Colon Cancer

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Background

• 2nd overall leading cause of cancer death in the United States
  – 3rd in each sex
• Approximately 6% of individuals in the US will develop a cancer of the colon or rectum within their lifetime
• 944,717 incident cases worldwide in 2000
Definition

- Colorectal Cancer is the cancer affecting caecum, colon and rectum.
- Anal canal and Appendix are not considered in the definition, and are treated as separate entities.

Anatomic Distribution

- Incidence rates for colorectal cancer differ by sub-sites.
Histopathology

- Vast majority of colorectal cancers are adenocarcinomas, which are preceded by adenomas or adenomatous polyps in most cases
- Only around 10% of adenomas will develop into cancers, a process that takes at least 10 years

Mortality and Incidence in the United States

- 147,500 colorectal cancer cases in 2003
  - 105,500 colon
  - 42,00 rectum
- 57,100 deaths from colorectal cancer
Incidence

- SECOND most common cause of Cancer related deaths in North America
- Estimated new cases and deaths from colon and rectal cancer in the United States in 2009*
  
  - New cases: 106,100 (colon); 40,870 (rectal)
  - Deaths: 49,920 (colon and rectal combined)

*Source – National Cancer Institute
Cancer Related Mortality

- Overall 5 year survival rate is 61.9%
  - Differs by race, age, and distribution of disease
- Survival rates are lower among blacks than whites
  - 52.8% vs. 62.6%
- Survival rates are highest for localized cancers
**Age**

- Incidence rates start to increase after age 35 with a rapid increase after age 50, when more than 90% of colorectal cancers develop

**Gender**

- Overall age-standardized incidence rates were 65.1 per 100,000 for men and 47.6 per 100,000 for women
  - Male-female ratio=1.37
- Mortality rates were also higher in men than women
  - 25.4 versus 18.0 per 100,000
• Race and Ethnicity
  – Higher rates and mortalities among blacks than whites

• Socioeconomic status
  – Possible association between low SES and colorectal cancer mortality

• Fruit, Vegetables, and Fiber
  – Majority of case-control studies have shown an association between higher intake of vegetables and lower cancer risk
  – Recent large cohort studies have shown weak or non-existent association between fiber and colon cancer risk

• Folate
  – Higher intake of folate has been relatively consistently associated with lower colon cancer risk
Lifestyle Factors - Nutrition

• Calcium
  – Avoidance of low intakes of calcium may minimize risk of colon cancer

• Fat, Carbohydrates, and Proteins
  – Excess energy intake leading to obesity increases the risk of colon cancer
  – Possible association of red meat with increased risk

Lifestyle Factors - BMI

• Higher BMI is associated with an increased risk of colon cancer
  – Approximately twofold higher risk in individuals who are overweight or obese
Lifestyle Factors- Physical Activity

- Individuals who are more physically active have a decreased risk of colon cancer
- Some benefits appear to be independent of BMI
  - Studies have shown dose-response relationship between physical activity and colorectal cancer
  - Highest risk observed in persons who are both physically inactive and have high BMIs

Lifestyle Factors-Other

- Alcohol
  - Somewhat controversial, but appears that high alcohol intake increases risk
- Tobacco
  - Most studies indicate excess risk in smokers
High Risk Factors

- Familial Adenomatous Polyposis
- Hereditary Non Poliposis Colon Cancer
- Family history of Colo Rectal Carcinoma
- Previous Colo Rectal CA, Ovarian, Endometrial, Breast CA
- Age >50
- Inflammatory Bowel Disease (UC > CD)
- Poor Diet (increased fat, red meat, decreased fibre)
- Smoking
- Diabetes mellitus & Acromegaly
- Streptococcus Bovis Bacteremia?
- Ureterosigmoidostomy?

Genetic Susceptibility Syndromes

- Familial Adenomatous Polyposis (FAP)
  - Rare, inherited, autosomal dominant syndrome
  - Causes occurrence of multiple colorectal adenomas in individuals in their 20s and 30s that untreated, will lead to cancer
- Hereditary Nonpolyposis Colorectal Cancer (HNPCC)
  - Autosomal dominant inherited disorder
Other Host Factors

• Family history of colorectal cancer
• History of adenomatous polyps
• Several low-penetrance genes
• Type 2 Diabetes
• Growth factors
  – High insulin-like growth factors
  – Hyperinsulinemia

Related Medical Conditions

• Inflammatory Bowel Disease
• Gallstones and Cholecystectomy
• Glucose Intolerance, Non-Insulin Dependent Diabetes Mellitus
• Acromegaly
Primary Prevention

• Prevention of smoking
• Prevention of weight gain
• Maintenance of a reasonable level of physical activity in adulthood
• Limit red and processed meats, high-fat dairy products, highly refined grains and starches, and sugars

Prevention

• Increase fibre in diet
• Decrease animal fat and red meat,
• Decrease smoking and EtOH
• Increase exercise and decrease BMI
• Secondary prevention with screening
Screening

- Early detection and removal of colorectal adenomas reduces risk of cancer
- Screening is recommended for adults beginning at age 50
  - Fecal occult blood test (FOBT) annually
  - Sigmoidoscopy every 5 years
  Or
  - Colonoscopy every 10 years
- For high risk individuals, screening should be tailored to their expected risk

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Distribution</th>
<th>Histology</th>
<th>Malignant Potential</th>
<th>Other Lesions</th>
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</thead>
<tbody>
<tr>
<td>Familial Adenomatous Polyposis</td>
<td>Large Intestine</td>
<td>Adenoma</td>
<td>Common</td>
<td>none</td>
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<td>Gardner Syndrome</td>
<td>Large and Small Intestine</td>
<td>Adenoma</td>
<td>Common</td>
<td>Multiple Malignancies</td>
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<td>Turcot Syndrome</td>
<td>Large Intestine</td>
<td>Adenoma</td>
<td>Common</td>
<td>Brain Tumors</td>
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<tr>
<td>Nonpolyposis Syndrome</td>
<td>Large Intestine</td>
<td>Adenoma</td>
<td>Common</td>
<td>Endometrial and Ovarian Tumors</td>
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<tr>
<td>Peutz Jegher's Syndrome</td>
<td>Small, Large Intestine, Stomach</td>
<td>Hamartoma</td>
<td>Rare</td>
<td>Multiple Malignancies</td>
</tr>
<tr>
<td>Juvenile Polyposis</td>
<td>Large and Small Intestine</td>
<td>Hamartoma</td>
<td>Rare</td>
<td>Congenital Anomalies</td>
</tr>
</tbody>
</table>
Genetic Changes in CRC

**GENETIC CHANGES**
- Activation of proto-oncogenes (K-ras)
- Loss of tumour-suppressor gene activity (APC, DCC)
- Abnormalities in DNA repair genes (hMSH2, hMLH1), especially HNPCC syndromes

**MECHANISM** - the mutational activation of an oncogene followed by and coupled with the loss of genes that normally suppress tumorigenesis

Colorectal Polyps

[Diagram of colon with colon polyps]
Screening Tools

Digital rectal exam (DRE): most common exam, but not recommended as a screening tool

Fecal occult blood test (FOBT):
- proper test requires 3 samples of stool
- still recommended annually by the World Health Organization (WHO)
- results in 16-33% reduction in mortality in RCTs
- Minnesota Colon Cancer Study: RCT showed that annual FOBT can decrease mortality rate by 1/3 in patients 50-80 years old

Sigmoidoscopy:
- can identify 30-60% of lesions
- sigmoidoscopy + FOBT misses 24% of colonic neoplasms
Screening Tools

Colonoscopy:
- can remove or biopsy lesions during procedure
- can identify proximal lesions missed by sigmoidoscopy
- used as follow-up to other tests if lesions found
- disadvantages: expensive, not always available, poor compliance, requires sedation, risk of perforation (0.2%)

Virtual colonoscopy: 91% sensitive, 17% false positive rate
Air contrast barium enema: 50% sensitive for large (>1 cm) adenomas, 39% for polyps
Carcinogenic embryonic antigen (CEA): to monitor for recurrence q3 months

Screening for Colorectal Cancer

- Average risk individuals, at age 50 (incl. those with <2 relatives with CRC) – recommendations are variable:

- American Gastroenterology Society and American Cancer Society - Yearly fecal occult blood test (FOBT), flexible sigmoidoscopy q5y, colonoscopy q10y
Screening for Colorectal Cancer

Family Hx (>2 relatives with CRC/adenoma, one being a 1st degree relative): start screening 10 years prior to the age of the relative’s age with the earliest onset of carcinoma

• FAP genetic testing +ve:
• yearly sigmoidoscopy starting at puberty (“B” recommendation)
• HNPCC genetic testing +ve:
• yearly colonoscopy starting at age 20 years

Investigations

• Colonoscopy (best), look for synchronous lesions -Alternative: air contrast barium enema (“apple core” lesion) + sigmoidoscopy
• If a patient is FOBT +ve, microcytic anemia or has a change in bowel habits, do colonoscopy
• Metastatic workup: CXR, abdominal CT/ultrasound
• Bone scan, CT head only if lesions suspected
• Labs: CBC, urinalysis, liver function tests, CEA (before surgery baseline)
Colonoscopy

Capsule (Colonoscopy)

Optical dome
Laser diode
Illuminating LEDs
Lens
Battery
Antenna

Standard colonoscopy showing inflammation around the taenial folds.
Capsule Endoscopy

Capsule Endoscopy
A capsule endoscopy is a small device that can be swallowed to examine the small intestine and other areas of the gastrointestinal tract. The capsule is equipped with a camera that transmits images to a computer where they can be viewed in real-time. The procedure typically takes about 8 hours to complete, during which the patient remains mobile and can continue with their normal activities. After 8 hours, the capsule is excreted and is not harmful. The procedure is comfortable and does not require any special preparation. It is often used to diagnose small bowel bleeding or other conditions that cannot be seen with traditional endoscopy. The capsule endoscopy is a non-invasive and minimally invasive procedure that provides detailed images of the small intestine and other areas of the gastrointestinal tract.
Virtual Endoscopy

Virtual Colonoscopy
Apple Core Lesion in Colorectal Cancer

Ulcerating Carcinoma
Clinical Features

- Often asymptomatic
- Hematochezia / melena, abdominal pain, change in bowel habits
- Weakness, anemia, weight loss, palpable mass, obstruction

Pattern of metastasis/spread
- Direct extension, lymphatic, hematogenous (liver most common, lung, rarely bone and brain)
- Peritoneal seeding: ovary, Blumer’s shelf (pelvic cul-de-sac)
- Intraluminal

Clinical Presentation

<table>
<thead>
<tr>
<th></th>
<th>Right Colon</th>
<th>Left Colon</th>
<th>Rectum</th>
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</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>25%</td>
<td>35%</td>
<td>30%</td>
</tr>
<tr>
<td>Pathology</td>
<td>Exophytic lesions with occult bleeding</td>
<td>Annular invasive lesions</td>
<td>Ulcerating lesions</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Weight loss, weakness, rarely obstruction</td>
<td>Constipation, alternating bowel patterns, abdominal pain, decreased stool caliber, rectal bleeding</td>
<td>Obstruction, tenesmus, bleeding</td>
</tr>
<tr>
<td>Signs</td>
<td>Fe-Deficiency Anemia</td>
<td>Bright Red Blood Per Rectum, Large Bowel Obstruction</td>
<td>Palpable mass on rectal exam. Bright Red Blood Per Rectum</td>
</tr>
</tbody>
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TNM Classification

<table>
<thead>
<tr>
<th>Primary Tumor</th>
<th>Regional Lymph Nodes</th>
<th>Distant Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0 No Primary Tumor</td>
<td>N0 No Regional LN</td>
<td>M0 No Metastasis</td>
</tr>
<tr>
<td>Tis CA in situ</td>
<td>N1 Metastasis in 1-3 pericolic nodes</td>
<td>M1 Distant Metastasis</td>
</tr>
<tr>
<td>T1 Invasion into submucosa</td>
<td>N2 Metastasis into 4 or more pericolic nodes</td>
<td></td>
</tr>
<tr>
<td>T2 Invasion into muscularis propria</td>
<td>N3 Metastasis into any nodes along the course of named vascular trunks</td>
<td></td>
</tr>
<tr>
<td>T3 Invasion into serosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4 Invasion into adjacent structures</td>
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Stages of Colorectal Cancer
Treatment

SURGERY
(indicated in potentially curable or symptomatic cases - not always in stage IV)
- Curative: wide resection of lesion (5 cm margins) with nodes and mesentery
- Palliative: if distant spread, then local control for hemorrhage or obstruction
- 80% of recurrences occur within 2 years of resection
- Improved survival if metastasis consists of solitary hepatic mass that is resected
Treatment

Colectomy:
- most patients get primary anastomosis (e.g. hemicolectomy, low anterior resection (LAR)

- if cancer is below levators in rectum, patient may require an abdominal perineal resection (APR) with a permanent end colostomy, especially if lesion involves the sphincter complex

- complications: anastomotic leak or stricture, recurrent disease, pelvic abscess, enterocutaneous fistula

RADIOTHERAPY & CHEMOTHERAPY
- Chemotherapy (5 FU based regimens): for patients with node-positive disease
- Radiation: for patients with node-positive or transmural rectal cancer (pre ±post-op), not effective in treatment of colon cancer
- Adjuvant therapy – chemotherapy (colon) and radiation (rectum)
- Palliative chemotherapy/radiation therapy for improvement in symptoms and survival
Local Excision, Resection Anastomosis

Resection and Colostomy
Case Finding

- Case finding for colorectal cancer (symptomatic or history of UC, polyps, or CRC)
- Surveillance (when polyps are found): colonoscopy within 3 years after initial finding
- Patients with past CRC: colonoscopy every 3-5 years, or more frequently
- IBD: some recommend colonoscopy every 1-2 years after 8 years of disease (especially UC)

Follow up

- Intensive follow up improves overall survival in good risk patients
- Currently there is no data suggesting optimal follow up
- Combination of periodic CT chest/abdo/pelvis, CEA and colonoscopy is recommended
Conclusions

• CRC is a leading cause of death
• Life style modification is important in preventing CRC
• Early stages are detectable and Screening can prevent CRC
• Advances in chemotherapy and targeted therapy doubled survival in last 10 years
• Case finding of familial colon cancer and intense monitoring is important

KP Souther California

“Goal of reducing mortality from colorectal cancer by 50% in next 10 years.”

Michael Kanter, MD