Non-Ulcer Dyspepsia
Piyush Ranjan

Introduction

Dyspepsia is a common term used to characterize abdominal pain centered in the epigastrium, sometimes combined with other gastrointestinal complaints. Historically, the word ‘dyspepsia’ was used for a heterogeneous group of abdominal symptoms. Functional (previously nonulcer) dyspepsia (FD) is the focus of this review, and usually indicates abdominal discomfort or pain with no obvious organic cause that could be identified by endoscopy.

The term ‘dyspepsia’ originates from the Greek ‘dys’ and ‘pepsis’, popularly known as indigestion. It was first recorded in the mid 18th century and since then it has been widely used. In the 18th century dyspepsia was thought to be one of the ‘nervous disorders’ along with hypochondria and hysteria. In addition to the term ‘functional dyspepsia’, several other descriptions of dyspepsia are in use, each of which reflects various amounts of investigation into upper gastrointestinal symptoms of the patient. Uninvestigated dyspepsia refers to patients with either new or possibly recurrent dyspeptic symptoms in whom no investigations have previously been undertaken. After those investigations dyspeptic complaints may be called investigated dyspepsia and should be differentiated into organic dyspepsia and FD. Organic dyspepsia means that there is a clear anatomic or pathophysiologic reason for the dyspeptic complaints, such as an ulcer disease or mass. In contrast, when a diagnosis of FD has been made, it means that a number of investigations were performed including upper gastrointestinal endoscopy, and were found to be normal.

Definition

The recommended definition for functional dyspepsia was a symptom or a set of symptoms that are considered by most physicians to originate from gastroduodenal region.

Rome criteria were developed by a committee of experts and modified subsequently. They include Rome I, Rome II and Rome III. Rome I and Rome II did not include meal related symptoms and this was the fundamental change in Rome III.

Rome I

In 1991, the Rome I committee considered dyspepsia to represent persistent or recurrent abdominal pain or abdominal discomfort centered in the upper abdomen.

The discomfort could be described as post-prandial fullness, early satiety, nausea, retching, vomiting, or upper abdominal bloating, and could be intermittent or continuous.

Three categories of dyspepsia were identified:

i. Dyspepsia with identified cause that if treated leads to improvement, such as chronic peptic ulcer disease, reflux esophagitis, malignancy, or pancreaticobiliary disease;

ii. Dyspepsia with an identified abnormality of uncertain significance, such as H. pylori gastritis, duodenitis, idiopathic gastroparesis, gastric dysrhythmias, or small bowel dysmotility;

iii. Dyspepsia with no explanation identified.

Of these three categories, the Rome I criteria considered both dyspepsia with an identified abnormality of uncertain significance and dyspepsia with no explanation as functional dyspepsia.

The symptoms of functional dyspepsia were described as chronic or recurrent abdominal pain or discomfort centered in the upper abdomen lasting at least three months. Symptoms had to have been present at least 25% of the time. This classification of functional dyspepsia did not include irritable bowel syndrome (IBS), gastroesophageal reflux disease (GERD), biliary tract disease, or aerophagia.

Functional dyspepsia was further divided in to three subgroups:

i. Ulcer-like functional dyspepsia, wherein there was predominant pain and three or more of the following symptoms were present: pain that was very well localized to a small area, pain relieved by food, or antacids or antisecretory therapy, pain before meals or when hungry, night pain, or periodic pain.

ii. Dysmotility-like functional dyspepsia, wherein the symptoms suggest gastric stasis. Symptoms were described as three or more of the following in the absence of predominant pain: early satiety, post-prandial fullness, nausea, recurrent retching/vomiting, bloating without visible distention, or discomfort often aggravated by food.

iii. Unspecified functional dyspepsia that did not fit into the ulcer like or dysmotility type categories.

Rome II

In 1999, the Rome II made changes to the criteria for functional dyspepsia. Notably, Rome II sought to attribute each functional dyspepsia subtype with a single predominate (most bothersome) complaint rather than with a cluster of complaints as was the case in Rome I. For ulcer-like functional dyspepsia the predominant symptom was epigastric pain. For dysmotility-like functional dyspepsia, the predominant symptom was a non-painless discomfort characterized as abdominal fullness, early satiety, bloating or nausea. Categorizing sub-groups by a predominant symptom sought to better identify the underlying pathophysiologic disturbance and to target treatment.

The time course of functional dyspepsia was revised for all criteria symptoms had to be present for at least 12 weeks over a 12-month period which need not be consecutive, although this definition later proved clumsy and was abandoned by Rome III. It has been difficult to reliably identify distinct groups of patients within functional dyspepsia. There were several drawbacks to the Rome I and II criteria in this regard. Frequently, patients cannot distinguish pain from discomfort. Some patients think of mild pain as discomfort while others don’t make this distinction at all. Not everyone fitted into the sub-groups of the Rome classification. And even those who did fit into the subgroups showed instability in their categorization, even over the short term. There is still no acceptable understanding of the term ‘predominant’ as used in the Rome II criteria. To compound the difficulties, subdividing patient groups according to the predominant symptom failed to identify subgroups with...
Post-Prandial Distress Syndrome

2. Epigastric Pain Syndrome

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other key symptoms (early satiety and fullness) should be meal
suggested pain must be in the more precise epigastric area, while
onset at least 6 months previously (Table 1).

Criteria should be fulfilled for at least 3 months with symptom
onset of symptoms at least six months previously, with one or
both of the following symptoms.

- bothersome postprandial fullness
- early satiety
- epigastric pain
- epigastric burning

and
- no evidence of structural disease (including upper endoscopy)
that is likely to explain the symptoms

Table 2: Rome III criteria for functional gastroduodenal disorders

<table>
<thead>
<tr>
<th>B Functional gastroduodenal disorders</th>
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<tbody>
<tr>
<td>B1 Functional dyspepsia (for application in clinical practice but not otherwise useful)</td>
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<tr>
<td>B1a Postprandial distress syndrome</td>
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<tr>
<td>B1b Epigastric pain syndrome</td>
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<td>B2 Belching disorders</td>
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<td>B2a Aerophagia</td>
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<tr>
<td>B2b Unspecified excessive belching</td>
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<td>B3 Nausea and vomiting disorders</td>
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<td>B3a Chronic idiopathic nausea</td>
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<td>B3b Functional vomiting</td>
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<td>B3c Cyclic vomiting syndrome</td>
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<td>B4 Rumination syndrome in adults</td>
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</tbody>
</table>

homogeneous underlying pathophysiological mechanisms.12

Rome III

In 2006, Rome III radically reformulated the functional
dyspepsia classification. Till now this is the most current
definition of functional dyspepsia.

According to the most recent 2006 Rome III criteria FD
must include one or more of following symptoms: bothersome
postprandial fullness, early satiation, epigastric pain, epigastric
burning with no evidence of structural disease, excluded by
upper endoscopy, which is likely to explain the symptoms.
Criteria should be fulfilled for at least 3 months with symptom
onset at least 6 months previously (Table 1).

In Rome III, dyspepsia was redefined; from a description of
symptoms centered in the upper abdominal area, the Committee
suggested pain must be in the more precise epigastric area, while
other key symptoms (early satiety and fullness) should be meal
related. In Rome III, discomfort was replaced by either post-
prandial fullness or early satiety. The Rome III criteria moved
away from the use of the predominant symptom to classify sub-
types, and recognized that there is no one symptom present in the
vast majority of patients previously labeled as having functional
dyspepsia. Finally, and most notably, the very term functional
dyspepsia was abandoned in favor of a new classification as
described in Table 2.

In Rome III classification functional dyspepsia has been
classified as

1. Post-Prandial Distress Syndrome
2. Epigastric Pain Syndrome

Post-Prandial Distress Syndrome

This is a new concept. Post-prandial distress syndrome (PDS)

Table 3: Rome III diagnostic criteria for epigastric pain syndrome.

At least 3 months, with onset at least 6 months previously, with ALL of the following symptoms:

1. Pain or burning localized to the epigastrium of at least moderate severity, at least once per week.
2. Pain is intermittent.
3. Pain is not generalized or localized to other abdominal or chest regions.
4. Pain is not relieved by defecation or passage of flatus.
5. Pain does not fulfill criteria for gallbladder or sphincter of Oddi disorders.

- Supportive criteria
  1. Upper abdominal bloating or postprandial nausea or excessive belching can be present.
  2. May coexist with epigastric pain syndrome.

Table 4: Rome III diagnostic criteria for postprandial distress syndrome.

At least 3 months, with onset at least 6 months previously, with one or both of the following symptoms.

1. Bothersome postprandial fullness, occurring after ordinary-sized meals, at least several times per week.
2. Early satiation that prevents finishing a regular meal, at least several times per week.

- Supportive criteria
  1. Upper abdominal bloating or postprandial nausea or excessive belching can be present.
  2. May coexist with epigastric pain syndrome.

(Table 3) refers to unexplained regular meal-induced dyspeptic symptoms (namely bothersome post-prandial fullness after an ordinary-sized meal that occurs at least several times per week or early satiation that prevents the finishing of a regular sized meal at least several times per week. By Rome III, one or both of these must have been present for at least the last three months with an onset of symptoms at least six months prior to diagnosis. PDS can also coexist with symptoms of upper abdominal bloating, post-prandial nausea and epigastric pain.

Epigastric Pain Syndrome

Epigastric pain syndrome (EPS) (Table 4) refers to pain or burning localized to the epigastrium of at least moderate severity at least once per week. The pain must be intermittent in nature though not relieved by defecation or passage of flatus. Likewise, the pain characteristics should not fulfill criteria for biliary pain that occurs in functional gallbladder or sphincter of Oddi disorders. Again the pain must have been present for at least the last three months with an onset of symptoms at least six months prior to diagnosis. EPS can include burning, though without a retrosternal component distinguishing it from heartburn. The pain is thought to be commonly precipitated or relieved by meals, but can also occur during fasting. Symptoms of PDS can also occur, although the degree of overlap remains currently undefined. EPS is not a new concept.

Functional Dyspepsia Post Rome III

Under current criteria, the symptoms of dyspepsia are thought to originate in the gastroduodenal region. Dyspepsia is defined by Rome III to comprise the presence of one or more of the following symptoms:
1. **Post prandial fullness**: Bothersome post-prandial fullness that can be described as an unpleasant sensation like prolonged persistence of food in the stomach.

2. **Early satiety**: Early satiation which can be described as a feeling that the stomach is overfilled soon after starting to eat. This feeling is out of proportion to the size of the meal and results in the patient being unable to finish the meal.

3. **Epigastric pain**: Epigastric pain which is pain located between the umbilicus and lower end of sternum in-between the mlddclavicular lines. The pain is a subjective and clearly unpleasant feeling and is difficult otherwise to describe, although it may be akin to a feeling of tissue being damaged.

4. **Epigastric burn**: Epigastric burning is pain located in the epigastrium that has a burning quality but does not radiate to the chest.

**What about Coexistent Heartburn?**

Though past definitions have included heartburn (a retrosternal burning pain) as a cardinal symptom of dyspepsia, and while some authorities still insist this should be the state of the art, heartburn is neither necessary nor sufficient to diagnose gastroesophageal reflux disease (GERD), and commonly co-occurs in patients labeled in clinical practice as having gastroesophageal reflux disease (GERD), and commonly objective findings such as reflux esophagitis. However, dominant heartburn is a poor predictor for identifying reflux symptoms should be provisionally classified as GERD. Though past definitions have included heartburn (a retrosternal burning pain) as a cardinal symptom of dyspepsia, and while some authorities still insist this should be the state of the art, heartburn is neither necessary nor sufficient to diagnose gastroesophageal reflux disease (GERD), and commonly co-occurs in patients labeled in clinical practice as having functional dyspepsia, it still remains unclear whether these are a cause or not of symptoms in this broad patient grouping.

**Conclusions and Future**

There are some obvious limitations to the new Rome III criteria and these need exploring. Recent literature reflects controversy about the nature of functional dyspepsia, and there currently remains a divide between the symptom experience and abnormal pathophysiology which may not be addressed by the new classification. While much work has looked at putative mechanisms including gastric emptying and gastric accommodation in functional dyspepsia, it still remains unclear whether these are a cause or not of symptoms in this broad patient grouping.

**References**


