Surgery and Crohn's Disease Timing is Everything

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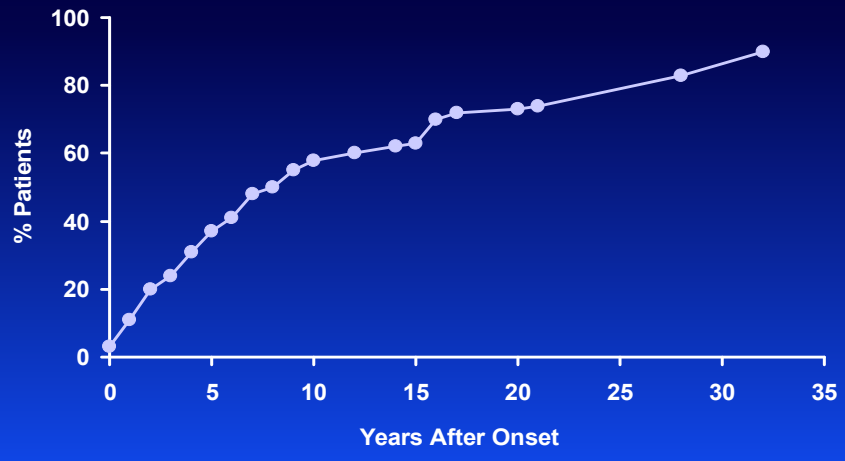
Outline

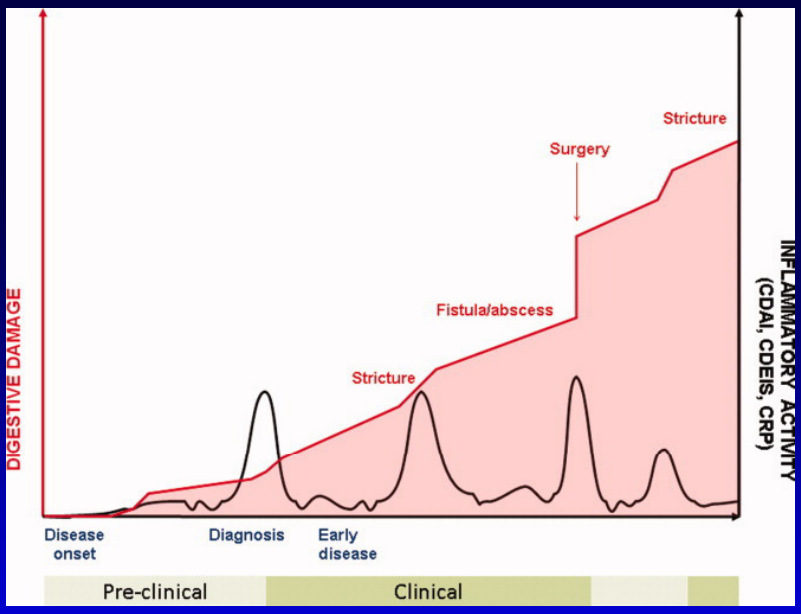
- Natural history of Crohn's Disease
- Identification of the high risk patient
- Can we alter the natural history of Crohn's Disease?
- Indications for surgery
- Do anti-TNFs increase risk of postop complications?
- Who needs postoperative prophylaxis?

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



Mekhjian HS, et al. Gastroenterology. 1979;77(4 Pt2):907-913.



Pariente B, et al. Inflamm Bowel Dis. 2011 Jun; 17(6): 1415–1422.

Predictors of Disabling Crohn's Disease

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

Factor	OR	95% CI
Steroid Use	3.1	2.2 – 4.4
< 40 years old	2.1	1.3 – 3.6
Perianal disease	1.8	1.23 – 2.8

Positive Predictive Value

# Factors	%
0	61
1	67
2	91
3	93

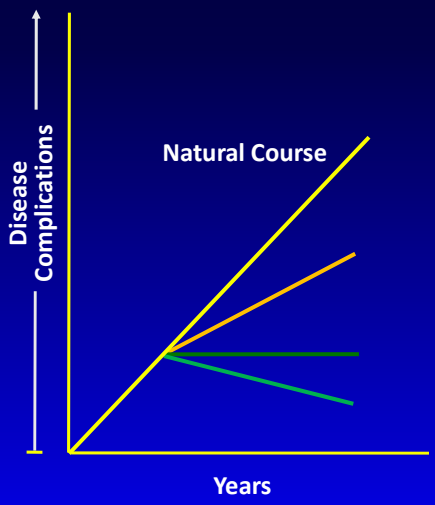
Beaugerie et al. Gastroenterology. 2006; 130:650-6

Predictors of Rapid Progression to Surgery

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

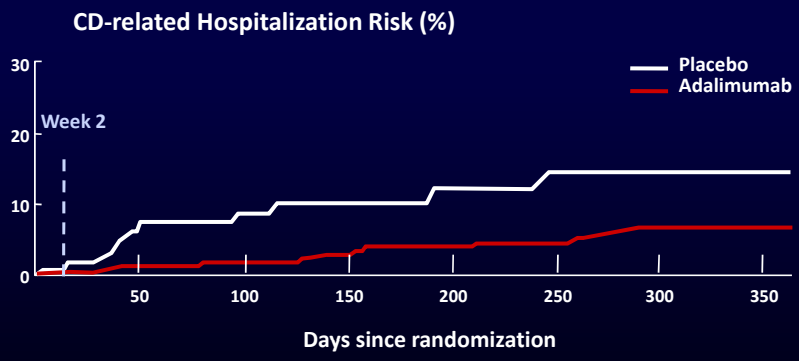
Sands et al, Am J Gastroenterol. 2003 Dec;98(12):2712-8

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



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%)

Feagan BG, et al. Gastroenterology. 2008;135(5):1493-9.

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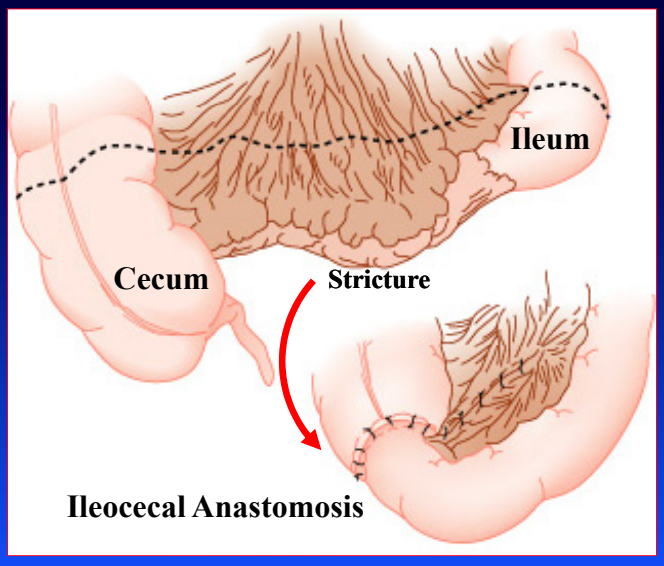
Crohn's Disease: Indications for Surgery

- 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

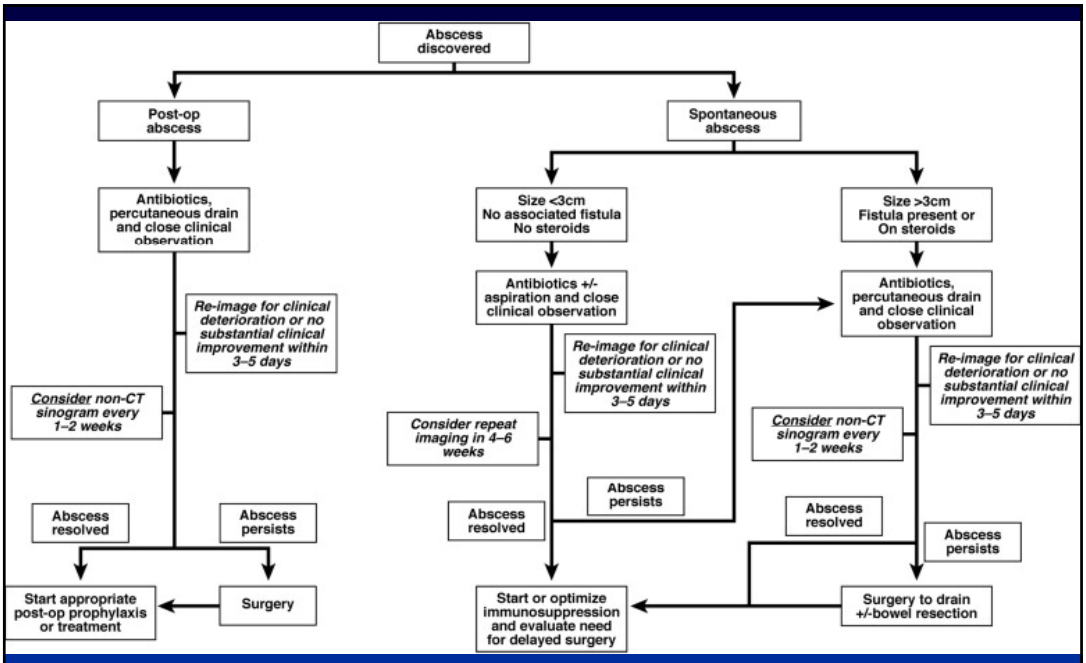
Endoscopic Therapy of Crohn's Strictures

- 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



Feagins LA, et al. Clin Gastroenterol Hepatol. 2011 Oct;9(10):842-50.

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.

Billioud V, Ford AC, Tedesco ED, Colombel JF, Roblin X, Peyrin-Biroulet L. Preoperative use of anti-TNF therapy and postoperative complications in inflammatory bowel diseases: a meta-analysis. J Crohns Colitis. 2013 Dec;7(11):853-67.

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.

Narula N, Charleton D, Marshall JK. Meta-analysis: peri-operative anti-TNFα treatment and post-operative complications in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2013 Jun;37(11):1057-64.

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

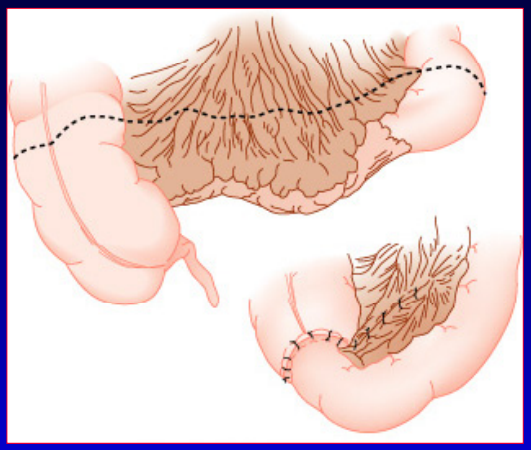
Anti-TNFs and Postop Complications

- PUCCINI: Prospective Cohort of Ulcerative Colitis and Crohn's Disease Patients Undergoing Surgery to Identify Risk Factors for Post-Operative INfection I

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

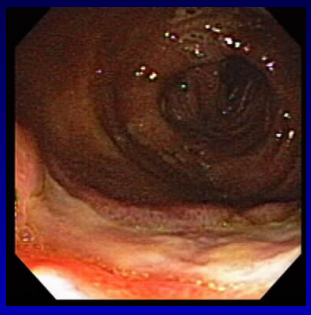


Stratify Postoperative Patients into Low, Moderate and High Risk and Immediately Treat Only Moderate or High Risk Patients

Risk Stratification

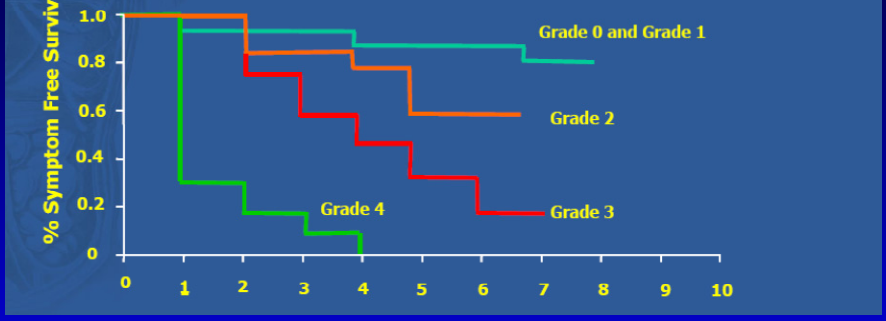
- Low Risk
  - Longstanding Crohn's disease (>10 years)
  - Indication for surgery is a short (<10 cm) fibro-stenotic stricture
- Moderate Risk
  - Short duration of disease (<10 years) prior to surgery
  - Resection for a long segment (>10 cm) of small bowel inflammation
- High Risk
  - Penetrating 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

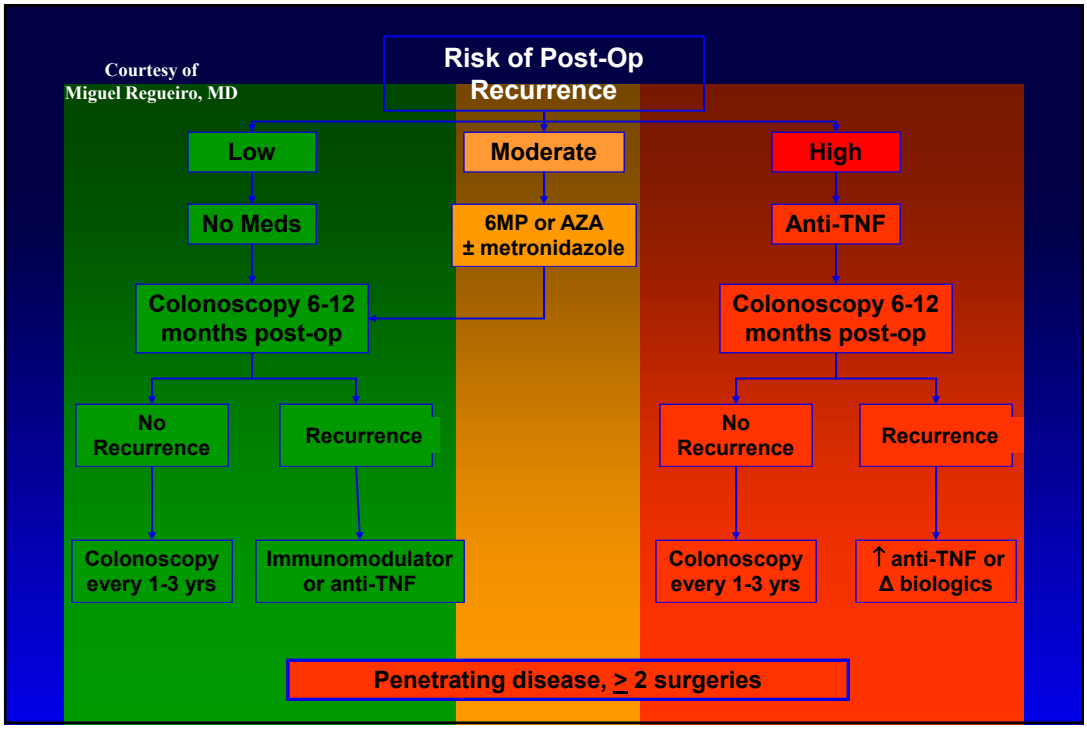


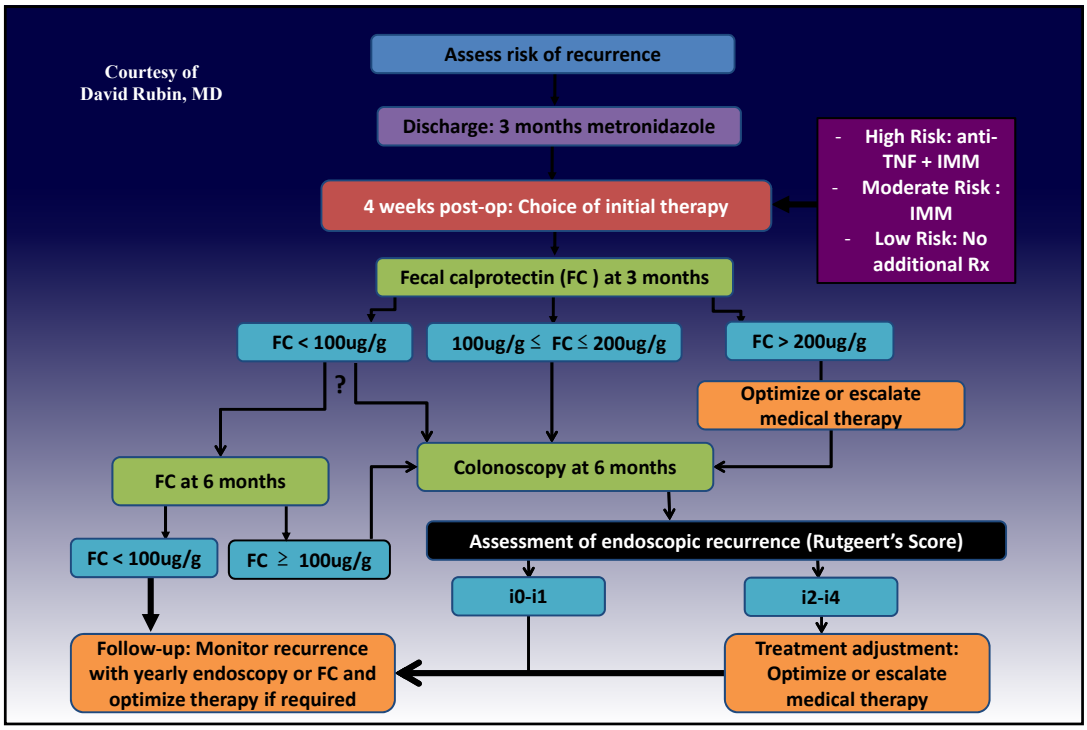
Rutgeerts Score and Symptomatic Recurrence

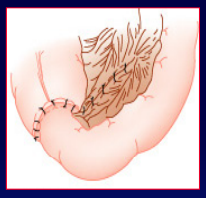
Individuals with grade 3 and 4 lesions at colonoscopy one year postop were more likely to have earlier symptomatic recurrence than those with grade 1 and 2 lesions.



Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn's disease. Gastroenterology. 1990;99(4):956-63.







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