trunk fat and lower body fat were also measured. The fat fraction was calculated as the total body fat mass divided by the sum of the total lean body mass plus total body fat mass. The ratio of fat to lean mass was calculated by dividing total fat mass by total lean mass. The ratio of fat mass to BMI (fat/BMI) and lean mass to BMI (lean/BMI) was calculated by dividing the total fat mass or total lean mass (respectively) by BMI. The ratio of trunk fat to lower-extremity fat was calculated by dividing the truncal fat mass by the lower-extremity fat mass.

Biochemical Measurements

Serum leptin was determined using a commercially available radioimmunoassay kit (Linco Research, St. Charles, MO). The antibody used in this kit was raised against highly purified human leptin. In our laboratory, it has an intraassay coefficient of variation of 4.7%. All samples were measured in a single assay. The serum testosterone level was measured as previously described,[20,21] with interassay and intraassay coefficients of variation of 4.7% and 5.8%, respectively. The serum estradiol level was measured with an extraction radioimmunoassay from Pantex (Santa Monica, CA), which has an intraassay coefficient of variation of 4.7% and an interassay coefficient of variation of 8.5%. The serum free-thyroxine index (FTI) was measured in a commercial laboratory (Metrolab, St. Louis, MO).

Strength

Grip strength was measured using a Jaymar dynamometer (J.A. Preston, Jackson, MS) as previously described.[21] The mean of three force measurements (in kilograms) was used to assess grip strength. The coefficient of variation for this test was determined in 11 elderly subjects to be 5.7%.

Statistical Analysis

Data are expressed as the mean ± SEM. Statistical analyses were performed using a commercially available statistics package, after obtaining professional statistical advice (Statistica; Statsoft, Tulsa, OK). The following statistics were used where appropriate: simple regression analysis, ANOVA, multiple regression analysis, and Tukey's t test. Results of post hoc testing are only reported when ANOVA yielded a statistically significant value with P less than .05. In addition, a general fitting procedure was used to estimate the "goodness of fit" of a nonlinear function, as well as the best estimate of the constants of that function, using the statistical package according to the manufacturer's instructions. Linear regression is a specific application (using a linear function) of this general procedure. In the general procedure, linearity of the regression function is not necessarily specified. We used a cosinor function and minimized the residual variance (sum of squared residuals) around the regression line using the Quasi-Newton method. The methodology generates the best least-square estimation for the cosinor function using the experimental data and a systematic stepwise substitution for the unknown constants in the specified function. For multiple regression analysis, data were transformed using the cosinor function and constants derived as already described. A P value less than .05 was considered significant in all analyses.

RESULTS

To document the changes associated with age in women, we first analyzed all of the data together. We then performed a subgroup analysis in AAF and CF to evaluate potential differences related to ethnicity. Age and total body fat were not linearly related in the entire group or in AAF, but were linearly related in CF (r = .37, P = .02). Nonlinear analysis for the entire group (r = .35, P = .0007; Fig 1A), AAF (r = .42,

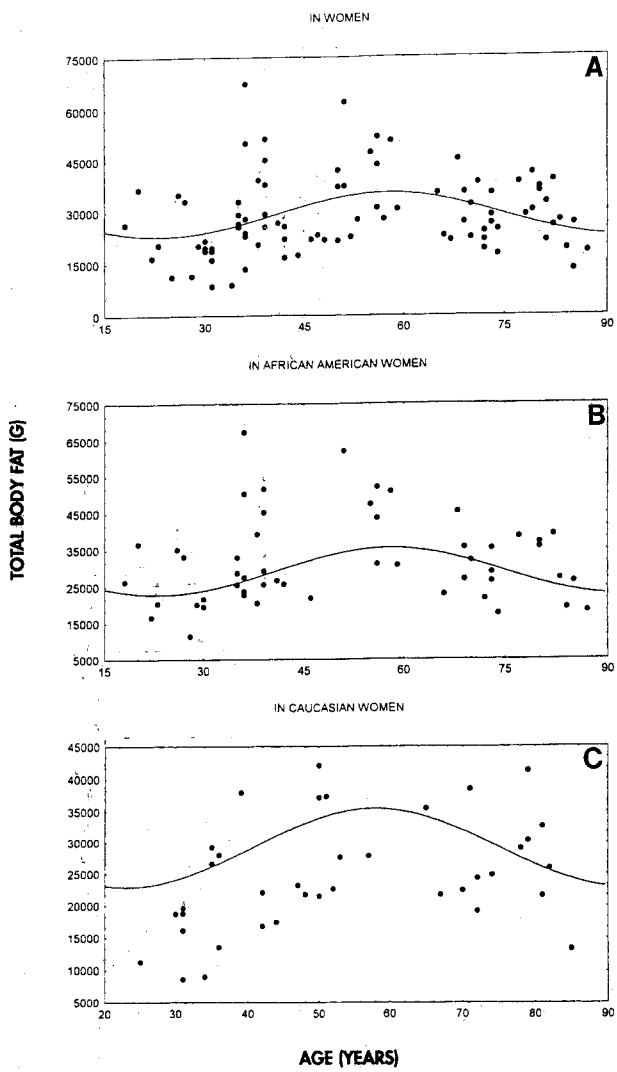

Fig 1. Age versus total body fat in the entire group (A), AAF (B), and CF (C). For A, the correlation coefficient for the linear regression is r = .12 (NS), and for the nonlinear regression line shown, r = .35 (P = .0007). For B, the correlation coefficient for the linear regression is r = .05 (NS), and for the nonlinear regression line shown, r = .42 (P = .002). For C, the correlation coefficient for the linear regression is r = .37 (P = .02), and for the nonlinear regression line shown, r = .46 (P = .002).

$P = .002$; Fig 1B), and CF ($r = .46$, $P = .004$; Fig 1C) demonstrated a significant relationship between fat mass and age. BMI was not linearly related to age in either the whole group or AAF, but there was a significant relationship between age and BMI in CF ($r = .37$, $P = .02$). Using nonlinear analysis, a significant relationship between BMI and age was evident in the entire group ($r = .27$, $P < .05$), AAF ($r = .44$, $P = .001$), and CF ($r = 0.40$, $P = .02$).

Serum leptin concentrations were linearly related to BMI in the entire group ($r = .83$, $P < .0001$), as well as in AAF ($r = .79$, $P < .001$) and CF ($r = .84$, $P < .001$). Serum leptin concentrations were also linearly related to total fat mass in the entire group and in AAF ($r = .87$, $P < .001$) and CF ($r = .93$, $P < .001$). However, serum leptin levels were nonlinearly related to age ($r = .28$, $P = .03$; Fig 2), with a pattern similar to that found for both BMI and total body fat (Fig 1).

Clearly, fat and muscle mass are affected by stature, training, and age, as well as other factors. In an attempt to correct for differences in fat and muscle mass potentially related to height, physical activity, or other factors, we corrected the measures of body composition for BMI (fat/BMI and lean/BMI) or the fat mass for lean mass (fat to lean ratio). We then examined the relationships between age and total fat mass to BMI, and the fraction of mass that was fat, the fat to lean ratio, fat distribution, and total lean mass to BMI. These indices were not linearly related to age. Nonlinear analysis generated a significant relationship between fat mass per BMI and age in the entire group ($r = .40$, $P = .0001$; Fig 3A), AAF ($r = .36$, $P = .009$; Fig 3B), and CF ($r = .54$, $P = .0005$; Fig 3C). A similar cosinor analysis of the relationship between the fraction of mass that was fat and age showed significant correlations in the entire group ($r = .40$, $P = .0001$), AAF ($r = .34$, $P = .01$), and CF ($r = .54$, $P = .001$). The fat to lean ratio was also similarly significantly related to age in the entire group ($r = .39$, $P = .0002$), AAF ($r = .38$, $P = .006$), and CF ($r = .58$, $P = .001$). Fat distribution as assessed by the ratio of trunk fat to lower-extremity fat was linearly related to age in the entire group ($r = .36$, $P = .001$), AAF ($r = .27$, $P = .05$), and CF ($r = .50$, $P = .001$).

Total lean body mass and age were inversely related in the entire group ($r = .28$, $P = .008$) and CF ($r = -.38$, $P = .017$), but were not significantly related in AAF ($r = .23$, $P = .10$). Similarly, lean body mass per BMI was inversely related in the entire group ($r = -.37$, $P = .0005$) and CF ($r = -.65$, $P < .0005$), but were not significantly related in AAF ($r = -.23$, $P = .11$). As might be expected, a practical measure of lean body mass, mean grip strength in the dominant hand, was linearly related to age in the entire group ($r = -.46$, $P = .0005$), AAF ($r = -.37$, $P = .01$), and CF ($r = -.52$, $P = .003$).

Table 1 examines the effect of ethnicity on body composition. The BMI was greater ($P < .05$) in AAF than in CF up to 71 years of age. Total fat, fat/BMI, and mean dominant grip strength were greater ($P < .05$) in young AAF compared with young CF. Total lean mass was not significantly different between AAF and CF, although at all ages the mean values were greater in AAF. In the oldest versus youngest CF, significant ($P < .05$) declines in strength and the ratio of lean mass to BMI and an increase in trunk to lower-extremity fat were evident (Table 1).

As already noted, the relationship between serum leptin and both total body fat and BMI (Figs 2 and 3) was similar in both AAF and CF. Serum leptin also correlated with regional measures of fat in both AAF and CF. The correlations were similar for both lower- and upper-extremity fat in the two groups (data not shown). However, correlations between leptin and trunk fat were significantly different in AAF and CF (Fig 4). In addition, the relationship between leptin and trunk to lower-extremity fat was significant in CF ($r = .67$, $P = .001$) but not in AAF ($r = .05$, NS; Fig 5).

On simple regression analysis, significant correlations were evident (data not shown) for testosterone and estradiol with BMI, in addition to that noted with leptin, in the whole group. Serum leptin correlated with testosterone ($r = .257$, $P = .047$) and estradiol ($r = .268$, $P = .038$).

For the entire group, multiple regression techniques showed that age (either transformed with the nonlinear function or not), leptin, and FTI were independent predictors for measures of body composition. For AAF, hormonal measurements, primarily the FTI and leptin, were the most consistent independent predictors of body composition. For CF, age and these hormonal

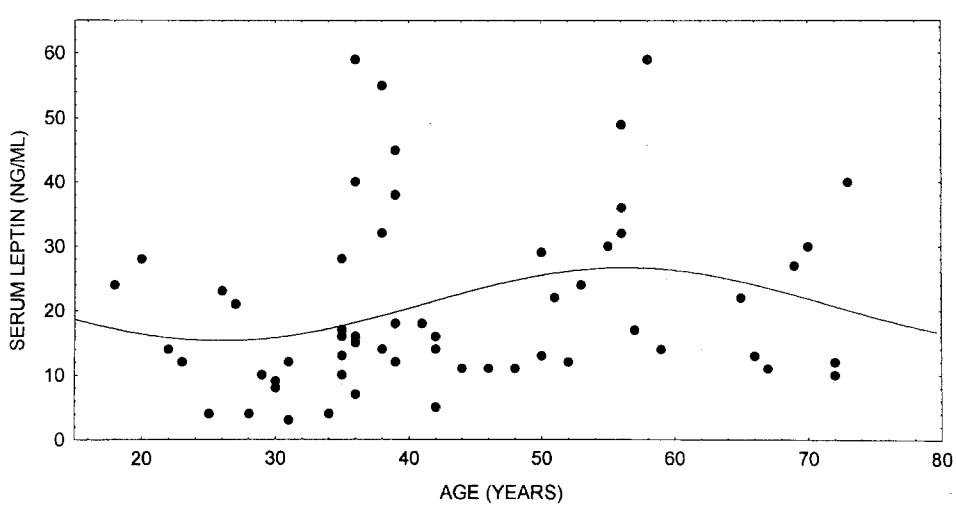

Fig 2. Serum leptin versus age in the entire group. The correlation coefficient for the nonlinear analysis is $r = .281$ ($P = .03$).

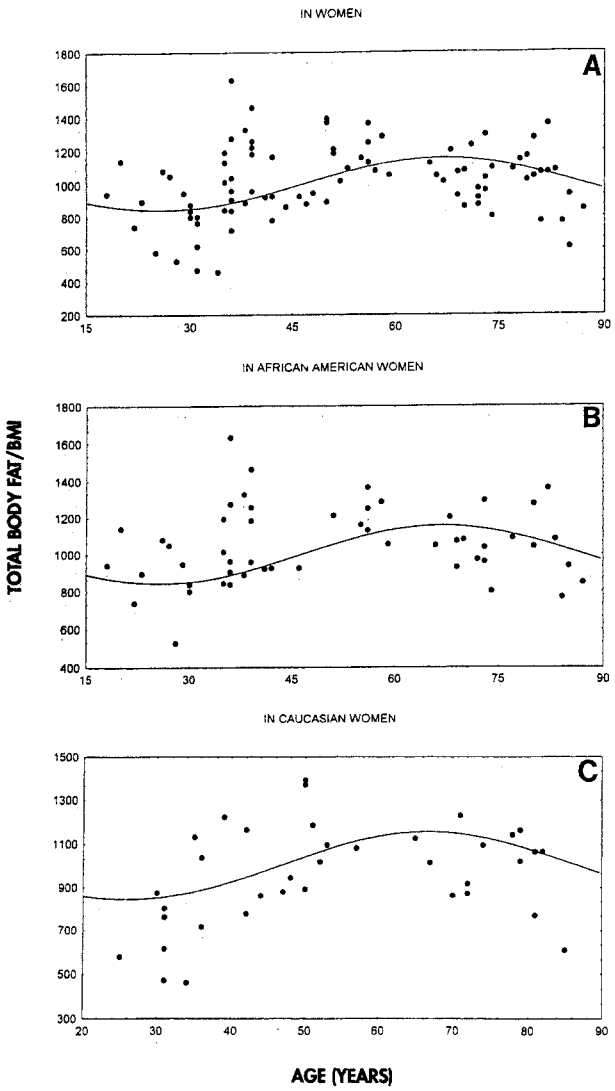

Fig 3. Age versus total fat per BMI in the entire group (A), AAF (B), and CF (C). For A, the correlation coefficient for the linear regression is $r = .18$ (NS), and for the nonlinear regression line shown, $r = .40$ ($P = .0001$). For B, the correlation coefficient for the linear regression is $r = .12$ (NS), and for the nonlinear regression line shown, $r = .36$ ($P = .009$). For C, the correlation coefficient for the linear regression is $r = .30$ (NS), and for the nonlinear correlation, $r = .54$ ($P = .0005$).

measures were consistent in dependent predictors of body composition (Table 2).

Multiple regression analyses for leptin were overwhelmed by the correlation with fat mass or a proxy (BMI, fat BMI, or fat fraction), so only single regressions were significant.

DISCUSSION

This study demonstrated that in the entire group all measures of body fat have a nonlinear relationship to age, with an increase in middle age and a decrease in old age as hypothesized.[18] As expected, a linear decline in lean body mass with aging was also evident in the entire group. Correcting lean body mass (linearly related to age) for BMI (nonlinearly related to age) demonstrated a significant linear relationship between age and lean body mass. The observed decrease in grip strength with age is consistent with this reduction in lean body mass. This decrease in strength is consistent with a decrease in function with age.[22,23]

These studies confirm the previous findings of Silver et al[18] and are similar to those of Cohn et al,[24] who found a peak in percent body fat between 50 and 60 years of age and then a subsequent decline. However, in the latter study, no correction was made for BMI. Steen et al[25] reported a decline in body fat in a longitudinal study of persons between 70 and 80 years of age. A similar decrease in body fat has been demonstrated by Rico et al[26] in women aged 65 to 80 years.

Despite the nonlinear relationship of age to measures of fat mass, the distribution of fat was linearly related to age in the entire group, so the ratio of trunk fat to lower-body fat increased linearly with aging. This is compatible with the age-related increase in the waist to hip ratio in women.[27] Our study showed a similar increase in truncal fat with advancing age in both AAF and CF.

Leptin is a protein product of adipose cells.[12] In this study, we found a highly significant relationship between serum leptin levels and total body fat or BMI (Fig 2), as previously reported.[14-16] However, there are other studies that suggest a curvilinear (exponential) relationship between leptin and fat.[28,29] In our study, the relationship between body fat and leptin appears almost perfect for the entire group, as well as for CF and AAF considered as separate groups. In a separate analysis, we noted that a curvilinear (exponential) relationship was a statistically significant descriptor of the data (data not shown). The relationship was not as good as the linear description. Interestingly, we found a difference in the relationship between trunk fat and leptin in the two groups (Figs 5 and 6). The difference we observed may potentially be accounted for by differing rates of production of leptin from different fat depots, as previously reported.[30] In turn, this finding confirms our third hypothesis. However, a previous report has suggested some variance in the measurement of fat distribution by dual-energy techniques.[31] In the absence of data suggesting a systematic difference in dual-energy measurements of truncal fat in AAF versus CF, we believe our results demonstrate differences in leptin production related to ethnicity. However, we acknowledge the potential limitation in this finding.

In simple regression analysis, two hormones were correlated with leptin, namely testosterone and estradiol. Higher plasma leptin levels have been previously reported to occur in females,[32] although hormone replacement therapy in older women has been reported not to alter serum leptin concentrations.[28]

Age (transformed or not) was clearly a consistent factor in predicting body composition. There was no apparent dissociation of serum leptin and body fat with age. In this case, if leptin regulates appetite, there is no evidence that alterations in serum leptin with age cause the decreased fat mass we observed in the elderly. In addition, serum leptin and the FTI were also consistent independent predictors of various measures of body composition. A higher FTI appeared to be predictive of abdominal obesity. Testosterone was also an important independent predictor of abdominal obesity and of lean BMI. A number of studies have shown a relationship between testosterone and

Table 1. Comparison of Body Composition Measures at Different Ages in AAF and CF

Parameter	Age Group (yr)					
	≤40		41-71		72-87	
	AAF	CF	AAF	CF	AAF	CF
No. of subjects	25	12	15	16	13	13
BMI (kg/m²)	28.9 ± 1.1*	23.4 ± 1.1	32.9 ± 1.9*	25.4 ± 1.0	27.4 ± 1.2	26.3 ± 1.2
Total fat (g)	30,571 ± 2,619*	19,812 ± 2,611	37,062 ± 3,175	27,271 ± 2,040	28,718 ± 2,186	26,284 ± 2,440
Fat/BMI	1,030 ± 50†	818 ± 76	1,105 ± 36	1,058 ± 46	1,037 ± 51	1,336 ± 37
Fat fraction	0.404 ± 0.017	0.325 ± 0.030	0.455 ± 0.019	0.413 ± 0.019	0.427 ± 0.020	0.419 ± 0.017
Ratio of trunk to lower-extremity fat	0.95 ± .04	0.84 ± .07‡	1.10 ± .06	0.94 ± .05	1.05 ± .06	1.14 ± .08
Lean/BMI	1,522 ± 59	1,694 ± 73‡	1,345 ± 68	1,519 ± 67	1,398 ± 63	1,336 ± 38
Total lean (g)	42,855 ± 1,401	38,808 ± 1,110	42,762 ± 1,619	37,703 ± 900	37,616 ± 1,110	35,273 ± 1,337
Dominant mean (kg)	31.5 ± 1.0*	29.4 ± 1.4‡	29.8 ± 1.5	27.3 ± 1.0	24.0 ± 1.9	22.4 ± 1.7

*$P < .05$ *v* CF of same age group.
†$P = .05$ *v* CF of same age group.
‡$P < .05$ *v* oldest age group of same ethnicity.

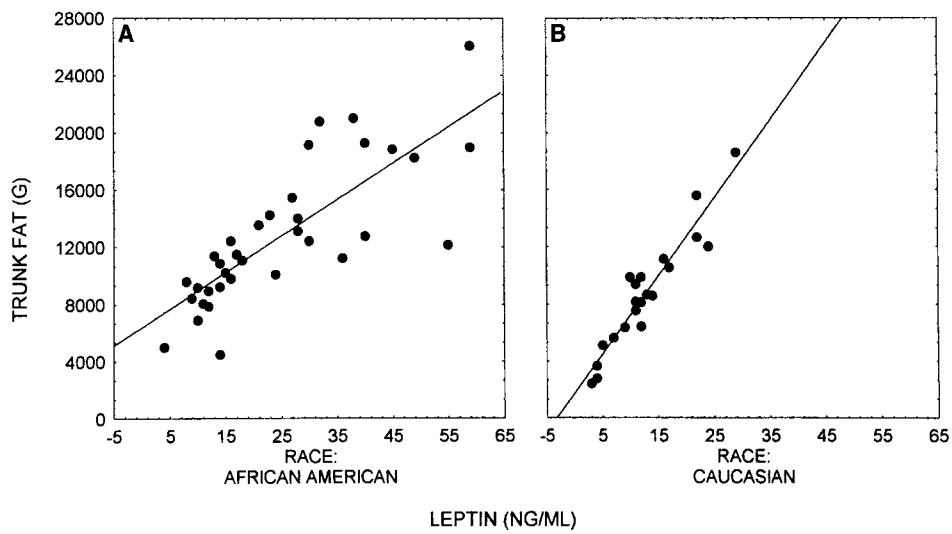

Fig 4. Serum leptin versus trunk fat mass in AAF (A) and CF (B). For A, the correlation coefficient is $r = .81$, and for B, $r = .95$. These were statistically significantly different ($P = .014$).

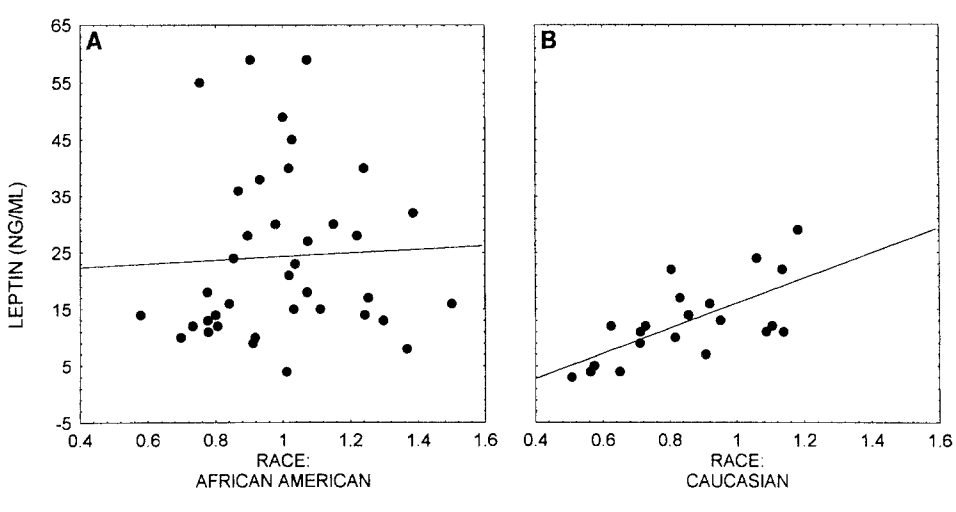

Fig 5. Ratio of trunk to lower-extremity fat versus leptin in AAF (A) and CF (B). For A, the correlation coefficient is $r = .67$ ($P = .001$).

Table 2. Multiple Regression Analysis for Measures of Body Composition in the Whole Group and AAF and CF Subgroups

	Age	Age Cos	T	FTI	Leptin
Whole group					
BMI (r = .849)					
β			−.13		.84
P			.08		.000
Fat BMI (r = .845)					
β		−.21		.15	.75
P		.010		.050	.000
Fat fraction (r = .854)					
β	.21			.24	.75
P	.008			.002	.000
Trunk/low fat (r = .649)					
β	−.58		−.47	.28	
P	.000		.000	.01	
Lean/BMI (r = .760)					
β	−.29		−.27	.32	−.49
P	.007		.012	.001	.000
AAF					
BMI (single regression only)					
Fat BMI (r = .874)					
β				.29	.80
P				.001	.000
Fat fraction (r = .885)					
β				.37	.77
P				.000	.000
Trunk/low fat (r = .538)					
β	−.52		−.40	.27	
P	.001		.01	.07	
Lean/BMI (r = .693)					
β				−.44	−.51
P				.002	.000
CF					
BMI (r = .920)					
β	.28			.42	.79
P	.35			.001	.000
Fat BMI (single regression only)					
Fat fraction (r = .968)					
β	.30		−.16	.30	.84
P	.004		−.48	.001	.000
Trunk/low fat (single regression only)					
Lean/BMI (r = .932)					
β	−.64	−.34		.54	−.75
P	.000	.041		.000	.000

Abbreviations: Age Cos, the age of the individual transposed by the same nonlinear function used to calculate BMI; T, testosterone; fat BMI, total body fat per BMI; fat fraction, total body fat divided by the sum of total body lean and fat mass; trunk/low fat, trunk fat divided by lower-extremity fat; lean BMI, total body lean mass divided by BMI.

visceral fat accumulation.[33-37] Our study found that increasing levels of total testosterone predicted a greater truncal fat and more lean body mass.

This study provides further information regarding the association of body fat and BMI across the life span in both CF and AAF. Leptin levels were demonstrated to be more strongly correlated with body fat or BMI than with age or ethnicity. This relationship argues that changes in leptin levels are not associated with decreased fat mass in very old women. Finally, we have demonstrated a significant difference between the relationship of leptin to trunk fat in AAF and CF.

REFERENCES

1. Morley JE: Nutrition and the older female. J Am Coll Nutr 12:337-343, 1993
2. Allen TH, Anderson EC, Langham WH: Total body potassium and gross body composition in relation to age. J Gerontol 15:348-357, 1960
3. Forbes GB, Hursh JB: Age and sex trends in lean body mass calculated from ^{40}K measurements: With a note on the theoretical basis for the procedure. Ann NY Acad Sci 110:225-263, 1963
4. Meneely GR, Heyssel RM, Ball COT, et al: Analysis of factors affecting body composition determined from potassium content in 915 normal subjects. Ann NY Acad Sci 110:271-281, 1963
5. Flynn MA, Nolph GB, Baker AS, et al: Total body potassium in aging humans: A longitudinal study. Am J Clin Nutr 50:713-717, 1989
6. Blanehard J, Conrad KA, Harrison GG: Comparison of methods for estimating body composition in young and elderly women. J Gerontol 45:B119-B124, 1990
7. Durnin JV, Womersley J: Body fat assessed from total body density and its estimation from skinfold thicknesses: Measurements on 481 men and women aged 16 to 72 years. Br J Nutr 32:77-97, 1974
8. Novak LP: Aging, total body potassium, fat-free mass and cell mass in males and females between ages 18 and 85 years. J Gerontol 27:438-443, 1972
9. Mazariegos M, Wang ZM, Gallagher D, et al: Differences between young and old females in the five levels of body composition and their relevance to the two-compartment chemical model. J Gerontol 49:M201-M208, 1994
10. Young CM, Blondin J, Tensuar R, et al: Body composition of "older" women. JAMA 43:344-348, 1963
11. Najjar MF, Rowland M: Anthropometric reference data and prevalence of overweight. Vital Health Stat 11, 238:1-73, 1987
12. Zhang Y, Proenca R, Maffei M, et al: Positional cloning of the mouse obese gene and its human homologue. Nature 372:425-432, 1994
13. Halaas JL, Gajiwala KS, Maffei M, et al: Weight reducing effects of the plasma protein encoded by the obese gene. Science 269:543-546, 1995
14. Considine RV, Sinha MK, Heiman ML, et al: Studies of circulating leptin by radioimmunoassay in humans with and without obesity. N Engl J Med 334:292-295, 1996
15. Maffei M, Halaas J, Ravussen E, et al: Leptin levels in human and rodent. Measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nat Med 1:1155-1161, 1995
16. McGregor GP, Desaga JF, Ehlenz K, et al: Radioimmunological measurement of leptin in plasma of obese and diabetic human subjects. Endocrinology 137:1501-1504, 1996
17. Kleerekoper M, Nelson DA, Peterson EL, et al: Body composition and gonadal steroids in older white and black women. J Clin Endocrinol Metab 79:775-779, 1994
18. Silver AJ, Guillen CP, Kahl MJ, et al: Effect of aging on body fat. J Am Geriatr Soc 41:211-213, 1995
19. Perry HM III, Horowitz M, Morley JE, et al: Aging and bone metabolism in African American and Caucasian women. J Clin Endocrinol Metab 81:1108-1117, 1996
20. Kaiser FE, Viosca SP, Morley JE, et al: Impotence and aging: Clinical and hormonal factors. J Am Geriatr Soc 36:511-519, 1988
21. Morley JE, Perry HM, Kaiser FE, et al: Effects of testosterone replacement therapy in old hypogonadal males: A preliminary study. J Am Geriatr Soc 41:149-152, 1993
22. LaCroix AZ: Determinants of Health—Exercise and Activities of

Daily Living in Health Statistics on Older Persons, United States, 1986. Vital Health Statistics, series 3, no. 25, DHHS, 1986, pp 1387-1409

23. Brocklehurst JC, Exton-Smith AN, Lempert Barber SM, et al: Fracture of the femur in old age. A two-centre study of associated clinical factors and the cause of the fall. Age Ageing 7:2-15, 1978

24. Cohn SH, Ellis KJ, Vartsky D, et al: Comparison of methods of estimating body fat in normal subjects and cancer patients. Am J Clin Nutr 34:2839-2847, 1981

25. Steen B, Lundgren RK, Jackson B: Body composition at age 70, 75, 79 and 81: A longitudinal population study, in Chandra RK (ed): Nutrition, Immunity and Illness in the Elderly. New York, NY, Pergamon, 1985, pp 49-58

26. Rico H, Revilla M, Villa LF, et al: Four-compartment models of body composition of normal elderly women. Age Ageing 22:265-268, 1993

27. Shimokata H, Tobin JD, Muller DC, et al: Studies in the distribution of body fat: I. Effects of age, sex and obesity. J Gerontol 44:M66-M73, 1989

28. Kohrt WM, Landt M, Birge SJ Jr: Serum leptin levels are reduced in response to exercise training, but not hormone replacement therapy, in older women. J Clin Endocrinol Metab 81:3980-3985, 1996

29. Weigle DS, Ganter SL, Kuijper JL, et al: Effect of regional fat distribution and Prader-Willi syndrome on plasma leptin levels. J Clin Endocrinol Metab 82:566-570, 1997

30. Masuzaki H, Ogaway, Isse N, et al: Human obese gene expression. Adipocyte-specific expression and regional differences in the adipose tissue. Diabetes 44:855-858, 1995

31. Snead DB, Birge SJ, Kohrt WM: Age-related differences in body composition by hydrodensitometry and dual-energy x-ray absorptiometry. J Appl Physiol 74:770-775, 1993

32. Rosenbaum M, Nicolson M, Hirsch J, et al: Effects of gender, body composition, and menopause on plasma concentrations of leptin. J Clin Endocrinol Metab 81:3424-3427, 1996

33. Kaye SA, Folsom AR, Soler JT, et al: Associations of body mass and fat distribution with sex hormone concentrations in postmenopausal women. Int J Epidemiol 20:151-156, 1991

34. Evans DJ, Hoffman RG, Kalkhoff RK, et al: Relationship of androgenic activity to body fat topography, fat cell morphology, and metabolic aberrations in premenopausal women. J Clin Endocrinol Metab 57:304-310, 1983

35. Kirschner MA, Samojlik E, Drejka M, et al: Androgen-estrogen metabolism in women with upper body versus lower body obesity. J Clin Endocrinol Metab 70:473-479, 1990

36. Hauner H, Ditschuneit HH, Pal SB, et al: Fat distribution, endocrine and metabolic profile in obese women with and without hirsutism. Metabolism 37:281-286, 1988

37. Goodman-Gruen D, Barrett-Connor FB: Total but not bioavailable testosterone is a predictor of central adiposity in postmenopausal women. Int J Obes 19:293-298, 1995