**Differential Diagnosis in Functional Dyspepsia**

Amarender S Puri, Vishal Garg

Dyspepsia refers to symptoms centered in the upper abdominal region, such as pain, heartburn, feeling discomfort after eating, and heavy feeling in the stomach. Dyspepsia affects up to 40 percent of adults each year, and about 10 percent of those affected seek medical care. Most cases in patients who seek care are eventually diagnosed as functional dyspepsia. Functional (non-ulcer) dyspepsia is defined as the presence of postprandial fullness, early satiation, or epigastric pain or burning in the absence of causative structural disease.

### Defining the Problem

Recent guidelines distinguish dyspepsia from heartburn and gastroesophageal reflux symptoms, which often coincide with dyspepsia but are considered separate entities. Previous studies have used a variety of definitions for dyspepsia. Currently Rome III guidelines are in use for definition of functional dyspepsia, which define functional dyspepsia as, presence of at least one of the following: bothersome postprandial fullness, early satiation, epigastric pain, epigastric burning and no evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms (criteria must be fulfilled for the past three months, with symptom onset at least six months before diagnosis).

### Pathophysiology

Dyspepsia is a symptom and not a diagnosis. Dyspepsia is a heterogeneous group of disorder and there are no definitive pathophysiologic mechanisms for functional dyspepsia. Several studies implicate gastric dysmotility in the pathophysiology of functional dyspepsia. Studies have documented altered gastric motility (e.g., gastroparesis, gastric dysrhythmias, abnormal fundus accumulation, pyloric sphincter dysfunction) in up to 80 percent of patients with functional dyspepsia. However, the degree of dysmotility does not correlate with symptoms. The relationship between functional dyspepsia and acid secretion is unclear. One study demonstrated a lower pH level in the duodenum of patients with functional dyspepsia compared with those in the control group, although the pH level did not correlate with symptoms. The role of Helicobacter pylori infection in functional dyspepsia has also been investigated. Large population studies have shown an increased incidence of H. pylori infection in patients with functional dyspepsia.

### Diagnostic Approach to a Patient with Dyspepsia

The differential diagnosis of dyspepsia is shown in Table 2. While important clues to symptom aetiology may be obtained from interview and examination, symptom patterns alone do not discriminate organic from functional dyspepsia. In 50%–60% of cases, no cause is identified and patients are considered to have functional dyspepsia. The prevalence of peptic ulcer disease is 15%–25% and oesophagitis prevalence is 5%–15%. Upper digestive cancer is seen in typically <2%.

Functional dyspepsia is a diagnosis of exclusion; therefore, physicians should focus on excluding serious or specifically treatable diseases, without spending too much time investigating symptoms. Functional dyspepsia is the most prevalent diagnosis, making up 70 percent of dyspepsia cases.

The physician should perform a detailed history and physical examination at the initial presentation, noting any findings that point to a diagnosis other than functional dyspepsia (e.g., right upper-quadrant pain with cholelithiasis, exercise association with coronary artery disease, radiation to the back with pancreatitis). Detailed evaluation of the drug history should be done to ascertain the cause of dyspepsia.

For patients unresponsive to acid suppressive therapy or H pylori eradication, mechanisms of symptom generation are largely speculative. This means therapeutic interventions are also speculative. A variety of potential causes have been proposed (Table 3).

Three aetiologies deserve particular attention: dysmotility, visceral hypersensitivity, and psychiatric disorders. Abnormalities of gastric neuromuscular function can be detected by scintigraphic gastric emptying studies, electrogastrography, or antroduodenal manometry in between 30% and 60% of patients. In addition to impaired motor function, a subset

### Table 1: Rome III diagnostic criteria for Functional Dyspepsia

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<th>Presence of at least one of the following:</th>
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<td>Bothersome postprandial fullness</td>
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<td>Early satiation</td>
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<td>Epigastric pain</td>
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<tr>
<td>Epigastric burning</td>
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<td>and</td>
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<tr>
<td>No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms</td>
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Note: Criteria must be fulfilled for the past three months, with symptom onset at least six months before diagnosis

### Table 2: Differential diagnosis of dyspepsia

- Non-ulcer dyspepsia.
- Gastro-oesophageal reflux disease.
- Peptic ulcer disease.
- Medication related: non-steroidal anti-inflammatory drugs, antibiotics, iron, potassium supplements, digoxin.
- Carbohydrate malabsorption (lactose, fructose, sorbitol).
- Cholelithiasis or choledocholithiasis.
- Chronic pancreatitis.
- Systemic disorders (diabetes, thyroid, parathyroid, hypoadrenalism, connective tissue disease).
- Intestinal parasites.
- Abdominal malignancy (especially pancreatic and gastric cancer).
- Chronic mesenteric ischaemia.
Table 3: Potential causes of non-ulcer dyspepsia

- Duodenogastric reflux.
- Duodenitis.
- Carbohydrate malabsorption (lactose, fructose, sorbitol).
- Cholelithiasis or choleclocholithiasis.
- Chronic pancreatitis.
- Systemic disorders (diabetes, thyroid, parathyroid, hypoadrenalism, connective tissue disease).
- Intestinal parasites.
- Psychiatric disorders.
- Visceral hypersensitivity.
- Gastric/small intestinal dysmotility.
- Gallbladder/iliary dysmotility.

of dyspeptics has impaired postprandial relaxation of the proximal stomach. Some investigators have suggested that certain symptoms are associated with altered gastric physiology. Predictors of delayed gastric emptying include female sex, excessive postprandial fullness, and severe vomiting.24 Impaired postprandial relaxation of the proximal stomach has been associated with early satiety.20,21 The acute administration of the interstitial serotonin receptor (5-HT1) agonists, buspirone and sumatriptan, has been shown to improve accommodation and tolerance to balloon distension of the proximal stomach.21,22 However, most studies have failed to demonstrate a relationship between disturbed gastrointestinal motor function and symptoms.

Much recent attention has focused on the concept that patients with functional dyspepsia have augmented perception of visceral pain or visceral hypersensitivity. Many patients with dyspepsia will report pain at levels of balloon distension in the stomach or proximal intestine that are not perceived as adverse by controls.23-25 Although, tricyclic antidepressants have been shown to have efficacy in treating the hyperalgesia of irritable bowel syndrome and non-cardiac chest pain, there is presently no evidence for their efficacy in the treatment of non-ulcer dyspepsia. As visceral hypersensitivity is common to these disorders, use of tricyclics in functional dyspepsia would seem reasonable even if unstudied.

The coexistence of psychiatric disturbances and dyspeptic symptoms is well documented. Importantly, it appears that dyspeptic consultors do not differ from non-consultors with respect to objective symptoms, but they tend to perceive their symptoms as more severe and have greater associated anxiety.26

In conclusion, functional dyspepsia is a diagnosis of exclusion. Patients with alarm features should undergo prompt endoscopic evaluation to rule out organic causes of dyspepsia.

References