Updates in Evaluation and Management of Dyspepsia and H. Pylori Infection

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Disclosures

None
Session Objectives

- Review 2017 recommendations for diagnosis, evaluation, and treatment of dyspepsia
- Summarize 2017 H. Pylori screening and treatment guidelines
- Review risks and benefits of PPI therapy
What Is Dyspepsia?

- Postprandial fullness, early satiation, epigastric pain, and/or epigastric burning, possibly associated with nausea
- Affects about 40% adults/year
- Uninvestigated vs investigated
# Dyspepsia: Differential Diagnosis

<table>
<thead>
<tr>
<th>Table 1. Possible Underlying Causes of Symptoms of Dyspepsia.</th>
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<tbody>
<tr>
<td>Functional dyspepsia</td>
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<tr>
<td>Peptic ulcer disease and infection with <em>Helicobacter pylori</em></td>
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<tr>
<td>Gastroesophageal cancer</td>
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<td>Gastroparesis</td>
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<td>Gallstones, sphincter of Oddi dysfunction, biliary dyskinesia, or gallbladder cancer</td>
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<td>Drugs (e.g., nonsteroidal antiinflammatory drugs, iron, calcium antagonists, angiotensin-converting–enzyme inhibitors, methylxanthines, and glucocorticoids)</td>
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<td>Chronic pancreatitis or pancreatic cancer</td>
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<td>Parasites (e.g., <em>Giardia lamblia</em>, strongyloides, and anisakis)</td>
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<td>Hepatocellular carcinoma</td>
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<td>Chronic mesenteric ischemia</td>
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<td>Crohn’s disease</td>
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<td>Infiltrative diseases (e.g., eosinophilic gastroenteritis and sarcoidosis)</td>
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Functional Dyspepsia (FD)

- >70% dyspepsia attributable to FD
- **Rome Classification and Criteria**
  - “Functional” GI disorders → Disorders of “gut-brain interaction”
  - Basis for categorizing patients into study cohorts
American College of Gastroenterology & Canadian Association of Gastroenterology: 2017 Practice Guideline: Management of Dyspepsia

- Dyspepsia = predominant epigastric pain lasting at least one month
  - May be associated with epigastric fullness, nausea, emesis, or heartburn
  - *Epigastric pain is primary concern*

- Functional Dyspepsia = endoscopy and/or other testing has ruled out structural or anatomic etiology for above symptoms
ACG/CAG 2017 Guidelines: What They Did

- Systematic review for all pharmacologic treatment methods

- Quality of evidence rating:
  - High (H): new data would be unlikely to change noted effect
  - Moderate (M)
  - Low (L)
  - Very low (VL): estimate of effect is very uncertain

- Strength of recommendation
  - Strong (S)
  - Conditional (C)
ACG/CAG Guideline: Why Do Endoscopy?

- Purpose is to exclude gastric neoplasia
  - Third most common cause of cancer mortality worldwide
  - Often presents with dyspepsia and can be detected early
- Gold standard, but expensive and invasive
- In dyspepsia patients, >75% normal
Case #1

Which of the following patients presenting with dyspepsia should have an endoscopy as their initial work-up?

A. 44 yo Caucasian man c/o epigastric pain and early satiety x 3 months, noted to have 5# weight loss.
B. 55 yo Chinese-American woman c/o epigastric pain and early satiety x 3 months, noted to have 5# weight loss.
C. 62 yo African-American man c/o epigastric pain and post-prandial nausea.
D. 50 yo Latina c/o epigastric pain and food “sticking” when she swallows x 3 months.
Perform endoscopy on patients ≥ 60 years old (C/VL)

- Age is biggest risk factor

- Other risk factors: male sex, born and/or childhood spent in high-risk regions, eg East Asia (half of cases occur there)
ACG/CAG 2017 Guideline: Alarm Features ≠ Endoscopy

Don’t do endoscopy for alarm features in patients < 60 years old to exclude upper GI neoplasia (UGIN). (C/M)

- Studies looking at predictive value of alarm features don’t support their reliability
- Even though data has shown people with individual alarm features have 2-3x risk of UGIN, *typical* risk so low in N. America, still far <1%
ACG/CAG 2017 Guideline: Who <60 Should Have an Endoscopy?

- While typical risk is <1% even with individual alarm features, consider endoscopy in certain sub-groups:
  - Alarm features are prominent (e.g., progressive dysphagia, >20# weight loss)
  - Combination of alarm features present
  - Family history UGIN
  - Older age
  - Born and/or childhood in high risk geographic region
Getting Back to Case #1

Which of the following patients presenting with dyspepsia should have an endoscopy as their initial work-up?

A. 44 yo Caucasian man c/o epigastric pain and early satiety x 3 months, noted to have 5# weight loss.

B. 55 yo Chinese-American woman c/o epigastric pain and early satiety x 3 months, noted to have 5# weight loss.

C. 62 yo African-American man c/o epigastric pain and post-prandial nausea.

D. 50 yo Latina c/o epigastric pain and food “sticking” when she swallows x 3 months.
ACG/CAG 2017 Guideline: Recommended Evaluation for Patients <60

Test patients <60 yo for H. Pylori non-invasively and treat if positive. (S/H)

- Use urea breath test or fecal H. Pylori Ag
- Wait 4 weeks after treatment before assessing response
  - 6 trials (2399 patients) compared test and treat (T/T) and prompt EGD: no difference in global dyspepsia at end of f/u and only 25% in T/T group had EGD during f/u period
- Prior recommendation: PPI first if local prevalence <15%
H. Pylori and Dyspepsia

- Major cause of gastritis and PUD
- RF for MALT lymphoma and gastric adenocarcinoma
- Associated with a variety of motility, endocrine, and anti-secretory abnormalities
- H. Pylori eradication has a *small*, but statistically significant effect on reducing functional dyspepsia; also increases rates of DUD healing and reduces rates of DUD recurrence (compared to ulcer-healing med alone)
Additional Benefits Test and Treat: Reduced Gastric Cancer?

- H. Pylori treatment in asymptomatic H. Pylori+ adults *may* lead to reduced incidence gastric cancer
  - Meta-analysis 24 studies (22 done in Asian countries)
  - 2014 Cochrane review and meta-analysis 6 RCT
  - Highest benefit in regions or populations with highest gastric cancer rates
H. Pylori Infection: Epidemiology

- Chronic, usually acquired in childhood, can be asymptomatic
- Worldwide risk factors for infection
  - low socio-economic status
  - increased number of siblings
  - infected parent
- Prevalence in North America
  - Non-Hispanic whites < other racial/ethnic groups
  - African-Americans with higher > lower proportion African ancestry
  - Overall lower rates than many regions, including Asia, Central and South America
Case #2

Which of the following patients should you screen for H. Pylori?

A. 52 yo man with well-controlled DM2, HTN, and dyslipidemia who is starting low-dose ASA prophylaxis.

B. 48 yo woman with h/o endoscopy-proven peptic ulcer disease treated with PPI course.

C. 45 yo obese man with bilateral knee DJD taking ibuprofen tid for past year.

D. 55 yo woman c/o heartburn and excessive burping.
How to Approach H. Pylori Testing and Treatment?

American College of Gastroenterology 2017 Clinical Guideline: Treatment of H. Pylori

- Indications for test and treat
- Review of evidence for treatment regimens
- Recommendations for antibiotic treatment and follow-up
ACG 2017 Treatment of H. Pylori Guidelines: Who Should We Test & Treat?

Anyone with:

- Active PUD or h/o PUD not previously tested
- Uninvestigated dyspepsia < 60 years old
- Daily low dose ASA
- Initiation chronic NSAIDs
- Unexplained iron-deficiency anemia despite work-up
- Adults with immune thrombocytopenia (ITP)
- H/o endoscopic resection early gastric cancer
- Low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma
What About Testing in GERD?

- No proven causal association
- Not recommended to test if epigastric symptoms not present
- Negative association between H. Pylori prevalence and GERD on geographic basis
- Treating may make it worse! Data mixed.
Case #3

54 yo man with COPD and HTN has a positive fecal H. Pylori antigen test in a work-up for dyspepsia. His initial treatment regimen should be:

A. Clarithromycin, amoxicillin and omeprazole x 7 days.
B. Clarithromycin, amoxicillin and omeprazole x 14 days.
C. Bismuth, omeprazole, tetracycline, and metronidazole x 7d
D. Clarithromycin, amoxicillin, omeprazole and metronidazole x 7d
ACG 2017 Clinical Guideline: Principles of H. Pylori Treatment

- Few trials in North America assessing updated regimens
- Treatment is usually empiric
- Antibiotic sensitivity testing for H. Pylori typically not done
- Find out about local (geographic) antibiotic resistance rates and local (patient) prior antibiotic use
- 10-14 days superior to 7 days
ACG 2017 Clinical Guideline: H. Pylori Treatment Regimen

1. **Clarithromycin Triple Therapy x 14 days (C/L)**
   - Clarithromycin, PPI, amoxicillin (or metronidazole if PCN-allergy)
   - Use where local clarithromycin resistance (CR) <15% and patient has no prior macrolide use
   - Eradication rates: 14d > 7d (still close to 80%)

2. **Bismuth Quadruple Therapy x 10-14d (S/L)**
   - Bismuth, PPI, tetracycline and nitroimidazole
   - If PCN-allergic, prior macrolide use, or CR >15%
   - Mean eradication rate 91%, but Q.I.D. dosing
ACG 2017 Clinical Guideline: H. Pylori Treatment Regimen

3. **Concomitant Treatment 10-14d (S/LQ)**
   - PPI, clarithromycin, amoxicillin, and nitroimidazole
   - No N. America RCTs but meta-analysis 19 clinical trials: 3-10 day treatment mean cure rate 88%

4. **Sequential Treatment 10-14d (C/LQ)**
   - Several iterations, some with clarithromycin others with levofloxacin
   - Best international data: PPI + amox for 5-7d *then* PPI, levofloxacin + nitroimidazole for 5-7d (pooled rate 87.8%)
ACG 2017 Clinical H. Pylori Guideline: Predicting Treatment Success

- Host Factors:
  - Adherence
  - Cigarette smoking
  - Diabetes

- H. Pylori Factors:
  - Antibiotic sensitivity

<table>
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<th>Antibiotic</th>
<th>Resistance rate (%)</th>
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<tbody>
<tr>
<td>Metronidazole</td>
<td>20</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>16</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>31</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>&lt;2</td>
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ACG 2017 H. Pylori Clinical Guideline: Confirm Eradication?

- Confirm H. Pylori eradication with urea breath test, fecal H. Pylori Ag or endoscopic biopsy at least 4 weeks after treatment completion and 2 weeks off PPI
  - Data doesn’t support this as cost-effective except in patients with bleeding PUD
  - Consider in patients with FD who have persistent symptoms

- What if the H. Pylori is eradicated but the symptoms are not?
Getting Back to Dyspepsia: When There’s No H. Pylori

If <60 years old, use PPIs if H. Pylori eradicated or H. Pylori negative (S/H) or FD (S/M)

- H. Pylori negative or persistent symptoms after eradication
  - 6 RCTs (2709 pts): once daily PPI vs placebo or antacid (NNT=6); persistent symptoms 50% PPI vs 73% placebo group
  - Low dose = standard dose in FD (Cochrane Review, 2017)

- What about H2-blockers?
  - Head to head RCTs didn’t show statistically significant difference
Case #4

You are weighing prescribing a PPI for a 62 yo woman with H. Pylori-negative functional dyspepsia, who also has DM2, HTN, and DJD bilateral knees. She is on metformin, benazepril, atorvastatin and ASA. You counsel her that a PPI may decrease her risk of stomach bleed and:

A. PPI may decrease her kidney function.

B. PPI may increase her risk of ASCVD events.

C. PPI may increase her risk of developing pneumonia.
PPIs: Evidence for Adverse Effects

**Caveat:** most of the evidence is based on observational data, and so it’s possible that:

- PPI users are sicker than non-users
- Effects are cased by other drugs or conditions associated with PPI use

That said…
PPIs: Evidence for Adverse Events

Observational and/or Population-Based Studies Support

- Chronic Kidney Disease
- Acute Kidney Injury
- Hypomagnesemia
- Clostridium difficile infection and recurrence
- Hip and spine fracture
PPIs: Evidence for Adverse Events

Conflicting Data: Overall No Clear Evidence

- Community-Acquired Pneumonia
- Increase risk ASCVD events
ACG/CAG 2017 Guideline

Patients <60 years old or with diagnosis FD who are unresponsive to PPI or H. Pylori eradication should be offered TCA (C,L) or pro-kinetic (C/VLQ).

- 3 FD studies TCA vs placebo showed significant effect
- 3 low quality trials of PPI vs PK show trend toward PPI
- TCA > PK in terms of efficacy in functional dyspepsia
Take Home Points

- In patients with dyspepsia, investigate with endoscopy for >60 years old or higher risk population, not isolated alarm features
- In patients <60 years old with dyspepsia, test and treat for H. Pylori first, then try low-dose PPIs
- Screen patients with PUD or starting ASA or NSAIDs for H. Pylori
- Assess for local and individual antibiotic resistance factors before choosing an H. Pylori treatment regimen
- Use PPIs judiciously at lowest effective dose for short periods of time to minimize risk
References