Pouchitis - Full Clinical Guideline

Reference no.: CG-GASTRO/2020/028

This guideline covers the diagnosis and medical management of acute and chronic idiopathic pouchitis.

Keywords: Pouch, Pouchitis, IPAA, ileal pouch anal anastomosis

Contents:

Abbreviations

IBD: Inflammatory Bowel Disease

UC: Ulcerative Colitis

CD: Crohn's Disease

CMV: Cytomegalovirus

IPAA: Ileal Pouch Anal Anastomosis

FAP: Familial Adenomatous Polyposis

1. Overview of pouchitis

- Restorative proctocolectomy with ileal- pouch anal anastomosis (IPAA) is the surgical procedure for patients with refractory ulcerative colitis (UC), dysplasia in colitis or familial adenomatous polyposis (FAP) of the colon (apart from other less common indications such as synchronous colorectal cancer).
- The pouch procedure provides an opportunity for the patient to prevent a permanent ileostomy.
- Patients with normally functioning healthy pouches 12 months after pouch creation can expect to have around 4 to 7 bowel movements a day (including one to two movements at night), with continence and ability to defer a bowel movement for up to an hour.
- Pouchitis refers to idiopathic chronic non-specific inflammation of the ileal reservoir (pouch) causing symptoms (see below) with endoscopic and histologic features of pouch inflammation. It is common in those who had the pouch for UC and exceedingly rare in those who had it for cancer or FAP.
- Up to 50% of patients will develop pouchitis at any point after IPAA and the incidence of acute pouchitis is around 20% in the first year and 40% at 5 years after IPAA.
- Increased bacterial concentration and dysbiosis in the ileal reservoir have been identified as the possible mechanisms for pouchitis substantiated by the efficacy of antibiotic therapy in treating flares.
- Acute pouchitis refers to symptoms less than 4 weeks. Chronic pouchitis is defined as persistence of symptoms more than 4 weeks despite treatment.
- Typical symptoms of pouchitis include:
    - Urgency
    - Diarrhoea with or without rectal bleeding
    - Increased bowel frequency
    - Nocturnal seepage or incontinence
    - Tenesmus
    - Abdominal cramps
    - Pelvic discomfort
    - Extraintestinal manifestations (iritis, arthritis, pyoderma gangrenosum, erythema nodosum etc)
    - Lethargy (iron and other vitamin deficiencies are very common due to reduced absorption/ inflammation)
- Approach to the patient with pouch dysfunction (Fig. 1) involves a thorough history/ timeline of symptoms and examination; exclusion of other causes such as infection, NSAID use, coeliac disease, medications, Crohn’s disease, pelvic sepsis/ collection, cuffitis and irritable pouch syndrome.
- In patients with IPAA and above-mentioned symptoms, other causes such as coeliac disease, small intestinal bacterial overgrowth, faecal incontinence from sphincter damage, irritable pouch syndrome and lactose intolerance should be considered if normal histology from pouch mucosa is noted.
- Pouchitis can have an adverse impact on physical as well as mental health with implications on socioeconomic factors such as daily activities, socialising and work. Urgency, incontinence and nocturnal seepage can be devastating symptoms for patients. Timely diagnosis and management help to improve morbidity and outcomes.

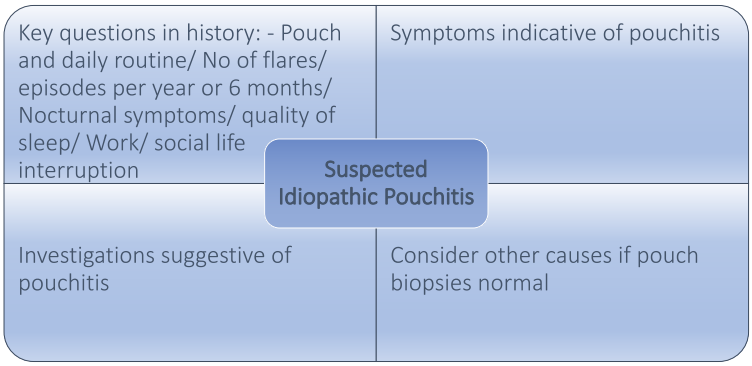

Figure 1: Factors to consider during assessment of idiopathic pouchitis

2. Types of pouchitis and practical points in assessment

- *Idiopathic pouchitis*- the *commonest* type in a patient with previous IBD- UC. It can be acute (< 4 weeks- duration of symptoms), acute relapsing (above with more than 4 episodes a year) or chronic (>4 weeks).
    - The disease course can be *antibiotic- responsive, antibiotic-dependent or antibiotic- refractory* (Fig. 2). 20- 30% of patients with antibiotic refractory chronic pouchitis can be due to secondary pouchitis.

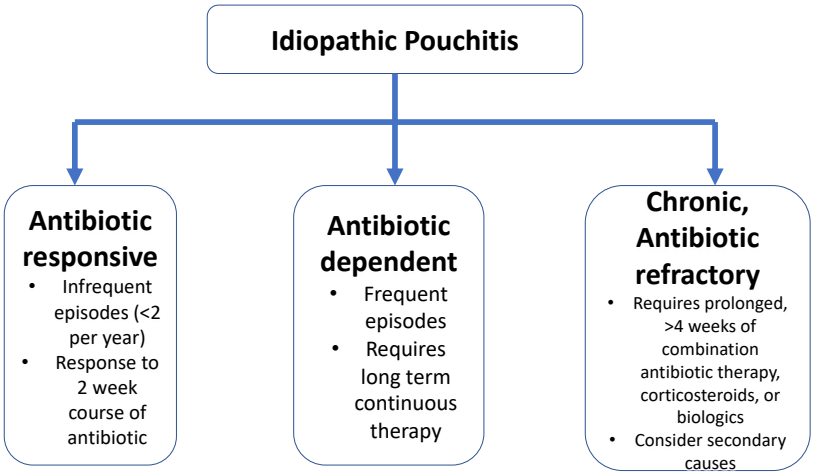

Figure 2: Spectrum of idiopathic pouchitis based on antibiotic treatment response

- *Secondary Pouchitis (less common)*
    - Clostridium difficile pouchitis (chronic antibiotic therapy is a predisposing factor)
    - Other infective pouchitis (E coli, Klebsiella and other coliforms)
    - Candida pouchitis
    - CMV pouchitis
    - Ischaemic pouchitis
        - Characteristically found in the afferent limb
        - Plane of demarcation of inflammation during pouchoscopy along the suture line
        - Poor response to antibiotics and immunomodulator therapy

- NSAID- induced pouchitis
- Autoimmune pouchitis- features include:
    - Chronic pouchitis refractory to antibiotic therapy
    - Concurrent autoimmune conditions might be present
    - Extraintestinal manifestations or Primary Sclerosing Cholangitis (PSC) are associations
    - Elevated serum IgG4 and/or infiltration of the pouch mucosa with IgG4 expressing plasma cells (need to request histopathologist for IgG4 stain from biopsies)
    - Management involves immunosuppression
- Crohn's disease of the pouch
    - Can develop *de novo* in UC patients after colectomy with IPAA; can be challenging to diagnose
    - Mechanical defects can mimic CD of the pouch (short interval between index IPAA and onset of symptoms should raise suspicion)
    - Features that can lead to suspicion of CD of the pouch include
        a. Development of a new perianal fistula more than 12months after IPAA surgery
        b. Narrowing (structuring) of the pouch inlet or the efferent limb
        c. Inflammation of the pre-pouch ileum that extends well beyond 10 cm above the pouch
        d. Systemic symptoms- weight loss, nausea, vomiting
    - Behaviour can be inflammatory, fibro-stenotic or fistulising
    - Strictures may be encountered in endoscopy (avoid dilatation without assessing with imaging)
    - Immunomodulators recommended early with a view to pouch preservation if not responsive to antibiotics
    - Presence of a fistula does not automatically suggest Crohn's disease and needs further evaluation (especially pouch-vaginal fistula)
- Cuffitis
    - Indicates inflammation of the rectal cuff in the area between the anastomosis and the dentate line
    - May represent UC in the rectal cuff and is particularly common when IPAA formed with stapled anastomosis without mucosectomy (check surgical notes).
    - Surveillance for dysplasia is required in this group of patients if recurrent flares

- Irritable pouch syndrome
    - Characterised by symptoms of pouchitis but no endoscopic or histologic activity
    - Consider other causes such as coeliac disease, small intestinal bacterial overgrowth or food intolerances namely lactose/ fructose/ gluten intolerance/ sphincter dysfunction

3. Investigations

- Stool cultures
- Blood investigations- ensure iron, B12, folate and Vitamin D checked and supplemented if low; iron deficiency anaemia is common in pouchitis and some patients may require iron infusions if poor response to oral supplementation
- Pouch endoscopy with biopsies- biopsies needed even if mucosa appears normal (see separate guideline on endoscopy in a patient with a pouch)
- MRI of the pelvis- to exclude collections or fistulae (not routinely needed) and if Crohn's disease suspected (for example stricture noted in pouch endoscopy)
- Examination under anaesthesia (EUA) may be required if MRI shows pelvic collections or fistulae- these are ideally discussed in the IBD MDT and needs liaising with the colorectal team.

4. Management of pouchitis

Antibiotics reduce bacterial counts, improves villous atrophy, induces short chain fatty acid formation in the pouch and reduces leucocyte infiltration in the pouch. Ciprofloxacin and metronidazole were compared for treatment in acute pouchitis in a randomised trial; Ciprofloxacin was superior in efficacy with less side effects.

- ***Acute Pouchitis (symptoms less than 4 weeks, negative stool cultures)***
    - First line therapy includes Ciprofloxacin 500mg BD or Metronidazole 400mg tds for *2 weeks*
    - Second line therapy comprises the following regimes for a total of *4 weeks:*
        - Ciprofloxacin 500mg BD and Metronidazole 400mg tds, or
        - Ciprofloxacin 500mg BD and Tinidazole 1gram, or
        - Ciprofloxacin 500mg BD and Rifaximin 1gram BD (note cost)

- ***Chronic Pouchitis (symptoms for more than 4 weeks)***
    - Combination antibiotics (as above) if not tried before
    - VSL#3 at 1 or 2 sachets per day recommended as maintenance *only* for antibiotic dependent patients with chronic pouchitis.
        - Consider stopping probiotics if recurrent flares despite on probiotic maintenance
    - Rotating antibiotics to control symptoms for a total of 8 weeks
    - Antidiarrhoeals- loperamide to control frequency may be needed
    - If not resolved or if rapid relapse (refractory pouchitis), initiate oral Budesonide 9mg/day for 8 weeks or oral Beclomethasone 10mg/ day for 8 weeks
    - If still not resolved, refer to IBD MDT for consideration of biological therapy. Immunomodulator monotherapy (thiopurines), alicaforsen enemas, bismuth and tacrolimus remain other options but there is very little evidence on efficacy.
    - Consider colorectal surgical team review (pouch excision) if pouch failure despite above.

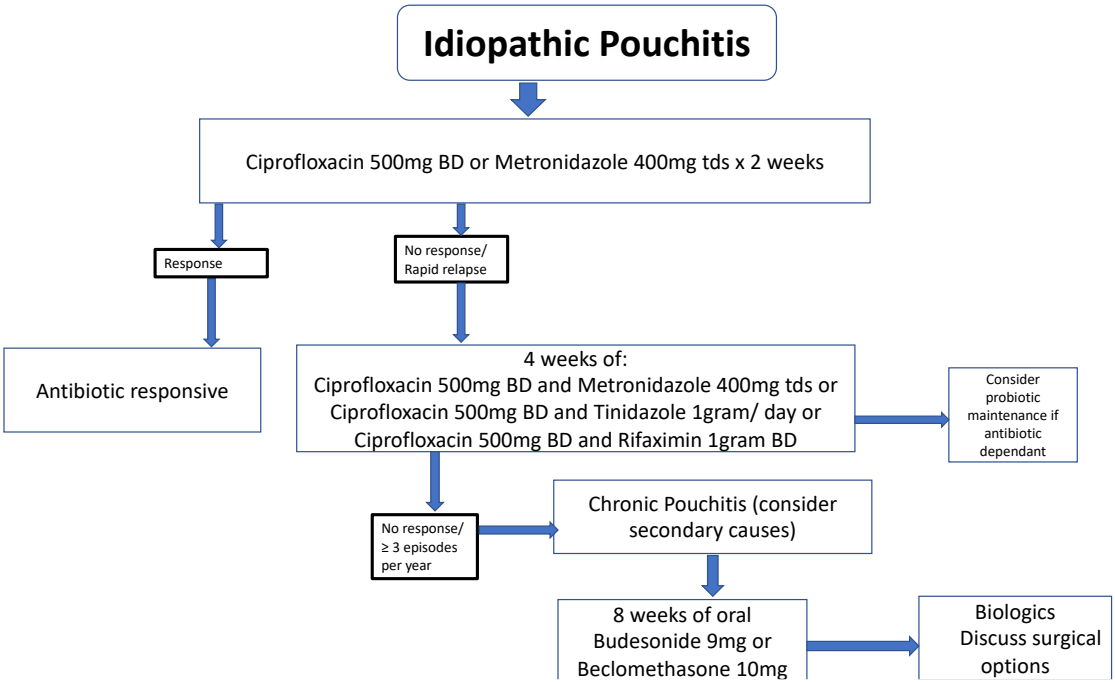

Figure 3: Idiopathic pouchitis management pathway

- ***Cuffitis***
  - Management is similar to ulcerative proctitis with topical mesalamine/ topical steroids, thiopurine and biologics

5. **Surveillance**
   - Risk of neoplasia in pouches is low, with cancer risk of 0.02% at 20 years
   - Cancer may arise from the rectal cuff, the pouch or separately from the anal mucosa
   - Yearly pouch surveillance is recommended for the following group of patients at increased risk for dysplasia or cancer:
     - Colorectal carcinoma or dysplasia in the colectomy specimen
     - Primary Sclerosing Cholangitis
     - Chronic pouchitis with type C ileal pouch mucosa (moderate to severe villous atrophy, severe pouchitis occurring rapidly after pouch formation)
     - Long retained rectal cuff
   - In the absence of above risk factors, the benefits of surveillance are uncertain and should be discussed with the patient.

References:

1. Lamb, Christopher Andrew, Nicholas A. Kennedy, Tim Raine, Philip Anthony Hendy, Philip J. Smith, Jimmy K. Limdi, Bu'Hussain Hayee et al. "British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults." *Gut* 68, no. Suppl 3 (2019): s1-s106.
2. Pardi, Darrell S., Geert D'Haens, Bo Shen, Simon Campbell, and Paolo Gionchetti. "Clinical guidelines for the management of pouchitis." *Inflammatory bowel diseases* 15, no. 9 (2009): 1424-1431.
3. Landy, J., H. O. Al-Hassi, S. D. McLaughlin, S. C. Knight, P. J. Ciclitira, R. J. Nicholls, S. K. Clark, and A. L. Hart. "Etiology of pouchitis." *Inflammatory bowel diseases* 18, no. 6 (2012): 1146-1155.
4. Magro, Fernando, Paolo Gionchetti, Rami Eliakim, Sandro Ardizzone, Alessandro Armuzzi, Manuel Barreiro-de Acosta, Johan Burisch et al. "Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders." *Journal of Crohn's and Colitis* 11, no. 6 (2017): 649-670.
5. Benlice, Cigdem, Bo Shen, and Scott R. Steele. "Prevention and Medical Treatment of Pouchitis In Ulcerative Colitis." *Current drug targets* 20, no. 13 (2019): 1399-1408.
6. Shen, Bo. "Pouchitis: what every gastroenterologist needs to know." *Clinical Gastroenterology and Hepatology* 11, no. 12 (2013): 1538-1549.
7. Nguyen, Nghia, Bing Zhang, Stefan D. Holubar, Darrell S. Pardi, and Siddharth Singh. "Treatment and prevention of pouchitis after ileal pouch-anal anastomosis for chronic ulcerative colitis." *Cochrane Database of Systematic Reviews* 11 (2019).
8. Segal, Jonathan P., Nik S. Ding, Guy Worley, Simon Mclaughlin, S. Preston, O. D. Faiz, S. K. Clark, and A. L. Hart. "Systematic review with meta-analysis: the management of chronic refractory pouchitis with an evidence-based treatment algorithm." *Alimentary pharmacology & therapeutics* 45, no. 5 (2017): 581-592.
9. Zezos, Petros, and Fred Saibil. "Inflammatory pouch disease: the spectrum of pouchitis." *World Journal of Gastroenterology: WJG* 21, no. 29 (2015): 8739.
10. Shen, Bo, Feza H. Remzi, Aaron Brzezinski, Rocio Lopez, Ana E. Bennett, Ian C. Lavery, Elaine Queener, and Victor W. Fazio. "Risk factors for pouch failure in patients with different phenotypes of Crohn's disease of the pouch." Inflammatory bowel diseases 14, no. 7 (2008): 942-948.
11. Benlice, Cigdem, Bo Shen, and Scott R. Steele. "Prevention and Medical Treatment of Pouchitis In Ulcerative Colitis." *Current drug targets* 20, no. 13 (2019): 1399-1408.
12. Shen, B., A. Brzezinski, V. W. Fazio, F. H. Remzi, J-P. Achkar, A. E. Bennett, K. Sherman, and B. A. Lashner. "Maintenance therapy with a probiotic in antibiotic-dependent pouchitis: experience in clinical practice." *Alimentary pharmacology & therapeutics* 22, no. 8 (2005): 721-728.
13. Lichtenstein, Lev, Irit Avni-Biron, and Ofer Ben-Bassat. "The current place of probiotics and prebiotics in the treatment of pouchitis." *Best Practice & Research Clinical Gastroenterology* 30, no. 1 (2016): 73-80.
14. Gionchetti, Paolo, Fernando Rizzello, Claudia Morselli, Gilberto Poggioli, Rosi Tambasco, Carlo Calabrese, Patrizia Brigidi, Beatrice Vitali, Giulia Straforini, and Massimo Campieri. "High-dose probiotics for the treatment of active pouchitis." *Diseases of the Colon & Rectum* 50, no. 12 (2007): 2075-2084.
15. Sandborn, William J. "Pouchitis following ileal pouch-anal anastomosis: definition, pathogenesis, and treatment." *Gastroenterology* 107, no. 6 (1994): 1856-1860.
16. Mahadevan, U., and William J. Sandborn. "Diagnosis and management of pouchitis." *Gastroenterology* 124, no. 6 (2003): 1636-1650.

17. Penna, C., R. Dozois, W. Tremaine, W. Sandborn, N. LaRusso, C. Schleck, and D. Ilstrup. "Pouchitis after ileal pouch-anal anastomosis for ulcerative colitis occurs with increased frequency in patients with associated primary sclerosing cholangitis." *Gut* 38, no. 2 (1996): 234-239.
18. Sandborn, William J., and Darrell S. Pardi. "Clinical management of pouchitis." *Gastroenterology* 127, no. 6 (2004): 1809-1814.
19. McLaughlin, Simon D., Susan K. Clark, Siwan Thomas-Gibson, Paris P. Tekkis, Paul J. Ciclitira, and John R. Nicholls. "Guide to endoscopy of the ileo-anal pouch following restorative proctocolectomy with ileal pouch-anal anastomosis; indications, technique, and management of common findings." Inflammatory bowel diseases 15, no. 8 (2009): 1256-1263.
20. Segal, Jonathan P., Stephanie X. Poo, Simon D. McLaughlin, Omar D. Faiz, Susan K. Clark, and Ailsa L. Hart. "Long-term follow-up of the use of maintenance antibiotic therapy for chronic antibiotic-dependent pouchitis." *Frontline Gastroenterology* 9, no. 2 (2018): 154-158.
21. Dalal, Robin L., Bo Shen, and David A. Schwartz. "Management of pouchitis and other common complications of the pouch." *Inflammatory bowel diseases* 24, no. 5 (2018): 989-996.

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