

Pouchitis

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Bullet Points

- Pouches (ileal reservoirs) are the procedure of choice for most patients with ulcerative colitis and FAP requiring colectomy.
- Pouchitis, pelvic sepsis and poor function, including apparent recurrent Crohn's disease, are the most common causes of pouch failure.
- Most biopsied pouches have inflammation and the following should be reported: quantity of acute and chronic inflammation, the presence of erosions and ulcers, the presence of pseudopyloric metaplasia, granulomas, presence of dysplasia (or adenomas in FAP) or carcinoma.
- Other complications can be associated with "pouchitis" such as prepouch ileitis, Crohn's disease, "cuffitis," polyps, dysplasia and carcinoma.
- About 10% of pouches end up being resected for various complications.

Pouches

- Patients undergoing colectomy for inflammatory bowel disease (IBD), usually but not always for ulcerative colitis (UC) (and also familial adenomatous polyposis - FAP), are frequently considered for an ileostomy sparing procedure with an anastomosis between the terminal ileum to the lower rectum. Part of the procedure is to form an ileal reservoir – the pouch, allowing reasonably normal physiological function. This is called euphemistically called "restorative proctocolectomy with ileal pouch - anal anastomosis" (IPAA) – the latter is the business end of the procedure.
- There are numerous anatomical variants of pouches but the procedure of choice is frequently the J pouch – formed from a loop of ileum turned back on itself (the J), with division of the intervening wall to form the reservoir, and anastomosis of the lower part of the J to the upper end of the anal canal. Invariably a small fragment of lower rectal mucosa overlying the sphincter muscles is deliberately left intact, as this provides the greatest chance of being continent. The remaining rectal mucosa is called the "rectal cuff". In both persistent UC and FAP this means that the cuff is potentially the site of persistent UC ("cuffitis"), and therefore dysplasia and carcinoma, and in FAP of adenomas and carcinomas. Pouches therefore have an afferent limb, often a small blind loop in the left upper part of the J, and the efferent limb which is the part anastomosed to the upper anal canal/rectal cuff.
- Pouches have long been the procedure of choice for most patients with ulcerative colitis who require colectomy for medically refractory disease or a complication such as dysplasia, and for FAP, but are sometimes also performed, advertently or inadvertently, for patients with Crohn's disease.
- Adverse sequelae include mechanical, inflammatory, functional, neoplastic, and metabolic conditions.(1)
- Pouchitis, pelvic sepsis and poor function, including apparent recurrent Crohn's disease, are the most common causes of pouch failure.

Pouchitis

- Pouchitis, which is the most common complication after IPAA, is an idiopathic chronic inflammatory condition that may occur in the ileal pouch in up to 60% of patients after IPAA for ulcerative colitis, but <5% of patients with FAP.
- The greater the extent of UC, the more likely is pouchitis to develop. Patients with pancolitis and backwash ileitis are therefore at greatest risk. Other predisposing causes include: genetic polymorphisms of the interleukin-1–receptor antagonist, of the NOD2/CARD gene, and noncarrier status of tumor-necrosis factor allele; proctocolectomy thrombocytosis; preoperative corticosteroid use; extra-intestinal manifestations, especially primary sclerosing cholangitis; the presence of perinuclear antineutrophil cytoplasmic antibodies (p-ANCA); being a non-smoker, and the use of NSAIDs (1)
- While the etiology of pouchitis remains unclear, it frequently responds to antibiotics, which have long implicated ileal flora in its etiology.
- The most common symptom from pouchitis is diarrhea, but there are numerous other causes of diarrhea in pouch patients. Increasingly, specific infections such as *C. difficile*, and less commonly CMV, are recognized as treatable causes of diarrhea in pouch patients(2, 3). However it is important to recognize that non-inflammatory causes of diarrhea (irritable pouch syndrome – which has been reported to be associated with enterochromaffin cell hyperplasia but is not practical as a routine(4), and other diseases causing diarrhea) can result in pouchoscopy and biopsies asking “is there pouchitis?”
- There is a poor correlation between symptoms, endoscopy and pathology, so that initial antibiotic therapy is the rule, and investigation usually reserved for patients with unresponsive or persistent symptoms.

Pouches for Crohn’s disease

This is sometimes done inadvertently when review of prior colectomy slides shows granulomas not attributable to other causes (mucin, foreign material), and/or transmural lymphoid hyperplasia typical of CD. However it is sometimes performed especially in young patients with Crohn’s disease limited entirely to the large bowel, without evidence of terminal ileal or perianal disease, in an attempt to shepherd them through their formative teens and twenties without having an ileostomy at this time of their lives. Although there is a high incidence of pouchitis, this policy can be very successful.

Sequelae of pouchitis

- Inflammation in the pouch occurs within the first few weeks, and most patients in whom pouchitis will be a problem have symptoms in the first year. (5)
- Changes which were thought to be adaptive occur in many patients with changes resembling colonic metaplasia. However these are likely a response to the inflammation rather than the presence of a pouch.(6)

Histological diagnosis of pouchitis

- If biopsies are without significant abnormality – say so.
- Most pouches coming to biopsy have some degree of inflammation which may be localized, patchy or diffuse, and have erosions and ulcers, and sometimes openings of fistula tracts endoscopically. The latter are *not* synonymous with Crohn’s disease (CD),

tend to occur at the ileo-anal anastomosis line. However the later they occur after the pouch procedure the more likely they are to represent CD.

- Because all inflammation is “non-specific”, it is a waste of space using this term.
- Biopsies are usually best reported descriptively regarding (7, 8)
 - quantity of acute and chronic inflammation (mild, moderate, severe - tradition rather than value), and if considered necessary, loss of villous height (also a waste of space as severe inflammation is always accompanied by loss of villous height and therefore inevitable if severe)
 - the presence of erosions and ulcers.
 - the presence of pseudopyloric metaplasia (ulcer-associated cell lineage) – which is indicative of prior ulceration
 - granulomas, and whether related to ruptured crypts (mucin) or foreign body. These are not indicative of Crohn’s disease
 - presence of dysplasia or adenomas in FAP, or carcinoma
 - other findings – e.g. intraepithelial lymphocytosis - ? celiac, a subepithelial collagen band – collagenous pouchitis.(9, 10)

Other complications in pouches that can result in biopsies

- ***Prepouch ileitis*** (inflammation in the afferent limb of the pouch). This is an increasing problem. Inflammation can be in continuity with inflammation in the pouch (some liken this to backwash ileitis but in the pouch), but sometimes occurs only in the afferent limb (often an inlet problem), and sometimes with a skip of normal mucosa between an inflamed pouch and the lesion. The latter in particular raises the question of CD, but it is impossible (unless overt well formed granulomas of no other cause, or overt CD elsewhere in the small bowel) to make the diagnosis. ***Beware*** interpreting any biopsies as “consistent with Crohn’s disease”. We have no idea what pre-pouch ileitis is. Some respond to anti-inflammatory medication but that does not mean they are CD. Your diagnosis of c/w CD will make this “Crohn’s disease confirmed on biopsy” for the clinician.(11-15)
- ***Crohn’s disease***. The diagnosis of CD is primarily clinical / endoscopic, and even here unless overt the distinction from pouchitis can be difficult or impossible as there is huge overlap between where severe pouchitis stops and CD of the pouch starts. There are no good criteria for doing this. Biopsies to support a clinical diagnosis of CD are contraindicated. There are NO good criteria for distinguishing inflammation secondary to pouchitis from that of CD (I state this in my reports). Unless you are going to write the definitive paper on this biopsies are contraindicated for this purpose. Do NOT sign out any pouch inflammation as “c/w Crohn’s disease” unless you also state the other things is also c/w, as the patient will be labelled as having Crohn’s disease (biopsy proven again).(10, 16)
- ***Cuffitis*** If taken from rectal mucosa these can show all of the features of the underlying IBD (or FAP). However, while inflamed large bowel can be villous, the presence of villi (well or poorly formed), pseudopyloric metaplasia, and particularly numerous Paneth cells in all crypts, suggests that the mucosa is really ileal and not rectal. Whether ileal

mucosa can ever grow into the rectal cuff mucosa is speculative. It can be difficult to see exactly where you are clinically.(17)

- ***Polyyps*** These can occur within the pouch and may be related to pouchitis (inflammatory), are rarely dysplastic (unless in FAP), or of other types that have nothing to do with the pouch (e.g. inflammatory fibroid polyps, other mesenchymal tumors) (18, 19)
- ***Dysplasia*** Dysplasia is rare in pouches but can occur. The rate is so low that routine screening in IBD cannot be justified, although in FAP adenomas regularly occur in the pouch and rectal cuff and may be biopsied. It is unclear what to do about dysplasia in a pouch but if visible endoscopically it can be removed and biopsies taken around the excision site to ensure that it has been completely removed. Dysplasia in the rectal cuff is part of the underlying IBD, is rare. There is no good solution other than also trying to remove it locally as the anal sphincter mechanism is at risk, while resection means the pouch also has to be taken down. (20-24)
- ***Carcinoma*** Carcinoma is seen in pouches but can represent involvement from dysplasia and carcinoma in the rectal cuff, represent involvement of the pouch from recurrent carcinoma in patients with carcinoma in their colectomy specimens that reaches the mucosa, or may genuinely occur in the pouch. All are bad news and result in excision of the pouch. However carcinomas and even carcinoids can occur in the rectal cuff(25-28), and also adenocarcinoma in the anal mucosa(26)
- ***Upper GI disease*** In patients in whom severe pouchitis leads to consideration of CD, an upper endoscopy (or enteroclysis, or capsule endoscopy) may be carried out looking for evidence of CD. However, patients with active pouchitis can have all of the extraintestinal, and extra pouch, complications seen in UC, including upper GI involvement. Data are scant but about 10% are said to have CD, and another 10% other inflammatory changes, and 3% peptic ulcer disease. Interpret these with caution. (29)
- ***Ileal endoscopy*** This is carried out looking for evidence of CD either because that diagnosis has been raised on the colectomy resection (transmural lymphoid hyperplasia, granulomas of no other cause), or in defunctioned pouches in whom CD of the pouch is suspected and the ileum is intubated looking for other evidence of the disease. Because changes secondary to the ostomy itself are very localized, changes proximal to the ileostomy may represent CD. However these are analogous to chronic active inflammation in terminal ileal biopsies, which are very likely to represent CD, but other causes (NSAIDS, infections) always need to be considered.

Resected pouches

About 10% of pouches end up being resected. Indications for pouch excision included pelvic or perineal sepsis in (60%), pouchitis (23%), and poor pouch function (17%). Persistent perineal sinus is present in about in (40%). Around 20% of these patients are considered to have Crohn's disease(30). Resected pouches are one of the classic morphological mimics of CD, and like other mimics (diversion disease, some diverticular disease, "Crohn's appendicitis"), often

have the transmural lymphoid hyperplasia so characteristic of CD. In one study (abstract only) only 2/80 pouches with these changes ever had evidence of CD elsewhere in the GI tract. Also, many of these patients have been treated with anti TNF antagonists which further mutes the inflammatory reaction, further confounding the differential diagnosis. Unless changes are so “barn door” that it is impossible to entertain any other diagnosis, or there are numerous granulomas not attributable to any other cause, changes are likely attributable to the underlying pouchitis.

- **Diversion pouchitis.** Many pouches that are ultimately resected may have undergone prior defunctioning with formation of what was hoped to be a temporary ileostomy. However ultimately a decision is made to excise the pouch. The effect of diversion on pouch morphology is still unclear. However established diversion proctitis frequently also has transmural lymphoid hyperplasia, so the role of diverting the pouch on potentiating further transmural lymphoid hyperplasia remains unclear. (31)

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