

Vesalius SCALpel™ : Colorectal Cancer (see also: colorectal folios)

Cancer incidence, mortality

new cases	M	F
	prostate 33%	breast 32%
	lung 14%	lung 12%
	colon 11%	colon 11%
mortality		
	lung 31%	lung 25%
	prostate 10%	breast 15%
	colon 10%	colon 11%

cancer is the leading cause of large bowel obstruction in the US

diverticulitis is second

fecal occult blood screening detects higher than the expected number of early colon cancers

positive predictive value 10% for cancer, 30% for adenomas

Genetic syndromes

familial adenomatous polyposis (FAP)

loss of adenomatous polyposis coli (APC) tumor suppressor gene

germline mutation 5q21

codes for protein that causes cell adhesion, suppresses neoplasm

mutation found in 75% of FAP, 35% of sporadic colon cancers

mutation occurs early in carcinogenesis

autosomal dominant, loss of two alleles, generalized polyposis, < age 30

< 1% of all colorectal Ca

start screening family members with sigmoidoscopy at puberty

rectal polyps always present if disease is present

association with gastric cancer (diffuse form), duodenal polyps and cancer

extraintestinal manifestations (relatively low incidence)

2% lifetime risk thyroid cancer, pancreatic cancer, hepatoblastoma, CNS

tumors (esp. medulloblastoma), benign adrenal adenomas

Gardner's: variant of FAP with extraintestinal manifestations:

osteomas, desmoid, exostoses

1/3 of pts have duodenal polyps, 28% gastric

periampullary carcinoma 2nd most common cause of death

Turcot's: another possible variant of FAP with CNS tumors (medulloblastoma), no small bowel polyps

hereditary non-polyposis colon cancer (HNPCC/Lynch syndrome)

loss of function of a series of DNA/mismatch genes

germline mutation plus somatic mutation leads to cancer sequence

mismatch repair gene abnormalities: hMSH2, hMLH1, PMS

APC (5q), p53 (17p13)

type 1: colon only, 75% risk by age 75
 type 2: also endometrial (risk 40%), ovarian (<10%), breast, gastric, upper GU (renal cell)
 follow with colonoscopy, urinalysis, vaginal ultrasound
 < 30-40, R colon > L
 5-10% of colon cancers
 increased synchronous and metachronous cancers
 better survival stage for stage than non HNPCC cancers
 start screening family 10y before age of youngest with cancer
 Peutz-Jegher's: autosomal dominant, hamartomas most jejunal/ileal plus some stomach
 and colorectal
 obstruction, intussusception, bleeding
 oral, sole and palm melanin spots
 malignant potential
 (Cronkhite-Canada: hamartomas without cancer)
 Juvenile polyps
 70% solitary, 60% within 10cm of anal verge
 malignant association
 polyp to cancer sequence, same genetic changes
 sporadic gene changes: APC, hMSH2, hMLH1, DCC, p53, K-ras
 APC loss early in development of polyps
 tumor suppressor gene chromosome 5
 mutation found in 75% of FAP, 35% of sporadic colon cancers
 p53, K-ras higher expression in sporadic cancers
 p53 tumor suppressor gene codes for nuclear phosphoprotein which binds to
 DNA, regulates transcription
 chromosome 17
 mutant p53 binds wild p53 and inactivates
 K-ras, oncogene chromosome 12
 codes plasma protein for transduction growth & differentiation
 found in 50% of colorectal cancers
 DCC (deleted in colon cancer): chromosome 18
 cell protein regulates cell contact
 found in 73% of colon cancer
 mutation late in carcinogenesis
 chromosomal, microsatellite instability
 normal mucosal cells divide only in crypts, division at all levels of adenomas
 most (75%) polyps tubular adenoma, 10% malignant
 villous adenoma: 10% of polyps, 45% malignant
 tubulovillous: 15%, intermediate malignancy incidence
 30% incidence of synchronous adenomatous polyp if one found

 presentation: bleeding (R classically), obstruction (L), abd pain, wt loss
 colonoscopy sensitive and specific

Staging

Basic workup: Liver enzymes, CT, CXR, Endoscopic US rectal

T1 mucosa/submucosa 12% incidence of positive nodes

T2 into muscularis propria 22% incidence of positive nodes

T3 through “

T4 invading adjacent structures

N0, N1 (1-3nodes), N2 (> 3 nodes)

stage

I T1,2 N0 M0 90% 5y

II T3 “ 70%

III any T N+ 40%

IV any T any N M1 < 5%

75% of patients present as stage II or III

Rectal cancer

new safe distal margin 2cm (v 5 previously) adequate to prevent locoregional recurrence

pain and tenesmus usually means sphincter involvement, requires APR

radial resection margin more important: total mesorectal excision

presacral plane to tip of coccyx

local bladder, vaginal involvement does not preclude coloanal anastomosis

5% local recurrence with surgery alone

local Rx

endoscopic US 90% accurate for T stage

(CT, PET, endoscopy do not accurately assess T)

MRI acceptable alternative

trans-anal excision for early low rectal 10% failure v abdominal perineal 5%

criteria: T1,2, well differentiated, distal rectal, less than 1/3 of circumference

negative path features: no lymphovascular invasion, negative margins with full-thickness excision

better functional result

adjuvant Rx

indicated for locoregionally advanced, not for metastatic

stage III 5FU X 6mo

neoadjuvant higher sphincter salvage rate

stage IIb or III rectal: combined radiation & systemic 5FU, pre (preferable) or post-op reduces local recurrence

Anal (epidermoid) Ca

types: squamous, basaloid, cloacogenic, mucoepidermoid, transitional

risk: HIV, human papilloma virus (HPV 16, 18), immunosuppression

chemoradiation primary therapy (Nigro protocol: fluorouracil, mitomycinC)

nodal and distal mets (liver, lung) most important prognostic factors
no prophylactic groin dissection
82-87% 5y survival
5-10% have positive inguinal nodes at Dx
inguinal nodes included in radiation fields
 radiation decreases incidence of metachronous nodal disease
synchronous positive nodes poorer prognosis
chemorad 90% control of synchronous inguinal LN mets
occurrence of metachronous nodes better prognosis than synchronous
 preferred initial Rx v inguinal lymph node dissection
abdominal perineal for recurrence

anal marginal Ca: outside anal verge
most, well differentiated, slow-growing, spread to inguinal LNs
wide excision (v Nigro chemorad)
graft or flap for wide defect
recurrence repeat excision
(no role for topical fluorouracil)

Bowel prep

only mechanical cleansing plus antibiotics reduces rate of wound infection

References:

Hriesik C et al. Update for surgeons: recent noteworthy changes in therapeutic regimens for cancer of the colon and rectum. JACS, 468-478.