Similarities and Differences Between Diabetic and Idiopathic Gastroparesis

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This article has an accompanying continuing medical education activity on page e134. Learning Objective—At the end of this activity, the learner should distinguish the similarities and differences between diabetic gastroparesis and idiopathic gastroparesis.

BACKGROUND & AIMS: Gastroparesis can be diabetic or idiopathic, yet little is known about differences in their presentation. We compared clinical characteristics, symptoms, and gastric emptying in patients with type 1 or type 2 diabetic (DG) or idiopathic (IG) gastroparesis. **METHODS:** We analyzed data from 416 patients with gastroparesis who were enrolled in the National Institute of Diabetes and Digestive and Kidney Diseases Gastroparesis Registry; 254 had IG (most were female and white), and 137 had DG (78 had type 1 and 59 had type 2). Registry data included detailed histories, physical examinations, results from gastric emptying scintigraphy, and responses to validated symptom questionnaires. **RESULTS:** Patients with type 2 diabetes mellitus (DM) were an average of 13 years older at the onset of symptoms of gastroparesis and heavier than patients with IG. Patients with type 1 DM had more hospitalizations in the past year than patients with IG. Symptoms that prompted evaluation more often included vomiting for DG and abdominal pain for IG. Patients with DG had more severe retching and vomiting than those with IG, whereas patients with IG had more severe early satiety and postprandial fullness subscores. Compared with IG, gastric retention was greater in patients with type 1 DM. More than 50% of patients with type 1 DM had severe retention (>35% at 4 hours); they took prokinetic agents more frequently and were more likely to receive gastric electric stimulation. **CONCLUSIONS: There are similarities and differences in clinical characteristics of DG and IG. Gastroparesis is a heterogeneous disorder; its etiology affects symptoms and severity. Long-term studies are needed to determine whether the differences in symptoms and gastric emptying affect progression and treatment responses.**

Keywords: Stomach Disorder; Nausea; Vomiting; Gastric Emptying; Digestion; NIDDK Gastroparesis Clinical Research Consortium.

Gastroparesis can result from several disorders including diabetic gastroparesis (DG) and idiopathic gastroparesis (IG).[1,2] Symptoms of gastroparesis are variable. Early satiety, postprandial fullness, and vomiting are associated with delayed emptying in functional dyspepsia.[3,4] In IG, increasing gastric retention is associated with increasing severity of vomiting.[5] Abdominal pain can be present in some patients and seems to be more prevalent in IG.[6,7] In diabetes, abdominal fullness and bloating have been associated with delayed gastric emptying.[8]

DG and IG appear to have different pathophysiologies. Patients with DG might have vagal nerve dysfunction, whereas patients with IG do not.[9] Common cellular abnormalities are loss of interstitial cells of Cajal, inflammatory infiltrate, and decreased nerve fibers.[10,11] Nitric oxide synthase expression appears to be decreased in more IG patients compared with DG patients.[11]

Most studies of gastroparesis have combined patients with DG and IG, but whether DG and IG differ in their phenotypic presentation is not known. The aim of this study was to describe the similarities and differences between patients with DG and IG, focusing on demographics, symptom profiles, gastric emptying, and quality of life.

Methods

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Gastroparesis Clinical Research Consortium is a cooperative network of 7 clinical centers and 1 Data Coordinating Center. The Gastroparesis Registry (http://ClinicalTrials.gov identifier: NCT00398801) was implemented as an observational study of patients with gastroparesis. En-

Abbreviations used in this paper: BDI, Beck Depression Inventory; BMI, body mass index; DG, diabetic gastroparesis; GCSI, Gastroparesis Cardinal Symptom Index; IG, idiopathic gastroparesis; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; OR, odds ratio; PAGI-SYM, Patient Assessment of Upper GI Symptoms; PAG-QoL, Patient Assessment of Upper Gastrointestinal Disorders Quality of Life; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; STAI, State-Trait Anxiety Inventory; T1DM, type 1 diabetes mellitus; T2, type 2 diabetes mellitus.

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rolled patients met specific entry criteria: 18 years or older; symptoms of at least 12-week duration; delayed gastric emptying; and no structural abnormality on upper endoscopy.

During interviews, case report forms were completed including data relating to symptoms, associated medical conditions, and medication and supplemental therapies. Clinical severity of gastroparesis[12] 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 as shown by the patient having emergency department visits, frequent doctor visits or hospitalizations, and/or inability to maintain nutrition via an oral route).

The Patient Assessment of Upper GI Symptoms (PAGI-SYM) questionnaire assesses symptoms of gastroparesis, dyspepsia, and gastroesophageal reflux disease[13] including symptoms of the Gastroparesis Cardinal Symptom Index (GCSI).[14] Severities of symptoms during the previous 2 weeks were graded from 0–5: no symptoms = 0 and very severe = 5.

Disease-specific quality of life was assessed with the Patient Assessment of Upper Gastrointestinal Disorders Quality of Life (PAGI-QOL) survey, which scores 30 factors from 0 (none of the time) to 5 (all of the time) during the past 2 weeks.[15] Overall PAGI-QOL scores were calculated by taking means of all subscores after reversing item scores; a mean PAGI-QOL score of 0 represents poor quality of life, whereas 5 reflects the best life quality.

The Medical Outcomes Study 36-Item Short-Form Health Survey version 2 (SF-36v2) was used to assess the patients' views of overall physical and mental health. The 8 subscales were standardized to the 1998 U.S. general population with a mean (± standard deviation) of 50±10. A higher score reflects higher QoL.[16]

Psychological functioning was assessed by using Beck Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI). BDI is a 21-question inventory assessing depression, cognition, and physical well-being.[17] Each answer is scored on a scale of 0–3. Higher total scores indicate more severe depressive symptoms. 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).[18]

Investigator-derived independent outcomes measure score includes parameters associated with healthcare resource use: intensity of service, severity of illness, and number of nongastrointestinal organ systems involved.[19] Each parameter is rated on a 10-point scale, and they are summed for a total score ranging from 0–30.

Gastric emptying scintigraphy was performed by using a low-fat, egg white meal, with imaging at 0, 1, 2, and 4 hours.[20,21] Delayed gastric emptying (gastric retention >60% at 2 hours and/or >10% at 4 hours) was graded according to the gastric retention at 4 hours: mild (≤20% gastric retention at 4 hours), moderate (>20%–35%), and severe (>35%).[21]

This report focuses on patients with either IG or DG enrolled from January 2007–March 15, 2010. Because studies with DG have suggested some differences between type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM),[22] the data in diabetic patients are reported for T1DM and T2DM. Some data included in this article were included in prior publications of earlier, smaller cohorts of subjects in the Gastroparesis Registry IG[5] and psychological dysfunction in gastroparesis.[23]

Statistical Methods

We conducted an exploratory analysis of a set of baseline characteristics of scientific merit including demographic, lifestyle, anthropometric, gastroparesis-specific medical history, symptom severity scores, gastric emptying results, medications, comorbidities, psychological inventory scores, and QoL assessments. The set of characteristics were analyzed by using univariate and multivariate logistic regression analyses for each of the gastroparesis subgroups of interest (idiopathic, T1DM, T2DM). Univariate results are expressed as mean ± standard deviation or by percentages. Statistical significance of differences in clinical features comparing all diabetics and each of the diabetic subgroups with IG was tested by using a χ^2 test for nonordered categories, Fisher exact test, or a Cochran-Armitage test for trend for ordered categorical features. Continuous features were analyzed by using a Kruskal-Wallis test.[24]

Independent characteristics associated with either T1DM and IG or T2DM and IG were determined from fitting the pooled set of characteristics with significance at the .05 level from bidirectional step-wise (both forward and backward) multiple binary logistic analyses.[25] Both final models had respectable goodness of fit by using the Hosmer-Lemshow goodness-of-fit test.

P values are two-sided and nominal, with a level of .05 considered to be statistically significant. Both SAS version 9.1 (SAS Institute, Cary, NC) and Stata release 11 (Stata Corp, College Station, TX) statistical software were used.

Results

Study Subjects

Of 416 patients with gastroparesis, 25 patients were diagnosed with other causes of gastroparesis (eg, postsurgical) and were too few to be included. There were 391 patients with IG or DG enrolled into the NIDDK Gastroparesis Registry at the time of data analyses (November 15, 2010), 254 patients with IG and 137 with DG (78 patients with T1DM and 59 patients with T2DM).

Demographics

The majority of the patients were women (83% overall) regardless of etiology; IG patients were most likely to be female (idiopathic, 89%; T1DM, 71%; T2DM, 76%; $P < .001$) (Table 1). Most patients were white (85% overall); IG patients were more commonly white (90% IG, 77% T1DM, 76% T2DM; $P = .001$). Patients with T2DM were older at enrollment (41 ± 14 years for IG, 39 ± 11 years T1DM, 53 ± 11 years T2DM; $P < .001$) and heavier (body mass index [BMI] of 25.7 ± 6.9 kg/m^2 for IG, 26.1 ± 6.0 kg/m^2 T1DM, 33.4 ± 7.5 kg/m^2 T2DM; $P < .001$) than patients with IG. Overall, 71% of patients with T2DM were obese (BMI > 30 kg/m^2) compared with 26% for IG and 28% for T1DM.

Symptoms

T2DM patients were older at onset of symptoms (36 ± 15 years IG, 34 ± 10 years T1DM, 49 ± 11 years T2DM; $P <$