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Pouch outcomes among children with ulcerative colitis treated with calcineurin inhibitors before ileal pouch anal anastomosis surgery

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Abstract

Purpose: The purpose of this article is to describe the outcomes of the pouches of 14 children with ulcerative colitis (UC) who were pretreated with calcineurin inhibitors before they underwent their ileal pouch anal anastomosis (IPAA) surgery.

Methods: An institutional review board–approved retrospective review of the charts of consecutive patients with UC treated with calcineurin inhibitors before undergoing IPAA surgery at a tertiary pediatric center between 1998 and 2003 was performed. The primary endpoint was pouch outcome after at least 2 years of follow-up (healthy pouch, acute pouchitis, chronic refractory pouchitis, or pouch failure); the secondary endpoints were early postoperative complications, number of stages, and time between stages.

Results: Fourteen of 53 consecutive patients who underwent IPAA for UC were treated with calcineurin inhibitors before their surgery (26%; 6 with cyclosporine and 8 with tacrolimus). All 14 patients were concomitantly treated with systemic steroids. Ten patients (71%) were also taking 6-mercaptopurine or azathioprine, and 9 (64%) were also taking mesalamine. Three patients (21%) had healthy pouches with no clinical evidence of pouchitis, 6 (43%) had at least one episode of acute pouchitis (average of 2 episodes per year), 3 (21%) had chronic relapsing pouchitis, and 2 (14%) were later determined to have Crohn's disease. There was no pouch failure. Two patients (14%) had an early postoperative complication (intraabdominal abscess, anastomotic stricture). Five patients (36%) had a 2-staged procedure, and 8 (64%) had a 3-staged procedure. For the 2-staged procedures, the mean time between the first and second stages was 3.14 months (range, 3-4 months). For the 3-staged procedures, the mean time between the first and second stages was 4.25 months (range, 2-6 months) and that between the second and third stages was 4 months (range, 2.5-6 months).

Conclusions: In this series, chronic pouchitis was an infrequent complication among children who were pretreated with calcineurin inhibitors. Calcineurin inhibitor use did not lead to or portend increased early postoperative complications or affect the number or duration of surgical stages. Further studies are required to determine if preoperative calcineurin inhibitors improve pouch outcomes or facilitate the performance of 2-staged procedures.

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Approximately 150 000 Americans younger than 18 years suffer from ulcerative colitis (UC), a form of inflammatory bowel disease (IBD) [1]. Although most patients can be treated medically, 20% to 30% ultimately require surgical intervention owing to medical intractability, bleeding, obstruction, or perforation [2]. Ileal pouch anal anastomosis (IPAA) has become the preferred surgical procedure for patients with UC who require removal of the colon and rectum. The surgery involves abdominal colectomy and rectal mucosectomy with construction of an ileal pouch that is anastomosed to the anus. It takes advantage of the fact that UC is a mucosal disease limited to the rectum and colon, allowing preservation of the rectal muscular cuff and anal sphincter.

Although most patients enjoy a high quality of life and good functional outcomes after IPAA, the surgery can be associated with significant complications such as sepsis, small bowel obstruction, strictures, incontinence, and pouch inflammation [3]. The most common long-term complication after IPAA is nonspecific inflammation of the ileal pouch, a condition referred to as *pouchitis*. Pouchitis is defined as a clinical syndrome of watery and frequent diarrhea or hematochezia accompanied by urgency, incontinence, abdominal cramping, malaise, and fever [4]. This definition encompasses endoscopic and histologic evidence of inflammation in addition to the clinical symptoms [5,6]. Pouchitis rarely occurs in patients who have undergone IPAA surgery for indications other than IBD, such as familial adenomatous polyposis [7]. Therefore, it has been postulated that pouchitis may be a form of IBD recurring in the pouch.

In patients with severe steroid refractory colitis, calcineurin inhibitors (cyclosporine and tacrolimus) may be used to induce remission. Although these agents are often effective in controlling severe diseases, potential toxicities limit their usefulness as a long-term maintenance therapy. They are therefore used either as "bridge" agents to maintenance immunosuppression with 6-mercaptopurine/azathioprine or as a way of controlling and "cooling down" a disease before IPAA. However, the long-term outcome of IPAA in children with severe colitis treated with cyclosporine or tacrolimus is not well described. In this article, we report on the outcomes of the pouches of 14 patients who were treated with calcineurin inhibitors before they underwent their IPAA surgery.

1. Materials and methods

A retrospective review of the charts of consecutive patients with UC treated with calcineurin inhibitors before their IPAA surgery at a tertiary pediatric center between 1998 and 2003 was performed. Approval for the study was obtained from the institutional review board of the Children's Hospital Boston before it was initiated. Fifteen patients who underwent IPAA surgery and received systemic calcineurin inhibitors before their surgery were identified. One patient was lost to follow-up before 2 years and was therefore excluded from our analysis. The medical records of these patients were reviewed to identify age, medical therapy, clinical course before surgery, operative course, and postoperative course. All surgeries were performed by the same 2 surgeons. A synchronous abdominoperineal approach was used with rectal mucosectomy and preservation of the transitional anorectal mucosal epithelium. A J pouch of the ileum was constructed with handsewn IPAA. Temporary diverting ileostomy was always used. Total abdominal colectomy was performed in conjunction with IPAA if the condition of the rectal mucosa permitted it. The final stage involved closure of the ileostomy after a contrast enema had demonstrated satisfactory healing of the IPAA.

The primary endpoint was pouch outcome after at least 2 years of follow-up. Pouch outcome was categorized into the following groups: healthy pouch, acute pouchitis, chronic relapsing pouchitis, and pouch failure. Acute pouchitis was defined as less than 3 episodes of pouchitis per year that were responsive to antimicrobial therapy. It was usually diagnosed clinically. Chronic relapsing pouchitis was defined as 3 or more episodes of pouchitis per year as diagnosed by clinical, endoscopic, and histologic evidence. Pouch failure was defined as a requirement for enteric diversion. The secondary endpoints were early postoperative complications, number of stages required, and time between stages.

2. Results

Of 53 consecutive patients with UC who underwent IPAA at the Children's Hospital Boston between 1998 and 2003, 14 (26%) received systemic calcineurin inhibitor therapy to control their disease before undergoing colectomy (6 with cyclosporine and 8 with tacrolimus). The mean age of the patients was 14.6 years (range, 5.5-18.6 years). There were 8 girls and 6 boys. Twelve patients (86%) had pancolitis, and 2 (14%) had left-sided disease. Tacrolimus was given twice daily and titrated to maintain trough levels between 10 and 12 ng/mL. Cyclosporine was also given twice daily to maintain trough levels between 150 and 300 ng/mL. The mean duration of calcineurin inhibitor therapy was 3.5 months (range, 10 days to 9 months). All patients were concomitantly treated with systemic steroids. Ten patients (71%) were also taking 6-mercaptopurine or azathioprine, and 9 (64%) were also taking mesalamine.

Two patients (14%) had an early postoperative complication (intraabdominal abscess, anastomotic stricture). Five patients (36%) had a 2-staged procedure (combined total colectomy and IPAA followed by subsequent ileostomy closure). Nine patients (64%) had a 3-staged procedure. For the 2-staged procedures, the mean time between the first and