

# Gastroparesis and Symptoms-Sketchy Relationships

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### Abstract

The relation between gastric emptying and symptoms is still unclear. The conception that improvement of gastric outflow or motoric function by Gastric Peroral Endoscopic Pyloromyotomy (G-POEM) or Gastric Electrical Stimulation (GES) would improve gastrointestinal symptoms simplifies the complexity of gastric dysfunction. It is still unclear why some patients with gastroparesis and dyspeptic symptoms benefit from GES. Besides placebo effects alteration of visceral perception has been suggested.

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### Introduction

#### Gastric dysfunction is caused by complex gastrointestinal pathophysiology

Normal gastric emptying is controlled by complex gastrointestinal physiologic functions. These comprise regular fundic tone with sufficient receptive and adaptive relaxation, tonic and peristaltic contractions, regular antroduodenal coordination, effective antral motor pump with grinding, gastric eurhythmia, normal sensory function and duodenal feedback. The predominant and clinical measurable gastric dysfunction is Gastroparesis (GP) with delay of gastric emptying. GP can be secondary through cerebral damage, vagal nerve disturbance, medical side effect, paraneoplasia, endocrinological diseases and infection. However, nearly half of the cases are classified as idiopathic. The diagnosis of clinically relevant idiopathic GP is based on the combination of characteristic symptoms in conjunction with objective evidence of delayed gastric emptying in the absence of mechanical obstruction [1-3].

#### Poor relationship between gastric dysfunction and clinical symptoms

Measurement of delayed gastric emptying time as part of multiple gastric dysfunctions time by scintigraphy and breath tests is established in clinical practice. Most clinicians believe that GP is the main cause for clinical symptoms such as nausea, vomiting, epigastric pain, early satiety, and weight loss. However, the relationship between gastric dysfunction and symptoms are not as clear-cut as considered by many physicians. This problem is evident by the finding that only disturbed gastric fundic relaxation significantly correlates with early satiety [4], whereas all the other gastric dysfunctions do not significantly match with symptoms. Especially, the relation between gastric emptying and symptoms is still unclear [5-14]. In addition, interpretation of gastrointestinal symptoms in GP in relation to its pathophysiology is challenging because they show a great overlap with other disorders such as functional dyspepsia or irritable bowel syndrome [2]. Furthermore, gastric emptying as measured by scintigraphy or breath tests show a wide range of normality making differentiation between clinically relevant normal and abnormal gastric emptying difficult in some cases.

## Pitfalls in the treatment of GP and symptoms

Because of the poor relationship between gastric emptying and symptoms and the heterogeneous patient group rational pathophysiological-based treatment in idiopathic GP is difficult. The conception that improvement of gastric outflow or motoric function by gastric peroral endoscopic pyloromyotomy (G-POEM) or Gastric Electrical Stimulation (GES) would improve gastrointestinal symptoms simplifies the complexity of gastric dysfunction. This dilemma [15,16] is obvious in two recent studies of Gastric Peroral Endoscopic Pyloromyotomy (G-POEM) and Gastric Electrical Stimulation (GES) in patients with idiopathic GP [17] and a randomized double-blind study in patients with refractory emesis with and without GP [18]. In addition, numerous metaanalyses point to the low quality of studies with GES [19] and failed to find robust effects of GES on gastric emptying [20-22]. Major criticism of the metaanalyses were potential bias because many studies were conducted by one group and sponsored by Medtronic (Minneapolis, USA), variation in the methods used to assess the improvement in symptoms in the patients with GES implants [20], substantial discrepancies between the reported results of controlled and open label GES studies, raising questions about the use of GES outside of defined clinical trials [21]. The lack of randomized controlled trials demonstrating benefit suggests the possibility of an underlying placebo effect [22]. However, it is still unclear why some patients with GP and dyspeptic symptoms benefit from GES. Besides placebo effects which may reach up to 50% in functional dyspepsia alteration of visceral perception as it has been suggested with endoscopic reflux therapy [23-25] may be an explanation. Further studies to elucidate this problem are necessary [26].

## Conclusion

Regulation of gastric functions is complex. Gastric emptying and dyspeptic symptoms show poor correlation. Treatment by Gastric Electrical Stimulation (GES) or Gastric Peroral Endoscopic Pyloromyotomy (G-POEM) are beneficial only in subgroups of patients with gastroparesis. GES has only minor effect of gastric emptying. Besides placebo effects, alteration of visceral perception may be a potential mechanism.

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