Seymour Katz, M.D., Series Editor

Ileal Pouch-anal Anastomosis (IPAA) for Ulcerative Colitis; Management of Complications and Follow-up in Primary Care

Simon D. McLaughlin

Sue K. Clark

Ileal pouch-anal anastomosis (IPAA) is one of the greatest advances in colorectal surgery in the last 30 years and is the procedure of choice for the one-third of ulcerative colitis patients who eventually require surgery. Most patients have an excellent functional outcome, but there is considerable overall morbidity. The most common complications include pouchitis, rectal cuff inflammation and pelvic sepsis. Anemia from iron or vitamin B_{12} deficiency is common. A significant reduction in fertility occurs in female patients. The development of cancer is rare, however, long-term endoscopic surveillance is recommended.

This article aims to provide primary care physicians with an excellent understanding of IPAA including the investigation and management of patients with dysfunction in order to improve the long-term functional outcome of these patients.

BACKGROUND

About one-third of patients with ulcerative colitis (UC) will eventually require surgery (1,2) due to failed medical treatment or because of neoplastic change. Essentially the surgical options include conventional proctocolectomy with end ileostomy or restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA); sometimes termed "pouch surgery."

IPAA was first described in 1978 and is one of the greatest advances in colorectal surgery in the last 30 years. It is now accepted as the procedure of choice in UC patients requiring surgery because it retains anal sphincter function and avoids the need for a long-term ileostomy. The numbers of patients having this opera-

(continued on page 29)

Dr. Simon D. McLaughlin, Research Fellow, Department of Gastroenterology, Miss Sue K. Clark, Consultant, Colorectal Surgeon, Department of Surgery, St. Mark's Hospital, London, UK.

(continued from page 24)

tion are ever increasing, and it is being performed both within and outside specialist units. A good understanding of the associated complications and management is essential to all physicians who may be involved in the care of these patients.

SURGICAL PROCEDURE

IPAA is an elective procedure: acutely unwell patients first require conventional subtotal colectomy and ileostomy, with completion proctectomy and IPAA following an interval of at least three months. IPAA is performed in one-or-two stages depending on the preference of the surgeon. In a one-stage procedure proctocolectomy, pouch construction and restoration of intestinal continuity are performed in one operation. In a two stage procedure proctocolectomy, pouch construction and a temporary diverting ileostomy are performed. The ileostomy is then closed about eight weeks later.

Various pouch configurations have been described, however most surgeons now form a two limb "J" pouch, constructed from the last 40 cm of small bowel, with a capacity of about 400 mL, which is anastomosed to the anal canal. (Figure 1)

NORMAL POUCH FUNCTION

Following IPAA mean bowel frequency is six-to-eight times in 24 hours with the passage of loose or semi-formed stool. About 50% of patients will need to evacuate once or twice overnight. Most patients should be able to defer for one hour. Loperamide and codeine are useful in patients who are troubled by frequency, and are safe and well tolerated. The dose of each may be titrated up to the maximum recommended daily dose.

LONG-TERM OUTCOME

Failure of IPAA occurs in patients who require pouch excision or a permanent ileostomy for poor function or other complications. The highest rate of failure occurs in the first year following surgery. Following this the rate of failure increases slowly with time and is about 4% at five years rising to about 10% at 20 years (3). The most common causes of failure are pelvic sepsis, pouchitis and poor function.

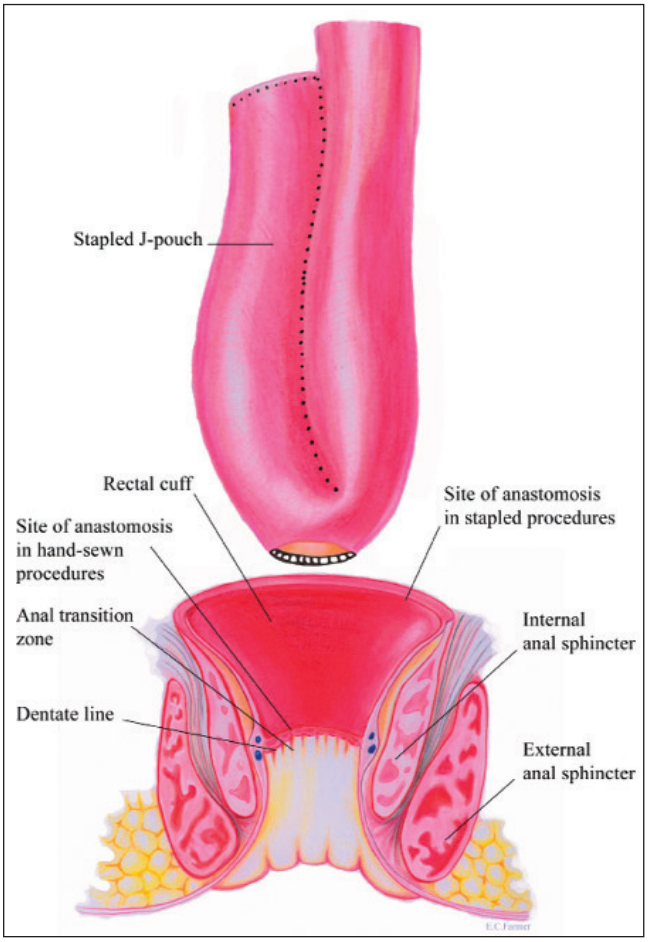

Figure 1. Ileo-anal J-pouch anatomy.

Patients may be reassured that pouch function is stable over time with only a small increase in urgency and seepage over a 25-year period.

RECOMMENDED FOLLOW-UP IN PRIMARY CARE

Endoscopic Surveillance

The risk of dysplasia following IPAA is small; so far there have been about 20 reports of cancer developing in the pouch or residual anorectal mucosa, and in virtually all of these patients dysplasia or cancer was present at the time of IPAA (4). The risk is increased in patients with chronic pouchitis and primary sclerosing cholangitis. There are no national guidelines for sur-

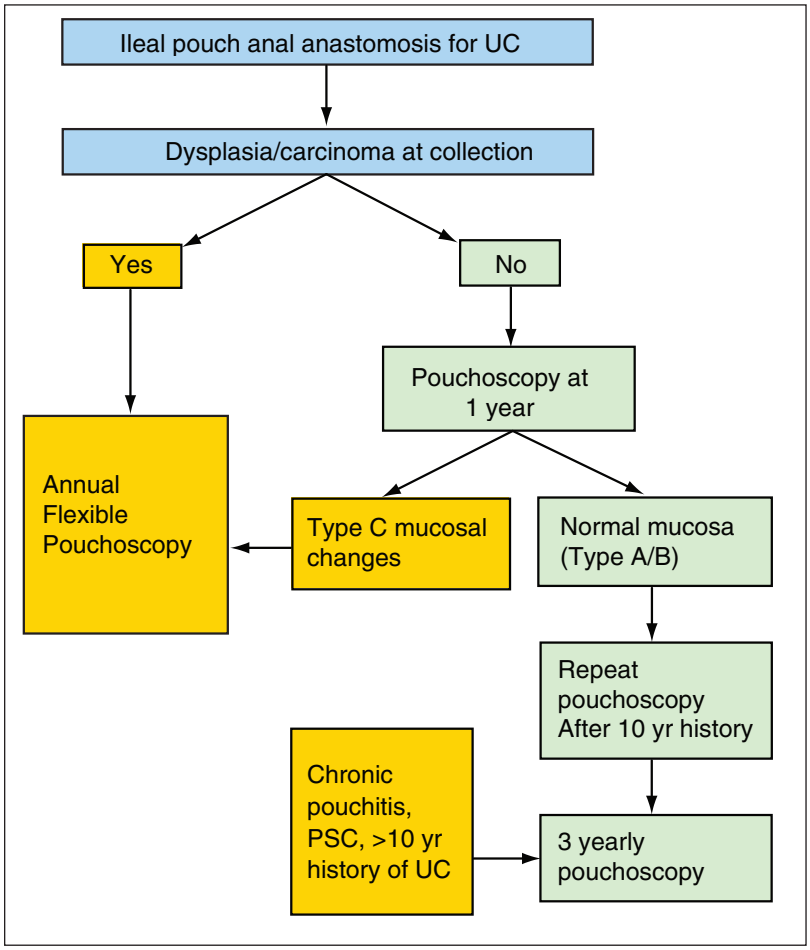

Figure 2. Endoscopic surveillance.

veillance; we recommend that surveillance flexible pouchoscopy should be undertaken every three years in patients with UC of more than 10 years duration. In those with previous dysplasia annual surveillance is recommended.

An algorithm used at our institution is illustrated in Figure 2.

Annual Blood Tests

We recommend an annual complete blood count, ferritin, B_{12}, folate, and liver function tests. Anemia following IPAA is common. Vitamin B_{12} deficiency occurs due to impaired absorption (the terminal ileum forms part of the pouch) and iron deficiency may occur due to pouch or rectal cuff inflammation. Standard replacement regimes are appropriate, but many IPAA patients do not tolerate oral iron well and may require parenteral replacement. Liver function tests are recommended since any patient with UC may later develop primary sclerosing cholangitis.

COMPLICATIONS FOLLOWING IPAA

Fertility, Pregnancy and Childbirth

IPAA is known to cause a three-fold reduction in fecundity in females (5); this is probably due to pelvic adhesions. Its incidence is similar to those who undergo conventional pan-proctocolectomy. Females who require surgery and have not yet completed their family may wish to consider a subtotal colectomy (with retained rectum) as an interval procedure and undergo IPAA later. Those patients who have difficulty conceiving following IPAA should be referred to an infertility specialist for consideration of in vitro fertilization since this has been shown to be successful in most patients (6).

During pregnancy pouch function often worsens with increased stool frequency, seepage and incontinence. Patients should be reassured that after delivery normal pouch function rapidly returns.

There is no absolute contraindication to vaginal delivery, but most colorectal surgeons would advocate elective caesarean section because even mild unrecognized anal sphincter damage that can occur during vaginal delivery may later cause increased seepage as anal sphincter function deteriorates with age. Patients should be encouraged to discuss the mode of delivery with their colorectal surgeon and obstetrician.

Erectile Dysfunction

Impotence (partial or complete) occurs in about 1% of males following IPAA (7) and due to iatrogenic pelvic nerve damage during surgery. Many patients will benefit from drugs such as sildenafil.

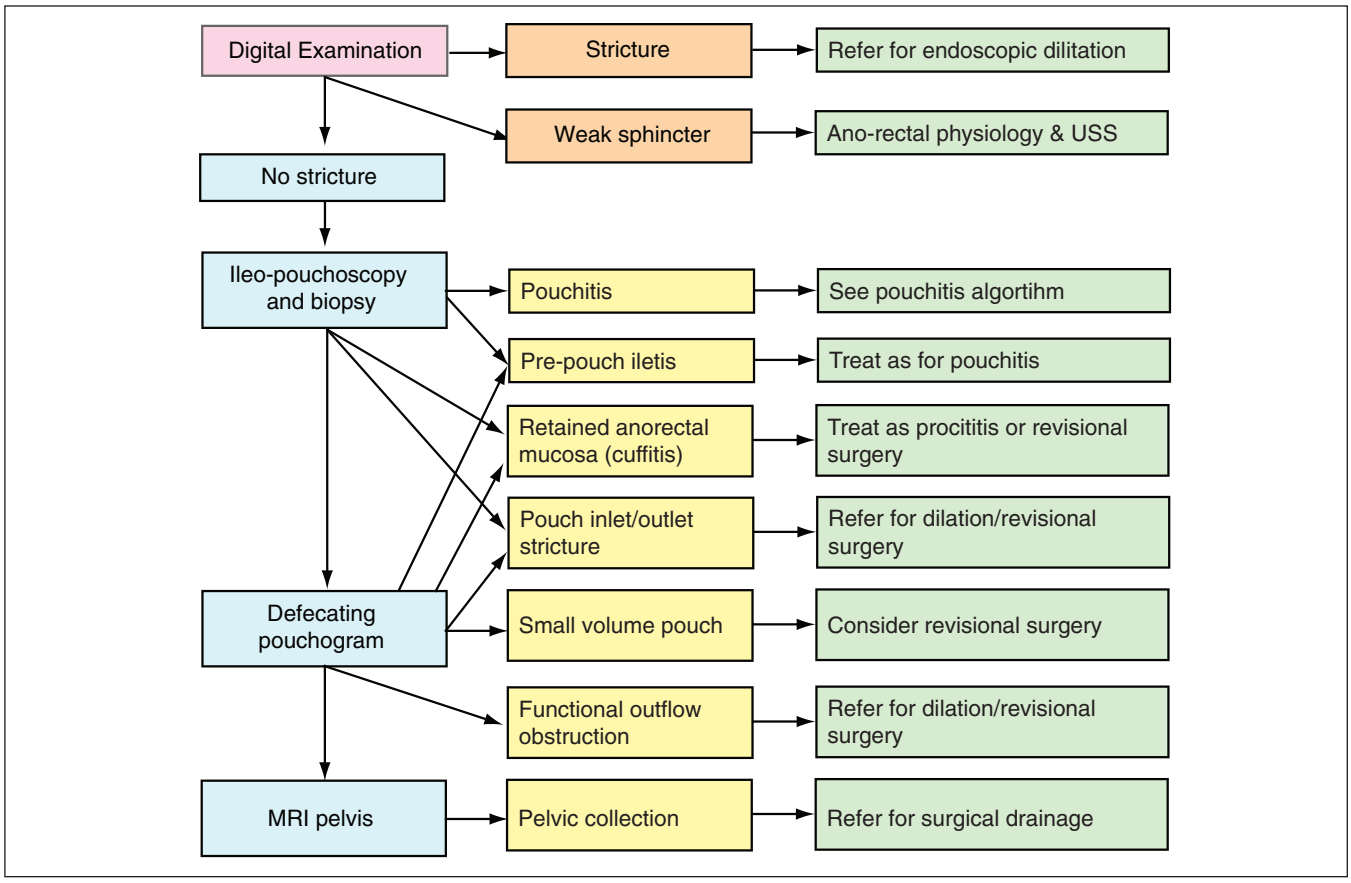

Figure 3. Algorithm for the investigation of pouch dysfunction in primary care.

Ejaculatory dysfunction with ejaculatory failure or retrograde ejaculation occurs in about 4% of males. Both of these complications have a similar incidence in patients undergoing conventional pan-proctocolectomy (7).

Pouch Dysfunction

The various causes of pouch dysfunction often present with similar symptoms such as frequency and urgency, therefore a structured approach to investigation is recommended. Initial investigations should include stool antigen testing to exclude *Clostridium difficile* and cytomegalovirus as well as Celiac antibody screening. If these tests are normal referral for a flexible pouchoscopy is recommended. Further investigations to consider include a defacating pouchogram to delineate pouch volume and exclude incomplete evacuation and pelvic MRI to exclude anastomotic leak and pelvic sepsis. Anal physiology should be considered in those where there is a suspicion of anal sphincter weakness.

An algorithm used at our institution for the investigation for pouch dysfunction is illustrated in Figure 3.

POUCHITIS

Inflammation of the ileal-pouch mucosa is the most common complication following IPAA. It occurs in about 20%–50% of patients. Symptoms include stool frequency, urgency and, in a small proportion of patients, bleeding. It is associated with NSAID use and withdrawal may be sufficient to induce remission (8). Enteric infections such as *Clostridium difficile* or Cytomegalovirus should be excluded.

Pouchitis is diagnosed following endoscopically proven pouch inflammation and confirmatory histol-

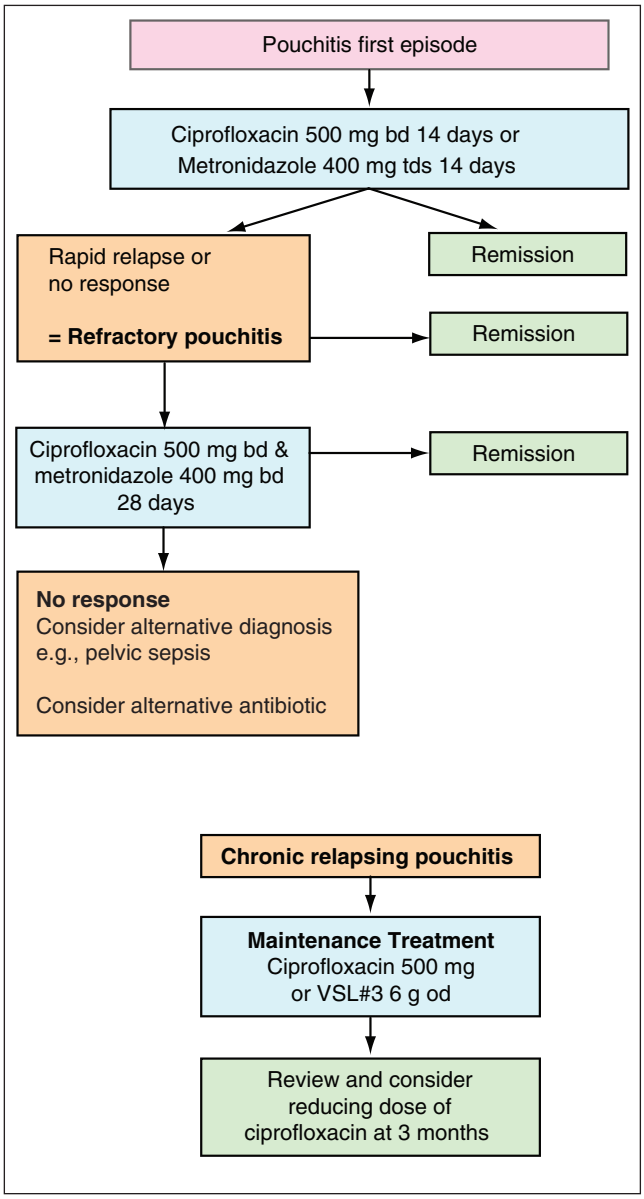

Figure 4. Algorithm for the management of pouchitis

ogy in patients with symptoms. Asymptomatic pouch inflammation found incidentally at routine pouchoscopy is common and does not require treatment.

The majority of patients will have a single episode of pouchitis or infrequent episodes which are easily treated with a single antibiotic agent; ciprofloxacin 500 mg bd for 14 days is first line treatment. In those where this is ineffective a four-week course of combined ciprofloxacin 500 mg bd and metronidazole 400 mg bd (9) is highly effective, alternative regimes include ciprofloxacin 500 mg bd and rifaxamin 1 g bd (10). Chronic relapsing pouchitis occurs in about 5% of patients and is defined as three or more episodes of pouchitis per year. Such patients are best treated with long term maintenance therapy; ciprofloxacin 250–500 mg bd. VSL#3 at a dose of 900 billion bacteria per day (four sachets) may be considered; however, results in clinical practice have been less favorable than in the original studies, and most insurance companies will not reimburse its use (11,12).

An algorithm used for the management of pouchitis at our institution is illustrated in Figure 4.

RETAINED RECTAL CUFF INFLAMMATION ("CUFFITIS")

The pouch-anal anastomosis can be formed in two ways: the first is to hand-sew the pouch to the anal canal; the second (and most common) is to use a stapling device. This requires leaving a 0.5 cm to 2 cm cuff of rectum (i.e., residual UC) in-situ. In about 13% of patients the rectal cuff becomes sufficiently inflamed to give symptoms similar to proctitis with bleeding, urgency and frequency (13). This condition is termed retained rectal cuff inflammation or "cuffitis." The diagnosis may be suspected when a high anastomosis is palpable; however, a flexible pouchoscopy with biopsies should be performed to confirm the diagnosis and exclude pouchitis. Treatment is similar to proctitis; mesalamine suppositories 500 mg bd (14) or prednisolone suppositories 5 mg bd for one month are usually effective, but relapse is common. In a small proportion of patients revisional surgery may be required.

PRE-POUCH ILEITIS

Pre-pouch ileitis is inflammation in the ileum proximal to the pouch and occurs in 14% of patients with concurrent pouchitis. It should be treated as chronic pouchitis. It does not imply Crohn's disease (15).

(continued on page 35)

(continued from page 32)

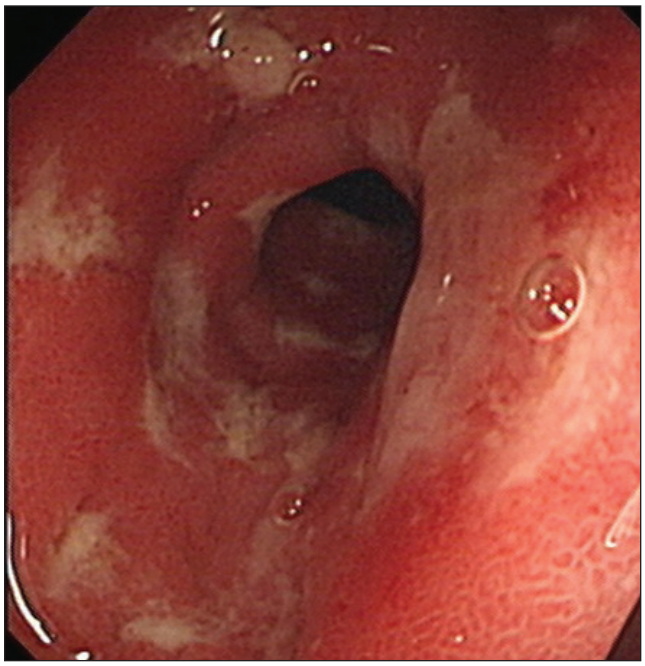

Figure 5. Endoscopic view of inflamed J-pouch.

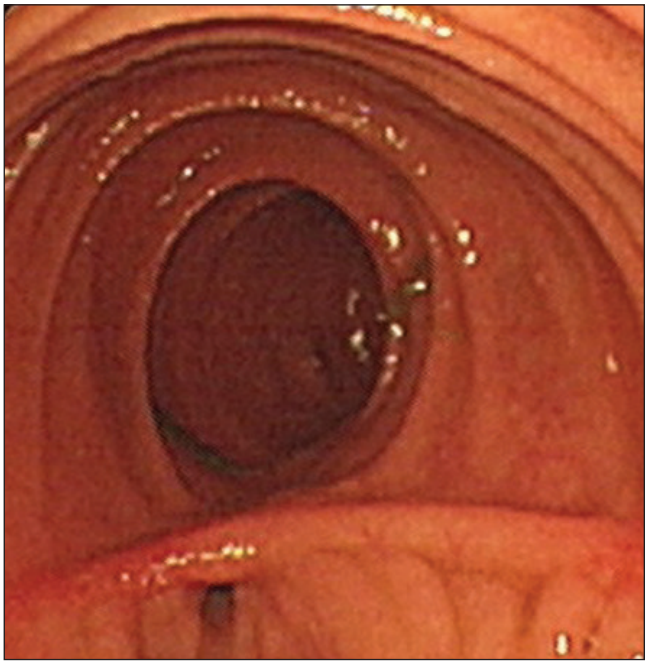

Figure 6. Endoscopic view of normal J-pouch.

CROHN'S DISEASE

Most surgeons agree that IPAA should not be performed in patients with Crohn's disease because of the high failure rate (40%–60%) (16); however, about 2%–3% of patients thought to have ulcerative colitis or indeterminate colitis will later be reclassified with Crohn's disease (3). Such patients usually present with problematic pouchitis or anal fistulae; however, it should be appreciated that fistulae occur in 5%–10% of patients following IPAA and in most cases this does not indicate Crohn's disease (17). Patients with confirmed Crohn's disease should be treated in a conventional manner.

PELVIC SEPSIS

Pelvic sepsis is most common in the immediate postoperative period but may occur at any time (even years) following IPAA. It occurs due to a leak at the pouch-anal anastomosis and often presents insidiously with poor pouch function, and in some cases pain and/or systemic symptoms. It may easily be confused with pouchitis. A pelvic MRI is diagnostic and should be considered in any patient with unexplained pelvic pain or poor pouch function. Some cases will require surgical drainage and others will resolve with antibiotic treatment.

ANAL-ANASTOMOTIC STRICTURE

Fibrotic stricturing at the pouch anal anastomosis following IPAA is common. This only requires treatment if a single digit cannot easily be inserted past the anastomosis. Dilitation can be performed endoscopically or under general anaesthesia. Those with recurrent strictures should be taught to regularly self-dilate with a Hegar dilator. In those where stricturing is due to a long retained rectal cuff revisional surgery should be considered.

WEAK SPHINCTER

Sphincter weakness may lead to seepage and incontinence. Sphincter damage may have occurred at vaginal delivery or during IPAA itself. Endo-anal ultrasound and physiology is diagnostic. Treatment is difficult, conservative measures such as codeine and loperamide

should be trialed, if these are unsuccessful an end ileostomy should be considered.

SMALL VOLUME POUCH

In some cases a pouch of inadequate volume will have been constructed giving rise to symptoms of stool frequency. Revisional surgery should be considered.

FUNCTIONAL OUTFLOW OBSTRUCTION

A functional outflow obstruction presents with symptoms similar to an anastomotic stricture with pouch frequency and defacatory difficulty. It may occur due to abnormal pelvic descent during defacation resulting in occlusion of the efferent limb or due to compression of the efferent limb during pouch filling. Clinical and endoscopic examination is normal. A defacating pouchogram (contrast enema) is diagnostic. Most patients will benefit from biofeedback and self-catheterization of the pouch using a medina catheter. In others pouch revision may be considered.

CONCLUSION

This revolutionary surgical procedure has become widespread since its description in the late 1970s. There is a steadily expanding population of individuals living with an ileoanal pouch, and avoiding a permanent ileostomy. While in the majority the outcome is excellent, complications do occur, often many years after the procedure was performed. Many of these can be simply and effectively investigated and managed, but others are more problematic and require specialist referral. ■

Acknowledgement

Figures 1 and 2 reproduced from: McLaughlin SD, Clark SK, Tekkis PP, Ciclitira PJ, Nicholls RJ. Review Article: restorative proctocolectomy, indications, management of complications and follow-up: a guide for gastroenterologists. *Aliment Pharmacol Ther,* 2008.

References

1. Hendriksen C, Kreiner S, Binder V. Long term prognosis in ulcerative colitis—based on results from a regional patient group from the county of Copenhagen. *Gut* 1985; 26(2): 158-163.
2. Langholz E, Munkholm P, Davidsen M, Binder V. Colorectal cancer risk and mortality in patients with ulcerative colitis. *Gastroenterology*, 1992; 103(5):1444-1451.
3. Hahnloser D, Pemberton JH, Wolff BG, Larson DR, Crownhart BS, Dozois RR. Results at up to 20 years after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Br J Surg,* 2007; 94(3):333-340.
4. Das P, Johnson MW, Tekkis PP, Nicholls RJ. Risk of dysplasia and adenocarcinoma following restorative proctocolectomy for ulcerative colitis. *Colorectal Dis,* 2007; 9(1): 15-27.
5. Waljee A, Waljee J, Morris AM, Higgins PD. Threefold increased risk of infertility: a meta-analysis of infertility after ileal pouch anal anastomosis in ulcerative colitis. *Gut*, 2006; 55(11):1575-1580.
6. Cornish JA, Tan E, Teare J, Teoh TG, Rai R, Darzi AW, et al. The effect of restorative proctocolectomy on sexual function, urinary function, fertility, pregnancy and delivery: a systematic review. *Dis Colon Rectum,* 2007; 50(8):1128-1138.
7. Colwell JC, Gray M. What functional outcomes and complications should be taught to the patient with ulcerative colitis or familial adenomatous polyposis who undergoes ileal pouch anal anastomosis? *J Wound Ostomy Continence Nurs.* 2001; 28(4): 184-189.
8. Shen B, Fazio VW, Remzi FH, Bennett AE, Lopez R, Lavery IC, et al. Effect of Withdrawal of Nonsteroidal Anti-Inflammatory Drug Use on Ileal Pouch Disorders. *Dig Dis Sci,* 2007.
9. Mimura T, Rizzello F, Helwig U, Poggioli G, Schreiber S, Talbot IC, et al. Four-week open-label trial of metronidazole and ciprofloxacin for the treatment of recurrent or refractory pouchitis. *Aliment Pharmacol Ther,* 2002; 16(5):909-917.
10. Gionchetti P, Rizzello F, Venturi A, Ugolini F, Rossi M, Brigidi P, et al. Antibiotic combination therapy in patients with chronic, treatment-resistant pouchitis. *Aliment Pharmacol Ther,* 1999; 13(6):713-718.
11. Mimura T, Rizzello F, Helwig U, Poggioli G, Schreiber S, Talbot IC, et al. Once daily high dose probiotic therapy (VSL#3) for maintaining remission in recurrent or refractory pouchitis. *Gut*, 2004; 53(1):108-114.
12. Shen B, Brzezinski A, Fazio VW, Remzi FH, Achkar JP, Bennett AE, et al. Maintenance therapy with a probiotic in antibiotic-dependent pouchitis: experience in clinical practice. *Aliment Pharmacol Ther,* 2005; 22(8):721-728.
13. Lavery IC, Sirimarco MT, Ziv Y, Fazio VW. Anal canal inflammation after ileal pouch-anal anastomosis. The need for treatment. *Dis Colon Rectum,* 1995; 38(8):803-806.
14. Shen B, Lashner BA, Bennett AE, Remzi FH, Brzezinski A, Achkar JP, et al. Treatment of rectal cuff inflammation (cuffitis) in patients with ulcerative colitis following restorative proctocolectomy and ileal pouch-anal anastomosis. *Am J Gastroenterol,* 2004; 99(8):1527-1531.
15. Mclaughlin SD, Clark SK, Bell AJ, Tekkis PP, Ciclitira PJ, Nicholls RJ. Incidence and implications of pre-pouch ileitis in patients following restorative proctocolectomy. *Gut*, 2008;57 [Supp I]. 1-3.
16. Reese GE, Lovegrove RE, Tilney HS, Yamamoto T, Heriot AG, Fazio VW, et al. The effect of Crohn's disease on outcomes after restorative proctocolectomy. *Dis Colon Rectum,* 2007; 50(2):239-250.
17. Groom JS, Nicholls RJ, Hawley PR, Phillips RK. Pouch-vaginal fistula. *Br J Surg,* 1993; 80(7):936-940.