Surgical Update: Pouchitis, Pouch Loss and Early Surgery for Crohn’s

Richard C Thirlby MD FACS
Virginia Mason
March 20.2015
Pouchitis
Guidelines for Management

- Etiology/Risk Factors
- Diagnosis
- Treatment
Pouchitis
Etiology/Risk Factors/Incidence

- Bacterial overgrowth.
- Incidence much higher in UC patients than FAP patients.
- Incidence increases with time.
- Other risk factors
Pouchitis
Etiology/Risk Factors/Incidence

- Bacterial overgrowth still cause.
- Incidence much higher in UC patients than FAP patients:
  - UC: 30-60% incidence at 10 years
  - FAP: only about 5%
Pouchitis
Etiology/Risk Factors/Incidence

- Bacterial overgrowth still cause.
- Incidence much higher in UC patients than FAP patients
- Incidence increases with time
- Other risk factors
Incidence of Pouchitis Increases with Time

<table>
<thead>
<tr>
<th>Years post IPAA</th>
<th>% Pouchitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
</tr>
</tbody>
</table>
Pouchitis

Etiology/Risk Factors/Incidence

- Bacterial overgrowth still cause.
- Incidence much higher in UC patients than FAP patients
- Incidence increases with time
- Other risk factors
Predictive Factors for Acute Pouchitis

- UC vs FAP
- Extraintestinal Symptoms
- Primary Sclerosing Cholangitis
- Preoperative thrombocytosis
  - But not fulminant colitis!
- Genetic factors
  - IL-1ra, CARD 15, TNF genes
  - pANCA data conflicting
Short- and Long-Term Surgical Outcomes in Patients Undergoing Proctocolectomy With IPAA in the Setting of Primary Sclerosing Cholangitis. Mathis et al Dis Colon Rectum 2011

- Retrospective study of 100 patients with PSC who underwent IPAA between 1994 and 2005.
- Mean follow-up time = 5.9 years.
- Risk factors for Short and Long-term complications studies.
Short- and Long-Term Surgical Outcomes in Patients Undergoing Proctocolectomy With IPAA in the Setting of Primary Sclerosing Cholangitis.
Mathis et al Dis Colon Rectum 2011

- Short term complications occurred in 39% of patients.
- Steroids, BMI, age, MELD not risk factors.
- Pouch failure rate was only 3/100 (3%).
Primary Sclerosing Cholangitis Is Associated with Endoscopic and Histologic Inflammation of the Distal Afferent Limb in Patients with Ileal Pouch–Anal Anastomosis

Bo Shen, MD,* Ana E. Bennett, MD,† Udayakumar Navaneethan, MD,* Lei Lian, MD,‡§ Zhuo Shao, MD,¶ Ravi P. Kiran, MD,† Victor W. Fazio, MB, MS,‡ and Feza H. Remzi, MD‡

Inflammatory Bowel Disease 2011
Primary Sclerosing Cholangitis and Pouchitis in IPAA

<table>
<thead>
<tr>
<th></th>
<th>IPAA + PSC (N=39)</th>
<th>IPAA (N=91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Pouchitis</td>
<td>36%</td>
<td>14%</td>
</tr>
<tr>
<td>Acute Pouchitis</td>
<td>23%</td>
<td>14%</td>
</tr>
<tr>
<td>Afferent limb inflam</td>
<td>54%</td>
<td>17%</td>
</tr>
<tr>
<td>Pouch Loss</td>
<td>8%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Shen et al, Inflammatory Bowel Dis 2011
Predictive Factors for Acute Pouchitis

- UC vs FAP
- Extraintestinal Symptoms
- Primary Sclerosing Cholangitis
- Preoperative thrombocytosis
  - But not fulminant colitis!
- Genetic factors
  - IL-1ra, CARD 15, TNF genes
  - pANCA data conflicting
Pouchitis Incidence

- At 10 years, at least 50% of patients will have had pouchitis.
- Of those, about 10-20% will develop chronic pouchitis.
- Thus, about 5-10% of all patients will develop chronic pouchitis.
- At least 3-5% will “loose” their pouch.
  - In my experience, many of these patients probably have Crohn’s.
Pouchitis
Clinical Features

- Increased stool frequency
- Abdominal cramps
- Urgency
- Nocturnal soilage
- Fecal Incontinence
- Bleeding
  - anemia
- Extraintestinal manifestations
**Pouchitis Disease Activity Index - PDAI**

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool frequency/usual</td>
<td>0</td>
</tr>
<tr>
<td>2/day more than usual</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 3 /day more than usual</td>
<td>2</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0</td>
</tr>
<tr>
<td>Urgency</td>
<td>0</td>
</tr>
<tr>
<td>Fever</td>
<td>0</td>
</tr>
<tr>
<td>Endoscopy: edema, granularity, Friable, loss vasc, exudate ulcers</td>
<td>1 each</td>
</tr>
<tr>
<td>Histology, PMN’s1</td>
<td>1</td>
</tr>
<tr>
<td>Ulceration: &lt;25%/low power field</td>
<td>1</td>
</tr>
<tr>
<td>25-50%</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 50%</td>
<td>3</td>
</tr>
</tbody>
</table>
Pouchitis
Differential Diagnosis

- Crohn’s
- Infection: CMV, C. dif
- Decrease pouch compliance
- Irritable Pouch Syndrome
- Cuffitis
- Anastomotic Stricture
- Poor pouch emptying
- Pelvic Floor dysfunction
- Pouch stricture/ischemia
- Anal sphincter

- “At the first episode of symptoms suggesting acute pouchitis, it is important to confirm the diagnosis with endoscopy and histology.”
- “The severity of symptoms often does not correlate with the degree of endoscopic or histologic inflammation of the pouch.”

Shen and co-workers, Inflammatory Bowel Disease, 2009
How should you work up a patient with symptoms of Pouchitis?

- “Patients with symptoms suggesting pouchitis should be assessed by a combined evaluation of history, physical examination, pouch endoscopy and biopsy, all of which are necessary for an accurate diagnosis of pouchitis and for differentiating it from other inflammatory diseases.”

Shen and co-workers, Inflamm Bowel Dis, 2009
Pouchitis
Differential Diagnosis

- Crohn’s
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Role of Endoscopy in Patients with Sxs of Pouchitis

“Some clinicians make an empiric diagnosis of pouchitis...given that pouchitis is the most common cause...This strategy may lead to an incorrect diagnosis of pouchitis in patients who have another cause of pouch dysfunction.”

Pouchitis
Diagnostic Testing after Endoscopy

- Pouchogram
- Physical Exam:
  - Dilate anal stenosis
- Anal Manometrics
- Stool Culture/C. diff
  - C. diff common in Cleveland, never seen in Rochester, rare in Seattle
- Nuclear scintigraphy
Preoperative C. difficile is not associated with an increased risk for infection in ileal pouch patients.

Sun, Du, Shen. Dig Dis Sci 2014

- 102 patients with C. difficile infections prior to colectomy; and 21 patients with C. diff in ileal pouches were studied.

- Risk factors for C diff infections identified.
Preoperative C. difficile is not associated with an Increased Risk for Infection in ileal Pouch Patients
Sun, Du, Shen. Dig Dis Sci 2014

- Significant risk factors were male, preoperative co-morbidities and use of antibiotics for other indications.

- Preoperative C diff infection was not a risk factor.
Pouchitis
Differential Diagnosis

- Crohn’s
- Infection: CMV, C. dif
- Decrease pouch compliance
- Irritable Pouch Syndrome
- Cuffitis
- Anastomotic Stricture
- Poor pouch emptying
- Pelvic Floor dysfunction
- Pouch stricture/ischemia
- Anal sphincter
Pouchitis
Differential Diagnosis

“The absence of endoscopic, radiographic or histologic abnormalities in the afferent limb, pouch and rectal cuff in patients with symptoms would suggest the diagnosis of “irritable pouch syndrome.”

Shen and co-workers, Cleveland Clinic, 2009
Pouch Endoscopy
Key Elements

- Anal dilation of anastomotic stenosis
  - Finger usually is adequate
  - Young dilators for firm stricture
Pouch Endoscopy
Key Elements

- Anal dilation of anastomotic stenosis
- **Inspect the afferent limb** (the ileum above the pouch)
  - Significant inflammation in the afferent limb suggests Crohn’s or PSC
Pouch Endoscopy

Key Elements

- Anal dilation of anastomotic stenosis
- Inspect the afferent limb (the ileum above the pouch)
- Biopsy both normal and abnormal appearing mucosa (don’t biopsy small ulcers on the staple line)
  - Look for CMV, granulomas
  - Normal appearing mucosa can have significant inflammation on histology.
  - Chronic inflammation is normal; acute inflammation is diagnostic of pouchitis.
Pouch Endoscopy
Key Elements

- Anal dilation of anastomotic stenosis
- Inspect the afferent limb (the ileum above the pouch)
- Biopsy both normal and abnormal appearing mucosa (don’t biopsy small ulcers on the staple line)

Read the op note to find out if the patient has a stapled or hand-sewn anastomosis (possible cuffitis)

- A stapled anastomosis usually will leave 1-3 cm’s of rectal mucosa which can result in urgency, pruritus, increased stool frequency etc.
Pouch Endoscopy
Key Elements

- Anal dilation of anastomotic stenosis
- Inspect the afferent limb (the ileum above the pouch)
- Biopsy both normal and abnormal appearing mucosa (don’t biopsy small ulcers on the staple line)
- Read the op note to find out if the patient has a stapled or hand sewn anastomosis (possible cuffitis)
Acute Pouchitis Treatment

- Ciprofloxacin  500 mg BID
- Metronidazole  750-1500 mg/day
  - I rarely exceed 250 mg/TID

- Moxifloxacin (Avelox)
- Rifaximin
- Anything!
Flagyl vs Cipro?
Randomized Trial for Acute Pouchitis

- 16 patients randomized to Cipro 1 gm/day or Flagyl 20mg/kg/d.
- Significantly better response of PDAI in Cipro patients compared to the Flagyl patients
- 33% of Flagyl patients had side effects.

Shen et al. Inflamm Bowel Dis 2001
FDA Boxed Warning on Fluoroquinolones

- Fluoroquinolones are associated with an increased risk of tendon rupture.
- Risk increased in age > 60, on steroids, immunosuppressed.
- Patients with pain should stop taking their quinolones.
Classification of Pouchitis

- **Acute vs. Chronic**
  - Acute: sx less than 4 weeks
  - Chronic: sx more than 4 weeks

- **Antibiotic dependence**
  - Antibiotic-responsive
  - Antibiotic-dependent
  - Antibiotic-refractory
Chronic Pouchitis: Multi-drug Rx

- 8 patients with antibiotic resistant chronic pouchitis treated with rifaximin 1 g bid plus Cipro 500 mg bid.
- 7/8 patients had marked improvement (n=2) or resolution (n=5) of their sxs.
- At 30 months, all 7 were still in remission. 2 needed extended course.

Abdelrazeq et al, York UK, Colorectal Dis, 2005
Antibiotic Dependent Pouchitis
Second Line RX

- Mesalamine Suppository
  - Canasa Suppository 1 gm qhs
- Oral or topical Budesonide
- Oral or topical Azathioprine
Prophylaxis of Pouchitis
Role of Probiotics
Chronic Pouchitis
Role of Probiotics

- 40 patients with antibiotic-dependent chronic pouchitis were randomized to VSL#3, 6 grams/day or placebo for 9 months.
- Patients seen monthly, endoscopy every 2 months

Gionchetti et al, Bologna Gastro 2000,
Chronic Pouchitis
Role of Probiotics

- Relapse in VSL#3 group: 15%
- Relapse in placebo group: 100%

Gionchetti et al, Bologna Gastro 2000,
Prophylaxis of Pouchitis
Role of Probiotics

- 40 patients with IPAA randomized to VSL#3 (1 packet) or placebo immediately after ileostomy closure.

- Followed for 1 year with endoscopy at 1, 3, 6, 9 and 12 months.

- Pouchitis occurred
  - VSL#3 = 10%
  - Placebo = 40%

Gionchetti et al  Gastroenterology 2003
Efficacy of Infliximab Rescue Therapy in Patients with Chronic Refractory Pouchitis

Acosta et al, Inflamm Bowel Dis: 2011

- Retrospective, multi-center study
- 33 patients with chronic refractory pouchitis treated with IFX 5 mg/kg.
- Patients assessed clinically (no endoscopy) at 2, 26 and 52 weeks.
Efficacy of Infliximab Rescue Therapy in Patients with Chronic Refractory Pouchitis
Acosta et al, Inflamm Bowel Dis: 2011

<table>
<thead>
<tr>
<th></th>
<th>8 weeks</th>
<th>26 weeks</th>
<th>52 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial response</td>
<td>63%</td>
<td>33%</td>
<td>18%</td>
</tr>
<tr>
<td>Complete response</td>
<td>21%</td>
<td>33%</td>
<td>27%</td>
</tr>
<tr>
<td>Withdrew</td>
<td></td>
<td></td>
<td>39%</td>
</tr>
</tbody>
</table>
Pouchitis after IPAA Summary

- Empiric Treatment of patients with new onset sx s c/w pouchitis
- Start with Cipro 1g/d for 10-14 days.
- Flagyl 750-1000mg/d for failures
- Endoscopy with biopsies and anal dilation in non-responders. Examine afferent limb.
- Don’t’ forget “cuffitis”
- Rifaximin or Avelox for failures, consider dual therapy.
- Canasa Suppositories or Budesonide for failures.
- Infliximab
Pouchitis Management

1. Ciprofloxacin or
2. Metronidazole

Response

No Response

Infrequent recurrences

Prompt recurrence or multiple recurrences

Switch Cipro for Metronidazole

Endoscopy with biopsy

No Pouchitis

Pouchitis

Tincture of Opium

Avelox

Prompt recurrence

Chronic antibiotics (best response antibiotic)

Add probiotics

Rifaximin

Response

Cycling Antibiotics

Chronic Probiotics

Mesalazine Suppository
Dosing for Pouchitis

Ciprofloxacin 500 mg. BID x 10 days
Metronidazole 250 mg. TID x 10 days
Avelox 400 mg qd. X 10 days
Rifaximin 200 mg TID x 5 days
Mesalamine suppository 1 gm qhs x 30 days
Tincture of opium 10% solution 0.6 cc. po BID
Probiotics VSL #3 (www.vsl3.com) 2-4 packets/day x 30 days
   Initial dose 2 packets BID, chronic dose is 1 packet BID

Chronic antibiotics = 30 days
Ileoanal Pouch Procedures
Failure rates and Salvage

- Current reviews suggest about a 5% pouch loss rate or failure rate after IPAA.
- Pouch loss is related to:
  - Crohn’s
  - Pouchitis
  - Mechanical failure.
- Crohn’s is associated with a pouch loss rate of 16-45%.
Salvage Procedures after Ileoanal Pouch Procedures

- Systematic Review and Meta-analysis

- 77 studies with 2,103 patients

- Salvage procedures divided into
  - Local/perineal
  - Revisional
  - Redo

Wexner and co-workers, JACS 2015
Salvage Procedures

Indications

- Pelvic Sepsis #1
- Crohn’s Disease
- Pouch Fistulas
- Pouch Vaginal fistulas
- Small Volume Reservoirs
- Incontinence
- Stenoses
# Salvage Procedures Success Rates

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>% Success at 2 Years</th>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redo</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>Revisional</td>
<td>79%</td>
<td>44%</td>
</tr>
<tr>
<td>Local/Perineal</td>
<td>68%</td>
<td>14%</td>
</tr>
</tbody>
</table>
IPAA Salvage Procedures

- Redo and revisional procedures (combined abdominal and perineal) are more successful.
- However, there is much less morbidity with local/perineal procedures.
- Therefore, some authors recommend attempted transanal procedure first.
- Data suggests 3-fold higher reoperation rate
Salvage Procedures

Pouch Vaginal Fistulas

- Revisional procedure with ileoanal advancement is optimal procedure

- Advancement of endo-anal flap less likely to work

- Add Gracilis flap improves results.
## Salvage Procedures
### Pouch-Vaginal Fistulas

<table>
<thead>
<tr>
<th>Success Rates</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High</strong> (72%)</td>
<td>Abd-Perineal pouch advancement</td>
</tr>
<tr>
<td><strong>Moderate</strong> (75% in 1 small series)</td>
<td>Ileoanal advancement with gracilis muscle</td>
</tr>
<tr>
<td><strong>Low</strong> (I’ve never seen it work)</td>
<td>Fibrin glue, Button plug, seton</td>
</tr>
</tbody>
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# Salvage Procedures

## Pelvic abscess/Fistula

<table>
<thead>
<tr>
<th>Success Rates</th>
<th>Procedures</th>
</tr>
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<tbody>
<tr>
<td>High</td>
<td>Abd-Perineal pouch advancement</td>
</tr>
<tr>
<td>Moderate</td>
<td>Ileoanal advancement</td>
</tr>
<tr>
<td>Low</td>
<td>Fibrin glue, Collagen plug, seton, fistula excision.</td>
</tr>
</tbody>
</table>
Summary

- Pouch salvage in patients with significant ileal pouch disease is now possible in about 2/3 of patients.

- Local procedures usually don’t work, however the morbidity of failed procedures is relatively low.

- Revisions via combined abdominal and perineal approach are possible in many patients.
What is the Role for Early Surgery in Patients Presenting with Ileocelecal Crohn’s?

- 207 patients with ileo-cecal Crohn’s were reviewed.
- 83 underwent surgery at presentation.
- 124 underwent delayed surgery at an average of 54 months.
- End point was clinical recurrence.
- Secondary endpoint was need for immunosuppression and surgery.

Aratari et all, Alimentary Pharm & Therap 2007
What is the Role for Early Surgery in Patients Presenting with Ileocelecal Crohn’s?

- At 10 years, 60% of the early resection group was free of clinical recurrence.
- Only 16% of the delayed surgery group was free of clinical recurrence.
- However, the same percentage of patients had repeat surgery at 10 years.
- On multivariate analysis, early surgery was the only independent variable associated with reduced risk for clinical recurrence.

Aratari et al, Alimentary Pharm & Therap 2007
Transverse Incisions for Resection of Ileocolic Crohn’s Disease

MICHAEL J. CAMPBELL, M.D., NATHANIEL B. PAULL, M.D., RICHARD C. THIRLBY, M.D.
From the Department of General Surgery, Virginia Mason Medical Center, Seattle, Washington

American Surgeon, 2013
Ileocectomy for Crohn’s

- 39 patients undergoing first operation for Crohn’s through small transverse incision

 Short-term
  - OR time 91 minutes
  - LOS 4 days
  - Major complications: none

 Long-term
  - Reoperation for Crohn’s = 2 (7%)
  - Stoma’s = 0
  - Sx free = 61%

Campbell et al. American Surgeon 2013
What is the Role for Early Surgery in Patients Presenting with Ileocelecal Crohn’s?

- If we can all agree that “top-down” treatment is the optimal management strategy for patients presenting with Crohn’s, then
- Why not really start at the “top” and resect the disease at presentation and start with a patient in complete surgical “remission.”

Thirlby et al, 2015
Summary

- Pouchitis is the “Achilles Heel” of the IPAA, occurring in at least 50% of patients.

- Many IPAA’s with major technical problems can be salvaged.

- “To cut is to cure.”
Pouchitis Management

1. Ciprofloxacin or
2. Metronidazole

Response

No Response

Infrequent recurrences

Prompt recurrence or multiple recurrences

Switch Cipro for Metronidazole

Endoscopy with biopsy

No Pouchitis

Tincture of Opium

Pouchitis

Avelox

Prompt recurrence

Chronic antibiotics (best response antibiotic)

No Response

Add probiotics

Rifaximin

Cycling Antibiotics

Response

Chronic Probiotics

Mesalazine Suppository

No Response

Oral or topical budesonide

Oral or topical Immunosuppressive drugs (e.g. azathioprine)

Biologic (infliximab)

Surgical consultation
Ciprofloxacin 500 mg. BID x 10 days
Metronidazole 250 mg. TID x 10 days
Avelox 400 mg qd. X 10 days
Rifaximin 200 mg TID x 5 days
Mesalamine suppository 1 gm qhs x 30 days
Tincture of opium 10% solution 0.6 cc. po BID
Probiotics VSL #3 (www.vsl3.com) 2-4 packets/day x 30 days
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