Benign Strictures in Crohn’s Disease

Insights into epidemiology, diagnosis and management

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Strictures in Crohn’s Disease
Strictures in Crohn’s Disease

Pathogenesis

• At diagnosis, predominantly inflammatory
• Mesenchymal cells (fibroblasts, myofibroblasts, etc) ➔ ECM components (collagen, etc)
• Fibrosis can progress independently of inflammation
Strictures in Crohn’s Disease

Epidemiology

- At diagnosis:
  - 11% Strictures, 16% fistulae
- Cumulative complications over time:
  - 48-52% at 5 years
  - 70% at 10 years
- 1/3 of Crohn’s patients develop strictures
- Risk of surgery: 40-70% within 10 years
- Gradual progression (data lacking)

2. Cosnes et al. Inflam Bowel Dis 2002;8:244
Strictures in Crohn’s Disease

Distribution of Strictures

Ileocolonic Region 40-60%
Ileum alone 30-45%
Colon Alone 15-25%
Upper GI tract 5-10%
Risk Factors

Clinical Factors:

- Age < 40 years
- Perianal disease
- Need for steroids during 1\textsuperscript{st} flare
  \quad \text{PPV 90\% for disabling disease if 2 or more present} \textsuperscript{1,2}
- Smoking \textsuperscript{2,3}
- Ileal disease \textsuperscript{3} (likely due to smaller lumen caliber)

1. Beaugerie et al. Gastroenterology 2006;130:650
Risk Factors

Genetic factors and Biomarkers:

- Not specific for strictures

- NOD2/CARD15 gene
  - Surgery more frequent and earlier in the course for stricturing disease
  - Earlier recurrence post-op
  - Ileal disease (confounding factor)

- ASCA / CBir1 / Anti-I2 / OmpC

Diagnosis of Crohn’s Strictures:

- Imaging
  - SBFT
  - CT
  - MRI
- Colonoscopy
- Capsule Enteroscopy
Imaging of Crohn’s Strictures

CT Enterography (CTE)

- “Negative” oral contrast to accentuate the bowel wall
- Luminal and extra-luminal pathology
- New dose-reduction techniques result in less radiation
- Metaclopramide / Glucagon

Cons:
- Requires IV contrast
- Radiation
Imaging of Crohn’s Strictures

CT Enterography (CTE)

- Inflammation (Active CD):
  - Fat stranding, mucosal hyper-enhancement, transmural inflammation, lymphadenopathy, vasa recta engorgement

- Fibrotic strictures:
  - Stenosis in the absence of active CD
Imaging of Crohn’s Strictures:

CT Enterography (CTE):

- Replaced Barium SBFT
- Superior to conventional CT for SB pathology
- Strictures\(^1,2\):
  - Sensitivity: 85-93%
  - Specificity: 90-100%
- CTE alters management in \(\approx 50\%\) of patients \(^2\)
- Over/underestimates the extent of complicated disease in 31% \(^3\) (on subsequent surgical evaluation)

1. Fiorino et al. Inflamm Bowel Dis 2011;17:1073
MR Enterography
Imaging of Crohn’s Strictures

MR Enterography (MRE)

- Strictures:
  - Sensitivity: 75 – 100%
  - Specificity: 91 – 100%
- MRE vs. MR Enteroclysis (equivalent – No need for ND tube)
- Vs. CTE:
  - Eliminates radiation exposure
  - Higher cost / Longer exam time
  - Direct comparison (Italian Group, 44 patients)
    - Comparable sensitivity/specificity overall
    - MRE possibly better at detecting strictures (p=0.04, small numbers)

2. Fiorino et al. Inflamm Bowel Dis 2011
Treatment of Crohn’s Strictures

What are the important points?

• 70% of Crohn’s patients undergo surgery within 10 years of diagnosis (many for strictures)
• Active Crohn’s (Fibrosis vs. Inflammation)?
  • Combination of clinical factors, biochemical markers (CRP, ESR) and Imaging
• Medical Therapy vs. Endoscopic Treatment vs. Surgery
• Goal of bowel preservation, clinical resolution and quality of life
Treatment of Crohn’s Strictures

Medical Therapy (Inflammatory strictures):

• Traditionally: Steroids then AZA/6-MP
  • No decrease in strictures or surgery
• Earlier and prolonged use of immunosuppressive meds may decrease surgery / hospitalizations (CHARM)

Pannacione et al Ailment Pharmacol Ther 2010
CHARM Study

56 weeks

Surgeries : Patients

0% 1% 2% 3% 4%

ADA weekly
ADA eow
Placebo

0.8% 0.4% 3.8%

p≤0.01 for all comparisons with placebo

Source: CHARM
Treatment of Crohn’s Strictures

Medical Therapy

- Adalimumab
  - Hospitalization rates at 1 year: 13.9% placebo vs. 5.9% ADA (CHARM)
  - ↓ Hospitalizations at 3 years (ADHERE)
- Combination therapy (AZA/6-MP + anti-TNF) early for strictures
- No current medical treatment for fibrotic strictures
Treatment of Crohn’s Strictures

Medical Therapy in Acute Obstruction

- 26 patients, Acute SBO secondary to Crohn’s strictures
- Rx: NG, Bowel rest, steroids
- 25 / 26 relieved within 72 hours
- 75% had recurrence within mean of 52 months
  - All responded to treatment
- 46% eventually underwent elective surgery
- If symptom-free for 8 months after 1st episode ➔ 17%
- Pre anti-TNF era

Yaffe et al. J Clin Gastroenterol 1983
Treatment of Crohn’s Strictures

Endoscopic Dilation

- Indicated when medical rx fails or fibrotic stricture
- TTS dilation balloon
Treatment of Crohn’s Strictures

Endoscopic Dilation

• Systematic Review
  • 13 studies, 347 CD patients, 1990-2007, TTS balloon dilation
  • Mean stricture length 2.7 cm, Majority post-surgical pts
  • Technical success: 86%
  • Long-term efficacy: surgery-free (mean f/u 33 months): 58%
  • Major complications: 2% (perforation, bleeding)
  • Stricture < 4 cm associated with surgery-free outcome

Hassan et al. Aliment Pharmacol Ther 2007;26
## Endoscopic Balloon Dilation

### Recent Prospective Cohorts:

<table>
<thead>
<tr>
<th>Ref.</th>
<th>No.</th>
<th>Stricture Length (cm)</th>
<th>Stricture Diameter (mm)</th>
<th>Balloon max insuff diameter</th>
<th>Insuff Interval (seconds)</th>
<th>Initial Success Rate %</th>
<th>F/U Interval (months)</th>
<th>Long term success</th>
<th>Major Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Assche et al (Belgium) 2010</td>
<td>138</td>
<td>&lt;5</td>
<td>NA</td>
<td>18</td>
<td>120</td>
<td>97%</td>
<td>70</td>
<td>76%</td>
<td>3%</td>
</tr>
<tr>
<td>Scimeca et al (Italy) 2011</td>
<td>37</td>
<td>3.4</td>
<td>6</td>
<td>10-20</td>
<td>60-90</td>
<td>51%</td>
<td>26.3</td>
<td>89%</td>
<td>0%</td>
</tr>
<tr>
<td>Mueller et al (Germany) 2010</td>
<td>55</td>
<td>3</td>
<td>NA</td>
<td>15-18</td>
<td>60</td>
<td>95%</td>
<td>44</td>
<td>76%</td>
<td>2%</td>
</tr>
</tbody>
</table>
Clinical Outcomes after Endoscopic Dilation

- Immediate success: 97.1%
- No new dilatation: 54.3%
- No surgery: 76.0%
- Dilatation/surgery free: 44.2%

Median follow up: 5.8 yrs (IQR:3.0-8.4)

Median time to new dilation or surgery: 12.5 months
Endoscopic Balloon Dilation

Van Assche et al, Gut 2010 (Belgium)

a) Impact of Endoscopic Activity on the Dilatation/Surgery free Survival

Log Rank: p = 0.90

Impact of CRP on the dilatation/surgery free survival

Log Rank: p = 0.98

CRP

**normal**

> 5 mg/L

.00-censored

Cum Survival

Cum Survival

Years

Years
Van Assche et al, Gut 2010 (Belgium)

*Follow up longer in 5-ASA group since older practice
Retrospective data: disease activity may have influenced treatment decisions
Treatment of Crohn’s Strictures

**Intra-lesional Corticosteroids:**

- Triamcinolone injection in 4 quadrants
- Retrospective series suggest:
  - Lower recurrence rate
  - Delayed time to recurrence
- GIE 2010 (Dinardo et al., Italy)
  - Randomized double-blind trial in pediatric Crohn’s strictures
  - 29 patients, injection done after ED
  - Longer time to re-dilation and surgery vs. placebo
  - Short term follow up (12 months)
Treatment of Crohn’s Strictures

Adjuvant Endoscopic Treatments

Stents (Biodegradable)

Needle-knife Stricturotomy
Treatment of Crohn’s Strictures

Endoscopic Dilation and Adjuvant treatments:

- Technically feasible, safe
- Conscious sedation
- May need repeat dilations in the future (in up to 50% of patients)
- Shorter, straight strictures (<4-5 cm)
- Balloon diameters up to 20 mm (increased risk in larger diameters) with gradual 
- Triamcinolone injection
- Biopsy any suspicious strictures
Surgical Treatment of Crohn’s Strictures

Stricturoplasty

Heineke-Mikulicz technique

Finney technique

Side-to-side isoperistaltic technique

Image from Rieder et al. Gut 2013
Surgical Treatment of Crohn’s Strictures

**Stricturoplasty**

- **Indications:**
  - Multiple strictures over extensive bowel length
  - Prior significant bowel resection
  - Uncomplicated strictures (no phlegmon or fistula)
  - Duodenal strictures
  - Safe in active disease

- **Contraindications:**
  - Abscess or phlegmon or septic fistula
  - Suspicion for carcinoma (contraindicated in colon)
  - Perforation
Surgical Treatment of Crohn’s Strictures

Stricturoplasty Statistics

- Recurrence rates: 28-41% at 5 years
- Disease recurrence at stricturoplasty site:
  - Similar to intestinal resection
- Major complications 6%
  - Leak, abscess, fistula, sepsis
Strictures In Crohn’s Disease

Conclusions and Unanswered Questions

- Progress has been made in diagnosis and management of Crohn’s strictures
- Medical therapy likely to improve
  - Research into anti-fibrotic therapies (Is fibrosis reversible?)
- Novel biomarkers are needed
  - To predict outcomes
  - To utilize medical and surgical therapies more effectively
- Endoscopic therapies promising
  - Controlled trials are needed
Thank you