Published in final edited form as:

Gastroenterol Clin North Am. 2015 March ; 44(1): 9–19. doi:10.1016/j.gtc.2014.11.002.

EPIDEMIOLOGY AND NATURAL HISTORY OF GASTROPARESIS

Adil E. Bharucha¹

¹Clinical Enteric Neuroscience Translational and Epidemiological Research Program and Division of Gastroenterology and Hepatology Mayo Clinic, Rochester, Minnesota

Keywords

Gastroparesis; epidemiology; quality of life; natural history; diabetic gastroparesis; idiopathic gastroparesis

INTRODUCTION

Gastroparesis is a syndrome characterized by delayed gastric emptying (GE) and symptoms thereof in the absence of gastric outlet obstruction. In diabetes mellitus (DM), delayed GE is often asymptomatic.¹ This term should be reserved for patients with delayed GE and upper gastrointestinal symptoms. DM and “idiopathic causes” are the 2 primary etiologies associated with gastroparesis. Only 2 studies have evaluated the epidemiology of gastroparesis in the population.^{2, 3} Even these studies are based on data collected from patients who presented for medical attention rather than a random sample of people in the community. At present, GE can only be assessed by scintigraphy, which requires specialized laboratories and radiation exposure, limiting population-based studies of the epidemiology of gastroparesis. Hence, our understanding of many facets of the epidemiology of gastroparesis is primarily based on case series or hospital-based databases rather than the population. These studies suggest that gastroparesis is not uncommon and can impair quality of life. The incidence of hospitalizations associated with a diagnosis of gastroparesis has increased considerably since 2000.⁴ Several organic diseases affect gastric neuromuscular functions by causing an extrinsic or enteric neuropathy or a myopathy. Among patients who do not have an underlying disorder that is known to be associated with gastroparesis, the pathogenesis of gastroparesis is poorly understood.

PREVALENCE AND INCIDENCE

There is only 1 study on the epidemiology of idiopathic gastroparesis in the population.² That study, which was conducted in the Rochester Epidemiology Project, defined

© 2014 Elsevier Inc. All rights reserved.

Affiliation: Professor of Medicine, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905. bharucha.adil@mayo.edu

Disclosures: Dr. Bharucha has received consulting fees from Asubio Pharmaceuticals, Ironwood Pharmaceuticals, GICare Pharmaceuticals, and Medspira Inc; licensed a patent to Medspira Inc.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

gastroparesis as definite (i.e., delayed gastric emptying by standard scintigraphy and typical symptoms for more than 3 months), probable (i.e., typical symptoms and food retention on endoscopy or upper gastrointestinal study), and possible (i.e., typical symptoms alone or delayed gastric emptying by scintigraphy without gastrointestinal symptoms). There were 83 patients with definite, 127 with definite or probable gastroparesis, and 222 any of the 3 definitions of gastroparesis. On January 1, 2007, the age-adjusted prevalence of definite gastroparesis per 100,000 persons was approximately four fold higher in women [37.8 (95% CI, 23.3–52.4)] than in men [9.6 (95% CI, 1.8–17.4)]. Likewise, the age-adjusted incidence per 100,000 person-years of definite gastroparesis for the years 1996–2006 was approximately four fold higher in women [9.8 (95% CI, 7.5–12.1)] than men [2.4 (95% confidence interval [CI], 1.2–3.8)].

Earlier reports from tertiary referral centers observed that up to 60% of patients with long-standing T1DM and gastrointestinal symptoms had diabetic gastroparesis.^{5, 6} However, these studies predated the routine use of intensive insulin therapy for T1DM.

More recently, population-based studies of GI symptoms in DM have been based on symptoms alone or symptoms and delayed GE. Compared to the studies in selected populations above, the cumulative incidence of diabetic gastroparesis among patients with DM in the community is lower. In the only community-based study from Olmsted County, MN, the cumulative incidence of symptoms and delayed gastric emptying over 10 years was 5% in type 1 DM (HR 33 [95% CI 4.0, 274] adjusted for age and gender versus controls), 1% in type 2 DM (HR 7.5 [95% CI 0.8, 68] adjusted for age and gender versus controls) and 1% in controls.³ (Table 1) The risk of gastroparesis in type 1 DM was significantly greater than in type 2 DM (HR 4.4 [95% CI 1.1, 17]). Gastroparesis was documented by physician diagnosis, by evaluating gastric emptying with scintigraphy, or by symptoms and retained food at endoscopy. Because gastroparesis was identified only in people who presented for care, people in whom GE was not evaluated may not have been identified. Hence, this study assessed the cumulative incidence of diabetic gastroparesis (over 10 years) rather than the prevalence of diabetic gastroparesis.

Several studies have evaluated the epidemiology of upper gastrointestinal symptoms but not GE among diabetics in the community. In most community-based studies, the prevalence of GI symptoms was not significantly higher in diabetics than in asymptomatic controls. In the Rochester Diabetic Neuropathy Study from Olmsted County, only 1% of patients had symptoms of gastroparesis.⁷ (Table 2). Another study from Olmsted County observed that the prevalence for nausea and/or vomiting or dyspepsia was not significantly different in type 1 or 2 diabetes relative to controls.⁸ That study did not assess GE. However, in an Australian community-based study of 423 patients with predominantly (95%) type 2 DM, the prevalence of several upper gastrointestinal (GI) symptoms including abdominal pain or discomfort, early satiety, postprandial fullness, bloating, heartburn, nausea, vomiting, and dysphagia, was higher in a sample of people predominantly with type 2 DM than in controls.⁹ Taken together, these data suggest that GI symptoms are not uncommon among people with DM. The risk of gastroparesis is higher in type 1 than type 2 DM.

Longitudinal studies from Australia suggest that similar to functional GI disorders, GI symptom turnover also occurs in DM. Turnover refers to appearance and disappearance of symptoms over time. In the first study, there was considerable turnover in GI symptoms 3 years after the initial assessment in patients with type 2 DM.¹⁰ However, appearance and resolution were balanced; hence overall prevalence was comparable at follow-up. Several factors, but not glycemic control, predicted symptom change; these factors varied among symptoms. In another cohort of 139 diabetic subjects of whom approximately 50% had type 1 DM and 5% had severe autonomic dysfunction, symptom turnover varied between 15–25% in the diabetic group and was not significantly different from controls.¹¹ Symptom turnover was not associated with glycemic control or autonomic neuropathy but rather with depression (i.e., appearance and disappearance of depression were associated with gain and loss of GI symptoms respectively).

No studies that have assessed symptoms and GE among randomly selected people in a community, perhaps because scintigraphy is cumbersome and involves radiation exposure. Gastric emptying breath tests utilize ¹³C, which is a stable isotope, and offer an alternative approach for measuring solid phase GE without elaborate detection equipment or radiation exposure in the office or bedside.^{12, 13} The Food and Drug Administration is currently reviewing a ¹³C-spirulina GE BT for use in the United States. Gastric emptying can also be measured by a nondigestible capsule, SmartPill™, which records luminal pH, temperature, and pressure during GI transit providing a measure of GE time.¹⁴

While most attention has focused on delayed GE, DM is also associated with rapid GE. In a Mayo Clinic, tertiary referral study of 129 patients with diabetes and upper GI symptoms undergoing scintigraphy, 42% had normal, 36% delayed and 22% rapid gastric emptying.¹⁵ There were approximately an equal number of patients with type 1 and type 2 diabetes in each category. However, the prevalence of rapid GE among diabetics in the community is unknown.

HOSPITALIZATION

While the incidence of gastroparesis did not change significantly between the periods 1996–2000 and 2001–2006,² data from the Nationwide Inpatient Sample (NIS), which comprises a nationally representative sample of 5–8 million hospitalizations, demonstrate a 138% increase in the hospitalizations related to gastroparesis between 1995 and 2004.⁴ DM was listed as a comorbidity in 21% of these patients in 1995 and 26.7% in 2004. Gastroparesis was the primary or secondary diagnosis for these hospitalizations. The former increased by 158% between 1995 and 2004 and most of this change (138%) occurred between 2000 and 2004. In comparison, changes over that period in diabetes-related hospitalizations (+53%), all hospitalizations (+13%), and hospitalizations with 4 other GI conditions, i.e., gastroesophageal reflux disease (GERD), gastric ulcer, gastritis, or nonspecific nausea/vomiting as the primary diagnosis (–3% to +76%) were smaller. Conceivably, this increase in hospitalizations for gastroparesis may reflect an increased prevalence of DM or gastroparesis, changes in diagnostic criteria, severity, and treatment of gastroparesis, or better recognition and/or diagnosis of this disorder. There are several possible explanations for the striking increase after 2000. The withdrawal of the prokinetic agent cisapride from

the market might have increased the number of symptomatic patients. The U.S. Food and Drug Administration (FDA) provided humanitarian device exemption to gastric electric stimulation around 2000. This device often entails hospitalization for surgical placement of the stimulator.¹⁶ Increased recognition of this disorder and a change in hospital coding practices may also contribute. Compared to these 4 GI conditions as the primary diagnosis, the length of stay was also longer (+15.4% to +66.2%, all $P < 0.001$) for gastroparesis listed as the primary diagnosis. The total charges for hospitalization in patients with gastroparesis listed as the primary (\$20,573) or secondary (\$24,965) diagnosis in 2004 were also higher than these 4 diagnoses except for gastric ulcer, for which the total charge was \$23,259. Similar trends for gastroparesis versus other diagnoses were observed in 1995.

The Nationwide Inpatient Sample study did not clearly discriminate between hospitalization for idiopathic versus diabetic gastroparesis. In the NIDDK consortium, patients with gastroparesis due to type 1 DM reported more hospitalizations (ie, 5.1 ± 6.4 per year, Mean $\pm$ SD), mostly for vomiting and dehydration, than those with idiopathic (1.6 ± 3.0) or type 2 DM (2.7 ± 5.7).¹⁷ In a study from the Beth Israel Deaconess Medical Center and the Joslin Diabetes Center, patients with DM gastroparesis also had more hospital days than patients with DM and GI symptoms but normal GE (i.e., 25.5 versus 5.1 per 1000 patient days).¹⁸

RISK FACTORS AND ASSOCIATED CONDITIONS

Table 2 identifies the mechanisms of gastroparesis and diseases associated with the same. Among patients who do not have such underlying disorders, the pathogenesis of gastroparesis is poorly understood. A tertiary referral series of patients with idiopathic gastroparesis observed that the onset of symptoms was consistent with a viral etiology in 23% and began after a cholecystectomy in 8%.¹⁹ In the NIDDK Gastroparesis Consortium, approximately 19% of patients with idiopathic and 14% each with type 1 and type 2 DM had features of an infectious prodrome; 36% of patients with idiopathic or diabetic gastroparesis had a cholecystectomy.^{17, 20} Patients with cholecystectomy had more comorbidities, particularly chronic fatigue syndrome, fibromyalgia, depression, and anxiety. It is unclear if cholecystectomy is an independent risk for gastroparesis.

Acute hyperglycemia delays gastric emptying.²¹ However, the relationship between long-term control of glycemia and gastric emptying is unclear. Increased HbA1c levels were associated with gastrointestinal symptoms in people with type 2 DM.²² However, HbA1c levels were not significantly different among participants with DM with GI symptoms and delayed GE, DM with GI symptoms and normal GE, and DM without GI symptoms.¹⁸ Also, improved glycemic control did not accelerate gastric emptying in participants with T1DM or T2DM and delayed gastric emptying.²³ This is in contrast to the findings of the Diabetes Control and Complications Trial (DCCT), wherein 6.5 years of intensive insulin therapy reduced the risk of diabetic retinopathy, nephropathy, peripheral and cardiac autonomic neuropathy by 40–60% compared to conventional insulin therapy.²⁴ Moreover, these differences between the former intensive and conventional treatment groups have persisted for as long as 14 years despite the loss of glycemic separation.^{25–27}

Other than an association with autonomic neuropathy²⁸ the relationship between diabetic gastroparesis and other complications of longstanding DM is incompletely understood. In the only community-based study, symptoms of peripheral or autonomic neuropathy were not associated with diabetic gastroparesis.³

NATURAL HISTORY AND OUTCOMES

In the Olmsted County epidemiology study, one third of all incident cases of gastroparesis patients died and another one third required hospitalization, medications, or tube feeding related to gastroparesis.² Overall survival in patients with gastroparesis was significantly lower than that of the Minnesota white population.

There is minimal data on the natural history of diabetic gastroparesis. From a group of 86 patients assessed at a tertiary referral center, 20 patients, of whom 16 had type 1 DM, were reevaluated 12 years later and only 13 patients (12 had type 1 DM) were reevaluated approximately 25 years after the first study.^{23, 29} While gastric emptying was not significantly different 25 years after the baseline assessment, correlation between initial and subsequent assessments was limited, as evidenced by a correlation coefficient of 0.56.²³

IMPACT ON QUALITY OF LIFE

While nausea and vomiting are the cardinal symptoms of gastroparesis, data from the NIDDK Gastroparesis Clinical Research Consortium suggest that upper abdominal pain or discomfort is not uncommon and often severe.³⁰ Moderate to severe pain was associated with more severely delayed GE, worse quality of life, depression and anxiety.³⁰ Moreover, among patients with moderate to severe pain, 48% were taking opiates. The SF-36 physical and mental component scores indicate a severe impact on QOL. To what extent this impact is related to GI symptoms per se versus comorbid conditions (eg, depression) and/or medications (eg, opiates) is unclear.

Data on the impact of GI symptoms on QOL among patients with gastroparesis in the community are limited. Among a cohort of people with predominantly T2DM in the community, the physical and mental QOL as assessed by the SF-36 were lower in diabetics with GI symptoms compared with population norms.³¹ The QOL scores in all subscales decreased markedly with increasing numbers of distinct GI symptom groups. The association between GI symptoms and poorer quality of life in DM was independent of age, gender, smoking, alcohol use, and type of diabetes. However, the absolute SF-36 scores in this study were considerably, (ie, approximately twofold) higher than the data from the NIDDK consortium.^{30, 31} Race is also associated the impact of GI symptoms on QOL in DM. Thus, nonwhite patients with gastroparesis had more severe symptoms, poorer QOL, and utilized more health care resources than white patients.³² The 2 groups differed in health care utilization: 49% of nonwhite patients reported more than 4 gastroparesis-related emergency department visits and 42% reported more than 4 gastroparesis-related hospitalizations, as compared with 20% and 14% of white patients, respectively. In this study, nonwhite race, sex, age, and age of onset were independently associated with symptom scores, whereas etiology of gastroparesis and gastric emptying times were not.

High unemployment rates, lower household income, and work absenteeism are also variably associated with gastroparesis.^{17, 33}

MORTALITY RATES

Overall survival in patients with idiopathic gastroparesis was significantly lower than the age- and sex-specific expected survival computed from the Minnesota white population.² A review of several case series observed that the mortality rates in patients with gastroparesis range from 4% and 38%.³⁴ The best outcomes were observed in a largely outpatient-based group of patients followed for about 2 years and the highest death rates were reported in diabetic patients with gastroparesis requiring nutritional support.^{2, 19, 23, 35–38} In a study of 86 patients with diabetes, approximately 25% had died by follow up at least 9 years later; gastroparesis was not associated with mortality after adjustment for other disorders.³⁹ However, this study did not ascertain the relationship between diabetic gastroparesis and other medical conditions. Whether this increased mortality is driven by gastroparesis is unknown. Data on long-term natural history in the community are lacking.

CLINICAL IMPLICATIONS

The clinical features of gastroparesis are detailed in other chapters. This section will focus on selected aspects that pertain to the epidemiology of gastroparesis.

During GE scintigraphy, postprandial scans at 1 hour can identify accelerated GE while scans at 2 and 4 hours distinguish normal function from delayed GE with a sensitivity of 90% and a specificity of 70%.⁴⁰ For solid-phase testing, most centers use a 99mTc sulfur colloid-labeled egg sandwich as the test meal, with imaging at 0, 1, 2, and 4 hours. The Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society recommend a 4-hour test using radiolabelled EggBeaters® meal with jam, toast, and water.⁴¹

The cardinal upper gastrointestinal symptoms of dyspepsia and gastroparesis are similar. While dyspepsia is not defined by delayed GE, approximately one-third of patients with functional dyspepsia have delayed GE.⁴² Hence, the distinction between, dyspepsia with delayed GE and gastroparesis, either functional or diabetic, is blurred.⁴² Because the term gastroparesis implies a paralyzed stomach, its use should be restricted to patients with severe symptoms and markedly delayed GE. There is no accepted GE value to discriminate between delayed GE and gastroparesis. When the delay in GE is not severe, the term dyspepsia is perhaps more appropriate.

Up to 40% of patients with diabetic gastroparesis are asymptomatic.¹ Likewise, there is a limited correlation between symptoms and delayed GE in idiopathic gastroparesis.⁴² During therapeutic trials for gastroparesis, improvements in GE and symptoms were not correlated.⁴³ Hence, the utility of using GE as an endpoint in therapeutic trials for gastroparesis has been questioned.⁴³ Perhaps this limited correlation between symptoms and delayed GE is explained, among other factors, by other features such as vagal dysfunction⁴⁴ or increased sensitivity to gastric distention⁴⁵ that influence the expression of gastric emptying disturbance (i.e., as symptoms). Similar discrepancies between symptoms and objective

findings exist in other diseases (eg, Crohn's disease). For example, in one study, the correlation between symptoms evaluated by the Crohn's Disease Activity Index and endoscopic findings in Crohn's disease was not significant.⁴⁶ In addition to gastrointestinal symptoms, delayed GE may also predispose to hypoglycemia in type 1 DM.⁴⁷ Hence, consideration should be given to evaluating GE in patients with unexplained hypoglycemia without GI symptoms.

By convention, delayed GE is defined by scintigraphy. However, delayed GE may also manifest with retained food in the stomach after an overnight fast. Our clinical observations suggest that some patients with retained food in the stomach at endoscopy have normal GE by scintigraphy. This discrepancy may be explained by day-to-day variations in GE, the use of medications (e.g., opioids) which can delay GE before either study, ingestion of food before an endoscopy, or differences between the gastric motor mechanisms responsible for antral motility and emptying of smaller particles during scintigraphy (i.e., type 2 antral motor activity) and indigestible larger particles (i.e., 3 mm size) ingested with meals which are emptied by the antral component of the migrating motor complex during fasting or sleeping.

Among patients with an idiopathic disorder, DM, an autonomic neuropathy or postural orthostatic tachycardia syndrome, dyspeptic symptoms may also be associated with rapid GE.^{48–54} Because symptoms are of limited utility for discriminating between delayed and rapid GE, it is essential to measure gastric emptying to ascertain whether patients have normal, delayed or rapid GE.

SUMMARY and CONCLUSIONS

Diabetic and idiopathic gastroparesis are not uncommon conditions that can substantially impair the quality of life. Most studies on the epidemiology of gastroparesis have been conducted in selected case series rather than in the population. More studies are necessary to better understand the incidence and prevalence, risk factors, and natural history of gastroparesis.

Acknowledgments

This work was supported in part by USPHS NIH Grant P01 DK68055

References

1. Camilleri M, Bharucha AE, Farrugia G. Epidemiology, mechanisms, and management of diabetic gastroparesis. *Clin Gastroenterol Hepatol*. 2011; 9:5–12. quiz e7. [PubMed: 20951838]
2. Jung HK, Choung RS, Locke GR 3rd, Schleck CD, Zinsmeister AR, Szarka LA, Mullan B, Talley NJ. The incidence, prevalence, and outcomes of patients with gastroparesis in Olmsted County, Minnesota, from 1996 to 2006. *Gastroenterology*. 2009; 136:1225–33. [PubMed: 19249393]
3. Choung RS, Locke GR 3rd, Schleck CD, Zinsmeister AR, Melton LJ 3rd, Talley NJ. Risk of gastroparesis in subjects with type 1 and 2 diabetes in the general population. *Am J Gastroenterol*. 2012; 107:82–8. [PubMed: 22085818]
4. Wang YR, Fisher RS, Parkman HP. Gastroparesis-related hospitalizations in the United States: trends, characteristics, and outcomes, 1995–2004. *American Journal of Gastroenterology*. 2008; 103:313–22. [PubMed: 18047541]

5. Feldman M, Schiller LR. Disorders of gastrointestinal motility associated with diabetes mellitus. *Ann Intern Med.* 1983; 98:378–384. [PubMed: 6402969]
6. Jones KL, Russo A, Stevens JE, Wishart JM, Berry MK, Horowitz M. Predictors of delayed gastric emptying in diabetes. *Diabetes Care.* 2001; 24:1264–9. [PubMed: 11423513]
7. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM, O'Brien PC, Melton LJ 3rd, Service FJ. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study [Erratum appears in *Neurology* 1993 Nov;43(11):2345]. *Neurology.* 1993; 43:817–24. [PubMed: 8469345]
8. Maleki D, Locke GR 3rd, Camilleri M, Zinsmeister AR, Yawn BP, Leibson C, Melton LJ 3rd. Gastrointestinal tract symptoms among persons with diabetes mellitus in the community. *Archives of Internal Medicine.* 2000; 160:2808–16. [PubMed: 11025791]
9. Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M. Prevalence of gastrointestinal symptoms associated with diabetes mellitus: a population-based survey of 15,000 adults. *Archives of Internal Medicine.* 2001; 161:1989–96. [PubMed: 11525701]
10. Talley NJ, Howell S, Jones MP, Horowitz M. Predictors of turnover of lower gastrointestinal symptoms in diabetes mellitus.[comment]. *American Journal of Gastroenterology.* 2002; 97:3087–94. [PubMed: 12492194]
11. Quan C, Talley NJ, Jones MP, Spies J, Horowitz M. Gain and loss of gastrointestinal symptoms in diabetes mellitus: associations with psychiatric disease, glycemic control, and autonomic neuropathy over 2 years of follow-up. *American Journal of Gastroenterology.* 2008; 103:2023–30. [PubMed: 18796098]
12. Szarka LA, Camilleri M, Vella A, Burton D, Baxter K, Simonson J, Zinsmeister AR. A stable isotope breath test with a standard meal for abnormal gastric emptying solids in the clinic and in research. *Clin Gastroenterol Hepatol.* 2008; 6:635–643. [PubMed: 18406670]
13. Bharucha AE, Camilleri M, Veil E, Burton D, Zinsmeister AR. Comprehensive assessment of gastric emptying with a stable isotope breath test. *Neurogastroenterol Motil.* 2013; 25:e60–9. [PubMed: 23216872]
14. Kuo B, McCallum RW, Koch KL, Sitrin MD, Wo JM, Chey WD, Hasler WL, Lackner JM, Katz LA, Semler JR, Wilding GE, Parkman HP. Comparison of gastric emptying of a nondigestible capsule to a radio-labelled meal in healthy and gastroparetic subjects. *Alimentary Pharmacology & Therapeutics.* 2008; 27:186–96. [PubMed: 17973643]
15. Bharucha AE, Camilleri M, Forstrom LA, Zinsmeister AR. Relationship between clinical features and gastric emptying disturbances in diabetes mellitus. *Clin Endocrinol (Oxf).* 2008; 70:415–420. [PubMed: 18727706]
16. Cutts TF, Luo J, Starkebaum W, Rashed H, Abell TL. Is gastric electrical stimulation superior to standard pharmacologic therapy in improving GI symptoms, healthcare resources, and long-term health care benefits? *Neurogastroenterology and Motility.* 2005; 17:35–43. [PubMed: 15670262]
17. Parkman HP, Yates K, Hasler WL, Nguyen L, Pasricha PJ, Snape WJ, Farrugia G, Koch KL, Calles J, Abell TL, McCallum RW, Lee L, Unalp-Arida A, Tonascia J, Hamilton F. National Institute of Diabetes Digestive Kidney Diseases Gastroparesis Clinical Research Consortium. . Similarities and differences between diabetic and idiopathic gastroparesis. *Clin Gastroenterol Hepatol.* 2011; 9:1056–64. quiz e133–4. [PubMed: 21871247]
18. Hyett B, Martinez FJ, Gill BM, Mehra S, Lembo A, Kelly CP, Leffler DA. Delayed radionucleotide gastric emptying studies predict morbidity in diabetics with symptoms of gastroparesis. *Gastroenterology.* 2009; 137:445–52. [PubMed: 19410575]
19. Soykan I, Sivri B, Sarosiek I, Kiernan B, McCallum RW. Demography, clinical characteristics, psychological and abuse profiles, treatment, and long-term follow-up of patients with gastroparesis. *Digestive Diseases & Sciences.* 1998; 43:2398–404. [PubMed: 9824125]
20. Parkman HP, Yates K, Hasler WL, Nguyen L, Pasricha PJ, Snape WJ, Farrugia G, Koch KL, Calles J, Abell TL, Sarosiek I, McCallum RW, Lee L, Unalp-Arida A, Tonascia J, Hamilton F. Cholecystectomy and clinical presentations of gastroparesis. *Digestive Diseases and Sciences.* 2013; 58:1062–73. [PubMed: 23456496]

21. Fraser RJ, Horowitz M, Maddox AF, Harding PE, Chatterton BE, Dent J. Hyperglycaemia slows gastric emptying in type 1 (insulin-dependent) diabetes mellitus. *Diabetologia*. 1990; 33:675–80. [PubMed: 2076799]
22. Bytzer P, Talley NJ, Hammer J, Young LJ, Jones MP, Horowitz M. GI symptoms in diabetes mellitus are associated with both poor glycemic control and diabetic complications. *Am J Gastroenterol*. 2002; 97:604–11. [PubMed: 11922554]
23. Jones KL, Russo A, Berry MK, Stevens JE, Wishart JM, Horowitz M. A longitudinal study of gastric emptying and upper gastrointestinal symptoms in patients with diabetes mellitus [see comment]. *Am J Med*. 2002; 113:449–55. [PubMed: 12427492]
24. Kilpatrick ES, Rigby AS, Atkin SL. The Diabetes Control and Complications Trial: the gift that keeps giving. *Nat Rev Endocrinol*. 2009; 5:537–45. [PubMed: 19763126]
25. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus. *JAMA*. 2002; 287:2563–9. [PubMed: 12020338]
26. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. *JAMA*. 2003; 290:2159–67. [PubMed: 14570951]
27. Martin CL, Albers JW, Pop-Busui R. DCCT/EDIC Research Group. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. *Diabetes Care*. 2014; 37:31–8. [PubMed: 24356595]
28. Bharucha AE, Camilleri M, Low PA, Zinsmeister AR. Autonomic dysfunction in gastrointestinal motility disorders. *Gut*. 1993; 34:397–401. [PubMed: 8472990]
29. Chang J, Russo A, Bound M, Rayner CK, Jones KL, Horowitz M. A 25-year longitudinal evaluation of gastric emptying in diabetes. *Diabetes Care*. 2012; 35:2594–6. [PubMed: 22891253]
30. Hasler WL, Wilson LA, Parkman HP, Koch KL, Abell TL, Nguyen L, Pasricha PJ, Snape WJ, McCallum RW, Sarosiek I, Farrugia G, Calles J, Lee L, Tonascia J, Unalp-Arida A, Hamilton F. Factors related to abdominal pain in gastroparesis: contrast to patients with predominant nausea and vomiting. *Neurogastroenterology and Motility*. 2013; 25:427–38. e300–1. [PubMed: 23414452]
31. Talley NJ, Young L, Bytzer P, Hammer J, Leemon M, Jones M, Horowitz M. Impact of chronic gastrointestinal symptoms in diabetes mellitus on health-related quality of life. *American Journal of Gastroenterology*. 2001; 96:71–6. [PubMed: 11197290]
32. Friedenberg FK, Kowalczyk M, Parkman HP. The influence of race on symptom severity and quality of life in gastroparesis. *Journal of Clinical Gastroenterology*. 2013; 47:757–61. [PubMed: 23426455]
33. Bielefeldt K, Raza N, Zickmund SL. Different faces of gastroparesis. *World Journal of Gastroenterology*. 2009; 15:6052–60. [PubMed: 20027677]
34. Bielefeldt K. Gastroparesis: concepts, controversies, and challenges. *Scientifica*. 2012; 2012:424802. [PubMed: 24278691]
35. Chaudhuri TK, Fink S. Prognostic implication of gastroparesis in patients with diabetes mellitus. *Clinical Autonomic Research*. 1992; 2:221–4. [PubMed: 1392540]
36. Fontana RJ, Barnett JL. Jejunostomy tube placement in refractory diabetic gastroparesis: a retrospective review. *American Journal of Gastroenterology*. 1996; 91:2174–8. [PubMed: 8855743]
37. Dudekula A, O'Connell M, Bielefeldt K. Hospitalizations and testing in gastroparesis. *Journal of Gastroenterology and Hepatology*. 2011; 26:1275–82. [PubMed: 21443672]
38. McCallum RW, Lin Z, Forster J, Roeser K, Hou Q, Sarosiek I. Gastric electrical stimulation improves outcomes of patients with gastroparesis for up to 10 years. *Clinical Gastroenterology & Hepatology*. 2011; 9:314–319. e1. [PubMed: 21185396]
39. Kong MF, Horowitz M, Jones KL, Wishart JM, Harding PE. Natural history of diabetic gastroparesis. *Diabetes Care*. 1999; 22:503–7. [PubMed: 10097936]

40. Camilleri M, Zinsmeister AR, Greydanus MP, Brown ML, Proano M. Towards a less costly but accurate test of gastric emptying and small bowel transit. *Dig Dis Sci*. 1991; 36:609–15. [PubMed: 2022162]
41. Abell TL, Camilleri M, Donohoe K, Hasler WL, Lin HC, Maurer AH, McCallum RW, Nowak T, Nusynowitz ML, Parkman HP, Shreve P, Szarka LA, Snape WJ Jr, Ziessman HA. American Neurogastroenterology and Motility Society and the Society of Nuclear M. Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine.[reprint in *J Nucl Med Technol* 2008 Mar;36(1):44–54;]. *American Journal of Gastroenterology*. 2008; 103:753–63. [PubMed: 18028513]
42. Lacy BE. Functional dyspepsia and gastroparesis: one disease or two? *Am J Gastroenterol*. 2012; 107:1615–20. [PubMed: 23160285]
43. Janssen P, Harris MS, Jones M, Masaoka T, Farre R, Tornblom H, Van Oudenhove L, Simren M, Tack J. The relation between symptom improvement and gastric emptying in the treatment of diabetic and idiopathic gastroparesis. *American Journal of Gastroenterology*. 2013; 108:1382–91. [PubMed: 24005344]
44. Rathmann W, Enck P, Frieling T, Gries FA. Visceral afferent neuropathy in diabetic gastroparesis. *Diabetes Care*. 1991; 14:1086–9. [PubMed: 1797493]
45. Farre R, Vanheel H, Vanuytsel T, Masaoka T, Tornblom H, Simren M, Van Oudenhove L, Tack JF. In functional dyspepsia, hypersensitivity to postprandial distention correlates with meal-related symptom severity. *Gastroenterology*. 2013; 145:566–73. [PubMed: 23702005]
46. Jones J, Loftus EV Jr, Panaccione R, Chen L-S, Peterson S, McConnell J, Baudhuin L, Hanson K, Feagan BG, Harmsen SW, Zinsmeister AR, Helou E, Sandborn WJ. Relationships between disease activity and serum and fecal biomarkers in patients with Crohn's disease. *Clinical Gastroenterology & Hepatology*. 2008; 6:1218–24. [PubMed: 18799360]
47. Chang J, Rayner CK, Jones KL, Horowitz M. Diabetic gastroparesis and its impact on glycemia. *Endocrinology and Metabolism Clinics of North America*. 2010; 39:745–62. [PubMed: 21095542]
48. Phillips WT, Schwartz JG, McMahan CA. Rapid gastric emptying of an oral glucose solution in type 2 diabetic patients. *Journal of Nuclear Medicine*. 1992; 33:1496–500. [PubMed: 1634941]
49. Frank JW, Saslow SB, Camilleri M, Thomforde GM, Dinneen S, Rizza RA. Mechanism of accelerated gastric emptying of liquids and hyperglycemia in patients with type II diabetes mellitus. *Gastroenterology*. 1995; 109:755–65. [PubMed: 7657103]
50. Schwartz JG, Green GM, Guan D, McMahan CA, Phillips WT. Rapid gastric emptying of a solid pancake meal in type II diabetic patients [see comment]. *Diabetes Care*. 1996; 19:468–71. [PubMed: 8732711]
51. Charles F, Phillips SF, Camilleri M, Thomforde GM. Rapid gastric emptying in patients with functional diarrhea. *Mayo Clinic Proceedings*. 1997; 72:323–8. [PubMed: 9121178]
52. Weytjens C, Keymeulen B, Van Haleweyn C, Somers G, Bossuyt A. Rapid gastric emptying of a liquid meal in long-term Type 2 diabetes mellitus. *Diabetic Medicine*. 1998; 15:1022–7. [PubMed: 9868975]
53. Bertin E, Schneider N, Abdelli N, Wampach H, Cadiot G, Loboguerrero A, Leutenegger M, Liehn JC, Thieffn G. Gastric emptying is accelerated in obese type 2 diabetic patients without autonomic neuropathy. *Diabetes & Metabolism*. 2001; 27:357–64. [PubMed: 11431601]
54. Lawal A, Barboi A, Krasnow A, Hellman R, Jaradeh S, Massey BT. Rapid gastric emptying is more common than gastroparesis in patients with autonomic dysfunction. *American Journal of Gastroenterology*. 2007; 102:618–23. [PubMed: 17100966]
55. Janatuinen E, Pikkarainen P, Laakso M, Pyorala K. Gastrointestinal symptoms in middle-aged diabetic patients. *Scandinavian Journal of Gastroenterology*. 1993; 28:427–32. [PubMed: 8511503]
56. Hammer J, Howell S, Bytzer P, Horowitz M, Talley NJ. Symptom clustering in subjects with and without diabetes mellitus: a population-based study of 15,000 Australian adults. *American Journal of Gastroenterology*. 2003; 98:391–8. [PubMed: 12591060]

KEY POINTS

- Gastroparesis is a syndrome characterized by delayed gastric emptying and symptoms thereof in the absence of gastric outlet obstruction.
- Most studies on the epidemiology of gastroparesis have been conducted in selected case series rather than in the population at large.
- In the only community-based study, the age-adjusted prevalence of idiopathic gastroparesis per 100,000 persons was higher in women [37.8 (95% CI, 23.3–52.4)] than men [9.6 (95% CI, 1.8–17.4)].
- In the only community-based study of gastroparesis in DM, the average cumulative incidence of symptoms and delayed gastric emptying over 10 years was higher (i.e., 5%) in type 1 DM than in type 2 DM (1%) in and in controls (1%).
- In the United States, the incidence of hospitalizations related to gastroparesis increased substantially between 1995 and 2004 and particularly after 2000.

Table 1
Community-Based Epidemiological Studies of Gastrointestinal Symptoms in Diabetes Mellitus (DM)

	Respondents	Response rate (number of respondents)	Key Findings
Dyck, 1993 ⁷	Residents of Rochester, MN with DM	44% (102 DM1, 278 DM2)	Gastroparesis: (0% DM1, 1% DM2)
Janatuinen, 1993 ⁵⁵	All residents in a hospital district with DM and a randomly selected control group	92% to 100% (89 DM1, 481 DM2, 635 controls)	Symptoms of nausea and vomiting were not different between cases with DM and controls without
Maleki, 2000 ⁸	Samples of Olmsted County residents with DM1, DM2 and corresponding age- and sex-stratified controls	59% (138 DM1, 217 DM2, 388 controls)	No difference in proportions with stomach symptoms between DM and controls; less heartburn reported by DM1 patients
Bytzer, 2001 ⁹ Hammer, 2003 ⁵⁶	Gender-stratified sample of 15,000 people in Sydney, Australia	60% for entire sample (423 of 8555 respondents had DM, 95% had DM2)	Small differences were detected with the highest adjusted OR for vomiting 1.7% vs 1.1% (mean OR 2.51). When upper gut dysmotility symptoms were evaluated, the results were 18.2% vs 15.3% (OR 1.75)
Talley, 2002 ¹⁰	Two surveys of subjects with DM2 on mailing list of Diabetes Australia at 3-year interval	64% returned second survey (892 DM2 in first survey)	Not applicable
Choung, 2012 ³	Follow-up of 1374 subjects (269 with DM1, 409 DM2) and controls matched for age and gender (735) in Olmsted County, MN	89% (1226 subjects) authorized review of medical records; questionnaires at interviews were not performed	Over 10 years, gastroparesis developed in 5.2% (DM1), 1% (DM2), and 0.2% (controls). Higher risk (HR 4.4, CI 1.1, 17) in DM1 than DM2.

NA – not applicable; DM1 = type 1 diabetes mellitus; DM2 = type 2 diabetes mellitus; All surveys used a mailed questionnaire
Data from Refs 3,7–10,55

Table 2

Pathogenesis and Etiology of Gastroparesis

Mechanism	Common causes	Uncommon causes
Extrinsic neuropathy	Iatrogenic vagotomy (eg, surgery for peptic ulcer disease, fundoplication), DM neuropathy	Other CNS diseases (eg, stroke, other causes of autonomic neuropathy, Parkinson's disease, spinal cord injury)
Intrinsic or enteric neuropathy	Post-infectious gastroparesis ¹ , DM	Paraneoplastic syndrome
Myopathy		Polymyositis, scleroderma ²
Drugs and metabolic disorders		Opiates, anticholinergic drugs, hypothyroidism, hyperparathyroidism, Addison's disease
Miscellaneous		After lung transplantation, anorexia nervosa, pregnancy