Dyspepsia

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- Dyspepsia is a common symptom with an extensive differential diagnosis and a heterogeneous pathophysiology.

- It occurs in approximately 25 percent of the population each year, but most affected people do not seek medical care

- Although dyspepsia does not affect survival, it is responsible for substantial health care costs and significantly affects quality of life

- According to the Rome III criteria, dyspepsia is defined as one or more of the following symptoms:
- Postprandial fullness (classified as postprandial distress syndrome)
- Early satiation (inability to finish a normal sized meal, also classified as postprandial distress syndrome)
- Epigastric pain or burning (classified as epigastric pain syndrome)

- Approximately 25 percent of patients with dyspepsia have an underlying organic cause.

- However, up to 75 percent of patients have functional (idiopathic or nonulcer) dyspepsia with no underlying cause on diagnostic evaluation

- Dyspepsia secondary to organic disease
- Although there are several organic causes for dyspepsia,
- the main causes are peptic ulcer disease, gastroesophageal reflux, gastric malignancy, and NSAID-induced dyspepsia

Peptic ulcer disease

- Upper abdominal pain or discomfort is the most prominent symptom in patients with peptic ulcers.
- Although discomfort from ulcers is usually centered in the epigastrium, it may occasionally localize to the right or left upper quadrants.
- While the pain may radiate to the back, back pain as the primary symptom is atypical of peptic ulcer disease.

- While classic symptoms of duodenal ulcer occur when acid is secreted in the absence of a food buffer (ie, two to five hours after meals or on an empty stomach),
- peptic ulcers can be associated with food-provoked symptoms.

- Peptic ulcers can also be associated with postprandial belching, epigastric fullness, early satiation, fatty food intolerance, nausea, and occasional vomiting.

Gastro-esophageal reflux

- **Gastro esophageal reflux — The most common symptoms of gastroesophageal reflux disease (GERD) are retrosternal burning pain and regurgitation.**

- **GERD should be suspected when these symptoms accompany dyspepsia and are the predominant complaints**

Gastro-esophageal malignancy

- Gastroesophageal malignancy is an uncommon cause of chronic dyspepsia in the Western hemisphere but the incidence is higher in patients of Asian extraction.

- The incidence of malignancy also increases with age. When present, abdominal pain tends to be epigastric, vague and mild early in the disease but more severe and constant as the disease progresses.

Biliary pain

- Classic biliary pain is characterized by episodic acute and severe upper abdominal pain, usually in the epigastrium or right upper quadrant. It is not colicky.
- The pain typically lasts for at least one hour and may persist for several hours. The pain may radiate to the back or scapula, and is often associated with restlessness, sweating, or vomiting.
- Episodes are typically separated by weeks to months and patients are completely pain free between attacks

Drug-induced dyspepsia

- Nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 selective inhibitors can cause dyspepsia even in the absence of peptic ulcer disease.

- Several other drugs have been implicated as causes of dyspepsia. However, data to support the role of these medications in drug induced dyspepsia are limited. These medications include calcium channel blockers, methylxanthines, alendronate , orlistat , potassium supplements, acarbose and certain antibiotics, including erythromycin

Other causes

- Celiac disease and chronic pancreatitis may rarely present with dyspepsia alone.

- Other rare causes for dyspepsia include infiltrative diseases of the stomach (eg, eosinophilic gastritis, Crohn's disease, sarcoidosis), diabetic radiculopathy, metabolic disturbances (eg, hypercalcemia, heavy metal), hepatoma, steatohepatitis, and intestinal angina

Functional dyspepsia

- Functional (idiopathic or nonulcer) dyspepsia is defined as the presence of one or more of the following:
- postprandial fullness, early satiation, epigastric pain or burning, and no evidence of structural disease to explain the symptoms. These criteria should be fulfilled for the last three months with symptom onset at least six months before diagnosis.

- A diagnosis of functional dyspepsia can therefore only be established exclusion of other causes of dyspepsia. The pathophysiology and treatment of functional dyspepsia are discussed in detail, separately.

INITIAL EVALUATION

- A history, physical examination, and laboratory evaluation are the first steps in the evaluation of a patient with new onset of dyspepsia.

- One important goal of the initial evaluation is to identify alarm features for gastroesophageal malignancy, which will direct the diagnostic approach.

Alarm features in dyspepsia

Age older than 55 years with new-onset dyspepsia

Family history of upper gastrointestinal cancer

Unintended weight loss

Gastrointestinal bleeding

Progressive dysphagia

Odynophagia

Unexplained iron deficiency anemia

Persistent vomiting

Palpable mass or lymphadenopathy

Jaundice

History

- A detailed history is necessary to narrow the differential diagnosis and to identify GERD and NSAID-induced dyspepsia, as well as patients with alarm features

- A dominant history of heartburn, regurgitation, or cough is suggestive of GERD
- NSAID use raises the possibility of NSAID dyspepsia and peptic ulcer disease.
- Radiation of the pain to the back, a personal or family history of pancreatitis may be indicative of underlying chronic pancreatitis.

- Significant weight loss, anorexia, vomiting, dysphagia, odynophagia, and a family history of gastrointestinal cancers suggest the presence of an underlying malignancy.

- The presence of severe episodic epigastric or right upper quadrant abdominal pain lasting more than an hour or pain that occurs at any time is suggestive of symptomatic cholelithiasis.

Physical examination

- The physical examination in patients with dyspepsia is usually normal, except for epigastric tenderness.

- Abdominal tenderness on palpation should be evaluated with the Carnett sign to determine if it is due to pain arising from the abdominal wall rather than due to inflammation of the underlying viscera.

- The presence of increased local tenderness during muscle tensing (positive Carnett's sign) suggests the presence of abdominal wall pain.

- However, if the pain is decreased (negative Carnett's sign), the origin of pain is not from the abdominal wall and likely from an intra-abdominal organ, as the tensed abdominal wall muscles protect the viscera.

- Other informative findings on physical examination may include: a palpable abdominal mass (eg, hepatoma) or lymphadenopathy (eg, left supraclavicular or periumbilical in gastric cancer), jaundice (eg, secondary to liver metastasis) or pallor secondary to anemia.

- Ascites may indicate the presence of peritoneal carcinomatosis. Patients may have evidence of muscle wasting, loss of subcutaneous fat, and peripheral edema due to weight loss.

Laboratory tests

- Routine blood counts and blood chemistry including liver function tests should be performed to identify patients with alarm features (eg, iron deficiency anemia) and underlying metabolic diseases that can cause dyspepsia (eg, diabetes, hypercalcemia)

DIAGNOSTIC STRATEGIES AND INITIAL MANAGEMENT

- The approach to and extent of diagnostic evaluation of a patient with dyspepsia is based on the presence or absence of alarm features, patient age, and the local prevalence of *Helicobacter pylori* (*H. pylori*) infection

- Patients with GERD and NSAID-induced dyspepsia should be treated with an empiric trial of proton pump inhibitors (PPI) for eight weeks and NSAIDs should be discontinued

- Further evaluation should be pursued if these patients continue to have symptoms after eight weeks of PPI therapy or earlier if they have alarm features

Early upper endoscopy

- Upper endoscopy should be performed for the evaluation of new onset dyspepsia in patients with alarm features or those over age 55 years.

- Upper endoscopy provides a gold standard for establishing a specific cause in patients with upper abdominal pain. Biopsies of the stomach should be obtained to rule out *Helicobacter pylori*

- Patients with *H. pylori* should receive eradication therapy in addition to treatment based on the underlying diagnosis.

Patient without alarm features and age ≤55 years

- The two main strategies in patients ≤55 years without alarm features are to test and treat for *H. pylori* and to provide empiric antisecretory therapy.

- The efficacy of the *H. pylori* test and treat strategy varies based on whether it is employed in primary or secondary care settings and the local prevalence of *H. pylori*

- Patients ≤55 years of age without alarm features should be tested and treated for *H. pylori* if the local prevalence of *H. pylori* is high (>20 percent).

- Empiric treatment with a proton pump inhibitor (PPI) should be recommended in areas with prevalence <5 percent

- In areas with a prevalence of 5 to 20 percent, the strategies of test and treat *H .pylori* or empiric PPI therapy may be equivalent in terms of dyspepsia resolution, patient satisfaction, and cost

Test and treat for Helicobacter pylori

- The rationale for *H. pylori* testing in patients with dyspepsia is based upon the recognition of *H. pylori* as an etiologic factor in peptic ulcer disease.

- Testing for *H. pylori* should be performed with a urea breath test or stool antigen assay. Serologic testing should not be used due to their low positive predictive value

EVALUATION OF PERSISTENT SYMPTOMS

- Despite the approaches described above, some patients continue to have symptoms of dyspepsia. Patients with continued symptoms of dyspepsia fall into the following categories:

- patients with persistent *H. pylori* infection, patients with an alternate diagnosis, and patients with functional dyspepsia.

- According to the Rome III criteria, functional dyspepsia is defined as the presence of one or more of the following:

- postprandial fullness, early satiation, epigastric pain or burning and no evidence of structural disease (including at upper endoscopy) to explain the symptoms

PATHOPHYSIOLOGY

- While several mechanisms have been proposed, the pathogenesis of functional dyspepsia remains unclear :

- Gastric motility and compliance
- Visceral hypersensitivity
- Helicobacter pylori infection
- Altered gut microbiome
- Psychosocial dysfunction

TREATMENT
Initial approach

- Patients with functional dyspepsia should be tested and treated for *H. pylori* if the local prevalence of *H. pylori* is high
- Proton pump inhibitors (PPIs)
- Antisecretory therapy
- H2 receptor antagonists
- Antidepressants

Subsequent approach

- There are few therapeutic options for patients with functional dyspepsia who fail to respond to initial management with *H. pylori* eradication, empiric PPI, and tricyclic antidepressant.
- Prokinetic agents like methochlopramide and dompridon
- Fundic relaxant drugs for example buspirone
- Antinociceptive agents like Pregabalin which can be considered in patients who fail a four-week trial of prokinetic agents and in patients who cannot tolerate prokinetics.
- Psychological therapy