Colon Cancer

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03/10/2015

Epidemiology

- In the United States, CRC incidence rates have declined about 2 to 3 percent per year over the last 15 years
- Death rates from CRC have declined progressively since the mid-1980s in the United States
- The lifetime incidence of CRC in patients at average risk is about 5 percent, with 90 percent of cases occurring after age 50

Risk Factors that alter screening recommendations

- Hereditary CRC syndromes:
- Familial adenomatous polyposis (FAP)
- Lynch Syndrome: is an autosomal dominant syndrome, which is more common than FAP, and accounts for approximately 3 to 5 percent of all colonic adenocarcinomas
- Personal or family history of sporadic CRCs or adenomatous polyps
- Ulcerative colitis/Crohn's disease
- Abdominal radiation especially in childhood malignancies

Risk factors that do not alter screening recommendations

- Diabetes mellitus and insulin resistance
- Use of androgen deprivation
- Cholecystectomy
- Alcohol abuse
- Obesity

Protective factors

- Regular physical activity
- Diet: Fiber, resistant starch, folic acid and folate, calcium and dairy products,Pyridoxine, Vitamin D and fish
- Drugs: ASA, postmenopausal hormone therapy, Statins, antioxidants, bisphosphonates,

Clinical Presentation

Frequency and duration of symptoms and signs in a series of 194 consecutive colorectal cancers

Variable	N (percent)	Median duration in weeks (25 to 75 percent)*
Fecal occult blood test positive	149 (77)	2 (1 to 7)
Rectal bleeding	113 (58)	8 (3 to 19)
Anemia•	110 (57)	2 (1 to 5)
Abdominal pain	100 (52)	8 (3 to 20)
Weight loss	76 (39)	27 (9 to 42)
Anorexia	53 (27)	9 (4 to 24)
Constipation	53 (27)	10 (3 to 20)
Altered stools	48 (25)	9 (4 to 19)
Fatigue	49 (25)	14 (5 to 27)
Diarrhea	43 (22)	5 (3 to 15)
Nausea or vomiting	42 (22)	2 (1 to 5)
Tenesmus	16 (8)	5 (4 to 21)
Mucus in stools	12 (6)	12 (6 to 28)
Rectal pain	10 (5)	14 (10 to 22)
Obstruction	7 (4)	1 (1 to 4)

* Interquartile range.
• Anemia: a homoglobin of <13.4 g/dL (male) and <12.3 g/dL (female).

Diagnosis

- Colonoscopy
- Flexible sigmoidoscopy(inadequate)
- Barium enema
- CT colonography
- PiLLCAM: Capsule colonoscopy(when colonoscopy not complete)

Staging studies

- CT Abdomen and pelvis
- Chest imaging
- PET scans(does not add benefit)

TNM staging for colorectal cancer, 7th edition

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria*
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into pericolorectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum¶
T4b	Tumor directly invades or is adherent to other organs or structures¶Δ
Regional lymph node (N)◇	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1–3 regional lymph nodes
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2–3 regional lymph nodes
N1c	Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in four or more regional lymph nodes
N2a	Metastasis in 4–6 regional lymph nodes
N2b	Metastasis in seven or more regional lymph nodes
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (eg, liver, lung, ovary, nonregional node)
M1b	Metastasis in more than one organ/site or the peritoneum

Anatomic stage/prognostic groups§

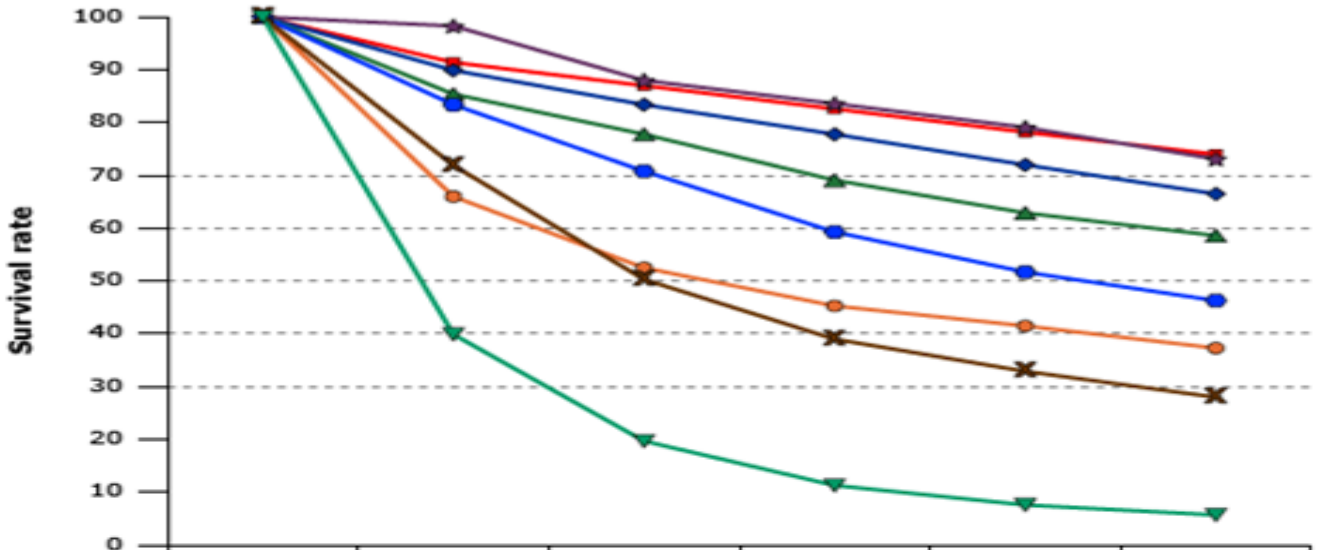
Stage	T	N	M	Dukes¥	MAC¥
0	Tis	N0	M0	-	-
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1–2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3–T4a	N1/N1c	M0	C	C2
	T2–T3	N2a	M0	C	C1/C2
	T1–T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3–T4a	N2b	M0	C	C2
	T4b	N1–N2	M0	C	C3
IVA	Any T	Any N	M1a	-	-
IVB	Any T	Any N	M1b	-	-

* Tis includes cancer cells confined within the glandular basement membrane (intraepithelial) or mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.
¶ Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina).
Δ Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1–4a depending on the anatomical depth of wall invasion. The V and L classifications should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN site-specific factor should be used for perineural invasion.
◇ A satellite peritumoral nodule in the pericolorectal adipose tissue of a primary carcinoma without histologic evidence of residual lymph node in the nodule may represent discontinuous spread, venous invasion with extravascular spread (V1/2), or a totally replaced lymph node (N1/2). Replaced nodes should be counted separately as positive nodes in the N category, whereas discontinuous spread or venous invasion should be classified and counted in the Site-Specific Factor category Tumor Deposits (TD).
§ cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pretreatment (eg, ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).
¥ Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any TN1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.

Major prognostic indicators

- Extent of invasion
- Lymph node involvement
- Mesenteric nodules
- Nodal micrometastatic disease
- Vascular invasion
- Residual tumor
- Other factors are like microsatellite instability may influence outcome, tumor grade,margins, focal neuro-endocrine involvement

Observed survival rates for 28,491 cases with adenocarcinoma of the colon



	0	1	2	3	4	5
I	100.0	91.4	87.0	82.6	78.2	74.0
IIA	100.0	89.9	83.4	77.8	72.0	66.5
IIB	100.0	85.4	77.8	69.1	62.9	58.6
IIC	100.0	66.0	52.5	45.3	41.5	37.3
IIIA	100.0	98.3	88.0	83.6	79.1	73.1
IIIB	100.0	83.4	70.8	59.3	51.7	46.3
IIIC	100.0	71.9	50.3	39.0	32.9	28.0
IV	100.0	39.9	19.7	11.3	7.6	5.7

Years from diagnosis

Data from the SEER 1973-2005 Public Use File diagnosed in years 1998-2000. Stage I includes 7417; Stage IIA, 9956; Stage IIB, 997; Stage IIC, 725; Stage IIIA, 868; Stage IIIB, 1492; Stage IIIC, 2000; and Stage IV, 5036.

Treatment

- Surgical resection
- Pathologic staging
- Adjuvant treatment after curative resection: the goal of postoperative (adjuvant) chemotherapy is to eradicate micrometastases, thereby reducing the likelihood of disease recurrence and increasing the cure rate.
- The benefits of adjuvant chemotherapy have been most clearly demonstrated in patients with stage III (node-positive) disease, who have an approximately 30 percent reduction in the risk of disease recurrence and a 22 to 32 percent reduction in mortality with modern chemotherapy.

Adjuvant treatment

- Stage I: No further treatment is recommended after complete surgical resection
- Stage III: Node positive disease adjuvant treatment is recommended
- Chemotherapy recommended: Oxalipatin based regimen(Folfox, Xelox), 5 FU and leucovorin, Capcitabine

Stage II disease

- Most trials have shown at least a disease-free survival (DFS) benefit for adjuvant chemotherapy in patients with stage II disease.
- Small change in Overall survival
- Higher risk features: poorly differentiated histology , lymphovascular invasion , perineural invasion ,bowel obstruction or perforation,close indeterminate, or positive margins; inadequately sampled lymph nodes (less than 13 in the surgical specimen) a high preoperative serum carcinoembryonic antigen (CEA) level and occult nodal metastasis
- MSI testing

Stage IV disease

- Chemotherapy backbone:
- ●FOLFOX or XELOX +/- Avastin
- ●FOLFIRI +/- panitumumab or cetuximab
- ●FU/LV +/- avastin
- ●FOLFOXIRI

Toxicity

- Nausea, vomiting, diarrhea and constipation
- Myelosuppression
- hand-foot syndrome
- neuropathy
- bleeding
- Thromboembolic issues

Surveillance/Survicorship

- Survivorship: person is a cancer survivor from the moment of a cancer diagnosis, through the balance of his or her life

ASCO Guidelines

- H&P: Every 3 to 6 months for 5 years
- CEA: Every 3 to 6 months for 5 years
- CT scan: Abdomen and chest annually for 3 years; pelvis: rectal cancer only, annually for 3 to 5 years
- Colonoscopy: Colonoscopy at one year; subsequent studies dictated by prior findings. If negative, every five years.

NCCN Guidelines

- H&P: Every 3 to 6 months for 2 years, then every 6 months for 3 years
- CEA: Every 3 to 6 months for 2 years for ≥T2 disease; then every 6 months for 3 years
- CT scanning: Abdomen/pelvis and chest annually for up to 5 years; for resected metastatic disease, abdomen/pelvis and chest every 3 to 6 months for 2 years, then every 6 months up to total 5 years
- Colonoscopy: Colonoscopy at 1 year; subsequent studies dictated by prior findings. If no advanced adenoma, repeat at 3 years, then every 5 years; if advanced adenoma at one year, repeat at one year.

Psychosocial Issues

- Psychological distress and depression
- Social relationships and employment
- Bowel and anorectal problems
- Urinary dysfunction
- Sexual dysfunction
- Fatigue
- Neuropathy