Functional Dyspepsia

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Functional Dyspepsia

- Pathophysiology
- Clinical manifestation and classification
- Treatment “strategy”
- Therapies
There Is Significant Overlap Among GI Disorders

- 29% of GERD patients have Chronic Constipation*
- Diagnoses can shift from one disorder to another over time†
- Possible common pathophysiological mechanisms‡‡

Uninvestigated dyspepsia vs. Investigated dyspepsia

(functional, non-ulcer or endoscopy-negative dyspepsia)
Symptoms of Dyspepsia

- Discomfort in the upper abdomen
- Bloating
- Early satiety
- Abdominal distension
- Nausea
- Indigestion

Normal gastric function:

- **Fasting**
- **Accommodation**
- **Emptying**

**Perception**

Pathophysiological abnormalities in functional dyspepsia:

- H. pylori infection
- Hypersensitivity to gastric distention
- ANS/CNS disorder
- Impaired accommodation
- Unsuppressed phasic contractile activity
- Abnormalities of gastric electrical rhythm
- Delayed emptying
- Duodenal lipid or acid hypersensitivity
- Small intestinal dysmotility

Normal Proximal and Distal Stomach Function
Gastric Distension and Functional Dyspepsia

Food → Vagus (transient LES relaxation) → Vagus (Sensation) → Distension
Proximal Gastric Accommodation to Meals

Tack et al. Gastroenterol 1998;115:1346 (Barostat in normal volunteers)
Impaired Proximal Gastric Accommodation

About 41% of patients have impaired gastric accommodation

Liquid Load Test for FD

Abnormal Proximal and Distal Stomach Function

- Reservoir
- Antral Pump
- Tonic Contraction
- Decrease In Volume
- (Accommodation) Relaxation
  - Increase In Volume
Probable Pathophysiology of Functional Dyspepsia

- Impaired Fundic Accommodation
- Rapid Proximal Gastric Emptying
- Antral Distension
- Dyspeptic Symptoms
Delayed Gastric Emptying in Functional Dyspepsia

**Vomiting-Predominant**
- Vomiting
- Dehydration
- Hospitalizations
- Weight loss

**Regurgitation-Predominant**
- Refractory heartburn
- Effortless regurgitation

**Dyspepsia-Predominant (Functional Dyspepsia)**
- Epigastric pain
- Bloating
- Abdominal distension

N=339 patients presenting to University of Louisville

## Classification of Gastroparesis Based on Predominant-Symptom Presentation

<table>
<thead>
<tr>
<th>Type of Gastroparesis</th>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Vomiting-predominant gastroparesis</td>
<td>Vomiting with retching and nausea are the most bothersome symptoms</td>
</tr>
<tr>
<td>2. Dyspepsia-predominant gastroparesis</td>
<td>Discomfort centered in upper abdomen is the most bothersome symptom; may be characterized by upper abdominal fullness, early satiety, bloating, or nausea</td>
</tr>
<tr>
<td>3. Regurgitation-predominant gastroparesis</td>
<td>Effortless regurgitation of acid or undigested food or heartburn is the most bothersome symptom</td>
</tr>
</tbody>
</table>

Patients with Diabetic Gastroparesis Presents with Vomiting-Predominant Symptoms

* p<0.01 compared to other symptom groups

Delayed Gastric Emptying Does Not Correlate with Clinical Presentation

Delayed Gastric Emptying in Functional Dyspepsia

- Occur in 23 to 32% of patients with functional dyspepsia
- Poor correlation between gastric emptying and functional symptoms
- Delayed gastric emptying is not likely the cause of dyspepsia in most patients
Normal gastric function:

- Fasting
- Perception
- Accommodation
- Emptying

Pathophysiological abnormalities in functional dyspepsia:

- H. pylori infection
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Past Classification of Functional Dyspepsia

- Ulcer-like
- Dysmotility-like
- Reflux-like
- Non-specific

But symptoms overlap and unstable over time
Symptom Clusters in Patients with Functional Dyspepsia

- **Cluster 1**: Bloating (17% (N=1,644))
- **Cluster 2**: Nausea/Vomiting (7% (N=671))
- **Cluster 3**: F/ES (44% (N=4,143))
- **Cluster 4**: H/R (28% (N=2,665))
- **Cluster 5**: Undefined (4% (N=357))

Abbreviations:
- F/ES = Fullness/Early Satiety
- H/R = Heartburn/Regurgitation

Analysis included symptomatic respondents (those reporting the specific symptom ≥ 1 time per month for the past 3 months).

Telephone survey of 21,128 adults
New Classification for Functional Dyspepsia (Rome III)

- **Postprandial Distress Syndrome**
  - Postprandial fullness after ordinary sized meals and/or
  - Early satiety preventing finishing a regular meal
  - Supportive criteria
    - Upper abdominal bloating
    - Postprandial nausea
    - Excessive belching

- **Epigastric Pain Syndrome**
  - Epigastric pain or burning and
  - Pain is intermittent and
  - Not generalized or localized to other abdominal regions and
  - Not relieved by defecation or passage of flatus and
  - Not gallbladder and sphincter of Oddi disorders
Dyspepsia or Epigastric pain

TO SCOPE OR NOT TO SCOPE?
Non-Ulcer ("Functional") Dyspepsia is Very Common

- Functional Dyspepsia: 60%
- Peptic Ulcer: 15% - 25%
- GERD: 5% - 15%
- Malignancy: <2%

Treatment Approach to Uninvestigated Dyspepsia

Alarm Symptoms/Risk Factors

Yes
Endoscopy
Test for treat strategy for *H. pylori*

No
Acid-suppression

Others
- Treat bacterial overgrowth
- Improve accommodation
  - Sildenafil (↑ NO-smooth muscle relaxation)
  - Buspirone (5-HT1A agonist)
  - Sumatriptan (5-HT1P agonist)
- Complimentary alternative medicine
- Psychologic intervention

Prokinetics
Alarm Symptoms in Patients Presenting with Dyspepsia

- New onset at age >55 years
- Unexplained weight loss >10%
- Progressive dysphagia
- Gastrointestinal bleeding
- Iron deficiency anemia
- Persistent vomiting
- Previous esophagogastric cancer
- Previous documented peptic ulcer
- Family history of gastrointestinal cancer
- Lymphadenopathy or abdominal mass on exam

Patients with uninvestigated dyspepsia

Age > 55 or alarm features

- EGD

Age ≤ 55
No alarm features

HP prevalence <10%

- PPI trial
  - Fails
    - Test and treat for H. pylori
      - Fails
        - Consider EGD

HP prevalence ≥ 10%

- Test and treat for H. pylori
  - Fails
    - PPI trial
      - Fails
        - Consider EGD

Talley et al. 2005. Practice guideline for dyspepsia, ACG
Test-and-Treat for H. pylori Strategy
For Uninvestigated Dyspepsia
# Accuracy of Tests for *H pylori* Infection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea Breath Test</td>
<td>94.7</td>
<td>95.7</td>
</tr>
<tr>
<td>Stool Antigen Test</td>
<td>93.1</td>
<td>92.8</td>
</tr>
<tr>
<td>Rapid Urease Test From Gastric Biopsy</td>
<td>71.1</td>
<td>87.6</td>
</tr>
<tr>
<td>Serum IgG Antibody</td>
<td>85.0</td>
<td>79.0</td>
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# Uninvestigated Dyspepsia: 1-Year Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>Test-and-Treat n = 223</th>
<th>Endoscopy n = 224</th>
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<tbody>
<tr>
<td><strong>Symptom-Free</strong></td>
<td>50%</td>
<td>55%</td>
</tr>
<tr>
<td><strong>Average Doctor Visits per Year</strong></td>
<td>0.98</td>
<td>0.66</td>
</tr>
<tr>
<td><strong>PPI Therapy</strong></td>
<td>52</td>
<td>59</td>
</tr>
<tr>
<td><strong>Endoscopies/Patients</strong></td>
<td>0.50</td>
<td>1.25*</td>
</tr>
<tr>
<td><strong>Dissatisfied With Care</strong></td>
<td>12%</td>
<td>4%†</td>
</tr>
</tbody>
</table>

*P*<0.0001; †*P*<0.013.

H. Pylori Treatment for
Functional (Non-Ulcer) Dyspepsia
Benefit of H. Pylori Therapy for Functional Dyspepsia is Minimal

H. Pylori Treatment for FD

H. Pylori and Functional Dyspepsia

- No significant evidence to show:
  - H. pylori causes FD or
  - H. pylori treatment improves FD or
  - H. pylori eradication success did not correlate with treatment success
Acid Suppression Therapy for Functional Dyspepsia
Prevalence of GERD in FD

N=247 pts with FD without dominant heartburn

Acid Suppression Therapy for Functional Dyspepsia is Suboptimal

- *P = 0.002
- †P = 0.02
- ‡P<0.05
- §P = 0.08

Prokinetics for Functional Dyspepsia
Tegaserod (*Zelnorm) for Functional Dyspepsia with **Normal** Gastric Emptying

Tack J et al. DDW 2002 (N=271, 71% females, normal EGD and 4-hr GET)

*Not an FDA approved indication

*p<0.05
Tegaserod (*Zelnorm) for Functional Dyspepsia with Delayed Gastric Emptying

Retention (%) at 4 hours post meal

- Baseline (%)
- 8 weeks (%)

- Tegaserod dose:
  - 24: ↓67%
  - 18: ↓71%
  - 12: ↓35%
  - Placebo: ↓38%

*‘Normal’ gastric retention rate at 4 hours is 6.3%

Tougas G et al. DDW 2003

*Not an FDA approved indication
Complimentary Alternative Medicine
Iberis amara
(Annual Candytuft, Clown’s Mustard)
**STW-5 (Iberogast®)**

Nine herbal extracts

- Clown's Mustard (*Iberis amara*)
- Peppermint leaves
- Caraway fruit
- Angelica root
- Milk thistle fruit
- Greater celandine
- Liquorice root
- Camomile flowers
- Lemon balm leaves

20 drops tid

$49.95

$29.71
STW 5 in Guinea-Pig

- Fundus and corpus muscle strips
  - Dose-dependently relaxation of circular and longitudinal muscle
- Antral muscle strips
  - Increase contraction
- Effects resistant to tetrodotoxin, atropine, capsaicin
  - Pathways not involving nitric oxide or vagus
- STW 5 alters gastric motility in a region-specific manner, may improve:
  - Impaired fundus accommodation
  - Antral hypomotility

Phytotherapy of Functional Dyspepsia with STW 5 (Iberogast)

Red Pepper (Capsaicin) for FD

Red pepper powder
0.5 g capsules - 5 per day
vs.
Placebo (tomato powder)

n=30

Summary: Functional Dyspepsia

- “Patient needs a doctor, not an endoscopist”
- Investigated vs. Uninvestigated dyspepsia
- Differentiate postprandial distress vs. epigastric pain syndrome
- PPI OK, H. Pylori treatment not helpful in FD
- Valid role for CAM