Prediction of Low Body Weight at Long-Term Follow-Up in Acute Anorexia Nervosa by Low Body Weight at Referral

Johannes Hebebrand, M.D., Günther W. Himmelmann, M.D., Wolfgang Herzog, M.D., Beate M. Herpertz-Dahlmann, M.D., Hans-Christoph Steinhausen, M.D., Ph.D., Margit Amstein, M.D., Reinhold Seidel, M.D., Hans-Christian Deter, M.D., Helmut Remschmidt, M.D., Ph.D., and Helmut Schäfer, Ph.D.

Objective: *The authors investigated the hypothesis that in acute anorexia nervosa a low body weight predicts a poor weight prognosis for the future.* *Method:* *The body mass indexes at referral of 272 female patients were examined in relation to the body mass indexes of these patients after a mean follow-up of 9.5 years.* *Results:* *The overall correlation between body mass indexes at referral and at follow-up was r=0.33. Despite this low correlation, the 100 patients with body mass indexes less than 13 kg/m² at referral had low weights at long-term follow-up. Eleven of the 12 deceased patients were among these 100 patients, as were 24 of the 46 surviving patients whose body mass indexes were 17.5 kg/m² or less at follow-up.* *Conclusions:* *For patients with anorexia nervosa, a body mass index less than 13 kg/m² at referral indicates a substantial risk for chronic anorexia nervosa and death related to emaciation.*

(Am J Psychiatry 1997; 154:566–569)

Single follow-up studies have identified a low body weight at referral as a poor prognostic indicator for intermediate or long-term follow-up (1, 2). Morgan and Russell (3) observed an association between low body weight (less than 60% average body weight, roughly equivalent to a body mass index of 12.5 kg/m^2 in females aged 17–19 years) at referral and poor general outcome after 5 years. In a previous study (4), we found that 24 patients with body mass indexes less than 13 kg/m^2 at referral had significantly lower body mass indexes at follow-up than 57 patients who had higher body mass indexes at referral; the mean follow-up period was 11.7 years. Possible explanations for the discrepancies regarding the prognostic implications of a low body weight at referral include small sample sizes and crude categorizations of the weight outcome.

The hypothesis of the present study was that a low body mass index at referral predicts a low body mass index at long-term follow-up. To test this hypothesis we assessed body mass indexes at referral and at follow-up in a large study group (N=272) to determine their interrelationship and to assess the influence of age at onset, age at referral, and age at follow-up, respectively.

Received Sept. 25, 1995; revision received Aug. 7, 1996; accepted Oct. 25, 1996. From the Departments of Child and Adolescent Psychiatry of the Universities of Marburg, Zürich, and Berlin. Address reprint requests to Dr. Hebebrand, Clinical Research Group, Department of Child and Adolescent Psychiatry of the University of Marburg, Hans-Sachs-Str. 6, 35033 Marburg, Germany; Hebebran@post.med.uni-marburg.de (email).

Supported by the Deutsche Forschungsgemeinschaft.

METHOD

The study group was a composite of five study cohorts with a total of 341 consecutively ascertained inpatients with anorexia nervosa. Twenty-four of the patients were males. The ascertainment, diagnostic assessment according to DSM-III-R, and outcome of these study cohorts have been described in detail elsewhere (4–9). For the present analysis, all 24 of the males, seven females with additional somatic diseases at referral, and seven pretreated females whose body mass indexes at referral were greater than 17.5 kg/m^2 were excluded; 31 additional females could not be traced at follow-up. The final study group included 272 females whose body mass indexes at referral and body mass indexes at follow-up or time of death were available. Their mean ages at referral and at follow-up were 16.7 years (SD=4.5, range=10–42) and 26.2 years (SD=6.9, range=15–58), respectively. Mean length of follow-up was 9.5 years (SD=5.3, range=0–33.6) and included the survival times of the 12 patients who had died after a mean of 4.2 years (SD=4.0, range=0–13). Deaths were related to the sequelae of emaciation in 10 patients and to suicide in two patients.

The patients' body mass indexes at referral were plotted against their body mass indexes at follow-up and Pearson's correlation was calculated. Body mass indexes were plotted in 1-kg/mg^2 intervals from 9 to 27 kg/mg^2. Patients with low body mass indexes at referral were compared with patients with higher body mass indexes at referral by using repeated U tests. Significance was adjusted for multiple testing (10). We also charted the proportion of patients whose body mass indexes at follow-up were 17.5 kg/m^2 or less, those whose body mass indexes were in the fifth percentile or below, and those whose body mass indexes were in the 10th percentile or below. Body mass index percentiles were based on the German National Nutrition Survey (11).

Age at onset, age at referral, age at follow-up, duration of illness before index admission, and length of follow-up were considered as possible further influence factors. The duration of illness before admission was determined by asking either the patient or her parents at the time of referral. Age at onset was estimated by subtracting this duration from the age at referral. Logistic regression was performed on body mass index at follow-up with the criterion of 17.5 kg/m^2 or

less (the alternative ICD-10 weight criterion for a diagnosis of anorexia nervosa) as the dependent variable. The proportion of deceased patients whose body mass indexes at referral were less than 13 kg/m^2 was compared with the proportion of deceased patients whose body mass indexes at referral were 13 kg/m^2 or more by using an alpha-adjusted Fisher's exact test (10).

We used SAS-OS/2 V 6.10 and applied the procedures UNIVARIATE, MEANS, NPAR1WAY, CORR, FREQ, LOGISTIC, and GPLOT.

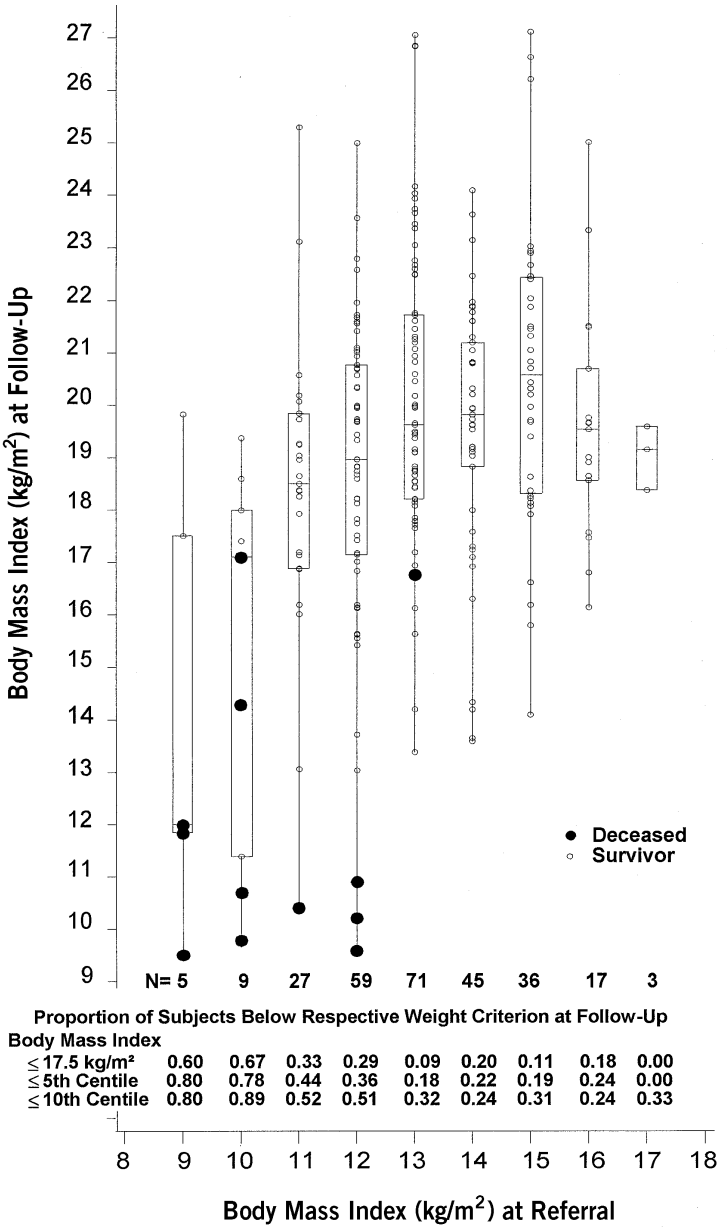
RESULTS

Patients with low body mass indexes at referral had lower body mass indexes at follow-up than patients with higher body mass indexes at referral (figure 1). The cutoff point was at 13 kg/m^2 (p=0.0000008, corrected for multiple U tests). The mean body mass index at follow-up of patients with body mass indexes less than 13 kg/m^2 at referral was 18.0 kg/m^2 (SD=3.4, range=9.5–25.3), and the mean body mass index at follow-up of patients with body mass indexes of 13 kg/m^2 or more at referral was 20.0 kg/m^2 (SD=2.6, range=13.4–27.1). This difference of 2 kg/m^2 (post hoc U test; chi-square approximated p<0.05) amounts to 5.78 kg in a female with a height of 1.7 m. The mean follow-up intervals of the two groups were similar: 9.6 years (SD=6.1, range=0–33) for the patients with body mass indexes less than 13 kg/m^2 at referral and 9.4 years (SD=4.9, range=3.2–33.6) for the patients with body mass indexes of 13 kg/m^2 or more at referral. However, the duration of the eating disorder before referral differed between the two groups by almost 1 year (mean=2.2 years, SD=3.3, range=0–19, versus mean=1.3 years, SD=1.73, range=0–16, respectively) (post hoc U test; chi-square approximated p<0.05).

The correlation between body mass index at referral and body mass index at follow-up was r=0.33 (p<0.00001); this changed to r=0.19 with the exclusion of the deceased patients (p= 0.002). The proportions of patients with follow-up body mass indexes of 17.5 kg/m^2 or less, patients in the fifth percentile or less, and patients in the 10th percentile or less declined with increasing body mass index at referral (figure 1). The trend of these proportions was similar when the deceased patients were excluded (data not shown explicitly).

The logistic regression is logit=0.0904 (SE= 0.0833) for age at onset (p=0.28) + 0.1532 (SE= 0.0712) for age at referral (p=0.03) – 0.0969 (SE=0.0357) for age at follow-up (p=0.007) – 0.2042 (SE=0.0480) body mass index at referral (p=0.00002). Thus, body mass index at referral had the highest loading; age at referral and age at follow-up were also significant predictors for a body mass index at follow-up of 17.5 kg/m^2 or less. Exclusion of the deceased patients did not change the general pattern of predictor variables. The duration of the disorder before admission and the follow-up interval were linear combinations of the aforementioned age variables.

FIGURE 1. Relationship of Body Mass Indexes (kg/m^2) at Referral to Body Mass Indexes at Follow-Up in 272 Female Patients With Anorexia Nervosa[a]



[a]Filled dots represent deceased individuals. Boxes encompass those patients whose body mass indexes at follow-up were within the second and third quartiles of the respective group; the vertical line within a box represents the median body mass index at follow-up for the respective group. Numbers below box plots indicate number of patients in the respective group. The insert presents proportions of individuals in whom body mass indexes at follow-up were equal to or less than 17.5 kg/m^2, were in the fifth percentile of body mass index or below, or were in the 10th percentile of body mass index or below, respectively. The fifth and 10th percentiles in the German population almost completely overlap with percentiles calculated for the U.S. population (11).

The mortality rate of 11% (11 out of 100) in patients whose body mass indexes at referral were less than 13 kg/m^2 was significantly different from the rate of 0.6% (one out of 172) of the patients whose body mass indexes at referral were 13 kg/m^2 or more (p=0.0001, alpha-adjusted Fisher's exact test). Ten of the deceased patients died with body mass indexes less than 15 kg/m^2, reflecting severe emaciation. Twelve survivors also had body mass indexes of less than 15 kg/m^2 at follow-up.

DISCUSSION

The results clearly reflect the clinical implications of a low body mass index at referral. The seemingly continuous weight range at follow-up shows a cutoff point at 13 kg/m^2 for the body mass index at referral; below this cutoff point the weight prognosis is less favorable. This is corroborated by the substantially higher proportions of patients with body mass indexes at referral less than 13 kg/m^2 remaining in differently defined low-weight outcome groups (figure 1). The prognostic significance of a low body mass index at referral can be picked up in a follow-up study only if a sufficiently large number of patients at referral have body mass indexes in this critical range. Future research on possible influencing factors on the outcome of anorexia nervosa should address the phenomenon that a cutoff point suggests a nonrandom underlying process.

The clinical implications of a low-weight outcome include chronic anorexia nervosa and death related to emaciation. Data on marasmic females collected during a famine revealed that the risk of mortality increased sharply when the body mass index went below 11 kg/m^2 (12). Of the 14 patients in our study who had body mass indexes less than 11 kg/m^2 at referral, only seven survived. The surviving patients whose body mass indexes at follow-up were less than 15 kg/m^2 are presumably at substantial risk for death related to emaciation. Figure 1 suggests that they form a subgroup distinct from the surviving patients whose body mass indexes at follow-up were greater than 15 kg/m^2.

The pattern underlying weight regulation in anorexia nervosa is possibly stronger than our data suggest because body mass index at referral is only a crude measure that is influenced by several variables (e.g., premorbid weight, tolerance of extreme underweight, body composition, treatment, and familial factors). The minimal body mass index achieved during the disorder is possibly of greater prognostic significance. This is indirectly substantiated by the fact that patients with body mass indexes less than 13 kg/m^2 at referral had a longer duration of anorexia nervosa before the key admission than those with higher body mass indexes, thus implying that the eating disorder had run more of its course in the former group. A longer duration of illness before referral has been associated with a poor general outcome (1, 2). Retrospective assessment of the minimal body mass index during the course of anorexia nervosa is complicated by the fact that patients who have not reached their adult height frequently cannot reliably recall their height at the time their lowest body weight occurred.

The mechanisms underlying weight regulation in anorexia nervosa can only be speculated upon. First, a simple explanation is that the amount of future weight gain is limited by the extent of underweight achieved during the acute stage of anorexia nervosa. Accordingly, an early goal of therapeutic interventions should be to prevent further weight loss. Second, the severity of a psychological conflict might influence both the degree of underweight reached in the acute stage and the recovery rate. Finally, genetic factors could underlie the aberrant weight regulation (13). The impact of anorexia nervosa on future body weight is substantiated by the fact that in our study only nine patients reached body mass indexes at follow-up greater than 25 kg/m^2. It will be of interest to assess the prognostic implications of plasma leptin levels at referral of patients with anorexia nervosa (14).

Obviously, focusing on weight outcome alone is unsuitable for assessment of the general outcome of anorexia nervosa, which for the patients in the present study has been described elsewhere (5–9). Nevertheless, persistence of underweight has far-reaching implications justifying attempts to adequately define a poor weight outcome. Categorizations of weight outcomes according to body mass indexes at follow-up of 17.5 kg/m^2 or less, the fifth percentile or less, or the 10th percentile or less are directly or indirectly based on the ICD-10 and DSM-IV diagnostic criteria and allow comparison with body mass index distributions in the general population (11). They offer an alternative to the criterion of within 15% average body weight used in the Global Outcome Score (3).

However, assessment of the weight outcome with any dichotomous categorization should be viewed with caution. In simple terms, a female with a body mass index corresponding to the fifth percentile at follow-up is most likely to be somatically and psychopathologically healthier than a female with a body mass index of 13.5 kg/m^2. The beneficial effect of a gain of 6 kg/m^2 in a patient with an initial body mass index of 10.5 kg/m^2 is not adequately reflected in her categorization in the poor weight outcome group. Therefore, it is important to stress individual courses.

REFERENCES

1. Herzog W, Rathner G, Vandereycken W: Long-term course of anorexia nervosa, in The Course of Eating Disorders. Edited by Herzog W, Deter H-C, Vandereycken W. Berlin, Springer, 1992, pp 15–29
2. Steinhausen H-C, Rauss-Mason C, Seidel R: Follow-up studies of anorexia nervosa: a review of four decades of outcome research. Psychol Med 1991; 21:447–451
3. Morgan HG, Russell GFM: Value of family background and clinical features as predictors of long-term outcome in anorexia nervosa: four-year follow-up study of 41 patients. Psychol Med 1975; 5:355–371
4. Hebebrand J, Himmelmann GW, Wewetzer C, Gutenbrunner C, Heseker H, Schäfer H, Remschmidt H: Body weight in acute

anorexia nervosa and at follow-up assessed with percentiles for the body mass index. Int J Eating Disorders 1996; 19:347–357
5. Deter H-C, Herzog W: Anorexia nervosa in a long-term perspective: results of the Heidelberg-Mannheim study. Psychosom Med 1994; 56:20–27
6. Herpertz-Dahlmann BM, Wewetzer C, Remschmidt H: The predictive value of depression in anorexia nervosa: results of a seven-year follow-up study. Acta Psychiatr Scand 1995; 91:114–119
7. Remschmidt H, Wienand W, Wewetzer C: The long-term outcome of anorexia nervosa, in Anorexia Nervosa. Edited by Remschmidt H, Schmidt MH. Toronto, Hogrefe & Huber, 1990, pp 127–136
8. Steinhausen H-C, Seidel R: Outcome in adolescent eating disorders. Int J Eating Disorders 1993; 14:487–496
9. Steinhausen H-C, Amstein M, Reitle M, Seidel R: The outcome of adolescent eating disorders in two different European regions, in Eating Disorder in Adolescence: Anorexia and Bulimia Nervosa. Edited by Steinhausen H-C. Berlin, de Gruyter, 1995, pp 359–370
10. Miller R, Sigmund D: Maximally selected chi square statistics. Biometrics 1982; 38:1011–1016
11. Hebebrand J, Heseker H, Himmelmann GW, Schäfer H, Remschmidt H: Use of percentiles for the body mass index in anorexia nervosa: diagnostic, epidemiological and therapeutic implications. Int J Eating Disorders 1996; 19:359–369
12. Collins S: The limit of adaptation to starvation. Nature Med 1995; 1:810–814
13. Hebebrand J, Remschmidt H: Anorexia nervosa viewed as an extreme weight condition: genetic implications. Hum Genet 1995; 95:1–11
14. Hebebrand J, van der Heyden J, Devos R, Köpp W, Herpertz S, Remschmidt H, Herzog W: Plasma concentrations of obese protein in anorexia nervosa. Lancet 1995; 346:1624–1625