Colon Cancer Screening: What’s New

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Overview

- Epidemiology and Pathogenesis of CRC
- Colon cancer screening
  - Colonoscopy, FOBT, Flexible sigmoidoscopy
  - Virtual colonoscopy
  - Stool DNA testing
- ASGE quality indicators for CRC screening
  - Non-polypoid neoplasms
  - Colonoscopy withdrawal time
Epidemiology of CRC

- 4th most common cancer in US
- 2nd leading cause of cancer-related death
- 140,000 new cases/year
- 50,000 deaths/year
- Lifetime risk is similar in both sexes
- >90% of CRC after age 50
- AAM: screening should start at age 45
Cancers of the Colon and Rectum (Invasive):
Average Annual Age-Specific SEER Incidence and
U.S. Mortality Rates By Gender, 1995-1999

![Graph showing age-specific incidence and mortality rates for colon and rectal cancer, with separate lines for male and female rates.]
Epidemiology

• Age > 50 with adenoma: 25-40%
• Age > 50 with advanced* adenoma: 3-10%
• Lifetime risk of CRC at age 50: 5%

→ Most adenoma do not develop into CRC
→ Advanced adenoma are at greatest risk

*Advanced adenoma: >1cm, >25% villous adenoma, HGD
Risk factors

- Age > 50
- PMH/FH of adenoma, CRC
- IBD
- FAP, HNPCC

- Pelvic irradiation
- Diet/lifestyle: high red meat, high fat, alcohol, tobacco, obesity
Colorectal Cancer (CRC)

Sporadic (average risk) (65%–85%)

Family history (10%–30%)

Hereditary nonpolyposis colorectal cancer (HNPCC) (5%)

Familial adenomatous polyposis (FAP) (1%)

Rare syndromes (<0.1%)

Rare syndromes (<0.1%)
Protective Factors

- High fiber diet/vegetables/fruits
- High calcium diet
- High folate diet
- High physical activity
- ASA/NSAIDs use
CRC Pathogenesis

- Normal Colon
  - APC
  - hMSH2
  - hMLH1 abnormalities (Hereditary Syndromes)

- Hyperproliferative epithelium
  - Methylation abnormalities
  - APC
  - hMSH2
  - hMLH1 inactivation

- Adenoma
  - K-ras mutation
  - DCC deletion
  - p53 deletion
  - Further accumulation of genetic abnormalities

- Carcinoma
CRC Survival Rates

• 5-year survival rate:
  – Early stage: 90%
  – Metastatic disease <10%

• 5-year overall survival rates:
  – White: 60-65%
  – AA: 50%
Definition

• Screening: search for CRC in asymptomatic patient w/o prior CA
• Surveillance: evaluation of patient at high-risk of CRC: h/o adenoma/CRC, IBD.
• Diagnosis: Evaluation of symptomatic patient
5 Key Points for CRC Screening

- CRC can be prevented
- Screening decreases mortality from CRC
- All individuals age > 50 need screening
- High-risk individuals begin earlier screening
- Any screening test is better than no test
Comparison of Colorectal Cancer Test Use with other Cancer Screening Tests, NHIS 2000*

* Among appropriate populations that receive screening tests
Medicolegal issues for PCP

• Delay in CRC diagnosis accounts for > 50% of all litigation against PCP for GI disease:
  – Attributing rectal bleeding to hemorrhoids
  – Inadequate evaluation of positive FOBT
  – Failure to screen/recommend screening
2008 joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer and the American College of Radiology
Screening of average risk individuals

• Start screening at age 50 (age 45 AAM?)
• Preferred modality: Colonoscopy (ASGE, ACG)
  – Every 10 years
  – Visualize entire colon
  – Diagnosis/histology and treatment/resection
  – National Polyp Study: Polypectomy ↓ ↓ the incidence of CRC by 76%-90% when compared to 3 historic reference groups
  – Indirect evidence that it ↓ ↓ CRC-related mortality
Observed and Expected Colorectal Cancer Incidence in National Polyp Study Cohort After Colonoscopic Polypectomy

Cumulative incidence, percent

Years followed

NPS expected (Mayo Clinic)
NPS expected (St. Mark's)
NPS expected (Seer)
NPS observed

Screening Methods
Colonoscopy

Disadvantages of colonoscopy:

• Bowel preparation
• Cost
• Risk of sedation
• Risk of perforation: 1/1,000
• Miss rate:
  – 27% for polyp<5 mm
  – 6%-11% for polyp>1cm
  – Associated w quality of prep, skills of endoscopist, withdrawal time
Screening Methods
Alternatives to Colonoscopy

- FOBT every year
- Flexible sigmoidoscopy every 5 years
- FOBT and FlexSig every 5 years
  - If any test positive \(\rightarrow\) colonoscopy
- But 50% of patients with advanced adenoma/CRC in proximal colon have no distal polyp

Lieberman et al; Imperiale et al, NEJM 2000
Screening Methods
The Knew Kids on the Blocks

• Virtual Colonoscopy
• Fecal DNA testing
Screening Methods
Virtual Colonoscopy

• CT Scanning of colon after bowel and prep and colonic distension

• For polyp > 10mm
  – Sensitivity 55%-100% (vs 98% for colonoscopy)
  – Specificity 94%-98%

• For polyp 6-9mm: Sensitivity:
  – 39%-94%
  – Specificity: 79%-92%

• Likely misses non-polypoid neoplasia
Screening Methods
Virtual Colonoscopy

- No consistent patient preference VC vs colonoscopy
- Still need to prep; no sedation
- If polyp seen → need colonoscopy
- Radiation exposure
- Not covered by Medicare and private insurers
- Not endorsed for CRC screening by medical societies
- Colonoscopy is more cost-effective
Screening Methods
Virtual Colonoscopy

Use:

• Patients who refuse colonoscopy
• Incomplete colonoscopy
• Patient at high-risk for sedation and at low-risk for positive exam
Screening Methods
Fecal DNA testing

• Based on the molecular genetics of CRC: chromosomal instability, microsatellite instability, and CpG island methylation

• Sensitivity:
  – For CRC: 62%-91%
  – For advanced adenomas: 27%-82%

• Specificity: 93%-96%

• Not recommended for CRC screening
Screening for High-Risk individuals (30%)

• FH of CRC, colon polyp:
  – Colonoscopy starting at age 40 or 10 years younger than the affected relative, whichever comes first
  – Every 5 years

• IBD:
  – Colonoscopy every 1-2 years after 7-10 years of disease

• FAP (APC mutation):
  – Genetic testing (positive in 80%)
  – FlexSig starting at age 10, yearly
  – once adenomas appears → total colectomy

• HNPCC (Mismatch repair genes mutation):
  – Colonoscopy starting at age 20, every 1-2 years (yearly after age 40)
Non-Polypoid CR Neoplasms

- Slightly elevated, flat or depressed lesions
- Described by the Japanese in the 80’s
- 1,819 subjects from the Palo Alto VA
- NP-CRN
  - Found in 9.3% of patients
  - Found in 15% of patients in surveillance program
  - 5x as likely as polypoid neoplasms to harbor in situ or invasive CA
  - Depressed type has the highest risk (33%)

Soetikno et al JAMA 2008
NP-CRN
NP-CRN

- Highlights importance of excellent prep
- Slow withdrawal time
- Learn to distinguish subtle changes of NP-CRN from the surrounding normal mucosa
Colonoscopy Withdrawal Time

- Compared rate of detection of neoplasia with withdrawal time of 6 min or more vs withdrawal time <6min

- Detection of:
  - Any neoplasia: 28% vs 11%
  - Advance neoplasia: 6.4% vs 2.6%

Barclay et al, NEJM, Dec 2006
Colonoscopy Withdrawal Time

• Compared detection of neoplasia with withdrawal time of 8min or more vs withdrawal time < 8min

• Detection of:
  – Any neoplasia: 37.8% vs 23.3%
  – Advanced neoplasia: 6.6% vs 4.5%

Summary

• Colon cancer is a preventable disease
• Importance of screening
• Colonoscopy: Gold standard for screening
• New methods being evaluated
• Importance of high quality exam in detecting CR neoplasia