

# ACG Clinical Guideline: Management of Gastroparesis

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## **Abstract**

This guideline presents recommendations for the evaluation and management of patients with gastroparesis. Gastroparesis is identified in clinical practice through the recognition of the clinical symptoms and documentation of delayed gastric emptying. Symptoms from gastroparesis include nausea, vomiting, early satiety, postprandial fullness, bloating, and upper abdominal pain. Management of gastroparesis should include assessment and correction of nutritional state, relief of symptoms, improvement of gastric emptying and, in diabetics, glycemic control. Patient nutritional state should be managed by oral dietary modifications. If oral intake is not adequate, then enteral nutrition via jejunostomy tube needs to be considered. Parenteral nutrition is rarely required when hydration and nutritional state cannot be maintained. Medical treatment entails use of prokinetic and antiemetic therapies. Current approved treatment options, including metoclopramide and gastric electrical stimulation (GES, approved on a humanitarian device exemption), do not adequately address clinical need. Antiemetics have not been specifically tested in gastroparesis, but they may relieve nausea and vomiting. Other medications aimed at symptom relief include unapproved medications or off-label indications, and include domperidone, erythromycin (primarily over a short term), and centrally acting antidepressants used as symptom modulators. GES may relieve symptoms, including weekly vomiting frequency, and the need for nutritional supplementation, based on open-label studies. Second-line approaches include venting gastrostomy or feeding jejunostomy; intrapyloric botulinum toxin injection was not effective in randomized controlled trials. Most of these treatments are based on open-label treatment trials and small numbers. Partial gastrectomy and pyloroplasty should be used rarely, only in carefully selected patients. Attention should be given to the development of new effective therapies for symptomatic control.

## **Introduction**

This clinical guideline addresses the definition, diagnosis, differential diagnosis, and treatment of gastroparesis, including nutritional supplementation, glycemic control, pharmacological, endoscopic, device, and surgical therapy.

Each section of this document will present the key recommendations related to the section topic and a subsequent summary of the evidence supporting those recommendations. An overall summary will be presented in the first table. A search of OVID Medline, Pubmed, and ISI Web of Science was conducted for the years from 1960 to 2011 using the following major search terms and subheadings including “gastroparesis,” “electrical stimulation,” “botulinum toxin,” “drug therapy,” “glycemic control,” “dietary therapy,” and “alternative therapy”. We used systematic reviews and meta-analyses for each topic when available, followed by a review of clinical trials.

The GRADE system was used to evaluate the strength of the recommendations and the overall quality of evidence (1) (**Table 1**). The strength of a recommendation was graded as “strong” when the desirable effects of an intervention clearly outweigh the undesirable effects and as “conditional” when there is uncertainty about the trade-offs. The quality of evidence could range from “high” (implying that further research was unlikely to change the authors’ confidence in the estimate of the effect) to “moderate” (further research would be likely to have an impact on the confidence in the estimate of effect) or “low” (further research would be expected to have an important impact on the confidence in the estimate of the effect and would be likely to change the estimate).

<b>Table 1. Criteria for assigning grade of evidence</b>
<i>Type of evidence</i>
Randomized trial=high
Observational study=low
Any other evidence=very low
<i>Decrease grade if:</i>
Serious (-1) or very serious (-2) limitation to study quality
Important inconsistency (-1)
Some (-1) or major (-2) uncertainty about directness
Imprecise or sparse data (-1)
High probability of reporting bias (-1)
<i>Increase grade if:</i>
Strong evidence of association—significant relative risk of >2 (<0.5) based on consistent evidence from two or more observational studies, with no plausible confounders (+1)
Very strong evidence of association—significant relative risk of >5 (<0.2) based on direct evidence with no major threats to validity (+2)
Evidence of a dose response gradient (+1)
All plausible confounders would have reduced the effect (+1)
<i>Definitions of grades of evidence</i>
<i>High</i> = Further research is unlikely to change our confidence in the estimate of effect
<i>Moderate</i> =Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
<i>Low</i> =Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
<i>Very low</i> =Any estimate of effect is very uncertain

## **Definition of Gastroparesis Syndrome and Gastroparesis Symptoms**

### **Recommendations**

1. The diagnosis of gastroparesis is based on the combination of symptoms of gastroparesis, absence of gastric outlet obstruction or ulceration, and delay in gastric emptying. (Strong recommendation, high level of evidence)
2. Accelerated gastric emptying and functional dyspepsia can present with symptoms similar to those of gastroparesis; therefore, documentation of delayed gastric emptying is recommended before selecting therapy with prokinetics agents or gastric electrical stimulation (GES). (Strong recommendation, moderate level of evidence)

## **Identifying the Cause of Gastroparesis**

### **Recommendations**

1. Patients with gastroparesis should be screened for the presence of diabetes mellitus, thyroid dysfunction, neurological disease, prior gastric or bariatric surgery, and autoimmune disorders. Patients should undergo biochemical screen for diabetes and hypothyroidism; other tests are as indicated clinically. (Strong recommendation, high level of evidence)
2. A prodrome suggesting a viral illness may lead to gastroparesis (postviral gastroparesis). This condition may improve over time in some patients. Clinicians should inquire about the presence of a prior acute illness suggestive of a viral infection. (Conditional recommendation, low level of evidence)
3. Markedly uncontrolled ( $> 200$  mg/dl) glucose levels may aggravate symptoms of gastroparesis and delay gastric emptying. (Strong recommendation, high level of evidence.) Optimization of glycemic control should be a target for therapy; this may improve symptoms and the delayed gastric emptying. (Moderate recommendation, moderate level of evidence)
4. Medication-induced delay in gastric emptying, particularly from narcotic and anticholinergic agents and glucagon like peptide-1 (GLP-1) and amylin analogs among diabetics, should be considered in patients before assigning an etiological diagnosis. Narcotics and other medications that can delay gastric emptying should be stopped to establish the diagnosis with a gastric emptying test. (Strong recommendation, high level of evidence)
5. Gastroparesis can be associated with and may aggravate gastroesophageal reflux disease (GERD). Evaluation for the presence of gastroparesis should be considered in patients with GERD that is refractory to acid-suppressive treatment. (Conditional recommendation, moderate level of evidence)

## **Diagnosis of Gastroparesis**

### **Recommendations**

1. Documented delay in gastric emptying is required for the diagnosis of gastroparesis. Scintigraphic gastric emptying of solids is the standard for the evaluation of gastric emptying and the diagnosis of gastroparesis. The most reliable method and parameter for diagnosis of gastroparesis is gastric retention of solids at 4 h measured by scintigraphy. Studies of shorter duration or based on a liquid challenge result in decreased sensitivity in the diagnosis of gastroparesis. (Strong recommendation, high level of evidence)
2. Alternative approaches for assessment of gastric emptying include wireless capsule motility testing and  $^{13}\text{C}$  breath testing using octanoate or spirulina incorporated into a solid meal; they require further validation before they can be considered as alternates to scintigraphy for the diagnosis of gastroparesis. (Conditional recommendation, moderate level of evidence)

3. Medications that affect gastric emptying should be stopped at least 48 h before diagnostic testing; depending on the pharmacokinetics of the medication, the drug may need to be stopped > 48 h before testing. (Strong recommendation, high level of evidence)
4. Patients with diabetes should have blood glucose measured before starting the gastric emptying test, and hyperglycemia treated with test started after blood glucose is < 275 mg/dl. (Strong recommendation, moderate-high level of evidence)

### **Exclusion Criteria and Differential Diagnosis**

#### **Recommendations**

1. The presence of rumination syndrome and/or eating disorders (including anorexia nervosa and bulimia) should be considered when evaluating a patient for gastroparesis. These disorders may be associated with delayed gastric emptying, and identification of these disorders may alter management. (Strong recommendation, moderate-high level of evidence)
2. Cyclic vomiting syndrome (CVS) defined as recurrent episodic episodes of nausea and vomiting, should also be considered during the patient history. These patients may require alternative therapy. (Conditional recommendation, moderate level of evidence)
3. Chronic usage of cannabinoid agents may cause a syndrome similar to CVS. Patients presenting with symptoms of gastroparesis should be advised to stop using these agents. (Conditional recommendation, low level of evidence)

### **Management of Gastroparesis**

#### **Recommendations**

1. The first line of management for gastroparesis patients should include restoration of fluids and electrolytes, nutritional support and in diabetics, optimization of glycemic control. (Strong recommendation, moderate level of evidence.)
2. Oral intake is preferable for nutrition and hydration. Patients should receive counseling from a dietician regarding consumption of frequent small volume nutrient meals that are low in fat and soluble fiber. If unable to tolerate solid food, then use of homogenized or liquid nutrient meals is recommended. (Conditional recommendation, low level of evidence)
3. Oral intake is the preferable route for nutrition and hydration. If oral intake is insufficient, then enteral alimentation by jejunostomy tube feeding should be pursued (after a trial of nasoenteric tube feeding). Indications for enteral nutrition include unintentional loss of 10% or more of the usual body weight during a period of 3–6 months, and/or repeated hospitalizations for refractory symptoms. (Strong recommendation, moderate level of evidence)
4. For enteral alimentation, postpyloric feeding is preferable to gastric feeding because gastric delivery can be associated with erratic nutritional support. (Conditional recommendation, low level of evidence)
5. Enteral feeding is preferable to parenteral nutrition. (Conditional recommendation, low level of evidence)

**Table 2.** Intubations for decompression and feeding in patients with gastroparesis

Type of evidence	Usefulness	Disadvantages
Nasogastric tube	Gastric decompression in acute management	Not meant for long-term use Large tube size often causes is comfort Is a poor choice for feeding due to delayed gastric emptying as significant gastroesophageal reflux can occur
Nasoduodenal/ nasojejunal tube	Used to give trial feedings to determine if jejunal feedings are tolerated. May be acceptable if there are no other options	Not for long-term use Vomiting may expel the tube into the stomach
Gastrostomy tubes	May be used for venting of secretions to decrease vomiting and fullness	Poor choice for feeding due to delayed gastric emptying May prevent proper electrode placement for gastric electrical stimulation
PEG-J or Jet-PEG	Allows the patient to vent gastric secretions to decrease/ prevent persistent emesis Provides jejunal feedings New PEG-Js have distal feeding ports to reduce duodenogastric reflux	Migration of the J-tube extension into stomach Pyloric obstruction from J-tube May prevent proper electrode placement for gastric electrical stimulation
Jejunostomy (surgical, endoscopic, radiographic)	Stable access for reliable jejunal nutrient delivery Avoids gastric penetration that would interfere with proper electrode placement for gastric electrical stimulation	Cannot vent stomach
Dual gastrostomy and jejunostomy	Two sites—one for venting and one for enteral nutrition	Increased risk of leakage, infection Cosmetic issues

PEG, percutaneous endoscopic gastrostomy; PEG-J, percutaneous endoscopic gastrostomy with jejunal extension tube.

Table created from text of ref. (63).

## **Glycemic Control in DG (diabetic gastroparesis)**

### **Recommendations**

1. Good glycemic control should be the goal. Since acute hyperglycemia inhibits gastric emptying, it is assumed that improved glycemic control may improve gastric emptying and reduce symptoms. (Conditional recommendation, moderate level of evidence)
2. Pramlintide and GLP-1 analogs may delay gastric emptying in diabetics. Cessation of these treatments and use of alternative approaches should be considered before initiation of therapy for gastroparesis. (Conditional recommendation, low level of evidence)

## **Pharmacologic Therapy**

### **Recommendations**

1. In addition to dietary therapy, prokinetic therapy should be considered to improve gastric emptying and gastroparesis symptoms, taking into account benefits and risks of treatment. (Strong recommendation, moderate level of evidence)
2. Metoclopramide is the first line of prokinetic therapy and should be administered at the lowest effective dose in a liquid formation to facilitate absorption. The risk of tardive dyskinesia has been estimated to be < 1%. Patients should be instructed to discontinue therapy if they develop side effects including involuntary movements. (Moderate recommendation, moderate level of evidence)
3. For patients unable to use metoclopramide, domperidone can be prescribed with investigational new drug clearance from the Food and Drug Administration (FDA) and has been shown to be as effective as metoclopramide in reducing symptoms without the propensity for causing central nervous system side effects; given the propensity of domperidone to prolong corrected QT interval on electrocardiogram, a baseline electrocardiogram is recommended and treatment withheld if the corrected QT is > 470 ms in male and 450 ms in female patients. Follow-up electrocardiogram on treatment with domperidone is also advised. (Moderate recommendation, moderate level of evidence)
4. Erythromycin improves gastric emptying and symptoms from delayed gastric emptying. Administration of intravenous (IV) erythromycin should be considered when IV prokinetic therapy is needed in hospitalized patients. Oral treatment with erythromycin improves gastric emptying also. However, the longterm effectiveness of oral therapy is limited by tachyphylaxis. (Strong recommendation, moderate level of evidence)
5. Treatment with antiemetic agents should occur for improvement of associated nausea and vomiting but will not result in improved gastric emptying. (Conditional recommendation, moderate level of evidence)
6. Tricyclic antidepressants (TCA) can be considered for refractory nausea and vomiting in gastroparesis but will not result in improved gastric emptying and may potentially retard gastric emptying. (Conditional recommendation, low level of evidence)

## **Intrapyloric Botulinum Toxin Injection**

### **Recommendation**

1. Intrapyloric injection of botulinum toxin is not recommended for patients with gastroparesis based on randomized controlled trials. (Strong recommendation, high level of evidence.)

## **Gastric Electrical Stimulation**

### **Recommendation**

1. GES may be considered for compassionate treatment in patients with refractory symptoms, particularly nausea and vomiting. Symptom severity and gastric emptying have been shown to improve in patients with DG, but not in patients with IG (idiopathic gastroparesis) or PSG (Postsurgical gastroparesis). (Conditional recommendation, moderate level of evidence.)

## **Surgical Treatments: Venting Gastrostomy, Gastrojeunostomy, Pyloroplasty, and Gastrectomy**

### **Recommendations**

1. Gastrostomy for venting and/or jejunostomy for feeding may be performed for symptom relief. (Conditional recommendation, low level of evidence)
2. Completion gastrectomy could be considered in patients with PSG who remain markedly symptomatic and fail medical therapy. (Conditional recommendation, low level of evidence)
3. Surgical pyloroplasty or gastrojeunosotomy has been performed for treatment for refractory gastroparesis. However, further studies are needed before advocating this treatment. Partial gastrectomy and pyloroplasty should be used rarely, only in carefully selected patients. (Conditional recommendation, low level of evidence)

## **Complementary and Alternative Medicines**

### **Recommendation**

1. Acupuncture can be considered as an alternative therapy. This has been associated with improved rates of gastric emptying and reduction of symptoms. (Conditional recommendation, low level of evidence)

### **Suspected gastroparesis**

Step 1: Diagnosis: 4 h Gastric emptying by scintigraphy

Step 2: Exclude iatrogenic disease

Dietary: low fat, low fiber diet

Glycemic control among diabetics

Step 3: Pharmacological Rx:

- Prokinetics: metoclopramide, erythromycin, domperidone
- Antiemetics: anti-histamine<sub>1</sub> receptors; 5-HT<sub>3</sub> antagonists

Step 4: Nutritional support: Enteral formula

Step 5: Non-pharmacological Rx

Pyloric injection of botulinum toxin

Venting gastrostomy, feeding jejunostomy

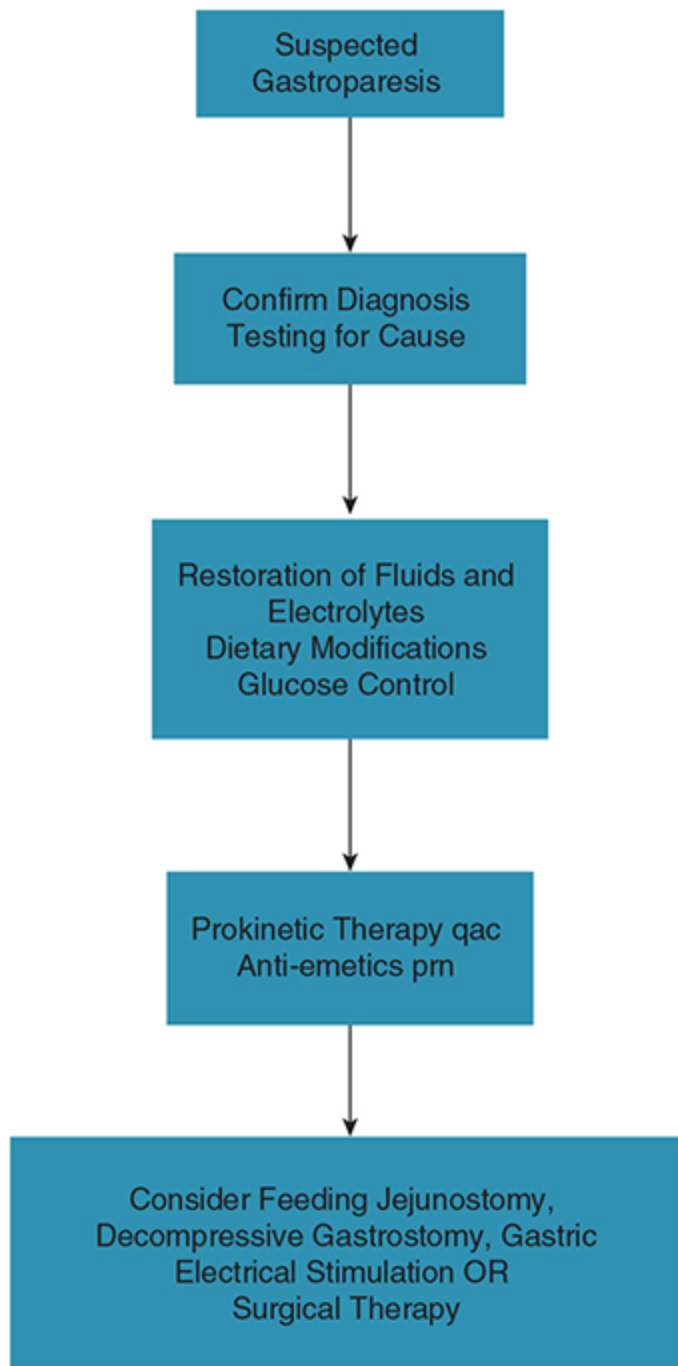
Parenteral nutrition

Gastric electrical stimulation

Pyloroplasty

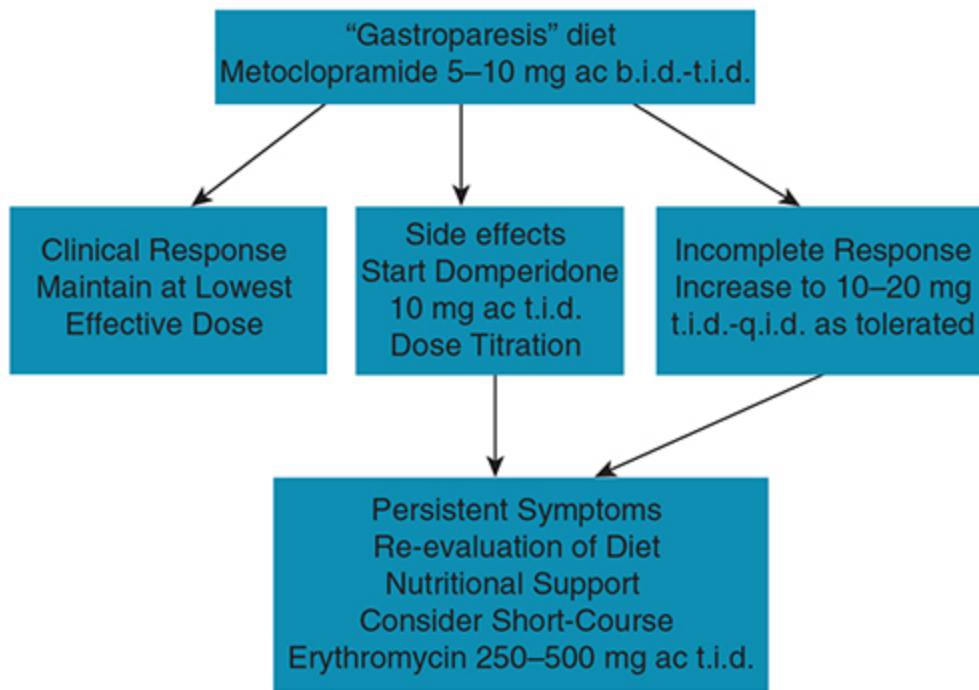
Partial gastrectomy

**Figure 1.** Stepwise algorithm for gastroparesis diagnosis and management.



**Figure 2.** Treatment algorithm for gastroparesis.





**Figure 3.** Algorithm for prokinetic therapy in gastroparesis.