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Gastroparesis
A Review

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IMPORTANCE Gastroparesis is a condition of delayed gastric emptying in the absence of gastric outlet obstruction. Based on a 2018 US administrative health insurance claims database study, prevalence of definite gastroparesis (with documented delayed gastric emptying) was 21.5 per 100 000 persons.

OBSERVATIONS Gastroparesis, which is caused by reduced contractions of the distal stomach or abnormal pyloric relaxation, is more common among females than males (ratio, 2:1-4:1) and typically causes nausea, vomiting, early satiety, bloating, and abdominal pain or discomfort. In a large US epidemiological study involving 82.6 million patients, the most common causes of gastroparesis were type 2 diabetes (51.7%), postsurgical effects (15%), medication-induced (11.8%), idiopathic (11.3%), type 1 diabetes (5.7%), and other (4.5%). Other risk factors include neurological disorders (eg, Parkinson disease), hypothyroidism, amyloidosis, connective tissue disorders (eg, scleroderma), and viral infections (eg, norovirus, cytomegalovirus, Epstein-Barr virus, SARS-CoV-2). The 2022 American College of Gastroenterology and the 2025 American Gastroenterological Association (AGA) guidelines define the criterion standard diagnostic test for gastroparesis as gastric emptying scintigraphy with more than 10% gastric retention at 4 hours in patients with symptoms of gastroparesis without mechanical obstruction based on upper endoscopy or abdominal imaging such as computed tomographic (CT) scan. The carbon 13 spirulina stable isotope breath test is also approved for diagnosing gastroparesis by the US Food and Drug Administration. Based on the percentage of gastric retention at 4 hours, gastroparesis is categorized in the 2022 AGA clinical practice update as mild (10%-15%), moderate (16%-35%), or severe (>35%). Treatment includes discontinuation of medications that delay gastric emptying such as opioids, cannabis, anticholinergics, and glucagon-like peptide-1 receptor agonists and for patients with diabetes, optimizing glycemic control. First-line therapies according to the AGA 2022 clinical practice update are a small particle diet (food that is blended or chopped into small pieces) that is low in fat and nondigestible fiber and antiemetics (eg, serotonin 5-hydroxytryptamine 3 [5-HT_3] receptor antagonists, histamine H_1 receptor antagonists) for mild gastroparesis; antiemetics and prokinetics (metoclopramide, erythromycin) for moderate gastroparesis, and liquid diet or jejunal enteral feeding for severe gastroparesis. Severe refractory gastroparesis may be treated with gastric peroral endoscopic myotomy (G-POEM), which involves endoscopic-guided incision of the pylorus sphincter muscle, or gastric electrical simulation, in which an implanted neurostimulator sends electrical pulses to the stomach muscle.

CONCLUSIONS AND RELEVANCE Gastroparesis is a condition of delayed gastric emptying without gastric outlet obstruction that is diagnosed based on a gastric emptying study. First-line treatments include a small particle diet and antiemetics and prokinetics. Severe refractory gastroparesis may be treated with procedures such as G-POEM or gastric electrical simulation.

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Supplemental content

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Gastroparesis is a condition of delayed gastric emptying in the absence of gastric outlet obstruction. Symptoms of gastroparesis include nausea, vomiting, early satiety, postprandial fullness, bloating, and upper abdominal pain (**Box**).[1,2] Abdominal pain is more frequent among patients with idiopathic gastroparesis compared with other etiologies.[3] Based on a US national claims database of 82.6 million people, gastroparesis was identified in 267.7 per 100 000 people and was up to 8-fold higher in the southeast US than in other states with lowest prevalence, such as Illinois and North Dakota.[4] The most common causes of gastroparesis are type 2 diabetes (51.7%), postsurgical adverse effects (15%), medication-induced (11.8%), idiopathic (11.3%), type 1 diabetes (5.7%), and other etiologies (4.5%).[4]

Gastroparesis is associated with emergency department visits, hospitalization, decreased quality of life (QOL), and loss of work productivity. Among 406 patients in the National Institutes of Health Gastroparesis Consortium database, reasons for hospitalization included nausea (83%), vomiting (78%), abdominal pain (70%), and dehydration (59%).[5] This review summarizes the pathogenesis, epidemiology, diagnosis, treatment, and prognosis of gastroparesis.

Box. Frequently Asked Questions About Gastroparesis

What are risk factors for gastroparesis?

Risk factors for gastroparesis include type 1 and type 2 diabetes; prior gastric, esophageal, or thoracic surgery; drugs (opioids, cannabis, glucagon-like peptide-1 [GLP-1] receptor agonists, or anticholinergics); neurological disorders (eg, Parkinson disease); amyloidosis; hypothyroidism; and connective tissue diseases (eg, scleroderma). Gastroparesis may also develop after viral infections (norovirus, rotavirus, cytomegalovirus, Epstein-Barr virus, herpes viruses, enterovirus, or SARS-CoV-2) but often resolves within months to a year.

How is gastroparesis diagnosed?

Gastroparesis is diagnosed when patients with suggestive symptoms such as nausea, vomiting, and postprandial fullness have delayed gastric emptying at 4 hours on gastric emptying scintigraphy or a stable isotope carbon 13 spirulina breath test after ingestion of a solid meal and have no evidence of upper gastrointestinal obstruction on upper endoscopy or abdominal computed tomographic scan.

How is gastroparesis treated?

Patients with gastroparesis should discontinue medications that delay gastric emptying such as opioids, cannabis, anticholinergics, and GLP-1 receptor agonists. Those with diabetes should optimize glycemic control. For mild gastroparesis (typically 10%-15% gastric retention at 4 hours), recommended treatments include consumption of a small particle diet (food that is blended or chopped into small pieces), reduction of nondigestible fiber (2 g per serving) and fat content (low-fat foods but no recommended daily fat consumption), and use of antiemetics such as serotonin (5-hydroxytryptamine 3 receptor [5-HT_3]) receptor antagonists (eg, ondansetron) and histamine H_1 receptor antagonists (eg, promethazine, diphenhydramine, meclizine). Moderate gastroparesis (16%-35% retention at 4 hours) is treated with the addition of prokinetic agents (eg, metoclopramide, erythromycin). Treatment of severe refractory gastroparesis may involve a liquid diet or enteral nutrition via jejunal feeding tube and consideration of gastric peroral endoscopic myotomy or gastric electrical stimulation.

Methods

A PubMed search was conducted for English-language articles from 1950 to March 15, 2026, using the following keywords: *gastroparesis*, *epidemiology*, *prevalence*, *gastric emptying*, *pylorus*, *gastrointestinal motility*, *prokinetics*, *antiemetics*, *gastric electrical stimulation*, *peroral endoscopic myotomy*, *pathophysiology*, *gastric motor function*, *manometry*, *randomized controlled trials*, *systematic reviews*, and *meta-analyses*. Of 1986 retrieved articles, 108 were included, consisting of 57 observational studies, 23 randomized clinical trials, 12 systematic reviews with meta-analyses, 9 reviews or systematic reviews, and 7 guidelines or position statements.

Observations

Physiology of Normal Gastric Motor Function

After ingestion, solid food is initially stored in the proximal stomach, then transferred to the distal stomach where gastric antral contractions lead to food trituration (eg, breakdown) to 1-2 mm diameter particle size, after which it passes from the stomach to the duodenum. These motor functions are controlled by extrinsic (predominantly vagal cholinergic) and enteric or intrinsic nerves that include excitatory (eg, cholinergic and tachykinergic) or inhibitory (eg, nitrergic) neurons, pacemaker cells (interstitial cells of Cajal and platelet-derived growth factor receptor α–positive fibroblast-like cells),[6] and smooth muscle activity (**Figure 1**).

Pathophysiology

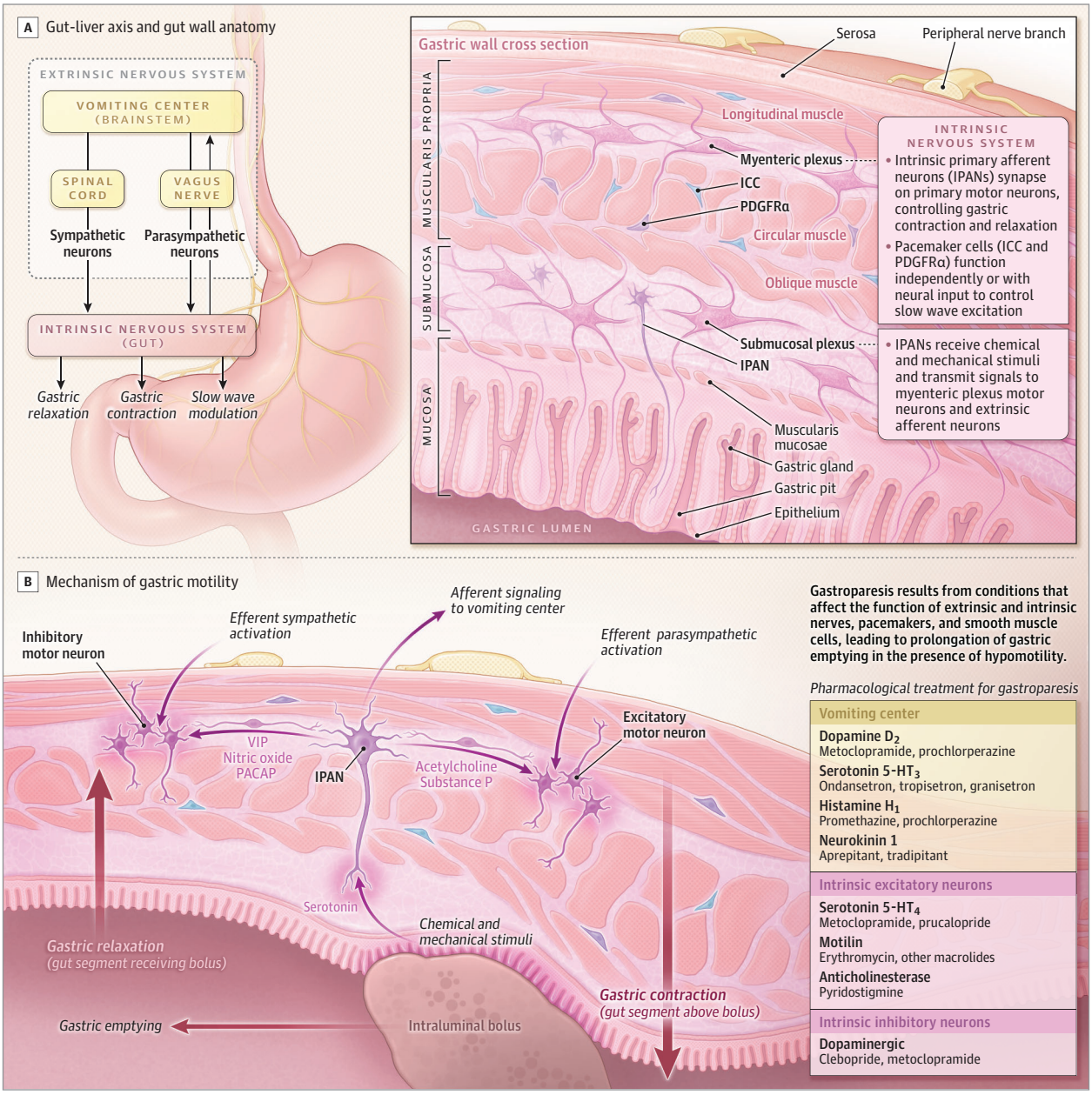
Gastroparesis results from conditions that affect the function of extrinsic and intrinsic nerves, pacemakers, and smooth muscle cells of the stomach and pylorus, leading to prolongation of gastric emptying in the presence of antral hypomotility.[7,8] Disorders of gastric motility are broadly classified as neuropathic disorders, which involve reduced frequency of the distal antral contractions and increased pyloric contractions (eg, diabetic autonomic neuropathy, postvagotomy),[9] or myopathic disorders, which involve normal frequency but decreased amplitude of antral and small intestinal contractions (eg, scleroderma, amyloidosis).[8,10] Examples of abnormal antropyloroduodenal manometry in patients with diabetic or postfundoplication gastroparesis are illustrated in **Figure 2**.

Diabetic gastroparesis may be associated with loss of intrinsic or enteric inhibitory neurons and pacemaker cells[11] and loss of intrinsic cholinergic neurons in the stomach.[12] Based on full-thickness gastric biopsies from patients with gastroparesis, particularly those with diabetes, hyperglycemia may be associated with oxidative stress and inflammation.[13] Hyperglycemia may cause mitochondrial dysfunction in enteric neurons by inducing M1 macrophages, which increase production of reactive oxygen species that cause inflammation and reduce M2 macrophages, which limit the ability to control inflammation and promote recovery of the enteric neurons.[14]

Risk Factors

Risk factors for gastroparesis include type 1 and type 2 diabetes, prior surgery involving the stomach, esophagus, or thorax (mediated by

Figure 1. Illustration Depicting the Intrinsic and Extrinsic Neural Control of Peristalsis and Gastric Emptying and Pharmacological Drug Classes and Agents Modulating the Vomiting Center and Intrinsic Excitatory and Inhibitory Neurons in the Gut Wall



A, Shows the central nervous system and the vomiting center in the brainstem with the predominant receptors. The inset shows the organization of the layers in the wall of the gastrointestinal tract.

B, Shows the apparatus involved in gastrointestinal peristalsis with IPANs stimulated by transmitters such as serotonin from enteroendocrine cells in response to chemical or mechanical stimuli (eg, intraluminal bolus) in the lumen. The IPANs stimulate excitatory motor neurons to release transmitters such as acetyl choline and substance P that result in contraction above an intraluminal bolus, as well as inhibitory motor neurons that release transmitters including vasoactive intestinal polypeptide, nitric oxide, and pituitary adenylate cyclase–activating peptide (PACAP) resulting in relaxation in the receiving segment.

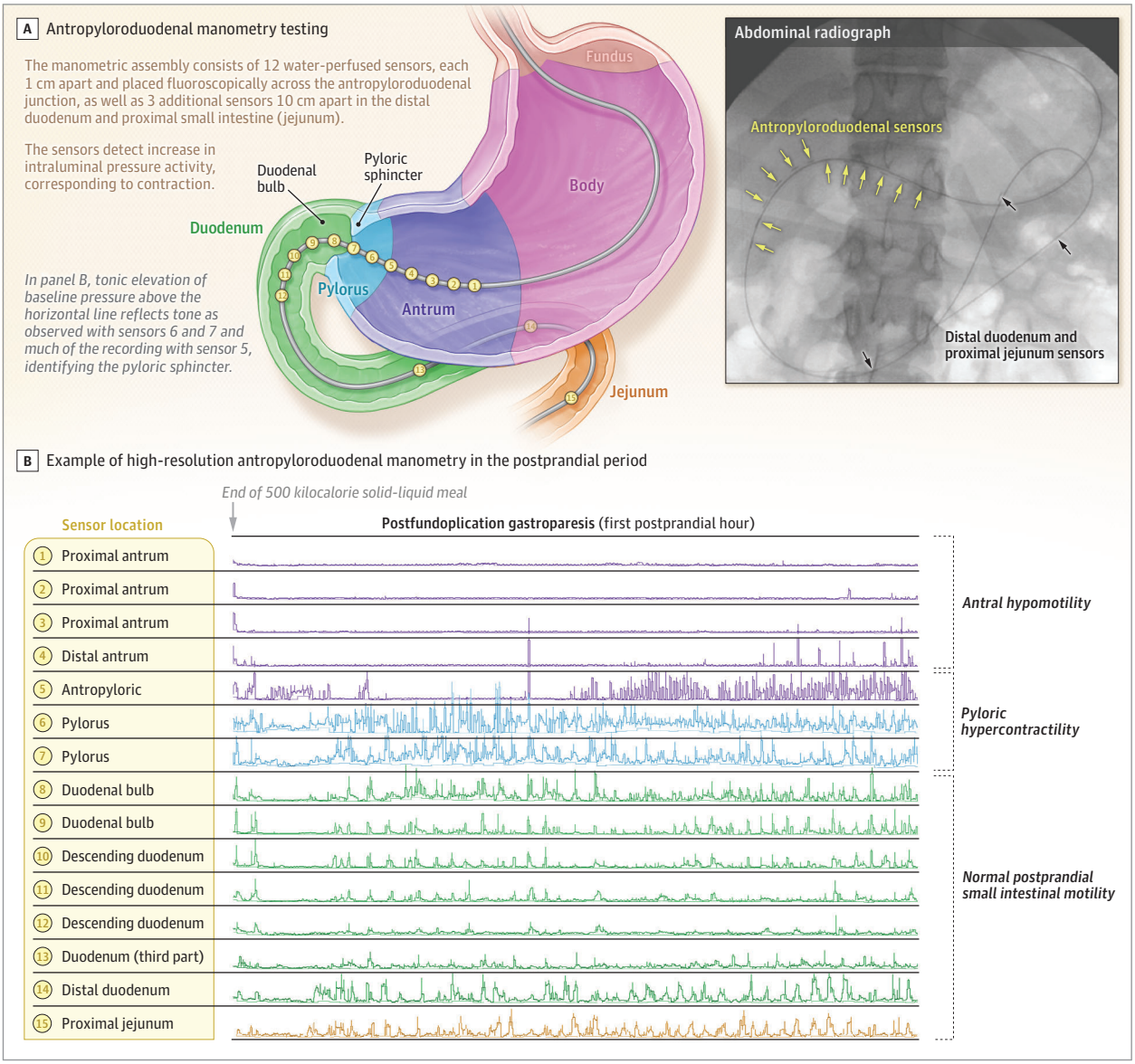
5-HT indicates 5-hydroxytryptamine; ICC, interstitial cells of Cajal; PACAP, pituitary adenylate cyclase–activating polypeptide; PDGFRα, platelet-derived growth factor receptor α-fibroblast-like cell; VIP, vasoactive intestinal peptide.

vagal injury); viral infections (such as norovirus, rotavirus, cytomegalovirus, Epstein-Barr virus, herpes viruses, enterovirus, and SARS-CoV-2, which often resolve by approximately 1 year after infection); medications (eg, opioids, cannabis, anticholinergics, and glucagon-like peptide-1 [GLP-1] receptor agonists); neurological disorders (eg, Parkinson disease); and amyloidosis, hypothyroidism, and connective tissue diseases (eg, scleroderma, Ehlers-Danlos syndrome, and systemic lupus erythematosus).

Epidemiology

Based on a 2018 US national administrative health insurance claims database including 57 million individuals, the diagnostic prevalence

Figure 2. Illustration Depicting Placement of Sensors for Antropyloroduodenal Manometry and Example of Recordings in the Postprandial Period in a Patient With Gastroparesis



An example of high-resolution antropyloroduodenal manometry in the postprandial period in a patient with postfundoplication gastroparesis. The postfundoplication gastroparesis is associated with activation of pyloric activity demonstrated by the elevation of baseline pressure in combination with phasic contractions, and the paucity of distal antral contractions above the level of the pylorus, which demonstrates antral hypomotility and pyloric hypercontractility. Separate gastric emptying studies (not shown) showed transfer of food to the distal stomach within the first hour and manometry documented antral hypomotility and pyloric hypercontractility.

of definite gastroparesis (by gastric emptying scintigraphic test and persistent symptoms for >3 months) was 21.5 per 100 000 persons (95% CI, 20.6-22.4) in 2018.[4] The most common causes of gastroparesis were type 2 diabetes (51.7%), postsurgical adverse effect (15%), induced by drugs (11.8%), idiopathic (11.3%), type 1 diabetes (5.7%), and other (4.5%). The mean ages assessed a mean of 28 (SD, 29.3) months after gastroparesis diagnosis, were 52.4 (SD, 15.8) years in patients with type 1 diabetes, 63.3 (SD, 13.5) years in those with type 2 diabetes, and 50.7 (SD, 18.9) years with idiopathic gastroparesis.[4] However, some studies have reported higher rates of idiopathic gastroparesis than were reported in this US database study.[4] Among individuals seeking medical care, the study found that gastroparesis was more common among females than males, with a female to male ratio of 2:1[4] and up to 4:1 in some studies.[15] In a single-center US study of 146 patients with gastroparesis, the mean age at onset of gastroparesis symptoms was 33.7 (SD, 9.1) years.[16]

In a community-based study of individuals with diabetes, the 10-year incidence of gastroparesis (slowed gastric emptying documented by scintigraphy) was 5% among 227 patients with type 1 diabetes and 1% among 360 patients with type 2 diabetes compared with 0.2% in 639 control participants.[17] A 2023 systematic review

and meta-analysis of 14 studies (12 cross-sectional, 1 cohort, and 1 case-control study) including 3.2 million patients with diabetes reported prevalence of gastroparesis of 12.5% (95% CI, 7.7%-17.3%) among patients with type 2 diabetes and 8.3% (95% CI, 6.4%-10.2%) among patients with type 1 diabetes based on scintigraphic data in 6 studies and symptoms in 8 studies.[18] In a US cohort of 69 950 patients with gastroparesis, 28.3% were diagnosed with idiopathic gastroparesis,[19] and prevalence of idiopathic gastroparesis[19] was 39.4% among 1145 patients with gastroparesis in a UK cross-sectional study,[20] and 49.4% among 83 patients with definite gastroparesis in a retrospective observational study in Olmsted County Minnesota.[21] eTable 1 in Supplement 1 summarizes the epidemiology of gastroparesis.[4,17,19-21]

Clinical Presentation

Common symptoms of gastroparesis include nausea, vomiting, early satiety, abdominal pain, and bloating. In a study of 1013 patients with gastroparesis[3] (607 idiopathic, 361 diabetes, 45 postfundoplication) enrolled in a National Institutes of Health gastroparesis registry, presenting symptoms included nausea (31%), vomiting (20%), abdominal pain (20%), bloating (9%), postprandial fullness or early satiety (4%), heartburn (4%), and constipation (3%).[3] Patients in this registry had substantially impaired QOL measured with the Patient Assessment of Upper Gastrointestinal Disorders QOL (PAGI-QOL), which is based on a 0 to 5 Likert scale with lower scores reflecting poorer QOL; mean scores at presentation were 2.6 (SD, 1.1).[3]

Diabetic Gastroparesis

Hyperglycemia is associated with delayed gastric emptying. An observational study of 74 patients with type 1 diabetes from the Diabetes Control and Complications Trial (DCCT),[22] reported that participants with delayed gastric emptying (measured using the ^{13}C spirulina breath test) had a longer mean (SEM) duration of type 1 diabetes (90 [8] vs 69 [8] months; $P = .04$) than participants with normal gastric emptying and a higher baseline mean (SEM) hemoglobin A_{1c} (HbA_{1c}) level (9.6% [0.3%] vs 8.3% [0.2%]; $P = .002$) over a mean follow-up of 27 years prior to optimized glycemic control. In a single-center study, 30 patients with poorly controlled type 2 diabetes (HbA_{1c} >9.0) had mostly asymptomatic, delayed gastric emptying at 4 hours (>97 minutes based on the ^{13}C spirulina breath test).[23]

In a National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Gastroparesis Registry study of 159 patients with gastroparesis, the vomiting score (based on 0-5 scale) was more severe in those with diabetic gastroparesis (1.9, [SD, 1.8]) than idiopathic gastroparesis (0.9 [SD, 1.4]; $P < .001$).[24]

Drug-Induced Gastroparesis

The most common drugs associated with gastroparesis are opioids, cannabis, GLP-1 receptor agonists, and anticholinergics. In a tertiary care academic center, among 223 patients with gastroparesis and confirmed delayed gastric emptying, 19.3% were taking scheduled opioids for more than 1 month with a median morphine equivalent of 60 mg/d, and 9.9% were taking opioids only as needed.[25] Compared with individuals not using scheduled opioids, those taking scheduled opioids had long duration of daily nausea symptoms (median, 7 hours per day vs 4 hours per day; $P = .04$), and more daily vomiting episodes (median, 3 vs 2 days; $P = .002$).[25] In the NIDDK Gastroparesis Consortium[26] study of 583 patients with gastroparesis, 41% were taking opioids, of those, 82% were taking potent opioids (eg, morphine, oxycodone, fentanyl). These patients experienced more severe symptoms of gastroparesis, worse QOL, and more frequent hospitalizations for gastroparesis in the prior year (65% taking opioids, 50% not taking opioids; $P = .03$). Additionally, annual hospitalizations for gastroparesis were higher (58% vs 40%) for patients receiving potent vs weaker opioids (eg, tramadol or codeine).[26]

Treatment with GLP-1 receptor agonists is associated with nausea, vomiting, and early postprandial fullness. A bayesian network meta-analysis[27] of 48 randomized clinical trials (RCTs) involving GLP-1 receptor agonists (27 729 participants) reported an 11.66% overall incidence of gastrointestinal adverse events: nausea (21.49%), diarrhea (10.62%), vomiting (9.10%), dyspepsia (8.67%), constipation (7.92%), and decreased appetite (5.49%). A prospective study of 60 patients with overweight or obesity without diabetes treated with the GLP-1 receptor agonist liraglutide for 16 weeks reported that 60% developed delayed gastric half-emptying time of more than 175 minutes (95th percentile of 319 healthy adults)[28] of solids (320 kcal, 30% fat egg meal) measured scintigraphically over 4 hours at 5 weeks, but only about 30% had delayed gastric emptying after 16 weeks of treatment.[29] A systematic review of 10 placebo-controlled RCTs of GLP-1 receptor agonists involving 25 872 patients receiving a GLP-1 receptor agonist or 25 531 controls) reported respectively 12 cases of gastroparesis in the GLP-1 receptor agonist group and 5 cases in the control group.[30] The relative risk (RR) of reported gastroparesis with GLP-1 receptor agonists compared with controls was not statistically significant (RR, 1.52; 95% CI, 0.57-4.03; $P = .40$). However, because the diagnosis was made clinically without requirement for gastric emptying studies, gastroparesis was likely underreported or underdiagnosed.[30] A systematic review and meta-analysis of 23 observational studies involving 262 018 patients reported that people who took GLP-1 receptor agonists compared with those who did not had an increase in retained gastric contents during upper gastrointestinal endoscopy despite standard preparation with overnight fast (7.53% vs 0.53% for people who did not take GLP-1 receptor agonists; odds ratio [OR], 4.54; 95% CI, 3.30- 6.24) and premature endoscopy termination (1.26% vs 0.15%; OR, 4.54; 95% CI, 3.05-6.75) but no significant difference in the risk of aspiration pneumonia (0.19% for both groups; OR, 0.96; 95% CI, 0.53-1.75).[31] Nevertheless, a 2024 AGA clinical practice update recommends cessation of GLP-1 receptor agonists prior to elective procedures including surgery and endoscopy, with discontinuation of liraglutide 1 day prior and semaglutide and tirzepatide 7 days prior, based on their different half-lives.[32]

Surgically Induced Gastroparesis

Postsurgical gastroparesis is caused by accidental vagal injury or dysfunction, which may be reversible if the vagus is stretched or compressed but not severed, after fundoplication, a surgical treatment for gastroesophageal reflux disease or hiatal hernia. Postsurgical gastroparesis causes postprandial antral hypomotility,[33] upper gastrointestinal symptoms such as bloating, postprandial abdominal pain and early satiety, and delayed gastric emptying consistent with gastroparesis.[34] Esophageal, gastric, and thoracic procedures such as lung transplant may also cause vagal injury, resulting in gastroparesis. A meta-analysis of 21 observational studies included 18

retrospective studies and 3 prospective studies to determine the risk of gastroparesis among patients who had undergone either a lung transplant or a lung and heart transplant. Among these studies, 17 made the diagnosis of gastroparesis with scintigraphy, 4 with clinical diagnosis, and 1 with both methods. Of the 2888 patients, 44.89% (95% CI, 17.05%-76.35%) in the lung and heart transplant group had documented gastroparesis vs 26.95% (95% CI, 15.46%-42.68%) of those in the lung transplant alone group.[35]

Assessment and Diagnosis

When evaluating patients with possible gastroparesis, clinicians should elicit gastrointestinal symptoms (nausea, vomiting, early satiety, abdominal pain, bloating, and constipation), symptoms of autonomic dysfunction (postural dizziness, difficulties with vision when exposed to bright lights, absence of sweating), and symptoms suggestive of peripheral neuropathy (numbness or tingling in hands or feet, foot drop, and difficulty grasping objects). Physical examination should assess pupillary constriction in response to light, postural hypotension, and presence of a succussion splash or loud, high-pitched, hyperactive bowel sounds (borborygmi) suggestive of abdominal or gastric obstruction. Prior to making the diagnosis of gastroparesis, mechanical obstruction (eg, pyloric stenosis, peptic ulcer disease, malignancy, stricture) must be excluded with upper gastrointestinal endoscopy or abdominal computed tomographic (CT) scan. Methods to diagnose gastric motor dysfunction associated with slow gastric emptying are summarized in eTable 2 in the Supplement 1.

Measurement of Gastric Emptying

The 2 standard methods recommended by the 2022 ACG and 2025 AGA gastroparesis guidelines for diagnosis of gastroparesis are the 4-hour scintigraphic study (criterion standard)[2] and the carbon13 spirulina (^{13}C-spirulina) breath test. For radioscintigraphy, patients ingest a solid, low fat meal, typically containing 250 kcal, 2% fat[36,37] or alternatively with 2 real eggs (320 kcal, 30% fat),[28,38] along with radiolabeled with technetium 99m and undergo abdominal imaging with a γ-camera immediately after eating, and 1, 2, and 4 hours after ingestion. For patients with an egg protein intolerance or allergy, a plant-based alternative has been developed that has similar performance as 2 real eggs.[39]

The ^{13}C-spirulina breath test, approved by the US Food and Drug Administration (FDA), involves eating a standardized nonradioactive meal (230 kcal, 30% fat) enriched with ^{13}C-spirulina. Breath samples are collected for up to 4 hours and analyzed with gas isotope ratio mass spectrometry for carbon dioxide 13, which is generated by the liver after spirulina is digested and reflects the rate of stomach emptying. Compared with radioscintigraphy, ^{13}C-spirulina is 89% sensitive and 80% specific for diagnosis of delayed gastric emptying.[40]

Differential Diagnosis

The differential diagnosis of gastroparesis includes functional dyspepsia (persistent dyspepsia without gastrointestinal structural abnormalities on upper gastrointestinal endoscopy and/or CT imaging), rumination syndrome (repetitive regurgitation of gastric contents within minutes after meals, and involving a conscious decision to reswallow or spit out the food),[41] cyclical vomiting (intermittent recurrent episodes of severe nausea and vomiting lasting hours to days), and cannabinoid hyperemesis syndrome. Cannabis and cannabidiol can delay gastric emptying.[42,43] Cannabinoid hyperemesis syndrome, which is considered a subset of cyclical vomiting syndrome, is a condition of cyclical emetic episodes associated with chronic daily use of cannabis.

Management

Patients with gastroparesis should discontinue medications that delay gastric emptying such as opioids, cannabis, anticholinergics, and GLP-1 agonists, and those with diabetes should optimize glycemic control. Based on the 2022 AGA clinical practice update,[44] choice of therapy is determined by severity of delay in gastric emptying and tolerance of oral nutrition.

Hydration and Nutrition

Guidelines recommend that all patients with gastroparesis should undergo assessment of nutritional state[1,2] and be advised to drink fluids sufficient to maintain normal urine output (typically 1-1.5 L/d), and adhere to a homogenized (solid food particle size, 1-2 mm), low-fat diet (fat content of 25%-30% of calorie intake[45]) with low nondigestible fiber (≤2 g per serving), and small frequent meals typically 4 to 6 times per day. This diet reduces upper gastrointestinal symptoms in patients with diabetic gastroparesis.[45] For patients with persistent gastroparesis despite these dietary modifications, stepwise nutritional interventions include oral nutrition supplements, liquid meals, enteral nutrition, and parenteral nutrition.[46] Patients requiring enteral nutrition usually receive iso-osmolar formula (≈300 mOsm/kg) at least 60 mL per hour over 12 to 15 hours per day.[47]

Pharmacological Agents

Metoclopramide is the only FDA-approved medication for gastroparesis, but due to the risk of tardive dyskinesia, the FDA recommends only short-term use (typically up to 12 weeks). The 2025 AGA guideline[2] issued a conditional recommendation (low quality of evidence) for use of metoclopramide and erythromycin but recommended against use of an antiemetic (aprepitant), prokinetics (domperidone and prucalopride), and neuromodulators (nortriptyline, buspirone) as first-line therapies. Figure 1 summarizes pharmacological approaches targeting vomiting center receptors and neurons in the enteric nervous system. **Table 1**[48-65] summarizes currently used medications for gastroparesis. **Figure 3** outlines the 2025 AGA treatment algorithm for gastroparesis.

Medication Treatment by Gastroparesis Severity

For patients with mild gastroparesis (10%-15% gastric retention at 4 hours), antiemetics such as serotonin 5-HT$_3$ receptor antagonists (eg, ondansetron) and histamine H$_1$ receptor antagonists (eg, promethazine) were recommended by the 2022 AGA clinical practice update on an as-needed basis.[44] For moderate gastroparesis (16%-35% gastric retention at 4 hours), the 2022 AGA update[44] recommended treatment with antiemetics and prokinetics, and the 2025 AGA guideline[2] provided a conditional recommendation for the prokinetic agents, metoclopramide or erythromycin. For severe gastroparesis, addition of other medications (such as prucalopride, domperidone, aprepitant, nortriptyline, or buspirone) may be prescribed based on shared decision-making and consideration of potential adverse effects (Supplement 1).[2,45,50,51,55-59,61,64-83]

Table 1. Medications for Gastroparesis

Study	Study type	Drug name and dose	Mechanism of action	No. of patients	Effects and efficacy in treatment of gastroparesis symptoms	Common adverse effects	Special considerations
Guideline recommended first-line treatment							
Ingrosso et al,[48] 2023	Systematic review and meta-analysis of 2 placebo-controlled 3-wk studies	Metoclopramide: oral, 10 mg 3/d vs placebo	Prokinetic (weak potency serotonin 5-HT_4 RA) and antiemetic dopamine D_2 RAnt	91 Patients	Reduced nausea: RR, 0.46 (0.21-1.00) Global symptoms: RR, 0.48 (95% CI, 0.23-0.99); postprandial fullness: RR, 0.78 (95% CI, 0.65-0.94) Bloating: RR, 0.53 (95% CI, 0.30-0.93)	Hyperprolactinemia, involuntary movements, headache, somnolence; increased risk of adverse events: RR, 0.38 (95% CI, 0.15-0.99)	Risk of tardive dyskinesia estimated as 1:1000 FDA-approved for treatment of gastroparesis
MacCallum et al,[49] 2024	RCT	Metoclopramide: 10 mg intranasally 4/d vs placebo	Prokinetic (weak potency serotonin 5-HT4 RA) and antiemetic dopamine D2 RAnt	205 Patients with diabetic gastroparesis (12% type I diabetes)	No overall symptom benefit but significant reduction in nausea and upper abdominal pain for all 4 wk	Headache and abdominal pain	Risk of tardive dyskinesia estimated as 1:1000 FDA-approved for treatment of gastroparesis
Parkman et al,[50] 2015	Phase 2B randomized clinical trial	Metoclopramide: 10 mg-14 mg 4/d vs placebo	Prokinetic (weak potency serotonin 5-HT4 RA) and antiemetic dopamine D2 RAnt	285 Patients with diabetic gastroparesis(17.5% type I diabetes)	Symptom scores reduced in females vs placebo: 10 mg: mean, 1.2 (SD, 1.8); $P = .03$ 14 mg: mean, 1.3 (SD, 0.94; $P = .02$)	Dysgeusia, headache, and fatigue	Risk of tardive dyskinesia estimated as 1:1000 FDA-approved for treatment of gastroparesis
Maganti et al,[51] 2003	Systematic review	Erythromycin: 250 mg 2/d or 500 mg 2/d and at bedtime open-label studies	Prokinetic motilin RA	35 Patients (5 idiopathic, 30 diabetic gastroparesis)	2 Open-label studies showed a reduction in symptom scores in about 40% of patients 1 Study showed no difference between erythromycin and metoclopramide	Nausea, vomiting, abdominal pain, and diarrhea; may prolong QTc on ECG	Tachyphylaxis is common, so should be used for a few wk
Guideline recommended for symptom relief and mild gastroparesis							
Varma et al,[52] 2024	RCT	Ondansetron: 4-8 mg 2/d or as needed vs placebo	Antiemetic, Serotonin 5-HT3 Ant	40 Patients with type I diabetes with dyspepsia	Ondansetron and placebo improved daily symptoms from baseline; no differences between treatments	Constipation	Extensive clinical use as needed or even long term
Friedenberg and Parkman,[53] 2006	Opinion by experts	Prochlorperazine: 5-10 mg orally or 25 mg by suppository	Phenothiazine, Antiemetic, Histamine H_1 RAnt		Take every 4-6 h to control nausea	Prolonged QT on ECG, tardive dyskinesia, neuroleptic malignant syndrome	
	No clinical trials	Promethazine: 12.5-25 mg orally or rectally every 4-6 h as needed	Phenothiazine, Antiemetic, Histamine H_1 RAnt		Used as needed to control nausea	Dermatitis, urticaria, xerostomia, CNS depression, dizziness, extrapyramidal disease, lowered convulsive threshold, sedation, somnolence	May be habit forming; therefore, used as a second-line or rescue agent
Zikos et al,[54] 2020	4-Section survey study	Diphenhydramine: 12.5 to 25 mg every 4-6 h as needed	Histamine H_1 RAnt	153 Patients treated for nausea (40% due to gastroparesis) rated efficacy of diverse antinausea medications	Overall, diphenhydramine was not effective in relief of nausea, but patients with more severe nausea responded better to diphenhydramine	Xerostomia, dizziness, dyskinesia, somnolence	Used as needed to control severe nausea

(continued)

Table 1. Medications for Gastroparesis (continued)

Study	Study type	Drug name and dose	Mechanism of action	No. of patients	Effects and efficacy in treatment of gastroparesis symptoms	Common adverse effects	Special considerations
	No clinical trials	Meclizine: 12.5-25 mg 2/d as needed	Histamine H_1 RAnt		FDA approved for motion sickness	Xerostomia; somnolence	Used as needed to control nausea
Guideline recommended treatments for severe gastroparesis, generally as part of shared decision-making in refractory cases							
Carbone et al,[55] 2017	Double-blind RCT	Prucalopride: 2 mg/d vs placebo	Prokinetic and serotonin 5-HT_4 RA	Crossover 28 patients with idiopathic and 6 with diabetic gastroparesis Each phase with 2 wk washout	Improved mean (SD) total GCSI: 1.65 (0.19) vs 2.28 (0.20); $P < .001$ Improved 3 GCSI subscales: nausea and vomiting: mean (SD), 1.02 (0.20) vs 1.42 (0.24); $P < .01$; fullness and satiation: 2.16 (0.26) vs 2.81 (0.26); $P < .001$);bloating and distension: 1.58 (0.28) vs 2.50 (0.29); $P < .001$ Improved overall mean (SD) PAC-QOL score: 1.15 (0.16) vs 1.44 (0.16); $P < .05$ Accelerated gastric emptying by GEBT Efficacy mostly in idiopathic gastroparesis No improvement in GCSI or meal-related symptom score	Diarrhea, abdominal pain, and small bowel volvulus (1 serious AE)	Indicated particularly for patients with constipation
Andrews et al,[56] 2020	Double-blind crossover RCT	Prucalopride: 4 mg/d vs placebo	Prokinetic, serotonin 5-HT_4 RA	13 Patients with diabetes and 2 with connective tissue disease	No improvement in GCSI or meal-related symptom score	Abdominal pain, headache, diarrhea	
Pasricha PJ,[57] 2018	RCT	Aprepitant: 125 mg/d	Antiemetic neurokinin-1 RAnt	126 Patients with idiopathic or diabetic gastroparesis (57% slow gastric emptying)	Symptoms of nausea (primary end point) not reduced, but reduced symptom severity of nausea, vomiting, and overall gastroparesis symptoms	Gastrointestinal AEs (symptoms not specified)	
Midani and Parkman,[58] 2016	Prescription registry	Transdermal granisetron: 34.3 mg/d	Antiemetic serotonin 5-HT_3 RAnk	51 Patients (25% diabetic and 69% idiopathic gastroparesis)	Reduced nausea and/or vomiting in 76% (39/51)	Constipation	Used as rescue most often
Parkman et al,[59] 2013	RCT	Nortriptyline: 10, 25, 50, and 75 mg at bedtime with dose escalation every 3 wk vs placebo:	Central neuromodulator tricyclic with anticholinergic effects	130 Patients (65 in each group) with idiopathic gastroparesis	Nortriptyline not superior to placebo in alleviating symptoms (GCSI score): 23% vs 21% had improved scores, respectively; No appraisal of gastric emptying performed	Serious AEs with nortriptyline: 1 allergic reaction, 2 vomiting, 1 GI-related event, and 1 cardiac event vs 1 (abdominal pain) with placebo	Restricted for patients with prominent abdominal pain; potential slowing of gastric emptying

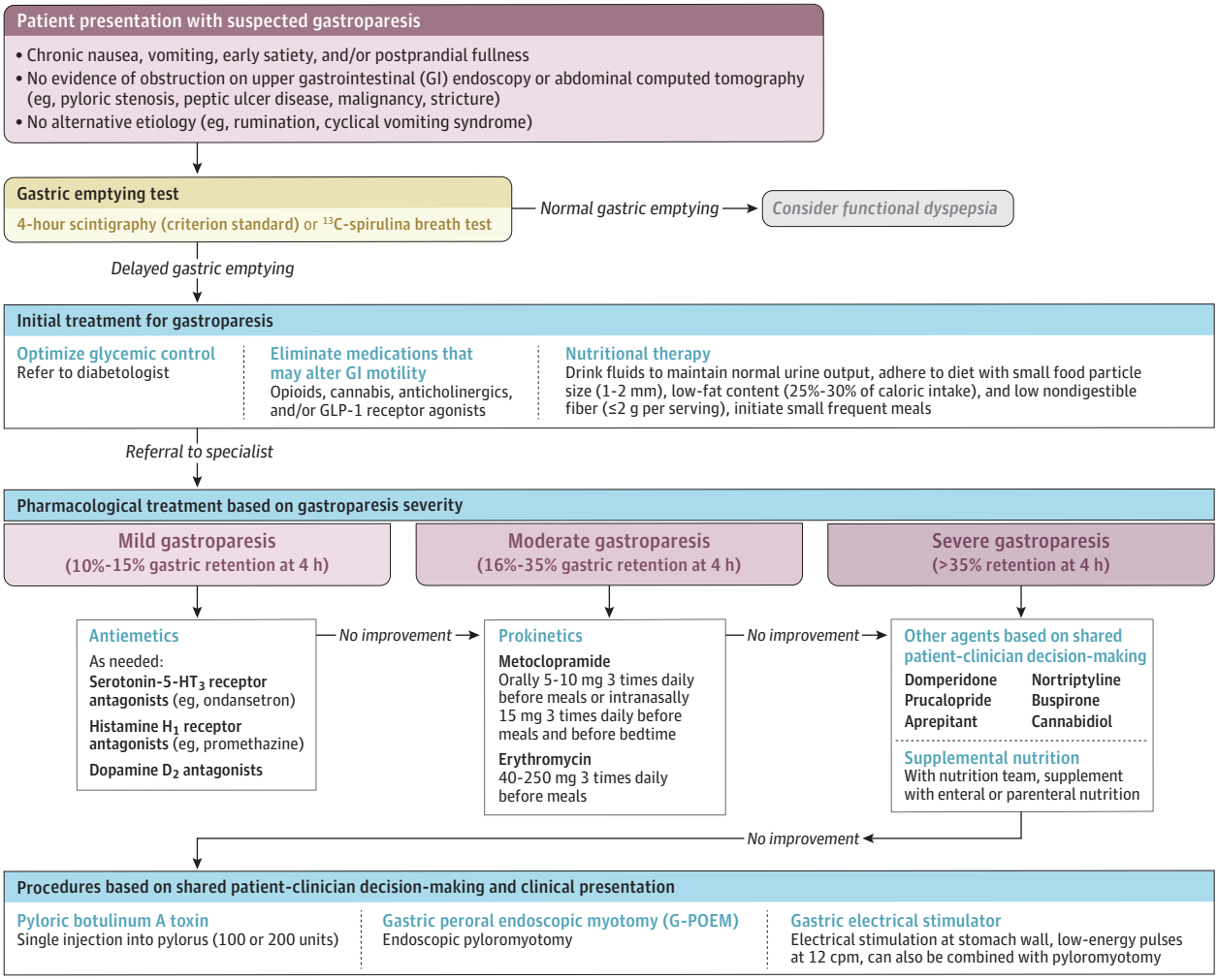
(continued)

Table 1. Medications for Gastroparesis (continued)

Study	Study type	Drug name and dose	Mechanism of action	No. of patients	Effects and efficacy in treatment of gastroparesis symptoms	Common adverse effects	Special considerations
Parkman et al,[60] 2023	RCT	Buspirone: 10 mg 3/d vs placebo	Serotonin 5-HT$_1$ RA and anxiolytic	96 Patients (37 diabetic and 59 idiopathic gastroparesis); 47 buspirone, 49 placebo	No between-groups difference in the mean (SD) early satiety and postprandial fullness subscore: −1.16 (1.25) for buspirone vs −1.03 (1.29) for placebo However, buspirone is more likely to benefit patients with severe to very severe bloating at baseline No effect on GE by scintigraphy or satiation by water load test	GI, particularly diarrhea, abdominal pain, and nausea; somnolence; and dizziness in both groups	Possibly indicated in patients with severe bloating
Malamood et al,[61] 2016	Open-label study 4-wk study	Mirtazapine: 15 mg at bed time	RA at several serotonin 5-HT RA and tetracyclic antidepressant and α2-RAnt	30 Patients (4 had diabetic gastroparesis); 24 completed the study	Improved nausea, vomiting, retching, loss of appetite, and assessment of severity vs pretreatment; enhanced gastric accommodation	Drowsiness, lethargy or fatigue, constipation, mood swings, and slurred speech	20% Stopped treatment due to AEs
Roldan et al,[62] 2017	RCT	Haloperidol: 5 mg vs placebo intravenously	Antiemetic, antipsychotic, analgesic γ-Aminobutyric acid and dopamine D$_2$ RAnt	33 Patients with acute exacerbation of gastroparesis: 15 haloperidol, 18 placebo	Reduced pain and nausea scores 1 h after administration of haloperidol vs placebo	QTc prolongation and arrhythmia; hypotension	Restricted to use in emergency department for acute exacerbation of nausea and pain
Stirrup et al,[63] 2023	Retrospective analysis	Droperidol: 1.25 mg intravenously	Antiemetic, antipsychotic, analgesic γ-Aminobutyric acid and dopamine D$_2$ RAnt	233 Patients with gastroparesis in the emergency department	Reduced the number of patients requiring opioid therapy, patient-reported pain, and antiemetic therapy requirement	QTc prolongation and arrhythmia; hypotension	Restricted to use in emergency department for acute exacerbation of nausea and pain
Friedenberg et al,[64] 2008	RCT crossover	Pyloric botulinum toxin vs placebo	Single injection into pylorus of 100 units botulinum A toxin	32 Patients (16 in each group)	No significant effect on symptoms (GCSI) or gastric emptying	Headache, fatigue, no serious AEs	Risk of fibrosis which may impair efficacy of subsequent G-POEM
Arts et al,[65] 2007	RCT crossover	Pyloric botulinum toxin vs placebo	2 Injections of 100 units	23 Patients (12 in botulinum toxin group; 11 in placebo group)	No significant effect on symptoms (GCSI) or gastric emptying	Headache, fatigue, no serious AEs	Risk of fibrosis which may impair efficacy of subsequent G-POEM

Abbreviations: 5-HT-5, 5-hydroxytryptamine, serotonin; AE, adverse event; CNS, central nervous system; ECG, electrocardiogram; FDA, US Food and Drug Administration; GCSI, Gastroparesis Cardinal Symptom Index; GEBT, gastric emptying breath test; GI, gastrointestinal; G-POEM, gastric peroral endoscopic myotomy; PAC-QOL, Patient Assessment of Constipation Quality of Life; RA, receptor agonist; RAnt, receptor antagonist; RCT, randomized clinical trial; RR, relative risk.

Figure 3. Algorithm of Management of Gastroparesis and Choice of Therapies in Accordance With the 2025 American Gastroenterological Association Clinical Guideline on Gastroparesis



Note the positive recommendations including the use of diet, nutritional support, antiemetics, metoclopramide, and erythromycin. All other medications and procedures are based on joint decision-making between the clinician and the patient. The Figure is adapted from the 2025 American Gastroenterological Association Clinical Guideline on Gastroparesis.[2] ^{13}C-spirulina indicates 13 carbon spirulina; GLP-1, glucagon-like peptide-1.

Refractory Gastroparesis

Nutrition

Refractory gastroparesis is defined by 2022 AGA update[44] as persistent symptoms despite dietary modifications with metoclopramide as a first-line therapeutic agent. If patients cannot maintain oral nutrition, a percutaneous feeding tube should be placed, and enteral feeding should be delivered directly into the jejunum because jejunal extension tubes from gastrostomy may "flip back" into the stomach, which can cause retching or vomiting. Jejunal feeding is generally safe, although complications such as infection may occur at the abdominal wall insertion site.[46] In a single-center study of 26 patients with diabetic gastroparesis receiving jejunal feeding, 39% had improved nausea and vomiting, 52% reported fewer hospitalizations, 56% reported improved nutritional status, and 83% reported improved overall health during the 47-month follow-up (range, 1-130 months).[84] Severe nutritional deficiencies may require short-term parenteral nutrition. Long-term parenteral nutrition is used for patients with jejunal feeding intolerance. Complications associated with central lines used for parenteral feeding include infection and thrombosis.[46]

Other Therapies

The 2025 AGA guideline[2] advises against routine use of botulinum toxin injection into the pyloric sphincter during upper endoscopy, citing low-quality evidence and a lack of benefit in randomized trials. However, the guideline allows consideration of pyloric botulinum toxin injection via shared decision-making in refractory cases and when attempting to predict potential for symptom improvement with pyloromyotomy, which involves endoscopic or surgical incision of the pyloric valve muscle to widen the opening from the stomach to the duodenum. For patients with refractory gastroparesis, the 2025 AGA guideline recommends consideration of gastric peroral endoscopic myotomy, and gastric electrical stimulation, and did not provide a recommendation about surgical pyloroplasty, due to insufficient evidence (Figure 3 and Table 2[85-92]).

Table 2. Nonpharmacological Therapies for Patients With Refractory Gastroparesis

	Gastric per oral endoscopic myotomy	Gastric electrical simulation	Laparoscopic pyloroplasty
Method	Endoscopic pyloromyotomy	Surgical placement of electrical leads on the stomach wall for delivery of electrical stimulation, low-energy pulses at 12 cycles per minute	Minimally invasive surgical procedure in which incisions are made to reconfigure the pyloric muscle so that it remains permanently open
Study outcomes	2 Sham-controlled RCTs reported relief of symptoms: RCT of 41 patients: reduction of GCSI > 50% from baseline at 6 mo: 71% (95% CI, 50 to 86) after G-POEM vs 22% (8-47) after sham (P = .005).[85] RCT of 52 patients all with diabetic gastroparesis: showed relief of 3 GCSI subscales[86]: • Nausea and vomiting: −1.67 (IQR, −3.00 to −0.83) vs 1 (IQR, 0.08 to - 1.33; P = .001)[86] • Postprandial fullness and early satiety: −2.25 (IQR, −3.00 to −1.00) vs 0.25 (IQR, 0 to 0.75; $P \leq .001$)[86] • Bloating and distention: −1.5 (IQR, −2.00 to −1.00) vs 0.25 (IQR, 0.88 to 1.00; P = .03)[86] • RCT also showed relief of pain (0-4 scale), −2 (IQR, −2.00 to 0) vs 0 (IQR, −1.00 to 0.00; P = .04)[86] Improved gastric emptying in both trials, particularly in diabetic gastroparesis in first RCT[85] Numerous open-label observational studies and systematic review and meta-analyses document clinical benefit[87]	Multicenter, crossover trial including 172 patients in France[88] Single-center cohort of 110 patients in the US followed up ≤5 y:[89] Benefits in all 9 gastrointestinal symptoms, total GCSI score, reduced use of prokinetics and antiemetics, and reduced hospitalizations for gastroparesis	A study of 177 patients with refractory gastroparesis who underwent laparoscopic pyloroplasty reported 90% of patients had improved gastric emptying at 3 mo after surgery and improvement of nausea, vomiting, bloating, and abdominal pain at 1 and 6 mo after surgery[90]
Adverse events	Pneumoperitoneum requiring resuturing (1 of 18)[86] pyloric channel ulcer, gastric mucosal injury, dumping syndrome (1 of each adverse events in 21 patients)[85]	Abdominal wall pain at site of implant (n = 28), infections at the abdominal pouch (battery location; n = 16), hematoma (n = 1); in 3 cases, the device-related adverse events were serious enough to prompt device removal	Intraoperative adverse event rate was 6.8%, including 2 inadvertent gastrotomies requiring repair and 2 suture line leaks (1.1%) requiring further surgery[90]
Considerations	On multivariable analyses, the predictors of positive outcome with G-POEM were shorter duration of gastroparesis, nondiabetic etiology, lower body mass index, and improvement with intrapyloric botulinum toxin injection	Additional benefit observed with GES together with pyloroplasty;[91,92] In an RCT of 38 patients with diabetic or idiopathic gastroparesis[91] at 3 mo, patients with activated GES vs nonactivated GES had GCSI improvement from baseline (median difference, −1.33 [95% CI, −2.34 to −0.33]; P = .01).; a single-center cohort of 49 patients with gastroparesis with GES and pyloroplasty showed beneficial effects on clinical symptoms, patient satisfaction, and gastric emptying at median follow-up of 47 mo (range, 5-90 mo)[92]	Largely replaced by G-POEM; There is evidence of adding benefit when combined with GES[92]

Abbreviations: G-POEM, gastric peroral endoscopic myotomy; GCSI, Gastroparesis Cardinal Symptom Index; GES, gastric electrical stimulation; RCT, randomized clinical trial.

Gastric Peroral Endoscopic Myotomy

Pyloromyotomy is recommended over no treatment for refractory gastroparesis symptoms,[34] based on open-label studies and 2 sham-controlled trials of 6 months' duration. Currently, pyloromyotomy is almost exclusively performed with gastric peroral endoscopic myotomy,[93] which involves an endoscopic incision of the pyloric muscle and is a same-day procedure in 85% of patients.[94] In a trial of 86 patients randomized to gastric peroral endoscopic myotomy or a sham , treatment success (defined as a decrease in the Gastroparesis Cardinal Symptom Index [GCSI] by at least 50%) at 6 months was higher after gastric peroral endoscopic myotomy than after the sham procedure: 89% (95% CI, 56%-98%) vs 17% (95%,CI, 3%-57%) in patients with diabetic gastroparesis, 67% (95%, CI, 30%-90%) vs 20% (95%, CI, 3%-67%) in patients with idiopathic gastroparesis, and 50% (95%, CI, 18%-82%) vs 29% (95% CI, 7%-67%) in patients with postsurgical gastroparesis.[85]

Another RCT involving 52 patients with diabetic gastroparesis reported significant decreases of at least 40% relative to baseline in 3 GCSI subscales (0-4 scale) with gastric peroral endoscopic myotomy and significant median differences from the sham procedure: nausea and vomiting subscale, −1.67 (IQR, −3.00 to −0.83) vs 1 (IQR, 0.08 to 1.33; P = .001); postprandial fullness and early satiety, −2.25 (IQR, −3.00 to −1.00) vs 0.25 (IQR, 0 to 0.75; $P \leq .001$); bloating and distention, −1.5 (IQR, −2.00 to −1.00) vs 0.25 (IQR, 0.88 to 1.00; P = .03); and decreased abdominal pain, −2 (IQR, −2.00 to 0) vs 0 (IQR, −1.00 to 0; P = .038).[86]

A systematic review and meta-analysis of gastric peroral endoscopic myotomy of 15 observational studies (7 retrospective, 8 prospective) involving 982 patients with gastroparesis (290 postsurgical, 287 idiopathic, and 286 diabetic) reported pooled clinical success rates (defined by at least a 1-point decrease in the GCSI score or 25%-50% improvement in symptoms and improved gastric emptying times) in 65% of patients.[95] However, there was substantial heterogeneity in outcomes among the 15 studies.[95]

Another systematic review and meta-analysis of 20 cohort studies reported that 979 patients who had undergone gastric peroral

endoscopic myotomy had a weighted mean difference compared with the preprocedure GCSI score (range, 0-4) of −1.56 (95% CI, −1.89 to −1.24, with minimum clinically important difference of 1).[96] Another systematic review and meta-analysis showed reduced nausea, satiety and bloating, although there was substantial heterogeneity in symptom responsiveness.[97] Predictors of positive outcomes with gastric peroral endoscopic myotomy were shorter duration of gastroparesis, nondiabetic gastroparesis, lower body mass index, and response to intrapyloric botulinum toxin.[87] A meta-analysis of 23 studies (prospective or retrospective observational studies with at least 6 months of follow-up [maximum 60 months]) reported that gastric peroral endoscopic myotomy was associated a pooled response rate of 73.25% (95% CI, 64.3% to 81.3%) at 12 months, and 69.76% (95% CI, 58.31% to 80.1%) at 36 months.[98]

Gastric Electrical Stimulation

Gastric electrical simulation involves open or laparoscopic surgical placement of electrical leads on the stomach for delivery of electrical stimulation by a subcutaneously placed device. Gastric electrical simulation delivers high-frequency, low-energy pulses at 12 cycles per minute. The basal electrical rhythm of the pacemaker of the human stomach is 3 cycles per minute, so the gastric electrical simulation does not accelerate gastric emptying, but alters visceral afferent function to reduce symptoms of gastroparesis such as nausea.[99] Although trials of gastric electrical simulation have had mixed results,[34] a single-center cohort of 157 US patients (57 with diabetic gastroparesis, 93 with idiopathic gastroparesis, and 7 with postsurgical gastroparesis) reported statistically significant improvements in all 9 assessed symptoms (nausea, vomiting, retching, stomach fullness, inability to finish meal, feeling full after meals, loss of appetite, bloating, and stomach visibly larger) at the 1-year (n = 141) and 5-year (n = 110) follow-up visits after gastric electrical simulation ($P < .05$) compared with preoperative values. The study also reported a significant decrease in use of prokinetic and antiemetic medications. In addition, the mean number of hospitalizations for gastroparesis decreased from 3.7 (SD, 1.9) preoperatively to 1.5 (SD, 0.4]) at 1 year and 1.6 (SD, 0.4) at 5 years postoperatively ($P < .05$).[89]

A meta-analysis of 9 studies (7 randomized trials, 2 observational studies) involving 730 participants who had undergone gastric electrical simulation reported sustained improvement in total symptom scores (for 6 symptoms: vomiting, nausea, early satiety, bloating, postprandial fullness, and epigastric pain based on a 0-4 scale, 4 indicates very severe) at 12 months compared with before treatment (mean difference [MD], −6.07; 95% CI, −4.5 to −7.65) and reduced frequency of weekly vomiting episodes (MD, −15.59; 95% CI, −10.29 to −20.9); however, there were no significant differences in weekly vomiting frequency between the gastric electrical simulation group and the control group (MD, −1.76; 95% CI, −6.15 to 2.63; $P = .43$).[100]

Laparoscopic Pyloroplasty

Laparoscopic pyloroplasty is a minimally invasive surgical procedure in which incisions are made to reconfigure the pyloric muscle, so that it remains permanently open. A study of 177 patients with refractory gastroparesis who had undergone laparoscopic pyloroplasty reported that 90% of patients had improved gastric emptying at 3 months after surgery and improvement of nausea, vomiting, bloating, and abdominal pain at 1 and 6 months after surgery.[90] However, the intraoperative adverse event rate was 6.8%, including 2 inadvertent gastrotomies that required repair and 2 suture line leaks (1.1%) requiring further surgery.

Comparisons of Procedures

A comparison of 2 multicenter cohorts of patients with medically refractory gastroparesis with predominant nausea and vomiting, of whom 34 were treated with gastric electrical simulation and 30 had undergone gastric peroral endoscopic myotomy, showed equivalent efficacy of these procedures in treating individual symptoms and in overall daily GCSI scores at 24 months.[101] Mean scores of the nausea and vomiting subscale after 24 months decreased with gastric electrical simulation (from 3.0 at baseline to 1.6; $P < .001$) and gastric peroral endoscopic myotomy (from 2.6 at baseline to 1.2; $P < .001$). The difference in nausea and vomiting subscales adjusted from baseline scores was −0.28 (96% CI, −0.77 to 0.19; $P = .24$), suggesting no significant difference in efficacy between the 2 gastric electrical stimulation and gastric per oral endoscopic myotomy.[101] A systematic review and network meta-analysis of 55 observational studies of gastric peroral endoscopic myotomy (21 studies with 1199 participants), pyloroplasty (5 studies with 179 participants), gastric electrical simulation (11 studies with 272 participants), and intrapyloric botulinum toxin A injection (4 studies with 80 participants) reported that gastric peroral endoscopic myotomy and gastric electrical simulation were the most effective treatments for gastroparesis.[102]

Prognosis

Nutritional deficiencies are frequent among patients with gastroparesis. Based on dietary questionnaires of 305 patients with diabetic or idiopathic gastroparesis enrolled in the National Institute of Diabetes and Digestive and Kidney Diseases Gastroparesis Registry, 194 patients (64%) reported caloric-deficient diets, defined as less than 60% of estimated total energy requirements. Based on the Block Brief Food Frequency Questionnaire,[103] these patients had deficiencies (relative to recommended daily intake) in vitamin K (70.1%), vitamin C (66.5%), vitamin B_1 (62.4%), vitamin B_6 (55.2%), and vitamin A (49.5%); 86.1% had iron deficiency, and 70.1% were zinc deficient.[104] Rarely, patients with gastroparesis develop substantial fluid or metabolic derangements (eg, ketoacidosis, kidney insufficiency, hyperglycemia) due to nausea and vomiting that require oral or intravenous hydration and repletion of electrolytes (eg, potassium, calcium, and magnesium).[105]

Patients with gastroparesis have an increased mortality risk compared with age- and sex-matched individuals without gastroparesis,[15] which may partially be due to underlying conditions such as diabetes. A study involving electronic health record review by a gastroenterologist of individuals in Olmsted County, Minnesota,[21] identified 222 patients with gastroparesis based on symptoms or delayed gastric emptying by scintigraphy and reported 5-year survival rates of 67% in those with gastroparesis vs 81% among comparable controls without gastroparesis, adjusting for age and sex but not for comorbidities ($P < .05$). Among the 69 patients with gastroparesis who died, the most common causes of death were cardiovascular disease (24.6%), respiratory failure (23.2%), malignancy (15.9%), and chronic kidney failure (15.9%).[21]

In a cross-sectional study that included 1145 UK patients with gastroparesis, over 20 years of follow-up, the hazard ratio (HR) for death was significantly higher among patients with type 1 diabetic gastroparesis (adjusted HR, 2.6; 95% CI, 1.6-4.2) and type 2 diabetic gastroparesis (HR, 2.0; 95% CI, 1.2-3.4) than among those with idiopathic gastroparesis.[20] Absolute rates of death were 82 of 426 patients (19.2%) with diabetic gastroparesis vs 39 of 447 patients (8.7%) with idiopathic gastroparesis.[20]

Discussion

Practical Considerations

Gastroparesis is frequently overdiagnosed, if the diagnosis is based only on symptoms or suboptimal measurement of gastric emptying (eg, 2-hour). In a retrospective observational study from a tertiary care center, only 15.5% of 339 patients referred for suspected gastroparesis based on symptoms or suboptimal measurement of gastric emptying had the diagnosis of gastroparesis confirmed after a 4-hour scintigraphic gastric emptying study.[106]

Gastroparesis is associated with treatment dissatisfaction, decreased QOL, depression, and anxiety. In a survey of 1423 adults with average duration of gastroparesis symptoms of 9.3 years, patients rated their feeling about gastroparesis treatment as being dissatisfied (33%), somewhat dissatisfied (27%), neutral (14%), somewhat satisfied (15%), and satisfied (4%).[107] These patients had a decreased QOL measured by the Short-Form 36 Health Survey, and their physical health QOL score was negatively correlated with symptoms including nausea, abdominal pain, and early satiety ($P < .001$).[107] The mean composite summary normed score for physical health was 33.1 (SD, 10.3) and for mental health was 36.0 (SD, 12.1) among patients with gastroparesis, both of which were lower than normal values of 50 (SD, 10) for the general healthy population. Among these patients with gastroparesis, 41.7% were diagnosed with anxiety and 41.3% with depression.[107] In a multicenter cohort study of 299 patients with gastroparesis (100 with diabetes, 199 with idiopathic origin), scores on the Beck Depression Inventory and State-Trait Anxiety Inventory were higher with increasing gastroparesis severity ($P < .05$), and with GCSI higher than the median score of 3.1 vs less than 3.1 ($P < .05$).[108] For example, the mean Beck Depression Inventory scores were 15.9 (SD, 9.3) in 148 patients with GCSI of 3.1 or less and 22.2 (SD, 11.2) in 149 patients with GCSI of more than 3.1.

Use of a multidisciplinary team including primary care clinicians, gastroenterologists, dietitians, and psychologists can help patients with gastroparesis manage symptoms and implement a high nondigestible fiber diet. In addition, clinicians should avoid prescribing central neuromodulators such as tricyclic agents that may impair gastric emptying due to anticholinergic effects.

Limitations

This review has several limitations. First, some relevant articles may have been missed. Second, systematic evaluation of the quality of evidence was not performed. Third, the review of medications was restricted to those available in the US or those being evaluated in phase 2B and phase 3 trials for treatment of gastroparesis.

Conclusions

Gastroparesis is a condition of delayed gastric emptying without gastric outlet obstruction that is diagnosed based on a gastric emptying study. First-line treatments include a small particle diet and use of antiemetics and prokinetics (metoclopramide and erythromycin). Severe refractory gastroparesis may be treated with G-POEM or gastric electrical simulation.

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Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Kristin Walter, MD, at kristin.walter@jamanetwork.org.

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