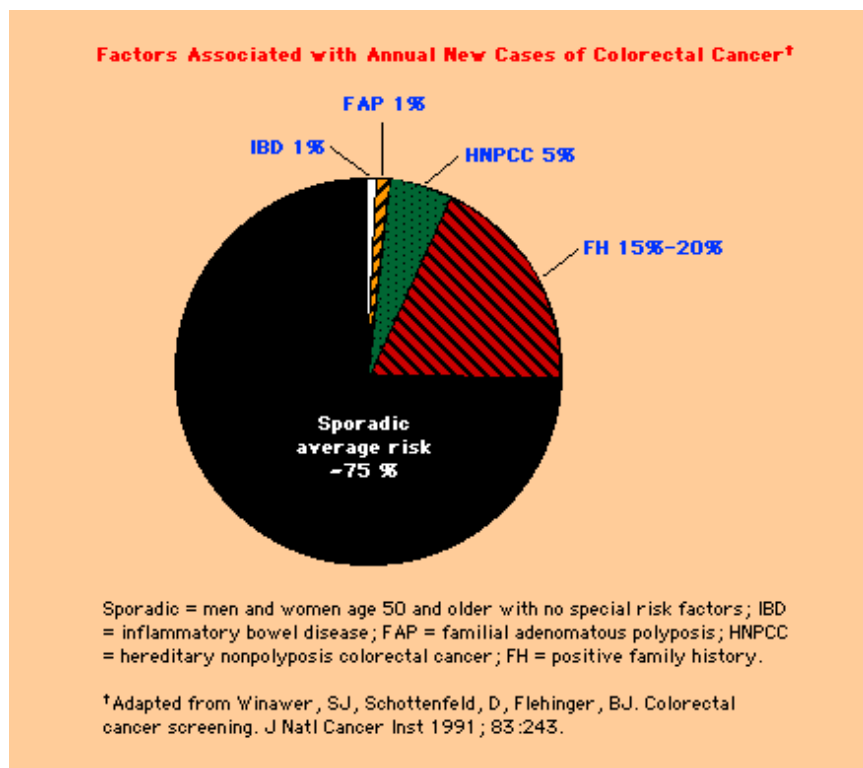


INFLAMMATORY BOWEL DISEASE AND COLORECTAL CANCER

Epidemiology/Risk Factors



Crohn's Disease

- median age at diagnosis 55
- overall <100 cases/year in US
- 2.5 relative risk overall vs 5.6 if disease restricted to colon
- increased risk if
 - male sex <30 years old at initial diagnosis (RR of 21 compared to patients diagnosed >30 years old)
 - longer duration of disease (>10 years)
 - greater extent of colonic involvement
 - stricturing (6.8% increase in colorectal cancer compared to those without)
 - risk increases with increased duration of disease
 - coexisting PSC

Ulcerative Colitis

- median age at diagnosis 43-49
- increased risk with
 - longer duration of disease (5-10% post 20 years disease, 12-20% post 30 years)
 - more extensive disease (greatest risk when extending to hepatic flexure)
 - more severe inflammation and/or backwash ileitis
 - stricturing

- coexisting PSC
- proctitis or proctosigmoiditis alone not risk factor

Pathogenesis

- Most likely different from sporadic CRC based on
 - younger mean age at cancer diagnosis (vs 70 y/o for sporadic CRC)
 - cancer preceded by chronic inflammation (vs discrete non inflammatory polyps)
 - decreased number of sporadic mutations in *ras* proto-oncogene (vs 40-60% in sporadic)
 - earlier loss of p53 heterozygosity

Pathology

- most adenocarcinomas but increased incidence of poorly differentiated anaplastic and mucinous variants
- may be diffuse and extend over more than 1 segment of bowel; may infiltrate bowel wall causing stricturing
- may look ulcerated, polypoid, nodular or plaque-like but up to 1/3 of Crohn's associated cancers are found in normal appearing bowel
- dysplasia
 - characterized by increased mitoses, back to back gland pattern, increased nuclear size and pleomorphism and polychromasia
 - may remain stable, progress or regress but there is currently no reliable way to predict which outcome will be most likely
 - Classification (UC guidelines 1983)
 - 1- normal
 - 2- IND (indefinite for dysplasia)
 - further classified as
 - probably negative
 - unknown
 - probably positive
 - 3- LGD (low grade dysplasia)
 - 4- HGD (high grade dysplasia)
 - DALM (dysplasia associated lesion/mass) – may be a marker for underlying invasive carcinoma especially when non-adenomatous (more studied in UC)
- inflammatory pseudopolyps NOT indicators for dysplasia and NOT a risk factor for CRC
- location
 - UC – most in rectum or sigmoid
 - CD – most in R colon and rectosigmoid; may be associated with fistulas
- synchronous tumors in up to 12% of Crohn's associated CRC and 14-40% of UC associated CRC (vs 3-5% of sporadic CRC)

Diagnosis

- Surveillance colonoscopy and biopsy as gold standard (see Recommendations); need at least 33 biopsy specimens from single colonoscopy to detect dysplasia with 90% confidence

Future possibilities

- molecular markers
 - Sialosyl-Tn – precedes CRC dysplasia by few years
 - p53, Rb, mcc, APC all found in UC associated dysplasia and cancer
- chemoendoscopy - methylene blue and indigo carmine dyes have been found to show intraepithelial neoplasia in UC patients.

Diagnostic Recommendations

- Crohn's and Colitis Foundation of America
 - UC – screening colonoscopy post 8-10 years of symptoms; surveillance q 1-2 years for patients with extensive left sided colitis vs surveillance as for general population for those with proctosigmoiditis; surveillance could be reduced to q 3 years post 2 negative scopes until >20 yrs disease duration at which time q 1-2 year surveillance should be resumed; colonoscopy for all patients with concomitant PSC at time of PSC onset;
 - CD – patients who have no colonic involvement are not considered high risk and should be managed according to the recommendations for the general population; screening colonoscopy post 8-10 years of symptoms; surveillance q 1-2 years; surveillance could be reduced to q 3 years post 2 negative scopes until >20 yrs disease duration at which time q 1-2 year surveillance should be resumed;
 - Screening colonoscopy for all patients with PSC without known IBD to determine status
- AGA
 - UC – screening colonoscopy post 8 years of disease in pancolitis vs post 15 years if disease restricted to left colon and surveillance colonoscopies q1 year thereafter
 - CD – same recommendations due to comparable risk
- ACG
 - UC – screening colonoscopy post 8-10 yrs of disease in patients who are surgical candidates with multiple biopsies at regular intervals;
 - CD – no definitive guidelines
- ASGE
 - UC – screening colonoscopy post 8 years of disease in patients with pancolitis with 4 biopsy specimens per 10 cm from cecum to rectum;
 - CD – no definitive guidelines

Treatment Recommendations

- Crohn's and Colitis Foundation of America
 - UC
 - Indefinite for dysplasia should be followed by surveillance exam within 3-6 months
 - LGD in flat mucosa – prophylactic colectomy should be offered (due to risk of synchronous CA); if LGD is found to be multifocal or repetitive (2+ exams) the patient should be strongly encouraged to undergo total proctocolectomy; if patient defers surgery, a repeat exam should be done within 3-6 months of initial LGD finding
 - HGD in flat mucosa – total proctocolectomy

- Raised lesions/polyps with dysplasia – may be amenable to complete polypectomy; if surrounding biopsy negative and there is no dysplasia elsewhere in colon a follow up exam should be done within 6 months and regular surveillance resumed; if surrounding mucosa dysplastic complete proctocolectomy is recommended;
 - Stricture – strong indication for colectomy due to high risk of underlying cancer
 - CD
 - Recommendations for management of abnormal findings equal to those for UC; for patients with segmental Crohn’s colitis it is not known whether segmental resection alone is sufficient or whether total proctocolectomy should be considered
 - Stricture – repeat evaluation within 1 year; if patient with >20 yrs of disease total colectomy or segmental resection is appropriate due to 12% risk of concomitant CRCA
- ACG
 - definite dysplasia confirmed by a pathologist is indication for colectomy
- ASGE
 - any findings of dysplasia or cancer is indication for colectomy

Yevgenia Pashinsky, MSSM 3
April 11, 2005