

POST – OP RECURRENCE OF CROHN’S DISEASE

- I. Definition based on clinical, endoscopic, radiologic, or surgical criteria
 - Endoscopic recurrence occurs very early after ileocolic anastomosis.
 - *Rutgeerts et al and Olaison et al* – endoscopic recurrence in 73% - 93% of patients after 1 year and 85% - 100% after 3 years (however recurrence was 30% in 3 months)
 - Review article by *Assche et al* reports clinical recurrence is estimated at 20% - 30% after 1 year.
 - The need for repeated surgery or endoscopic dilation of the anastomosis is between 15% and 45% 3 years post-operatively and 26% - 65% after 10 years
- II. Disease behavior is not influenced by surgical resection. The extent of ileal disease in a patient with post-operative recurrence is most often comparable with what was observed pre-operatively.
- III. Fecal stream is an important in the pathogenesis of recurrent Crohn’s disease. Following ileocolic anastomosis postoperative lesions can develop within 2 weeks. However, fecal stream diversion with loop ileostomy proximal to the anastomosis prevents recurrence. New lesions are induced within weeks following restoration of fecal stream after closing the ileostomy.

Assessment of postoperative recurrence

Endoscopic severity score for postoperative Crohn’s (proposed by Rutgeerts et al)

- i0: Absence of any lesions at the site of anastomosis and in the neo-terminal ileum
- i1: <5 aphthous ulcers (<5mm)
- i2: >5 aphthous ulcers with normal mucosa between lesions or lesion confined to the ileocolic anastomosis (<1cm)
- i3: Diffuse aphthous ileitis with diffusely inflamed mucosa
- i4: Diffuse ileitis with large ulcers, nodularity, or narrowing

Risk factors for early postoperative recurrence

- I. Location – ileocolic anastomosis > colocolic anastomosis.
 - Surgical disease recurrence for ileocolic anastomosis is between 25% - 60% at 5 years and between 40% - 91% at 15 years.
 - Surgical recurrence for colocolic anastomosis vary between 8.5% - 42% at 5 years and from 2% - 40% at 15 years.
 - Recurrence rates in the small intestine proximal to the ileorectal anastomosis are thought to follow the pattern of colocolic anastomosis.
- II. Disease phenotype – perforating disease recurrence > nonperforating disease
 - *Greenstein et al* – time to reoperation in the perforating group was 4.7 years compared to 8.8 years in the nonperforating group.
- III. Smoking
 - *Cotton et al* – After 6years of surgery 60% of nonsmokers, 41% of ex-smokers and 27% of smokers were free of clinical recurrence.

- *Sutherland et al* – Repeat surgery was performed in 20% of nonsmokers and 36% of smokers. At 10 years the figures increase to 41% and 70% respectively.
- Females with small bowel disease were at the highest risk for recurrence.

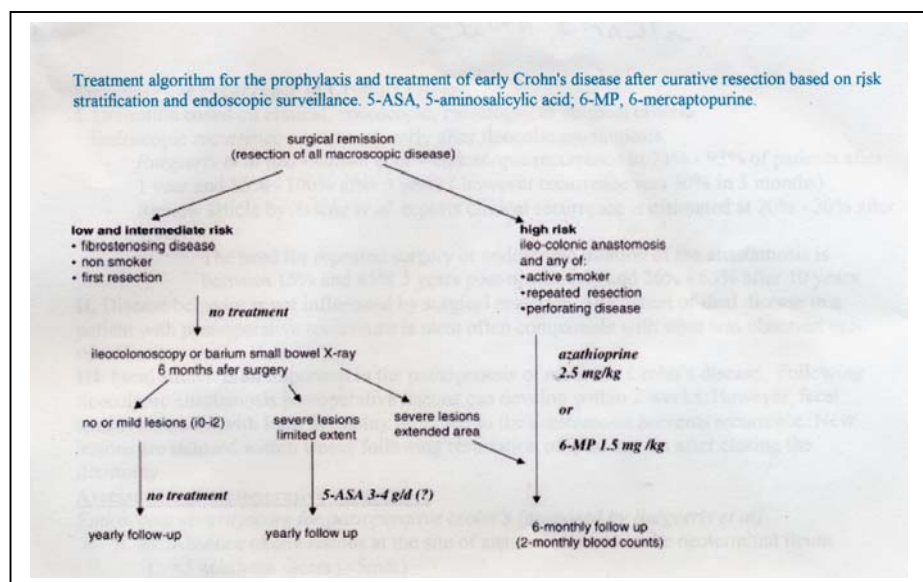
Prevention of clinical recurrence

- Aminosalicylates: sulfasalazine and mesalamine
 - 3 studies looking at the effect of sulfasalazine initiated early after surgery.
 - *Bergman and Krause and Wenckert et al* – no benefit over placebo
 - *Ewe et al* – surgical and radiologic recurrence of 16% in sulfasalazine group at 1 year compared to 28% in placebo group. 3 year recurrence rate were the same (38%).
 - *Caprilli et al* – 2 studies
 - 1994 - showed the benefit for 5-ASA (Asacol 2.4g)
Clinical recurrence – 18% receiving Asacol vs 41% placebo
 - 2003 – compared two doses of Asacol (4g vs 4.8g)
clinical recurrence – 12% in 4g Asacol group vs 14% in 4.8g Asacol group.
No difference in endoscopic recurrence
- Placebo-controlled trials investigating role of 5-ASA in prophylaxis of post-operative Crohn's
 - *McLeod et al 1995* – the only study showed a significant benefit with the 3 year clinical recurrence rate was 31% with 1.5 gram of ASA twice a day vs. 41% in the control group
- Budesonide
 - *Heller's et al* – double blind placebo-controlled trial included 129 patients randomized to budesonide 6mg / day or placebo within 2 weeks from surgery (for fibrostenotic disease). No difference was noted between both the groups at 3 and 12 months.
 - A subanalysis showed a significant reduction in endoscopic lesions with budesonide – 32% reduction vs 65% after 12 months – only in patients operated on for inflammatory luminal disease
- Purine Analogues
 - *Adler and Korelitz* – have provided preliminary data supporting a role for 6-MP in the prevention of post-operative recurrence.
 - *Hanauer et al* – trial comparing 6-MP, 50mg, with 5-ASA, 3g and placebo. Absence of endoscopic recurrence was seen in 32% of patients on 6-MP vs 20% with Pentasa and 10% with placebo. 6-MP was also more efficacious at preventing severe endoscopic relapse. Clinical recurrence reduction was only achieved with 6-MP.
- Nitromidazole
 - *Rutgeerts et al* – first double- blind placebo-controlled trial explored the effect of **metronidazole**, 20mg/kg body weight, during 3 months and started within 1 week from surgery. 3 months total endoscopic recurrence rate were not significantly decreased in the metronidazole group – 52% vs 75%. However, severe endoscopic lesions were lower in the active treatment (13% vs 43%). Clinical recurrence was suppressed at the 1-year, not 2 or 3 year.

- *Rutgeerts et al* – trial using **ornidazole**, 500mg twice a day or placebo initiated within 1 week for 1 year after surgery – severe lesions (> i2) were detected in 74% of the patients in the placebo group vs 41% in the ornidazole. Clinical recurrence was only suppressed only at 1 year (8% vs 37%)
- **Biologic Agents(infliximab)**
 - no data available on their efficacy to prevent post-surgical relapse
- **Probiotics**
 - *Campieri et al* - indicated VSL#3 had therapeutic potential as compared with mesalamine
 - *Prantera et al* - found no difference between placebo and Lactobacillus GG6 10 colony forming twice a day given for 12 months. Endoscopic recurrence was seen 60% in the probiotics group and 35% in the placebo. Clinical recurrence was present in 17% of probiotics treated and in 10.5% of placebo treated.

References

1. *Assche G, Rutgeerts P*. Medical management of postoperative recurrence in Crohn's disease. *Gastroenterology Clinics*. 2004; 33:
2. *Caprilli R, Cottone M, Tonelli F, Sturniolo G, Castiglione F, Annese V, et al*. Two mesalazine regimens in the prevention of the postoperative recurrence of Crohn's disease : a pragmatic, double-blind, randomized controlled trial. *Aliment Pharmacol Ther* 2003; 17: 517-23
3. *Rutgeerts P, Geboes K, Vantrappen G, et al*. Predictability of the postoperative course of Crohn's disease. *Gastroenterology* 1990; 99:956-63.



Suchie Chawla, M.D.
September 6, 2004