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Effect of Nutritional Rehabilitation on Gastric Motility and Somatization in Adolescents with Anorexia

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Abstract

Objective—To examine gastric function, as well as the presence of somatic complaints, anxiety symptoms, and functional gastrointestinal disorders (FGIDs), in adolescents with anorexia nervosa (AN) before and after nutritional rehabilitation.

Study design—Sixteen females with AN and 22 healthy controls with similar demographic profiles were included. Gastric emptying (measured as residual gastric volume) and gastric accommodation (measured as postprandial antral diameter) were assessed with abdominal ultrasonography. Participants completed the Children's Somatization Inventory (CSI), the Screen for Child Anxiety-Related Emotional Disorders, and the Questionnaire on Pediatric Gastrointestinal Symptoms–Rome III version. All testing was repeated 3–4 months later.

Results—Body mass index in the AN group improved over time ($P = .012$). Fasting gastric parameters were similar in the 2 groups. Maximum postprandial antral diameter was significantly greater in controls compared with the AN group ($P = .008$). Only adolescents with AN demonstrated a significant increase in maximum postprandial diameter at repeat testing ($P = .009$). There was no difference in residual gastric volume between the 2 groups. Initial CSI scores were higher in adolescents with AN ($P < .0001$), including higher scores for nausea and abdominal pain. CSI scores were significantly lower in adolescents with AN ($P = .035$). Initial scores on the Screen for Child Anxiety-Related Emotional Disorders were significantly higher in adolescents with AN ($P = .0005$), but did not change over time. Adolescents with AN met significantly more criteria for FGIDs ($P = .003$).

Conclusion—Adolescents with AN have impaired gastric accommodation that improves after nutritional rehabilitation, have significantly more somatic complaints, and meet more criteria for anxiety disorders and FGIDs. After nutritional rehabilitation, somatization improves and FGIDs become less common, but symptoms of anxiety persist.

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The authors declare no conflicts of interest.

Disordered eating behaviors and weight concerns are common among adolescents. Almost two-thirds of adolescent girls and almost one-third of adolescent boys report trying to lose weight, and almost 50% of adolescent girls use unhealthy measures in an attempt to lose weight.[1] Eating disorders affect more than 11 million people in the US alone. Anorexia nervosa (AN) is the third most common chronic illness in female adolescents and young adults, after obesity and asthma, and carries significant medical, social, psychological, and economic costs.[2–5] AN is a clinical diagnosis characterized by the refusal to maintain body weight at or above a minimally normal level for age and height, as well as an intense fear of gaining weight and a disturbance in body image.[6] Although the etiology and pathogenesis of AN remain unclear, the morbidity and mortality are profound, and the majority of affected patients are diagnosed with comorbid psychiatric disorders.[7,8]

AN is associated with a variety of medical complications, with gastrointestinal disturbances particularly common.[9] Bloating, nausea, abdominal distension, and gastric fullness are reported in as many as 78% of those with AN, and multiple studies in adults with AN have demonstrated delayed gastric emptying.[10–12] Currently, scintigraphy is considered the gold standard for measuring gastric emptying, and the barostat balloon and single photon emission computed tomography testing are used to measure gastric volume and assess gastric accommodation.[13] These methods have several disadvantages, however, particularly in the pediatric population, including exposure to ionizing radiation, the invasive nature of the studies, increased expense, and the need for specialized equipment and training. Ultrasonography offers a safe, well-tolerated alternative to these methods of assessing gastric emptying and gastric volumes,[14–19] and has been validated against the gold standard.[20,21] There is strong evidence indicating that the longer the duration of illness, the more difficult the recovery.[22] This suggests that the prevention of long-term comorbidity in adolescents with AN through early detection and treatment is possible. Improved understanding of the pathophysiology of gastrointestinal symptoms may be useful in the treatment of adolescents with AN, who are more likely to respond to concrete statements about the effects of malnutrition and poor eating habits on their physical health.[2]

In this prospective controlled study, we sought to examine the differences in gastric motility and accommodation in pediatric patients with AN before and after nutritional rehabilitation, and to examine the differences in self-reporting of somatic complaints, anxiety symptoms, and functional gastrointestinal disorders (FGIDs) between healthy controls and adolescents with AN before and after nutritional rehabilitation.

Methods

The study subjects included female patients with AN aged 10–21 years who met the criteria for medical admission, including severe bradycardia, orthostatic hypotension, electrolyte abnormalities, inability to maintain weight, and hypothermia. Exclusion criteria included a history of gastric surgery, concurrent use of motility agents, past history of diseases associated with gastroparesis (including, but not limited to, diabetes, cystic fibrosis, inflammatory bowel disease, and celiac disease), and inability to complete the questionnaires or provide appropriate consent/assent. Controls were age-matched females recruited from an adolescent primary care clinic and via a mass e-mail sent out to all hospital employees. The control subjects recruited from the clinic had presented for vaccinations or sports physicals. The inclusion and exclusion criteria for the control group were the same as above, with the additional exclusion criteria of a diagnosed FGID and a body mass index <5th percentile or ≥95th percentile.

After appropriate consent and assent were obtained, participants completed questionnaires regarding somatic complaints, symptoms of anxiety, and gastrointestinal symptoms and

underwent limited abdominal ultrasonography surrounding a standard liquid meal to obtain gastric measurements including, but not limited to, antral diameter and gastric emptying time (as described in detail below). This baseline/initial testing is termed T1. All analyses were repeated 14 ± 2 weeks later; this follow-up testing is designated T2. The research protocol was approved by the Nationwide Children's Hospital Institutional Review Board.

Weight, height, vital signs, medications, medical and social history, and calorie counts (with the aid of a food diary) were recorded. All ultrasound examinations were completed in the morning after an overnight fast of at least 8 hours. Patients were given a 300-mL liquid meal consisting of a 1-kcal/mL liquid supplement (Ensure; Abbott, Columbus, Ohio). Sonographic measurements (including antral diameter as a measure of gastric accommodation and gastric volumes)[14–17] were obtained just before and immediately after the meal, and then at 10-minute intervals for the next 1 hour. Multiple measurements were taken at each interval. Residual gastric volume (RGV) at the end of the 60-minute measurement period was calculated as a measure of gastric emptying. The personnel performing ultrasonography were blinded to the overall aims of the study, and the radiologist was blinded to the type of patient (AN vs control) at the time of image interpretation. All patients cooperated with ultrasonography without difficulty.

The Children's Somatization Inventory (CSI)[23,24] is a tool developed to better characterize the breadth and severity of somatic symptoms in pediatric patients. The short form is a 19-item scale. The response format is a 5-point Likert scale, with responses ranging from “not at all” (0) to “a whole lot” (4). Symptoms include headaches, abdominal pain, nausea, and bloating. The standard time period for symptom reporting is 2 weeks. Total CSI scores can range from 0 to 76, obtained by summing all item ratings, with higher scores corresponding to increased somatization. The CSI has been validated in patients with recurrent abdominal pain, school children, and healthy patients aged 6–18 years. It has demonstrated good internal consistency and test-retest reliability.

The Screen for Child Anxiety-Related Emotional Disorders (SCARED)[25] is a 41-item self-report questionnaire designed to screen for the presence of anxiety disorders in children and adolescents aged 9–18 years. The response format is a 3-point Likert scale, with responses ranging from “not true or hardly ever true” (0) to “often true or very true” (2). Total SCARED scores can range from 0 to 82, obtained by summing all item ratings, with higher scores corresponding to increased anxiety. The scale has been validated in clinical and community samples, with good internal consistency and good test-retest stability even at 12 weeks.[26]

The Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III version (QPGS-RIII)[27] is an adaptation and abbreviation of the Questionnaire on Pediatric Gastrointestinal Symptoms. The self-report version of the QPGS-RIII is suitable for administration to children 10 years of age and older. It uses a 5-point scale to measure frequency, severity, and duration of symptoms. In addition, it can be scored to assess whether a patient meets criteria for each of the individual FGIDs. The QPGS-RIII has been validated and has demonstrated good test-retest reliability.

Given a medium effect size, 2 covariates, significance level of 0.05, and power of 0.94, a minimum total sample size of 16 patients (study patients and controls) was required to detect a group difference in both gastric emptying time and gastric antral diameter between T1 and T2. For continuous variables with repeated measurements, we used the mixed procedure for comparisons between groups, with consideration of correlations within subjects. For categorical variables with repeated measurements, we used the GENMOD procedure for logistic regression, with consideration of correlations within subjects. For categorical

variables at time period 0 only, we used logistic regression. We examined correlations between gastric emptying and gastric accommodation both before and after nutrition, as well as CSI scores, SCARED scores, and QPGS-RIII scores before and after nutrition, using a paired-sample *t* test and generalized linear model. All analyses were performed using SAS 9.2 (SAS Institute, Cary, North Carolina).

Results

A total of 16 female patients with AN and 22 female controls were enrolled, and all subjects completed the study. Demographic characteristics were similar in the 2 groups (Table I; available at www.jpeds.com), although the groups did differ slightly in medication use. The patients with AN were more likely to be taking a psychotropic medication (antidepressants or anxiolytics) as treatment for a comorbid condition. One-half of the patients with AN had been diagnosed within 6 months of enrollment. As expected, daily caloric intake was significantly lower in the patients with AN compared with controls ($P < .0001$). In the AN group, caloric intake increased from <1200 kcal/day in T1 to ≥1800 kcal/day at T2 ($P < .0001$). Initial body mass index was significantly lower in the AN group compared with controls (17.3 vs 20.7; $P = .0006$), and increased from T1 to T2 in the AN group (from 17.3 to 18.3; $P = .012$).

Fasting gastric volumes and antral diameters and the time to reach maximum postprandial antral diameter were similar in the 2 groups. Maximum postprandial antral diameter was significantly greater in the controls compared with the AN group (14.08 cm^2 vs 7.9 cm^2; $P = .008$). Although controls had similar results at follow-up, the AN group showed a significant increase in maximum postprandial antral diameter at follow-up (7.9 cm^2 vs 10.8 cm^2; $P = .009$). RGV was not significantly different in the 2 groups at either T1 or T2 (Table II).

Initial CSI scores were higher in the AN group compared with controls ($P < .0001$) (Table III). The patients with AN reported higher scores on almost all 19 items on the questionnaire, including headache ($P = .007$), low energy ($P = .002$), hot or cold spells ($P = .03$), weakness ($P = .01$), nausea ($P = .0007$), constipation ($P = .0004$), diarrhea ($P = .02$), abdominal pain ($P < .0001$), bloating ($P < .0001$), and “food making you sick” ($P = .002$). CSI scores did not change over time in the controls, but decreased significantly in the adolescents with AN ($P = .035$).

Initial SCARED scores (Table IV) were significantly higher in the AN group compared with controls ($P = .0005$). These scores did not change significantly over time.

The patients with AN also met significantly more criteria for FGIDs compared with controls, with 75% meeting criteria for at least 1 FGID, vs 18% of controls ($P = .003$). Irritable bowel syndrome was the most prevalent FGID in the AN group. Nine of the 16 patients with AN (56%) met the criteria for irritable bowel syndrome at T1, and only 4 of these 16 patients (25%) met the criteria for irritable bowel syndrome at T2 ($P = .004$).

There was no correlation between the ultrasound findings (specifically RGV and maximum postprandial diameter) and questionnaire scores at either T1 or T2.

Discussion

In this study exploring disturbances in gastric motility in adolescent females with AN, the patients with AN had impaired gastric accommodation compared with healthy controls and showed improvement after nutritional rehabilitation. None of the patients with AN demonstrated delayed gastric emptying; even though this finding differs from the adult

literature, it does seem to be consistent with the major symptoms reported by our patients. Although the patients frequently complained of nausea, bloating, and abdominal pain (possibly reflecting abnormal gastric accommodation or gastric hyperalgesia), they reported less-frequent vomiting (which occurs more commonly in patients with delayed gastric emptying). This finding is an important initial step toward an improved understanding of the physiology of gastric disturbances in adolescents with AN.

Gastric motility has been shown to a key mediator of hunger and satiety.[28] Specifically, intragastric pressure has been directly correlated with satiation.[29] The antrum is particularly sensitive to distension, and increased feelings of satiety and fullness in patients with impaired accommodation may originate from the antrum.[30] Multiple studies have demonstrated the importance of gastric accommodation in relation to food intake in patients with functional dyspepsia, healthy patients, and obese patients who have undergone surgical intervention.[31–40] These studies indicate that impaired gastric accommodation is associated with decreased food intake. Although the long-term effects on body weight are not clear, it can be postulated that in patients with impaired gastric accommodation, such as the patients with AN in the present study, the feelings of increased satiety lead to decreased food intake and decreased hunger, thereby accelerating the weight loss or contributing to the inability to gain weight.

We found that the patients with AN had significantly more somatic complaints than the healthy controls. Somatization can be significant in AN and is not solely limited to gastrointestinal-specific symptoms. AN has been linked to significant levels of alexithymia[41] and reduced ability to accurately perceive bodily signals and visceral sensations.[42] This combination of alexithymia and impaired interoception likely results in poor emotional awareness and generalized somatization. In this study, somatization improved significantly after nutritional rehabilitation, as has been described in adults.[8]

Patients with AN also met more criteria for anxiety disorders and FGIDs than the healthy controls. In terms of FGIDs, adult studies have demonstrated that even after 12 months of treatment, almost 80% of adults with AN continue to meet the criteria for FGIDs,[43] suggesting that FGIDs can persist independent of treatment outcome; however, in our study cohort, FGIDs were less common at T1 than has been reported in adults. Irritable bowel syndrome was the most common FGID in our patients with AN, and even this became less common after nutritional rehabilitation, suggesting that early intervention in a younger population may help prevent the development of long-term comorbidities. Symptoms of anxiety persisted at the follow-up visit in our patients with AN. This finding is supported by long-term outcome data demonstrating that both affective disorders and anxiety disorders, such as obsessive compulsive disorder, continue to be more common in adolescents with AN compared with healthy adolescents even at 10 years after the onset of AN.[44] These data reinforce the significant psychological component in AN, and provides justification for the extended time often necessary to treat patients with AN. It also should be noted that the patients with AN not only met more criteria for anxiety disorders and FGIDs, but also were more likely to be taking a psychotropic medication for a comorbid condition. A potential relationship among gastric motility, intake of psychotropic medications, and presence of a comorbid psychiatric condition was not explored in the present study, but should be considered for future investigation.

The time frame necessary to observe changes in gastric motility after refeeding has not yet been well established. Although some studies have suggested that changes are not seen until 22 weeks of nutritional rehabilitation,[11] others have reported that gastric emptying improves after 30 ± 7 days.[45] Given the variable time courses reported in the liter-ature, we chose an interval of 14 ± 2 weeks for repeat testing, given that it may take up to 3 months of

treatment to begin to establish consistent weight recovery in AN.[46] Thus, long-term follow-up might reveal different results that those reported here.

In addition, it also has been suggested that the time to achieve recovery in AN exceeds 12 months. The risk of relapse is greatest during the initial 12-month period after diagnosis.[47] Thus, it was not surprising that although our patients with AN showed some improvement in somatization and the presence of FGIDs, they were still significantly different from healthy controls at our 3- to 4-month follow-up assessment. It also is not surprising that the symptoms of anxiety did not improve during this short study period. Follow-up at 12–15 months from the initial visit, particularly in those patients with a new diagnosis, would better coincide with true recovery.

To date, scintigraphy has been considered the gold standard for measuring gastric emptying, and the electronic barostat and single photon emission computed tomography testing have been used to measure gastric volumes and assess gastric accommodation.[13] Ultrasonography offers a safe, well-tolerated alternative to these methods. Ultrasound examination has been used to assess gastric emptying, gastric volumes, and accommodation in healthy patients,[17–19] as well as in patients with functional dyspepsia,[48] diabetes,[49] gastroesophageal reflux and esophagitis,[50] recurrent abdominal pain,[51] and obesity.[52] Ultrasonography has been shown to yield comparable results to the gold standard tests,[20,21] with antral diameter providing a measure of gastric accommodation and RGV reflecting gastric emptying, and to have good reliability and reproducibility, as well as low interobserver variation and error.[16] We further addressed variability concerns in the present study by obtaining multiple measurements of both antral diameter and gastric volume at each time point, using the same select group of ultrasonographers to perform all of the studies, and using the same radiologist to interpret all of the studies. A 4-hour scintigraphy study is more useful than the standard 1- or 2-hour study for diagnosing delayed gastric emptying.[53,54] This difference in timing has not yet been examined in ultrasound techniques, and there have been no direct comparison studies examining the difference between 4-hour scintigraphy studies and ultrasound studies.

We recognize that there are many other potential contributing factors that were not addressed in this study. These factors could include, but certainly might not be limited to, severity and duration of malnutrition, presence of purging behaviors such as self-induced vomiting, coping skills, family functioning, and symptoms of depression or other psychological factors. The gastrointestinal disturbances in AN, such as constipation and lower gastrointestinal tract function, which may affect foregut function, should be explored as well. The roles of other gastric areas, such as the fundus, and of hormones, such as motilin, also warrant further investigation, as does the use of pharmacotherapy to treat the gastric motility disturbances in patients with AN.

Larger and longer-term follow-up studies are needed to better characterize this patient population. There is also currently no consistent approach to refeeding in patients with AN. An improved understanding of the pathophysiology of gastrointestinal disturbances associated with AN could lead to the development of a more standardized approach to management in these patients and may better explain some of the symptoms, such as nausea, fullness, and early satiety, that often make it difficult to treat patients with AN.

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Glossary

AN	Anorexia nervosa
CSI	Children's Somatization Inventory
FGID	Functional gastrointestinal disorder
QPGS-RIII	Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III version
RGV	Residual gastric volume
SCARED	Screen for Child Anxiety-Related Emotional Disorders
T1	Baseline/initial testing
T2	Follow-up testing

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Table I

Demographic and clinical characteristics

Characteristic	AN group	Controls	*P* value
Age, years, mean	15.5	16.8	NS
Caucasian race/ethnicity, n	16	22	NS
Maternal education level, n (%)			NS
Some high school or high school graduate	2 (12.5)	0	
Some college or more	14 (87.5)	22 (100)	
Paternal education level, n (%)			NS
Some high school or high school graduate	2 (12.5)	2 (9)	
Some college or more	14 (87.5)	20 (91)	
Average annual household income (self-reported), n (%)			NS
<$75 000	5 (31.25)	4 (18)	
≥$75 000	11 (68.75)	18 (82)	
Family structure, n (%)			NS
Mother and father	12 (75)		
Other (including stepparents, single parents)	4 (25)		
Medications, n (%)			
Acne medications	1 (6.25)	2 (9)	NS
Contraceptives	4 (25)	6 (27)	NS
Vitamins/supplements	9 (56.25)	3 (13.6)	.007
Laxatives/stool softeners	2 (12.5)	0	NS
Psychotropic medications	9 (56.25)	2 (9)	.002
Other	8 (50)	6 (27)	NS
Time since diagnosis of AN, n (%)			
Within 6 months of enrollment	8 (50)	NA	
More than 6 months after enrollment	8 (50)	NA	
Body mass index at T1, mean	17.3	20.7	.0006
Body mass index at T2, mean	18.32	21	.02

NA, not applicable; *NS*, not significant.

Table II

Measures of gastric motility

	Maximum antral diameter at T1, cm^2	Maximum antral diameter at T2, cm^2	
AN	7.9 (SD, 2.969; SE, 0.74)	10.8 (SD, 4.452; SE, 1.19)	*P* = .009
HC	14.08 (SD, 5.113; SE, 1.07)	13.1 (SD, 4.377; SE, 0.91)	*P* = NS
	P = .008	*P* = NS	

	RGV at T1, %	RGV at T2, %	
AN	43 (SD, 31.81; SE, 7.95)	60 (SD, 26.567; SE, 7.1)	*P* = .04
HC	56 (SD, 28.413; SE, 5.92)	50 (SD, 28.242; SE, 5.88)	*P* = NS
	P = NS	*P* = NS	

HC, healthy controls. Note: Maximum antral diameter is a measure of gastric accommodation, and RGV is a measure of gastric emptying.

Table III

CSI scores

	Mean CSI score at T1	Mean CSI score at T2	
AN	26.4 (SD, 11.202; SE, 2.8)	20.3 (SD, 12.25; SE, 3.28)	$P = .035$
HC	8.5 (SD, 7.556; SE, 1.57)	8.4 (SD, 8.193; SE, 1.7)	P = NS
	$P < .0001$	$P = .04$	

Table IV

SCARED scores

	Mean SCARED score at T1	Mean SCARED score at T2	
AN	28 (SD, 11.33; SE, 2.83)	27 (SD, 11.683; SE, 3.12)	*P* = NS
HC	14.8 (SD, 10.971; SE, 2.29)	13.4 (SD, 10.32; SE, 2.15)	*P* = NS
	P = .0005	*P* = .0005	