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Percent Body Fat is a Risk Factor for Relapse in Anorexia Nervosa: A Replication Study

Lindsay P. Bodell, BA and Laurel E.S. Mayer, MD*

Eating Disorders Research Unit, Department of Psychiatry, College of Physicians and Surgeons of Columbia University/New York State Psychiatric Institute, New York, New York

Abstract

Objective—We aimed to replicate and extend our previous findings of an association between percent body fat in recently weight-restored patients with Anorexia Nervosa (AN) and clinical outcome in the year following treatment.

Method—Twenty-two hospitalized, weight-restored women with AN underwent whole body MRI to determine percent adipose tissue. Following hospital discharge, patients were contacted regularly, and at the end of the year, clinical outcome was determined using modified Morgan-Russell (MR) criteria: full, good, fair or poor. Identical to our previous study, outcome was dichotomized into “full, good or fair” and “poor” groups.

Results—Data from 21 subjects were available for analysis. Percent body fat was significantly lower in the poor outcome group ($22\% \pm 5\%$) compared to the “full, good or fair” outcome group ($27\% \pm 4\%$) ($p < 0.035$). To further examine the relationship, we combined data from the current study with data from the 26 subjects on whom we had previously reported. Univariate analysis of variance (ANOVA) demonstrated a significant difference in percent adipose tissue across the four MR outcome groups ($F = 3.416$, $df = 3$, $p < 0.03$).

Discussion—Lower percent adipose tissue after short-term weight normalization is associated with poor clinical outcome in the year following inpatient treatment. These findings may be important in the assessment of risk for relapse in patients with AN.

Anorexia Nervosa (AN) is a serious psychiatric illness with high rates of recidivism. Reported relapse rates range from 30% to 50%,¹ with the greatest risk of relapse occurring in the first year following hospitalization.^{2,3} Identifying factors associated with relapse would greatly aid the development of effective treatments. Some studies have suggested that longer duration of illness^{1,4} and older age of onset¹ are associated with worse outcome. Other studies suggest greater concern with shape and weight^{3,5,6} or excessive exercise⁵ is associated with relapse. More recently, Schebendach and colleagues⁷ described an association between diet and risk of relapse in a cohort of recently weight-restored inpatients with AN. Patients consuming an overall diet of lower energy density or of a limited variety

of foods were more likely to relapse in the year following hospital discharge compared to those individuals with more varied diets and a higher overall energy density. Studies exploring risk factors such as body mass index (BMI) indicate that a higher BMI at presentation for treatment may be associated with better outcomes.^{1,8,9} Additionally, in a multi-site relapse prevention trial¹⁰ in which all patients had achieved a minimally normal body weight before entry, the only factors associated with relapse were BMI at the end of acute treatment and the rate of weight loss in the first four weeks following hospitalization.¹¹ Leptin levels are generally positively correlated with BMI and body fat,¹² thus these findings suggest that higher leptin levels would be associated with improved outcome. Somewhat paradoxically, Holtkamp and colleagues¹³ reported that higher leptin levels at discharge in inpatients with AN predicted greater weight loss in the 2 months after hospitalization and worse outcome in the year following hospitalization; in this study, patients remained significantly underweight at hospital discharge. Mayer and colleagues¹⁴ reported that percent body fat was significantly associated with clinical outcome. Specifically, lower percent body fat among women with AN restored to at least 90% of ideal body weight predicted worse outcome in the year following inpatient treatment. The aims of the current study were to replicate, in a new sample, our previous finding of an association between body composition and dichotomous clinical outcome according to the Morgan-Russell scale (“full, good or fair” versus “poor”).¹⁵

Method

Participants were 22 women with AN between the ages of 18–45 years participating in a longitudinal study examining changes in body composition and body fat distribution in the year following inpatient treatment on an eating disorders unit. Participants met DSM-IV-TR criteria for AN, with the exception of the amenorrhea criterion.^{16,17} Patients were excluded if they were taking psychotropic or other medications known to affect weight, appetite or body composition, or if they had non-removable metal in or on their body. As described below, we also examined data from 26 subjects meeting identical criteria who had participated in our previous study.¹⁴

This study was approved by the Institutional Review Board of the New York State Psychiatric Institute and Columbia University Department of Psychiatry. The study was described to the participants and written informed consent was obtained prior to participation.

All participants received inpatient treatment on the Eating Disorders Service of the General Clinical Research Unit (GCRU) at the New York State Psychiatric Institute at the Columbia University Medical Center. Inpatient treatment consisted of a structured behavioral program aimed at normalizing weight and eating behavior.^{10,14} Patients were prescribed three meals and one snack per day and were expected to gain >1 kg/week. If weight gain was not sufficient on food alone, then additional calories were prescribed in the form of a liquid nutritional supplement (ENSURE or ENSURE PLUS). Patients restored weight to at least 90% of ideal body weight (IBW) ($BMI = \sim 19.5 \text{ kg/m}^2$) as defined by the Metropolitan Life actuarial tables.¹⁸ Body composition was assessed in participants after they maintained 90% of IBW for two to four weeks.

On the morning of testing, weight was measured to the nearest [1/4] lb with a calibrated physician's beam balance scale (Detecto, Madison WI), and patients ate a standardized breakfast (~ 300 kcal). Total body MRI was performed at the Program for Imaging in Cognitive Sciences (PICS) of Columbia University Medical Center (CUMC) using a 1.5T, GE Systems MRI machine (GE, Milwaukee WI). MRI images were analyzed for body composition by the Image Analysis Laboratory affiliated with the New York Obesity Research Center. Percent adipose tissue was calculated as total adipose tissue (TAT) divided by body weight times 100, and this calculation was used as a proxy for percent body fat.

Upon completion of the inpatient program, patients were discharged to treatment in the community. Follow up information regarding eating disorder symptoms and weight status was obtained during monthly phone calls by research staff, and by in-person evaluations conducted every three months for up to one year following hospital discharge.

Clinical outcome was evaluated at the end of one year or at the point of last contact. Clinical outcome was determined using modified Morgan-Russell criteria¹⁵: full, good, fair, and poor (Table 1). Patients followed for less than eight weeks, were assigned to an "other" category, as evaluation of the modified Morgan-Russell criteria requires an 8-week interval. As in the prior study, because of the brief duration of follow up, reliable, long-term clinical outcome could not be determined in the "other" group, and they were excluded from analyses. Identical to the previous study,¹⁴ outcome was dichotomized into Morgan-Russell classification of "full, good or fair" and "poor"

Statistical Analyses

Clinical characteristics of "full, good or fair" and "poor" outcome groups were compared using independent samples *t*-tests. Effect size (Cohen's *d*) was calculated to assess the magnitude of the difference between the groups. A binary logistic regression model was constructed to further evaluate the relationship between percent body fat and dichotomous clinical outcome.

In order to examine the relationship between body composition and all four Morgan-Russell outcome groups with greater statistical power, we combined data from the current study with data from the 26 subjects on whom we had previously reported.¹⁴ These patients had achieved weight restoration on the same clinical unit using identical clinical procedures. Body composition of these subjects was also assessed identically, but MRI images were acquired on a different 1.5 T GE Systems MRI machine (affiliated with the New York Obesity Research Center at St. Luke's-Roosevelt Hospital). Analysis of variance (ANOVA) was used to compare percent body fat and BMI among the four Morgan-Russell outcome groups (full, good, fair, poor). The data were also subjected to non-parametric analysis for ordered categories with the Kruskal-Wallis test.

All analyses were performed with SPSS for Windows (version 17.0, SPSS, Chicago). Means are reported $\pm$ standard deviation. Significance level was set at 0.05.

Results

Follow up information was obtained on 21 of the 22 subjects, as one participant did not return phone calls after hospital discharge. Nineteen of the 21 participants completed follow-up assessments 9–12 months after hospitalization and provided sufficient information to determine Morgan-Russell criteria. One participant provided information at 3 months post discharge, but did not return phone calls after that visit. Another participant remained in contact with the clinic for seven months, but was then lost to follow-up. For these two patients, Morgan-Russell classification was determined by information collected at the point of last contact.

Demographic and clinical information is presented in Table 2. Of the 21 participants included in the analyses, outcome for 10 patients was categorized as “full (N = 4), good (N = 1), or fair (N = 5)” and for 11 patients as “poor” outcome. One subject was maintaining a BMI of 18.2 and was menstruating regularly, and thus was included in the fair category. As expected by outcome classification, mean BMI at follow-up was significantly different between the “full, good or fair” and “poor” outcome groups ($20.8 \pm 2.5 \text{ kg/m}^2$ compared to $16.2 \pm 1.2 \text{ kg/m}^2$, $p < 0.001$). At the time of initial testing, age, duration of illness, diagnostic subtype, and BMI were not significantly different between the “full, good or fair” and “poor” groups. Percent body fat, however, was significantly lower in the “poor” outcome ($22\% \pm 5$) compared to the “full, good or fair” outcome ($27\% \pm 4$) group ($t = 2.275$, $df = 19$, $p < 0.035$, Cohen’s $d = 1.10$). In the binary logistic regression model, the relationship between percent body fat and clinical outcome nearly reached statistical significance ($\text{Exp}[B] = 0.762$, $df = 1$, $p < 0.056$).

In order to further explore the relationship between body composition and the range of Morgan-Russell outcome categories, we examined data from the 21 participants described above combined with identical data from the 26 participants previously described.¹⁴ In the combined sample, the outcomes of six participants were categorized as full recovery, the outcomes of 15 as good, of five as fair, and of 21 as poor. Analysis of variance (one-way ANOVA) demonstrated that percent body fat varied significantly ($F = 3.416$, $df = 3$, $p < 0.03$) across the Morgan-Russell outcome groups (see Fig. 1). Non-parametric analysis for ordered categories using the Kruskal-Wallis test also yielded significance across outcome groups (chi-square 8.9, $df = 3$, $p < 0.03$).

Discussion

The results of the current study provide additional data supporting our previous finding¹⁴ that among fully weight-restored women with AN on an inpatient unit, there is a significant association between body composition and longer-term outcome. Specifically, lower percent body fat prior to hospital discharge is associated with worse outcome in the year following inpatient treatment. Recommended percent body fat for women 18–45 years of age ranges from 20%–30%,¹⁹ thus, on average, patients who achieved minimal normalization of percent body fat had a poorer outcome compared to those who normalized body fat above the minimum recommended percent.

Replicated predictors of relapse are few. Higher BMI at the time of hospital discharge has been shown to be associated with lower risk of relapse¹¹; however, in the current study, no significant difference in BMI between the “full, good or fair” and “poor” outcome groups was observed. Although consistent with the finding of our previous study,¹⁴ it is somewhat surprising that in the absence of a significant difference in BMI, percent body fat was different. Given the relatively narrow range of BMI in the current study, it is possible that in a larger sample, a difference in BMI between the groups might have been detected. Another way to explore this apparent discrepancy would be to evaluate leptin levels. It is well established that serum leptin levels are strongly, positively correlated with body fat¹²; therefore, the current results suggest that higher leptin levels would be associated with improved outcome. Paradoxically, Holtkamp and colleagues¹³ described that higher leptin levels at hospital discharge in patients with AN were associated with weight loss in the first two months after hospitalization. Of note, patients were significantly underweight at discharge (mean BMI ~ 17.3 kg/m²), and thus, these apparently inconsistent findings may reflect the short-term effects of “over-feeding” (or acute nutritional status) on leptin levels²⁰ in the Holtkamp study and, in the present study, the longer-term relationship between leptin level and body composition.

Unfortunately, there is no universally-accepted definition of recovery or of relapse in AN. Previous studies on relapse and relapse prevention in AN have successfully used Morgan-Russell criteria to define outcome.^{3,10} However, a significant limitation of the Morgan-Russell criteria is the primary emphasis on weight status and the relative lack of consideration of other important aspects of the symptoms of AN, for example binge eating, purging, or body image concerns. The relationship between body composition immediately following weight restoration and other definitions of recovery and relapse is unknown.

There are a number of other limitations to the current study. Our report is the result of a secondary analysis of data, the sample size was small, and this limited our ability to conduct analyses among the Morgan-Russell outcome groups or identify other predictors of relapse. By pooling the current data with data from our previous publication, we attempted to address this statistical limitation somewhat. Another limitation of the current study was the use of total body MRI to measure adipose tissue. In the previous study, percent body fat was assessed by dual x-ray absorptiometry (DXA). While total body MRI allows for the direct visualization and measurement of adipose tissue, percent total adipose tissue assessed via MRI is not identical to percent body fat as assessed by DXA,²¹ although the two are highly correlated.^{22,23} In our sample, the correlation between percent body fat determined by DXA and percent adipose tissue by MRI was $r = 0.846$, $p < 0.001$ (unpublished data).

In addition, other factors such as physical activity and dietary intake may have directly or indirectly contributed to percent body fat, and in turn, risk of relapse. At the time of testing, patients were in the weight-maintenance phase of the inpatient treatment program, and although formal exercise was discouraged, the amount of physical activity patients engaged in was not controlled. It is possible that those who were more active had lower percent body fat, and it was the level of physical activity, rather than the percentage of body fat *per se* that was associated with outcome. Similarly, variations in dietary intake may have contributed to differences in body composition and/or outcome. Schebendach and colleagues⁷ reported

associations between dietary energy density and diet variety and clinical outcome. Thus, the differences in body composition described in this sample may reflect differences in physical activity, diet, or other factors.

Full recovery from AN includes resumption of regular menstrual cycles. It is well-established that body fat stores are related to reproduction function.²⁴ Specifically in AN, resumption of menses is associated with more complete normalization of weight.²⁵ In the current study, only 8 of the 22 women (36%) had return of menstrual function with acute normalization of weight to 90% IBW. Thus, we cannot evaluate the relationship between percent body fat, return of menses, and recovery.

Despite the limitations, these data suggest that lower percent body fat in recently-weight restored women with AN may be a risk factor for relapse, and normalization of body fat may be an important contributor to long-term recovery from AN. While it is quite premature to recommend that the achievement of a specific level of body fat be a target of acute treatment, body composition assessment may be helpful as part of a profile of “risk factors for relapse.” Additional study of the interplay between body composition and other factors affecting long-term outcome of AN is important.

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FIGURE 1.

Percent body fat shortly after weight normalization in hospitalized patients with AN is associated with Morgan-Russell outcome classification in the year following discharge. Analysis of variance (one-way ANOVA) demonstrate that percent body fat varies significantly ($F = 3.416$, $df = 3$, $p < 0.03$) across outcome groups.

TABLE 1

Definition of modified Morgan–Russell criteria for patients with anorexia nervosa

Outcome	Definition
Full	No DSM-IV-TR criteria for AN for a minimum of 8 weeks
Good	BMI 18.5; normal menses, may have some binge eating or purging behavior or psychological symptoms of AN
Fair	BMI 18.5; amenorrhea
Poor	BMI 18.5

Demographic and clinical information at time of discharge from acute care of outcome groups ($N = 21$)**TABLE 2**

	Mean $\pm$ SD		<i>t</i>	df	<i>p</i>	Cohen's <i>d</i>
	Full, Good, or Fair Outcome ($N = 10$)	Poor Outcome ($N = 11$)				
Age (years)	27.9 $\pm$ 7.5	25.4 $\pm$ 3.4	1.01	19	.32	0.43
Duration of illness (years)	7.3 $\pm$ 6.6	6.8 $\pm$ 5	0.19	19	.85	0.09
Length of follow-up (months)	10 $\pm$ 2.8	11.8 $\pm$ 3.5	-1.32	19	.20	-0.57
Body mass index (kg/m ²)	20.3 $\pm$ 0.4	20.0 $\pm$ 0.4	1.38	19	.18	0.75
Percent body fat	27 $\pm$ 4	22 $\pm$ 5	2.28	19	.035	1.10