Weight loss and body-composition changes in men and women infected with HIV[1–3]

Janet E Forrester, Donna Spiegelman, Eric Tchetgen, Tamsin A Knox, and Sherwood L Gorbach

ABSTRACT

Background: The nature of body-composition changes in HIV-associated weight loss is unclear.

Objective: We examined the relation between the initial percentage of body fat and the composition of weight loss in men and women with HIV infection.

Design: HIV-positive adults were seen at semiannual clinic visits, at which time weight, fat, and fat-free mass were determined. The unit of analysis was the person-interval.

Results: Five hundred fifty-one persons contributed 2266 intervals of data, of which 311 (14%) were intervals in which weight loss was ≥5% of initial (start of interval) weight. Of these, 208 (67%) intervals met the criteria for analysis (123 from men and 85 from women). Loss of fat-free mass was dependent on the initial percentage of body fat in the men with < 32% body fat. A plot of the initial percentage of body fat compared with loss of fat-free mass (kg) suggested a nonlinear relation over the range of body fat examined. There was no clear relation between the initial percentage of body fat and loss of fat-free mass in the women.

Conclusions: In men with HIV-associated weight loss, the weight lost as fat-free mass depends on the initial percentage of body fat at low levels of body fat but appears to be independent of initial percentage of body fat at high levels of body fat. In women with HIV-associated weight loss who have normal-to-high body fat stores, loss of fat-free mass is independent of the initial percentage of body fat. *Am J Clin Nutr* 2002;76:1428–34.

KEY WORDS HIV infection, body composition, fat-free mass, percentage of body fat, bioelectrical impedance analysis, nutritional assessment, men, women

INTRODUCTION

The causes of weight loss in HIV infection are unknown and controversial. Early in the AIDS epidemic, Kotler et al (1) found in a cross-sectional study that homosexual men with advanced AIDS had a greater relative depletion of body cell mass (the intracellular component of lean body mass) than of fat mass when compared with healthy homosexual men. Women in the same study had a greater relative depletion of fat than of body cell mass when compared with healthy control subjects. It was postulated that wasting in men with HIV infection is a cachectic process in which weight loss is disproportionately a loss of lean body mass, with relative conservation of fat (1–3) and that AIDS wasting in men differs from simple starvation because of metabolic disturbances that prevent nitrogen sparing (2). Thus, fat loss was deemed a poor marker of AIDS wasting (1–3). However, later studies were contradictory: some found that weight loss was mainly loss of lean body mass (4, 5); others found principally fat loss or a loss of both fat and lean mass (6–9). Mulligan et al (10), in a longitudinal study of weight loss in 32 men with HIV, showed that those with initial body fat < 15% lost more lean mass than did those with > 15% body fat. These investigators concluded that, as in healthy men (11–13), the loss of lean body mass in men with HIV is dependent on the percentage of body fat before the weight loss. Here, using longitudinal data from a cohort of men and women with HIV infection, we set out to examine the relation between initial body fat stores and subsequent changes in body composition during periods of weight loss. We believe that this is the first reported longitudinal study addressing this question in women with HIV.

SUBJECTS AND METHODS

Study design

The Nutrition for Healthy Living Study, initiated in February 1995, is a prospective study that aims to determine the role of nutritional status in the progression of HIV infection. The subjects were HIV-positive adults. Those persons fulfilling any of the following criteria were excluded: diagnosed diabetes mellitus, thyroid disease, or malignancies (other than HIV-associated malignancies); pregnant at recruitment; and inadequate English language fluency. The subjects were seen at 1 of 3 sites: the New England Medical Center or the Fenway Community Health Center, in Boston, or the Miriam Hospital in Providence, RI, for semiannual clinic visits. Measurements of weight, body composition, and medical history,

[1] From the Department of Family Medicine and Community Health, Tufts University School of Medicine, Boston (JEF, ET, and SLG); the Departments of Epidemiology and Biostatistics, Harvard School of Public Health, Boston (DS); and the Department of Medicine, New England Medical Center, Boston (TAK).

[2] Supported by National Institute of Diabetes and Digestive and Kidney Diseases grant DK4 5734-07 and National Institute on Drug Abuse grant DA 11598. The General Clinical Research Center of the New England Medical Center, Boston, is supported by the Division of Research Resources of the NIH, grant no. MO1-RR00054.

[3] Address reprint requests to JE Forrester, Department of Family Medicine and Community Health, Tufts University School of Medicine, 136 Harrison Avenue (Stearns 203A), Boston, MA 02111. E-mail: janet.forrester@tufts.edu.

Received May 31, 2001.

Accepted for publication January 30, 2002.

TABLE 1
Initial percentage of body fat and weight lost as fat or fat-free mass (FFM) after ≥5% weight loss in the men

	Overall	Quartile of initial percentage of body fat: 1	2	3	4	P for trend
Person-intervals	123	30	31	31	31	
Initial body fat (%)	27 (21, 31)[1]	17 (15, 19)	25 (22, 25)	28 (27, 30)	34 (32, 37)	
Change in weight (kg)	−5.5 (−7.9, −4.5)	−4.8 (−5.8, −4.2)	−5.4 (−7.5, −4.5)	−5.3 (−8.5, −4.5)	−7.5 (−8.7, −5.5)	<0.01
Change in FFM (kg)	−1.8 (−4.2, 0.62)	−2.6 (−5.5, −1.7)	−2.0 (−3.9, −0.5)	−0.5 (−3.3, 2.3)	−0.8 (−4.0, 1.1)	<0.01
Change in fat (kg)	−4.1 (−12.2, −1.8)	−2.0 (−4.1, 0.19)	−3.7 (−5.9, −1.5)	−5.7 (−8.8, −3.0)	−5.8 (−8.5, −3.5)	<0.001
Weight lost as FFM (%)	31	57	35	8	12	

[1] Median; 25th and 75th percentiles in parentheses.

including medications, were taken at each visit. The subjects gave their written, informed consent. Confidentiality of records was preserved according to regulations stipulated by human studies review committees at each participating institution. The protocol was approved by institutional review boards at each site.

Data collection

Body composition was determined by bioelectrical impedance analysis (BIA) after the subjects fasted for 5 h, following the manufacturer's recommended procedures (RJL Systems Inc, Clinton, MI). The equations of Lukaski (14) were used to derive measures of fat-free mass (FFM; principally lean body mass, including bone). BIA measures of FFM determined by using the equation of Lukaski agreed well with FFM measured by dual-energy X-ray absorptiometry in a substudy of 71 male subjects (r = 0.91). Because estimates of FFM by BIA can be influenced by hydration, the subjects were advised not to exercise or drink alcohol during the 48 h before the visit. The subjects were examined for edema, and their data were excluded from the analyses if edema was present at the time of the BIA measures. We used the data from the baseline and all available follow-up visits to create person-intervals (the unit of analysis), where an interval was defined as the time between any 2 successive visits. For example, a subject with a baseline and 2 follow-up visits contributed 2 person-intervals to the analyses. Thus, only persons who had at least one follow-up visit were included. We focused on the person-intervals in which ≥5% of initial (start of interval) weight was lost over the interval. Because we were interested in the changes in fat and FFM that occur in persons with HIV who lose weight in the absence of deliberate efforts to change body composition, we excluded the persons-intervals in which the subject reported doing strength-building exercises, such as lifting weights. We also excluded person-intervals during which the subject reported taking medications such as anabolic steroids, human growth hormone, or megesterol acetate and person-intervals following the use of those medications. We examined the changes in body composition in each interval of weight loss in relation to the initial (start of interval) percentage of body fat in 2 ways. First, we compared the median change in FFM or fat (expressed in kg) and median percentage of weight lost as FFM in relation to the quartile of initial percentage of body fat. For each quartile of initial percentage of body fat, we calculated the percentage of weight lost as FFM by expressing the change in FFM as a proportion of the sum of change in FFM and fat mass as measured by BIA. Second, we examined the shape of the relation (linear compared with nonlinear) between change in fat or FFM and initial percentage of body fat treated as a continuous variable. We were unable to examine the percentage of weight lost as FFM as a function of initial percentage of body fat in our data because some individuals did not lose FFM and some even gained FFM over the interval of weight loss. Thus, percentage of weight lost as FFM was undefined for these persons. This limitation did not apply to the data in **Tables 1** and **2** because the reported proportion of weight lost as FFM was based on the overall and group-specific median change in weight and FFM. Because change in FFM depends on the weight lost, we adjusted for the weight lost (kg) in the regression analyses. In our final analysis, we divided the intervals into 2 groups: *1*) those in which the subject had lost predominantly FFM and *2*) those in which the subject had lost predominantly fat. We then compared the distribution of pre-weight-loss percentage of body fat between the groups.

Statistical analyses

We expressed the results in Table 1 as medians (25th and 75th percentiles) because the outcome data were skewed in some quartiles. Tests for trend across the quartiles of body fat were done by regressing the change in FFM or fat on the quartile (coded 1–4). We used the technique of restricted cubic splines to assess the

TABLE 2
Initial percentage of body fat and weight lost as fat or fat-free mass (FFM) after ≥5% weight loss in the women

	Overall	Quartile of initial percentage of body fat: 1	2	3	4	P for trend
Person-intervals	85	21	21	21	22	
Initial body fat (%)	38 (34, 43)[1]	31 (28, 32)	36 (35, 36)	40 (39, 42)	46 (45, 49)	
Change in weight (kg)	−5.5 (−7.6, −4.2)	−4.0 (−5.2, −3.4)	−5.3 (−8.1, −4.1)	−5.6 (−7.4, −4.6)	−6.6 (−9.3, −5.5)	<0.05
Change in FFM (kg)	−1.9 (−3.9, −0.7)	−1.3 (−3.9, 0.04)	−2.5 (−3.7, −1.0)	−1.8 (−2.3, −1.3)	−1.8 (−4.5, −0.2)	0.70
Change in fat (kg)	−4.1 (−6.3, −1.8)	−2.7 (−4.8, −1.3)	−4.1 (−6.3, −1.4)	−4.1 (−6.9, −2.3)	−5.8 (−8.0, −3.3)	0.06
Weight lost as FFM (%)	32	33	38	31	24	

[1] Median; 25th and 75th percentiles in parentheses.

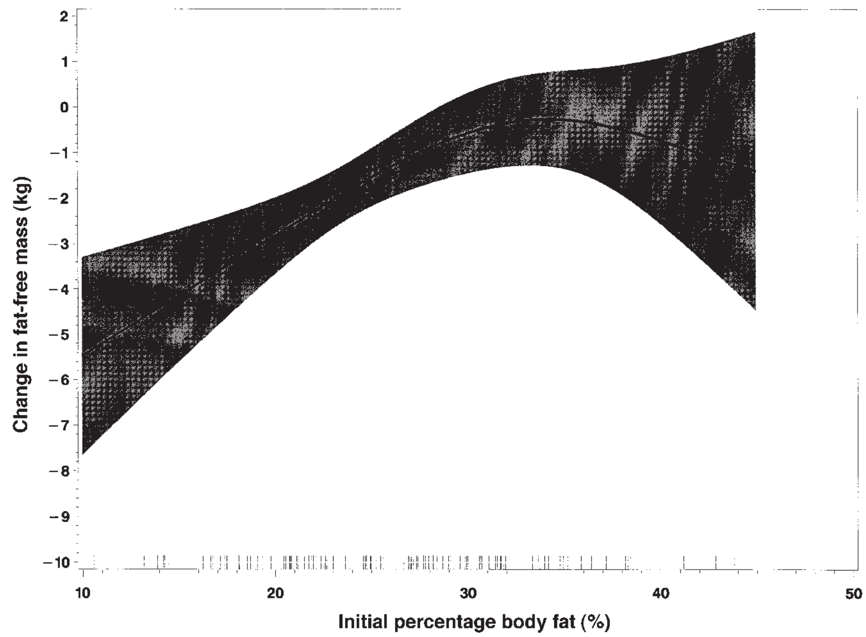

FIGURE 1. Change in fat-free mass in relation to the initial percentage of body fat in the men. The ticks along the *x* axis indicate the initial percentage of body fat of each observation. The shaded region is the CI for the spline.

evidence for possible nonlinear associations between the initial percentage of body fat and change in FFM in the interval (15). Analyses were done in the MIXED procedure of SAS version 8.0 (SAS Institute, Cary, NC). All inferences were conducted by using the empirical SE to account for within-person correlation (16). This allows valid statistical inferences to be made on data that come from more than one observation per person. Separate analyses were performed for men and women. Alpha (two-tailed) was set at 5%.

RESULTS

The Nutrition for Healthy Living Study had 678 subjects enrolled as of 17 August 17 1999. One hundred twenty-seven subjects died, withdrew, or were lost to follow-up before the first follow-up visit. Thus, 551 subjects came to the first follow-up visit and contributed at least one person-interval of observation. The median number of follow-up visits of enrolled subjects was 4 (minimum = 1, maximum = 11). There were 2267 intervals of follow-up among the 678 study subjects.

Of the 2267 person-intervals available for analysis, 363 (16%) were person-intervals in which ≥5% of preinterval body weight had been gained during the interval, and 311 (14%) were person-intervals in which ≥5% of preinterval body weight had been lost during the interval. The remaining 1593 (70%) intervals were those during which weight at the end of the interval was within 5% of the weight at the start of the interval. The median length of the intervals was 6.5 mo (25th percentile, 6.0; 75th percentile, 7.9)

Of the 311 intervals in which ≥5% of weight had been lost (intervals for 204 males and 107 females), the distribution of intervals of weight loss per person was the following: 180 persons had 1 interval of ≥5% weight loss, 47 persons had 2 intervals of ≥5% weight loss, 11 persons had 3 intervals of ≥5% weight loss, and 1 person had 4 intervals of ≥5% weight loss.

We excluded from the analyses 35 intervals in which the subject reported current or past use of anabolic steroids, megesterol acetate, or human growth hormone. Data on strength-building exercises were available at baseline for 614 of the 678 subjects enrolled in the study. At baseline, 133 of 435 (31%) men and 19 of 179 (11%) women reported doing strength-building exercises. This corresponded to 42 of the 276 (15%) remaining intervals. These intervals were also excluded from further analyses. Body-composition data were missing for 26 of the intervals. Thus, there were 208 intervals available for analyses. Of the 123 intervals from men, 74 (60%) were from white men, 34 (28%) were from African American men, and 15 (12%) were from men of other races. Of the 85 intervals from women, 33 (39%) were from white women, 42 (49%) were from African American women, and 10 (12%) were from women of other races. The mean age in the intervals contributed by men was 43 y, and the mean age in the intervals contributed by women was 41 y.

The median change in weight, FFM, and fat and the median percentage of weight lost as FFM overall and in each quartile of initial percentage of body fat are presented in Tables 1 (men) and 2 (women). Among the men there was a trend to greater loss of weight ($P < 0.01$), FFM ($P < 0.01$), and fat ($P < 0.001$) with lower initial percentage of body fat. The men in the highest 3 quartiles of percentage of body fat lost predominantly fat, and the men in the lowest quartile of body fat lost predominantly FFM. Among the women, weight loss was predominantly loss of fat in all 4 quartiles of percentage of body fat. In addition, there was no relation between initial percentage of body fat and the change in FFM over the quartiles of percentage of body fat in the women ($P = 0.7$).

When we looked at the change in kilograms of FFM as a function of initial percentage of body fat, with initial percentage of body fat treated as a continuous variable (**Figure 1**), we found a linear relation below 32% body fat in the men ($P < 0.001$). Above 32% initial body fat, the slope of the relation leveled off, suggesting that the change in FFM was not dependent on initial percentage of body fat above 32% body fat. The test for this nonlinear (compared with linear) component of the relation was of borderline significance

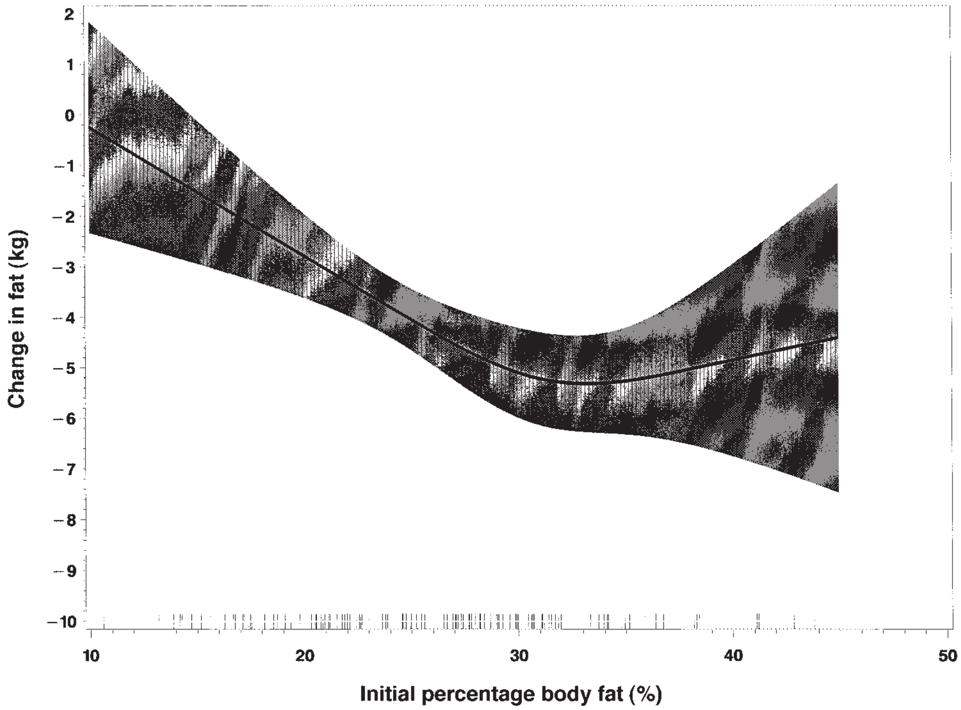

FIGURE 2. Change in fat in relation to the initial percentage of body fat in the men. The ticks along the *x* axis indicate the initial percentage of body fat of each observation. The shaded region is the CI for the spline.

($P = 0.07$). The relation of change in fat mass to initial percentage of body fat also appeared to be curvilinear, with an inflection point at ≈32% body fat (**Figure 2**). Below 32% initial body fat the amount of fat lost increased with increasing fat stores ($P < 0.001$), but above 32% initial percentage of body fat, the change in fat leveled off such that the change in fat mass appeared to be independent of fat stores. As in the case of FFM, the nonlinear component of the relation was of borderline significance ($P = 0.07$).

Among the women (**Figures 3** and **4**), the shape of the relation between initial percentage of body fat and change in FFM or fat

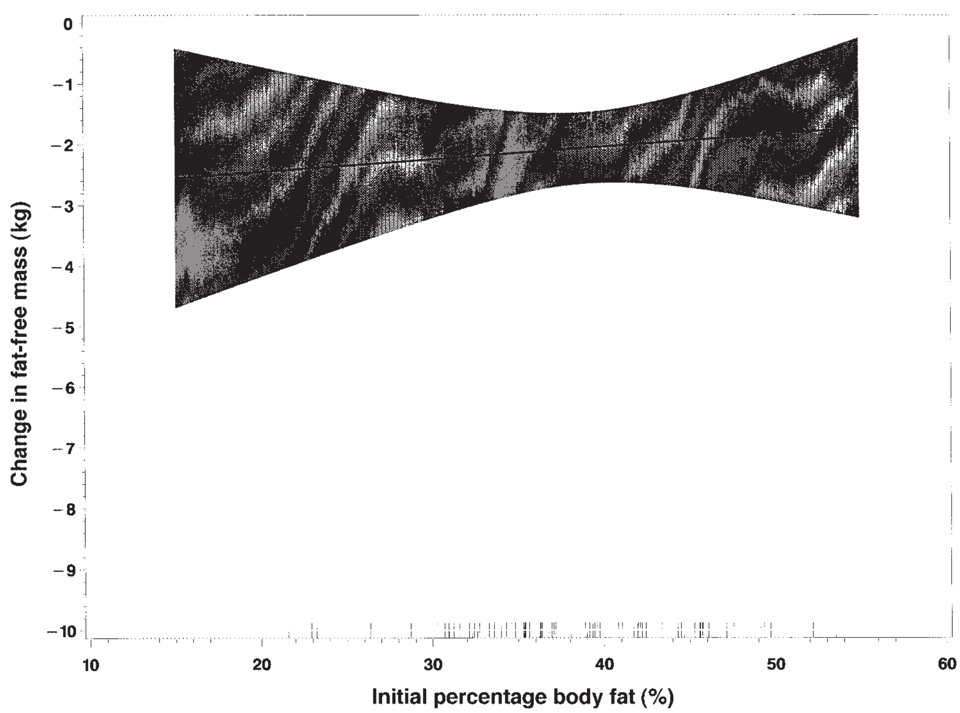

FIGURE 3. Change in fat-free mass in relation to the initial percentage of body fat in the women. The ticks along the *x* axis indicate the initial percentage of body fat of each observation. The shaded region is the CI for the spline.

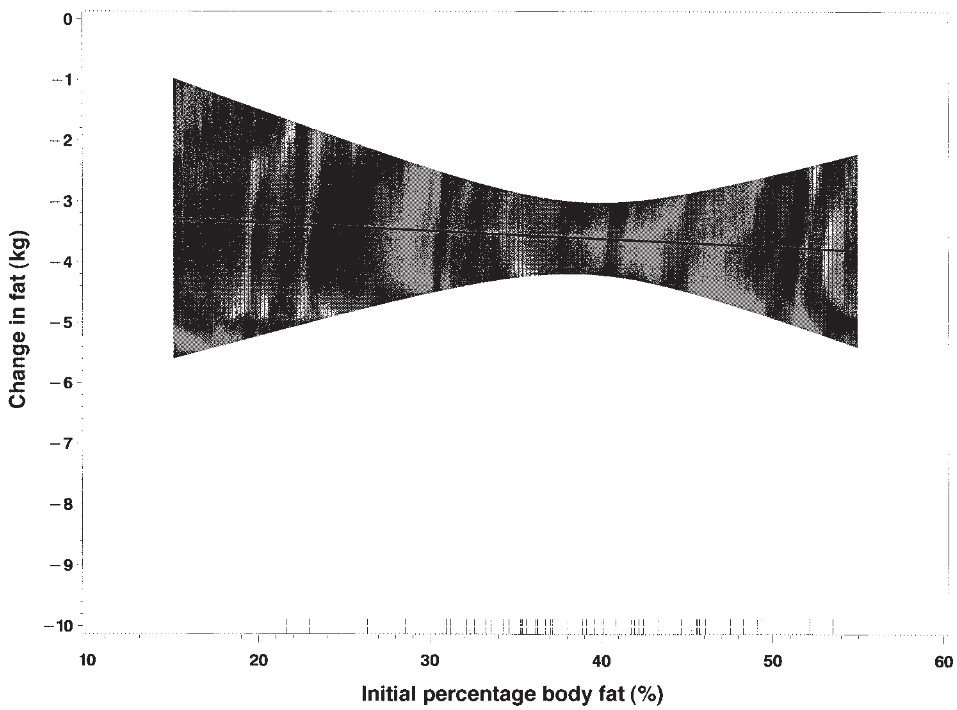

FIGURE 4. Change in fat in relation to the initial percentage of body fat in the women. The ticks along the *x* axis indicate the initial percentage of body fat of each observation. The shaded region is the CI for the spline.

mass over the range of body fat percentage examined (21.6–53.5%) showed no evidence of a linear ($P = 0.80$) or nonlinear relation between initial percentage of body fat and change in FFM. Thus, the change in FFM and fat appeared to be independent of fat stores.

Further multivariate analyses indicated that the relation between initial percentage of body fat and change in FFM in the men and women did not differ by race (African American compared with other), nor did it differ between those taking and those not taking highly active antiretroviral therapies.

Of the 123 intervals of weight loss among the men and the 85 intervals of weight loss among the women, 45 (37%) and 27 (32%), respectively, were intervals in which the weight lost was predominantly FFM. The distribution of initial percentage of body fat in intervals in which the weight loss was predominantly fat compared with intervals in which the loss was predominantly FFM in men and women, respectively, is shown in **Figures 5** and **6**. As expected, the intervals from men in which weight loss was predominantly fat mass had a higher average initial percentage of body fat than did the intervals in which weight loss was

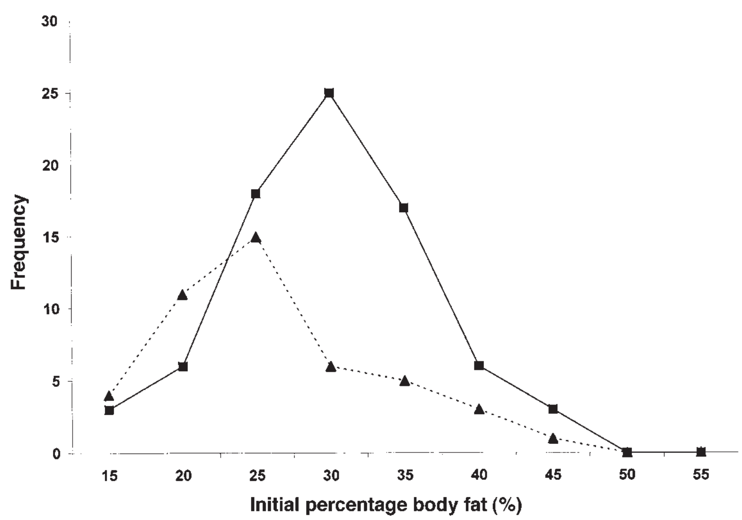

FIGURE 5. Distribution of the initial percentage of body fat in the men in intervals in which the weight loss was predominantly fat (■) compared with intervals in which the loss was predominantly fat-free mass (▲).

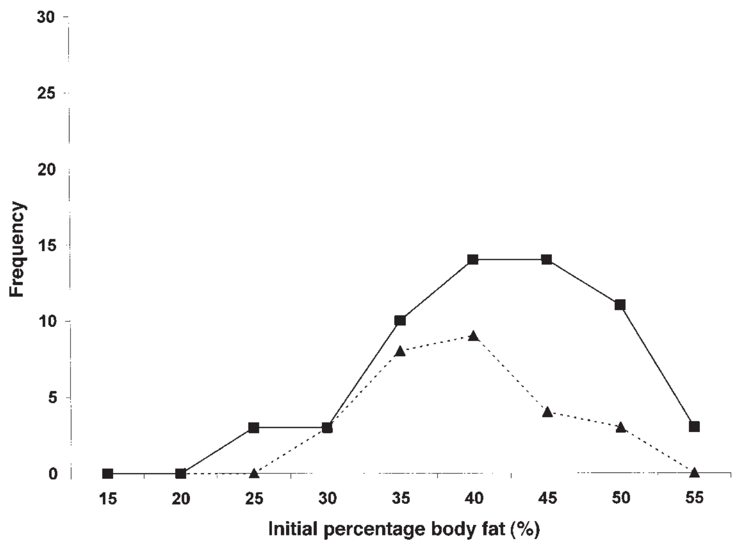

FIGURE 6. Distribution of the initial percentage of body fat in the women in intervals in which the weight loss was predominantly fat (■) compared with intervals in which the loss was predominantly fat-free mass (▲).

predominantly FFM (3.9%; SE 1.0, $P = 0.02$). However, the data in Figure 5 show that among the intervals in which weight loss was predominantly loss of FFM, there was a great deal of variability in the initial percentage of body fat, from a low of 11% to a high of 41%. Among the intervals from women in which weight loss was predominantly FFM, the distribution of initial percentage of body fat varied from 26% to 49%. As with the men, among the women there was a great deal of overlap in initial percentage of body fat between the groups. In the women, the test of the between-group difference in the average initial percentage of body fat was of borderline significance (2.7% in those women who lost predominantly fat; SE 1.2, $P = 0.08$).

DISCUSSION

Our aim was to examine the relation between the initial percentage of body fat and the change in FFM during intervals of weight loss in men and women infected with HIV. Only the men in the lowest quartile of initial body fat lost predominantly FFM; those in the 3 highest quartiles lost predominantly fat. These results agree with the results of a study by Mulligan et al (10) in HIV-infected men. Among the women, weight loss was, on average, predominantly fat in all quartiles of initial body fat.

In men, the relation of initial percentage of body fat to change in FFM appears to be nonlinear over the range of percentage of body fat examined. The shape of the curve suggests that the loss of lean body mass may be dependent on the initial percentage of body fat when the initial percentage of body fat is < 32% but independent of the initial percentage of body fat when it is > 32%. However, the borderline significance of the test for nonlinearity does not rule out a linear relation between the initial percentage of body fat and change in FFM in the men. In women, the loss of FFM appears not to depend on the initial percentage of body fat. Because most of the women in this study had body fat levels > 32%, our power to detect a relation between initial percentage of body fat and change in FFM at lower levels of body fat was limited. Thus, we cannot conclude decisively that loss of FFM in women is independent of the initial percentage of body fat over all levels of initial percentage of body fat.

The small number of women with a percentage of body fat in the lower ranges also limited our ability to examine differences between men and women. Thus, it is not clear whether the relation between initial percentage of body fat and subsequent loss of FFM mass is similar or differs between HIV-infected men and women who have the same initial percentage of body fat. Apparent differences between men and women in body-composition changes following weight loss may be caused by the higher average amounts of body fat in women in general. However, cross-sectional data from previous studies of HIV-infected women with low amounts of body fat suggest that the composition of weight loss in HIV-infected women may be fundamentally different from that found in men. The women in these studies had average body fat percentages varying from 11.7% to 38%. Differences in body composition from healthy control subjects were predominantly differences in fat, even among the women with a very low percentage of body fat (1, 8, 17).

Our observations in persons with HIV infection do not differ substantially from observations of body-composition changes in persons without HIV infection. Underfeeding experiments of healthy men and women showed a curvilinear relation between the pre-weight-loss body fat and the fraction of weight lost as FFM (12, 13), with relatively little loss of lean mass at high body fat stores. Among the obese women whose initial percentage of body fat varied from 35% to 48% and who were consuming very-low-energy diets, Donnelly et al (18) found no significant relation between pre-weight-loss body fat and loss of lean mass. These women lost predominantly fat. Young, anorexic women also showed a predominance of fat loss (19–21), implying sex-specific differences in the composition of weight loss in persons without HIV.

The averages discussed thus far do not describe the high degree of individual variability found in the data. Although most men and women with a high initial percentage of body fat lost predominantly fat, some individuals with a relatively high initial percentage of body fat lost predominantly FFM. In addition to fat stores, there may be other important factors that determine the relative loss of fat compared with FFM in HIV-infected persons. A high degree of variability in the initial percentage of body fat at which weight loss is predominantly lean mass has also been observed in healthy males (13), so these factors may include some that are not attributable to HIV infection. Previously reported determinants of the fraction of weight lost as lean mass in healthy adults include the severity of negative energy balance (11, 12) and the ratio of protein to energy in the diet (11).

A weakness of the present study is our inability to describe these data in relation to the presence of the fat redistribution syndrome in the study subjects. There is, as yet, no consensus on the defining characteristics of the syndrome, whether the syndrome is a consequence of antiretroviral therapy, or even its prevalence among persons with HIV. A recent study, which used patient self-report or physician report of changes in body-fat distribution, found an 18-mo cumulative incidence of 17% among HIV patients taking highly active antiretroviral therapy for the first time (22). In our study, one-half of the subjects were receiving highly active antiretroviral therapy over the period examined. However, the syndrome has been reported in persons who have never taken any form of antiretroviral therapy. There may be some persons in our study who lost fat but did not lose lean body mass as a consequence of lipodystrophy. This may have contributed to variability in the data. Because we found no evidence that the relation between the initial percentage of body fat and subsequent change in FFM differed between those taking and not taking highly active antiretroviral therapy therapy, we believe that the results of this study are, in the main, generalizable to persons who have HIV-associated weight loss.

Studies of the causes and prevention of HIV-related wasting are still of importance, especially to populations that do not have ready access to antiretroviral therapies. More studies are needed to examine the relation of the initial percentage of body fat and the subsequent loss of FFM in women with HIV. These studies should include adequate numbers of women with a low initial percentage of body fat. In addition, there is a need to identify other factors that influence the relative loss of lean body mass. Such information will help in the design of interventions to preserve lean mass in the presence of chronic diseases such as HIV infection.

We thank the participants of the study for their time and enthusiasm. Thanks to the research team for their diligence.

REFERENCES

1. Kotler DP, Wang J, Pierson RN. Body composition studies in patients with the acquired immunodeficiency syndrome. Am J Clin Nutr 1985;42:1255–65.
2. Grunfeld C, Feingold KR. Metabolic disturbances and wasting in the acquired immunodeficiency syndrome. N Engl J Med 1992;327:329–37.
3. Babameto G, Kotler DP. Malnutrition in HIV infection. Gastroenterol Clin North Am 1997;26:393–415.
4. Ott M, Lambke B, Fischer H, et al. Early changes of body composition in human immunodeficiency virus-infected patients: tetrapolar body impedance analysis indicates significant malnutrition. Am J Clin Nutr 1993;57:15–9.
5. Paton NIJ, Macallan DC, Jebb SA, et al. Longitudinal changes in body composition measured with a variety of methods in patients with AIDS. J Acquir Immune Defic Syndr 1997;14:119–27.
6. Schwenk A, Hoffer-Belitz E, Jung B, et al. Resting energy expenditure, weight loss and altered body composition in HIV infection. Nutrition 1996;12:595–601.
7. Sharkey SJ, Sharkey KA, Sutherland, LR, et al. Nutritional status and food intake in human immunodeficiency virus infection. J Acquir Immune Defic Syndr 1992;5:1091–8.
8. Grinspoon S, Corcoran C, Miller K, et al. Body composition and endocrine function in women with aquired immunodeficiency syndrome wasting. J Clin Endocrinol Metab 1997;82:1332–7.
9. Forrester JE, Spiegelman D, Woods M, et al. Weight and body composition in a cohort of HIV-positive men and women. Public Health Nutr 2001;4:743–7.
10. Mulligan K, Tai VW, Schamblean M. Cross-sectional and longitudinal evaluation of body composition in men with HIV. J Acquir Immune Defic Syndr 1997;15:43–8.
11. Durrant ML, Garrow JS, Royston P, et al. Factors influencing the composition of the weight lost by obese patients on a reducing diet. Br J Nutr 1980;44:275–85.
12. Forbes GB. Lean body mass-body fat interrelationships in humans. Nutr Rev 1987;45:225–31.
13. Dulloo AG, Jacquet J, Girardier L. Autoregulation of body composition during weight recovery in humans: the Minnesota experiment revisited. Int J Obes Relat Metab Disord 1996;20:393–405.
14. Lukaski HC. Use of bioelectrical impedance analysis to assess human body composition: a review. In: Livingston GE, ed. Nutritional status assessment of the individual. Trunbull, CT: Food & Nutrition Press, Inc, 1989:189–204.
15. Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med 1989;8:551–61.
16. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13–22.
17. Kotler DP, Thea DM, Heo M, et al. Relative influences of sex, race, environment, and HIV infection on body composition in adults. Am J Clin Nutr 1999;69:432–9.
18. Donnelly JE, Jacobsen DJ, Whatley JE. Influence of obesity on loss of fat-free mass during very-low-energy diets. Am J Clin Nutr 1994;60:874–8.
19. Mazess RB, Barden HS, Ohlrich ES. Skeletal and body composition effects of anorexia nervosa. Am J Clin Nutr 1990;52:438–41.
20. Heymsfield SB, McManus CB. Tissue components of weight loss in cancer patients. A new method of study and preliminary observations Cancer 1985;55:238–49.
21. Probst M, Goris M, Vandereycken W, et al. Body composition of anorexia nervosa patients assessed by underwater weighing and skinfold-thickness measurements before and after weight gain. Am J Clin Nutr 2001;73:190–7.
22. Martinez E, Mocroft A, Garcia-Viejo MA, et al. Risk of lipodystrophy in HIV-1 infected patients treated with protease inhibitors: a prospective cohort study. Lancet 2001;357:592–8.