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Clinical Features of Idiopathic Gastroparesis Vary with Sex, Body Mass, Symptom Onset, Delay in Gastric Emptying, and Gastroparesis Severity

The NIDDK Gastroparesis Clinical Research Consortium (GpCRC)*,†

Abstract

Background & Aims—Idiopathic gastroparesis (IG) is a common but poorly understood condition with significant morbidity. We studied characteristics of patients with IG enrolled in the NIDDK Gastroparesis Clinical Research Consortium Registry.

Methods—Data from medical histories, symptom questionnaires, and 4-hour gastric emptying scintigraphy studies were obtained from patients with IG.

Results—The mean age of 243 IG patients studied was 41 years; 88% were female, 46% were overweight, 50% had acute onset of symptoms, and 19% reported an initial infectious prodrome. Severe delay in gastric emptying (>35% retention at 4 hours) was present in 28% of patients. Predominant presenting symptoms were nausea (34%), vomiting (19%), and abdominal pain

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Members of the Gastroparesis Clinical Research Consortium are listed in supplemental table 1.

No conflicts of interest exist.

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(23%). Women had more severe nausea, satiety, constipation and overall gastroparesis symptoms. Patients who experienced acute onset IG had worse nausea than those with insidious onset. Overweight patients had more bloating and gastric retention at 2 hours, but less severe loss of appetite. Patients with severely delayed gastric emptying had worse vomiting, more severe loss of appetite and overall gastroparesis symptoms. Severe anxiety and depression was present in 36% and 18%, respectively. 86% met criteria for functional dyspepsia, primarily postprandial distress syndrome.

Conclusions—IG is a disorder that primarily affects young women, beginning acutely in 50% of cases; unexpectedly, many patients are overweight. Severe delay in gastric emptying was associated with more severe symptoms of vomiting and loss of appetite. IG is a diverse syndrome that varies by sex, body mass, symptom onset, and delay in gastric emptying.

Keywords

gastroparesis; gastric emptying; nausea; vomiting; functional dyspepsia

INTRODUCTION

Gastroparesis is a chronic gastric motility disorder characterized by delayed gastric emptying (1). Symptoms include early satiety, postprandial fullness, nausea, vomiting and abdominal discomfort. Gastroparesis can occur in several clinical settings, in particular as a complication of diabetes and gastric surgery. In many cases, the underlying cause is not known and the term idiopathic gastroparesis (IG) is used.

IG has significant morbidity, yet its clinical features are poorly characterized since reports have been limited by a relatively small number of patients. IG occurs more commonly in women. Two series of patients with IG published by McCallum *et al* (2) and Harrell *et al* (3) suggest that symptom onset and body mass might impact on patient presentation.

The National Insitutes of Diabetes and Digestive and Kidney Diseases (NIDDK) Gastroparesis Registry was established in 2006 in order to enroll a sufficiently large number of patients to elucidate the clinical features of gastroparesis. The aims of this study were to determine clinical and other features of IG and determine their association with gender, body mass, symptom onset, delay in gastric emptying, and gastroparesis severity.

METHODS

The NIDDK Gastroparesis Clinical Research Consortium (GpCRC) is a cooperative network of seven clinical centers and one Data Coordinating Center. The Gastroparesis Registry was implemented as an observational study of patients with gastroparesis (ClinicalTrials.gov Identifier: NCT00398801). The Registry consists of patients meeting specific entry criteria with symptoms of at least 12 weeks duration, delayed gastric emptying on scintigraphy, and no abnormality causing obstruction on upper endoscopy. Registry data at enrollment include detailed history and physical examinations, validated symptom questionnaires, upper endoscopy results (within 1 year of enrollment), 4 hour gastric emptying scintigraphy results (within 6 months of enrollment), and laboratory tests.

During face-to-face interviews with each subject, the study physicians or coordinators completed case report forms including data relating to symptoms, disease profile, associated medical conditions, and medication and supplemental therapies. Patients were questioned about the onset of their gastroparesis symptoms, being either acute or insidious onset, if they had an initial infectious prodrome with resultant chronic GI symptoms, and to specify the infectious prodrome symptoms: upper respiratory flu-like symptoms, food-poisoning

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symptoms, gastroenteritis, or other. The clinical severity of gastroparesis was graded on a scale originally proposed by Tack et al and reported in the American Neurogastroenterology and Motility Society (ANMS) review on treatment of gastroparesis (4). The severity was graded as grade 1: mild gastroparesis (symptoms relatively easily controlled and able to maintain weight and nutrition on a regular diet); grade 2: compensated gastroparesis (moderate symptoms with only partial control with use of daily medications, able to maintain nutrition with dietary adjustments); grade 3: gastric failure (refractory symptoms that are not controlled with the patient having ER visits, frequent doctor visits or hospitalizations and/or inability to maintain nutrition via oral route).

Each patient filled out the 20 item Patient Assessment of Upper Gastrointestinal Disorders Symptoms Severity Index (PAGI-SYM) questionnaire which assesses symptoms of gastroparesis, dyspepsia, and gastroesophageal reflux disease (5). It includes the nine symptoms of the Gastroparesis Cardinal Symptom Index (GCSI) which asks about nausea, retching, vomiting, stomach fullness, inability to finish meal, excessive fullness, loss of appetite, bloating, and abdominal distension (6,7). The GCSI equals the mean of the nausea/vomiting subscore, postprandial fullness/early satiety subscore, and bloating subscore where: Nausea/vomiting subscore = mean of scores for nausea, retching, and vomiting; Postprandial fullness/early satiety sub-score = mean of scores for stomach fullness, inability to finish meal, excessive fullness, and loss of appetite; and Bloating subscore = mean of scores for bloating and large stomach. The PAGI-SYM also inquires about symptoms of gastroesophageal reflux including daytime heartburn, heartburn lying down, daytime chest discomfort, nighttime chest discomfort, daytime reflux, nighttime reflux, and bitter taste. Patients are asked to assess the severity of their symptoms during the previous two weeks using a 0 to 5 scale where no symptoms = 0, very mild = 1, mild = 2, moderate = 3, severe = 4, and very severe = 5.

Psychological functioning was assessed using the Beck Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI). BDI is a widely used 21-question multiple-choice self-report inventory that relate to depression, cognition, and physical well-being and is extensively employed to quantify depression in a range of clinical conditions (8,9). Each answer is scored on a scale of 0 to 3. Higher total scores indicate more severe depressive symptoms with 29–63 indicating severe depression (8). The STAI consists of 20 questions relating to state anxiety (a temporary or emotional state) and 20 questions pertaining to trait anxiety (long standing personality trait anxiety with a general propensity to be anxious) and has been well validated (10). A score of >44 denotes significant anxiety.

A portion of the Rome III Diagnostic Questionnaire for Adult Functional GI Disorders relating to functional gastroduodenal disorders and irritable bowel syndrome was administered (11). An analysis program developed by the Rome Foundation was utilized to obtain Rome III diagnoses (http://www.romecriteria.org/rome_iii_sas/).

Gastric emptying scintigraphy was performed using a low-fat, egg white meal with imaging at 0, 1, 2, 4 hours after meal ingestion, as described by a multicenter study (12) and endorsed by the Society of Nuclear Medicine and ANMS (13). This protocol ensures standardized information about delayed gastric emptying across the seven sites. Delayed gastric emptying was graded according to the gastric retention at 4 hours: mild (≤20% gastric retention at 4 hours), moderate (>20 to 35%), and severe (>35%) (13,14).

Laboratory tests obtained on each patient included complete blood count with erythrocyte sedimentation rate (ESR) and C reactive protein (CRP).

Patients were prospectively enrolled at seven centers from January 2007 to March 15, 2010 into the ongoing NIDDK Gastroparesis Registry. This report focuses on patients with IG,

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that is, patients with delayed gastric emptying scintigraphy > 60% at 2 hours and/or > 10% at 4 hours, and the main reason for gastroparesis evaluation not being from diabetic, postsurgical causes, or other known causes.

Statistical Methods

A set of baseline characteristics including demographic, lifestyle, anthropomorphic, laboratory values, co-morbidities, co-medications, psychological evaluation test scores, gastroparesis specific medical history, gastric emptying scintigraphy results and symptom severity scores from the PAGI-SYM were analyzed in both univariable and multivariable logistic regression analyses to show the pattern of these characteristics among IG patients and to also show variations in these patterns across five major IG patient sub-groups: (1) sex – female vs. male, (2) body mass – overweight vs. normal, (3) symptom onset – acute vs. insidious, (4) severity of delay in gastric retention at 4 hours – mild, moderate or severe, and (5) gastroparesis severity using gastroparesis severity scale and symptom severity based on GCSI score. Univariable results are expressed as mean ± standard deviation (SD) or by percentages, where appropriate. The statistical significance of differences in clinical features within each of the IG sub-groups was tested using either a chi-square test for non-ordered categories, Fisher's exact test, or a Cochran-Armitage test for trend for ordered categorical features. Continuous features were analyzed using a Wilcoxon rank sum test or a Kruskal-Wallis test (15). A series of six bi-directional stepwise (forward and backward) multiple binary logistic regression analyses were used to determine the independent set of characteristics associated with each of the IG sub-groups. Characteristics identified by either the forward or backward procedures were combined into a single model from which the final set of significant and independent characteristics were selected (16). A P-value of 0.05 was used both for the addition or deletion of candidate characteristics in the stepwise procedures. The results for GCSI were derived from separate analyses which did not include the nine individual symptom scores that are components of the GCSI. All final models for each IG-subgroup were found to have adequate goodness of fit. All *P* values are two-sided, nominal, with a level of 0.05 considered to be statistically significant.

For analyses, both SAS v9.1 (SAS Institute, Cary, NC) and Stata release 11 (Stata Corp, College Station, TX) statistical software were used (17).

RESULTS

Demographic Information

243 patients with IG were enrolled in the NIDDK Registry at the time of data analysis (March 15, 2010). This represented 61% of the total number of patients with delayed gastric emptying enrolled (243 idiopathic, 131 diabetic, 27 other causes). Of the 243 patients with idiopathic gastroparesis, 214 (88%) were female and 218 (90%) were white (Table 1). At the time of enrollment, the mean age was 41±14 (SD) years with 30% age 30 years or less. Mean BMI was 25.6±6.9 kg/m^2 with 8% underweight (BMI<18), 47% normal weight (BMI 18 to <25), 20% overweight (BMI 25 to 30), and 26% obese (BMI>30). One third of the IG patients were well educated with college education or higher and over half had annual incomes of $50K or higher.

The predominant symptom prompting evaluation of these patients was nausea in 34%, vomiting in 19%, abdominal pain in 23%, bloating in 7%, and gastroesophageal reflux in 6%. Overall, 22% of patients reported chronic stable symptoms, 34% described their symptoms as chronic and worsening, 33% reported chronic symptoms with periodic exacerbations, while 11% had a cyclic pattern of symptoms. 29% had refractory symptoms and could not maintain nutrition orally (gastric failure). The onset of symptoms of

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gastroparesis was acute in 50% and 19% of patients reported an infectious prodrome with onset of their gastroparesis symptoms. In these patients with IG, 36% scored severe for anxiety state and 35% scored severe for anxiety trait on the STAI, and 18% scored severe depression on the BDI. Patients averaged 3.6 other comorbidities including migraine headaches in 40%, fibromyalgia in 13%, and chronic fatigue syndrome in 9%.

Gender

Female patients comprised 214 of the 243 (88%) patients with gastroparesis (Table 1). Fewer females were overweight (25–30 kg/m^2 BMI) (17% vs 41%, P=0.002) or had ever smoked regularly (30% vs 55%, P=0.008) compared to males. More females than males had migraine headaches (43% vs 24%, P=0.05). Females had an average of 7% higher gastric retention at 4 hours compared to males (28.9±19.4% vs 22.2±13.3%, P=0.10). Females had higher symptom severity scores than male patients for nausea (3.6±1.3 vs 2.8±1.7, P=0.02), stomach fullness (3.8±1.1 vs 3.0±1.3, P<0.001), inability to finish a meal (3.7±1.3 vs 2.8±1.7, P=0.003), excessive fullness after a meal (3.8±1.2 vs 3.2±1.5, P=0.05), bloating (3.4±1.5 vs 2.7±1.6, P=0.03), visible stomach distention (3.0±1.8 vs 2.0±1.9, P=0.008) and constipation (2.6±1.8 vs 1.4±1.5, P<0.001). The GCSI score was higher in females than in males (3.1±1.0 vs 2.5±1.1, P=0.008).

The 12 features associated with females with IG compared to males with IG identified from multiple logistic regression (Table 4) were: drank alcohol in past year (OR=3.49, P=0.04), higher waist to hip ratio category (overall P=0.002), less likely to be overweight or obese (OR=0.14, P=0.002), higher ESR (OR=1.89, P=0.004), more migraine headaches (OR=3.34, P=0.05) and anxiety disorder (7.92, P=0.03), less clinically severe depression (using BDI) (OR=0.20, P=0.01), more severe symptoms at enrollment including nausea (1.69, P=0.02), stomach fullness (OR=1.94, P=0.01), and constipation (OR=1.48, P=0.03), and less severe upper abdominal discomfort (OR=0.55, P=0.02) and diarrhea (OR=0.63, P=0.02). GCSI score was also higher in female compared to male IG patients (OR=1.89, P=0.02).

Body mass

Of 243 patients with idiopathic gastroparesis, 132 (54%) were either normal weight or underweight whereas 111 (46%) were overweight or obese, which for further analysis, were pooled and labeled overweight (Supplemental Table 2). Overweight (BMI≥25 kg/m^2) IG patients were older at symptom onset (38.1±14.4 vs 34.5±14.7 years, P=0.05) and were less educated (20% vs 44% college or more, P<0.001) than those who were not overweight (BMI<25 kg/m^2). Overweight patients had similar type of symptom onset compared to normal weight individuals (52% vs 48% acute onset, P=0.40). An infectious-like prodrome was present in only 11% of overweight patients compared to 25% of normal weight patients (P=0.005). Increased gastric retention at 2 hours was more likely in overweight compared to normal weight patients (67±17% vs 60±16% retention, P=0.001), but gastric emptying was not significantly different at 4 hours (31±21 vs 26±17%, P=0.19). Patients who were overweight had elevated inflammatory markers compared to normal weight patients (ESR: 19±16 vs 10±13 mm/hr, P<0.001; and CRP: 0.9±1.2 vs 0.5±1.2, P<0.001). Overweight patients reported less severe loss of appetite (2.7±1.5 vs 3.4±1.4, P<0.001), had a lower score for inability to finish a meal (3.4±1.4 vs 3.8±1.4, P=0.02) and had higher gastroesophageal reflux scores (2.2±1.4 vs 1.9±1.4, P=0.06) compared to normal weight patients.

Multiple logistic regression resulted in 11 features associated with overweight (BMI≥25 kg/m^2) versus normal weight (BMI<25 kg/m^2) IG patients: less likely to be females (OR=0.11, P<0.001), lower income (OR=0.21 $50K+, P<0.001), higher waist to hip ratio category (overall P=0.01), higher ESR (OR=1.69, P<0.001), higher CRP (OR=2.90, P=0.008),

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increased anxiety disorder (4.09, P=0.01), higher percent gastric retention at 2 hours (OR=1.03, P=0.004), increased severity of bloating (1.34, P=0.03) and lower abdominal discomfort (OR=1.79, P=0.03) and less severe appetite loss (OR=0.63, P<0.001) and lower abdominal pain (OR=0.48, p=0.009) (Table 4).

Symptom Onset

Of the 122 patients who presented with acute symptoms at onset (Supplemental Table 3), 27.1% reported an infectious etiology compared to 10% of IG patients with an insidious symptom onset (P<0.001). The average score on the BDI was lower in patients with acute symptom onset compared to those with insidious onset (17±10 vs 20±12, P=0.03), and there was less reported fibromyalgia (6% vs 20%, P=0.001) in the acute onset group. Acute onset patients reported taking more anti-emetic medications than the insidious onset group (80% vs 63%, P=0.003). Patients with acute onset had a shorter duration of symptoms (3.5±4.4 vs 6.1±7.9 years, P<0.001), and tended to have more gastric failure (34% vs 24%, P=0.07) compared to those with insidious onset. Patients with acute onset reported less severe lower abdominal pain (1.8±1.6 vs 2.5±1.7, P=0.001), lower abdominal discomfort (2.0±1.7 vs 2.6±1.6, P=0.01), and constipation (2.2±1.9 vs 2.7±1.8, P=0.02) than patients with insidious onset.

Eleven features were associated with IG patients with acute onset compared to insidious onset of symptoms by multiple logistic regression analyses (Table 4). These were: higher waist to hip ratio category (overall P=0.004; moderate risk category vs low risk OR=4.02, P=0.002), less fibromyalgia (OR=0.22, P=0.005), less likely to use prokinetics (OR=0.41, P=0.008) and less likely to use estrogen/progesterone (OR=0.43, P=0.03), more likely to use anti-emetics (OR=3.56, P=0.001), shorter duration of symptoms (overall P<0.001), an initial infectious prodrome (OR=4.43, P=0.001), more severe nausea (OR=1.37, P=0.01) and lower abdominal discomfort (OR=1.62, P=0.05), and less severe lower abdominal pain (OR=0.45, P=0.002) and constipation (OR=0.80, P=0.02).

Gastric emptying

Overall, of 242 IG patients with gastric emptying scintigraphy results at 4 hours, delayed gastric emptying was mild (≤20% gastric retention) in 45%, moderate (>20 to 35%) in 27%, and severe (>35%) in 28% (Table 2). Patients with severe gastric retention had the lowest percent of incomes > $50K (41% vs 56% vs 69%, P<0.001), and reported more co-morbidities: Chronic fatigue syndrome (16% vs 9% vs 5%, P=0.01), fibromyalgia (24% vs 17% vs 4%, P<0.001), major depression (34% vs 20% vs 16%, P=0.006). Patients with severe gastric retention also reported more use of co-medications: anti-emetics (90% vs 58% vs 69%, P<0.001), gastric acid suppressants (85% vs 76% vs 71%, P=0.04), narcotics (57% vs 44% vs 32%, P=0.001). Patients with more severe retention had the longest duration of symptoms (5.9±7.6 vs 4.7±7.1 vs 4.2±5.2 years, P=0.09), and reported an initial infectious prodrome less frequently (10% vs 19% vs 24%, P=0.02). Patients with severe gastric emptying were more likely to be classified as having gastric failure (35%) compared to 26% with mild and moderate delay (P=0.06) Patients with severe retention reported more severe nausea (3.8±1.2 vs 3.4±1.3 vs 3.3±1.6, P=0.05), vomiting (2.5±1.9 vs 1.7±1.9 vs 1.8±1.9, P=0.01), retching (2.3±1.9 vs 1.5±1.6 vs 1.7±1.7, P=0.02), loss of appetite (3.4±1.4 vs 3.2±1.4 vs 2.8±1.6, P=0.04), upper abdominal discomfort (3.7±1.4 vs 3.4±1.3 vs 3.1±1.6, P=0.05), gastroesophageal reflux scores (2.5±1.4 vs 1.8±1.3 vs 1.9±1.4, P=0.007), and had higher GCSI scores (3.3±1.0 vs 2.9±0.8 vs 2.9±1.1, P=0.04) compared to patients with moderate or mild retention, respectively.

Multivariable logistic regression comparing severe to not severe (mild plus moderate) gastric retention at 4 hours identified the following 9 features associated with severe

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retention (Table 4): lower income (OR=0.42, P=0.01), higher waist to hip ratio CVD risk category (overall P=0.02; high risk OR=3.19, P=0.006 vs low risk category), lower CRP (OR=0.42, P=0.03), more likely to have fibromyalgia (OR=6.97, P<0.001), use anti-emetics (OR=5.76, P<0.001), use gastric acid suppressants (OR=2.65, P=0.03) and less likely to have an initial infectious prodrome (OR=0.30, P=0.02). Patients with severe gastric retention had more severe vomiting (OR=1.25, P=0.02) and loss of appetite (OR=1.38, P=0.01). The GCSI score was significantly higher in patients with severe compared to less severe retention (OR=1.42, P=0.05).

Gastroparesis Symptom Severity

The severity of gastroparesis was also assessed using the gastroparesis severity scale (4) with gastroparesis severity graded as grade 1: mild gastroparesis, grade 2: compensated gastroparesis, and grade 3: severe gastroparesis with gastric failure (Supplemental Table 4). With increasing severity of gastroparesis, there were significantly increased symptoms of nausea, retching, vomiting, bloating, upper abdominal pain/discomfort, and symptoms of GERD. The GCSI score increased with increasing severity of gastroparesis (2.4±0.9 vs 3.0±1.1 vs 3.3±0.8, P<0.001). The retention at 2 and 4 hours was not significantly different among the different grades. There was an increase in the inflammatory markers CRP and ESR with increasing severity of gastroparesis. In addition, there were increased STAI and BDI scores. With increasing severity of gastroparesis, there were increased use of anti-emetics, narcotic pain medications, and nutritional support using TPN or jejunostomy tube. Multivariable logistic regression was used to identify independent characteristics of patients with IG that were associated with gastric failure compared to mild or compensated gastroparesis (Table 4). Use of antiemetic agents (OR=4.06; P=0.004), use of total/parenteral support (OR=6.41; P<0.001), nausea severity score (OR=1.45; P=0.006), and being married (OR=2.12; P=0.03) were associated with severe gastroparesis, whereas being postmenopausal was associated with mild/compensated gastroparesis (OR=0.30; P=0.004). In addition, the GCSI score was associated with severe gastroparesis (OR=1.49; P=0.02).

Symptom severity of gastroparesis was also assessed by dividing patients according to their GCSI score: mild or less (0–2.99), moderate (3.0–3.99), and severe (4.0–5.0) (Table 3). With increasing symptom severity, there was an increase in gastroparesis severity (P=0.004) and increased predominant symptom of nausea for gastroparesis evaluation. Percent gastric retention at 4 hours increased with increasing symptom severity (26±18% vs 27±18% vs 36±23%, P=0.06) and there was an increase in number of patients with severe delay in gastric emptying (P=0.03). Independent characteristics associated with severe symptom severity (GCSI≥3.5) compared to mild to moderate symptoms (GCSI<3.5) included more percent retention at 4 hours (OR=1.02; p=0.01), migraine headaches (OR=2.33; p=0.003), major depression disorder (OR=2.12; p=0.03), and less fibromyalgia (OR=0.29; p=0.01) (Table 4).

Functional GI disorders

Patients with IG were also classified according to Rome III criteria for functional dyspepsia and irritable bowel syndrome (Supplemental Table 5). Overall, 86.0% of the IG patients fit criteria for functional dyspepsia with 91.0% meeting criteria for postprandial distress syndrome (PDS), 1.2% for epigastric pain syndrome, 34.2% for chronic idiopathic nausea, 38.7% for functional vomiting, and 64.6% for irritable bowel syndrome (IBS). There were no statistically significant differences in any of these classifications between females and males. PDS was significantly higher in patients with severely delayed GE (96%), compared to moderately (92%), or mild delay (87%), P=0.05. There was a slightly higher prevalence of IBS in patients with severe delay in gastric emptying (74% vs 68% vs 58%, P=0.04; Supplemental Table 6). With increasing severity of gastroparesis, there was a higher

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prevalence of functional vomiting (8.8% for grade 1, 38.0% for grade 2, and 53.5% for grade 3; $p<0.001$) and a trend for higher prevalence of postprandial distress syndrome (85.3% for grade 1, 90.5% for grade 2, and 95.8% for grade 3; $p=0.06$) (Supplemental Table 7).

DISCUSSION

This study highlights the clinical and physiologic features of patients with IG. The 243 patients comprising this multicenter report is the largest series of patients with IG. The study confirms that IG is a disease that particularly affects young women. Half of cases presented acutely, often in association with an initial infectious-like prodrome. The predominant symptom prompting evaluation was nausea in 34%, vomiting in 19%, and abdominal pain in 23%. Although the majority of patients were normal or even underweight, many patients were overweight or obese at time of enrollment despite having nausea and vomiting. Severe delay in gastric emptying was associated with more severe symptoms of vomiting, loss of appetite. Thus, IG has phenotypic variability with gender, body mass, type of symptom onset, degree of delay in gastric emptying, and gastroparesis severity.

Most patients with IG are women. Our finding that 88% of IG were female with a mean age of 41 years is similar to several other studies (2,3). Harrell et al (3) and Soykan et al (2) showed that approximately 80% of patients with gastroparesis were female. Females have been also reported to comprise the majority of patients with diabetic gastroparesis (76%) and postsurgical gastroparesis (89%) (2).

Why gastroparesis has a predilection for young female subjects is not known. In normal subjects, gastric emptying is affected by gender, menopausal status, and phase of the menstrual cycle (18,19). In this series of patients with IG, women tended to have a more severe delay in gastric emptying than males with IG. Postmenopausal status was more frequent with less severe gastroparesis severity. Stanghellini et al reported female sex was an independent factor associated with delayed gastric emptying in patients with functional dyspepsia (20). Females may have less of a reserve of ‘normal function’ than males and therefore be more likely to develop symptoms to a given insult. Women may have delayed gastric emptying compared to men due to differences in ovarian hormones, altered enteric transmission and decreased contractility of the antrum, altered gastric fundal accommodation and sensation (18,19,21,22). In our series of patients with IG, females had higher symptom scores than male patients for nausea and stomach fullness. In a survey of adults in the community, symptoms of early satiety and nausea were found to be more common in females than in males (23).

Half of the patients with IG in this series had an acute onset of symptoms, with 19% having an initial infectious prodrome. A viral infection has been suggested to precede the development of gastroparesis symptoms in some patients (24). In another series of patients with gastroparesis, 23% of the idiopathic patients presented after an acute viral gastroenteritis-like illness (2,25). In our series of IG, patients with acute onset had on average a shorter duration of symptoms and were more likely to have an initial infectious prodrome compared to those with insidious onset. These patients tended to have more gastric failure than those with insidious onset. This potential viral etiology for gastroparesis suggests viral-induced dysfunction of the components that affect gastric contractility: nerves, interstitial cells of Cajal, and/or smooth muscle. These patients with infectious-like gastroparesis have been reported to have slow resolution of their symptoms over several years, in contrast to individuals with IG without a viral trigger who tend to show less improvement over time (24).

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The majority of IG patients were either normal body weight (47%) or underweight (8%). Interestingly, 46% of the IG patients were overweight or obese which was unexpected in these patients with chronic nausea and vomiting. Overweight and obese patients were also noted in the Harrell series (3). Of note, the prevalence of both overweight/obesity and obesity in this series of IG is lower than for adult white females in the general population (46% vs 58% for overweight/obese, 26% vs 31% for obese) (26). The reason for obesity in patients with delayed gastric emptying is unclear. Of the overweight patients, 30% were losing weight at the time of enrollment. The overweight patients had less severe loss of appetite and a lower score for inability to finish a meal compared to normal weight individuals. One explanation is that IG patients in the overweight or obese category are likely to have less severe anorexia and hence could ingest more calories. Greater body mass index and gastric volume have been associated with reduced satiation (32). On the other hand, obesity may be a cause rather than a consequence of the gastroparesis. Our study confirmed inflammatory markers are more common in obese/overweight patients and ongoing inflammation may be a contributory factor to the development of gastroparesis. Myenteric inflammation has been noted in the stomach of some patients with gastroparesis (28,29).

A common assumption is that symptoms of gastroparesis can be attributed to delay in gastric emptying. However, most investigations have observed only weak correlations between symptom severity and the degree of gastric stasis. In diabetics, the correlation between global gastric symptoms and gastric emptying is poor (30) with only postprandial fullness associating with delayed emptying (31). In functional dyspepsia, symptoms of early satiety, postprandial fullness, nausea, and vomiting are more prevalent in individuals with delayed gastric emptying (20,32). This study shows that patients with relatively severe delay in gastric emptying >35% retention at 4 hours had more severe nausea, vomiting, retching, and loss of appetite compared to patients with moderate or mild retention using univariable analysis, of which vomiting, loss of appetite, and higher GCSI scores persisted using multivariable logistic regression analysis.

There is overlap between gastroparesis and functional dyspepsia as both symptoms and gastric emptying results may meet definitions for both in some patients (4,41). Some patients with mild abdominal pain, nausea, vomiting, and evidence of delayed emptying are considered to have functional dyspepsia by some clinicians and gastroparesis by others. Functional dyspepsia is diagnosed by having symptoms of postprandial fullness, early satiation, epigastric pain/burning (33). Since these symptoms are non-specific and cover gastric symptomatology and since our patients had to have gastric symptoms to enter the study, it is not surprising that many IG patients met criteria for functional dyspepsia. Indeed, 86% of patients with IG met criteria for functional dyspepsia. Over 90% had PDS and the presence of PDS increased with the severity of the delay in gastric emptying. This relation of PDS with delayed gastric emptying has been reported previously (34).

Use of prokinetic agents, antiemetic agents, gastric acid suppressants, narcotic pain medications, and enteral/parenteral nutrition increased with increasing severity of delayed gastric emptying. This is not unexpected as these are the patients with more symptom burden. Use of narcotic analgesics which could potentially delay gastric emptying, however, was not associated with severely delayed gastric emptying in multivariable analysis.

The severity of gastroparesis was assessed by several methods including gastric retention on GES (13), a gastroparesis severity scale (4), and symptom severity using GCSI (7). Patients with severe gastric retention had more severe vomiting, loss of appetite, GCSI score, and more frequently used anti-emetics. Gastric failure was associated with nausea severity score, GCSI score, the use of antiemetic agents, and use of total/parenteral support, whereas being

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postmenopausal was associated with mild/compensated gastroparesis. Severe symptom severity was associated with increased gastric retention at 4 hours and depression. Thus, symptoms, gastric retention, current treatment, and psychosocial variables impact on the severity of the gastroparesis syndrome.

Patients in this multicenter study were recruited primarily from tertiary referral centers and may be more symptomatic and have higher number of co-morbid disorders than patients in the community. Interestingly, irritable bowel syndrome, fibromyalgia and major depression were greater in patients with severely delayed gastric emptying. Fibromyalgia by self report was also found to be present more often in patients with an insidious onset of gastroparesis, rather than an acute onset of symptoms. STAI and BDI scores tended to be higher in patients with severely delayed gastric emptying suggesting chronic gastroparetic symptoms in patients with IG can be associated with depression and anxiety. This is also seen in diabetic gastroparesis (35). Symptoms of functional dyspepsia, particularly PDS, have been associated with anxiety, depression, and somatization (36,37).

In conclusion, this study has shown that IG is a disorder that particularly affects young women. Half of cases presented acutely, often in association with an initial infectious prodrome. Patients with IG may be overweight or even obese. Severe delay in gastric emptying was associated with more severe symptoms of vomiting and loss of appetite. IG is a phenotypically diverse syndrome with substantial variations in symptom severity related to gender, body mass, type of symptom onset and degree of delayed gastric emptying and gastroparesis severity. The results provide the basis for studies to determine whether these variations of IG relate to differences in pathogenesis and whether they impact on clinical course and treatment outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of idiopathic gastroparesis patients overall and for females and males

Characteristic	Total (N = 243)		Females (N = 214)		Males (N = 29)		*P* value[†]
	No.	Statistic[*]	No.	Statistic[*]	No.	Statistic[*]	
Demographic and lifestyle:							
Age at enrollment (years):							0.49
18–30	72	29.6%	62	29.0%	10	34.5%	
31–44	80	32.9%	74	34.6%	6	20.7%	
45–59	67	27.6%	58	27.1%	9	31.0%	
60+	24	9.9%	20	9.3%	4	13.8%	
Average age	243	41.0 ± 14.1	214	40.9 ± 14.0	29	41.6 ± 14.9	0.78
Race:							1.00
White	218	89.7%	192	90.0%	26	90.0%	
Black	16	6.6%	14	6.5%	2	6.9%	
Other	9	3.7%	8	3.7%	1	3.5%	
Married (yes vs no)	143	58.9%	126	58.9%	17	58.6%	0.97
College degree or higher (yes vs no)	80	32.9%	71	33.2%	9	31.0%	0.82
Income $50,000+ (yes vs no)	139	57.2%	122	57.0%	17	58.6%	0.87
Ever smoked regularly[‡] (yes vs no)	81	33.3%	65	30.4%	16	55.2%	**0.008**
Ever drink (past yr)	96	39.5%	87	40.7%	9	31.0%	0.32
Anthropometry:							
Height (m)	243	1.64 ± 0.08	214	1.62 ± 0.06	29	1.76 ± 0.07	**<0.001**
Weight (kg)	243	68.6 ± 19.0	214	66.8 ± 18.1	29	82.0 ± 20.8	**<0.001**
Waist circumference (cm)	243	85.0 ± 17.7	214	83.5 ± 17.5	29	95.7 ± 15.8	**<0.001**
Waist to Hip ratio health risk (sex-specific)[‡]							**0.01**
Low	89	36.6%	73	34.1%	16	55.2%	
Moderate	62	25.0%	53	24.8%	9	31.0%	
High	92	37.9%	88	41.1%	4	13.8%	
BMI category:							**0.04**
Underweight (<18 kg/m^2)	19	7.8%	18	8.4%	1	3.5%	

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Characteristic	Total (N = 243)		Females (N = 214)		Males (N = 29)		*P* value†
	No.	Statistic*	No.	Statistic*	No.	Statistic*	
Normal (18–24 kg/m^2)	113	46.5%	102	47.7%	11	37.9%	
Overweight (25–30 kg/m^2)	49	20.2%	37	17.3%	12	41.4%	
Obese (>30 kg/m^2)	62	25.5%	57	26.6%	5	17.2%	
BMI (kg/m^2)	243	25.6 ± 6.9	214	25.4 ± 7.0	29	26.3 ± 5.9	0.21
Inflammatory markers:							
C-reactive protein (CRP) (mg/dL)	243	0.7 ± 1.2	214	0.7 ± 1.3	29	0.6 ± 0.7	0.45
C-reactive protein elevated (>0.8 mg/dL)	51	21.0%	44	20.6%	7	24.1%	0.66
Erythrocyte sedimentation rate (mm/hr)	243	14.4 ± 14.9	214	15.3 ± 15.2	29	7.4 ± 10.3	**<0.001**
ESR elevated (ESR > 20.0 mm/hr)	51	21.0%	49	22.9%	2	6.9%	**0.05**
Psychological function inventories:							
State Anxiety inventory average score	243	45.2 ± 13.5	214	44.9 ± 13.1	29	47.7 ± 16.3	0.46
State Anxiety inventory score ≥ 50 (severe)	88	36.2%	77	36.0%	11	37.9%	
Trait Anxiety inventory average score	243	43.9 ± 12.1	214	43.8 ± 12.1	29	45.0 ± 12.3	0.53
Trait Anxiety inventory score ≥ 50 (severe)	84	34.6%	71	33.2%	13	44.8%	
Beck Depression Inventory average score	243	18.6 ± 10.8	214	18.5 ± 10.7	29	19.3 ± 11.2	0.71
Beck Depression Inv score > 28 (severe)	44	18.1%	36	16.8%	8	27.6%	0.16
Medical history:							
Co-morbidities:							
Average number of co-morbidities	243	3.63 ± 2.69	214	3.68 ± 2.64	29	3.28 ± 3.10	0.22
Migraine Headache (yes vs no)	99	40.7%	92	43.0%	7	24.1%	**0.05**
Chronic fatigue syndrome (yes vs no)	22	9.1%	22	10.3%	0	0.0%	0.09
Fibromyalgia (yes vs no)	31	12.8%	30	14.0%	1	3.5%	0.14
Major depression (yes vs no)	53	21.8%	46	21.5%	7	24.1%	0.75
Severe anxiety (yes vs no)	30	12.4%	26	12.2%	4	13.8%	0.77
Co-medications:							
Gastric acid suppressants (yes vs no)	185	76.1%	162	75.7%	23	79.3%	0.67
Prokinetics (yes vs no)	118	48.6%	103	48.1%	15	51.7%	0.72
Anti-emetics (yes vs no)	174	71.6%	154	72.0%	20	69.0%	0.74
Estrogen, progesterone,OCP's (yes v no)	58	23.9%	57	26.6%	1	3.5%	**0.006**

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Characteristic	Total (N = 243)		Females (N = 214)		Males (N = 29)		*P* value†
	No.	Statistic*	No.	Statistic*	No.	Statistic*	
Narcotic pain medications (yes vs no)	103	42.4%	92	43.0%	11	37.9%	0.60
Medical marijuana use (yes vs no)‡	3	1.2%	2	0.9%	1	3.5%	0.32
Total enteral/parenteral support (yes vs no)	28	11.5%	25	11.7%	3	10.3%	1.00
Post-menopausal (yes vs no)	67	31.3%	67	31.3%		*n/a*	
Hysterectomy (yes vs no)	59	27.6%	59	27.6%		*n/a*	
Age at onset of symptoms (years):							0.64
9 – 20	41	16.9%	36	16.8%	5	17.2%	
21 – 30	59	24.3%	51	23.8%	8	27.6%	
31 – 44	71	29.2%	66	30.8%	5	17.2%	
45 – 60	59	24.3%	50	23.4%	9	31.0%	
61 +	13	5.4%	11	5.1%	2	6.9%	
Average age	243	36.1 ± 14.6	214	36.1 ± 14.6	26	36.0 ± 15.2	0.82
Duration of symptoms at enrollment (yrs):							0.20
0 – 1	93	38.3%	81	37.9%	12	41.4%	
2 –4	76	31.3%	67	31.3%	9	31.0%	
5 – 9	45	18.5%	43	20.1%	2	6.9%	
10+	29	11.9%	23	10.8%	6	20.7%	
Average duration	243	4.8 ± 6.5	214	4.8 ± 6.6	29	5.0 ± 6.1	0.83
Initial infectious prodrome:	45	18.6%	40	18.7%	5	17.9%	0.92
Upper respiratory flu-like illness	11	4.6%	8	3.7%	3	10.7%	
Food-poisoning like symptoms	11	4.6%	9	4.2%	2	7.1%	
Gastroenteritis	16	6.6%	16	7.5%	0	0.0%	
Other	8	3.3%	8	3.7%	0	0.0%	
Predominant symptom prompting evaluation:							
Nausea vs all others	83	34.2%	73	34.1%	10	34.5%	0.97
Vomiting vs all others	47	19.3%	43	20.1%	4	13.8%	0.42
Abdominal pain vs all others	56	23.1%	51	23.8%	5	17.2%	0.43
Bloating vs all others	17	7.0%	13	6.1%	4	13.8%	0.13
Gastroesophageal reflux vs all others	14	5.8%	12	5.6%	2	6.9%	0.67

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Characteristic	Total (N = 243) No.	Total (N = 243) Statistic*	Females (N = 214) No.	Females (N = 214) Statistic*	Males (N = 29) No.	Males (N = 29) Statistic*	*P* value†
Type of gastroparesis symptom onset:							0.86
Acute start	122	50.2%	107	50.0%	15	51.7%	
Insidious start	121	49.8%	107	50.0%	14	48.3%	
Nature of gastroparesis symptoms:							0.91
Chronic, but stable	54	22.2%	48	22.4%	6	20.7%	
Chronic, but worsening	82	33.7%	73	34.1%	9	31.0%	
Chronic with periodic exacerbations	80	32.9%	70	32.7%	10	34.5%	
Cyclic pattern	26	10.7%	22	10.3%	4	13.8%	
Gastroparesis severity:							0.85
Mild (grade 1)	34	14.0%	29	13.6%	5	17.2%	
Compensated (grade 2)	137	56.4%	121	56.5%	16	55.2%	
Gastric failure (grade 3)	71	29.2%	63	29.4%	8	27.6%	
Irritable bowel syndrome or IBS‡							0.68
Yes, pending exam/test	157	64.6%	137	64.0%	20	69.0%	
No	86	35.4%	77	36.0%	9	31.0%	
Gastric emptying (scintigraphy):							
Percent gastric retention at 2 hr	243	62.7 ± 16.6	214	63.1 ± 16.7	29	59.9 ± 16.0	0.38
Percent gastric retention at 4 hr	242	28.1 ± 18.8	213	28.9 ± 19.4	29	22.2 ± 13.3	0.10
Severity of delayed gastric emptying - 4hr:							0.14
Mild (0 – 20%)	108	44.6%	92	43.2%	16	55.2%	
Moderate (21% – 35%)	66	27.3%	58	27.2%	8	27.6%	
Severe (> 35%)	68	28.1%	63	29.6%	5	17.2%	
Severity of Symptoms:‡							
Nausea severity	243	3.5 ± 1.4	214	3.6 ± 1.3	29	2.8 ± 1.7	**0.02**
Retching severity	243	1.8 ± 1.8	214	1.9 ± 1.8	29	1.5 ± 1.5	0.29
Vomiting severity	243	1.9 ± 1.9	214	2.0 ± 1.9	29	1.5 ± 2.0	0.15
Feeling of stomach fullness severity	241	3.7 ± 1.2	213	3.8 ± 1.1	28	3.0 ± 1.3	**<0.001**
Inability to finish meal severity	243	3.6 ± 1.4	214	3.7 ± 1.3	29	2.8 ± 1.7	**0.003**
Excessively full after meal severity	243	3.7 ± 1.3	214	3.8 ± 1.2	29	3.2 ± 1.5	**0.05**

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Characteristic	Total (N = 243) No.	Total (N = 243) Statistic*	Females (N = 214) No.	Females (N = 214) Statistic*	Males (N = 29) No.	Males (N = 29) Statistic*	*P* value†
Loss of appetite severity	243	3.1 ± 1.5	214	3.1 ± 1.5	29	2.7 ± 1.7	0.24
Bloating severity	243	3.3 ± 1.5	214	3.4 ± 1.5	29	2.7 ± 1.6	**0.03**
Visibly larger stomach severity	243	2.9 ± 1.8	214	3.0 ± 1.8	29	2.0 ± 1.9	**0.008**
Cardinal symptom index (GCSI)‡	241	3.0 ± 1.0	213	3.1 ± 1.0	28	2.5 ± 1.1	**0.008**
Upper abdominal pain	243	3.2 ± 1.7	214	3.2 ± 1.6	29	2.7 ± 1.8	0.09
Upper abdominal discomfort	243	3.3 ± 1.5	214	3.4 ± 1.5	29	3.0 ± 1.6	0.30
GERD sub-scale‡	243	2.0 ± 1.4	214	2.0 ± 1.4	29	1.9 ± 1.3	0.73
Constipation severity	243	2.4 ± 1.8	214	2.6 ± 1.8	29	1.4 ± 1.5	< **0.001**
Diarrhea severity	243	1.9 ± 1.7	214	1.9 ± 1.7	29	2.1 ± 1.9	0.55

*Means ± standard deviations or percents (%).

†The significance of difference in categorical variables between groups was tested with either a chi-square test or Fisher's Exact Test for non-ordered categories, the Cochran-Armitage test for trend for ordered categories, or with the Wilcoxon rank sum test for continuous measures. All *P* values are two-sided.

‡Definitions:

Ever smoked regularly defined as smoking ≥ 20 packs of cigarettes in a lifetime or ≥ 1 cigarette per day for a year.

Waist to hip ratio cardiovascular disease and diabetes health risk category based on NIDDK guidelines defined as follows: Low risk (≤ 0.95 for males, ≤ 0.80 for females), moderate risk (0.96 to 1.0 for males, 0.81 to 0.85 for females), high risk (≥ 1.0 for males, ≥ 0.85 for females)

Medical marijuana use determined via self-reported use in an "other category" of alternative therapies.

Irritable Bowel Syndrome or IBS diagnosis determined from the Rome III Diagnostic Questionnaire analyzed using an analysis program developed by the Rome Foundation (http://www.romecriteria.org/rome_iii_sas/, accessed 03 February 2010).

Symptom severity from the PAGI-SYM (Patient Assessment of GI Symptoms) questionnaire, scores range from 0–5

Gastroparesis cardinal symptom index (GCSI) = mean of the sub-scores for nausea, postprandial fullness, and bloating where:

Nausea sub-score = mean of the scores for nausea, retching, and vomiting

Postprandial fullness/early satiety sub-score = mean of the scores for stomach fullness, inability to finish meal, excessive fullness, and loss of appetite

Bloating sub-score = mean of the scores for bloating and large stomach

Gastroesophageal (GERD) sub-scale = mean of the scores for daytime heartburn, heartburn lying down, daytime chest discomfort, nighttime chest discomfort, daytime reflux, nighttime reflux, and bitter taste

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Table 2

Characteristics of patients with idiopathic gastroparesis with mild, moderate, or severe delay in 4-hour gastric emptying

	Severity of delay in gastric emptying at 4 hours*						
	Mild (N = 108)		Moderate (N = 66)		Severe (N = 68)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Demographic and lifestyle:							
Age at enrollment (yrs)	108	39.9 ± 14.1	66	42.9 ± 14.8	68	41.0 ± 13.2	0.38
Gender: Females	92	85.2%	58	87.9%	63	92.7%	0.15
Married: (yes vs no)	67	62.0%	38	57.6%	38	55.9%	0.40
College degree or higher (yes vs no)	37	34.3%	23	34.9%	19	27.9%	0.42
Income $50,000+ (yes vs no)	74	68.5%	37	56.1%	28	41.2%	**<0.001**
Ever smoked regularly (yes vs no)§	36	33.3%	20	30.3%	24	35.3%	0.83
Ever drink (past year)	49	45.4%	25	37.9%	21	30.1%	0.45
Anthropometry:							
Waist circumference (cm)	108	83.7 ± 16.8	66	82.9 ± 18.4	68	88.6 ± 8.0	0.08
Waist to hip ratio	108	0.85 ± 0.09	66	0.84 ± 0.15	68	0.86 ± 0.08	**0.04**
Overweight: (yes vs no)§	44	40.7%	32	48.5%	34	50.0%	0.21
BMI (kg/m^2)	108	25.3 ± 6.8	66	24.5 ± 5.4	68	26.8 ± 8.0	0.37
Inflammatory markers:							
C-reactive protein (CRP) (mg/dL)	108	0.7 ± 1.4	66	0.6 ± 1.2	68	0.7 ± 1.0	0.65
CRP elevated (> 0.8 mg/dL)	23	21.3%	10	15.2%	18	26.5%	0.52
ESR rate (mm/hr)§	108	13.4 ± 13.3	66	13.1 ± 12.4	68	17.0 ± 19.0	0.49
ESR elevated (> 20 mm/hr)§	23	21.3%	11	16.7%	16	23.5%	0.60
Psychological function inventories:							
State Anxiety inventory average score	108	44.3 ± 13.9	66	44.1 ± 13.9	68	47.6 ± 12.4	0.21
State Anxiety inventory score ≥ 50	38	35.2%	21	31.8%	28	41.2%	0.09
Trait Anxiety inventory average score	108	43.0 ± 12.8	66	43.3 ± 11.8	68	45.9 ± 8.0	0.20
Trait Anxiety inventory score ≥ 50	35	32.4%	23	34.9%	26	38.2%	0.24
Beck Depression Inventory avg score	108	18.1 ± 10.6	66	17.1 ± 9.6	68	20.9 ± 11.9	0.18

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Characteristic	Severity of delay in gastric emptying at 4 hours*						*P* value‡
	Mild (N = 108)		Moderate (N = 66)		Severe (N = 68)		
	No.	Statistic†	No.	Statistic†	No.	Statistic†	
Beck Depression inventory > 28	18	16.7%	8	12.1%	18	26.5%	0.08
Medical history:							
Co-morbidities:							
Average number of co-morbidities	108	3.13 ± 2.01	66	3.35 ± 2.80	68	4.72 ± 3.23	**0.002**
Migraine Headache (yes vs no)	43	39.8%	25	37.9%	31	45.6%	0.63
Chronic fatigue syndrome (yes vs no)	5	4.6%	6	9.1%	11	16.2%	**0.01**
Fibromyalgia (yes vs no)	4	3.7%	11	16.7%	16	23.5%	< **0.001**
Major depression (yes vs no)	17	15.7%	13	19.7%	23	33.8%	**0.006**
Severe anxiety (yes vs no)	12	11.1%	5	7.6%	13	19.1%	0.13
Co-medications:							
Gastric acid suppressants (yes vs no)	77	71.3%	50	75.8%	58	85.3%	**0.04**
Prokinetics (yes vs no)	48	44.4%	31	47.0%	38	55.9%	0.15
Anti-emetics (yes vs no)	74	68.5%	38	57.6%	61	89.7%	< **0.001**
Estrogen, progesterone,OCP's (yes)	28	25.9%	14	21.2%	16	23.5%	0.78
Narcotic pain medications (yes vs no)	35	32.4%	29	43.9%	39	57.4%	**0.001**
Total enteral/parenteral support (yes/no)	11	10.2%	4	6.1%	13	19.1%	**0.05**
Post-menopausal (yes vs no)	28	30.4%	22	37.9%	17	27.0%	0.42
Age at symptom onset (years)	108	35.7 ± 14.5	66	38.2 ± 15.4	68	35.1 ± 14.2	0.42
Duration of symptoms at enrollment(yrs)	108	4.2 ± 5.2	66	4.7 ± 7.1	68	5.9 ± 7.6	0.09
Initial infectious prodrome: (yes vs no)	26	24.1%	12	18.5%	7	10.3%	**0.02**
Predominant symptom:							
Nausea vs all others	38	35.2%	20	30.3%	24	35.3%	0.77
Vomiting vs all others	17	15.7%	16	24.2%	14	20.6%	0.37
Abdominal pain vs all others	25	23.2%	13	19.7%	18	26.5%	0.68
Type of gastroparesis symptom onset:							0.37
Acute start	57	52.8%	34	51.5%	31	45.6%	
Insidious start	51	47.2%	32	48.5%	37	54.4%	
Nature of gastroparesis symptoms:							0.24

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	Severity of delay in gastric emptying at 4 hours*						
	Mild (N = 108)		Moderate (N = 66)		Severe (N = 68)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Chronic, but stable	21	19.4%	21	31.8%	12	17.7%	
Chronic, but progressively worse	35	32.4%	19	28.8%	28	41.2%	
Chronic with periodic exacerbations	38	35.2%	22	33.3%	19	27.9%	
Cyclic pattern	13	12.0%	4	6.1%	9	13.2%	
Gastroparesis severity:							0.17
Mild (grade 1)	13	12.0%	11	16.7%	10	14.7%	
Compensated (grade 2)	61	56.5%	43	65.2%	33	48.5%	
Gastric failure (grade 3)	34	31.5%	12	18.2%	24	35.3%	
Gastric failure vs less severe	34	31.5%	12	18.2%	24	35.3%	0.06
Irritable bowel syndrome or IBS§							**0.04**
Yes, pending exam/test	63	58.3%	44	66.7%	50	73.5%	
No	45	41.7%	22	33.3%	18	26.5%	
Gastric emptying (scintigraphy):							
Percent gastric retention at 4 hr.	108	13.3 ± 4.7	66	26.2 ± 4.1	68	53.5 ± 14.5	< **0.001**
Severity of symptoms:§							
Nausea severity	108	3.3 ± 1.6	68	3.4 ± 1.3	68	3.8 ± 1.2	**0.05**
Retching severity	108	1.7 ± 1.7	66	1.5 ± 1.6	68	2.3 ± 1.9	**0.02**
Vomiting severity	108	1.8 ± 1.9	66	1.7 ± 1.9	68	2.5 ± 1.9	**0.01**
Stomach fullness severity	106	3.7 ± 1.2	66	3.7 ± 1.1	68	3.8 ± 1.2	0.51
Inability to finish meal severity	108	3.4 ± 1.5	66	3.6 ± 1.3	68	3.8 ± 1.2	0.41
Excessively full post meal severity	108	3.6 ± 1.3	66	3.7 ± 1.3	68	3.9 ± 1.1	0.59
Loss of appetite severity	108	2.8 ± 1.6	66	3.2 ± 1.4	68	3.4 ± 1.4	**0.04**
Bloating severity	108	3.2 ± 1.7	66	3.3 ± 1.4	68	3.4 ± 1.4	0.71
Visibly larger stomach severity	108	2.8 ± 1.9	66	2.9 ± 1.8	68	3.0 ± 1.7	0.75
Cardinal symptom index (GCSI)§	106	2.9 ± 1.1	66	2.9 ± 0.8	68	3.3 ± 1.0	**0.04**
Upper abdominal pain	108	2.9 ± 1.8	66	3.1 ± 1.5	68	3.5 ± 1.6	0.12
Upper abdominal discomfort	108	3.1 ± 1.6	66	3.4 ± 1.3	68	3.7 ± 1.4	**0.05**

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	Severity of delay in gastric emptying at 4 hours*						
	Mild (N = 108)		Moderate (N = 66)		Severe (N = 68)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Lower abdominal pain	108	2.0 ± 1.8	66	2.2 ± 1.4	68	2.5 ± 1.8	0.20
Lower abdominal discomfort	108	2.1 ± 1.7	66	2.4 ± 1.5	68	2.6 ± 1.8	0.18
GERD sub-scale	108	1.9 ± 1.4	66	1.8 ± 1.3	68	2.5 ± 1.4	**0.007**
Constipation severity	108	2.2 ± 1.8	66	2.7 ± 1.6	68	2.7 ± 1.9	0.10
Diarrhea severity	108	2.0 ± 1.7	66	1.6 ± 1.6	68	2.0 ± 1.8	0.21

*Percent gastric retention at 4-hours: Mild= 20% or less, Moderate= 21% to 35%, Severe= >35%.

†Means ± standard deviations or percents (%).

‡The significance of difference in categorical variables between groups was tested with either a chi-square test or Fisher's Exact Test for non-ordered categories, the Cochran-Armitage test for trend for ordered categories, or with the Wilcoxon rank sum test for continuous measures. All *P* values are two-sided.

§Definitions:

Ever smoked regularly defined as smoking ≥ 20 packs of cigarettes in a lifetime or ≥ 1 cigarette per day for a year.

Overweight = BMI ≥ 25 kg/m^2

ESR = Erythrocyte sedimentation rate

Irritable Bowel Syndrome or IBS diagnosis determined from the Rome III Diagnostic Questionnaire analyzed using an analysis program developed by the Rome Foundation (http://www.romecriteria.org/rome_iii_sas/, accessed 03 February 2010).

Symptom severity from the PAGI-SYM (Patient Assessment of GI Symptoms) questionnaire, scores range from 0–5

Gastroparesis cardinal symptom index (GCSI) = mean of the sub-scores for nausea, postprandial fullness, and bloating.

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Table 3

Characteristics of patients with idiopathic gastroparesis with mild, moderate or severe symptoms based on the Gastroparesis Cardinal Symptom Index

	Severity of symptoms by GCSI*						
	Mild GCSI: 0 – 2.99 (N = 114)		Moderate GCSI: 3.0 – 3.99 (N = 86)		Severe GCSI:4.0 – 5.0 (N = 41)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Demographic and lifestyle:							
Age at enrollment (yrs)	114	41.6 ± 16.0	86	41.3 ± 12.2	41	39.2 ± 12.1	0.68
Gender: Females	95	83.3%	78	90.7%	40	97.6%	**0.01**
Married: (yes vs no)	63	55.3%	54	62.8%	25	61.0%	0.38
College degree or higher (yes vs no)	43	37.7%	25	29.1%	12	29.3%	0.21
Income $50,000+ (yes vs no)	72	63.2%	40	46.5%	26	63.4%	0.46
Ever smoked regularly (yes vs no)§	33	29.0%	37	43.0%	10	24.4%	0.82
Ever drink (past year)	53	46.5%	28	32.6%	14	34.2%	0.07
Anthropometry:							
Waist circumference (cm)	114	85.3 ± 18.3	86	85.1 ± 18.0	41	84.3 ± 16.0	0.98
Waist to hip ratio	114	0.85 ± 0.09	86	0.86 ± 0.13	41	0.84 ± 0.08	0.89
Overweight: (yes vs no)§	54	47.4%	39	45.4%	17	41.5%	0.52
BMI (kg/m^2)	114	25.7 ± 7.6	86	25.2 ± 6.1	41	25.8 ± 6.8	0.96
Inflammatory markers:							
C-reactive protein (CRP) (mg/dL)	114	0.7 ± 1.5	86	0.5 ± 0.6	41	1.0 ± 1.2	**0.02**
CRP elevated (> 0.8 mg/dL)	21	18.4%	14	16.3%	16	39.0%	**0.03**
ESR rate (mm/hr)§	114	13.4 ± 16.5	86	15.4 ± 13.4	41	14.8 ± 13.5	0.06
ESR elevated (> 20 mm/hr)§	20	17.5%	20	23.3%	10	24.4%	0.27
Psychological function inventories:							
State Anxiety inventory average score	114	42.8 ± 12.6	86	48.3 ± 14.2	41	45.8 ± 13.3	**0.03**
State Anxiety inventory score ≥ 50	36	31.6%	37	43.0%	15	36.6%	0.31
Trait Anxiety inventory average score	114	42.5 ± 12.0	86	46.2 ± 12.2	41	43.5 ± 11.7	0.12
Trait Anxiety inventory score ≥ 50	25	30.7%	35	40.7%	14	34.2%	0.42
Beck Depression Inventory avg score	114	15.5 ± 9.6	86	21.7 ± 11.0	41	21.0 ± 11.2	< **0.001**

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	Severity of symptoms by GCSI*						
	Mild GCSI: 0 – 2.99 (N = 114)		Moderate GCSI: 3.0 – 3.99 (N = 86)		Severe GCSI:4.0 – 5.0 (N = 41)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Beck Depression inventory > 28	13	11.4%	22	25.6%	9	22.0%	**0.04**
Medical history:							
Co-morbidities:							
Averag number of co-morbidities	114	3.29 ± 2.64	86	3.76 ± 2.45	41	4.32 ± 3.24	0.06
Migraine Headache (yes vs no)	36	31.6%	37	43.0%	24	58.5%	**0.002**
Chronic fatigue syndrome (yes vs no)	8	7.0%	10	11.6%	4	9.8%	0.42
Fibromyalgia (yes vs no)	16	14.0%	10	11.6%	5	12.2%	0.68
Major depression (yes vs no)	17	14.9%	25	29.1%	11	26.8%	**0.04**
Severe anxiety (yes vs no)	14	12.3%	10	11.6%	6	14.6%	0.78
Co-medications:							
Gastric acid suppressants (yes vs no)	86	75.4%	64	74.4%	34	82.9%	0.45
Prokinetics (yes vs no)	45	48.3%	45	52.3%	18	43.9%	0.83
Anti-emetics (yes vs no)	79	69.3%	58	67.4%	35	85.4%	0.12
Estrogen, progesterone,OCP's (yes)	30	26.3%	19	22.1%	9	22.0%	0.40
Narcotic pain medications (yes vs no)	43	37.7%	36	41.9%	23	56.1%	0.06
Total enteral/parenteral support (yes/no)	9	7.9%	9	10.5%	9	22.0%	**0.02**
Post-menopausal (yes vs no)	29	30.5%	26	33.3%	12	30.0%	0.95
Age at symptom onset (years)	114	36.9 ± 16.1	86	36.1 ± 12.9	41	34.6 ± 13.6	0.85
Duration of symptoms at enrollment(yrs)	114	4.7 ± 6.7	86	5.1 ± 7.1	41	4.6 ± 4.5	0.70
Initial infectious prodrome: (yes vs no)	19	16.8%	18	20.9%	8	19.5%	0.58
Predominant symptom:							
Nausea vs all others	34	29.8%	28	32.6%	20	48.8%	**0.05**
Vomiting vs all others	23	20.2%	18	20.9%	6	14.6%	0.55
Abdominal pain vs all others	25	21.9%	22	25.6%	8	19.5%	0.94
Type of gastroparesis symptom onset:							0.65
Acute start	57	50.0%	41	47.7%	23	56.1%	
Insidious start	57	50.0%	45	52.3%	18	43.9%	

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	Severity of symptoms by GCSI*						
	Mild GCSI: 0 – 2.99 (N = 114)		Moderate GCSI: 3.0 – 3.99 (N = 86)		Severe GCSI:4.0 – 5.0 (N = 41)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Nature of gastroparesis symptoms:							**0.005**
Chronic, but stable	32	28.1%	20	23.3%	2	5.0%	
Chronic, but progressively worse	26	22.8%	33	38.4%	22	55.0%	
Chronic with periodic exacerbations	42	36.8%	26	30.2%	12	30.0%	
Cyclic pattern	14	12.3%	7	8.1%	4	10.0%	
Gastroparesis severity:							**0.004**
Mild (grade 1)	26	22.8%	6	7.0%	2	4.9%	
Compensated (grade 2)	62	54.4%	50	58.1%	24	58.5%	
Gastric failure (grade 3)	25	21.9%	30	34.9%	15	36.6%	
Gastric failure vs less severe	25	21.9%	30	34.9%	15	36.6%	**0.03**
Irritable bowel syndrome or IBS§							0.34
Yes, pending exam/test	69	60.5%	60	69.8%	27	65.8%	
No	45	39.5%	26	30.2%	14	34.2%	
Gastric emptying (scintigraphy):							
Percent gastric retention at 2 hr.	114	63.0 ± 16.8	86	62.0 ± 16.1	41	64.6 ± 16.1	0.80
Percent gastric retention at 4 hr.	113	26.3 ± 17.6	86	27.2 ± 17.9	41	35.7 ± 22.6	0.06
Severity of delayed gastric emptying 4 hr:							**0.03**
Mild (0 – 20%)	55	48.7%	35	40.7%	16	39.0%	
Moderate (21% – 35%)	32	28.3%	28	32.6%	6	14.6%	
Severe (> 35%)	26	23.0%	23	26.7%	19	46.3%	
Severity of symptoms:*							
Nausea severity	114	2.7 ± 1.4	86	3.9 ± 1.0	41	4.7 ± 0.6	*n/a*
Retching severity	114	1.1 ± 1.4	86	1.9 ± 1.6	41	3.8 ± 1.4	*n/a*
Vomiting severity	114	1.2 ± 1.7	86	1.9 ± 1.8	41	4.0 ± 1.0	*n/a*
Stomach fullness severity	114	3.0 ± 1.1	86	4.2 ± 0.8	41	4.7 ± 0.5	*n/a*
Inability to finish meal severity	114	3.0 ± 1.5	86	4.1 ± 1.0	41	4.4 ± 0.8	*n/a*
Excessively full post meal severity	114	3.0 ± 1.3	86	4.3 ± 0.9	41	4.6 ± 0.6	*n/a*

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	Severity of symptoms by GCSI*						
	Mild GCSI: 0 – 2.99 (N = 114)		Moderate GCSI: 3.0 – 3.99 (N = 86)		Severe GCSI:4.0 – 5.0 (N = 41)		*P* value‡
Characteristic	**No.**	**Statistic†**	**No.**	**Statistic†**	**No.**	**Statistic†**	
Loss of appetite severity	114	2.4 ± 1.4	86	3.6 ± 1.3	41	3.9 ± 1.2	*n/a*
Bloating severity	114	2.2 ± 1.4	86	4.0 ± 1.0	41	4.8 ± 0.4	*n/a*
Visibly larger stomach severity	114	1.6 ± 1.5	86	3.7 ± 1.3	41	4.5 ± 0.7	*n/a*
Cardinal symptom index (GCSI)*	114	2.1 ± 0.6	86	3.5 ± 0.3	41	4.4 ± 0.3	*n/a*
Upper abdominal pain	114	2.4 ± 1.7	86	3.8 ± 1.2	41	3.9 ± 1.4	**< 0.001**
Upper abdominal discomfort	114	2.6 ± 1.6	86	3.9 ± 1.1	41	4.2 ± 1.0	**< 0.001**
Lower abdominal pain	114	1.5 ± 1.5	86	2.6 ± 1.6	41	3.3 ± 1.5	**< 0.001**
Lower abdominal discomfort	114	1.7 ± 1.5	86	2.7 ± 1.7	41	3.2 ± 1.5	**< 0.001**
GERD sub-scale	114	1.5 ± 1.2	86	2.2 ± 1.4	41	3.1 ± 1.4	**< 0.001**
Constipation severity	114	1.8 ± 1.6	86	2.8 ± 1.8	41	3.5 ± 1.7	**< 0.001**
Diarrhea severity	114	1.6 ± 1.5	86	2.0 ± 1.8	41	2.4 ± 1.9	**0.05**

*Severity of symptoms based on the Gastroparesis Cardinal Index Score from the PAGI-SYM (Patient Assessment of GI Symptoms) questionnaires, scores range from 0–5): Mild= 0–2.9, Moderate= 3.0–3.99, Severe= 4.0–5.0. Two subjects were excluded due to a missing score on the Stomach Fullness Severity score.
Gastroparesis cardinal symptom index (GCSI) = mean of sub-scores for nausea, postprandial fullness, and bloating

†Means ± standard deviations or percents (%).

‡The significance of difference in categorical variables between groups was tested with either the Cochran-Armitage test for trend for ordered categories or Fisher's exact test, or with the Wilcoxon rank sum test for continuous measures. All *P* values are two-sided.

§Definitions:
Ever smoked regularly defined as smoking ≥ 20 packs of cigarettes in a lifetime or ≥ 1 cigarette per day for a year.
Overweight = BMI ≥ 25 kg/m^2
ESR = Erythrocyte sedimentation rate
Irritable Bowel Syndrome or IBS diagnosis determined from the Rome III Diagnostic Questionnaire analyzed using an analysis program developed by the Rome Foundation (http://www.romecriteria.org/rome_iii_sas/).

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Table 4

Multivariable logistic regression analysis to identify independent characteristics of patients with idiopathic gastroparesis that are associated with either sex, overweight, symptom onset, severity of gastric emptying delay, or severity of gastroparesis

Characteristics Selected	Females Vs Males*		Overweight Vs Normal*		Acute Vs Insidious*		Severe delay Vs Not severe*		Gastric failure Vs Mild/Comp*		Severe Symptoms Vs Less*	
	OR†	*P*	OR†	*P*	OR†	*P*	OR†	*P*	OR†	*P*	OR†	*P*
Demographic and lifestyle:												
Sex: Females vs Males	n/a	n/a	0.11	**<0.001**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Married (yes vs no)	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	2.12	**0.03**	n/s	n/s
College or higher education (yesVno)	n/s	n/s	0.21	**<0.001**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Income: $50,000 or more (yes vs no)	n/s	n/s	n/s	n/s	n/s	n/s	0.42	**0.01**	n/s	n/s	n/s	n/s
Ever drink in past year	3.49	**0.04**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Anthropometry:												
Waist to hip ratio cardiovascular risk category (sex specific):‡		**0.002**		**0.01**		**0.004**		**0.02**		n/s		n/s
Low risk	1.00		1.00		1.00		1.00		n/s	n/s	n/s	n/s
Moderate risk	2.14	0.25	1.67	0.26	4.02	0.002	1.63	0.29	n/s	n/s	n/s	n/s
High risk	12.20	0.002	3.40	0.004	1.48	0.28	3.19	0.006	n/s	n/s	n/s	n/s
Overweight (BMI≥25 kg/m^2)	0.14	**0.002**	n/a	n/a	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Inflammatory markers:												
C-reactive protein (CRP) (√mg/dL)	n/s	n/s	2.90	**0.008**	n/s	n/s	0.42	**0.03**	n/s	n/s	n/s	n/s
ESR (√mm/hr)‡	1.89	**0.004**	1.69	**<0.001**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Medical history:												
Co-morbidities:												
Migraine headache (yes vs no)	3.34	**0.05**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	2.33	**0.003**
Fibromyalgia (yes vs no)	n/a	n/a	n/s	n/s	0.22	**0.005**	6.97	**<0.001**	n/s	n/s	0.29	**0.01**
Major depression (yes vs no)	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	2.12	**0.03**
Anxiety disorder (yes vs no)	7.92	**0.03**	4.09	**0.01**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Beck Depression Index score > 30‡	0.20	**0.01**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Co-medications:												
Gastric acid suppressants	n/s	n/s	n/s	n/s	n/s	n/s	2.65	**0.03**	n/s	n/s	n/s	n/s
Prokinetics	n/s	n/s	n/s	n/s	0.41	**0.008**	n/s	n/s	n/s	n/s	n/s	n/s

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Characteristics Selected	Females Vs Males*		Overweight Vs Normal*		Acute Vs Insidious*		Severe delay Vs Not severe*		Gastric failure Vs Mild/Comp*		Severe Symptoms Vs Less*	
	OR†	*P*	OR†	*P*	OR†	*P*	OR†	*P*	OR†	*P*	OR†	*P*
Anti-emetics	n/s	n/s	n/s	n/s	3.56	**0.001**	5.76	**<0.001**	4.06	**0.004**	n/s	n/s
Estrogen, progesterone, OCP's	n/a	n/a	n/s	n/s	0.43	**0.03**	n/s	n/s	n/s	n/s	n/s	n/s
Total enteral/parenteral support (yes)	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	6.41	**<0.001**	n/s	n/s
Post-menopausal (yes vs no)	n/a	n/a	n/s	n/s	n/s	n/s	n/s	n/s	0.30	**0.004**	n/s	n/s
Duration of symptoms at enrollment :		n/s		n/s		**< 0.001**		n/s		n/s		n/s
0 – 1.5 years	n/s		n/s		1.00		n/s		n/s		n/s	
1.6 – 4 years	n/s	n/s	n/s	n/s	0.27	0.001	n/s	n/s	n/s	n/s	n/s	n/s
5+ years	n/s	n/s	n/s	n/s	0.20	<0.001	n/s	n/s	n/s	n/s	n/s	n/s
Initial infectious prodrome (yesVno)	n/s	n/s	n/s	n/s	4.43	**0.001**	0.30	**0.02**	n/s	n/s	n/s	n/s
Gastric emptying (scintigraphy):												
Percent gastric retention at 2 hr	n/s	n/s	1.03	**0.004**	n/s	n/s	n/a	n/a	n/s	n/s	n/s	n/s
Percent gastric retention at 4 hr	n/s	n/s	n/s	n/s	n/s	n/s	n/a	n/a	n/s	n/s	1.02	**0.01**
Severity of symptoms:‡												
Nausea severity	1.69	**0.02**	n/s	n/s	1.37	**0.01**	n/s	n/s	1.45	**0.006**	n/a	n/a
Vomiting severity	n/s	n/s	n/s	n/s	n/s	n/s	1.25	**0.02**	n/s	n/s	n/a	n/a
Feeling of stomach fullness severity	1.94	**0.01**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/a	n/a
Loss of appetite severity	n/s	n/s	0.63	**<0.001**	n/s	n/s	1.38	**0.01**	n/s	n/s	n/a	n/a
Bloating severity	n/s	n/s	1.34	**0.03**	n/s	n/s	n/s	n/s	n/s	n/s	n/a	n/a
Upper abdominal discomfort	0.55	**0.02**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s		
Lower abdominal pain severity	n/s	n/s	0.48	**0.009**	0.45	**0.002**	n/s	n/s	n/s	n/s		
Lower abdominal discomfort severity	n/s	n/s	1.79	**0.03**	1.62	**0.05**	n/s	n/s	n/s	n/s		
Constipation severity	1.48	**0.03**	n/s	n/s	0.80	**0.02**	n/s	n/s	n/s	n/s		
Diarrhea severity	0.63	**0.02**	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s		
Cardinal Symptom Index (GCSI)‡	1.89	**0.02§**	n/s	n/s	n/s	n/s	1.42	**0.05§**	1.49	**0.02§**	n/a	n/a

*Females (N=213), Males (N=28)

Overweight defined as Body Mass Index (BMI) ≥ 25 kg/m^2 (N=111), Normal or less defined as BMI < 25 kg/m^2 (N=132)

Acute onset of symptoms (N=122), Insidious onset (N=120)

Severe delay in gastric emptying at 4-hours is % retention > 35% (N=68), Not severe delay (N=173)

Severe gastroparesis defined as Grade 3: gastric failure (N=72), Grade 1: mild and Grade 2: compensated gastroparesis (N=171) using the gastroparesis severity scale reported in the ANMS review on treatment of gastroparesis (4).

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Severity of symptoms based on the GCSI score from the PAGI-SYM questionnaire: Severe symptoms defined as GCSI ≥ 3.5 (N=90), Less severe symptoms defined as GCSI < 3.5 (N=150)

[†]Independent characteristics and associated odds ratios were determined from bi-directional multivariable logistic regression analysis for each sub-group (sex, body mass, symptom onset, severity of delayed gastric empting, gastroparesis severity) using the full candidate set of characteristics shown in Tables 1–4, 6–7
n/a = Characteristic not in model due to instability of model due to multicollinearity.
n/s = Characteristic not significant at the 0.05 level

[‡]Definitions:
Waist to hip ratio cardiovascular and diabetes health risk category based on NIDDK guidelines defined as follows:

Low risk (≤ 0.95 for males, ≤ 0.80 for females), moderate risk (0.96 to 1.0 for males, 0.81 to 0.85 for females, high risk (≥ 1.0 for males, ≥ for females)

ESR = Erythrocyte sedimentation rate
Beck Depression Index > 30 indicates clinically severe depression
Symptom severity from the PAGI-SYM (Patient Assessment of GI Symptoms) questionnaire, scores range from 0–5
Gastroparesis cardinal symptom index (GCSI) = mean of the sub-scores for nausea, postprandial fullness, and bloating where:

Nausea sub-score = mean of the scores for nausea, retching, and vomiting

Postprandial fullness/early satiety sub-score = mean of the scores for stomach fullness, inability to finish meal, excessive fullness, and loss of appetite

Bloating sub-score = mean of the scores for bloating and large stomach

[§]Odds ratios and *P* values determined from a separate model including GCSI instead of the 9 separate symptom severity scores.