Hereditary Colorectal Cancer: Operative Management

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Lynch Syndrome: Clinical Features

- CRC is most frequently encountered cancer
  - Proximal to splenic flexure (68% vs. 49% sporadic)
  - More likely to have associated synchronous cancers (7% vs. 1% sporadic)
  - Have increased metachronous cancers at 10 years

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Presence of MSI</th>
<th>Tumor progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microsatellite</td>
<td>High (MSI-H)</td>
<td>1-2</td>
</tr>
<tr>
<td>Monosomy</td>
<td>Low (MSI-L)</td>
<td>11-12</td>
</tr>
<tr>
<td>Signature</td>
<td>Intermediate</td>
<td>5-10</td>
</tr>
<tr>
<td>MSI-H</td>
<td>Low (MSI-L)</td>
<td>5-10</td>
</tr>
<tr>
<td>MSI-L</td>
<td>Low (MSI-L)</td>
<td>5-10</td>
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</tbody>
</table>

- Adenoma is precursor lesion
  - More likely to develop adenomas compared to controls
  - Malignant transformation occurs in 3 yrs. vs. 10 yrs

Diagnosis

- Many patients have surgery for CRC before diagnosis is made
- Criteria
  - Amsterdam Criteria
  - Bethesda Criteria – useful screen for triaging CRC for MSI testing; not for diagnosis
- Tumor MSI testing + IHC
- Histology
- Genetics

Surgical Management

- Colon Cancer –
  - Segmental colectomy
  - Complete colectomy with Ileorectal anastomosis
- Rectal Cancer
  - Low Anterior Resection, Abdominoperineal Resection
  - Total Proctocolectomy
  - Ileal pouch vs ileostomy

Metachronous cancer risk

QoL and bowel function

**Surgical Management: Colon Cancer**

- **Increased % metachronous cancer in partial colectomy**
- **In total colectomy, took 3x as long to develop second cancer**

**Risk of Colorectal Adenoma and Cacncerna After Colectomy for Colorectal Cancer in Patients Meeting Amsterdam Criteria**


<table>
<thead>
<tr>
<th>Colon Cancer (CRC)</th>
<th>Total Population</th>
<th>Emotional Impact</th>
<th>Total Population</th>
<th>Emotional Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial colectomy</td>
<td>181</td>
<td>36</td>
<td>88</td>
<td>17</td>
</tr>
<tr>
<td>Total colectomy</td>
<td>325</td>
<td>52</td>
<td>122</td>
<td>24</td>
</tr>
</tbody>
</table>

**Retrospective cohort study of metachronous cancer in 382 patients**

- Segmental colectomy – 16% at 10 yrs, 41% at 20, 62% at 30

- Risk of metachronous CRC not related to specific MMR gene
- Risk of metachronous CRC reduced by 31% for every 10 cm bowel removed (p=0.002)

**Quality of Life After Surgery for Colon Cancer in Patients With Lynch Syndrome: Partial Versus Subtotal Colectomy**

- 51 patients with partial colectomy, 53 with STC
  - No difference in SF-36 measures (QoL)
  - STC – higher stool frequency, social impact (p<0.01)

- Parry S et al. Gut 2011

- Why segmental colectomy?
  - Patient refusal
  - HNPCC may not be confirmed at time of cancer resection
  - Patients with poor anal tone or low life expectancy better served by limited resection
  - Prophylactic colectomy generally not recommended unless........
    - Severe penetrance with early age of cancer
    - Patient already undergoing abdominal hysterectomy for HNPCC-confirmed uterine cancer

Surgical Management: Rectal Cancer

- Between 20 – 30% of HNPCC patients develop rectal cancer
  - 15% of patients present w/ rectal cancer as index
  - 12% of pts will develop over 10 years following total colectomy w/ IRA
- Quality of life choices are more pronounced when considering permanent stoma, bowel function
  - Proctectomy w/ colorectal anastomosis yields less frequent BM and more normal function than IPAA

Prognosis

- When stage- and age-matched, better survival for HNPCC compared to sporadic CRC
  - Watson P et al.: HNPCC patients had lower stage and fewer distant metastases at diagnosis; after stage-stratification, HNPCC had improved survival (HR = 0.67)

Summary

- Surgery for known Lynch syndrome is infrequent
- Although complete colectomy decreases risk of metachronous CRC, it has a worse functional outcome
- Proctectomy alone for rectal cancer has a significant metachronous CRC rate
- If diagnosis of Lynch syndrome is known, total proctocolectomy should be considered

Risk of Colonic Neoplasia After Proctectomy for Rectal Cancer in Hereditary Nonpolyposis Colorectal Cancer


Prognosis

When stage- and age-matched, better survival for HNPCC compared to sporadic CRC

- Watson P et al.: HNPCC patients had lower stage and fewer distant metastases at diagnosis; after stage-stratification, HNPCC had improved survival (HR = 0.67)
### Polyposis Syndromes

- Familial Adenomatous Polyposis (FAP)
- Attenuated FAP (AFAP)
- MYH Polyposis
- Peutz-Jegher’s Syndrome (PJS)
- Juvenile Polyposis Coli (JPC)
- Hyperplastic Polyposis Syndrome (HPS)
- Bloom’s Syndrome
- 1307K APC Polymorphism

### FAP

- Most common known adenomatous polyposis syndrome
- Autosomal dominant, APC gene
- Prevalence 1/5,000-7,500
- Polyposis generally post-pubertal onset/early teens
- Colonic cancers present 10-15 years after onset
- Affects both genders equally
- 100% lifetime risk
- Avg age at dx of colorectal ca – 39
- Phenotype-rectal sparing

### Surgical Management

- Total proctocolectomy with ileostomy (TPC)
- Restorative proctocolectomy with ileal pouch anal anastomosis w or w/o mucosectomy (RPC/IPAA)
- Total abdominal colectomy with ileorectal anastomosis (IRA)

### End Ileostomy

A. ileostomy
B. Brooke ileostomy
TPC with End Ileostomy

**Advantages**
- Remove all disease
  - Lowest risk of polyp formation
  - Least risk of cancer
- No issues of bowel function
  - No urgency
  - More liberal diet
  - Less night waking
  - Fewer trips to BR
- Single operation

**Disadvantages**
- Permanent stoma
  - Leakage of bag
  - Skin problems
  - Money for supplies
  - Emotional issues
- Perineal wound

**Indications:**
- Older patients
- Distal rectal cancer
- Weak anal sphincter
- Want one operation

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Ileanal Pouch

**Indications:**
- Anyone who needs operation
- EXCEPT
  - Elderly, rectal ca, fecal incontinence
  - Patient preference

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TPC with IPAA

**Advantages**
- Remove disease up to anal transition zone
- Avoid permanent stoma
- Evacuate “normally” via anus

**Disadvantages**
- Leaves anal transition zone
  - Small amount of colonic tissue may remain
  - Highest rate of ileal polyp formation
  - Requires vigilant surveillance
- Pelvic surgery
- More than one operation
- Complications
  - Infections
  - Pouchitis
  - Bowel problems
    - Incontinence
    - Night waking
    - Perianal skin irritation
    - Diet restrictions

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Ileorectal Anastomosis
Ileorectal Anastomosis (IRA)

- **Advantages**
  - Cosmetically appealing – no stoma
  - Fecal continence generally preserved
- **Disadvantages**
  - Rectal tissue remains → higher risk of CA
  - More frequent stools
  - Requires vigilant surveillance

**Indications**
- Anyone who needs operation who
  - has rectal sparing
  - Can be compliant with surveillance

Selection of Surgical Approach

- Pt preferences (age, cosmesis, bowel function)
- Severity (number of polyps)
- Location of polyps (rectal sparing)
- Patient age
- Prophylaxis vs cancer treatment
- Extracolonic manifestations/severity of disease
- Possibly specific gene mutation in the future

IPAA vs. IRA

12 studies, 1002 pts
- Better functional outcome after IRA (stool freq 24h, night defecation, incontinence)
- Unclear urgency better in IPAA, no diff in stool frequency at night
- No sig diff in quality of life (diet, sexual fnxn)
- No sig diff in bowel obstruction, hemorrhage, sepsis, anastamotic leak, wound infection. 30d reop rate higher in IPAA
- "further research needed to determine which most benefits patients with FAP"
Staple or Sew?

- Better function with stapling
  - preserve anal sensory epithelium (better functional result)
  - reduce tension on anastomosis (decreased infectious/septic complications)
  - Easier to do
  - less incontinence
  - better sampling reflex
- More anal problems in handsewn group
  - abscess, leak
  - stenosis
  - pouch removal

Handsewn vs. Stapled

Meta-Analysis: 21 studies of 4183 patients

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pouch Failure</td>
<td>1737</td>
<td>0.06</td>
</tr>
<tr>
<td>Night seepage</td>
<td>465</td>
<td>0.001</td>
</tr>
<tr>
<td>Night pad use</td>
<td>225</td>
<td>0.007</td>
</tr>
<tr>
<td>Incontinence</td>
<td>285</td>
<td>0.009</td>
</tr>
<tr>
<td>MRP/MSP</td>
<td>341</td>
<td>-13.4</td>
</tr>
</tbody>
</table>


Handsewn n=474       Stapled n=2635

Kirat et al Surgery 2009
Downside to stapling?

- Cumulative risk of developing a polyp at the anastomotic site was 8% at 3.5 years and 18% at 7 years.
- The risk of developing a polyp at the anastomotic site within 7 years was 31% for patients with stapled vs. 10% for patients with a hand-sewn anastomosis with mucosectomy (P = 0.03 [log-rank test]).
- No one developed a cancer.
- Surveillance is critical with either operation.

**J Gastroint Surg 1999**

Downside to stapling?

- Mucosectomy for FAP reduced risk of adenoma formation.
- Cumulative risk at 10 years of 22.6% after mucosectomy with handsewn anastomosis and 51.1% after stapled IPAA.
- Median time to first adenoma was longer after mucosectomy with handsewn anastomosis than after stapled IPAA (10.1 vs 6.5 years).
- One cancer developed in handsewn group.
- SURVEILLANCE IS KEY!

**Von roon et al Ann Surg 2011**

Desmoid Tumors

- Common post surgical complication.
- May be fatal.
- Rapidly growing may respond to cytotoxic chemotherapeutics.
- Radiation possible – side effects may be worse.
- 85% recurrence after surgical resection.
- High predisposition for mesentery and mesenteric vessels.

Post-surgical Follow Up

- Regular lower GI endoscopic surveillance of pouch, proximal and distal ileum, rectum.
- Monitor for extracolonic disease manifestations:
  - Thyroid screening.
  - Neuro screening.
- Upper GI endoscopy:
  - Periampullary CA.

**Awad et al. Ann Surg March 2010**
Risk-Reducing Surgery in FAP: Role for Surgeons Beyond the Incision

Fig. 1. Patients' desired role in decision-making:

concluded that: "The decision on the type of colorectal surgery in patients with FAP depends on the age of the patient, the number of colorectal polyps, the risk of having children, the risk of developing adenomas, and perhaps the size of the polyps in the APC gene. The final decision must be made with the patient after being fully informed about the pros and cons of each surgical option." (1)