

Management of Acute Ulcerative Colitis

C. Tyler Ellis, M.D., M.S.C.R. • Alessandro Fichera, M.D.

Department of Surgery, University of North Carolina, Chapel Hill, North Carolina

CASE SUMMARY: A 42-year-old man with an 8-month history of ulcerative colitis (UC), controlled with mesalamine enemas, presented with frequent (10 times per day) bloody bowel movements. He was diagnosed with an acute flare of pancolitis started on intravenous (IV) steroids. Flexible sigmoidoscopy confirmed mucosal ulceration consistent with severe colitis (Fig. 1), and biopsies confirmed cytomegalovirus colitis. Valganciclovir was added to his IV steroid therapy. After 3 days with refractory hematochezia, infliximab was added. He responded and was able to be discharged from the hospital. After his second dose of infliximab, he represented with worsening hematochezia. Colorectal surgery was consulted.

At the time of surgical evaluation, the patient was on infliximab 10 mg/kg, methylprednisone 20 mg IV 3 times per day, and valganciclovir 900 mg orally twice per day. His vital signs were normal (temperature 36.1°C, heart rate = 79, and blood pressure = 120/66). His white blood cell count was 18,000/ μ L and his hemoglobin was 6.6 g/dL. *Clostridium difficile* testing remained negative. Toxic megacolon was ruled out on clinical examination and cross-sectional imaging (Fig. 2). C-reactive protein (CRP) and erythrocyte sedimentation rate were persistently elevated at 28 mg/L (normal, <10 mg/L) and 35 mm per hour (normal, <15 mm/h). He had lost 23 pounds over the last month because of poor oral intake for fear of worsening his symptoms (serum albumin = 1.7 g/dL). He was started on total parental nutrition and received a blood transfusion. The patient was counseled on the low likelihood that his disease would be responsive to continuing medical therapy, and

surgery was recommended. A total abdominal colectomy (TAC) with end ileostomy was performed (Fig. 3). He did well and was able to be discharged on postoperative day 5.

CLINICAL QUESTIONS:

- What are the indications and timing for surgery in a patient with an acute flare of UC?
- Which types of infectious colitis should be ruled out in patients with an acute exacerbation of UC?
- What operations are indicated in the acute setting?

BACKGROUND

UC is an inflammatory disease that may involve the entire colorectal mucosa¹ with varying severity in a continuous retrograde direction with sparing of the anus.² Unlike Crohn's disease, surgery is curative for UC; yet a majority ($\approx 70\%$) of patients with UC will be successfully managed with medical therapy alone.² Failure of medical management can be subjective, hard to predict, and difficult to manage. For this reason, medical and surgical UC specialists should work collaboratively to achieve the best outcomes.

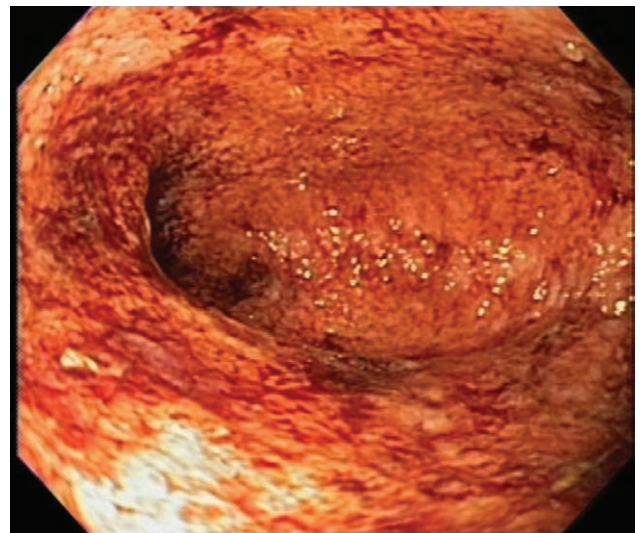


FIGURE 1. Endoscopic image of severe colitis associated with acute ulcerative colitis. Photo courtesy of Hans Herfarth, M.D., Ph.D.



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Funding/Support: None reported.

Financial Disclosure: None reported.

Correspondence: C. Tyler Ellis, M.D., M.S.C.R., University of North Carolina, Department of Surgery, 4001 Burnett-Womack Building, CB# 7050, Chapel Hill, NC 27599-7050. E-mail: ellistc@gmail.com

Dis Colon Rectum 2018; 61: 1010–1015

DOI: 10.1097/DCR.0000000000001173

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FIGURE 2. CT image, axial view, of an inflamed ascending and descending colon.

The majority of UC patients (>70%) that present with an acute flare can be rescued with medical therapy and do not require surgery.³ However, steroids and biological agents are associated with their own morbidity; they can confuse the clinical picture, leading to potential delays in the appropriate management and increased postoperative complications.

Indications for surgery in the acute phase of UC include the following acute flare unresponsive to medical

measures or life-threatening complication, such as toxic colitis, megacolon, perforation, or hemorrhage. Other indications, such as risk of malignancy, medical intractability, and growth retardation in children, are not discussed in this article.

A recent study found that TAC is surpassing total proctocolectomy as the most common initial operation for patients with UC in the United States.⁴ This suggests that patients may be presenting more frequently with acute illness and thus are unfit for a definitive operation.⁴ This trend coincides with the introduction of biological therapy in clinical practice. Infliximab, an antitumor necrosis factor (TNF)- α monoclonal antibody, was approved for use in UC for induction and maintenance therapy in 2005. Since that time, several other biological medications have been approved by the US Food and Drug Administration for the treatment of moderate-to-severe UC. Initial clinical trials demonstrated reduced rates of colectomy with infliximab use, and, as expected, anti-TNF medication use has increased over time.⁵ However, a recent report has shown an association between infliximab use and increased rates of colectomy.⁵ The association between infliximab and rates of colectomies for UC remains controversial; nevertheless, anti-TNF therapy may increase 3-stage procedures and postoperative complications after an IPAA.⁶

PRESENTATION AND DIAGNOSIS

An acute flare is often the initial presentation of UC, but it is also not uncommon in patients on maintenance therapy. In either case, it should be presumed that the patient is immunosuppressed and malnourished until proven otherwise. This information can be elucidated with a thorough history, physical examination, and serum laboratory markers (ie, albumin and prealbumin). Furthermore, patients on high-dose steroids may appear deceptively well.

Diagnostic criteria for severe and fulminant (ie, toxic) colitis are shown in Table 1.² Regarding biomarkers, erythrocyte sedimentation rate and CRP are 2 nonspecific



FIGURE 3. Colonic mucosa in advanced ulcerative colitis with pseudopolyps, mucosal thickening, and bridging.

TABLE 1. Diagnostic criteria for severe and fulminant (toxic) colitis

Signs and symptoms	Severe	Fulminant (toxic)
Bloody stools per day	6	10
Fever (temperature >37.5°C)	Yes	Yes
Tachycardia (heart rate > 90 beats per min)	Yes	Yes
Anemia (hemoglobin, <75% of normal)	Yes	Yes (requiring transfusion)
Elevated sedimentation rate (>30 mm/h)	Yes	Yes
Colonic dilation	—	Yes
Abdominal distention	—	Yes
Abdominal tenderness	—	Yes

markers of inflammation that can be elevated in patients with active UC.⁷ However, <50% of patients with an active flare of UC can demonstrate normal CRP levels.⁷ Fecal calprotectin is more specific for intestinal inflammation, and it has been used as a noninvasive assessment of disease relapse.⁷ Yet, there is no biomarker panacea for good clinical judgment, and biomarkers should only be used as an adjunct.

One should elucidate a history of perianal disease and review previous colonoscopies and cross-sectional imaging that may suggest small-bowel disease to rule out Crohn's disease and confirm the diagnosis of UC. Furthermore, superimposed infectious colitis, including *C. difficile* and cytomegalovirus colitis, affects <30% of patients with UC presenting with acute exacerbations, and it should be ruled out. Appropriate antibiotic and antiviral therapies are often successful in managing the acute presentation, thus avoiding urgent surgery.

Imaging should be obtained while taking into consideration the clinical scenario. An upright chest film with a flat plate of the abdomen at the bedside is usually sufficient to detect toxic megacolon and perforation, avoiding unnecessary cross-sectional imaging and associated delay in treatment. When the transverse colonic distention is >6 cm, the diagnosis of toxic megacolon should be entertained.² However, perforation may also occur without colonic dilation. These patients often do not exhibit classic signs of peritonitis.²

MANAGEMENT

During an acute exacerbation of UC in a stable patient, initial treatment with IV steroids, resuscitation, and bowel rest is indicated. Infectious colitis should be ruled out and the diagnosis confirmed with a flexible sigmoidoscopy. If a patient fails to show improvement after 3 days on steroids and treatment of concurrent infectious colitis, if indicated, consider second-line therapies, including escalating medical therapy with infliximab or cyclosporine, versus proceeding to surgery. Infliximab and cyclosporine have been shown to have success in decreasing colectomy rates in acute severe steroid-refractory UC in <75% of patients; however, their long-term efficacy is unclear.³

The patient should be closely followed to assess for improvements with medical therapy with serial abdominal exams and imaging as needed. Providers should consider supporting the patient with total parental nutrition during this time. Lack of response or worsening conditions will become apparent by day 5 to 7 after starting infliximab or cyclosporine. If infliximab is initiated and the patient fails to improve after

the first or second dose, surgery should be undertaken, because delay may increase the rates of postoperative complications.¹

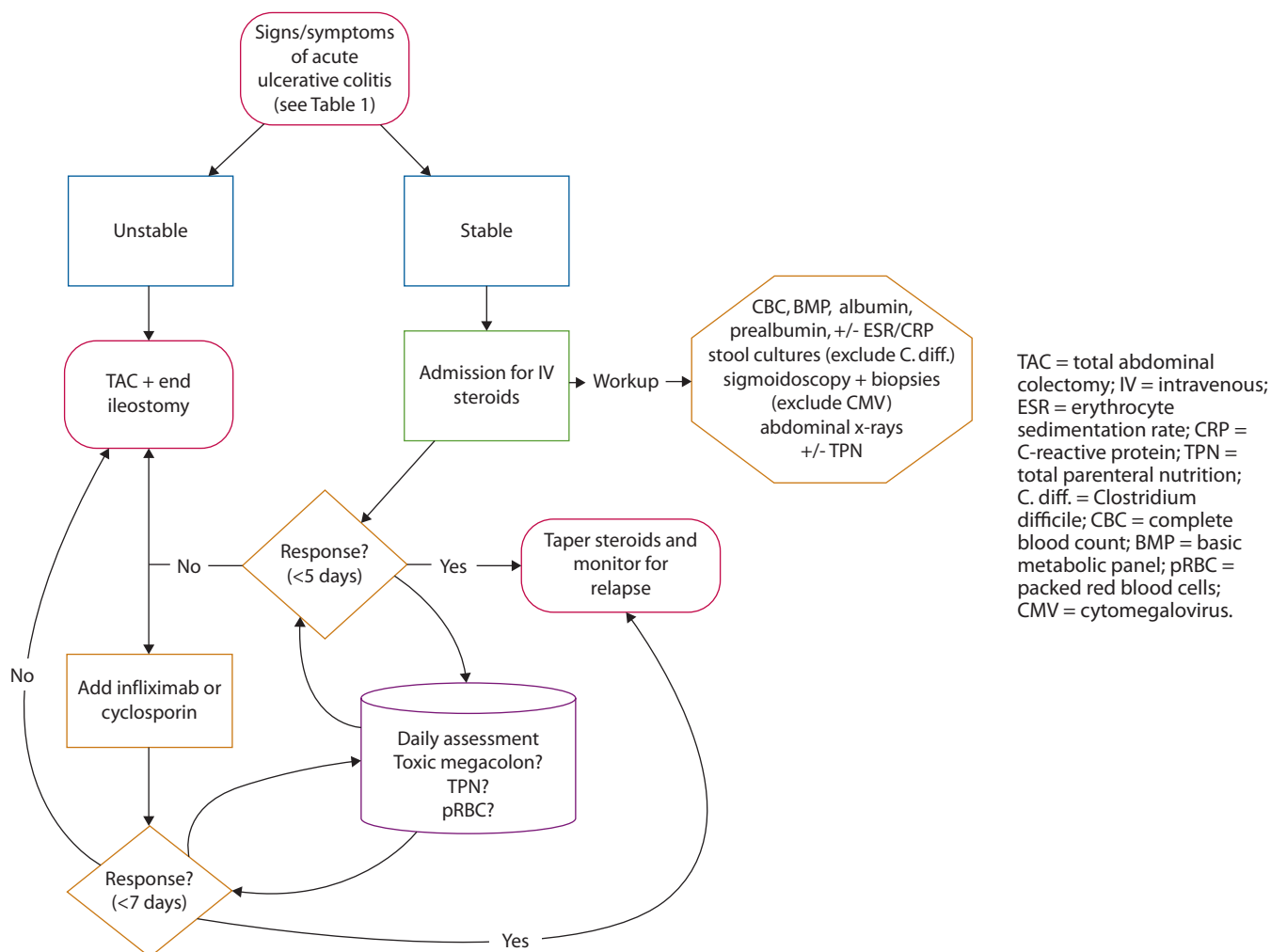
Under emergent conditions, alternatives to surgery are limited. Uncontrollable colonic bleeding, perforation, toxic colitis causing sepsis, and multisystem organ failure are indications for emergent surgery. The patient should be marked for an ostomy by a enterostomal therapist (if available), otherwise the stoma should be placed in an area overlying the patient's rectus muscle on the right side of the umbilicus that avoids skin folds and scars when the patient is sitting and supine. A TAC with end ileostomy and Hartmann pouch is the procedure of choice in the acute, urgent setting.⁸ Laparoscopic-assisted or hand-assisted approaches are considered safe and feasible even in the acute setting and are the authors' preference.⁹

A few technical considerations while performing a TAC include the following: avoid mobilizing the terminal ileum more than it is needed to bring it to the abdominal wall to preserve ileal length for a potential IPAA creation at a later date and preserve the inferior mesenteric pedicle to avoid any potential ischemia of a long rectal stump and avoid dissection of the rectum to facilitate pelvic dissection at the second surgery. Given the severity of the colonic disease, the possibility of a rectal stump blowout is a real concern. We prefer a temporary draining transanal rectal tube to minimize pressure in the rectal stump rather than creating a mucous fistula; however, both are acceptable options.

One alternative surgical approach is the Turnbull blowhole colostomy that has been described and used in the past for pregnant patients presenting with fulminant UC.¹⁰ This procedure includes a loop ileostomy and transverse colostomy.¹⁰ More recently, Dozois et al¹¹ have shown that a TAC with end ileostomy can be safely performed in pregnant patients when assisted by a multidisciplinary team that includes a high-risk obstetrician, gastroenterologist, and experienced surgeon.

The next step is a definitive operation. Surgical options included the following: a completion proctectomy with end ileostomy or a completion proctectomy with restorative IPAA, with or without a diverting loop ileostomy. This surgery should only be considered when the patient has improved his or her nutritional status and is free from immunosuppressive medications (usually >6 wk from the initial operation). Finally, patients with UC have a high risk of postoperative deep venous thrombosis; accordingly, postdischarge deep venous thrombosis prophylaxis should be considered after the initial and subsequent operations (see algorithm).¹²

EVALUATION AND TREATMENT ALGORITHMS



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