Surgery and Crohn’s Disease
Timing is Everything

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Outline

• Natural history of Crohn’s Disease
• Identification of the high risk patient
• Can we alter the natural history of Crohn’s Disease?
• Indications for surgery
• Do anti-TNFs increase risk of postop complications?
• Who needs postoperative prophylaxis?
Surgery for Crohn’s Disease is not curative, however, for specific patients, surgery can relieve symptoms and significantly improve quality of life.

Most Crohn’s Disease Patients Will Require Surgery

Predictors of Disabling Crohn’s Disease

Factors significantly associated with disabling Crohn's disease within 5 years of diagnosis (n=1123)

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid Use</td>
<td>3.1</td>
<td>2.2 – 4.4</td>
</tr>
<tr>
<td>&lt; 40 years old</td>
<td>2.1</td>
<td>1.3 – 3.6</td>
</tr>
<tr>
<td>Perianal disease</td>
<td>1.8</td>
<td>1.23 – 2.8</td>
</tr>
</tbody>
</table>

Positive Predictive Value

<table>
<thead>
<tr>
<th># Factors</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>61</td>
</tr>
<tr>
<td>1</td>
<td>67</td>
</tr>
<tr>
<td>2</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>93</td>
</tr>
</tbody>
</table>

Beaugerie et al. Gastroenterology. 2006; 130:650-6
Predictors of Rapid Progression to Surgery

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoker</td>
<td>3.1 (1.5–6.5)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1.8 (1.1–3.2)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>2.1 (1.0–4.1)</td>
</tr>
<tr>
<td>Ileal localization only</td>
<td>2.2 (1.3–3.8)</td>
</tr>
<tr>
<td>Oral steroid use in 1st 6months</td>
<td>3.8 (1.9–7.6)</td>
</tr>
</tbody>
</table>

Sands et al, Am J Gastroenterol. 2003 Dec;98(12):2712-8

Can Early Use of Highly Effective Therapy Alter Natural History of CD?

- Induce and maintain gastrointestinal healing
- Prevent strictures and penetrating complications
- Prevent extraintestinal complications
- Decrease hospitalization and/or surgery
- Decrease long-term cost of care
Kaplan-Meier CD-Related Hospitalization: CHARM

CD-related Hospitalization Risk (%)

Placebo
Adalimumab

Week 2

Days since randomization

50 100 150 200 250 300 350

n=778 randomized to adalimumab (ADA) 40 mg EOW or weekly, or placebo, through 56 weeks


3-month Hospitalization Risk

Placebo (%) 7.3
ADA (%) 1.6 (RR reduction: 78%)

12-month Hospitalization Risk

Placebo (%) 13.9
ADA (%) 5.9 (RR reduction: 57%)

Crohn’s Disease: Indications for Surgery

- Obstruction (fibrotic stricture w/o associated inflammatory component)
- Perforation
- Medically refractory disease including steroid dependent
- Medically intractable fistulous disease
- Hemorrhage/transfusion requirement
- Cancer or dysplasia
- Growth retardation in children
Anatomic Site Versus Clinical Course and Prognosis

- Need for operation
  - Ileocolic: 90%
  - Small intestine: 65%
  - Colon/anorectal: 58%

- Indications for surgery
  - Ileocolic: Fistula/abscess
  - Small intestine: Small bowel obstruction
  - Colon/anorectal: Megacolon/perianal disease

- Recurrence
  - Ileocolic: 53%
  - Small intestine: 44%
  - Colon/anorectal: 45%

Ileocecal Resection of Diseased Intestine
IBD-Related Strictures

- Endoscopy indicated to exclude malignancy (UC > CD)
- Asymptomatic
  - Do not require endoscopic therapy
- Obstructive symptoms
  - Medical Rx to reduce active inflammation
  - Consider endoscopic vs. surgical therapy
- No randomized controlled trials of endoscopic therapy compared to surgery

Endoscopic Therapy of Crohn’s Strictures

- 776 Dilations in 178 patients with Crohn’s
- 80% anastomotic strictures
- Technical success in 89%
- Surgery rate of 36% by year 5
- Complication rate 5.3%

Gustavsson A. Aliment Pharmacol Ther 2012;36:151-158.
Endoscopic Balloon Dilation

- Single stricture < 5 cm in length
- 10-20 mm balloon
- Perforation risk is 2 - 5%
- Anastomotic strictures respond better than de novo strictures
- Incremental dilation in 3 sizes, 30-60 seconds per insufflation
- 2 procedures generally required to achieve patency over 5 year period
- 50% long term efficacy, < 1/3 require surgical intervention

Anti-TNFs and Postop Complications

• Preoperative anti-TNF use slightly increases the occurrence of overall postoperative complications in IBD patients, and particularly infectious complications in CD patients.


Anti-TNFs and Postop Complications

• Anti-TNFα therapies appear to increase the risk of post-operative complications.
• The increase in risk is small, and may well reflect residual confounding rather than a true biological effect.
• Nevertheless, physicians should exercise caution when continuing biological therapies during the peri-operative period.

Decreasing Postop Complications

- Treat septic complications
- Improve nutrition
- Decrease or eliminate corticosteroids
- Do not start anti-TNF or hold dose if surgery is imminent

Ray Cross, MD and David Schwartz, MD, CCFA Advances 2013

Anti-TNFs and Postop Complications

- PUCCINI: Prospective Cohort of Ulcerative Colitis and Crohn’s Disease Patients Undergoing Surgery to Identify Risk Factors for Post-Operative Infection
Laparoscopic ileocolic resection versus infliximab treatment of recurrent distal ileitis in Crohn’s disease: A randomized multicenter trial (LIR!C)

- Assess comparison of the effectiveness and costs of infliximab treatment with laparoscopic ileo-colic resection in patients with Crohn’s disease of the distal ileum.

- Multicenter RCT of ileal Crohn’s disease patients that require infliximab treatment (moderate to severe disease) that fail to respond to steroid therapy or immunomodulatory therapy.

- Patients will be randomized to receive either infliximab or undergo a laparoscopic ileocolic resection.

- Primary outcomes are costs and treatment efficacy defined by hospital stay, early and late morbidity, sick leave, QOL and surgical recurrence.

Post Op Prophylaxis
Stratify Postoperative Patients into Low, Moderate and High Risk and Immediately Treat Only Moderate or High Risk Patients

Risk Stratification

- **Low Risk**
  - Longstanding Crohn’s disease (>10 years)
  - Indication for surgery is a short (<10 cm) fibro-stenotic stricture

- **Moderate Risk**
  - Short duration of disease (<10 years) prior to surgery
  - Resection for a long segment (>10 cm) of small bowel inflammation

- **High Risk**
  - Penetrating disease (e.g., abscess, perforation or internal fistula)
  - Smokers
  - Patients with prior surgery for Crohn’s disease
  - Patients who progressed to surgery despite treatment with immunomodulator
Use Ileocolonoscopy Findings at 6-12 Months to Identify High Risk Patients

Rutgeerts Score and Symptomatic Recurrence

Individuals with grade 3 and 4 lesions at colonoscopy one year postop were more likely to have earlier symptomatic recurrence than those with grade 1 and 2 lesions.

Risk of Post-Op Recurrence

- Low
  - No Meds
  - Colonoscopy 6-12 months post-op
  - Recurrence
    - Colonoscopy every 1-3 yrs
      - Immunomodulator or anti-TNF

- Moderate
  - 6MP or AZA ± metronidazole

- High
  - Anti-TNF
  - Colonoscopy 6-12 months post-op
  - Recurrence
    - Colonoscopy every 1-3 yrs
      - ↑ anti-TNF or Δ biologics

Penetrating disease, > 2 surgeries

Assess risk of recurrence

Discharge: 3 months metronidazole
4 weeks post-op: Choice of initial therapy

- High Risk: anti-TNF + IMM
- Moderate Risk: IMM
- Low Risk: No additional Rx

Fecal calprotectin (FC) at 3 months

- FC < 100ug/g
- 100ug/g ≤ FC ≤ 200ug/g
- FC > 200ug/g

Optimize or escalate medical therapy
Colonoscopy at 6 months
Assessment of endoscopic recurrence (Rutgeert's Score)

- i0-i1
- i2-i4

Treatment adjustment: Optimize or escalate medical therapy
Follow-up: Monitor recurrence with yearly endoscopy or FC and optimize therapy if required
Surgery should not be considered a “last ditch” treatment for CD

- Surgery is an important therapeutic option for patients with Crohn’s disease
- Surgery often results in a healthier, more active lifestyle and greater patient satisfaction
- Multidisciplinary team approach in patient management results in optimal long-term outcomes