



## Original article

## Higher Caloric Intake in Hospitalized Adolescents With Anorexia Nervosa Is Associated With Reduced Length of Stay and No Increased Rate of Refeeding Syndrome

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## A B S T R A C T

**Purpose:** To determine the effect of higher caloric intake on weight gain, length of stay (LOS), and incidence of hypophosphatemia, hypomagnesemia, and hypokalemia in adolescents hospitalized with anorexia nervosa.

**Methods:** Electronic medical records of all subjects 10–21 years of age with anorexia nervosa, first admitted to a tertiary children's hospital from Jan 2007 to Dec 2011, were retrospectively reviewed. Demographic factors, anthropometric measures, incidence of hypophosphatemia ( $\leq 3.0$  mg/dL), hypomagnesemia ( $\leq 1.7$  mg/dL), and hypokalemia ( $\leq 3.5$  mEq/L), and daily change in percent median body mass index (BMI) (%mBMI) from baseline were recorded. Subjects started on higher-calorie diets ( $\geq 1,400$  kcal/d) were compared with those started on lower-calorie diets ( $< 1,400$  kcal/d).

**Results:** A total of 310 subjects met eligibility criteria (age,  $16.1 \pm 2.3$  years; 88.4% female,  $78.5 \pm 8.3$  %mBMI), including 88 in the lower-calorie group ( $1,163 \pm 107$  kcal/d; range, 720–1,320 kcal/d) and 222 in the higher-calorie group ( $1,557 \pm 265$  kcal/d; range, 1,400–2,800 kcal/d). Neither group had initial weight loss. The %mBMI increased significantly ( $p < .001$ ) from baseline by day 1 in the higher-calorie group and day 2 in the lower-calorie group. Compared with the lower-calorie group, the higher-calorie group had reduced LOS ( $13.0 \pm 7.3$  days versus  $16.6 \pm 9.0$  days;  $p < .0001$ ), but the groups did not differ in rate of change in %mBMI ( $p = .50$ ) or rates of hypophosphatemia ( $p = .49$ ), hypomagnesemia ( $p = 1.0$ ), or hypokalemia ( $p = .35$ ). Hypophosphatemia was associated with %mBMI on admission ( $p = .004$ ) but not caloric intake ( $p = .14$ ).

**Conclusions:** A higher caloric diet on admission is associated with reduced LOS, but not increased rate of weight gain or rates of hypophosphatemia, hypomagnesemia, or hypokalemia. Refeeding hypophosphatemia depends on the degree of malnutrition but not prescribed caloric intake, within the range studied.

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### IMPLICATIONS AND CONTRIBUTION

In adolescents hospitalized with anorexia nervosa, commencing refeeding with 1,400–2,000 kcal/d is associated with reduced length of stay and no increased rates of hypophosphatemia, hypomagnesemia, or hypokalemia, compared with starting on  $< 1,400$  kcal/d. Refeeding hypophosphatemia depends on the degree of malnutrition but not prescribed caloric intake. Concerns about refeeding syndrome should not limit amount of calories prescribed, within the range studied.

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Hospitalized adolescents with anorexia nervosa (AN) are frequently started on low-calorie diets, based on national and international guidelines, because of concerns about refeeding syndrome [1–3]. The refeeding syndrome is a life-threatening constellation of clinical and metabolic changes induced by refeeding a malnourished patient, and is most likely to occur during the first week of refeeding. Those <70% of expected body weight are at particular risk [4,5]. The clinical features of the refeeding syndrome reflect cardiovascular, hematologic, respiratory, and neuromuscular compromise including arrhythmias, cardiac failure, hemolytic anemia, acute respiratory failure, seizures, coma, and sudden death [6,7]. Multiple case reports have described refeeding syndrome in AN [4,8–15]. Hypophosphatemia is the biochemical hallmark of the syndrome [4,6,7], but hypomagnesemia and hypokalemia may also contribute to the clinical consequences. Early detection and correction of these electrolyte abnormalities can help avert the full clinical syndrome [5,16,17].

Weight gain is an important early component of the treatment of AN, and is necessary to reverse the medical complications and enable effective psychological intervention. Hypocaloric diets can be associated with initial weight loss and prolonged length of stay (LOS). Garber et al. [18] recently found that starting patients on a diet of 1,200 kcal/d was associated with initial weight loss in 83% of subjects and significant weight gain was achieved only after 8 days of hospitalization. They found that prescribing higher calories at baseline was significantly associated with faster weight gain and shorter hospitalization. By “starting low and going slow,” both the amount and the rapidity of weight gain may be compromised.

Whereas initial weight loss during nutritional rehabilitation of malnourished patients is well known [19,20], the safety of more aggressive refeeding protocols has not been well studied. The risk of developing the refeeding syndrome needs to be balanced against the benefits of more rapid weight gain. Before national recommendations are revised, we need scientific evidence to demonstrate the safety and efficacy of more aggressive protocols. Such studies should include a large number of participants, and should specifically include subjects at highest risk for developing the refeeding syndrome: those <70% expected body weight.

The aim of the present study was to determine the effect of higher caloric intake on daily weight gain, LOS, and incidence of hypophosphatemia, hypomagnesemia, and hypokalemia in a large sample of hospitalized adolescents with AN, admitted to a tertiary children’s hospital for medical instability. We hypothesized that higher caloric intake would increase rate of weight gain and reduce LOS, and would not be associated with increased incidence of hypophosphatemia, hypomagnesemia, or hypokalemia.

## Methods

### Study population

Eligible subjects were adolescents aged 10–21 years with AN admitted to Lucile Packard Children’s Hospital inpatient eating disorders unit for medical stabilization, whose first admission occurred between January 2007 and December 2011. A child psychiatrist made the diagnosis of AN on presentation by according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition [21]. Criteria for admission to the unit include one or more of the following: severe malnutrition (<75% expected body weight), vital sign instability, (heart rate

<50 beats/minute during the day or 45 beats/minute at night), hypotension <90/45 mm Hg, hypothermia <36.3°C, orthostatic changes in pulse and blood pressure, dehydration, electrocardiographic abnormalities, or electrolyte disturbances, according to published national guidelines [1,22,23]. Patients with bulimia nervosa or eating disorder not otherwise specified were excluded. For subjects who were readmitted during the study period, only the first admission was included, to ensure that the response to refeeding analyzed in this study would not reflect prior medical interventions. Subjects who were transferred from another facility after nutritional rehabilitation had already been initiated, those who signed out against medical advice before they were medically stable, and those requiring nasogastric feeding were excluded.

### Study design

Electronic medical records of eligible subjects with AN were retrospectively reviewed. Duration of illness, rate of weight loss, demographic factors (age, race, and sex), anthropometric measures (height and daily weight), and the presence or absence of hypophosphatemia ( $\leq 3.0$  mg/dL), hypomagnesemia ( $\leq 1.7$  mg/dL), and hypokalemia ( $\leq 3.5$  mEq/L) were recorded. Duration of illness was ascertained from the history and physical performed by the admitting physician using a standardized template. One investigator (C.K.M.), a registered dietitian, reviewed the recorded 24-hour diet recall obtained by the unit dietitian in an interview with the patient within 24 hours of admission. Prescribed caloric intake on the first day of hospitalization and on the day of discharge were reviewed and recorded by C.K.M.

Body mass index (BMI) was calculated using the formula:  $BMI = \text{weight in kilograms} / \text{height in meters}^2$ . Median BMI (mBMI), the 50th percentile BMI for exact age, was determined using the sex-specific 2000 Centers for Disease Control and Prevention BMI-for-age growth charts for children and adolescents aged 2–20 years (<http://www.cdc.gov/growthcharts>). Percent median BMI (%mBMI) was calculated by dividing daily BMI by median BMI  $\times 100$ .

Baseline weight was defined as the weight obtained at 0600 hours on the first full day after admission. For each subject, change in %mBMI was calculated for each day of hospitalization from baseline. Length of stay was defined as the number of days from admission to discharge. Rate of change of %mBMI was calculated by dividing the total percent change in mBMI by the number of days hospitalized. Subjects started on a higher-calorie diet ( $\geq 1,400$  kcal/d) were compared with those started on lower-calorie diets (<1,400 kcal/d). The reason for selecting this cutoff is that most protocols based on the belief that caloric content predisposes to refeeding syndrome will start patients on <1,400 kcal/d.

The Stanford University Human Subjects Research Committee reviewed the protocol. A waiver of informed consent and a Health Insurance Portability and Accountability Act–compliant waiver of individual authorization were granted. The Stanford University Institutional Review Board approved data collection protocols.

### Protocol for refeeding and monitoring of daily weight and electrolytes on our unit

Weight is obtained daily at 0600 hours post-void in a hospital gown only. Three meals and two snacks are prescribed. All meals

and snacks are supervised by a staff member and any missed portions are replaced with a high-calorie liquid supplement. Before 2008, because of concerns about refeeding syndrome, patients were usually started on 1,000–1,200 kcal/d depending on their 24-hour diet recall on the day before admission. Since 2008, initial caloric prescriptions have been increased to 1,400–2,000 kcal/d with no other major changes to the program. Initial caloric prescription is decided by individual physicians on admission, based on their assessment of the degree of malnutrition and caloric intake preceding admission. Prescribed calories are increased by approximately 200 kcal every 24–48 hours, based on a daily weight gain goal of .2–.5 kg/d. Patients receive a balanced diet composed of approximately 40%–50% carbohydrate, 25%–30% protein, and 25%–30% fat, supplemented by a high-calorie liquid supplement consisting of 60% carbohydrate, 15% protein, and 25% fat. In a minority of cases, in which patients either refuse to eat at all or are unable to achieve adequate calories orally, nasogastric feeding is utilized in addition to oral food. Serum chemistries including magnesium and phosphorus are drawn on admission, and thereafter at 0600 hours every 24–48 hours for the first week, and afterward as clinically indicated. If phosphorus is  $\leq 3.0$  mg/dL, sodium potassium phosphate is administered, 250 mg/packet (8 mmol phosphorus and 7.1 mEq potassium), one to two packets three times a day by mouth. Some providers supplement phosphorus when levels approach 3.0 mg/dL (3.1–3.5 mg/dL) in severely malnourished patients in whom phosphorus levels are rapidly dropping.

For hypomagnesemia ( $\leq 1.7$  mg/dL), magnesium is supplemented as magnesium amino acids chelate (133 mg elemental magnesium per tablet), one to two tablets up to three times a day by mouth. Patients are discharged when their vital signs are stable for 24 hours, with weight  $> 75\%$  mBMI.

#### Statistical analysis

The primary outcome variable was the difference in rate of change of %mBMI between groups. Secondary outcome variables were differences in LOS and incidence of hypophosphatemia, hypomagnesemia, and hypokalemia between groups. Results were analyzed using independent *t* test for continuous variables and chi-square analysis for categorical data. For continuous variables, Levene's test was used for equality of variance and the Mann-Whitney U test was used when significant difference in variance was detected. The paired *t* test was used to compare change in %mBMI from baseline on each day of hospitalization. Multivariable linear regression was used to determine the effect of initial prescribed calories (treated as a continuous variable) on the rate of change of weight gain (controlling for potential confounders). The dependent variable was the rate of change of %mBMI during hospitalization. The predictor variables were: initial prescribed calories (treated as a continuous variable); kcal from 24-hour dietary recall from the day before admission, and %mBMI on admission and year of admission. We also included an interaction term between %mBMI on admission and initial prescribed calories (which was the product of these two variables). Date of admission was included in this model because of the change in our clinical practice that began in 2008. Logistic regression analysis was used to determine the effect of initial prescribed calories treated as a continuous variable on the presence of hypophosphatemia, hypomagnesemia, or hypokalemia. The dependent variable for this model was the development of hypophosphatemia, hypomagnesemia, or hypokalemia.

The predictor variables were: initial prescribed calories (continuous variable); kilocalories from 24-hour dietary recall from the day before admission; rate of weight loss before admission; year of admission; and initial %mBMI. Subgroup analyses were conducted for patients who were severely malnourished ( $<70\%$  mBMI). Data are presented as mean  $\pm$  standard deviation. Results were analyzed using SPSS v19.0 software (SPSS Inc, Chicago, IL).

#### Results

During the 5-year study period, 330 subjects met eligibility criteria for inclusion into the study. Twenty subjects were excluded for the following reasons: transferred from another facility ( $n = 10$ ), required nasogastric feeding ( $n = 8$ ), and signed out against medical advice before medically stable ( $n = 2$ ). The study sample was therefore composed of 310 subjects. They were predominantly female (88.4%) and Caucasian (82.9%). Mean age was  $16.1 \pm 2.3$  years (range, 10.4–21 years). They had lost on average  $13.7 \pm 9.6$  kg over a period of  $1.1 \pm 1.0$  years. Subjects were moderately malnourished ( $78.5 \pm 8.3\%$  mBMI) with a mean BMI of  $16.0 \pm 1.8$  kg/m<sup>2</sup>.

Table 1 shows that 88 subjects were in the lower-calorie group ( $1,163 \pm 107$  kcal/d; range, 720–1,320 kcal/d) and 222 in the higher-calorie group ( $1,557 \pm 265$  kcal/d; range, 1,400–2,800 kcal/d). In the higher-calorie group, 90% of subjects received 1,400–1,800 kcal/d and 95% received 1,400–2,000 kcal/d. At baseline, there were no significant differences in age, weight loss, rate of weight loss, 24-hour dietary recall on the day before admission, admit weight, admit BMI or %mBMI between groups. However, those started on a lower-calorie diet had been ill longer ( $p = .002$ ). At the end of hospitalization, absolute weight gain was higher in the lower-calorie group ( $p = .01$ ) but after correction for their longer LOS, rate of change of %mBMI did not differ between groups. Neither group had initial weight loss. The %mBMI increased significantly from baseline by day 1 in the higher-calorie group ( $p < .001$ ) and by day 2 in the lower-calorie group ( $p < .001$ ). By multivariable regression analysis, rate of change of %mBMI was significantly associated with lower %mBMI

**Table 1**  
Demographic and clinical features: higher-calorie versus lower-calorie groups

	Lower-calorie intake (n = 88)	Higher-calorie intake (n = 222)	<i>p</i>
Age, year	16.2 $\pm$ 2.4	16.1 $\pm$ 2.3	.69
Duration illness, year	1.39 $\pm$ 1.3	1.00 $\pm$ .9	.002
Weight loss, kg	14.4 $\pm$ 11.0	13.4 $\pm$ 9.0	.45
Rate of weight loss, kg/mo	1.6 $\pm$ 1.4	1.6 $\pm$ 1.6	.97
24-h dietary recall, kcal/24 hours	886 $\pm$ 631	973 $\pm$ 558	.30
Admit weight, kg	41.8 $\pm$ 6.5	42.9 $\pm$ 7.5	.21
Admit BMI, kg/m <sup>2</sup>	15.9 $\pm$ 2.2	16.1 $\pm$ 1.7	.48
Admit %mBMI	77.9 $\pm$ 9.6	78.7 $\pm$ 7.8	.44
Initial prescribed calories	1,163 $\pm$ 107	1,557 $\pm$ 265	<.001
Discharge BMI, kg/m <sup>2</sup>	17.2 $\pm$ 1.9	17.1 $\pm$ 1.5	.63
Discharge %mBMI	84.3 $\pm$ 8.2	83.7 $\pm$ 6.9	.54
Discharge calories	2,531 $\pm$ 608	2,560 $\pm$ 598	.70
Weight gain, kg	3.6 $\pm$ 2.3	2.9 $\pm$ 1.9	.01
% Change mBMI	9.3 $\pm$ 6.9	7.2 $\pm$ 5.5	.01
Rate of change %mBMI	.57 $\pm$ .30	.55 $\pm$ .37	.50
Length of stay, days	16.6 $\pm$ 9.0	13.0 $\pm$ 7.3	<.0001

Data are means  $\pm$  standard deviation.

BMI = body mass index; mBMI = mean BMI.

**Table 2**

Multivariable regression analysis of effects of initial prescribed calories, 24-hour dietary recall, percent mean body mass index on admission (mBMI), and date of admission on rate of change of percent mBMI

Model	Standardized coefficient, $\beta$	<i>p</i>
Constant		.63
%mBMI on admission	-.347	<.0001
Initial prescribed calories	-.026	.69
24-hour recall of calorie intake	-.059	.33
Admit date, year	-.013	.84

at baseline ( $p \leq .0001$ ) but not with initial prescribed calories ( $p = .69$ ), 24-hour dietary recall ( $p = .33$ ), or date of admission ( $p = .84$ ) (Table 2). There was no evidence of interaction between initial %mBMI and initial prescribed calories treated as a continuous variable ( $p = .92$ ).

Length of hospital stay was significantly shorter in the high-calorie group  $13.0 \pm 7.3$  days versus  $16.6 \pm 9.0$  days;  $p \leq .0001$ . A total of 49 subjects developed hypophosphatemia (15.8%), 47 developed hypomagnesemia (15.2%), and 62 developed hypokalemia (20.0%). Figure 1 shows there was no significant difference in the rates of hypophosphatemia ( $p = .49$ ), hypomagnesemia ( $p = 1.0$ ), or hypokalemia ( $p = .35$ ) in the higher-calorie group compared with the lower-calorie group. No subjects in either group developed clinical refeeding syndrome. By logistic regression, hypophosphatemia was associated with % mBMI on admission ( $\beta = -.055$ ;  $p = .004$ ) and rate of weight loss prior to admission ( $\beta = .2$ ;  $p = .03$ ), but not caloric intake on admission ( $\beta = -.001$ ;  $p = .14$ ).

A total of 49 subjects were <70% mBMI on admission. In this subgroup, mean %mBMI was  $65.1\% \pm 3.8\%$  (range, 51%–69.9%) and mean BMI was  $13.7 \pm 1.2$  (range, 11.0–16.6). Of the 49 subjects in this severely malnourished group, 31 were in the

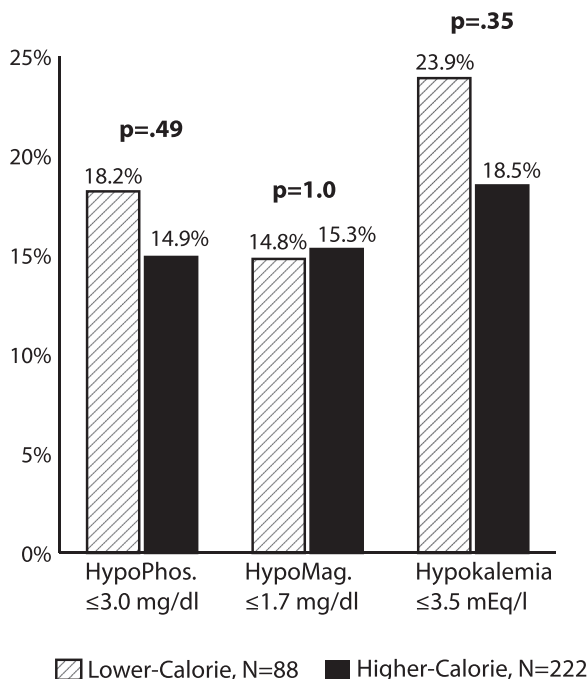
higher-calorie group and 18 were in the lower-calorie group. Those in the lower-calorie group had lost more weight than those in the higher-calorie group,  $22.5 \pm 13.2$  kg versus  $13.1 \pm 7.5$  kg,  $p = .01$ , but there were no other significant differences between groups in demographic or clinical variables. Similar to the total group, there was no significant difference in rate of change of %mBMI between groups. Length of stay was  $20.2 \pm 9.0$  days in the higher-calorie group compared with  $23.1 \pm 10.5$  days in the lower-calorie group. This difference did not reach statistical significance in this smaller sample, but the magnitude of the difference (approximately 3 days) is similar to that seen in the larger sample. In the higher-calorie group 8 of 31 (25.8%) developed hypophosphatemia, compared with 7 of 18 subjects (38.9%) in the low-calorie group,  $\chi^2 = .92$ ,  $p = .34$ . The incidence of both hypomagnesemia and hypokalemia was similar in the higher-calorie group and the lower-calorie group (5 of 31 [16.1%] versus 3 of 18 [16.7%],  $\chi^2 = .002$ ,  $p = .96$ ; and 8 of 31 [25.8%] versus 4 of 18 [22.2%],  $\chi^2 = .08$ ,  $p = .78$ ), respectively.

## Discussion

The results of our study demonstrate that in adolescents hospitalized with AN, starting patients on an average of 1,550 kcal/d (range, 1,400–2,000 kcal/d) is associated with reduced LOS and is not associated with increased rates of hypophosphatemia, hypomagnesemia, or hypokalemia. No subjects in either group developed clinical refeeding syndrome. Most important, we found no evidence of an association between higher prescribed calories and refeeding syndrome in those who are severely malnourished (<70% mBMI). Although statistical power was limited in this subgroup, the trend was toward lower rates of hypophosphatemia and hypokalemia in the higher-calorie group.

Our findings are in support of those of Garber et al. [18], who also found that higher caloric intake on admission predicted shorter hospital stay. Reduction in LOS is important not only because it reduces cost of treatment, but also because it enables the adolescent to return home sooner, where family-based treatment, the most effective treatment for adolescent with AN [24], can be initiated or continued. Earlier studies, also conducted in adolescents with AN, demonstrated initial weight loss for 5–8 days when started on hypocaloric diets of 1,000–1,200 kcal/d [18,20]. In contrast to these studies, in our present study, the higher-calorie group gained weight within 1 day and the lower-calorie group gained weight within 2 days of admission. The most likely reason for these differences is the higher amount of calories prescribed on admission. However, despite a greater rapidity of onset of weight gain and reduced LOS in the higher-calorie group, after correcting for LOS, we did not find an increase in the rate of weight gain in the higher-calorie group. This finding is in contrast to the study of Garber et al., in which the rate of weight gain was also higher in those prescribed higher calories. The reasons for these differences in rate of weight gain are not clear. One possible explanation is that in the study of Garber et al., although patients were started on fewer calories, they were discharged on more calories than were our patients ( $2,668 \pm 387$  kcal/d compared with  $2,547 \pm 603$  kcal/d). Presumably, caloric intake was increased more rapidly in that study.

Other investigators have documented the safety of more aggressive refeeding protocols in hospitalized patients with AN. In a small sample of 46 admissions of 29 adolescents with AN,



**Figure 1.** Prevalence of hypophosphatemia, hypomagnesemia and hypokalemia: higher-calorie vs. lower-calorie intake.

Whitelaw et al. [25] found that a protocol starting patients on a minimum of 1,900 kcal/d was associated with mild hypophosphatemia (serum phosphorus <3.4 mg/dL) in 38% of subjects, but was otherwise safe. In a population of severely malnourished young adults with AN (mean BMI,  $11.3 \pm .7$  kg/m<sup>2</sup>), Gentile et al. [26] utilized higher caloric intakes than recommended by current guidelines by using a combination of nasogastric and oral feeding, and demonstrated that with prophylactic supplementation of thiamine, phosphate, and potassium on a specialized unit, no subjects developed refeeding syndrome. Caloric prescription was based on indirect calorimetry measurements of resting energy expenditure. They argued that even the most severely malnourished patients could safely be treated on specialized units with careful monitoring. There is no consensus regarding prophylactic administration of phosphorus supplementation during the first weeks of nutritional rehabilitation, or whether to supplement phosphorus only when levels drop. A recent survey of adolescent medicine practitioners in North America who treat patients with eating disorders confirmed the wide variations in clinical practice in this regard [27].

With good reason, concerns about the refeeding syndrome have led to cautious recommendations regarding refeeding malnourished patients. The results of our study demonstrate that hypophosphatemia was associated with the degree of malnutrition, but not prescribed caloric intake. The relationship between both the refeeding syndrome and hypophosphatemia and the degree of malnutrition is well known [4,5,14,15,25,28], but there is an assumption that the refeeding syndrome is associated with the amount of calories prescribed during refeeding, without good data to support such an assumption. Case reports have shown that the refeeding syndrome can develop while consuming a wide variety of caloric intakes, including intakes as low as 500–800 kcal/d [4,15]. Whereas some organizations have deliberately avoided recommending a specific starting caloric amount to avoid refeeding syndrome, based on lack of available data [22,23], other organizations have made specific recommendations. The Academy of Nutrition and Dietetics recommends starting at 1,000–1,200 kcal/d, with incremental advances to achieve a weight gain of .5–1.0 lb/week [2]. The American Psychiatric Association recommends starting at 1,000–1,600 kcal/d [1]. The National Institute for Health and Clinical Excellence recommends starting on a maximum intake of 10 kcal/kg/d (500 kcal/d for a patient weighing 50 kg) for adults at high risk of developing refeeding problems (defined as those with one or more of the following: BMI <16 kg/m, unintentional weight loss > 15% within the prior 3–6 months, little or no nutritional intake for > 10 days or low levels of phosphate, magnesium, or potassium before feeding) [3]. These guidelines pertain to adults and not specifically to those with eating disorders. Caution is certainly warranted, especially in those who are severely malnourished, but the caution may need to focus more on careful monitoring of electrolytes and cardiac function than on the amount of calories prescribed. Even though electrolytes can be normal on admission, hypophosphatemia, hypomagnesemia, and hypokalemia may develop only after refeeding has been initiated, so electrolyte abnormalities and cardiac arrhythmias need to be anticipated and promptly treated to prevent clinical refeeding syndrome.

The predominant theory for the development of refeeding syndrome is electrolyte shifts from the extracellular to intracellular spaces with refeeding, stimulated by insulin secretion in response to reintroduction of carbohydrate. The intracellular

shifts of these minerals result in a drop of serum phosphorus, magnesium, and potassium, which can lead to cardiac and neuromuscular dysfunction. Whereas hypophosphatemia tends to occur early in refeeding, hypomagnesemia tends to occur later [28]. Because it is the carbohydrate component of the diet that primarily initiates the insulin surge, some investigators have advocated that development of hypophosphatemia depends more on the carbohydrate content of the diet rather than the amount of calories, and they have recommended restricting the carbohydrate content of the diet to <40% of total daily energy intake [29]. Our patients received balanced diets supplemented by a high-calorie liquid supplement, but we did not specifically document the macronutrient composition of daily meals for each patient.

The major strength of our study is the large sample size. We believe this to be the largest study of nutritional rehabilitation in adolescents with AN. Our sample also includes 49 subjects with severe malnutrition, who therefore were at highest risk for development of refeeding syndrome. In addition, our patients were all admitted to a specialized unit in which data were collected systematically. Data were collected on weight loss and caloric intake before admission, in addition to %BMI, which provided a richer assessment of the degree of malnutrition. The major limitation of this study is that it is a retrospective study subject to systematic bias. Subjects were not randomized into higher-calorie or lower-calorie groups, and the initial caloric prescription was made by individual providers based on their clinical assessments of the patient, which included the degree of malnutrition as well as the severity of caloric restriction in the days before admission. Furthermore, our reported prevalence of hypophosphatemia is an underestimate because some providers elected to supplement phosphorus prophylactically before levels dropped below 3.0 mg/dL. Finally, there is not a large difference in the amount of calories prescribed between the two groups, which may explain the lack of difference in rate of weight gain.

We agree with the comments of Katzman [30] that there is a need to challenge existing recommendations with scientific evidence demonstrating safety and efficacy of different protocols. The results of our study add to that body of literature to inform clinical practice. Our results demonstrate that in hospitalized adolescents with AN, compared with starting on a caloric intake of approximately 1,160 kcal/d, a higher caloric diet of approximately 1,550 kcal/d is associated with reduced LOS and no increased rates of refeeding syndrome. We found that refeeding hypophosphatemia depended on the degree of malnutrition but not prescribed caloric intake, within the range studied. Our study suggests that concerns about refeeding hypophosphatemia have unnecessarily limited the amount of calories prescribed to hospitalized adolescents with AN, and more aggressive feeding protocols should be implemented.

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