

## Functional Dyspepsia

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Dyspepsia is a common clinical condition associated with a complex of upper abdominal symptoms including: upper centered discomfort or pain, feeling of abdominal fullness, early satiety, abdominal distention and bloating, belching, and nausea. The exact prevalence of dyspepsia in the general population is not known, but it is estimated that as many as 25% to 40% of adults experience symptoms of dyspepsia in a given year. Patients with chronic or recurrent upper gastrointestinal (dyspeptic) symptoms usually undergo an array of investigative tests in an attempt to identify structural or biochemical abnormalities that can explain their symptoms. However, it is not unusual for a complete investigation to fail to reveal significant organic findings and the patient is then considered to have "Functional Dyspepsia" (FD).

### Definition and Classification

Prior to an investigational workup, patients with upper abdominal symptoms (i.e., dyspeptic symptoms) are considered to have "dyspepsia" or more accurately named "uninvestigated dyspepsia". It is important to recognize that dyspepsia/uninvestigated dyspepsia relates to a symptom complex rather than a true diagnosis or single medical disease/condition. In fact, dyspepsia may be indicative of a variety of possible conditions that may be the cause of the patient's dyspeptic symptoms. The differential diagnosis of dyspepsia includes: acid-related disorders such as gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD); gastric inflammatory conditions such as helicobacter pylori gastritis or nonsteroidal anti-inflammatory drug (NSAID) related erosions or gastropathy; and less common but still possible upper abdominal cancer (e.g., gastric, esophageal, pancreatic tumors).

When these conditions are excluded through appropriate investigations, the patient is given a diagnosis of "functional dyspepsia" (FD). Typically, this means the patient had a negative medical workup that included, at a minimum, an esophagogastroduodenoscopy (EGD), 24-hour esophageal pH monitoring, and H. Pylori assessment. This way, possible structural or acid-related causes for the patient's symptoms have been sufficiently ruled out. In the absence of specific structural (morphological) findings, FD is defined and diagnosed based on the clinical presentation. Symptom-based diagnostic criteria for FD were recently developed by a multinational working team known as the "Rome criteria". Over the years, there have been several attempts to sub-classify functional dyspepsia based on symptom predominance, such as GERD-like, ulcer-like, dysmotility-like, and a separate category of unspecified dyspepsia. However, the Rome II criteria for FD do not include the symptoms of heartburn, because the Rome II committees concluded that heartburn (GERD-like) predominant symptoms should be classified as part of GERD and not as dyspepsia.

This is due to increasing recognition that patients with heartburn-predominant symptoms behave more like patients with GERD (including a better response to acid suppression therapy) than patients with other sub-types of dyspepsia. The suggested sub-classification of dyspepsia is currently principally used for research purposes and seems to have less clinical utility/applicability. This is because: (a) a considerable number of patients do not fit into one of the sub-groups, (b) there is significant overlap between the symptom sub-groups, and (c) it does not seem to be helpful in understanding the underlying pathophysiologic mechanism/s or in directing the patient's treatment.

### **What causes Functional Dyspepsia?**

As previously mentioned, the diagnosis of FD implies that a complete diagnostic evaluation (including upper endoscopy) has been performed and that obvious structural gastrointestinal disease has been excluded. Beyond this "ruling out all other possible explanations", the pathophysiology of FD is not well established. However, a variety of pathophysiologic mechanisms have been proposed to explain functional dyspeptic symptoms.

#### ***Motility abnormalities***

Several specific motility abnormalities have been described in sub-groups of patients with FD. These abnormalities include: (a) a decrease in distal stomach motility (antral hypomotility) and delay in gastric emptying; (b) impaired reduction in gastric tone (impaired gastric accommodation) in response to meals which may lead to a decrease in the ability of the stomach to expand and allow the consumption of large meals; and (c) disordered gastric electrical activity as recorded by electrodes placed over the upper abdomen (electrogastrography/EGG). These findings suggest that some patients with FD may have gastric motor or electrical abnormalities. However, these findings of impaired motility and electrical function are found only in a minority of patients and there is only a small correlation between dyspeptic symptoms and detected motor abnormalities. Thus, motility and electrical abnormalities cannot account for the dyspeptic symptoms in the majority of patients.

#### ***Visceral sensory abnormalities***

Several studies have shown that patients with FD are significantly more sensitive to stomach distention (by an intragastric balloon) compared to healthy individuals. Moreover, patients with FD have reduced duodenal motor response and are more sensitive to intraduodenal acid infusion. Interestingly, hypersensitivity to mechanical distention was found to be correlated with symptoms of pain, belching and weight loss, while intraduodenal acid correlated more with nausea. Similar to the reported findings of abnormal gastric motility, the findings of gastric and duodenal sensory abnormalities have been found in only a portion of patients with FD and therefore cannot be considered a universal finding.

Furthermore, the pathophysiological mechanisms that underlie visceral hypersensitivity are not fully understood, particularly with regard to the relative importance and contribution of internal (e.g., stomach and duodenum) gastrointestinal physiological factors, external peripheral (e.g., vagal dysfunctions) factors, and central nervous system (CNS) processing of upcoming sensory GI information.

### *Psychological factors*

No unique psychological or personality profile has been found in patients with FD. However, epidemiological studies have shown that anxiety, neuroticism, somatization, and depression are more common in patients with FD compared to healthy controls. Symptom attentive behavior and alterations in illness behavior and coping styles have also been observed. In addition, several studies have shown a possible link between psychological factors and alterations in gut physiology. Other studies, including some from our group at UNC, have suggested that functional upper GI symptoms may have greater association with psychological factors than with abnormalities in GI physiology. Such examples are functional esophageal symptoms with anxiety and nausea with depression and anxiety.

### **Approach to Treatment**

As with other functional GI disorders, the treatment approach to FD depends on the severity of the disorder. Severity is determined by the intensity and constancy of the symptoms, the degree of psychosocial difficulties, and the frequency of need for health care assistance. Most patients with FD do not require chronic prescribed medications. They usually benefit from appropriate reassurance, education about the condition, and recommendations regarding dietary and life style changes. Patients are generally advised to eat smaller and more frequent meals, and to avoid food with high fat content and food that aggravates their symptoms. However, these recommendations have not been systematically studied and there has been no evidence linking specific food items to dyspeptic symptoms. In patients with mild or intermittent symptoms, short-term medication treatment can be prescribed at times of exacerbated symptoms. However, patients with more severe and persistent symptoms usually require chronic treatment.

The absence of a clear understanding of the mechanism/s that contribute to a patient's symptoms, the variety and unstable presentation of the symptoms, and the common overlap with other upper (GERD) and lower (IBS) functional GI symptoms may often lead to feelings of uncertainty and frustration for both patients and their (health) care providers. Furthermore, the poor correlation between physiological abnormalities and patient symptoms limits the physician's ability to use clinical symptoms as a logical guide for their selection of medical treatment. Moreover, attempts to direct the treatment toward the presumable nature of the underlying physiological disturbances (delayed gastric emptying, lack of gastric accommodation, hypersensitivity, etc.) has not yet proven to be more effective than empiric treatment (a trial-and-error approach).

Psychological interventions have been used and shown to be effective in patients with functional bowel disorders (e.g., IBS). However, data on the use of psychological interventions in patients with FD is still limited. A well-designed randomized controlled study using hypnotherapy in 126 patients with FD has shown greater symptom improvement in the hypnotherapy group as compared to medical treatment and support-only groups. Moreover, the hypnotherapy group also benefited from greater long-term improvement in quality of life and showed reduction in medication use and medical consultation rates.

A recent review assessing the effectiveness of different psychological interventions in patients with FD has identified only four trials and has led to the conclusion that there is currently insufficient evidence to confirm the efficacy of psychological interventions in FD. However, it seems reasonable to try psychological interventions in patients with severe symptoms and patients with significant associated psychosocial difficulties that have not responded to pharmacological therapy. Finally, in view of the difficulties in selecting the appropriate medication therapy and the currently limited availability of treatments for FD, it is important to view medication therapy as only one part of a more comprehensive management plan that recognizes and addresses both the physiological and psychosocial contributing factors.

### Suggested Readings

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4. Talley NJ, Stanghellini V, Heading RC, Koch KL, Malagelada JR, Tytgat GN. Functional gastroduodenal disorders. *Gut*. 1999;45:II37-42 Suppl 2.
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