

Management of Fulminant Ulcerative Colitis by Primary Restorative Proctocolectomy

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Severe acute ulcerative colitis unresponsive to medical management is characterized by multiple associated risk factors including anemia, hypoproteinemia, and high steroid requirements when urgent surgery is required. Current surgical options include use of primary ileal pouch-anal anastomosis (IPAA) *vs.* historic trends favoring colectomy with ileostomy. **PURPOSE:** To evaluate the efficacy of primary IPAA in patients with severe colitis, we reviewed our own experience in 20 patients with this condition. **METHODS:** Patients undergoing primary restorative proctocolectomy included 13 males and 7 females (mean age, 30.5 ± 2.4 years). Exclusion criteria for primary reconstruction included septic patients and patients with associated medical conditions such as pulmonary or cardiovascular disease. History of ulcerative colitis averaged 3.1 ± 1.1 years (range, 1 month to 19 years). Preoperative mean total serum protein concentration was 5.0 ± 0.2 g/dl, and mean albumin concentration was 2.1 ± 0.2 g/dl, reflecting disease severity. The average daily steroid requirement at the time of urgent colectomy was 58.0 ± 4.4 mg of prednisone (or intravenous equivalent). Primary IPAA included 18 "W" reservoirs, 1 "S" reservoir, and 1 "J" reservoir. **RESULTS:** Major surgical complications included mild pancreatitis (10 percent), anastomotic leak (5 percent), adrenal insufficiency (15 percent), an upper gastrointestinal bleed (5 percent), and small bowel obstruction (15 percent). There were no deaths, and no patients developed pelvic sepsis or required IPAA removal. At three and twelve months, 24-hr stool frequency averaged 7.3 ± 0.4 and 4.9 ± 0.3 , respectively. Overall day and night continence was excellent and not different from patients who underwent elective IPAA procedures for ulcerative colitis. **CONCLUSIONS:** Improved options such as primary IPAA may be safely used in selected patients requiring urgent surgery for severe or fulminant ulcerative colitis. Medical management should be abbreviated when disease control cannot be promptly achieved. [Key words: Fulminant; Ulcerative colitis; Ileal pouch]

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Surgical management of severe ulcerative colitis (UC) usually follows an initial attempt at aggressive medical therapy including bowel rest, high-dose steroids, hyperalimentation, and correction of associated electrolyte abnormalities and anemia.¹⁻³ The progression of disease that requires urgent surgical intervention can range from severe acute recurrent attacks in chronic disease to rapid fulminant courses that prove unresponsive to medical treatment.⁴⁻⁶ When parameters of severe UC are present as outlined by Danovitch¹ and Kambe *et al.*⁷ and aggressive medical treatment fails to improve significantly the disease status within the initial five days of therapy, surgery should be recommended. Truelove³ and others^{8,9} have noted that the probability of improving the outcome with continued medical treatment beyond five days is unlikely and increases the potential for life-threatening complications and compromised surgical results. The decision to terminate medical treatment and proceed with a pancolectomy or subtotal colectomy has, in large part, been responsible for a decrease in morbidity and mortality in patients with severe UC.^{8,10}

Ileal pouch-anal anastomosis (IPAA) has become the preferred option over total colectomy and permanent Brooke ileostomy for treatment of chronic UC.¹¹⁻¹³ The two-stage, elective procedure with temporary diverting ileostomy has been used for the most part in selected patients with less severe disease. The recommended approach for patients with free intra-abdominal perforation and sepsis continues to be subtotal colectomy and ileostomy placement with oversewing or diversion of the rectal stump, as advocated by Hawley¹⁴ and Goligher *et al.*⁸ Thus, surgical options in UC patients will vary depending on the two

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extremes of disease activity. However, the majority of patients with severe or more fulminant UC would not commonly present with perforation and sepsis-related problems if criteria for abbreviating medical management were more uniformly followed by the gastroenterology community. Together with extensive operative experience and improvements in perioperative management, an alternative approach for primary reconstructive procedures is supported by the understanding that many patients requiring urgent surgery may not have progressed to a critical disease status.

The judgment to proceed with a three-stage procedure *vs.* primary reservoir reconstruction has been based on historic trends, despite improvements in operative experience and perioperative management of more complex patients. Little information is available on the outcome or perioperative management of selected patients undergoing primary IPAA when criteria for severe disease are present. Additionally, the impact of severe hypoproteinemia and the ability to correct such deficits in the postoperative period to optimize recovery have not been examined along with operative strategies to minimize postoperative complications.

We report our experience with primary restorative proctocolectomy in patients with severe or rapidly progressing fulminant disease who failed to respond to aggressive medical therapy.

MATERIALS AND METHODS

From 1984 to 1992, 150 IPAA's were performed after total proctocolectomy for ulcerative colitis or familial polyposis at the University of Wisconsin Clinical Science Center, Madison, Wisconsin. Twenty-three of these patients have undergone urgent or emergent colectomy for severe or acute fulminant UC. All patients were hospitalized and referred by the gastroenterology service for colectomy after failure of aggressive medical therapy. All procedures were performed by the same surgical team.

All patients met three or more of the criteria for severe UC as defined by Danovitch¹ that includes: 1) anemia (hematocrit less than 5.0 and 3.0 g/dl, respectively); 3) severe UC requiring, but not improving with, bowel rest and hyperalimentation; 4) persistent tachycardia; 5) daily steroid requirements exceeding 40 mg of prednisone or equivalent intravenous dosage. Additional criteria distinguishing fulminant UC from severe disease included: 1) rapid course of dis-

ease requiring emergent surgery within seven days of medical treatment; 2) persistent fever over 38°C; 3) life-threatening hemorrhage; 4) findings of intra-abdominal perforation or clinical signs of sepsis.

All patients referred for urgent colectomy had the classic symptoms of severe disease, which included more than six bowel movements/day, crampy abdominal pain, and rectal bleeding. No significant improvement was evident with bowel rest, hyperalimentation, and administration of high doses of steroids in addition to correction of anemia and electrolyte abnormalities. No cases of toxic megacolon were treated during this time period; however, two patients were treated with colonic microperforations and positive intra-abdominal cultures for enteric organisms that were not associated with megacolon. Both presented with fulminant colitis and clinical sepsis (tachycardia, fever 38°C, and positive blood cultures).

Operative Management

All patients undergoing urgent colectomy and reservoir reconstruction were treated with antibiotics including ceftriaxone or had broad-spectrum coverage including an aminoglycoside. A limited preoperative mechanical bowel preparation with Golytely[®] (Braintree Laboratories, Inc., Braintree, MA) failed in seven patients because of severe abdominal cramping pain. Both patients who underwent emergent colectomy with findings of microperforations at celiotomy were excluded from any preoperative bowel preparation.

Twenty patients underwent immediate primary total colectomy, a 4-cm distal rectal mucosectomy, ileoreservoir reconstruction, and primary reservoir anal anastomosis with temporary diverting ileostomy. Because of associated factors (*i.e.*, cardiopulmonary disease, age, and sepsis from colonic perforation), the remaining three patients underwent a secondary reconstruction following initial subtotal colectomy with oversewing of the rectal stump.

Celiotomy was performed through a midline incision with meticulous dissection to prevent iatrogenic bowel perforation. The omentum was universally sacrificed as it was frequently adherent to the inflamed colon. A two-surgeon team was used to decrease overall operative time. All reservoirs, including W-shaped ileal reservoirs, were constructed as previously described.¹¹⁻¹² Pelvic hemostasis was ensured before reservoir placement in the pelvis to minimize the risk of pelvic bleeding and postoperative pelvic

abscess. A temporary loop ileostomy was placed in all patients.

Postoperative management principles included: 1) hyperalimentation to correct severe hypoproteinemia until patients were on a regular diet; 2) rapid tapering of steroid administration to an average of 15 mg of prednisone (or intravenous equivalent) by the fifth postoperative day.

Statistical Analysis

All results were expressed as mean \pm SEM. A computer-based statistics program (SYSTAT: The system for statistics, SYSTAT Inc., Evanston, IL) was used to perform all analyses. Paired *t*-tests followed by the Bonferroni procedure were used to evaluate changes from baseline. Paired analyses for total protein and albumin concentrations were performed. Unpaired *t*-tests were used to compare the effects of hypoproteinemia with steroid usage on complication frequency. A *P* value of ≤ 0.05 was considered statistically significant.

RESULTS

Demographic characteristics for patients with severe UC who underwent urgent or emergent primary restorative proctocolectomy are shown in Table 1. Among these patients were eight females and 15 males, with a mean age of 30.5 ± 2.4 years. The history of UC before presentation and surgery averaged 3.1 ± 1.1 years (range, 1 month to 19 years). The diagnosis of UC was confirmed by preoperative colonoscopy with biopsy and additionally by patho-

logic review at surgery. These patients had an average preoperative hospitalization of 14.1 ± 2.7 days (range, 1–48 days). Average weight loss before surgery was 7.7 ± 1.5 kg (or 9.7 ± 1.6 percent of body weight). Fifty percent of patients presented for surgery upon initial diagnosis of UC. The remaining patients had either continuous severe UC or chronic disease and had surgery as a result of an acute exacerbation. Four patients required emergent colectomy (within 48 hours of consultation) for fulminant UC on the basis of the outlined criteria, whereas 16 required urgent colectomy for severe disease. The majority (15/20) had total colonic involvement of UC, with the remaining being limited to left-sided disease only. One patient undergoing primary restorative proctocolectomy presented with signs and symptoms of colonic perforation, and transmural inflammation and colonic microperforations were confirmed at the time of surgery.

Table 2 summarizes the clinical characteristics of those patients meeting inclusion criteria for severe UC. Preoperatively, patients had a mean total serum protein concentration of 5.0 ± 0.2 (range, 3.8–6.6) g/dl, and mean albumin concentration was 2.1 ± 0.2 (range, 0.9–4.2) g/dl. Severe anemia was reflected by an average hematocrit of 30.5 ± 0.8 percent and a mean hemoglobin concentration of 10.1 ± 0.3 g/dl. At least 95 percent of patients presented with a hematocrit of less than 35 percent before surgery. At the time of surgery, steroid requirements averaged 58.0 ± 4.4 mg of prednisone/day (range, 20–100 mg) and 90 percent (18/20) requiring ≥ 40 mg/day. By the fifth postoperative day, mean daily steroid requirement was reduced to 13.1 ± 0.5 mg. Postoperatively, patients averaged 7.8 ± 0.6 days of

Table 1.
Patient Demographics*

	No. of Patients	%
Sex		
Male	13	65
Female	7	35
Extent of disease		
Left-sided	5	25
Total	15	75
Duration of disease		
<6 mo	8	40
6 mo–2 yr	8	40
>2 yr	4	20
Course of disease		
First attack	10	50
Intermittent	7	35
Continuous	3	15

* Age (yr) 30.5 ± 2.4 .

Table 2.
Preoperative and Perioperative Clinical Parameters of
20 Patients with Severe Ulcerative Colitis

		No. of Patients	%
Stool frequency (hr)	6–10/24	5	25
	10–14/24	8	40
	$\geq 15/24$	6	30
TSP (g/dl)	≤ 5.0	13	65
Albumin (g/dl)	≤ 3.0	19	95
Hgb (g/dl)	≤ 11	18	90
Hct (%)	≤ 30	13	65
	31–35	6	30
Transfusion requirement	<2	4	20
(packed cells) (units)*	2–4	10	50
	>4	6	30

* Operative and initial 24-hr perioperative period.

total parenteral nutrition. However, normoproteine-mia was not achieved in the immediate postopera-tive period by the time total parenteral nutrition was terminated. (Fig 1).

No mortality resulted from primary restorative proctocolectomy or in staged reconstruction. Three pa-tients with the outlined exclusion criteria precluding primary ileoanal reconstruction underwent a three-staged procedure with an initial subtotal colectomy and ileostomy. This group of patients all had success-ful delayed ileal pouch reconstructions 6 to 12 months after initial subtotal colectomy. Primary restorative proctocolectomy was accomplished with a "W" res-ervoir design in 18 patients, an "S" reservoir design in 1 patient, and a "J" reservoir in 1 patient (Table 3). The choice of reservoir design was primarily based on surgeon preference.

As a result of profound preoperative anemia, pa-tients were administered an average of 3.9 ± 0.5 units of packed red blood cells during surgery or within the initial perioperative 24 hours. Eighty percent (16/20) received two or more units. Fifteen patients received fresh frozen plasma averaging 4.4 ± 0.6 units/patient. Conservative intraoperative fluid management was reflected by an average crystalloid administration of 3.0 ± 0.3 liters. Operative time for primary restorative

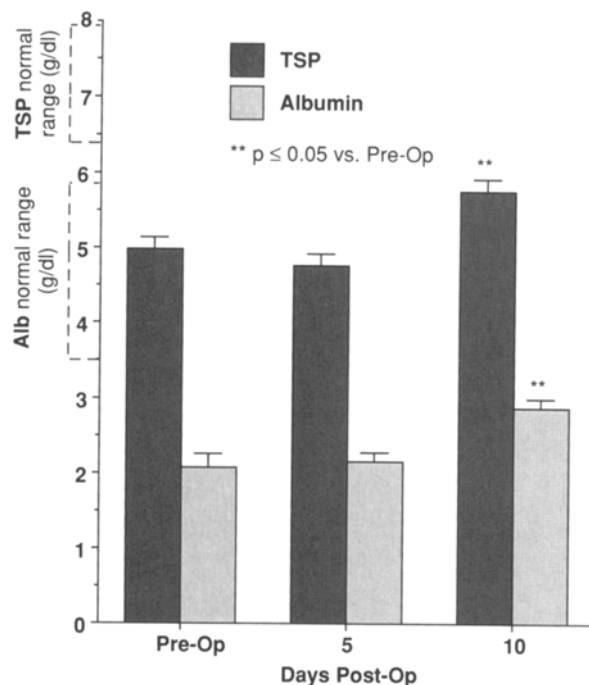


Figure 1. Preoperative and postoperative changes in plasma total protein (TSP) and albumin (Alb) concentrations following restorative proctocolectomy.

Table 3.
Surgical Procedures Performed in Patients
with Severe Ulcerative Colitis

Procedure	No. of Patients
Total proctocolectomy, W-pouch, ileostomy	18
Total proctocolectomy, S-pouch, ileostomy	1
Total proctocolectomy, J-pouch, ileostomy	1
Subtotal colectomy, ileostomy	3

proctocolectomy averaged 7.4 ± 0.2 hours. The mean postoperative hospital stay was 10.7 ± 0.9 days.

Complications

Successful reservoir reconstruction and function was accomplished in all patients undergoing primary or secondary ileoanal construction. Problems that could be directly attributed to high preoperative steroid requirements and rapid postoperative tapering included prolonged postoperative ileus (5 patients) and adrenal insufficiency symptoms including depression, postural hypotension, and dehydration (3 patients) (Table 4). Two patients also developed mild postoperative pancreatitis, which resolved readily with conservative management.

Major complications requiring reoperation included one wound dehiscence and three episodes of small bowel obstruction. One of these patients required adhesiolysis three weeks after surgery, and an early ileostomy takedown was performed to correct the obstruction. One patient developed an upper gastro-intestinal bleed, which was treated surgically. In another patient, a pouch-anal anastomotic disruption occurred, which was successfully managed by revi-

Table 4.
Incidence of Surgical Complications Following
Restorative Proctocolectomy for Severe
Ulcerative Colitis

Complication	No. of Patients	%
Infection		
Abdominal wound	2	10
Septicemia	1	5
Wound dehiscence	1	5
Pancreatitis	2	10
Adrenal insufficiency	3	15
DVT	2	10
Anastomotic disruption	1	5
Anal stricture	3	15
Small bowel obstruction	3	15
Upper gastrointestinal bleeding	1	5
Prolonged ileus	5	25

sion when the patient was nutritionally improved and off supplemental steroids.

Functional Characteristics

Postoperative follow-up was complete on all patients at one year after restorative proctocolectomy. There was a significant decrease ($P < 0.05$) in 24-hour stool frequency between 2 and 3 months and 1 year (7.3 ± 0.4 vs. 4.9 ± 0.3 , respectively) (Fig. 2). In addition, all patients reported complete continence during the day at 12 months, whereas 3 of 16 patients experienced minor occasional seepage at night. Postoperative assessment of anal sphincter pressure at 2 months confirmed overall excellent sphincter function with mean resting and maximal squeezing pressures of 51.8 ± 2.2 and 136.0 ± 11.1 mmHg, respectively.

DISCUSSION

Primary restorative proctocolectomy with the IPAA is commonly used in patients who require surgery for UC and has significantly improved quality of life; however, it is not routinely used in patients requiring urgent surgery for UC.¹⁵ The medical and surgical management of severe and fulminant UC has changed significantly since Goligher *et al.*⁸ recommended more aggressive and earlier operative intervention in patients with fulminant disease and toxic megacolon. Surgical trends have varied from preresection ileostomies and colostomies as advocated by Turnbull *et al.*¹⁶ to total proctocolectomy and ileostomy.⁸ However, morbidity has not decreased by including proctectomy *vs.* subtotal colectomy.¹⁴ In fact, it presents

an additional disadvantage by precluding eventual ileal reservoir reconstruction if the sphincter musculature is removed or damaged.

Hawley¹⁴ recently reviewed options in emergency surgery for UC and recommended a subtotal colectomy as the option of choice, thus preserving reconstructive options for the future. The advantage of this approach is obvious for patients presenting with toxic megacolon or major bowel perforation with peritonitis. However, the majority of patients in recent reports may not present with this degree of disease severity.¹ Recommendations to use a subtotal colectomy for severe disease apart from perforation or toxic megacolon do not take into account improvements in operative experience with ileal reservoir procedures and perioperative management of more complex patients. As historic trends have changed and strategies are used to limit perioperative morbidity, primary restorative proctocolectomy may not be automatically contraindicated. If critical disease status with free perforation or toxic megacolon is not present, as we have frequently observed, then a three-stage option (subtotal colectomy and delayed reconstruction with temporary ileostomy) may not be the procedure of choice. This may be especially true if the factors affecting morbidity (anemia, severe hypoproteinemia, and high steroid requirements) can be corrected in the perioperative period.

Additionally, the ultimate goal of optimal reservoir function without compromising morbidity is not necessarily improved by a three-stage procedure. Zenilman *et al.*,¹⁷ in one of the few reports comparing the two-stage and three-stage approaches, noted that functional results were compromised with an increased incidence of nocturnal incontinence and postoperative bowel obstruction in patients requiring three-stage procedures. Compromised reservoir function following a three-staged procedure was also reported by Nicholls *et al.*¹⁸ when compared with primary restorative proctocolectomy. A three-stage approach also does not guarantee eventual reconstruction following subtotal colectomy and ileostomy, as mesenteric scarring may make mobility to the anal canal difficult, especially in the overweight or male patients, and may compromise a potential staged reconstruction. Furthermore, the tendency to avoid surgery or a staged restorative proctocolectomy may prolong medical management, as we have observed, and increase the morbidity in an attempt to make the patient a better candidate for surgery.

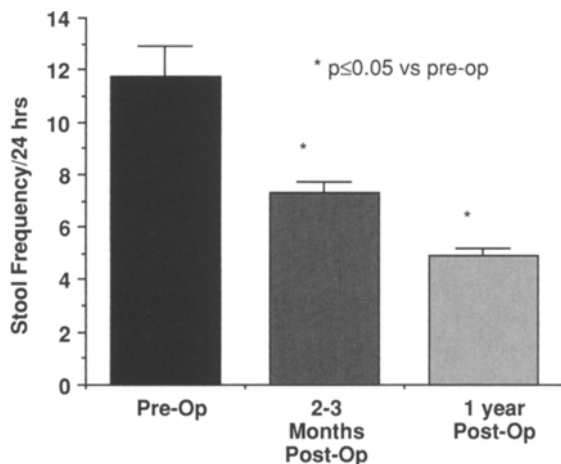


Figure 2. Stool frequency before and after restorative proctocolectomy.

Medical management of severe UC has improved greatly but still fails in over 80 percent of cases if the disease does not significantly improve within 5 days.³ Moreover, the possibility of reversing rapidly progressive fulminant disease in a febrile patient who is experiencing tachycardia and additional signs of sepsis after a 24-hour medical trial is improbable. Grant and Dozois⁴ concluded that in the extreme case of toxic megacolon, medical management should be exclusively regarded as preparation for surgery as 47 percent of patients that resolved with medical management required a later colectomy for recurrent severe disease. Despite these basic guidelines, our experience has been that gastroenterologists still tend to prolong medical management beyond an acceptable period as evidenced by our preoperative hospitalization of 14.1 ± 2.7 days. An aggressive, earlier surgical approach is not commonly considered by many in the gastroenterology community, even though IPAA has proved to be a tremendous advancement in the management of UC.

Previously reported guidelines for urgent colectomy for severe UC^{3, 8, 9} and our own experience with perioperative complications in patients that received prolonged medical management support early surgical intervention when patients with severe UC do not respond to medical treatment within one week. The trend to continue prolonged aggressive medical therapy may increase the potential for postoperative problems in the group of patients most likely to require future colectomy, even if the acute flare is controlled. All of our patients with severe UC who underwent primary restorative proctocolectomy had successful IPAA, obviating subsequent delayed reconstructive operative procedures with the attendant /operative morbidity. However, 58 percent of our patients sustained at least one minor or major complication (Table 4). This was significantly greater than the 33 percent incidence of complications reported by Wexner *et al.*¹⁹ and the 36 percent incidence reported in our own series for elective reconstructions.²⁰ One variable that significantly increased the risk for operative complications ($P < 0.05$) was a disease length of more than six months. A shorter duration of active disease significantly decreased operative risks and further supports the judgment to limit aggressive medical management when disease control cannot be rapidly achieved and maintained. Fifty percent of our patients manifested either intermittent disease with frequent flares or continuous disease requiring high steroid requirements. Only when severe disease sta-

tus was achieved were these patients referred for colectomy.

Ileal reservoir-related complications have decreased with time as operative experience and techniques have improved.^{21, 22} The most important determinant for successful outcome of primary IPAA remains proper patient selection. Patients with toxic megacolon or major perforation should not be considered as candidates for primary reconstruction; rather, a three-staged approach should be undertaken.¹⁴ Three patients in our series did not undergo primary reconstruction because of exclusion criteria that included 1) associated cardiopulmonary or renal disease; 2) age considerations (relative); 3) fulminant colitis with major perforation and sepsis; 4) toxic megacolon.

Additional factors that determine successful recovery from primary restorative proctocolectomy include correction of anemia, avoidance of infection-related problems such as pelvic abscesses, rapid steroid tapering, and correction of severe hypoproteinemia to optimize healing potential. Buckell *et al.*²³ demonstrated that protein depletion is an important determinant of disease activity, and treatment options such as hyperalimentation should be used early for primary medical treatment when the criteria for severe disease, as noted in Table 2, are present. Previous reports on emergent surgery for UC have not addressed the degree of protein deficits that occur or the ability to correct these deficiencies following surgery for severe or fulminant disease. Correction of severe protein deficits *via* hyperalimentation is unlikely in the preoperative period because of severe disease status (Fig. 1). However, even with aggressive nutritional support in the perioperative period, reversal of profound hypoproteinemia is difficult and does not begin to statistically normalize until the tenth postoperative day (Fig. 1). Correction of these severe deficits should be considered in the perioperative management course as parenteral nutrition is vital even in a supplemental role early after return of normal intestinal function. Failure to aggressively meet nutritional requirements may contribute to additional unnecessary morbidity. We feel the nutritional status, as reflected by the level of protein depletion and recovery, is an important gauge when selecting patients at greatest risk for perioperative complications. Nevertheless, we were unable to demonstrate a statistically significant effect of protein depletion on complication frequency. In the only other report comparing protein concentration and complication frequency in two-

stage and three-stage restorative proctocolectomy patients, Nicholls *et al.*¹⁸ was likewise unable to demonstrate a statistically significant correlation between preoperative albumin values <4 g/l and complication frequency.

The role of high-dose steroids in decreasing healing potential and increasing infection-related problems is well known.²⁴ Therefore, a rapid tapering schedule would seem to be mandatory for optimizing postoperative care and decreasing morbidity. However, aggressive steroid tapering from an average preoperative dose of 58.0 ± 4.4 to 13.1 ± 0.5 mg of prednisone (or intravenous equivalent) by the fifth postoperative day can lead to significant adrenal insufficiency symptoms, as developed in 15 percent of our patients with severe disease (Table 4). This was significantly higher than the six percent incidence of adrenal insufficiency reported for our series of elective patients in whom rapid tapering was not usually necessary.²⁰ Additionally, Stelzner *et al.*²⁵ reported frequent ileus and obstructive symptoms from a rapid taper approach following IPAA. We also found a high incidence of prolonged ileus (Table 4), which developed in 25 percent of our patients with severe disease compared with only 8 percent in our series of elective reconstructions.²⁰ The mechanism for prolonged ileus problems has not been clearly delineated; however, these findings confirm that such problems are frequently encountered following restorative proctocolectomy for severe UC. Consequently, nasogastric suction should not be quickly terminated in these patients as they may be more prone to develop hypomotility problems.²⁵

In the majority of patients presenting with severe or fulminant disease, associated factors such as hypoproteinemia and problems related to steroid tapering can be successfully managed in the perioperative period. Despite these complicating variables, all patients with severe UC that underwent restorative proctocolectomy had successful IPAA's with excellent functional results. The decline in 24-hour stool frequency to 4.9 ± 0.3 at 1 year (Fig. 2) is identical to that reported for our elective patients.²⁰ Furthermore, postoperative anal sphincter function, as reflected by resting and maximal squeezing pressures of 51.8 ± 2.2 and 136 ± 11.1 mmHg at 2 months, respectively, compared favorably with our elective series, in which we reported pressures of 46 ± 3.9 and 93 ± 2.1 mmHg at 2 months.²⁰

CONCLUSIONS

Selected patients presenting with severe UC who do not respond to aggressive medical treatment within the initial week of therapy should be considered for early surgical intervention. Additional reports corroborating our experience and evidence to support abbreviating unnecessarily prolonged medical management of severe or fulminant UC may further define the limits of using primary IPAA in this complex patient group. Urgent or emergent IPAA procedures must be clearly distinguished from elective IPAA in postoperative management to optimize the potential for successful outcome. These principles include correction of anemia, correction of severe hypoproteinemia *via* prolonged postoperative hyperalimentation, rapid steroid tapering, and awareness of problems related to adrenal insufficiency. Primary restorative proctocolectomy with IPAA may become a more viable option for carefully selected patients with severe or fulminant UC as experience with IPAA and perioperative management continue to improve.

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