SCREENING FOR COLON CANCER

By:
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I don’t represent or receive any sort of compensation from any anyone other than my employer

I am employed by Ivinson Memorial Hospital

I am paid a fixed salary

I regularly perform colonoscopy for screening

I am biased toward colonoscopy as the “best” form of colorectal cancer screening

I do not get paid more/less to perform or recommend colonoscopy or any other screening method
4th most commonly diagnosed cancer in US
Over 145,000 new cases of colorectal cancer to be diagnosed in 2019
Over 51,000 people will die from colorectal cancer in 2019
2nd leading cause of cancer deaths

1 in 20 people will get colorectal cancer (almost 5% of men and women)
5 year survival = 64.4% (all stages)
Stage 1 and 2 survival is 90%
Only 40% are diagnosed at stage 1/2
22% diagnosed at stage 4 (14.2% survival)

Scope of the Problem

- 1 in 3 people are NOT current with CRC screening
  - Over 30 million people between 50-75 years old
- 60% of deaths due to CRC could be prevented with adequate screening
- Incidence increasing in those <50yo in western countries
  - 1/10 colon cancers and almost 1/5 rectal cancers diagnosed <50yo
- ACS now recommends starting screening at 45yo

Colon and rectal cancer and polyps

For people at average risk for colorectal cancer, the American Cancer Society recommends starting regular screening at age 45. This can be done either with a sensitive test that looks for signs of cancer in a person's stool (a stool-based test), or with an exam that looks at the colon and rectum (a visual exam). Talk to your health care provider about which tests might be good.
Incidence of colorectal cancer is decreasing
Deaths from colorectal cancer are decreasing
5 year survival is improving


SEER 9.5-Year Relative Survival Percent from 1975-2011, All Races, Both Sexes. Modeled trend lines were calculated from the underlying rates using the Joinpoint Survival Model Software.
Risk Factors

- Age 50 and over
- Personal history of colorectal polyps or cancer
- Personal history of inflammatory bowel disease (ulcerative colitis or Crohn’s disease)
- Family history of colorectal cancer
- Family history of inherited polyposis or Lynch syndromes
- African American ethnicity
- Jews of Eastern European descent (Ashkenazi Jews)
- Type 2 Diabetes
- Diets high in red meats and low in fruits, vegetables, and whole grains
- Sedentary lifestyle
- Obesity
- Tobacco
- Heavy alcohol use
What Causes Colorectal Cancer?

- All cancer is due to Genetic Mutations
  - Acquired
  - Inherited
- Mutations in tumor suppressor genes lead to loss in control of cell growth and division
- Mutations in ProtoOncogenes convert the genes into Oncogenes and promote cell growth and division
Multi-Hit Principle

Tumors Are Clonal

Two-Hit Hypothesis
- No cancer
- Cancer
- Germline mutation
- Somatic mutation
- If first hit is a germline mutation, second somatic mutation more likely to enable cancer

Mutations in Tumor Suppressor Genes
- Normal genes (regulate cell growth)
- Tumor suppressor genes
- 1st mutation (susceptible carrier)
- 2nd mutation or loss (leads to cancer)
- No brakes!
- Active oncogene
Multiple mutations in multiple genes are required to cause colorectal cancer.
- Most mutations acquired
- Some congenital
  - Family h/o CRC
- 10 years from polyp to cancer
- Give us time to prevent CRC by removing polyps
Without Screening

- Wait for symptoms
  - Pain, rectal bleeding, obstruction, unexplained weight loss
- Cancer is advanced at time of diagnosis
Approaches to Screening

- Programmatic Screening
  - System-wide (National HealthCare Systems)
  - More organized
  - Better at tracking system-wide data

- Opportunistic Screening
  - PCP or other providers discusses screening with patient during routine visit
  - Less organized
Mostly opportunistic

World’s highest rates of CRC screening

- 60% of eligible population

Greatest reduction in CRC incidence and mortality in the world

Due to widespread awareness and legislation (insurance coverage)

Still, over 30% who should be getting screened are not
## Principals of Widespread Screening

- Disease being screened for should be common in the population
- Screening test should be effective and accurate (sensitive and specific)
- Screening test should be safe
- Should be able to intervene and improve outcomes based on the screening test results
- Screening test should be “relatively inexpensive”
Screening Tests

- Stool-based tests
- Imaging
- Endoscopic
Stool Based Tests

- gFOBT
- FIT-FOBT
- DNA-based testing (Cologuard)
Guaiac FOBT

- Looks for blood (heme) in stool
- Guaiac paper
  - Plant-based phenolic compound, alpha-guaiaconic acid
  - From the wood resin of the Guaiacum tree
- Application of hydrogen peroxide to the guaiac paper creates a blue reaction product
- Heme from blood catalyzes this reaction
Guaiac FOBT

- Advantages
  - Cheap ($3-20)
  - Easy
  - Stool sample can be collected at home
  - Non-invasive/no sedation
  - No bowel prep
  - Widespread use can lead to improved detection of CRC
Disadvantages

- Poor specificity
  - Detects blood in the stool from any source in GI tract
  - Bloody noses, PUD, bleeding gums, hemorrhoids, etc
  - Detects only intact heme, not other hemoglobin breakdown products
- False positives due to food
  - Red meat, cantaloupe, uncooked broccoli, turnips, radish, horseradish
  - NSAIDS, vitamin C can also lead to false positive results
  - These restrictions can act as a barrier to participation
- High false negative rate (30-50% sensitivity)
- Needs to be done annually
- Requires 3 samples
- Positive result = Colonoscopy
- Patient pays more out of pocket for subsequent colonoscopy
- Diagnostic vs screening
Fecal Immunochemical Test (FIT)

- Antibodies specific to globin moiety of human hemoglobin

- Qualitative = point of care
  - Differ in sensitivity/specificity by manufacturer

- Quantitative = laboratory based
  - Can adjust sensitivity/specificity
FIT

- Advantages
  - Cheap ($20-40)
  - Easy
  - Stool sample can be collected at home
  - Non-invasive/no sedation
  - No bowel prep
  - Widespread use can lead to improved detection of CRC
  - No pretest diet or medication changes
  - Requires only 1 stool sample
  - Better patient compliance/participation
Disadvantages

- Poor specificity (better than guaiac FOBT)
  - Detects blood coming from anywhere in GI tract
- Limited sensitivity (75%)
  - Will miss polyps or early cancers if no blood is being shed in to fecal stream
- Needs to be done annually
- Positive result = Colonoscopy
- Patient pays more for subsequent colonoscopy
  - Diagnostic vs screening colonoscopy
FIT-Fecal DNA

- Cologuard is the only commercially available test currently
- Detects DNA in fecal stream
  - Specifically looks for mutations in APC, K-ras, P53 genes and others
FIT-Fecal DNA

- Advantages
  - Fairly easy
  - Stool sample can be collected at home
  - Non-invasive/no sedation
  - No bowel prep
  - No dietary or medication changes
  - Complete every 3 years
FIT-Fecal DNA

- Disadvantages
  - More expensive ($500-900)
  - Patient has to collect entire BM
  - Will miss many polyps and some cancers (false negatives)
  - High rate of false positive rates
    - More subsequent colonoscopies needed
    - Potential for higher overall costs
  - Positive result = colonoscopy
  - Patient pays more for subsequent colonoscopy
    - Diagnostic vs screening
Imaging Based Tests

- Double Contrast Barium Enema
- CT Colonography
Double Contrast Barium Enema

- Contrast injected into rectum and forced into colon with hydrostatic pressure
- Requires bowel prep
- Does not require sedation
- Suitable for patients who choose not to have colonoscopy or cannot medically tolerate a colonoscopy
Double Contrast Barium Enema

- Will miss small (<1cm) polyps
- Will require colonoscopy if a tumor or polyp is found
- Can complete screening of right colon if colonoscopy incomplete
- Costs $250-1000
- Should be completed every 5 years
CT Colonography

- Requires bowel prep
- Does not require sedation
- Non-invasive
- Costs $500-2000
- Will require colonoscopy if any abnormalities are found
- Not available everywhere
- Should be completed every 5 years
Flexible Sigmoidoscopy

- Requires minimal bowel prep (enema)
- No sedation
- Only able to look at left colon and rectum
- Costs $800-2000
- Will need colonoscopy if polyps or tumor found
- Should be completed every 5 years
Colonoscopy

- 15,000,000/year in US
- Requires bowel prep
- Requires sedation (in most cases)
- Very small risk of colon perforation
  - 0.03-7%
- Looks at entire colon (in most cases)
Can perform intervention such as biopsy or polyp removal

Highest sensitivity and specificity of all screening modalities (Gold Standard)

Costs $1000-3000

Should be completed every 10 years for average risk individuals

Every 5 years in those with FH CRC or h/o polyps
# Summary of Options

## Table 1. Testing Options for the Early Detection of Colorectal Cancer and Adenomatous Polyps for Asymptomatic Adults Aged 50 Years and Older

<table>
<thead>
<tr>
<th>Tests that detect adenomatous polyps and cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSIG every 5 years, or</td>
</tr>
<tr>
<td>CSPY every 10 years, or</td>
</tr>
<tr>
<td>DCBE every 5 years, or</td>
</tr>
<tr>
<td>CTC every 5 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tests that primarily detect cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual gFOBT with high test sensitivity for cancer, or</td>
</tr>
<tr>
<td>Annual FIT with high test sensitivity for cancer, or</td>
</tr>
<tr>
<td>sDNA, with high sensitivity for cancer, interval uncertain</td>
</tr>
</tbody>
</table>
Harms, benefits and costs of fecal immunochemical testing versus guaiac fecal occult blood testing for colorectal cancer screening

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Table 1. Test characteristics of the screening tests used in the model.

<table>
<thead>
<tr>
<th>Screen test</th>
<th>Specificity (%)</th>
<th>Adenoma</th>
<th>Sensitivity * (%)</th>
<th>CRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>gFOBT</td>
<td>98</td>
<td>2</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>FIT 50</td>
<td>96</td>
<td>4</td>
<td>15</td>
<td>52</td>
</tr>
<tr>
<td>FIT 75</td>
<td>97</td>
<td>3</td>
<td>9</td>
<td>48</td>
</tr>
<tr>
<td>FIT 100</td>
<td>98</td>
<td>2</td>
<td>7</td>
<td>43</td>
</tr>
<tr>
<td>FIT 150</td>
<td>98</td>
<td>2</td>
<td>5</td>
<td>41</td>
</tr>
<tr>
<td>FIT 200</td>
<td>99</td>
<td>1</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>Colonoscopy‡</td>
<td>90</td>
<td>75</td>
<td>85</td>
<td>95</td>
</tr>
</tbody>
</table>

CRC, colorectal cancer; gFOBT, guaiac fecal occult blood test; FIT, fecal immunochemical test.

* Sensitivity is presented per participant for fecal occult blood tests and per lesion for colonoscopy.
† It was assumed that the probability a CRC bleeds and thus the sensitivity of gFOBT and FIT for CRC depend on the time to clinical diagnosis, based on a prior calibration of the MISCAN-Colon model to three gFOBT trials. This result is to be expected when cancers that bleed do so increasingly over time, starting in occult fashion and progressing to grossly visible bleeding.
‡ Colonoscopy was only used during follow-up and surveillance after a positive gFOBT or FIT. The lack of specificity of colonoscopy reflects the detection of hyperplastic polyps, which are not explicitly simulated by the MISCAN-Colon model. Additional biopsy costs were assumed for procedures where biopsies were performed and in which, in retrospect, no adenomas were detected.
FIT vs gFOBT

Fig. 1
Reported sensitivity and specificity for CRC of a range of gFOBT [27–28]

Fig. 4
Reported sensitivity and specificity for CRC of a range of FIT [38, 40, 48, 54, 55, 59–66]
Comparative Costs

- Fecal occult blood test: $3 to $40
- Fecal DNA testing: $400 to $800
- Double-contrast barium enema: $200 to $1,000
- Virtual colonoscopy: $750 to $2,000
- Sigmoidoscopy: $2,000 to $3,750
- Conventional colonoscopy: $2,000 to $3,750
Widespread colorectal cancer screening programs reduce the incidence and mortality from CRC

CRC screening is safe and effective

Offer CRC screening to your patients who are 50 years old or 10 years earlier than when relative was diagnosed, whichever is earlier

Future=45 years old?
Conclusions

- Start by recommending colonoscopy
- Recommend stool based screening (FIT or Cologuard) if patient will not get colonoscopy
  - Will need colonoscopy if positive
  - Insurance often covers less of colonoscopy as secondary test
    - Diagnostic vs screening
- The current “gold-standard” method is colonoscopy
Final Thoughts

- Have a well-developed CRC screening program in your clinic
- ANY CRC screening program is better than NO CRC screening program
  - Some are better than others
    - FIT is better than gFOBT
- Religiously screen your patients for
  - Eligibility for CRC screening
  - High risk or average risk
  - Up to date with CRC screening
CRC screening options do not apply to any patient at elevated risk of CRC due to family history, IBD, HNPCC, APC, h/o polyps, etc.

Patients at elevated risk of getting CRC **REQUIRE** a colonoscopy for adequate surveillance/screening
3 “best” options:

1. Recommend colonoscopy for everyone but use FIT or Cologuard testing for those that do not wish to start with colonoscopy (explain insurance implications if diagnostic colonoscopy needed)

2. Recommend FIT or Cologuard testing but explain the weaknesses in these screening modalities and explain insurance implications if they need subsequent diagnostic colonoscopy for positive results

3. Discuss Colonoscopy, FIT, and Cologuard on equal terms but explain the benefits and drawbacks of each as well as insurance implications of secondary diagnostic colonoscopy, if needed, and let the patient decide
Questions?