Indications for Colectomy in UC

Disorders of the Ileal Pouch

Chronic Refractory Pouch Dysfunction

Anatomy of Pelvic Pouches

Frequency of Chronic Pouchitis with Different Pouch Configurations

J, K Pouches vs. Ileostomy

Disorders of the Ileal Pouch

Updated from Shen B, et al. AJG2005;100:93-101
**Owl’s Eyes and Pouch Dysfunction**

**Endoscopic Predictors of Pouch Failure**

<table>
<thead>
<tr>
<th>Factor</th>
<th>HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s pouch</td>
<td>2.7 (1.2, 6.3)</td>
<td>0.018</td>
</tr>
<tr>
<td>Surgical complications</td>
<td>4.4 (1.7, 11.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Post-operative biologics</td>
<td>5.3 (2.5, 11.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2 abnormalities of ‘Owls’ beak</td>
<td>3.6 (1.5, 8.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Cuff endoscopy score</td>
<td>1.5 (1.3, 1.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

N = 426

Alder K, Shen B. IBDJ 2013

**Afferent Limb Syndrome**

**Efferent Limb Syndrome**


**S pouch (no owls’ eyes)**

**Twisted Pouch**
Pathogenetic Model of Pouchitis

Why not in FAP Pouches?

Therapeutic Target

Genetic Susceptibility

Abnormal Immune Response

Therapeutic Target

Mechanical factors (e.g., ischemia)

Alteration commensal bacteria (dysbiosis)

Pathogens

Luminal factors (e.g., NSAIDs)

Navaneethan U & Shen B. AJG 2010:105:51-64

Risk Factors for Pouchitis

- Extensive UC
- Backwash ileitis
- Primary sclerosing cholangitis
- P-ANCA
- IL-1ra, NOD2 polymorphisms
- NOD2 gene polymorphisms
- Precolectomy thrombocytosis
- Non-smoker
- NSAIDs
- Arthralgia
- Surgical techniques??

Navaneethan U & Shen B. AJG 2010:105:51-64

Shen B, et al. AJG 2005
Meier CB, et al. IBJD 2005
Shen B, et al. CGH 2006
Koturn W, et al. DCR 2011
RCT of Antibiotic Therapy in Pouchitis

<table>
<thead>
<tr>
<th>Authors</th>
<th>N</th>
<th>Type of pouchitis</th>
<th>Agent</th>
<th>Days</th>
<th>Median ∆ in PDAI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madden 1994</td>
<td>13</td>
<td>Chronic pouchitis</td>
<td>Metro 400 mg TID vs. placebo</td>
<td>7</td>
<td>N/A</td>
</tr>
<tr>
<td>Shen 2001</td>
<td>16</td>
<td>Acute pouchitis</td>
<td>Cipro 1 g/d vs. Metro 20 mg/kg/d</td>
<td>14</td>
<td>Cipro -6.7, Metro -5.9</td>
</tr>
<tr>
<td>Isaacs 2007</td>
<td>8</td>
<td>Acute or Chronic pouchitis</td>
<td>Rifaximin 1.2 g/d vs. placebo</td>
<td>28</td>
<td>-1.6 in study group</td>
</tr>
</tbody>
</table>

Open-labeled Trials of Antibiotics in Pouchitis

<table>
<thead>
<tr>
<th>Study Year</th>
<th>N</th>
<th>Type of pouchitis</th>
<th>Drugs</th>
<th>Duration (days)</th>
<th>Median ∆ in PDAI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shen 2006</td>
<td>51</td>
<td>Antibiotic dependent p.</td>
<td>Rifaximin 200 mg/d</td>
<td>30</td>
<td>Clin response in 3%</td>
</tr>
<tr>
<td>Shen 2007</td>
<td>16</td>
<td>Chronic anti refractory p.</td>
<td>Cipro 1 g/d+Rifaximin 5 mg/kg/d</td>
<td>15</td>
<td>-7</td>
</tr>
<tr>
<td>Gionchetti 2006</td>
<td>18</td>
<td>Chronic anti refractory p.</td>
<td>Cipro 1 g/d+Rifaximin 2 g/d</td>
<td>14</td>
<td>-12</td>
</tr>
<tr>
<td>Abdelrazaq 2005</td>
<td>8</td>
<td>Chronic anti refractory p.</td>
<td>Cipro 1 g/d+Rifaximin 5 mg/kg/d</td>
<td>14</td>
<td>-12</td>
</tr>
<tr>
<td>Kornbluth 2006</td>
<td>16</td>
<td>Chronic anti refractory p.</td>
<td>Rifaximin 550-890 g/d</td>
<td>21</td>
<td>Clin response in 87%</td>
</tr>
<tr>
<td>Mimura 2002</td>
<td>44</td>
<td>Refractory acute p.</td>
<td>Metro 800-1000mg d+ Cipro 1 g/d</td>
<td>28</td>
<td>-9</td>
</tr>
<tr>
<td>Hunt 1996</td>
<td>52</td>
<td>Acute anti responsive p.</td>
<td>Metro 750 mg/d or Cipro 1 g/d</td>
<td>7</td>
<td>Clin response in 94%</td>
</tr>
</tbody>
</table>

Management of “Conventional” Pouchitis

Idiopathic Pouchitis (dysbiosis-associated)

Probiotics in Primary or Secondary Prophylaxis of Pouchitis

<table>
<thead>
<tr>
<th>Authors Year</th>
<th>N</th>
<th>Design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gionchetti/Gastro 2000</td>
<td>40</td>
<td>RCT</td>
<td>Relapse 9 mo: 15% vs. 100%</td>
</tr>
<tr>
<td>Gionchetti/Gastro 2003</td>
<td>40</td>
<td>RCT</td>
<td>2 (10%) in study group, 6 (40%) in placebo group had pouchitis at 12 mo</td>
</tr>
<tr>
<td>Mimura/Gut 2004</td>
<td>36</td>
<td>RCT</td>
<td>Relapse 9 mo: 6% vs. 85%</td>
</tr>
<tr>
<td>Shen/APT 2005</td>
<td>31</td>
<td>Open labeled</td>
<td>On VSL3 at 8 mo: 19%</td>
</tr>
<tr>
<td>McLaughlin/DDW 2008</td>
<td>13</td>
<td>Open labeled</td>
<td>Remission 13%</td>
</tr>
</tbody>
</table>

Rationale for Antibiotic/Probiotic Therapy in Idiopathic Pouchitis

- “Shoot blindly”
- Target: dysbiosis
  - alteration in quality/quantity of commensal bacteria
- Consequences
  - Bacterial resistance
  - Opportunistic infection (C. difficile)
Fecal Coliform Culture in Pouchitis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number Patients</th>
<th>Resistant</th>
<th>Sensitive + Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. Coli</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coliform, not classified</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morganella</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4-wk treatment with sensitive antibiotics (N=15):
- Median 24-hr stool frequency: 14 → 9
- Median PDAI symptom score: 4 → 0

McLaughlin SD. CGH 2009;7:545

Range of *C. difficile* Pouchitis

![Image of pouchitis](https://example.com/pouchitis.png)

"Innocent?" superimposed "infectant"? or original culprit?

Secondary Pouchitis (with identifiable etiology/triggering factors)

- Pathogen-associated pouchitis
- NSAID-induced pouchitis
- Ischemic pouchitis
- Immune-mediated pouchitis

Campylobacter Pouchitis

![Image of Campylobacter](https://example.com/campylobacter.png)

Fever, malaise, dehydration

Rx: Erythromycin

He XS, Shen B. IBDJ 2010

*Clostridium difficile* Infection in Pouch

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>N</th>
<th>Prevalence</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manni/ DCR</td>
<td>2003</td>
<td>1</td>
<td>-</td>
<td>Recovered</td>
</tr>
<tr>
<td>Shen/ DDS</td>
<td>2006</td>
<td>1</td>
<td>-</td>
<td>Recovered</td>
</tr>
<tr>
<td>Shen/ CGH</td>
<td>2008</td>
<td>115</td>
<td>18%</td>
<td>Risk factors: Male (OR=5.0)</td>
</tr>
<tr>
<td>Shen/NRGH</td>
<td>2009</td>
<td>1</td>
<td>-</td>
<td>Fatal</td>
</tr>
<tr>
<td>Li/IBDJ</td>
<td>2013</td>
<td>196</td>
<td>11% (PCR for toxin B)</td>
<td>Refractory/Recurrence to vancomycin</td>
</tr>
</tbody>
</table>

![Image of Clostridium difficile](https://example.com/cdiff.png)

*Clostridium difficile* pouchitis

CMV Pouchitis

![Image of CMV pouchitis](https://example.com/cmvpouchitis.png)

He XS, Shen B. IBDJ 2010
**Ischemic Pouchitis**

**Clues:**
- Male
- "Difficult pouch" in operative note (the issue of "reach")
- Obese or excessive weight gain (>15% of baseline)
- Abdominal surgery (hernia repair, mesh)
- Portal vein thrombi
- Antibiotic refractory

---

**Implication of the Identification of Ischemic Pouchitis**

- Different from ischemic colitis or mesenteric ischemia
  - Necrosis/bowel infarction hardly occurs
  - Doppler or angiogram often negative
- Potential surgical treatment
  - Lysis of adhesion
  - Pouch revision or redo pouch (J → J; J → K)
Clinical Clues for Immune-mediated Pouchitis

- Pouchitis + enteritis
- Chronic antibiotic-refractory pouchitis
- Concurrent autoimmune disorders
- Serum autoantibodies

1-Year Budesonide in PSC-associated Pouchitis/Enteritis

<table>
<thead>
<tr>
<th></th>
<th>Pre-</th>
<th>Post-</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afferent limb Endoscopy Score</td>
<td>2.3 ± 1.9</td>
<td>0.8 ± 1.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Pouch Endoscopy Score</td>
<td>2.5 ± 2.2</td>
<td>0.7 ± 0.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- N = 18
- Induction: 9mg/day 1 – 3 months
- Maintenance: 3mg/day
- No impact on LFTs

Enteritis in PSC + UC with or without Colectomy and Ileal Pouch

IgG4-associated Pouchitis

- 29% in refractory pouchitis
- Serum IgG4 may be normal
- Current autoimmune disorders are common
- Budesonide-1st line therapy

PSC-associated Pouchitis/Enteritis

- Long segment of distal small bowel disease in addition to diffuse pouchitis
- Concurrent autoimmune disorders are common (31% vs. 6% in control)
- Budesonide 1st line therapy

Autoimmune (GVHD-like) Pouchitis

- Chronic antibiotic-refractory pouchitis
- Concurrent autoimmune diseases
- Serum auto-antibodies
- Budesonide, small dose immunomodulator

Navaneethan U., et al. JCC 2012;6:536-42

Navaneethan U., et al. JCC 2011;5:570-6

Shen B. IBD 2011;17:1890-900

Cuffitis: A Residual UC?

Ischemic/Collagenous Cuffitis

Surgical Complications
(Fistula, Sinus)

N = 14

Crohn’s Disease

N = 19

Pouch Excision/Revision/Diversion
N = 7

5ASA/steroid-responsive Cuffitis
N = 40

5ASA/steroid-refractory Cuffitis
N = 58

5ASA/steroid-dependent Cuffitis
N = 22

Cuffitis Diagnosis at the 1st Visit*

N = 120

Refractory Cuffitis

N = 25

Surgical Complications (Fistula, Sinus)
N = 14

Shen B, et al. IBDJ 2010

Lysis Adhesion in Treatment of “Refractory Cuffitis”

Wu B, et al. IBDJ 2013

Refractory Cuffitis - A Sign of CD?

Chronic Inflammation

Low-grade Dysplasia

High-grade Dysplasia

Invasive Cancer

3 Years

Mean duration of IBD before colectomy = 7.4 ± 7.2 yrs

Mean duration of the pouch = 7.1 ± 5.3 yrs

*Mean duration of IBD before colectomy = 7.4 ± 7.2 yrs

Wu B, et al. IBDJ 2013
Pouch Cancer/Dysplasia: Is Surveillance Endoscopy Indicated & Adequate?

7 months

Cox Model for Risk Factors for Pouch Neoplasia

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted HR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>1.16 (0.56-2.39)</td>
<td>0.686</td>
</tr>
<tr>
<td>Age at pouch</td>
<td>1.01 (0.98-1.04)</td>
<td>0.586</td>
</tr>
<tr>
<td>Duration of UC</td>
<td>1.01 (0.97-1.05)</td>
<td>0.547</td>
</tr>
<tr>
<td>PSC</td>
<td>0.41 (0.05-3.19)</td>
<td>0.394</td>
</tr>
<tr>
<td>Chronic pouchitis</td>
<td>0.69 (0.24-2.00)</td>
<td>0.497</td>
</tr>
<tr>
<td>Extensive colitis</td>
<td>1.53 (0.53-4.39)</td>
<td>0.430</td>
</tr>
<tr>
<td>Colectomy for cancer</td>
<td>13.43 (3.96-45.53)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Colectomy for dysplasia</td>
<td>3.62 (1.59-8.23)</td>
<td>0.002</td>
</tr>
<tr>
<td>Mucosectomy</td>
<td>0.78 (0.34-1.8)</td>
<td>0.559</td>
</tr>
</tbody>
</table>


Classification of Crohn’s Disease of Pouch

- Inflammatory
- Fibrostenotic
- Fistulizing

Pouch Neoplasia:
Cleveland Clinic Experience N=3203

Crohn’s Disease in Patients with IPAA

Summary

- A number of patients with chronic refractory pouch dysfunction in fact have surgery-associated mechanical or structural disorders.
- Pouchitis is disease spectrum with ranging etiopathogenetic pathways, disease course, and prognosis.
- De novo Crohn’s disease can occur in pouch patients with a preoperative diagnosis of UC.
- Emerging *C. difficile* infection is challenging.
- Cuffitis can in patients with restorative colectomy with ileal pouches.
- Cancer risk persists after colectomy.
- Most pouch cancer occurs at the cuff area.
Thank You!