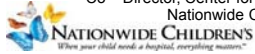



"Post - Operative
Management in Pediatric
Crohn's Disease: How
Should the Pediatric
Gastroenterologist Approach
This in 2015?"



Sandra C. Kim, MD
Associate Professor of Clinical Pediatrics
The Ohio State University College of Medicine
Co - Director, Center for Pediatric and Adolescent IBD
Nationwide Children's Hospital

Disclosures

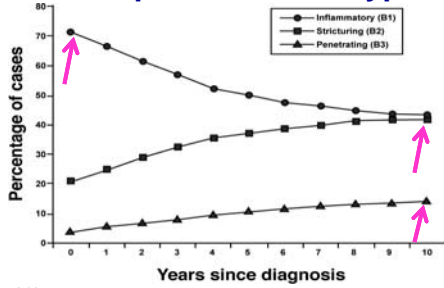
In the past 12 months, I have had the following
financial relationships:

Consultant: Abbott Laboratories and AbbVie

Objectives

- Describe the natural history of post-operative recurrence in patients with Crohn's disease
- Review different methods for defining, and monitoring for, post-operative recurrence
- Review the data on efficacy of different treatment regimens
- Discuss therapeutic approaches for effective management post-operatively
- Next steps?

Pediatric Crohn's Disease Progression to Complicated Phenotypes

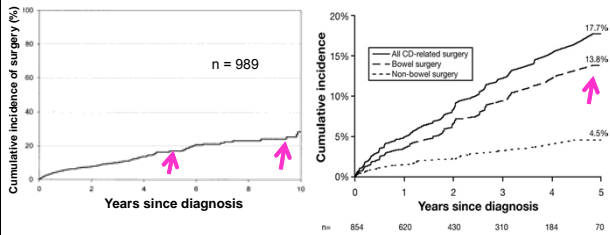


▪ n = 9114

▪ 34% surgery by 5 yrs

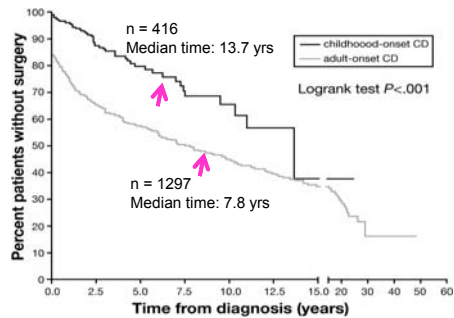
Vernier-Massouille, et al. 2008. *Gastroenterology*

Incidence and Risk for Surgery in Pediatric Crohn's Disease



Gupta, et al. 2006. *Gastroenterology*
Schaefer, et al. 2010. *Clin Gastroenterol Hepatol*

Children With Crohn's Disease Do Not Progress to Surgery As Quickly As Adults



Van Limbergen, et al. 2008. *Gastroenterology*

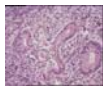
How Can We Predict Which Patients Will Have Post – Operative Recurrence?



The Natural History of Post-Operative Crohn’s Disease

Recurrence initially clinically silent →

Histologic



Within 1 week

Endoscopic



70-90% by 1 year

Clinical



30% 3 year
60% 5 year

Surgical



50% by 20 years

D’Haens, et al. 1998/ *Gastroenterology*
Olaison, et al. 1992. *Gut*
Rutgeerts, et al. 1990. *Gastroenterology*
Sachar DB. 1990. *Med Clin North Am*

What Are Predictive Factors for Post – Operative Recurrence in Pediatric Crohn’s?

- Retrospective review; multivariate analyses of 79 children undergoing 100 surgeries
- Clinical recurrence rates: 17% at 1 yr; 38% at 3 yrs, and 60% at 5 yr.
- Shorter post – op recurrence free interval:
 - Colonic Crohn’s (median 1.2 yr) vs. ileocecal (median 4.4 yr) or diffuse disease (median 3.0 yr) ($p = 0.01$).
 - High PCDAI at the time of surgery ($p = 0.01$)
 - Preoperative 6-MP ($p < 0.005$)

Baldassano, et al. 2001. *Am J Gastro*

Post - Op Recurrence in Adult vs. Pediatric Onset Crohn's Disease

- Retrospective review: patients with ileocecectomy or hemicolectomy
- Onset of disease: ≤16 yrs (n=34), >16 yrs (n=108)
 - Pediatric - onset ↑ pre-op immunomodulators
- Recurrence: 37% at 1 yr; 65% at 3 yrs; 78% at 5 yrs
 - *No difference between groups
- Predictors of delayed time to recurrence
 - Adult - onset: Post - op prophylaxis ≤4 weeks
 - Pediatric - onset: None

Bobanga, et al. 2014. *Am J Surgery*

Outcome After Resection in Pediatric CD

- Retrospective study of French population – based cohort (n=130)

	Risk of Disease Relapse	Cumulative Probability of 2 nd Surgery
2 Years	18%	8%
5 Years	34%	17%
10 years	47%	29%

- Increased risk of 2nd resection
 - Age < 14 years
 - Stricturing or fistulizing disease
 - Upper GI disease

Boualit, et al. 2013. *Inflamm Bowel Dis*

High Post - Op Recurrence in Children

- Danish National Patient Registry
 - N = 1545 (1978 – 2007); n = 422 (27%) underwent surgery
- Post – op recurrence defined as PGA and as need for step up or surgical therapy
- Cumulative recurrence rates: 50% at 1 yr, 73% at 5 yrs, and 77% at 10 yrs
- *No significant difference in post – op AZA for time to 2nd resection/operation

Hansen, et al. 2015. *JPGN*

Improved Growth Post - Operatively

- 1st surgery ≤ 3yrs from dx
 - Better catch-up growth and weight
- Age of patient: < 16 years
 - Pubertal or bone age delay

Boualil, et al. 2013. *Inflamm Bowel Dis*
 Hojsak, et al. 2015. *J Ped Surg*

How Do You Evaluate for Post-Op Recurrence?

- Ileocolonoscopy is the gold standard
- Endoscopic inflammation correlates with clinical recurrence by Rutgeerts' score
- Evaluation within 1 yr post – op recommended in ECCO guidelines

Rutgeerts, et al. 1990. *Gastroenterology*
 Van Assche, et al. 2010. *J Crohns Colitis*
 De Cruz, et al. 2012. *Inflamm Bowel Dis*

Evaluating for Endoscopic Recurrence

Score	Definition
i0	No lesions
i1	≤ 5 aphthous lesions
i2	> 5 aphthous lesions with normal mucosa between lesions, or skip areas of larger lesions, or lesions confined to ileocolonic anastomosis
i3	Diffuse aphthous ileitis with diffusely inflamed mucosa
i4	Diffuse inflammation with already larger ulcers, nodules, and/or narrowing

i0 and i1: Low likelihood of progression



i2,i3,i4: Higher likelihood of progression to surgery



Rutgeerts, et al. 1990. *Gastroenterology*

Capsule Endoscopy

- Capsule endoscopy (WCE) vs. colonoscopy
 - 6 months post - op (n=32)
 - WCE inferior (sensitivity 62-76%) at anastomosis
 - WCE revealed more proximal disease
- WCE vs. Small intestinal contrast USN (SICUS) vs. colonoscopy
 - 12 months post - op (n=22)
 - 5/22: Could not have WCE due to narrowing
 - 16/17: Recurrence detected by colonoscopy and WCE
 - 17/17: Recurrence detected by SICUS (1 false positive)

Bourrelle, et al. 2006. Gut
 Biancone, et al. 2007. Inflamm Bowel Dis

Radiographic Imaging

- MR enterography
 - Sensitivity 100%, specificity 89% in one study
 - MR score correlated well with Rutgeerts score
- Abdominal CT
 - Sensitivity 88%, specificity 97% in one study
 - Not recommended due to radiation exposure
- Ultrasound
 - Sensitivity 79%, specificity 95% in one study
 - Highly operator dependent; improved outcomes with PEG contrast (SICUS)

Saller, et al. 2008. Eur Radiol
 Kollakou, et al. 2010. Inflamm Bowel Dis
 De Cruz, et al. 2012. Inflamm Bowel Dis

Fecal Calprotectin

- Adult study compared FC at time of scope 1 yr post - op (n=30)
- Poor correlation; variability in patients with diarrhea
- FC > 600: 6/7 (86%) endoscopic recurrence
- FC < 100: 6/8 (75%) endoscopic remission

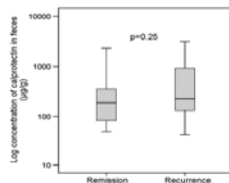


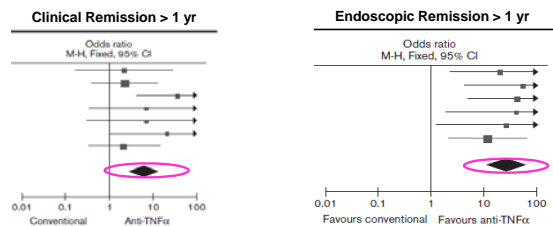
Table 3 Diagnostic precision of fecal calprotectin for prediction of endoscopic recurrence at different cut-offs.

Fecal calprotectin (µg/g)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
100	85	35	50	75
200	94	53	47	60
250	46	53	43	56

PPV, positive predictive value; NPV, negative predictive value.

Lasson, et al. 2014. J Crohns Colitis

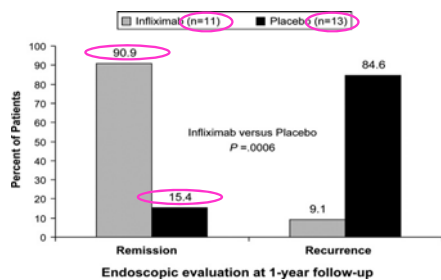
Anti-TNF is More Effective Than Conventional Therapy to Prevent Post-Op Recurrence



*High risk phenotypes: penetrating disease, smoking, perianal disease, and young age at diagnosis.

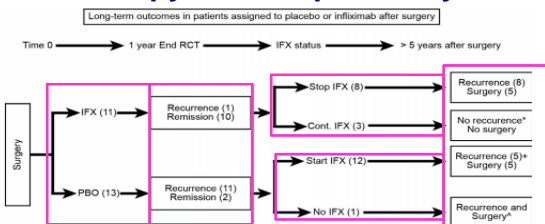
Nguyen, et al. 2014. *Eur J Gastroenterol Hepatol*

Endoscopic Recurrence Reduced in Infliximab Treated Patients



Regueiro, et al. 2009. *Gastroenterology*

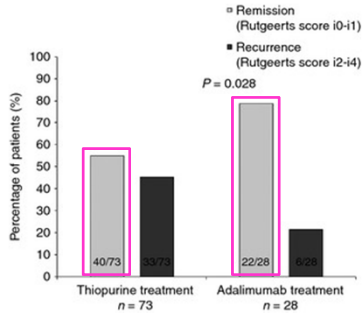
Long - Term Effects of Infliximab Therapy Post - Operatively



- Significant prevention of Crohn's recurrence or need for surgery when IFX continued > 1yr
- Discontinuation of infliximab in high risk post-op patients resulted in endoscopic recurrence, additional surgery

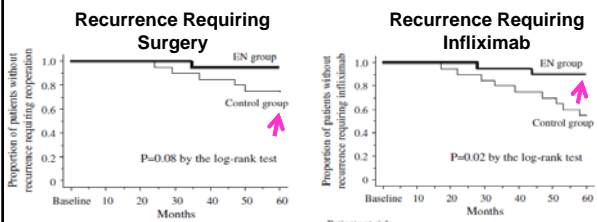
Regueiro, et al. 2014. *Clin Gastro Hep*

Adalimumab is More Effective Than Thiopurines in Preventing Early Recurrence



De Cruz, et al. 2015. *Aliment Pharm Ther*

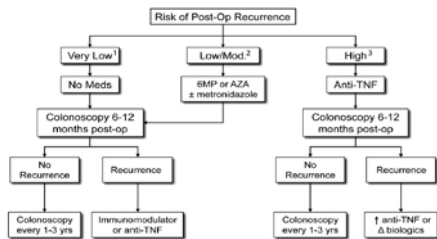
Long-term Prevention of Adult Post - Op Recurrence with Enteral Nutrition



Patients at risk	Baseline	10	20	30	40	50	60
EN	20	20	20	19	19	19	19
Control	20	20	18	17	16	15	15

EN: 50% of caloric needs from overnight elemental NG feeds and low fat diet + mesalamine (3 gm)
Control: Normal diet + mesalamine (3 gm)
 Yamamoto, et al. 2013. *Int J Colorectal Dis*

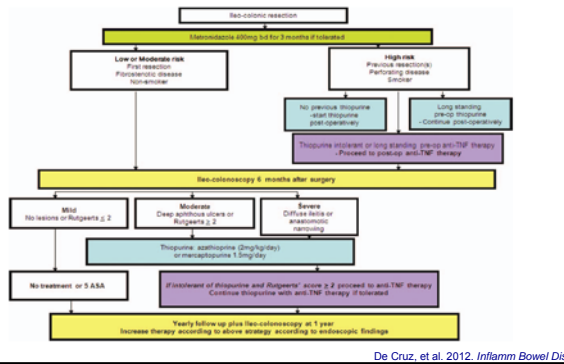
Traditional Adult CD Post-Operative Algorithm



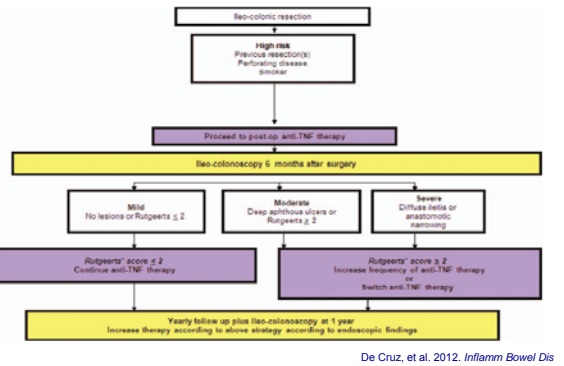
1. Long standing CD, 1st surgery, short stricture
 2. <4days CD long stricture or inflammatory CD
 3. Penetrating disease, > 2 surgeries

Regueiro, et al. 2009. *Inflamm Bowel Dis*

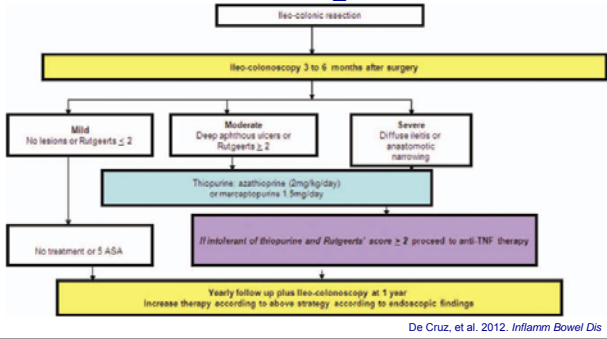
Immediate Post-Op Step-Up Prophylaxis



Post-Op Anti-TNF for High Risk Patients



Tailor Therapy to Post - Op Endoscopic Findings



Post – Operative Issues in Pediatric Crohn’s Disease: Summary

- Patients with Crohn’s disease have high recurrence rates post-operatively
- Risk factors includes extensive/severe disease, colonic disease, early age at disease onset, smoking
- Choice of post - operative prophylaxis essential, with anti – TNF agents more effective versus thiopurines, 5-ASA, antibiotics, and budesonide
- Surveillance is key, with ileocolonoscopy the gold standard

Post – Operative Care in Pediatric Crohn’s Disease: Recommendations

- All patients with Crohn’s disease who have undergone resection should undergo a post – operatively colonoscopy within 6 months after surgery
- Consider placing/continuing patients at high risk (prior IBD –related surgeries; presence of colonic disease; penetrating/perforating disease, tobacco usage) on anti – TNF therapy after resection

Post – Operative Issues in Pediatric Crohn’s Disease: Issues to Consider

- How do we define high risk in the pediatric population?
 - Additional factors: VEOIBD; growth failure
- Should all pediatric patients be started on medication prophylaxis post – operatively?
- Can we change the natural history of the disease?
 - Utilization of anti – TNF agents and other biologics
 - Role of enteral therapy and diet
 - Timing of surgery

What Do We Need to Do Next?



- Leverage/collect data from ongoing collaborative studies
- Develop best practice pathways for post-op management for pediatric Crohn's disease patients