



## Review Article

## Gastroparesis and functional dyspepsia: A diagnostic dilemma

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## ABSTRACT

Functional dyspepsia and gastroparesis are very frequently found gastric sensorimotor pathology encountered in gastrointestinal practice has adverse impact on quality of life of patients. As the etiopathophysiology of these two condition is not clearly understood, the diagnosis becomes quite challenging. Typical presentation of these condition consist of epigastric distress, burning or discomfort, along with complaints of early satiety, postprandial fullness, bloating, nausea and vomiting. The clinician face diagnostic dilemma which can be overcome by eliciting a through medical history and clinical examination along with the use diagnostic tools such a gastric endoscopy and a 4-hour solid phase gastric emptying scan. This review presents the dilemmas encountered by clinician in diagnosing FD or GP in a patients and diagnostic workout required to resolve the same.

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## 1. Introduction

Gastroparesis (GP) and functional dyspepsia (FD) are both stomach-related neuromuscular disorders that involve both motor and sensory dysfunctions. Functional FD is estimated to affect approximately 10% of the population, while GP has a prevalence of about 1.5-3%.<sup>1</sup> These conditions often lead to persistent abdominal symptoms in patients, resulting in a significant healthcare burden. Recent times have seen notable advancements in our comprehension of enteric neuromuscular dysfunctions and gastric sensorimotor dysfunctions linked to GP and FD. However, our understanding of the precise underlying causes and the connection between enteric neuromuscular dysfunctions, physiological changes, and symptoms remains limited.<sup>2</sup>

While GP and FD are typically categorized as two separate disorders, their differentiation is not always

straightforward. There is a substantial overlap in symptoms, and it's not uncommon to encounter cases where delayed gastric emptying and functional dyspepsia coexist. Functional gastrointestinal disorders (FGIDs) encompass a range of perplexing gastrointestinal (GI) symptom patterns that affect various parts of the GI tract. FD and GP are two significant conditions frequently found within this spectrum.<sup>3</sup>

Gastroparesis is a syndrome characterized by the delayed emptying of the stomach contents, and it typically occurs when there is no mechanical obstruction present.<sup>4</sup> The primary symptoms associated with GP include a feeling of fullness after eating, nausea, vomiting, and abdominal bloating. The causes of gastroparesis are diverse, with the main reasons are diabetes, idiopathic (of unknown cause), and post-gastric surgical disorders.

Functional dyspepsia is a clinical syndrome associated with long term symptoms originating from the gastroduodenal region.<sup>5</sup> As per the Rome criteria, established through expert consensus, the typical symptoms include

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recurring and troublesome sensations of post-meal fullness, an inability to complete a regular-sized meal (early satiety), as well as epigastric pain or a burning sensation in the context of a normal upper endoscopy.<sup>6</sup>

However, large number of patients with FD also struggle with other troublesome symptoms, such as vomiting sensation, abdominal gases, belching, and epigastric burning. In clinical practice, FD manifests as two distinct clinical syndromes, often with an overlap between them. One of these is Postprandial Distress Syndrome (PDS), which is consistently linked to meals and involves bothersome and frequent early satiety or post-meal fullness. These meal-related symptoms are more prevalent than heartburn and are reported by over 40% of the U.S. general population.<sup>7</sup> A frequent syndrome is epigastric pain syndrome (EPS), where patients present with recurrent and bothersome epigastric pain or less commonly epigastric burning.<sup>5</sup>

There is a pressing requirement for innovative approaches to aid in the diagnostic workout and management of these conditions. This course will provide an overview of the advancements made in comprehending the prevalence epidemiology, pathophysiology, diagnostic methods, and treatment options for GP and FD.

### 1.1. Clinical presentation

Researchers have raised the question of whether individual symptoms can reliably indicate the underlying pathophysiological mechanisms. Conversely, the results of pathophysiological assessments do not always correspond to the symptoms experienced in cases of FD and GP. Both conditions share certain symptoms, such as epigastric fullness, nausea, vomiting, and delayed gastric emptying.<sup>8</sup>

Individuals with GP often report symptoms such as epigastric pain, postprandial fullness, nausea, and vomiting. Numerous reports have highlighted the limited correlation between gastric emptying and these symptoms. Nevertheless, there are only a few interventions that target a specific mechanism. The positive response of both pathophysiological factors and symptoms to these therapeutic interventions convincingly underscores their interconnectedness.<sup>9</sup>

Patients with FD who exhibit abnormal fundic accommodation typically report symptoms like early satiety, epigastric pain or discomfort, postprandial bloating and nausea. In cases of FD, the dominant sensation of early satiety has been found to be closely linked to impaired accommodation. Notably, this sensation is reported by 25% of patients with delayed gastric emptying as well.<sup>10</sup> Furthermore, nausea and vomiting, which are hallmark symptoms of GP, occur in at least 20–50% of FD patients.<sup>11</sup>

### 1.2. Investigational workup

While various methods are available for the objective measurement of gastric emptying, the 4-hour solid-phase scintigraphic emptying scan is the most commonly performed. Typically, if there is greater than 10% gastric retention at the 4-hour mark, it is considered indicative of delayed gastric emptying of solid foods.<sup>12</sup> However, symptoms alone are often insufficient to distinguish between different categories of gastroparesis (GP) or the status of gastric emptying. When delayed gastric emptying is confirmed, the cause of the symptoms should be assessed by examining clinical features and potentially conducting additional tests. One perplexing issue that remains unresolved is the differentiation between GP and functional dyspepsia (FD). The challenge stems from the fact that slow gastric emptying can be observed in 25% of FD patients, but there is no distinct symptom complex associated with it. If GP is more strictly defined as involving a greater delay in gastric emptying (possibly exceeding 60% of a meal retained in the stomach after 4 hours), then symptoms like vomiting and weight loss could be more reliably associated with it. While this revised definition may lead to a decline in the reported incidence of GP,<sup>13</sup> it could facilitate a more definitive diagnosis of the condition.

Diagnosing functional dyspepsia (FD) still primarily relies on the exclusion of other conditions, requiring Esophagogastroduodenoscopy (EGD) to rule out peptic ulceration, esophagitis, and malignancy. The Rome III criteria, which aim to differentiate FD from structural diseases like peptic ulceration, do not offer significant improvement over earlier Rome definitions. These criteria have a diagnostic sensitivity of 61% and a specificity of 69%, both of which are less than ideal.<sup>14</sup> However, it's important to note that in patients presenting with typical dyspeptic symptoms (such as fullness, satiety, or epigastric pain) and no alarm features, the pre-test probability of FD is relatively high, approximately 0.7. Therefore, in clinical practice, provisional diagnoses can be considered for selected cases.

Possibly, the symptom that serves as the most robust indicator of functional dyspepsia (FD) is early satiety. This symptom, being highly distinctive, is now associated with a specific duodenal pathology. It's worth noting that many FD patients exhibit overlapping symptoms of Postprandial Distress Syndrome (PDS) and Epigastric Pain Syndrome (EPS), although in population-based studies, PDS and EPS tend to manifest more distinctly.<sup>15</sup> Additionally, there are several pathophysiological factors that are shared between gastroparesis (GP) and FD (see Table 1).

There is a considerable overlap between GP and FD when it comes to sensory dysfunction. However, in clinical practice, tests for assessing sensory abnormalities are limited. Presently, the available functional test methods primarily focus on evaluating motor function. It's important

**Table 1:** Pathophysiological characteristics of Gastroparesis and unctional dyspepsia

Pathophysiological findings	Gastroparesis	Functional dyspepsia	
		Epigastric pain syndrome	Postprandial distress syndrome
Visceral hypersensitivity	Undetermined	Yes	Undetermined
Delayed gastric emptying	Yes		Yes
Rapid gastric emptying		Yes	
Gastric dysrhythmias	Yes		Yes
Fundic accommodation	Yes		
Weak antral pump			
Antroduodenal discoordination	Yes		
Duodenal neuromuscular dysfunction	Yes		
Duodenal eosinophilia		Yes	
Abnormal duodenal feedback	Yes		
Sensitivity to acid, bile, and fats		Yes	

**Table 2:** Comparison of investigation procedures applied to evaluate gastric emptying

	Scintigraphy	Breath test	Capsule
Mechanisms of gastric emptying	Antral motor activity	Antral motor activity	Antral motor activity and migrating motor complex activity
Validation Studies	Extensive	Modest	Modest
Radiation exposure	+	-	-
Reproducibility (CV%)	Inter – 24%intra – 12%	Inter - 24%intra - 12%	Not evaluated
Limitations for testing	None	Malabsorption, liver failure, pancreatic/pulmonary disease	Obstruction
Evaluation of antral contractility	Feasible	-	+
Evaluation of small bowel and colonic transit	+	-	+

**Table 3:** Advantages and disadvantages of imaging techniques for assessment of gastric volumes

Technique	Advantages	Disadvantages
Single-Photon Emission Computed Tomography	Highly validated Can be used with scintigraphy to assess gastric emptying	Radiation exposure Limited temporal and spatial resolution
Ultrasound	No radiation Can also assess antral contractility and pyloric flow	Presence of air may limit visualization, especially in the fundus Highly operator-dependent
Magnetic Resonance Imaging	No radiation Validated Can also assess gastric air and fluid volumes, contractility, secretion, and emptying	Expense and limited availability

to note that abnormal gastric emptying time can be linked to broader dysmotility issues, akin to what is observed in the small bowel and colon. Additionally, there is a lack of validated algorithms for the diagnosis of GP and FD.<sup>16</sup>

Distinguishing between FD and GP through a differential diagnosis is crucial for gaining a better understanding of the specific symptoms and their underlying causes. This involves considering factors such as gastric emptying and alterations in peripheral and central sensory responses to gastric stimuli. A definitive diagnosis of GP is important as it helps rule out other potential causes, including peptic ulcer disease, gastric outlet obstruction, neoplasms, and small bowel obstruction. To achieve this, various diagnostic methods are employed.

The differential diagnosis process comprises two main steps. First, mechanical obstruction is excluded through imaging techniques, with upper gastrointestinal endoscopy, computed tomographic scans, or magnetic resonance enterography being preferred methods. Second, motility abnormalities are assessed using a range of tests, including gastric emptying tests and manometry.<sup>9</sup>

The evaluation of symptoms like nausea, vomiting, and dyspepsia often involves assessing the delay in gastric emptying. However, the interpretation of these findings can be limited due to the imperfect correlation between symptoms and the actual rates of stomach emptying. Furthermore, there is a relative lack of effective treatments for abnormal gastric emptying. Given that the stomach's

primary function is the emptying of triturated contents, changes in its emptying rate can serve as a marker for underlying neuromuscular issues.<sup>17</sup>

Several methods are available for assessing gastric emptying. Scintigraphy, an imaging technique, is widely accessible. More recent non-invasive options include the wireless motility capsule and gastric emptying breath testing, which offer standardization across different centers and can be performed within a gastroenterology practice. Supplementary imaging techniques, such as ultrasound, single-photon emission computed tomography (SPECT), and magnetic resonance imaging (MRI), are primarily used as research tools to evaluate factors like gastric volumes, contractility, the distribution of meals in the stomach, and the emptying process. A comparison of various tools for assessing gastric emptying is provided in Table 2.<sup>18</sup>

## 2. Gastric Emptying Scintigraphy

Scintigraphy is commonly used to gauge the emptying rate of solid meals from the stomach, but its sensitivity is lower when it comes to assessing liquid meals. However, it is considered a standard method for evaluating gastric emptying in clinical practice. Nonetheless, it is relatively expensive and involves radiation exposure. Consequently, it is typically reserved for assessing conditions such as dumping syndrome and post-surgical disorders.<sup>3</sup>

For solid-phase testing, many medical centers utilize a test meal consisting of a 99mTc sulfur colloid-labeled egg sandwich, which is recommended by a consensus statement from the ANMS (American Neurogastroenterology and Motility Society) and the Society of Nuclear Medicine.<sup>19</sup> Extending the duration of scintigraphy to 4 hours enhances its accuracy in detecting delayed gastric emptying. Unfortunately, many centers in the United States limit the postprandial scintigraphy to just 90 to 120 minutes, significantly reducing its clinical usefulness.<sup>3</sup>

Regional gastric emptying can evaluate intragastric meal distribution and transit from the proximal to distal portions gastric pouch. The findings may supply more knowledge regarding fundal and antral function. The symptoms of nausea, early satiety, and abdominal distension are related to proximal gastric retention; whereas vomiting is associated with delayed distal gastric retention.<sup>3,19</sup>

Assessing regional gastric emptying enables the evaluation of intragastric meal distribution and transit from the proximal to distal regions of the stomach. These findings can offer valuable insights into the functioning of both the fundus and antrum. Symptoms like nausea, early satiety, and abdominal distension are associated with proximal gastric retention, while delayed distal gastric retention is linked to vomiting.<sup>3,19</sup>

The use of gastric mucosal labeling with intravenous technetium-99m, followed by SPECT (Single-Photon Emission Computed Tomography) imaging, enables the

assessment of gastric volumes. Gastric volumes, particularly impaired accommodation, play a significant role in symptom development in both FD and gastroparesis. Scintigraphy and SPECT imaging enable the simultaneous measurement of gastric volumes and emptying.<sup>20</sup> Tables 4 highlights strengths, limitations, and role of these methods for further research.<sup>3</sup>

## 3. Wireless Capsule Motility for Assessment of Gastric Emptying

The wireless capsule motility method employs an indigestible capsule equipped with miniaturized wireless sensor technology capable of measuring pH, pressure, and temperature. As this capsule traverses the digestive tract, it detects the transition from the acidic pH of the stomach to the alkaline pH of the duodenum, thereby identifying gastric emptying. Its pH profile can also be utilized to assess transit times in the small bowel and colon. Additionally, pressure measurements provide insights into the motor functions of the stomach, small intestine, and colon. The SmartPill™ GI Monitoring System, which utilizes this technology, has received approval from the U.S. Food and Drug Administration (FDA) for evaluating gastric pH, gastric emptying, and total gastrointestinal transit time.<sup>3</sup>

The wireless capsule's readings exhibit a stronger correlation with the T-90% measurement for gastric emptying as compared to the T-50% measurement.<sup>21</sup> It tends to empty in sync with the phase III migrating motor complex, which signifies the completion of the postprandial phase and the transition back to the fasting state. When employing a 5-hour cutoff for assessing gastric emptying, this capsule can effectively differentiate between normal and delayed gastric emptying, achieving a sensitivity of 87% and a specificity of 92%.<sup>3</sup>

In the context of the small bowel fed response observed using the Wireless Motility Capsule (WMC) in both healthy individuals and patients with chronic constipation, it appears to be blunted in the presence of gastroparesis (GP). Abnormal contractions may indicate the presence of severe myopathy. A study that compared WMC and scintigraphy in a group of GP patients (n=61) demonstrated a reasonable correlation of 73% at the 4-hour mark.<sup>3</sup> Therefore, all three of these tests provide reasonably effective methods for estimating the presence of GP (see Table 2).

## 4. Gastric Emptying Breath Test (GEBT)

This test is employed to detect delayed gastric emptying by analyzing the values of breath samples. It utilizes a stable (non-radioactive) isotope called <sup>13</sup>C, typically in the form of octanoic acid, a saturated eight-carbon fatty acid, or derived from *Spirulina platensis*, a blue-green algae. Substrates containing <sup>13</sup>C are emptied from the stomach, absorbed in the small intestine, metabolized in the liver, and

become part of the body's bicarbonate pool. The exhalation of  $^{13}\text{CO}_2$  in the breath is then measured using mass spectrometry. The rate-limiting step in this entire process is the time it takes for the stomach to empty.<sup>22</sup>

Several research studies have concurrently measured gastric emptying using both scintigraphy and the breath test. The most well-validated meal for the Gastric Emptying Breath Test (GEBT) consists of a shelf-stable blend containing 238 kcal. This blend is made up of freeze-dried egg mix, saltine crackers, water, and 100 mg of  $^{13}\text{C}$  *Spirulina platensis*. When assessed against scintigraphy, which is considered the gold standard, this test meal exhibits a sensitivity of 89% and specificity of 80% at 150 and 180 minutes. Moreover, it achieves a sensitivity of 93% and specificity of 80% at 45 and 180 minutes.<sup>23</sup>

#### 4.1. Ultrasonography: 2D and 3D

Transabdominal ultrasonography offers a relatively straightforward, non-invasive, and cost-effective approach for evaluating gastrointestinal (GI) motor function. This technique can be applied to both structural and functional assessments of the stomach. It proves valuable in examining various aspects such as gastric distension and accommodation, antral contractility, mechanical deformation (strain), transpyloric flow, and gastric emptying. One of its unique advantages is its ability to simultaneously measure antral contractility, pyloric opening, pyloric flow, and potentially gastric emptying. However, the use of this technique in studying gastric motility is limited to a select few centers due to the significant technical expertise required for its application.<sup>24</sup>

Two-dimensional ultrasound (2D-US) offers an indirect means of assessing gastric emptying by quantifying changes in the antral area over time.<sup>24</sup> To obtain this measurement, a probe is placed on the abdomen to capture a parasagittal image of the antrum in the vicinity of the aorta and superior mesenteric vein. Studies employing 2D-US have investigated findings in both healthy individuals and those with various medical conditions, with validation against scintigraphy. These conditions include functional dyspepsia and diabetes. In functional dyspepsia, it is common to observe increased antral area (both in fasting and postprandial states), overall delayed gastric emptying, occasional faster 'early' emptying, and impaired proximal stomach accommodation. In diabetes, elevated antral area is frequently observed in both fasting and postprandial states, proximal stomach area is reduced, and gastric emptying is delayed in approximately 50% of patients.<sup>3</sup>

Two-dimensional ultrasonography (2D-US) offers a straightforward and practical method for clinically assessing gastric emptying. However, it has certain limitations when used for measuring gastric emptying, including its reliance on liquid meals and assumptions about stomach geometry based on a single parasagittal antral image. Additionally,

like other ultrasound techniques, it cannot image through air.<sup>3</sup>

In contrast, three-dimensional ultrasonography (3D-US) provides the capability to evaluate intragastric meal distribution, which is often irregular in cases of FD and GP. Studies employing 3D-US have confirmed increased antral volumes in both fasting and postprandial states among individuals with FD. Gastric accommodation, a key parameter, can be assessed by examining changes in the ratio of total to proximal gastric volume, and it is typically reduced in FD patients compared to healthy individuals. Furthermore, the assessment of proximal gastric volumes using 3D-US correlates closely with the results obtained from gastric barostat measurements. While 3D-US provides a wealth of information about gastric pathophysiology, it is a time-consuming technique that demands the expertise of a skilled operator and relatively expensive equipment.<sup>3</sup>

#### 5. MRI Assessment of GI Function

Magnetic resonance imaging for assessing GI function was previously limited to a small group of researchers. However, it is now advancing rapidly and has the potential to become a clinically relevant tool. In the past, it faced challenges due to abdominal motion and lengthy image acquisition times. However, with the development and refinement of ultra-fast echo-planar MRI techniques, body images can now be obtained in a fraction of a second, effectively overcoming issues related to motion artifacts and moving organs. Consequently, MRI now enables the real-time assessment of various aspects of GI function through dynamic imaging.<sup>3</sup>

MRI offers a comprehensive view of anatomy and provides complementary information about the tissues and composition of gut contents. It allows for the assessment of multiple parameters in individuals, including the delineation of gastric contents and the measurement of gastric volumes and emptying. In fact, MRI-based measurements of gastric emptying have been validated against other techniques, such as the simultaneous double marker indicator method and gamma scintigraphy, particularly for liquid and mixed solid/liquid meals. Furthermore, MRI proves effective in measuring gastric volumes with acceptable performance characteristics and good reproducibility.<sup>3,25</sup>

Recently, the application of MRI for studying GI function has gained traction in cases of GP and FD. It proves especially valuable in diabetic gastroparesis when investigating the effects of pharmacological interventions. In a specific study, 10 GP patients were administered a 400 ml high-caloric pudding. The study group exhibited reduced antral wave propagation speed and motility index (which is calculated as the product of velocity and depth of contraction) when compared to healthy volunteers.<sup>26</sup> Another study, involving 8 individuals with functional dyspepsia and 8 healthy controls, focused on assessing intersubject and intrasubject variability. This study found

excellent reproducibility between days in both groups in terms of meal volumes and gastric emptying times.<sup>3,27</sup>

MRI and ultrasound measurements of gastric volumes are considered more accurate and realistic compared to measurements obtained using a barostat because they do not artificially distend the stomach. MRI, in particular, offers superior temporal and spatial resolution and has been validated for these purposes, although it is not as commonly used as single-photon emission computed tomography (SPECT).<sup>25</sup>

Moreover, MRI possesses a unique capability to differentiate between gastric air and fluid, enabling the concurrent assessment of gastric emptying and secretion. With rapid MRI imaging sequences, gastric contractility can be effectively assessed. Additionally, MRI can visualize intestinal fluid content and caliber.

Functional gastrointestinal MRI offers several advantages, including rapid imaging, high image resolution, excellent contrast, three-dimensional coverage of the abdomen, and the ability to provide localized information on metabolites through spectroscopy. Additionally, MRI can measure various other parameters of pathophysiological significance, such as the distribution of food within the stomach, intragastric flow dynamics, and dilution of gastric contents due to secretion, gallbladder function, and blood flow to the gastrointestinal tract. MRI is patient-friendly, non-invasive, and safe, enabling the conduct of serial and dynamic studies. Moreover, it can acquire multiple parameters within a single session, making it a versatile tool for assessing gastrointestinal function.<sup>3</sup>

Patients scoring their symptoms during MRI scans enables a direct comparison with the measured MRI parameters. Nonetheless, MRI does come with certain limitations. It may not be suitable for individuals with metal implants or a large body frame. The studies are typically conducted with patients in the supine position, and there is often a lack of standardization across different protocols. Data processing can be complex and time-consuming, and MRI scan time can be relatively expensive.<sup>3</sup>

### 5.1. Meal testing

Meal-induced symptoms have gained recognition as a significant aspect of functional dyspepsia (FD). In a seminal study, patients with FD were administered a solid test meal. The study group included individuals who reported experiencing meal-induced symptoms like fullness or bloating, as well as those who did not perceive any connection between meals and their symptoms. Interestingly, the majority of subjects, despite their prior recollections, developed symptoms following the test meal. These symptoms were meticulously recorded every 15 minutes for a total of 240 minutes and were notably more pronounced when compared to healthy controls.<sup>28</sup>

What's intriguing is that individuals who self-reported having meal-induced symptoms typically experienced symptoms shortly after meal ingestion, often within the first 15 minutes, with a predominant presentation of fullness and bloating. On the other hand, those who self-reported no meal-related symptoms generally exhibited a delayed onset of postprandial symptoms, primarily characterized by pain or burning sensations.<sup>28</sup>

In functional dyspepsia (FD), there exists an objective test known as the nutrient test meal, which assesses meal-related symptoms. The standard procedure for this test begins with an 8-hour fast. Patients are then provided with a standardized enteral feeding solution, often Ensure, in 200 mL increments, with each 200 mL administered every 5 minutes until a cumulative volume of 800 mL is reached. Following each 200 mL portion, five key symptoms—fullness, abdominal pain, retrosternal/abdominal burning, nausea, and regurgitation—are assessed. These symptoms are evaluated using a standardized instrument with visual analogue scales ranging from 0 to 100. A cumulative symptom score is calculated across all five symptoms.<sup>29</sup> The findings from this test have been shown to correlate with gastric motor and sensory dysfunction and serve as an indirect measure of gastric accommodation. However, it's worth noting that parameter values tend to decrease with age.<sup>29</sup>

Despite its potential, the diagnostic utility of the nutrient test meal has not been thoroughly investigated in clinical settings, and it remains primarily an investigational tool. Notably, irregular meal ingestion and rapid eating behaviours are identified as risk factors for FD, as gastroduodenal dysfunction may restrict normal eating patterns and even lead to unintended weight loss.<sup>30</sup>

## 6. Gastroparesis Cardinal Symptom Index (GCSI)

The Gastrointestinal Symptom Rating Scale (GSRS) questionnaire is employed to assess the symptoms of GP. This questionnaire comprises three subscales, which are post-prandial fullness/early satiety (consisting of 4 items), nausea/vomiting (comprising 3 items), and bloating (including 2 items).<sup>(32)</sup> However, due to the overlapping symptoms between functional dyspepsia (FD) and GP, the GSRS questionnaire may not effectively differentiate between FD and GP patients. As a result, there is a recognized need for a more specific questionnaire that can aid in the diagnosis and differentiation of GP from FD.<sup>31</sup>

### 6.1. Differentiating FD from gastroparesis

Distinguishing between GP and FD remains a perplexing challenge that has yet to be definitively resolved. A fundamental issue lies in the fact that approximately 25% of individuals with FD exhibit slow gastric emptying, but without a clear-cut symptom complex.<sup>(34)</sup> The definition

of GP provided by the U.S. Gastroparesis Consortium is widely used. It characterizes gastroparesis as a condition associated with upper GI symptoms. However, the concept of slow gastric emptying is somewhat unhelpful in this broader patient cohort, as there is often only a modest to poor correlation between slow emptying and the presence of symptoms. Furthermore, slow gastric emptying may not consistently appear on repeat testing, and even when gastric emptying is accelerated using prokinetics, it may not accurately parallel the response of symptoms.<sup>32</sup>

Defining gastroparesis based on very slow gastric emptying (3 or more standard deviations from the normal) can effectively differentiate it from functional dyspepsia. In this case, symptoms like vomiting and weight loss would be clearly related to gastroparesis.<sup>33,34</sup>

Furthermore, it's important to note that symptoms of GERD can overlap with functional dyspepsia, as defined by the Rome III criteria, more frequently than expected by chance. In some cases of this overlap, individuals may indeed have pathological acid reflux. The escalation in gastric disaccommodation is associated with transient lower esophageal relaxations.<sup>34</sup> Considering that a subset of individuals with functional dyspepsia (up to 40%) also experience a failure of gastric accommodation, this may explain the overlap between functional dyspepsia and GERD. Therefore, a strict exclusion of all heartburn symptoms from the definition of functional dyspepsia can introduce significant selection bias.<sup>34</sup>

In clinical practice, other symptoms may accompany dyspepsia. If these are predominant, they can point to alternative diagnoses. In particular, frequent vomiting is a very unusual symptom in the dyspepsia symptom complex. In addition to considering GP and other rarer causes such as brain stem disease, drugs including cannabis (that can induce cyclic vomiting and sometimes compulsive bathing behaviour) need consideration. Persistent abdominal pain is not found in FD. Therefore presence of pain is suggestive of other possibilities such as functional abdominal pain syndrome or narcotic bowel syndrome.

It is essential to consider the presence of additional symptoms accompanying dyspepsia, as they can potentially indicate alternative diagnoses. Notably, frequent vomiting is an uncommon symptom within the dyspepsia symptom complex. When it is predominant, healthcare providers should explore other potential causes, including GP and less common conditions like brainstem diseases. Additionally, certain medications, including cannabis, which can induce cyclic vomiting and sometimes compulsive bathing behavior, should be taken into account. Persistent abdominal pain is typically not a characteristic feature of functional dyspepsia. Therefore, when pain is present, it should raise suspicion of other possibilities, such as functional abdominal pain syndrome or narcotic bowel syndrome.<sup>35</sup>

## 7. Conclusion

Despite the availability of various diagnostic tools, differentiating between FD and GP remains a challenging task. While both GP and FD are considered gastric neuromuscular disorders, relying solely on gastric emptying tests is often insufficient for accurately diagnosing these conditions. The rate of delay in gastric emptying does not consistently correlate with the severity of symptoms. Although delayed gastric emptying, when measured optimally, does show some correlation with GP symptoms, it is not a definitive diagnostic marker. Enteric dysmotility is a significant risk factor for the development of GP, and abnormalities in the duodenal barrier may play a role in the pathogenesis of FD. Functional brain MRI studies have revealed abnormalities in patients with both FD and GP, suggesting that alterations in central processing may be implicated in the symptoms of both conditions. Consequently, more research is needed to determine whether differentiating between FD and GP has practical implications for patient management and outcomes.

## 8. Source of Funding

None.

## 9. Conflict of Interest

None.

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