Article

Does Percent Body Fat Predict Outcome in Anorexia Nervosa?

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Objective: The goal of this study was to investigate the relationship of body composition and neuroendocrine levels with clinical outcome in women with anorexia nervosa in a relapse-prevention trial.

Method: Body composition and fasting cortisol and leptin levels were assessed before random assignment in 32 weight-recovered subjects with anorexia nervosa from the New York site of the Fluoxetine to Prevent Relapse in Women With Anorexia Nervosa trial. Clinical outcome at the end of study participation was defined using modified Morgan-Russell criteria (full, good, fair, poor), then dichotomized into treatment "success" or "failure."

Results: In a binary logistic regression model examining the effect of percent body fat, body mass index, anorexia nervosa subtype, waist-to-hip ratio, and serum cortisol and leptin levels on treatment outcome, only percent body fat was significantly associated with outcome.

Conclusions: In recently weight-restored women with anorexia nervosa, lower percent body fat was associated with poor long-term outcome.

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Relapse is a significant problem for individuals with anorexia nervosa, with relapse rates as high as 50% (1). Identification of predictors of relapse is a critical step in recognizing patients at increased risk for relapse and developing more successful treatment interventions (2). Persistent and excessive body image disturbances (2, 3) have been identified as potential psychological risk factors increasing the likelihood of relapse, but few studies have explored potential neurobiological risk factors for relapse. The role of body mass index has been examined, and studies (4, 5) have suggested that a higher body mass index at presentation for treatment is associated with better long-term outcome. Leptin levels following partial weight restoration have been inversely associated with relapse at 1-year follow-up (6). Despite the psychological fear of fat and weight gain that characterizes anorexia nervosa, to our knowledge, there are no published studies of body composition as a predictor of relapse.

This study aimed to investigate the relationship between body composition, hormones, and clinical outcome in a cohort of women with anorexia nervosa participating in a relapse-prevention study (7) and a longitudinal study of body composition in anorexia nervosa (8).

Method

The subjects were women between the ages of 18 and 45 years recruited from two studies: the Fluoxetine for Relapse Prevention in Women With Anorexia Nervosa trial (New York site only, reference 7) and Energy Homeostasis in Anorexia Nervosa, a longitudinal study involving the examination of changes in body composition (8). Thirty-two of the 45 relapse-prevention trial participants also participated in the body composition study. Reasons for nonparticipation in the body composition study included being less than 18 years old (N=5), taking psychotropic medications or medications known to affect body composition (N=2), the presence of a comorbid diagnosis of substance abuse (N=2), and the presence of nonremovable metal (N=1). In addition, two women participated in the relapse-prevention study before the initiation of the study of body composition, and one woman declined to participate. The subjects were free from medications for a minimum of 2 weeks (4 weeks for oral contraceptives) before testing.

After complete description of the studies to the subjects, written informed consent was obtained. These studies were approved by the institutional review boards of the New York State Psychiatric Institute, Columbia University, and St. Luke's–Roosevelt Hospital Center.

The subjects received inpatient treatment sufficient to normalize weight to at least 90% ideal body weight and were studied after maintaining ≥90% ideal body weight for 2–4 weeks (8) but before random assignment in the relapse-prevention trial. Menstruating subjects were tested during the follicular phase of the cycle.

Testing included fasting, morning blood sampling, and body composition assessment. Anthropometry and dual-energy X-ray absorptiometry for body composition measurement were performed at the Body Composition Unit of the New York Obesity Research Center at St. Luke's–Roosevelt Hospital Center.

The patients were assessed wearing a hospital gown and underwear. They were informed that measurements were for research purposes only and would not affect their clinical treatment. Height was measured using a wall-mounted stadiometer to the nearest millimeter. Weight was measured to the nearest 0.1 kg with a calibrated physician's office scale. Using a standard cloth tape measure, waist circumference was measured in millimeters at the level immediately below the lowest ribs, and hip circumference was measured below the iliac crest. Two trained assessors performed all assessments. The intraobserver coefficient of varia-

TABLE 1. Body Composition and Hormonal Data for Groups With Anorexia Nervosa Determined by Treatment Outcome

	Treatment Success (Morgan-Russell criteria: full, good, or fair) (N=16)		Treatment Failure (Morgan-Russell criteria: poor) (N=10)		Analysis		
Variable	Mean	SD	Mean	SD	t	df	p
Body mass index (kg/m^2)	20.59	0.62	20.52	0.70	–0.27	24	0.79
Percent body fat	26	4	21	4	–2.93	24	<0.007
Lifetime highest body mass index (kg/m^2)	21.72	2.83	22.79	3.17	0.89	24	0.38
Percent of lifetime highest body mass index	96	13	91	12	–0.97	24	0.34
Waist-to-hip ratio	0.84	0.05	0.87	0.03	1.31	24	0.20
Serum leptin (ng/ml)	21.7	15.5	13.0	12.4	–1.50	24	0.15
Serum cortisol (µg/dl)	20	7	17	6	–1.15	24	0.26
Days to study termination	244	133	122	96	–2.18	24	<0.02

tion was 1.0%. The waist-to-hip ratio was calculated as the quotient of the waist circumference divided by the hip circumference. Total body dual-energy X-ray absorptiometry was performed (DPX-L, GE Lunar, Madison, Wis.) to obtain percent body fat.

Cortisol was measured with solid-phase, chemiluminescent immunoassays (Immulite, Diagnostic Products Company, Los Angeles). Assay sensitivity was 0.2 µg/dl. Intra- and intercoefficients of variation were 7.6% and 10.2%, respectively.

Leptin was measured with a commercial immunoradiometric assay kit (Diagnostic Systems Labs, Inc., Webster, Tex.). Assay tubes were incubated overnight at room temperature. Assay sensitivity was 0.25 ng/ml. Intra- and interassay coefficients of variation were 2.5% and 3.6%, respectively.

Although survival analysis was the primary analysis used in the Walsh et al. (7) trial, subject outcome at study termination was also classified using the modified Morgan-Russell criteria (full, good, fair, or poor) (9, 10). The subjects were classified as "other" when they did not meet the time criteria (remaining in the study for at least 8 weeks) for Morgan-Russell determination (7). Outcome was dichotomized into "treatment success," defined as a Morgan-Russell categorization of full, good, or fair, and "treatment failure," defined as a Morgan-Russell categorization of poor. Consistent with the Morgan-Russell classification, we excluded six subjects whose outcome was categorized as "other"; thus, data from 26 subjects were available for analysis. Including subjects with an "other" outcome in the "treatment failure" group did not significantly change the results of the study.

Clinical variables were compared between those in the "treatment success" and "treatment failure" groups by using Student's t test. Logistic regression models were constructed to evaluate the effects of body mass index, percent body fat, subtype, waist-to-hip ratio, and serum cortisol and serum leptin levels on treatment outcome. Because no significant effect of fluoxetine was found on preventing relapse (7), medication assignment was not considered as a covariate in these analyses.

Lifetime highest body mass index was obtained by self-report, and percent of lifetime highest body mass index at testing was calculated as (body mass index/lifetime highest body mass index) * 100.

Analyses were performed with SPSS for Windows (version 10.1, SPSS, Chicago). Means and SDs are reported; t tests were two-tailed. Significance level was set at 0.05.

Results

Clinical variables are presented in Table 1. There were no significant differences between the success and failure groups on body mass index or percent lifetime body mass index. Percent body fat, however, was significantly different between the groups. Body fat (mean and SD) by Morgan-Russell outcome group was the following—full: mean=30%, SD=8%, N=2; good: mean=25%, SD=4%, N=11; fair: mean=26%, SD=4%, N=3; poor: mean=21%, SD=4%, N=10. Neither serum cortisol nor serum leptin level was significantly different between the groups. As expected, the mean number of days to termination in the relapse-prevention study was significantly greater for the "treatment success" group compared to the "treatment failure" group.

In the binary logistic regression model, with treatment "success" or "failure" as the outcome and body mass index, percent body fat, waist-to-hip ratio, and serum cortisol and serum leptin levels as the predictor variables, only percent body fat (Exp[B]=2.036, p=0.04) significantly predicted outcome.

Discussion

Among a group of recently weight-restored adult women with anorexia nervosa, lower percent body fat at the time of hospital discharge was associated with poorer outcome. This is the first study, to our knowledge, to describe a significant relationship between body composition after weight restoration and outcome.

It was somewhat unexpected that in the absence of a significant difference in body mass index, body composition was significantly different. In studies of individuals with a wider range of body mass indices, body mass index correlates significantly with level of body fat (11). The mean body mass index of the cohort in this study was well within the normal weight range, but the range of body mass index was small. The mean percent body fat in the "treatment failure" group was significantly below normal for adult women. Additionally, although relative central adiposity with acute weight gain has been described (8, 12) and hypothesized to contribute to long-term outcome, body fat distribution as measured by waist-to-hip ratio was not predictive of outcome.

Although patients had successfully regained weight to within a normal range, it could be argued that some remained below a body weight that might have been more appropriate for them. Indeed, patients were, on average, at 94% (SD=13%) of their lifetime highest body mass index. However, there was no significant difference between the treatment "success" and "failure" groups on lifetime

highest body mass index or percent of lifetime highest body mass index achieved.

Prior studies (13–15) have described that restoration of reproductive function is significantly associated with increases in weight and that end-of-hospitalization ovarian size may be associated with long-term outcome (13). It is commonly accepted that reproductive function is related to body fat stores and may be mediated by leptin. Combined with the findings from the current study, these data suggest that restoring body fat to normal levels may be integral to recovery.

There are a number of limitations to the current study. The outcome data were derived from a larger trial. Although participants were assessed before random assignment, the clinical trial was designed to examine the effect of fluoxetine on outcome. The number of subjects for whom body composition data were available was approximately one-third the total sample and included subjects from only one site (New York). Although there was no effect of medication on outcome in the larger trial, the New York site, lower initial body mass index, and the binge-purge subtype were associated with earlier relapse. In the current study, we found no significant effect of body mass index or subtype, which presumably reflects the reduced power of the smaller sample. Additionally, although all subjects were engaged in inpatient treatment where formal exercise was not permitted and meals were selected from a hospital menu, variations in levels of exercise or dietary intake may have contributed to differences in body composition.

Nevertheless, the results of this study are provocative. Without additional data linking percent body fat as a risk factor for relapse in anorexia nervosa, it would be premature to recommend that standard care include body composition testing after weight recovery. However, these data may be helpful to patients and to the clinicians caring for them in suggesting that, contrary to the fears characteristic of this disorder, increased body fat may serve to protect against relapse.

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