Gastroparesis is defined as a chronic motility disorder where there is delayed emptying of the stomach without an apparent mechanical obstruction. Usually, both solids and liquids are affected. Gastroparesis is usually of undetermined causes, but can also be linked to previous abdominal surgeries or diabetes mellitus. Symptoms include nausea, vomiting, and early satiety. Once diagnosed, the patient is instructed to follow a diet that has more liquid, promotility agents could be prescribed and antiemetics are used for symptomatic relief.

General Information

Patients with gastroparesis have delayed stomach emptying of food with no apparent obstruction. Gastric motility is controlled by the vagus nerve, smooth muscle cells, and enteric neurons. Each of these three control levels must be impaired for the patient to develop gastroparesis.

While most cases do not have a clear etiology, diabetes and abdominal surgeries have been both linked to the development of gastroparesis. It is more common in patients with Type 1 diabetes, but patients with Type 2 diabetes are also susceptible.

Symptoms of gastroparesis are non-specific, making diagnosis challenging. They include abdominal pain, early satiety, bloating, vomiting, and nausea. If left untreated, severe gastroparesis can cause esophagitis, bezoar formation, or Mallory-Weiss tears, which are due to repeated vomiting.
Epidemiology

Since the symptoms are non-specific, it is difficult to know the exact prevalence of gastroparesis in the USA. Some studies put the incidence of gastroparesis at 2.5 per 100,000 for men and 9.6 per 100,000 for women.

These numbers show that gastroparesis is more common in women, which is in agreement with another study of gastroparesis patients that reported 84% of the patients were women. Interestingly, healthy women usually have a delayed emptying rate compared to men which could, in theory, make them more predisposed to gastroparesis. However, few studies focus on specific populations that are known to have an increased risk of gastrointestinal symptoms.

Diabetes, in particular, has been strongly linked to gastrointestinal symptoms in general and gastroparesis in particular. Current studies show that diabetics are very likely to have delayed gastric emptying.

Gastroparesis-related hospitalizations have doubled in the last decade because of the increasing prevalence of diabetes and gastroesophageal reflux disease-related surgeries. Additionally, the total costs related to these hospitalizations are higher than those for gastric ulcers, gastritis, or gastroesophageal reflux disease.

Etiologies

The most commonly encountered etiologies of gastroparesis are idiopathic, followed by diabetes, and finally, post-gastric surgery related. Less common etiologies include Parkinson’s disease and collagen disorders.
Idiopathic gastroparesis means the exact etiology of delayed gastric emptying cannot be determined. Although several risk factors have been found in this subgroup of patients, the relationship is not strong enough to be considered an etiology.

For example, 21% of the idiopathic cases are thought to be postinfectious. Epstein-Barr, Hawaii, Norwalk, and rotavirus are all associated with an increased risk of gastroparesis after acute gastroenteritis, and this could be related to autonomic neuropathy. Most cases of viral gastroparesis resolve in 18 to 24 months.

Diabetes-related

About 20-30% of diabetics may have gastroparesis; some studies suggest this might be as high as 50% among Type 1 diabetics. Due to autonomic diabetic neuropathy, abdominal symptoms are less common in this subgroup of gastroparesis patients.

The pathophysiology of diabetic gastroparesis is better understood when compared to the idiopathic form. In long-standing diabetes, patients develop neuromyopathy, which is the cause of gastroparesis in these patients.
In addition to neuromyopathy, **oxidative injury, along with reduced insulin concentration** in diabetes, are responsible for the **loss of Cajal cells**. Cajal cells are responsible for the synthesis of **nitrous oxide NO neurotransmitter**, which relaxes the **fundus** and decreases the tone of the **pylorus**. Loss of Cajal cells in diabetes would result in an increased pyloric tone and, eventually, delayed gastric emptying. Additionally, **gastric slow waves** and **peristalsis** are both impaired in diabetic autonomic neuropathy.

### Postsurgical

In some abdominal surgeries, such as **fundoplication for gastroesophageal reflux disease** and **bariatric surgery for obesity**, there is a risk of **vagus nerve injury**. If injured, **gastric stasis** could develop, which, in turn, may lead to gastroparesis. **Gastrectomy, esophageal, and pancreatic surgeries** are also related to gastroparesis development. For example, up to 67% of patients who undergo **pancreatic cancer cryotherapy** have a high risk of temporary gastroparesis as a complication.

### Other Etiologies

**Tricyclic antidepressants** and **alpha-2 adrenergic agonists** slow gastric motility and could result in gastroparesis. **Parkinson’s disease** is associated with neuronal degeneration in the dorsal nucleus of the vagus nerve, which could result in gastroparesis. **Multiple sclerosis** has also been linked to the development of gastroparesis due to a different pathology that is linked to the involvement of the white matter in the vagus.
Clinical Presentation

Sometimes, it is a challenge to differentiate between gastroparesis and functional dyspepsia. In this section, we cover both the non-specific symptoms of gastroparesis and the more specific ones.

In gastroparesis, gastric motor dysfunction usually causes more severe symptoms than simple dyspepsia. Some, but not all, patients with gastroparesis experience weight loss, making it a less sensitive symptom.

Another important controversy related to gastroparesis is the relationship between the severity of the symptoms and the degree of the delayed stomach emptying, which is inconsistent.

The general symptoms of gastroparesis include abdominal pain, nausea, vomiting and, if severe enough, the formation of a food bezoar. Due to the poor relationship between the symptoms and gastroparesis, the doctor has to have a low threshold to order more specific tests to confirm the diagnosis in a high-risk patient.

Diagnostic Work-up

Laboratory investigations are only helpful for excluding other possible differential diagnoses, such as pancreatitis, but cannot diagnose gastroparesis definitively.

The first diagnostic test should be an esophagogastroduodenoscopy to exclude possible mechanical obstruction as the cause of delayed gastric emptying. If the endoscopy revealed no structural or mechanical cause for the patient’s symptoms, further studies are needed.

Gastric-emptying Scintigraphy

Gastric emptying scintigraphy (GES) is currently considered the gold standard for diagnosing gastroparesis. Before testing, the patient must be instructed to avoid smoking tobacco, tricyclic antidepressants, adrenergic agents, and promotility medications. Diabetic patients should maintain good control of hyperglycemia before attempting to do the test.

Before testing, the patient is instructed to eat a radiolabeled meal. Afterward, stomach imaging is conducted, along with a calculation of the remaining amount of the radiolabeled isotope.

The American Neurogastroenterology and Motility Society recently published diagnostic criteria for gastroparesis: If the patient has more than 90% retention of the radiolabeled material by 1 hour > 60% by 2 hours and > 10% by 4 hours, he or she is said to have delayed gastric emptying and possibly gastroparesis with high certainty.

Wireless Capsule Motility

The SmartPhill Corporation recently introduced a new wireless capsule that is indigestible
and is a safer alternative to GES. **The capsule measures pH, pressure, and temperature** and can be used to investigate both gastroparesis and constipation.

In gastroparesis, the capsule determines the time it took to pass the stomach by tracking the sudden change in pH, which demarcates the difference between the acidic and alkaline secretions of the **stomach** and **pancreas** in the duodenum, respectively. Usually, patients who are diagnosed to have gastroparesis with this method also have more than 90% retention one hour if GES was performed.

### Antroduodenal Manometry

This investigation is usually done during fasting to assess the **migrating motor complex (MMC)**, which helps in differentiating between **neuropathic and myopathy gastroparesis**.

Antroduodenal manometry, as the name implies, works by **measuring the intraluminal pressure in the antrum, pylorus, and duodenal areas**. Monitoring for 5 to 8 hours is usually needed. In **myopathic disease**, patients have low amplitude antral MMCs while, in **diabetic neuropathy**, the amplitude is normal but there is poor correlation between the three regions; the antrum, pylorus, and duodenal.

### Treatment Options

![Skeletal formula of domperidone](image)

Once the diagnosis of gastroparesis is confirmed, managing the condition usually involves **dietary modifications, medication**, and, in more severe cases, **endoscopic surgery**.

### Dietary Modifications

The first step in the management of gastroparesis is to switch to a diet with **smaller, more frequent meals with low-fat content and more liquid content**. Nausea, vomiting, bloating, and, to a lesser extent, abdominal pain, all improved after the introduction of a small-particle diet in diabetic gastroparesis. Unfortunately, such studies only provided short-term outcome results and long-term, follow-up studies are needed.

### Promotility Agents

Promotility agents, such as **TZP-102**, a **Ghrelin agonist**, are promising in the symptomatic relief of gastroparesis. Despite a significant decrease in the severity of the symptoms, researchers found no improvement in the rate of gastric emptying.

Despite this success, Ghrelin agonists are still in clinical trials, and more traditional **prokinetic agents**, such as **erythromycin**, are usually used as first-line therapy.
Metoclopramide nasal spray or tablets show good efficacy for symptomatic relief of gastroparesis but, again, they were not associated with an improvement in the gastric emptying rate.

Endoscopic Intervention and Surgery

Surgery should be the last resort and only for severe, medically refractory cases of gastroparesis. Near-total gastrectomy has been evaluated as a possible last resort for medically refractory gastroparesis with good results in terms of semiology. The study had a limitation because it did not show the rate of gastric emptying before the surgery, and the cohort had undergone several abdominal surgeries previously for gastroesophageal reflux disease and pyloromyotomies.

More recently, endoscopic pyloromyotomy was introduced as an option for gastroparesis. The procedure is similar to peroral endoscopic myotomy for achalasia and significantly improved gastroparesis-related symptoms. Larger, well-controlled clinical trials are still warranted to provide more evidence about this procedure’s efficacy.

Summary

While gastroparesis is common in certain populations, such as patients with diabetes, most cases have unknown causes. The main hallmark of gastroparesis is delayed gastric emptying which can be assessed by GES, a wireless capsule motility test, or antroduodenal manometry.

Once the diagnosis is confirmed, the patients are instructed to follow a small-particle diet with more liquids. If this is not sufficiently effective, promotility agents, such as erythromycin and antiemetics, such as metoclopramide, are prescribed. Novel treatments, such as Ghrelin agonists, are promising for symptomatic relief. Finally, surgery should be a last resort in gastroparesis; long-term follow-up and well-controlled clinical trials are still needed.

References


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