

COLORECTAL POLYPOSIS SYNDROMES

- Hereditary Colorectal Cancer:
- 1) Hereditary polyposis syndromes (i.e. FAP)
 - 2) Hereditary Non-polyposis Colorectal cancer (HNPCC)
- hereditary syndromes account for ~5% of all CRC. (130,000 new cases/year in the US).

Familial Adenomatous Polyposis (FAP)

- accounts for ~1% of all CRC, affecting about 1 in 10,000 individuals
- 100% of lifetime risk of developing CRC
- develops hundreds to thousands of colonic polyps (adenomas) by late teens. If left untreated majority develops cancer by age of 40-50.
- CHRPE lesions are unique clinical markers of FAP, it can be used as a screening tool at a young age in FAP positive families (CHRPE - congenital hypertrophy of the retinal pigment epithelium, best visualized by ophthalmoscopy)
- FAP individuals also at risk for other cancers:
 - Duodenal polyposis → small bowel cancer at the ampulla of Vater, requiring routine upper endoscopy. The lifetime risk is 4 - 12% for small bowel cancer.
 - Gastric Polyposis → usually benign in western cultures but higher incidence in Japan and Korea
 - Desmoids → induced by surgery, affect 10% of the individuals, may involve the SB mesentery or abdominal wall. Usually benign but can be difficult to excise.
 - Other tumors associated with FAP: osteoma, sarcoma, hepatoblastoma, pancreatic cancer, papillary thyroid cancer, medulloblastoma
- FAP Variants: Gardner's syndrome (+ soft tissue tumors, epidermoid cysts, osteoma, dental abnormalities), Turcot's syndrome (+ brain tumors), Attenuated FAP (AFAP - reduced # of polyps. <100. predominantly in right colon, cancer occurs a decade later)
- Genetics:
 - germ-line mutation on chromosome 5q21: APC (adenomatous polyposis coli)
 - APC controls the cell cycle by regulating the levels of B-catenin
 - Inherited a nonfunctional copy APC leading to accelerated progression to tumor initiation compared to normal individuals
 - Location of the mutation may dictate the phenotype (genotype ← → phenotype). Example: AFAP with mutations at either end of the gene
 - Genetic mutation analysis may be useful in screening, risk stratification, and prognosis.
 - Genetic testing on family members of affected FAP individuals is the standard of care
- Management: screening, early surveillance, prophylactic colectomy
- Chemoprevention: some studies showed that Celecoxib, Sulindac may cause regression of the polyps (reduce the size and number of adenomas)

Table 3. Options for cancer prevention in FAP for known or suspected gene mutation carriers.

Primary recommendations

- Annual flexible sigmoidoscopy beginning by the age of 10–12
- Annual colonoscopy, beginning by the age of 20, when attenuated FAP suspected
- Prophylactic colectomy in teen years or when polyps detected at colonoscopy
- Endoscopic surveillance every 4–6 months after ileorectal anastomosis and annually after ileoanal anastomosis
- Upper endoscopy, including duodenoscopy, every 6 months to 3 years starting by the age of 20–25

Secondary recommendations

- Annual thyroid examination beginning by the age of 10–12
- Annual palpation of liver during the first decade of life (consider annual hepatic ultrasound and measure of α -feto-protein)
- Consider serial MRI of brain in families with Turcot syndrome
- Consider serial MRCP or endoscopic ultrasound in families with multiple pancreatic cancers
- Consider use of sulindac or celecoxib chemoprevention in individuals with colorectal adenomas

Keeping Your Rectum: IRA vs. IPAA

- Pre- 1983: the only options are colectomy with ileorectal anastomosis (IRA) or colectomy with ileostomy.
- Advantages of IRA include: simpler operation without pelvic dissection and less likely to lead to impotence; more comfort and better bowel function experienced by patients

Bjork et al. (Dis Colon Rectum, 7/2001)

- retrospective study on surgical and functional outcomes between IRA, pIPAA, and sIPAA with 102 FAP patients in the Swedish Polyposis Registry from 1984-1996.
- Surgical complication rate was similar between IRA and pIPAA, but more patients suffered from complication in sIPAA than IRA.
- IRA patients reported better bowel function and quality of life than IPAA, however sIPAA patients favored IPAA over IRA.
- Sexual dysfunction was rare in all groups
- 2 / 47 IRA developed rectal cancer, none in IPAA
- However quality of life and comfort must be balanced with the increase risk of rectal cancer after IRA. The risk of rectal cancer after IRA ranged from 0-37%.
- Who should have IRA: (1) relatively few or no rectal polyps (2) good follow up compliance New IPAA technique may offer better functional outcomes in the future

Life After the Pouch:

- Significant remaining risk for developing other tumors/adenomas, such as SB adenoids, pouch adenoids, mesenteric desmoid tumor (MDT); requiring close follow up and routine endoscopic surveillance. (Parc et al Ann of Surgery 2004)

References:

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Table 1. Classification of hereditary colorectal cancer syndromes.
Polyposis syndromes (1% of all colorectal cancers)
Adenomatous polyposis syndromes
Familial adenomatous polyposis (<< 1% of all colorectal cancers)
Gardner syndrome
Turcot syndrome
Attenuated adenomatous polyposis coli
Hamartomatous polyposis syndromes (<< 1% of all colorectal cancers)
Peutz-Jeghers syndrome
Juvenile polyposis
Cowden syndrome
Hereditary non-polyposis colorectal cancer (2-3% of all colorectal cancers)
Lynch syndrome
Muir-Torre syndrome
Turcot syndrome