Screening and Surveillance in the Gut

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Objectives

- Review pathophysiology and screening recommendations for Barrett's esophagus
- Review screening recommendations for pre-malignant gastric conditions
- Review screening and surveillance guidelines for colorectal cancer

Pre-test Questions

Which of the following patient profiles presenting with long-standing heartburn is most likely to be diagnosed with Barrett's esophagus?

A.) 65 y/o Asian male with normal weight
B.) 55 y/o Caucasian male with abdominal obesity
C.) 60 y/o Caucasian female with abdominal obesity
D.) 70 y/o African-American male with abdominal obesity
Pre-test Questions

70 y/o female you have been following for several years in your practice was recently diagnosed with pernicious anemia. She also has complaints of chronic mild heartburn and dyspepsia symptoms. Which of the following should you consider given her recent diagnosis?

A.) CT abdomen/pelvis
B.) Upper GI contrast series
C.) EGD
D.) Monitor symptoms and observe only

Pre-test Questions

35 y/o patient presents to your office to discuss screening colonoscopy. He has no GI symptoms or alarm symptoms. Upon review of his family history, you discover his father had colon cancer diagnosed at age 70 and his brother had a large villous adenoma at age 45. When would you recommend he have a screening colonoscopy?

A.) Age 40
B.) Age 50
C.) Age 60
D.) Age 45

Barrett’s Esophagus Epidemiology

• Barrett’s esophagus is the condition in which metaplastic columnar epithelium replaces squamous epithelium in the distal esophagus
• Develops as a consequence of GERD
• Predisposes to the development of adenocarcinoma
• Usually discovered in middle-aged individuals undergoing endoscopy, mean age of 55
• Acquired condition, not congenital
• Uncommon in African Americans, Asians
• Male to female ratio 2:1
• Prevalence varies from 0.9 to 20 percent (depending on population studied)
Diagnostic Criteria

- Two criteria must be fulfilled:
  - Documentation of columnar epithelium in the distal esophagus
  - Histologic examination must reveal specialized intestinal metaplasia (gastric cardia-type epithelium not definitive)

Diagnostic Criteria, Continued

- Squamocolumnar (Z-line) and gastroesophageal (GEJ) junctions must be identified to further classify Barrett’s esophagus
  - Long segment Barrett's-distance between Z-line and GEJ >3cm
    - Pts tend to have more severe reflux (upright and supine)
  - Short segment Barrett's-distance between Z-line and GEJ <3cm
    - Less severe reflux (upright), higher LES pressures
- Identification of cardia-type epithelium above the Z-line is likely a precursor to intestinal metaplasia

Barrett's Esophagus
Pathophysiology

- Barrett's esophagus develops through the process of metaplasia
  - Tissue chronically exposed to noxious factors (reflux) promoting repair and aberrant differentiation
  - Metaplastic columnar cells appear to be more resistant to reflux-induced injury
  - Pattern of reflux may predispose to neoplasia
    - Pulsed acid exposure increases cell proliferation
    - Continuous acid exposure decreases proliferation

Barrett's Esophagus

- Metaplasia-dysplasia-carcinoma sequence

Dysplasia and Adenocarcinoma

- Estimates of cancer risk with Barrett's
  - General population of Barrett's pts- 0.25% per year
  - Low-grade dysplasia- poorly defined, somewhere between general population and high-grade
  - High-grade dysplasia- 4-8% per year
Screening

- There is no convincing evidence to suggest routine screening (endoscopy) of patients with GERD
- 40% of patients with adenocarcinoma of the esophagus had no history of GERD
- Studies have failed to prove targeted screening of patients with GERD has prevented deaths from adenocarcinoma
- Symptoms suggesting complicated GERD should undergo endoscopic evaluation:
  - Anorexia, wt loss, dysphagia, bleeding, odynophagia
- Consider screening pts with chronic gastroesophageal reflux disease, age >50 years, male sex, elevated body mass index with an abdominal pattern of fat distribution

Management Guidelines

- American College of Gastroenterology
  - The grade of dysplasia determines surveillance interval (should confirm by expert pathologist)
  - Non-dysplastic
    - Consider no surveillance. If surveillance is elected, perform EGD every 3 to 5 years. Consider endoscopic ablation in select cases
  - Low-grade dysplasia
    - Consider endoscopic ablation if no life-limiting comorbidities
    - Endoscopic surveillance every year is alternative
  - High-grade dysplasia (flat mucosa)
    - Endoscopic ablation recommended, RFA preferred
    - Alternative, repeat endoscopy in 3 months, irregular/nodular mucosa should undergo endoscopic mucosal resection for staging

Radiofrequency ablation
Premalignant gastric conditions

- Gastric polyps
  - Majority (70%-90%) of gastric epithelial polyps are fundic gland polyps (FGPs) or hyperplastic polyps
  - Most FGPs associated with long-term proton pump inhibitor use and are not associated with an increased risk of cancer in the absence of familial adenomatous polyposis syndrome (FAP).
  - Hyperplastic polyps are associated with an increased risk of gastric cancer. Polyps greater than 5mm should be removed.
  - Adenomatous polyps of the stomach should be endoscopically removed when possible
  - Gastric cancer has been found in 1.3% of patients during follow-up.
  - Endoscopy is recommended 1 year after adenomatous polyp resection, followed by surveillance endoscopy every 3 to 5 years.

Fundic gland polyps
Premalignant gastric conditions

- Pernicious anemia
  - Prevalence of gastric adenocarcinoma in patients with pernicious anemia, now considered to be associated with type A atrophic gastritis, is reported to be 1% to 3%.
  - Risk seems to be highest within the first year of diagnosis.
  - Benefits of endoscopic surveillance in patients with pernicious anemia have not been established.
  - Consider endoscopy soon after the diagnosis or when patients develop upper GI symptoms.

Premalignant gastric conditions

- Post-gastric surgery
  - May be an increased risk of gastric cancer in patients who have undergone partial gastrectomy for benign gastric or duodenal ulcer.
  - Reported frequencies of gastric remnant carcinoma range from 0.8% to 8.9%.
  - Dysplasia-to-carcinoma sequence has been described.
  - Risk appears to increase 15 to 20 years after the initial surgery.
  - No guidelines or strong recommendations for screening.

Colorectal Cancer

- Adenocarcinoma: 95%
  - Others: GIST, carcinoid, lymphoma
  - 4th most common cancer in U.S. and 2nd leading cause of cancer deaths
- Colon
  - 93,090 new cases of colon cancer
- Rectal
  - 49,700 new cases of rectal cancer
- Lifetime risk of colorectal cancer—men
  - 1 in 19 (5.2%)
- Lifetime risk in women
  - 1 in 20 (5%)
- Recent trend of increased incidence of CRC in young adults
Distribution of Colorectal Cancers

- Transverse: 15%
- Ascending/cecum: 20%
- Rectosigmoid: 10%
- Sigmoid: 25%
- Rectum: 20%
- Sigmoid: 25%
- Rectosigmoid: 10%

Only about half of all colon cancers are within reach of the flexible sigmoidoscope.

Adapted from Bresalier RS. Chapter 115. In Sleisenger & Fordtran's Gastrointestinal and Liver Disease. 7th ed.

Hereditary Colorectal Cancers

- Familial adenomatous polyposis (FAP)
  - APC gene
- Hereditary non-polyposis colorectal cancer (HNPCC)
  - MMR genes: hMSH2, hMLH1, hMSH6, hPMS1, hPMS2

Lynch syndrome (HNPCC)

- Most common cause of inherited colorectal cancer
  - AD inherited CRC secondary to mismatch-repair defect
- Amsterdam criteria
  - Three or more relatives with histologically verified Lynch syndrome-associated cancers (CRC, cancer of the endometrium or small bowel, transitional cell carcinoma of the ureter or renal pelvis), one of whom is a first-degree relative of the other two
  - Lynch syndrome-associated cancers involving at least two generations
  - One or more cancers were diagnosed before the age of 50 years
  - "3-2-1 rule" (3 affected members, 2 generations, 1 under age 50)
Reasons screening is effective

- CRC is a common malignancy with a long asymptomatic phase
- Can be prevented by detection and removal of precursor adenomas
- Emerges from a progression of several mutations in genes controlling cell growth and DNA repair
- Has a high survival rate if detected in its early stages
  - Survival rates for both colon and rectal cancers found early (stage I) have a 5 year survival rate of 75%

Screening Options

- **Prevention**
  - Rectal exam (rectal cancer)
  - Flexible sigmoidoscopy
  - Colonoscopy
  - Virtual colonoscopy (CT)

- **Detection**
  - Fecal occult blood testing (FOBT)
    - Hemoccult SENSA recommended
  - Fecal immunochemical testing (FIT)
    - No modification of diet or medications
  - Double-contrast barium enema (DCBE)
  - Fecal DNA testing

Colonoscopy: The Gold Standard

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<tr>
<th>Advantages</th>
<th>Limitations</th>
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<td>Ability to visualize entire colon, hence the highest detection rate for colonic polyps and cancer</td>
<td>Highest complication rate of all screening modalities (0.3%-0.56%)</td>
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<td>Can perform polypectomy without need for another procedure</td>
<td>Manpower and cost are major obstacles</td>
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<td>Potential for missed lesions remains (6% of advanced adenomas)</td>
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Adenomatous polyp (colonoscopy)

Screening Technologies:
CT Colonography (Virtual Colonoscopy)

American Cancer Society, the United States Multi-Society Task Force on Colorectal Cancer (ACS-MSTF) and American College of Radiology

- Options for screening
  - Colonoscopy every 10 years
  - Computed tomographic colonography (CTC) every five years
  - Flexible sigmoidoscopy every five years
  - Double-contrast barium enema every five years (now infrequently used as a screening strategy).
  - Fecal occult blood testing (FOBT) by sensitive guaiac method, performed annually
  - Fecal immunochemical-based testing (FIT) for blood, performed annually
### United States Preventive Services Task Force (USPSTF)

- **Options for screening**
  - Annual fecal occult blood testing (FOBT) with a sensitive test
  - Flexible sigmoidoscopy every five years, with sensitive FOBT every three years
  - Colonoscopy every 10 years
  - Consider discontinuation at age 75 or <10 yrs life expectancy
  - Patients over 85 should not be screened

### American College of Gastroenterology

- ACG recommends that clinicians have access to a “preferred” strategy for making CRC screening recommendations, as an alternative to the “menu of options” approach
- Preferred CRC prevention test is colonoscopy
  - Colonoscopy every 10 years, beginning at age 50. Begin at age 45 years in African Americans
- Alternative CRC prevention tests
  - Flexible sigmoidoscopy every 5–10 years
  - CT colonography every 5 years
- Preferred cancer detection test is annual FIT for blood
- Alternative cancer detection tests
  - Annual Hemoccult Sensa
  - Fecal DNA testing every 3 years

### Screening-high risk

- Recommendations for screening when family history is positive but evaluation for HNPCC considered not indicated (American College of Gastroenterology)
  - Single first-degree relative with CRC or advanced adenoma diagnosed at age >=60 years
    - Recommended screening: same as average risk
  - Single first-degree with CRC or advanced adenoma diagnosed at age <60 years or two first-degree relatives with CRC or advanced adenomas
    - Colonoscopy every 5 years beginning at age 40 years or 10 years younger than age at diagnosis of the youngest affected relative
Surveillance after polypectomy
(US Multi-Society Task Force on Colorectal Cancer)

- Average risk patients
  - No polyps
    - Repeat colonoscopy in 10 yrs
  - 1-2 small tubular adenomas (<10mm)
    - Repeat colonoscopy in 5-10 yrs
  - 3-10 tubular adenomas
    - Repeat colonoscopy in 3 yrs
- Adenomas >10mm
  - Repeat colonoscopy in 3 yrs
- Villous adenoma
  - Repeat colonoscopy in 3 yrs
- Tubular adenoma with high-grade dysplasia
  - Repeat colonoscopy in 3 yrs

Surveillance after CRC resection
(US Multi-Society Task Force on Colorectal Cancer)

- TNM stages I-III CRC, and selected patients with resected stage IV cancer
- Cumulative incidence of metachronous cancers of the colon and rectum is estimated to be about 0.3%-0.35% per year.
- Thus, postoperative colonoscopic surveillance is indicated long term, or until the benefit is outweighed by decreased life expectancy due to age and/or competing comorbidity.
- Patients should receive their first surveillance colonoscopy 1 year after surgery (colon cancer)
  - Interval to the next colonoscopy should be 3 years and then 5 years after that exam. Continue at every 5 yrs thereafter.

Surveillance after resected rectal cancer

- Important distinction is made between colon and rectal cancer because of the latter’s higher propensity for local recurrence
- Sigmoidoscopy or rectal EUS is recommended every 3 to 6 months for the first 2 or 3 years after surgery, in addition to colonoscopic surveillance for metachronous neoplasms
Colorectal screening and surveillance

- My thoughts
  - Incorporate a screening program and be consistent
  - Colonoscopy is preferred for detection but not right for every patient, know other methods
  - Remember to take accurate family history to detect need for earlier screening
  - 1/7 of all new colorectal pts are under 50-evaluate patients with symptoms!
  - Don’t forget to follow surveillance guidelines for polyps and cancers, unfortunately many pts don’t see gastroenterologist in follow-up

Post-test Questions

60 y/o caucasian male with chronic heartburn recently underwent EGD with endoscopic findings of long-segment Barrett’s esophagus. Biopsies showed intestinal metaplasia with high-grade dysplasia. What is the preferred treatment for this patient?

A.) Esophagectomy
B.) Surveillance EGD every 3-5 yrs
C.) Monitor for symptoms of dysphagia
D.) Endoscopic radiofrequency ablation

Post-test Questions

50 y/o female presents to your clinic to discuss screening colonoscopy. Her family history reveals three first-degree relatives with endometrial, colon, and bladder cancers. What is the most likely inherited form of CRC for this patient?

A.) Lynch Syndrome (HNPCC)
B.) Familial adenomatous polyposis
C.) Sessile serrated adenomatosis syndrome
D.) MUTYH-associated polyposis
Post-test Questions

25 y/o male presents to your office with recent mild rectal bleeding (which he feels are due to hemorrhoids), 20 lb unintentional weight loss over last 3 months and new onset of constipation. What should be your approach to this patient?

A.) Treat empirically for hemorrhoids
B.) Perform DRE and refer for colonoscopy
C.) Order CT abdomen/pelvis
D.) Recommend increased fiber intake and OTC laxative

Questions?

References

- The role of endoscopy in Barrett’s esophagus and other premalignant conditions of the esophagus. Gastrointest Endosc 2012;76:1087-1094
- Stuart Spechler, MD. Barrett's esophagus: Surveillance and management. UpToDate