Colorectal Cancer: Screening & Surveillance

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Advances in Internal Medicine

Objectives

• Brief overview – epidemiology and pathogenesis of colorectal cancer (CRC)
• To review screening modalities for CRC
• To review surveillance guidelines for CRC
• Limitations of Colonoscopy
• Optimization of colonoscopy
  – quality of the bowel preparation key to addressing limitations of colonoscopy
CRC: Overview

- 3rd most common cancer
- 2nd leading cause of cancer death among men and women in the US
- In 2012, colorectal cancer (CRC) was estimated to be diagnosed in 143,460 persons and responsible for the death of 51,690 persons in the US
- 1 in 3 people who develop CRC will die from this disease
CRC: The Good News

- The incidence of CRC has been declining over the last 2 decades
- Screening for and removal of adenomas appear to significantly reduce the incidence of and risk of dying from colorectal cancer
- The question is---- how to improve our screening rates?

CRC: Screening Rates

- Screening rates are still BELOW national targets
- Screening rates tend to be higher in:
  - Insured populations
  - Higher education
  - Non-Hispanic
  - Usual source of medical care
- 50% of CRC diagnosed in the US between 2004-2006 were late stage, particularly in older adults and African Americans (men and women)
Adults 50-75 with *Up-to-date* CRC Screening 2012

Fecal occult blood test (FOBT) during the previous year, a sigmoidoscopy within the previous five years and a FOBT within the previous three years, or a colonoscopy within the previous 10 years

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**Pathogenesis**

- Most CRCs arise from Adenomas
- Adenoma → Carcinoma takes approximately 10 years to occur
- The majority (2/3) of polyps are adenomas
  - 25% men, 15% women
- Hyperplastic polyps are generally benign
- Right vs. Left Sided CRCs
  - More R sided or proximal CRCs in women, older adults
  - Shift towards greater R sided lesions (may be due to colonoscopy)
CRC Screening Options

**Endoscopic/Radiology**
- Colonoscopy
- Flexible sigmoidoscopy
- CT Colonography
- Double-contrast Barium Enema

**Stool Based Tests**
- Guaiac-based fecal occult blood test (gFOBT)
- Fecal Immunochemical Test (FIT)
- Fecal DNA
Stool Based Tests

- Stool FOBT—need 3 consecutive stool samples using a sensitive guaiac test (Hemoccult SENSA)
- Older guaiac tests are NOT sufficiently sensitive for screening (Hemoccult II)
- FOBT detects the peroxidase activity of heme either as intact hemoglobin or free heme
- In the presence of heme and a developer (hydrogen peroxide), guaiac acid is oxidized producing a blue color

gFOBT

- Advantages include:
  - Noninvasive
  - Low cost
  - Evidence supporting effectiveness: 3 landmark RCT (33% reduction in CRC mortality over 13 yrs)
- Drawbacks include:
  - Dietary restriction (Vitamin C, red meat)
  - Medication restriction (ASA, NSAIDS)
  - If positive → colonoscopy
FIT vs. FOBT

- Employs an Antibody-Antigen reaction to test for human Hgb in stool
- FIT: no dietary restriction necessary
- FIT: better performance overall
- FIT: better sensitivity/ specificity and adherence
  - 82% vs. 64% SENA (SN)
  - 97% vs. 91% SENA (SP)
- Respond only to *Human* globin and do not detect UGIB or foods with peroxidase activity

FIT

- Advantages include:
  - Noninvasive with no dietary modification
  - Strong clinical data to support effectiveness
  - High adherence
  - Excellent sensitivity/specificity
  - Automated processing of sample
- Drawbacks include:
  - Sensitivity of one-time screening not ideal
  - Need for colonoscopy if positive

Cole et al. Gastroenterology, 2008
Van Rossum et al. Gastroenterology, 2008
Ragland et al. Gastroenterology, 2013
Flexible Sigmoidoscopy

- Once-only flexible sigmoidoscopy: RCT in UK showed FS reduced CRC mortality for at least 11 years\(^1\)
- Other randomized trials have shown mortality benefit with flexible sigmoidoscopy \(^2,3\)
- Adenomas in distal colon \(\rightarrow\) colonoscopy

\(^1\) Atkin et al, Lancet 2010
\(^2\) Segnan et al, J Natl Cancer Inst 2011
\(^3\) Schoen et al, N Engl J Med 2012

Double Contrast Barium Enema

- Infrequently used for screening
- Fewer adequately trained radiologists and techs in DCBE
- May be useful in resource limited settings
CT Colonography (CTC)

- NOT supported by USPTF
- Polyps > 6mm → colonoscopy (likely will need to re-prep if colonoscopy not scheduled after CT)
- 90% sensitive for polyp 1 cm or larger, sensitivity falls for smaller sized polyps
- CTC unable to detect polyps < 6 mm
- Risk of radiation is not insignificant and should be discussed with patients
- May lead to extracolonic findings

Colonoscopy

- No randomized controlled trials have been performed to test if colonoscopy reduces the incidence of CRC
- RCTs are ongoing but no results yet
National Polyp Study

- National Polyp Study followed 1418 patients in whom colonoscopies led to 1 or more polypectomies
- Mean f/u 6 years revealed incidence of CRC 88-90% lower than in patients who had polyps which were not removed

National Polyp Study

53% mortality reduction
CRC Screening: Average Risk

- In 2008 two important CRC screening guidelines were published:
  - American Cancer Society (ACS) and the US Multi-Society Task Force (MSTF) with the American College of Radiology
  - US Preventative Services Task Force (USPSTF)
- The USPSTF recently published updated surveillance guidelines in August 2012

CRC Screening Options: Average Risk

**ACS and MSTF**

- Colonoscopy every 10 years
- Double contrast BE every 5 years
- CT colonography (CTC) every 5 years
- Flex Sig every 5 years
- Annual screening with FOBT or FIT
- Start screening at 50 years old in average-risk persons
  - ACG states 45 years in African Americans
CRC Screening Options: Average Risk

USPSTF (50-75 years old)

- Colonoscopy every 10 years
- Sigmoidoscopy every 5 years with high sensitivity FOBT every 3 years
- Annual screening with high-sensitivity FOBT
  - FIT vs. guaiac-based tests
- The likelihood that detection and early intervention will yield a mortality benefit declines after age 75 because of the long average time between adenoma development and cancer diagnosis.

Above Average Risk for CRC

- Family History of CRC or Adenomatous Polyps
- Family History of FAP
- Family History of HNPCC/Lynch
- Personal History of Adenomatous Polyp
- History of Inflammatory Bowel Disease
Family History

- Single 1st degree relative with CRC or advanced adenoma (adenoma 1 cm in size, or with high-grade dysplasia or villous elements) diagnosed at age <60 years OR two 1st relatives with CRC or advanced adenomas.
  - Recommended screening: colonoscopy every 5 years beginning at age 40, or 10 years younger than age at diagnosis of the youngest affected relative

Family History

- Single 1st degree relative with CRC or advanced adenoma (adenoma 1 cm in size, or with high-grade dysplasia or villous elements) diagnosed over age 60 years
  - Recommended screening: same as average risk (colonoscopy every 10 years beginning at age 50 years)
Genetic Syndromes

- FAP
  - Flex sig every 12 months at puberty
  - If polyposis present, consider colectomy
- HNPCC (2-3% of all CRC)
  - Colonoscopy every 1-2 years starting at age 20-25 or 10 years earlier than the youngest CRC case in the family
  - At risk for other cancers including endometrial, stomach, and ovarian

Inflammatory Bowel Disease

- Surveillance colonoscopies necessary to look for dysplasia
- Start surveillance colonoscopy every 1-2 years after
  - 8-10 years of disease in patients with pancolitis
  - 15 years in patients with left sided colitis
- Biopsies are taken every 10 cm from all 4 quadrants
### 2012 Consensus Update by the USPSTF on Colorectal Cancer Surveillance

<table>
<thead>
<tr>
<th>Baseline colonoscopy: most advanced finding(s)</th>
<th>Recommended surveillance interval (y)</th>
<th>Quality of evidence supporting the recommendation</th>
<th>New evidence stronger than 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>No polyps</td>
<td>10</td>
<td>Moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>Small (&lt;10 mm) hyperplastic polyps in rectum or sigmoid</td>
<td>10</td>
<td>Moderate</td>
<td>No</td>
</tr>
<tr>
<td>1–2 small (&lt;10 mm) TA</td>
<td>5–10</td>
<td>Moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>3–10 TAs</td>
<td>3</td>
<td>Moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>&gt;10 adenomas</td>
<td>&lt;3</td>
<td>Moderate</td>
<td>No</td>
</tr>
<tr>
<td>1 or more TAs ≥10mm</td>
<td>3</td>
<td>High</td>
<td>Yes</td>
</tr>
<tr>
<td>1 or more VILLOUS adenomas</td>
<td>3</td>
<td>Moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>Adenoma with HGD</td>
<td>3</td>
<td>Moderate</td>
<td>No</td>
</tr>
</tbody>
</table>

### Baseline colonoscopy findings: Most advanced finding(s) | Recommended surveillance interval (y) | Quality of evidence supporting the recommendation | New evidence stronger than 2006 |

<table>
<thead>
<tr>
<th>Sessile serrated polyp(s) &lt;10 mm with no dysplasia</th>
<th>5</th>
<th>Low</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessile serrated polyp(s) ≥10 mm or</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sessile serrated polyp with dysplasia or</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Low</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Traditional serrated adenoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serrated polyposis syndrome</td>
<td>1</td>
<td>Moderate</td>
<td>NA</td>
</tr>
</tbody>
</table>
**Serrated Polyps**

- Heterogeneous group of polyps with variable malignant potential
  - Hyperplastic Polyps
  - Traditional Serrated Adenomas
  - Sessile Serrated Polyps or Sessile Serrated Adenomas
- Classification system for these polyps is still evolving

**Serrated Polyps**

- Hyperplastic
  - Usually in the rectosigmoid, <5mm
  - Benign
- SSA/SSP
  - Usually in proximal colon
  - Possibly higher potential for CRC compared to adenomas
  - ?Precursor lesions to sporadic MSI-H colon cancers
- TSA
  - Rectosigmoid
  - Will often have dysplasia
Limitations of Colonoscopy

- Colonoscopy not as effective in detecting proximal/right sided lesions
- Interval Colon Cancers
- Missed Adenomas
  - Operator factors (poor bowel prep, incomplete removal, missed lesions, etc.)
  - Tumor biology (sessile serrated adenomas, microsatellite instability)


Interval Colon Cancers

- Interval Cancers: CRC diagnosed within 6-36 months of a baseline examination negative for neoplasia (i.e. presumed missed on colonoscopy)
  - Up to 9% of CRC in a Canadian registry were interval cancers
  - SEER Medicare database 1994-2005: 7.2% of CRC were interval cancers
- Estimated that more than 70% of interval cancers are attributed to missed lesions
- Incomplete polypectomy accounting for another 10-27%

1 Gastroenterology 2011;140:65–72
2 Annals Gastro 2012 25:1-3
### Missed Adenomas

- Tandem colonoscopy studies have demonstrated adenoma miss rates of 21% to 24%
- Some investigators have suggested that the true miss rate could be even higher because the same technology was used twice, and lesions behind folds or flexures could be missed during both procedures.
- Pickhardt et. al. mapped locations of adenomas missed by colonoscopy but detected by CT colonography and found that 67% were on the proximal aspect of folds\(^1\)

\(^1\) Ann Intern Med. 2004;141:352–359

### Bowel Prep and ADR

- Washington University study of patients who had prior colonoscopy with inadequate prep
- Inadequate bowel preparation was reported on 373 patients
  - initial adenoma detection rate of 25.7%
- Of 133 patients who underwent repeat colonoscopy, 33.8% had at least 1 adenoma detected, and 18.0% had high-risk states detected
  - Per-adenoma miss rate was 47.9%.
- Majority of adenomas (64.8%) were missed in the proximal colon
  - 80% of advanced adenomas (adenomas ≥1 cm or with villous components or HGD) also were missed in the proximal colon

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Limitations of Colonoscopy

- Colonoscopy not as effective in detecting proximal/right sided lesions
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Optimization of Colonoscopy

- Compliance with recommended post-polypectomy surveillance guidelines
- Ensuring a direct referral is appropriate
- Optimize bowel prep
**ASGE/ACG Task Force on Quality in Endoscopy**

- Cecal Intubation
- Photodocumentation of cecum and landmarks
- Adenoma detection rate
  - 25% Men, 15% Women
- Quality of bowel prep should be documented in report

**Direct Referral to Colonoscopy**

UCSF Referral Smartphrases:

I have evaluated this patient and it is my assessment that this patient is safe for an endoscopic procedure with sedation.

__This patient has NOT had a recent MI or stroke

__This patient does NOT require home oxygen

__This patient is NOT on anticoagulation

__This patient does NOT have a history of chronic opiate use or substance abuse (drugs, ETOH)
Complications of Colonoscopy

- Conscious/Moderate Sedation
  - Cardiopulmonary Complications (most frequent complication related to sedation)
  - Hypoxemia, Arrhythmias, Aspiration
- Infection
- Bleeding (1-2% polypectomy)
- Perforation (0.01-0.1%)
- Missed Lesions

Consequences of an inadequate bowel preparation

- Reduced detection of polyps, adenomas and advanced adenomas
- Prolonged procedure time
- Decreased cecal intubation rates
- Repeat procedures \(\rightarrow\) increased costs to health care system, inconvenience for patients
Types of Bowel Preps (UCSF)

- Isosmotic Full Volume Preps (GoLYTELY)
  - Other brands include Colyte, TriLyte, NyLYTELY
- Isosmotic Low Volume Preps (MoviPrep)
  - Other brands include HalfLYTELY
- Hyper Osmotic Preps (OsmoPrep)
  - Other brands include LoSo Prep, Suprep
- Split Dose Preps (not used at UCSF) but recommended by ACG

Full Volume Preps

- GoLYTELY
- 8 oz every 10 minutes beginning at 5 or 6 pm evening prior to colonoscopy
- Total volume is 4 Liters!
Low Volume Preps

- MoviPrep (Salix Pharm)
  - 240 ml (8 oz) every 15 minutes at 5 to 6 pm evening before colonoscopy (1 Liter). Follow with at least 16 oz fluid
  - 240 ml (8 oz) every 15 minutes at least 3 to 4 hrs before colonoscopy (1 Liter) followed by 16 oz fluid

Hyperosmotic Preps

- Osmo Prep (Salix; Na P tablets)
  - 20 tablets (4 q15 min) at 5 to 6 pm evening before colonoscopy
  - Repeat with 12 tablets 10-12 hours later at least 3 hours before colonoscopy
Hyperosmotic Preps

- Fleet’s Phospho-soda withdrawn from market in 2008
- Rare but potentially irreversible acute phosphate nephrotoxicity
- Risk Factors: increased age, hypovolemia, acute colitis, kidney disease, ACEIs, ARBs, diuretics, NSAIDS
- BLACK BOX WARNING ON OSMOPREP

Split Preps

- Usually ½ taken the evening prior and the remainder morning of procedure
- Colonoscopy should be performed within 8 hours of last dosing (so for an AM procedure, 2\textsuperscript{nd} dose @ 2 AM)
- More effective and better tolerated than full dose PM
- Associated with
  - Better preparation
  - Less likely to discontinue prep
  - Reduced nausea
  - Willingness to repeat same prep
Split Preps

- Barriers
  - Needing to wake up in the middle of the night
  - Ongoing bowel activity in transit
  - Aspiration risk with sedation

Second Attempt Prep

- No clear guidelines
- Discontinue high residue foods at least 3 days before (corn, seeds, nuts, salads, high fiber foods)
- 2 days of clear liquids/8 L of PEG
- Mg Citrate at 12 pm, 10 mg Bisacodyl at 3 pm, 10 mg Metoclopramide, 4L split dosing
- Warning: Aggressive bowel preparation may lead to electrolyte disturbances and renal dysfunction in certain high risk patients
Summary

- CRC is among the leading causes of death among men and women in the US
- Screening is necessary to (and effective in) prevent CRC
- Options for colorectal cancer screening → Most roads ultimately lead to colonoscopy
- Colonoscopy surveillance guidelines
- Limitations to colonoscopy
- Factors that we can improve upon, including patient understanding of what to expect, risk/benefit, and bowel preparation

Thank you!! Questions?