Polyps in the Ileal Pouch

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ABSTRACT

Total proctocolectomy and ileal pouch–anal anastomosis is the operation of choice for patients with familial adenomatous polyposis. With this operation comes the risk of developing ileal pouch polyps. Although rare, ileal pouch carcinomas may also occur within the pouch. Periodic endoscopic surveillance of the retained rectum and ileal pouch is recommended. Endoscopic polypectomy of medium and large polyps should be performed. Sulindac is effective in the reduction and often in the elimination of numerous smaller pouch polyps. Future studies are necessary to determine the role of sulindac and other chemotherapeutic agents in preventing the development of these polyps.

KEYWORDS: Polyps, ileal pouch, familial adenomatous polyposis

Objectives: On completion of this article, the reader should be able to summarize the surveillance and management strategies of polyps in the ileal pouch in patients with familial adenomatous polyposis.

Total proctocolectomy and ileal pouch–anal anastomosis (IPAA) has become the operation of choice for treatment of familial adenomatous polyposis (FAP). It is a more attractive option than total proctocolectomy and end ileostomy because it maintains intestinal continuity and fecal continence. Total abdominal colectomy and ileorectal anastomosis is an acceptable alternative for patients with milder forms of the disease (< 20 rectal adenomas and < 1000 colonic adenomas).¹ It is known that adenomas and even adenocarcinomas may develop at the IPAA.² For this reason great controversy has arisen in the colorectal community as to whether the IPAA should be performed with or without mucosectomy. Proponents argue that the performance of a mucosectomy with total proctocolectomy (TPC) removes all of the rectal mucosa at risk for development of dysplasia and carcinoma. Others argue that removal of the anal transition zone leads to impaired rectal sensation and continence without an appreciable improvement in cancer prevention. Although overall a much

less-controversial entity, there is a growing body of literature documenting the development of neoplasia from the ileal mucosa of the intestinal pouch in patients with FAP. Identification and treatment of adenomatous polyps may be an important step in preventing the development of adenocarcinoma of the ileal pouch.

MORPHOLOGY AND PREVALENCE

In patients with FAP, ileal pouch polyps may vary in their size, number, and histology. Although most polyps tend to be small they may range in size from microadenomas (endoscopically invisible) to large villous lesions measuring > 3 cm to replacement of the pouch mucosa with adenomatous tissue, the so-called carpeting effect.^{2,3} The number of polyps ranges from as few as one to a countless number often demonstrating either tubular, tubulovillous, or villous histology.^{2,4–6} There are even reports of adenocarcinoma developing in the ileal pouch far above the IPAA.^{7,8}

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An early study performed at St. Marks Hospital (London, United Kingdom) suggested that the frequency of pouch adenomas was not significantly different than the frequency of adenomas in the ileum attached to the colectomy specimens.⁹ Thirteen percent of 38 FAP patients previously undergoing restorative proctocolectomy had adenomas whereas 8.9% of the historical cohort of 203 had ileal adenomas. They suggested that the ileal pouch does not predispose to the development of such adenomas. Subsequent studies have not agreed with this premise. Consistent within these later reports is the progressive development of ileal pouch polyposis over time. Parc et al⁴ endoscopically surveyed the ileal pouch of 85 patients with FAP following restorative proctocolectomy with mucosectomy. In this study, the risk of developing pouch adenomas at 5, 10, and 15 years after the procedure was 7%, 35%, and 75%. Additional prospective studies concur. In 1998, Wu et al published their series of 26 patients with FAP undergoing endoscopic surveillance. Forty-two percent of these patients had adenomatous polyps of the ileal pouch.¹⁰ They also noted that as the time from construction of the pouch increased so did the percentage of patients presenting with polyps within the pouch. Thompson-Fawcett et al state that the age of the pouch is extremely important as adenomas in their series of 33 patients are very common after 10 years.¹¹ Further, they recommend even closer follow-up for this high-risk population.

There are several other factors that have been examined in an attempt to help identify patients that are at risk for the development of ileal pouch adenomas. Unfortunately, age of the pouch has been the only consistent predictor. Groves et al suggested that the patient's age independently affects the number of polyps.⁶ A logistical regression model was used to analyze 34 patients with 362 pouch adenomas. Their data suggests that increased age of the patient was a stronger predictor of pouch polyposis than the length of follow-up following pouch creation. Parc et al did not agree with these findings and noticed that patients with pouch polyps were actually younger than those without polyps.⁴ This study did note that these patients also had a higher frequency of duodenal and ampullary adenomas. Seventy-seven percent of patients with adenomas of the ileal pouch had either duodenal or ampullary adenomas compared with 44% of those without disease of the pouch. However, the majority of studies have found no association between ileal pouch, duodenal, and ampullary polyposis.^{5,6,10,11} No study to date has identified a specific adenomatous polyposis coli (APC) mutation predisposing patients with FAP to develop ileal pouch adenomas.

ETIOLOGY

The exact mechanism describing the transition from normal ileal mucosa to adenoma in the ileal pouch of

patients with FAP has not been well established. Certainly, the ileal mucosa is not free from genetic alterations in the APC gene resulting in FAP. However, ileal adenomas in the segment just proximal to the pouch are much less common.^{10,11} Additionally, adenomatous disease of the ileal pouch is much more common than disease of the ileostomy.¹¹ Thompson-Fawcett et al found that 60% of patients with an ileal pouch had adenomas compared with 20% of patients with an ileostomy despite an older average age of the ileostomy. It has been suggested that fecal stasis of the ileal pouch somehow predisposes this mucosa to the development of adenomas.^{2,6,11,12} This theory is supported by the fact stasis is known to alter luminal contents which, in turn, affect the ileal mucosa. Natori et al demonstrated that ulcerative colitis and FAP patients with ileal pouches have significantly increased contents of anaerobic bacteria and unconjugated bile acids in their stool.¹³ Further, the concentrations of known carcinogens deoxycholic acid and lithocholic acid were found many times in the ileal pouch rather than in end ileostomy. Additional studies examining cause and effect in this area would be informative.

TREATMENT

There are no well-established treatment protocols to guide the management of ileal pouch polyposis. Nevertheless, there are essentially 4 treatment options. These include endoscopic polypectomy/coagulation, transanal excision, chemotherapy, and ileal pouch excision. Endoscopic polypectomy is the most common form of therapy. Nd:YAG laser and argon plasma coagulation have also been described.⁵ Advantages of all forms of endoscopic therapy are that they only require light sedation, patient discomfort is minimal, and the therapy is often definitive. However, replacement of the pouch mucosa with hundreds of polyps or by a carpet of polyps may present a significant barrier to complete endoscopic removal. Additionally, the ileal mucosa is thin and the risk of perforation is real.⁵ There are only a handful of studies reporting outcomes after polypectomy and coagulation so the risks, results, and complication rates have not been well delineated.

Transanal excision of adenomas is generally reserved for pouch-anal anastomotic adenomas. It may also be an option if there are distal pouch adenomas. However, difficulty traversing the pouch-anal anastomosis and potentially narrowed and fibrotic anal canal may result in suboptimal exposure and limited access to anything other than the anastomosis or most distal aspect of the pouch.

The effects of nonsteroidal antiinflammatory drugs, specifically sulindac, on regression of colon and rectal adenomas have been established.^{9,14} The mechanism of action is unknown, but may be related to

prostaglandin synthesis inhibition, induction of apoptosis, and prevention of cell cycle progression.¹⁵ There are case reports documenting the usage and effectiveness of sulindac in the treatment of FAP patients presenting with multiple small polyps in the ileal pouch after total proctocolectomy and IPAA. In 1996, Church et al described the effectiveness of the combination of endoscopic snare polypectomy or cautery of polyps > 5 mm and sulindac 150 mg twice daily for the remainder of polyps < 5 mm of which there were at least 40 in number. After 3 months the pouch was reevaluated endoscopically and found to have almost complete regression of all polyps.¹² Ho et al¹⁵ published their results after treatment of a similar patient with chemotherapy alone. This patient had partial regression of multiple polyps 2 to 3 mm in size after 3 months of therapy of sulindac 200 mg twice daily. This patient developed a pouch ulceration likely related to the higher dose of sulindac. The dose was reduced to 150 mg twice daily and the patient was treated with daily sucralfate enemas. Nine months later there was complete resolution of the polyps and ulcer. Church et al² published their updated recommendations after a review of the available literature in 2005. Polyps greater than 1 cm were removed endoscopically while multiple small adenomas (greater than 10) are treated with sulindac 150 mg twice daily. Schulz et al followed a protocol for treatment of pouch adenomas that included topical sulindac.¹⁶ Polyps > 5 mm were removed endoscopically. Patients diagnosed with pouch adenomas were immediately started on sulindac 150 mg suppository daily. This was reduced to 50 mg daily once adenomas could no longer be detected. Seven of eight patients in the study demonstrated complete response with no residual polyps detected endoscopically 6 months after the initiation of therapy. However, this study did not state the number of polyps found on initial endoscopy. Considering the available literature, sulindac represents a reasonable form of therapy for patients with large numbers of small ileal pouch polyps.

Ileal pouch excision can be performed if all other methods of controlling pouch neoplasia have failed. Unfortunately, reoperative pelvic surgery is associated with a significant rate of acute and long-term complications. Pelvic hemorrhage and ureteral injury may occur intraoperatively whereas urinary incontinence and sexual dysfunction (retrograde ejaculation, impotence, and dyspareunia) can result from inadvertent pelvic nerve injury.^{2,17}

SURVEILLANCE

Ileal pouch excision and aggressive endoscopic polypectomy for numerous ileal pouch polyps could theoretically be avoided by an appropriate surveillance strategy. Surveillance is justified based on the specific risks associated

with the IPAA. These include both persistence of rectal mucosa distal to the IPAA and the risk of adenomas and carcinomas developing within the ileal pouch.¹⁸ However, there are no studies documenting the effectiveness of one specific strategy over another. Additionally, there is no surveillance recommendation by the Standards Task Force of the American Society of Colon and Rectal Surgeons in the latest practice parameters for the treatment of patients with dominantly inherited colorectal cancer that have had a total proctocolectomy and IPAA.¹ Most authors have relied on personal experience to dictate surveillance regimens. There are numerous published endoscopic surveillance recommendations that include initial endoscopy anywhere from 3 months to 1 year after ileal pouch creation and then continued yearly or every other year for the life of the patient.^{2,16,18} Some have recommended the addition of indigo-carmin at the time of endoscopy to enhance identification of the flat adenoma.^{5,18}

In 2007, Schulz et al¹⁶ sought to determine the incidence of small intestine polyps presenting in patients with ileal pouch adenomas. They utilized a combination of endoscopy up to 40 cm proximal to the anal verge in combination with capsule endoscopy. In the 8 patients with pouch adenomas, they did not identify any polyps between the pouch and 40 cm by endoscopy. However, capsule endoscopy visualized numerous polyps in the proximal, middle, and distal portions of the small intestine. Barium contrast imaging, push enteroscopy, and even magnetic resonance imaging (MRI) have been used to identify polyps of the small intestine in patients with FAP. In studies prospectively comparing capsule endoscopy with barium contrast imaging and MRI, capsule endoscopy was the more effective method of detecting small bowel polyps in patients with FAP.^{19,20} However, capsule endoscopy may underestimate the number of polyps when compared with standard endoscopy. Wong et al²¹ suggest that although capsule endoscopy should not replace upper endoscopy in the management of patients with FAP, it may allow for identification of polyps in areas of the intestine not accessible by standard endoscopic techniques. The clinical impact of this evaluation has yet to be determined.

CONCLUSION

Ileal pouch polyps are extremely common in patients with FAP following total proctocolectomy and IPAA. As the age of these pouches increases so does the burden of disease. If left unchecked, carcinoma could develop in the pouches of these patients. No one surveillance strategy is appropriate in all patients, but yearly endoscopic examination of the retained rectum, pouch, and distal ileum appears to be a reasonable conservative approach. When applied safely, endoscopic polypectomy is the treatment of choice for polyps > 5 mm. Oral

sulindac reduces and may eliminate more abundant smaller polyps. Topical sulindac in the form of suppositories may be an alternative. Although there are an increasing number of studies examining the incidence, treatment, and surveillance methods for patients with FAP and ileal pouch polyps, no studies address the role of any forms of prevention. Future studies addressing the role of chemoprevention are needed.

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