Ileo-anal pouches and associated complications

Introduction

Approximately a third of patients with ulcerative colitis eventually require surgical intervention (Langholz et al, 1992). Restorative proctocolectomy with ileal pouch-anal anastomosis has become the established procedure for the majority of patients. With this procedure becoming more widespread physicians will increasingly encounter patients with complications post ileal pouch-anal anastomosis. This review summarizes what doctors in training need to know about ileal pouch-anal anastomosis and provides a practical approach to managing pouch dysfunction and complications.

Background

Advances in surgical techniques have resulted in restorative proctocolectomy with ileal pouch-anal anastomosis becoming the preferred procedure for patients with ulcerative colitis refractory to medical treatment or those with dysplasia or neoplasia. The procedure avoids formation of a long-term ileostomy and preserves anal sphincter function.

Ileal pouch-anal anastomosis can be performed as a one- or two-stage elective procedure. Patients with acute severe colitis requiring urgent subtotal colectomy would wait for several months before undergoing ileal pouch-anal anastomosis. The two-stage procedure involves excision of the rectum with formation of the ileal pouch anal anastomosis while a temporary defunctioning loop ileostomy is created. In a second procedure the defunctioning ileostomy is reversed and the pouch begins to function. An alternative one-stage procedure involves proctocolectomy with immediate formation and functioning of the ileal pouch-anal anastomosis.

The most common configuration of pouch is the 'J' pouch. This involves looping distal ileum back on itself to form two limbs which are stapled together to form a reservoir. An enterotomy is made at the distal end of the pouch which is anastomosed to the anal canal either by a stapled or hand-sewn technique. The more common stapled technique involves leaving 1–2 cm of columnar epithelium or 'rectal cuff' behind while the hand-sewn technique is performed after a mucosectomy of the anal transitional zone (*Figure 1*).

Normal pouch function

With pouches, the median stool frequency has been reported as four to eight bowel movements with approximately 600–700 ml of semi-formed stool per day (Fazio et al, 1995; Sagar and Pemberton, 1997). On average patients have been reported to have one bowel movement overnight. In one large series, frequent daytime and night-time incontinence (more than two episodes per week with interruption of daily activities) occurred in 7 and 12% of patients respectively, and did not change over a 10-year period. Thirty nine per cent of patients reported using an anti-diarrhoeal medication (Meagher et al, 1998).

Complications

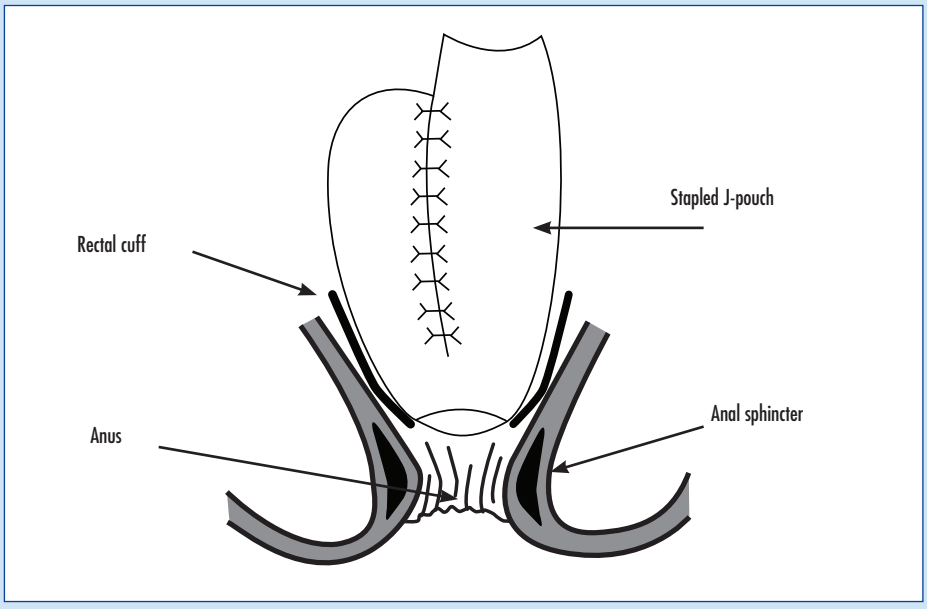
While the procedure has led to significant improvements in quality of life for patients with ulcerative colitis, inflammatory and non-inflammatory complications are common (*Figure 2*). The rate of pouch failure, resulting in pouch excision or permanent ileostomy, is highest in the first year after surgery. Since pouch disorders often present with a similar combination of symptoms it is important to develop a rigorous and structured diagnostic approach (*Table 1*).

Inflammatory complications

Pouchitis

Inflammation of the ileal pouch is the most common long-term complication following ileal pouch-anal anastomosis for ulcerative colitis. In one large series around 50% of patients developed at least one episode (Meagher et al, 1998). In addition, patients with co-existing primary sclerosing cholangitis have almost twice the risk of developing pouchitis as those without (Penna et al, 1996). Conversely, pouchitis rarely occurs in patients who undergo ileal pouch-anal anastomosis for familial adenomatous polyposis. The underlying aetiology and pathogenesis remain unclear.

Figure 1. Ileo-anal pouch anatomy.



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Pouchitis can cause a spectrum of symptoms including increased frequency, urgency, tenesmus, abdominal discomfort and rectal bleeding. Since symptoms are non-specific and can also occur in other pouch disorders it is important that these are considered together with endoscopic and histological findings to make an accurate diagnosis. Scoring systems have been developed in an attempt to standardize diagnostic criteria and severity, the pouchitis disease activity index being most commonly used in clinical trials (Sandborn et al, 1994). However, symptom scores often correlate poorly with objective endoscopic and histological findings.

A useful proposed method of classification is based on aetiology and symptom duration:

1. Idiopathic *vs* secondary
2. In remission *vs* active
3. Infrequent (<3 episodes per year) *vs* relapsing (>3 episodes per year).

Additionally, pouchitis can be classified on the basis of response to antibiotics:

1. Antibiotic responsive
2. Antibiotic dependent (need for continuous treatment to maintain remission)
3. Antibiotic refractory (Pardi et al, 2009).

Many patients will respond to antibiotics, with ciprofloxacin being regarded as a first-line choice as it appears more effective and associated with fewer side effects than metronidazole (Shen et al, 2001). Although the optimum duration of therapy is not clear, in practice a 14-day course is generally administered. A subset of these patients will subsequently develop frequent relapses and will be classified as having antibiotic-dependent pouchitis. Maintenance therapy options in these patients include probiotic therapy with VSL#3 which has demonstrated efficacy for maintaining antibiotic-induced remission (Mimura et al, 2004), or low-dose long-term antibiotics can be considered.

Patients who do not respond to an initial 14-day course of single agent antibiotic therapy are defined as having antibiotic-refractory pouchitis which is a common cause of pouch failure. It is important to exclude enteric infections such as cytomegalovirus or *Clostridium difficile*. The management of this challenging complication goes beyond the scope of this article but potential therapeutic options include combination antibiotic regimens, 5-aminosalicylates, corticosteroids and immunomodulators (Shen, 2012; Van Assche et al, 2013).

Figure 2. Overview of complications post ileal pouch-anal anastomosis.

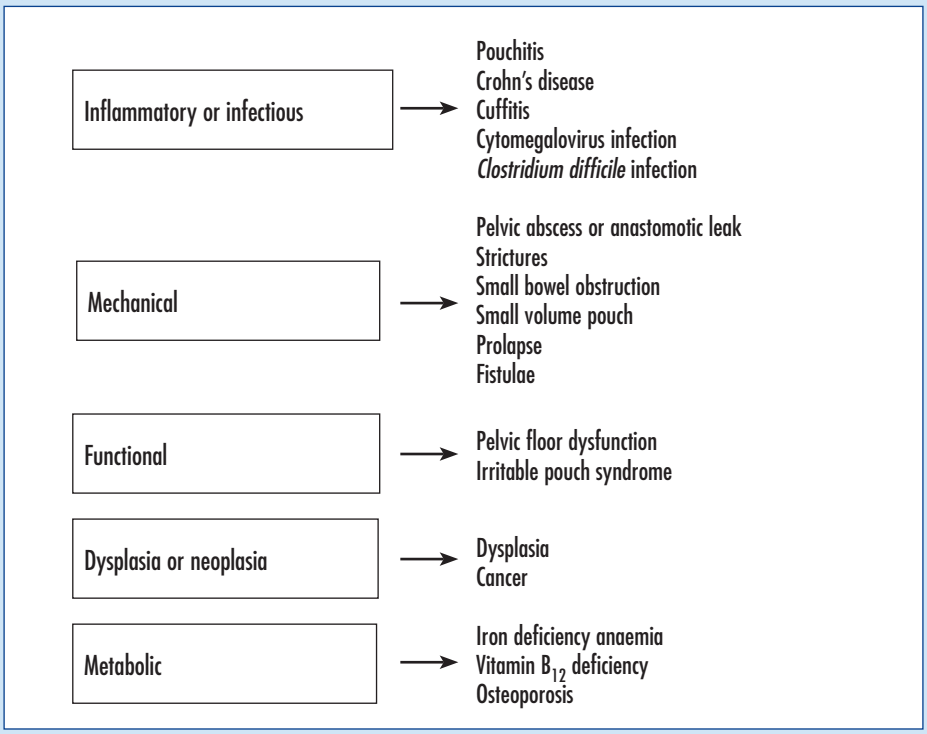

Table 1. Summary of investigations and management of complications post ileal pouch-anal anastomosis

Complication	Diagnosis	Treatment options
Pouchitis	Pouchoscopy and biopsy	Antibiotics
Cuffitis	Pouchoscopy and biopsies Pouchogram Computed tomography or magnetic resonance imaging enterography Computed tomography or magnetic resonance imaging pelvis	Dependant on disease phenotype – may require combination of pharmacological, endoscopic and surgical management
Pelvis sepsis	Magnetic resonance imaging of the pelvis Examination under anaesthesia	Antibiotics Drainage
Anastomotic strictures	Examination (digital examination) Pouchoscopy Examination under anaesthesia	Dilatation (endoscopic or surgical) Excision with pouch advancement
Small bowel obstruction	X-ray Computed tomography abdomen	Conservative (fluids and nasogastric suction) Surgery with adhesiolysis
Small volume pouch	Pouchogram	Surgical revision in selected cases
Pelvic floor dysfunction	Pouchogram Anorectal manometry	Biofeedback
Irritable pouch syndrome	Diagnosis of exclusion	Symptomatic treatment, e.g. antidiarrhoeals, antispasmodics

Cuffitis

Following a stapled anastomosis, some patients can develop inflammation of the residual cuff of rectum left behind. Presenting complaints are similar to those of pouchitis although bleeding is more

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likely to feature. Diagnosis should be confirmed by endoscopy with biopsies of the cuff. Anti-inflammatory topical agents such as mesalazine or corticosteroid suppositories are the mainstay of treatment.

Crohn's disease

A small proportion of patients who undergo ileal pouch-anal anastomosis for ulcerative colitis will subsequently be re-diagnosed with Crohn's disease. This should especially be considered in the setting of refractory pouchitis or fistula formation. However, diagnosis of Crohn's disease is particularly challenging in the context of ileal pouch-anal anastomosis since endoscopic and histological findings that mimic Crohn's disease can occur post-surgery; for instance fistulization at the anastomotic site or foreign body granulomas at biopsies from the suture line. Once the diagnosis is established it can be treated with pharmacological, endoscopic or surgical methods depending on disease phenotype.

Mechanical complications

Pelvic sepsis is more likely to present as an early postoperative complication as a result of an anastomotic leak. However, presentation can be delayed and it can present insidiously years post procedure. Presenting complaints include frequency, pelvic pain and patients can be systemically unwell with fever. The diagnosis is best demonstrated by magnetic resonance imaging. A conservative approach with antibiotics can be attempted although some patients will require definitive surgical drainage.

Anastomotic strictures are relatively common and appear to occur more frequently post stapled ileal pouch-anal anastomosis. Patients may complain of difficulty evacuating and frequency with small volume stools. These can be diagnosed on digital rectal examination or by pouchoscopy. Troublesome strictures can be dilated endoscopically or under anaesthesia. Some patients respond to regular self-dilatation using a Hegar dilator. In complex cases, it may be necessary to perform an anastomotic excision with pouch advancement.

Two large series have reported the incidence of small bowel obstruction post-ileal pouch-anal anastomosis as 13 and 25% respectively (Pemberton et al, 1987; Fazio et al, 1995). Adhesions are implicated in most cases since the operation requires both abdominal and pelvic dissection. Small bowel obstruction can be classified as an early or late postoperative complication. Most cases resolve with conservative management – nasogastric suction and intravenous fluids – although the need for surgical intervention appears more likely in cases of late small bowel obstruction.

Occasionally a pouch may be formed with insufficient volume which can lead to high stool frequency. Contrast X-ray of the pouch (pouchogram) and measurement via balloon insufflation can be used to determine pouch volume. In some cases the pouch reservoir may need augmentation.

Functional disorders

Patients presenting with outflow obstruction with symptoms such as difficulty evacuating and frequency need to be evaluated clinically and endoscopically. If these are normal then pelvic floor dysfunction should be suspected. Evaluation by pouch manometry and a defecating pouchogram is important. Patients can benefit from biofeedback which involves pelvic floor muscle re-training.

Irritable pouch syndrome is a functional disorder. It shares common clinical features with irritable bowel syndrome; patients may present with increased stool frequency, abdominal discomfort and pelvic discomfort. The diagnosis is one of exclusion where there is an absence of endoscopic, histological or mechanical abnormalities to account for the symp-

Case Example

A 47-year-old man with a history of ulcerative colitis was admitted with a 4-day history of diarrhoea. He underwent a proctocolectomy with ileal pouch-anal anastomosis after an episode of acute severe colitis 10 years ago. Pathological findings of the specimen were consistent with pancolitis without evidence of dysplasia. Following this the patient remained well with no postoperative complications.

He reported a 4-day history of frequency, opening his bowels twelve times a day with loose stools which was now waking him at night. There was no rectal bleeding, fever or abdominal pain. His past medical history included hypertension. Regular medication consisted of amlodipine 5 mg once daily. There had been no recent travel abroad.

Routine observations revealed a temperature of 36.6°C, blood pressure 125/70 mmHg, pulse rate 85 beats/minute and oxygen saturation 98% on room air. Physical examination was unremarkable. His abdomen was soft and non-tender. Rectal examination demonstrated normal tone and did not reveal any strictures or masses.

Initial laboratory investigations showed a haemoglobin of 130 g/litre, mean corpuscular volume 85 fl, white cell count 9.5 x10^9/litre, platelets 200 x10^9/litre, sodium 139 mmol/litre, potassium 3.5 mmol/litre, urea 7 mmol/litre, creatinine 80 μmol/litre, C-reactive protein 45 mg/litre. An abdominal X-ray did not detect any abnormality. Stool samples were negative on microscopy, culture and sensitivity. *Clostridium difficile* toxin was not detected.

Pouchoscopy revealed diffuse erythema, mucosal oedema and friability. Pathological examination of the biopsies taken showed superficial ulceration and inflammation of the epithelium with a polymorphonuclear infiltrate. No granulomas were identified and there was no histological evidence of cytomegalovirus colitis.

Diagnosis

Pouchitis is the most likely diagnosis given the acute history of frequency particularly with the endoscopic features of diffuse erythema, oedema and friability in conjunction with pathological findings of an acute inflammatory infiltrate.

Treatment

Recommended first-line treatment would be with ciprofloxacin as it is associated with fewer side effects than metronidazole. In practice a 14-day course is often prescribed.

This man remained well at follow up with no further episodes of pouchitis in the following year.

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toms. Routine use of antidepressants and/or anxiolytics is a risk factor for developing irritable pouch syndrome (Shen et al, 2006). Furthermore visceral hypersensitivity has been demonstrated in the ileal pouch with patients having a lower threshold for perception of gas, pain and urge to defecate (Shen et al, 2011). These observations have led some to suggest that there are common pathophysiological mechanisms between irritable pouch syndrome and irritable bowel syndrome. Similar therapeutic approaches may be helpful such as dietary modification and symptomatic management with antidiarrhoeals or antispasmodics.

Long-term follow up

Most patients have a good long-term outcome with failure rates of 10–20% reported at 20 years (McLaughlin et al, 2008). Annual routine follow up in the outpatient clinic is recommended for patients following ileal pouch-anal anastomosis unless complications warrant more frequent reviews. In addition to a gastrointestinal history, blood tests including haematinics (vitamin B_{12}, folate and iron studies) and liver function tests are recommended. Iron deficiency anaemia is common with inflammation. Iron replacement can improve quality of life with evidence that intravenous preparations are more effective and have fewer side effects than the oral route.

Although less common, vitamin B_{12} deficiency may occur and is likely to be multifactorial with proposed mechanisms including impaired absorption following ileal resection, small bacterial overgrowth and dietary restriction. Liver function tests are important since primary sclerosing cholangitis may subsequently be diagnosed in patients with ulcerative colitis and evidence suggests that co-concomitant primary sclerosing cholangitis is a risk factor for colorectal carcinoma.

Restorative proctocolectomy with ileal pouch-anal anastomosis formation in patients with ulcerative colitis does not completely remove the chance of subsequent neoplasia in the pouch or residual rectal mucosa. However, the risk appears to be low with few reports in the literature of cancer. In one of the larger case series of 3203 patients with ulcerative colitis who underwent ileal pouch-anal anastomosis, the cumulative incidence of pouch cancer at 25 years was 3.4% (Kariv et al, 2010). The predominant risk factor appears to be a preoperative diagnosis of dysplasia or cancer of the colon or rectum. Importantly mucosectomy was not shown to be a protective factor.

Guidelines for endoscopic surveillance do not exist. However, a reasonable approach that has been suggested in the literature is to offer annual surveillance for those with preoperative colorectal dysplasia or cancer. Surveillance endoscopy every 3 years is performed for others deemed to have a higher risk including those with chronic pouchitis, Crohn's disease of the pouch, severe mucosal atrophy, family history of colorectal cancer, concurrent primary sclerosing cholangitis and a duration of ulcerative colitis >10 years (McLaughlin et al, 2008; Liu et al, 2011). BJHM

KEY POINTS

- Restorative proctocolectomy with ileal pouch-anal anastomosis has become the procedure of choice for those with ulcerative colitis who require surgery and patients with familial adenomatous polyposis.
- The procedure has excellent long-term functional outcomes for the majority of patients. However, there is significant morbidity and important complications can occur.
- Complications can be divided into inflammatory, mechanical, functional, neoplastic and metabolic. The most common causes of pouch dysfunction include pouchitis, pelvic sepsis and rectal cuff inflammation.
- Since pouch disorders often present with a similar combination of symptoms it is imperative to develop a rigorous and structured diagnostic approach. Early specialist input is important in challenging cases.

Conflict of interest: none.

Fazio VW, Ziv Y, Church JM et al (1995) Ileal pouch-anal anastomoses complications and function in 1005 patients. *Ann Surg* **222**(2): 120–7

Kariv R, Remzi FH, Lian L et al (2010) Preoperative colorectal neoplasia increases risk for pouch neoplasia in patients with restorative proctocolectomy. *Gastroenterology* **139**(3): 806–12

Langholz E, Munkholm P, Davidsen M, Binder V (1992) Colorectal cancer risk and mortality in patients with ulcerative colitis. *Gastroenterology* **103**(5): 1444–51

Liu ZX, Kiran RP, Bennett AE, Ni RZ, Shen B (2011) Diagnosis and management of dysplasia and cancer of the ileal pouch in patients with underlying inflammatory bowel disease. *Cancer* **117**(41): 3081–92

McLaughlin SD, Clark SK, Tekkis PP, Ciclitira PJ, Nicholls RJ (2008) Review article: restorative proctocolectomy, indications, management of complications and follow-up--a guide for gastroenterologists. *Aliment Pharmacol Ther* **27**(10): 895–909

Meagher AP, Farouk R, Dozois RR, Kelly KA, Pemberton JH (1998) J ileal pouch-anal anastomosis for chronic ulcerative colitis: complications and long-term outcome in 1310 patients. *Br J Surg* **85**: 800–3

Mimura T, Rizzello F, Helwig U et al (2004) Once daily high dose probiotic therapy (VSL#3®) for maintaining remission in recurrent or refractory pouchitis. *Gut* **53**: 108–14

Pardi DS, D'Haens G, Shen B, Campbell S, Gionchetti P (2009) Clinical guidelines for the management of pouchitis. *Inflamm Bowel Dis* **15**(9): 1424–31

Pemberton JH, Kelly KA, Beart RW Jr, Dozois RR, Wolff BG, Ilstrup DM (1987) Ileal pouch-anal anastomosis for chronic ulcerative colitis. Long-term results. *Ann Surg* **206**(4): 504–13

Penna C, Dozois R, Tremaine W et al (1996) Pouchitis after ileal pouch anal anastomosis for ulcerative colitis occurs with increased frequency in patients with primary sclerosing cholangitis. *Gut* **38**(2): 234–9

Sagar PM, Pemberton JH (1997) Ileo-anal pouch function and dysfunction. *Dig Dis* **15**(3): 172–88

Sandborn WJ, Tremaine WJ, Batts KP, Pemberton JH, Phillips SF (1994) Pouchitis after ileal pouch–anal anastomosis: a pouchitis disease activity index. *Mayo Clin Proc* **69**(5): 409–15

Shen B (2012) Acute and chronic pouchitis--pathogenesis, diagnosis and treatment. *Nat Rev Gastroenterol Hepatol* **9**(6): 323–33

Shen B, Achkar JP, Lashner BA et al (2001) A randomized clinical trial of ciprofloxacin and metronidazole to treat acute pouchitis. *Inflamm Bowel Dis* **7**(4): 301–5

Shen B, Fazio VW, Remzi FH et al (2006) Risk factors for diseases of ileal pouch-anal anastomosis after restorative proctocolectomy for ulcerative colitis. *Clin Gastroenterol Hepatol* **4**(1): 81–9 [quiz 2–3]

Shen B, Sanmiguel C, Bennett AE et al (2011) Irritable pouch syndrome is characterized by visceral hypersensitivity. *Inflamm Bowel Dis* **17**(4): 994–1002

Van Assche G, Dignass A, Bokemeyer B et al (2013) Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations. *J Crohns Colitis* **7**(1): 1–33

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