Lecture #16
Title of Lecture ................. The Colon Cancer Problem, Early Diagnosis is the Key to Prevention: An Update Diagnostic and Therapeutic Considerations

Name ............................. Benjamin Krevsky, M.D., M.P.H.

OBJECTIVES
Following the completion of this lecture, participants should be able to:

1. Determine who in their practice needs screening for colorectal cancer.
2. Work with patients to help them decide the best screening technique.
3. Work with gastroenterologist, surgeon, and oncologist to optimize patient care.

EVIDENCE BASED RECOMMENDATIONS

1. Any colorectal cancer screening is better than none.
2. Colonoscopy is the most sensitive method for colorectal cancer screening, and permits therapeutics.
3. African American patients of average risk should start screening at a younger age (45 yo).
4. Chemotherapy can increase 5-year survival by 16%.

References:


The Colorectal Cancer Problem
Early Diagnosis is the Key to Prevention: An Update – Diagnostic and Therapeutic Considerations
Benjamin Krevsky, MD, MPH

Professor of Medicine
Director of Gastrointestinal Endoscopy
Temple University School of Medicine

Hirschowitz Fiberscope, 1960

Moderate (Conscious) Sedation
The Colorectal Cancer Problem
Early Diagnosis is the Key to Prevention: An Update – Diagnostic and Therapeutic Considerations
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Colorectal Cancer: Epidemiology

- Prevalent: 145,290 new cases diagnosed annually in US
  - Second leading cause of cancer mortality
  - 5% lifetime risk
- Deadly: 56,290 annual deaths
- Expensive: One of most expensive cancers to treat
- Treatable: 90% survival rate when detected early


Natural History: A Typical Case

10+ years

Normal → Adenoma → Carcinoma

~25% of the general population have polyps by age 50 years

Age-Specific Incidence of Colorectal Cancer in US (2000)

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Classification System of CRC


Early Detection Saves Lives

5-Year Survival Rates for Patients With Colorectal Cancer


Fecal Occult Blood Testing

Pros
• Evidence base is from randomized, controlled trials
• Non-invasive
• No bowel preparation required
• Readily performed by primary care practitioners
• Cost-effectiveness established

Cons
• Limited effectiveness
• Requires annual testing
• Patient resistance to handling stool
• Diet restrictions used in some practices
• False positives

Rex DK. Rev Gastroenterol Disord. 2002;2:82.
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Screening With Rigid Sigmoidoscopy

- Reduced risk of death from CRC by 59% for cancers in reach of the sigmoidoscope


Flexible Sigmoidoscopy

**Pros**
- Office-based procedure
- More practitioners trained than for colonoscopy
- More effective than FOBT
- Does not require sedation
- Preparation easier than for colonoscopy

**Cons**
- Patient discomfort
- Less effective than colonoscopy
- Preparation, expertise: limit insertion
- Perforation risk (1:10,000)


Double-Contrast Barium Enema

**Pros**
- Full colon evaluation
- Low risk
- Inexpensive

**Cons**
- Poor sensitivity vs. endoscopy
- Poor patient tolerance
- No data; only SCBE study
- Optimal screening interval unknown
- Radiologist expertise declining
- Same-day colonoscopy not possible

### The Colorectal Cancer Problem

*Early Diagnosis is the Key to Prevention: An Update – Diagnostic and Therapeutic Considerations*

**Benjamin Krevsky, MD, MPH**

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#### Colonoscopy

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most accurate test for detection of polyps and cancers (sensitivity: ~90%–95%)</td>
<td>• Highest “relative risk”</td>
</tr>
<tr>
<td>• Diagnostic and therapeutic</td>
<td>– Diagnostic perforation risk = 0.03%–0.61%&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Longest protective interval</td>
<td>– Therapeutic perforation risk = 0.07%–0.72%&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Reduced CRC mortality (indirect evidence)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Highest upfront cost</td>
</tr>
<tr>
<td>• Better patient satisfaction than with sigmoidoscopy</td>
<td>• Compliance Issues</td>
</tr>
<tr>
<td></td>
<td>– Patient limitation of activities (bowel preparation, medications, and time)</td>
</tr>
<tr>
<td></td>
<td>• Detection Limitations</td>
</tr>
<tr>
<td></td>
<td>– May miss interval cancers, flat lesions, and lesions obscured by suboptimal bowel preparation</td>
</tr>
</tbody>
</table>


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#### High Definition Endoscopy

- Uses HD scopes and monitors for greater resolution and field of view
- Narrow Band Imaging may permit “optical biopsy”

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#### Snare Polypectomy
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Polypectomy Significantly Reduced  
Expected Rates of Colorectal Cancer

![Chart showing observed and expected rates of colorectal cancer](image)

- Patients tested a mean of 5.9 years after polypectomy
- Reduced incidence by 76, 88, and 96% (P < 0.001)


Novel Screening Strategies  
Virtual Colonoscopy (CT colonography)

- 94% sensitive for detecting polyps ≥ 8mm (1233 participants screened)¹  
  - Sensitivity comparable with optical colonoscopy
- 55% sensitive for detecting polyps ≥ 10mm (615 participants screened)²  
  - Significantly lower sensitivity compared with conventional colonoscopy


Virtual Colonoscopy

**Pros**  
- Some studies show adequate sensitivity for polyps >1 cm  
- Low risk of perforation (1:25,000)  
- Same-day colonoscopy potential (to avoid back-to-back bowel preparation)  
- Extracolonic findings possible

**Cons**  
- Requires bowel preparation  
- Most expensive diagnosis-only strategy  
- High rate of false positives  
- Mixed results (vary by site)  
- Radiation exposure  
- Cost-effectiveness not established  
- Acceptability results variable (less than colonoscopy)

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Novel Screening Strategies:
Stool-Based DNA Screening

Pros
- “Total colon” examination
- Non-invasive, safe
- No bowel preparation
- Convenient (single sample collected at home)

Cons
- Less effective than colonoscopy

Capsule Endoscopy

Risk Factors for Colorectal Cancer

Average Risk
- Age ≥ 50 years; asymptomatic

High Risk
- Personal history of CRC or adenomas
- Family history of CRC or adenomas
- Genetic syndromes
  - Familial adenomatous polyposis (FAP)
  - Hereditary nonpolyposis CRC (HNPPC)
- Inflammatory bowel disease

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Recommended CRC Screening Strategies:
Average Risk
(ACS, ACG, AGA Guidelines)

Options Beginning at Age 50 Years
• Annual fecal occult blood testing (FOBT)
• Flexible sigmoidoscopy (FS) every 5 years
• Annual FOBT plus FS every 5 years
• Double-contrast barium enema (DCBE) every 5 years
• Colonoscopy every 10 years

Digital rectal examination is not an appropriate CRC screening method.

A Change In The Guidelines!

• CRC in African Americans > whites
• Mean age at dx is younger in African Americans
• Increased proximal distribution in African Americans

American College of Gastroenterology recommends starting screening at age 45 with colonoscopy
Agrawal, S. Am J Gastroenterol 2005;100:515-523

Recommended CRC Screening Strategies:
Increased Risk

Family History of Polyps or CRC
• Beginning at Age 40 Years (or 10 yrs < index case): Colonoscopy every 5 years
FAP(+)
• Flex sig starting at age 10, colectomy when polyps found
HNPCC
• Colonoscopy every 2 yrs starting age 25, or 5 years < earliest age of diagnosis of CRC.
Annual screening after age 40
Gastrointest Endosc. 2000 Jun;51:777-782
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**Recommended CRC Screening Strategies:**

**Increased Risk**

**Personal Hx Colorectal Cancer**
Clearance of rest of colon around time of resection, followed by colonoscopy at 3 yrs (1 yr?), then 3-6 yrs.

**Personal Prior adenomas**
After clearance, colonoscopy at 3 – 6 yr interval

**Ulcerative Colitis or Crohn’s Colitis**
After 8 years, colonoscopy every 1 – 3 yrs with systematic biopsies for dysplasia

*Gastrointest Endosc. 2000 Jun;51:777-782*

**Cost of Colorectal Cancer Screening Compared to Other Medical Procedures**

<table>
<thead>
<tr>
<th>Screening Method</th>
<th>Cost per life year saved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopy every 10 years</td>
<td>$6,600</td>
</tr>
<tr>
<td>Breast cancer screening</td>
<td>$22,000</td>
</tr>
<tr>
<td>Heart transplantation</td>
<td>$160,000</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>$250,000</td>
</tr>
</tbody>
</table>

*Colon cancer screening from age 55 is cost effective, but depends on compliance.*


**Summary of Post-Polypectomy Guidelines (ACG & AGA)**

- **1 or 2 tubular adenomas <1 cm**  →  5 years
- **>2 adenomas, HG dysplasia, >1 cm or villous**  →  3 years
- **Negative f/u**  →  5 years
- **Large sessile polyps >2 cm**  →  3 – 6 months
- **Malignant polyps**  →  3 months
- **Hyperplastic polyps**  →  10 years

*Gastrointest Endosc 2006;63:99*
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Primary Prevention of Colorectal Cancer
• Exercise
• Low-fat diet rich in fruits and vegetables
• Fiber?
• Chemoprophylaxis
  – NSAIDs (e.g. Celebrex®)
  – Calcium
  – Estrogen
  – Folate
  – Selenium

CDC. A Call to Action: Prevention and Early Detection of Colorectal Cancer.

Diagnosis and Staging
• Symptoms: fatigue, anemia, weight loss, obstruction
• 5% synchronous cancers, 30% synchronous polyps
• Imaging: CT, MRI, PET, intraoperative U/S
• Tumor size is not as important as depth of invasion and nodal status

Colon Cancer Surgery
• Can be curative
• Node positive?
• Obstruction
• Adjacent organs
• Laparoscopic
  – Earlier recovery
  – Fewer complications
  – Long learning curve

Right Hemicolecotmy
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Surveillance

• Fewer than 5% of recurrences after 5 yrs
• Recurrent disease is often resectable – 35% is curable
• Surveillance program:
  – Physician exam every 3 mos X 2 yrs
  – CEA and LFTs every 3 mos
  – Colonoscopy at 1 year and every 3 – 5 yrs afterwards if normal.
  – CT scan every 3 – 4 months

Adjuvant Therapy

• 50 – 60% of pts have micrometastatic disease post-op
• Chemo is given in effort to clear the micrometastatic disease (5-FU + leukovorin). Can increase 5-year survival by 16%
• Recommended for 6 months

Management of Metastases

• Surgical resection
• Chemotherapy
  – 5-FU + Leukovorin
  – Combinations with irinotecan or oxalplatin
  – Investigational protocols
• Radiation Therapy

Temple’s new linear accelerator
New Therapies & Combinations

• Bevacizumab – monoclonal antibody against vascular endothelial growth factor receptor in colon cancer
  – Improved median survival
• Cetuximab – monoclonal antibody against epidermal growth factor receptor
  – Higher response rate
  – Longer time to treatment failure
  – No improvement in median survival

5 Key Messages

• Screening reduces mortality from CRC
• Average risk persons aged ≥ 50 years should begin regular screening (≥ 45 if AA)
• Any screening test is better than no screening test
• Colorectal cancer can be prevented
• Aggressive therapy can be successful