

Original Article

# Surgical Management of Fulminant Colitis in Patients with Ulcerative Colitis

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## Key Words

Fulminant colitis;

Nutrition;

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**Purpose.** Ulcerative colitis disease is usually treated conservatively. Surgery is reserved for treating its complications. The experience of surgical treatment of ulcerative colitis, especially fulminant type in most physicians is relatively limited. This is a retrospective review of procedures and results of surgical treatment, and nutritional interventions upon fulminant colitis.

**Materials and Methods.** From December 1983 to October 2016, there were 50 patients with ulcerative colitis operated by a single surgeon. Twenty of them were female, and thirty were male. Age ranged from 16 to 82 years old, with an average of 47.3 years old when they were operated. Sixteen patients were considered to be fulminant colitis, four of them had total colonoscopy prior to the incidence. Six of them were female, and ten were male. Age ranged from 33 to 74 years old, with an average of 46.7 years old when they were operated.

**Results.** Among the sixteen fulminant ulcerative colitis patients, eight patients were treated with subtotal colectomies and ileorectal anastomoses. Four patients had colectomy with stomy. Four patients had restorative proctocolectomies with pouch anal anastomoses and diverting ileostomies. Sixteen patients had albumin less than 3.5 gm/dL prior to surgery. Fourteen patients received perioperative parenteral nutrition. One patient died of sepsis following colectomy with ileostomy for perforation of colon with peritonitis.

**Conclusion.** Surgery should be reserved for complicated ulcerative colitis, especially fulminant type. Malnutrition is common in the patients with ulcerative colitis who received the operation, and for the subgroup of fulminant colitis, some of the nutritional parameters were even worse. Restorative proctocolectomy can offer a good quality of life if the operation is successful. Total colonoscopy or colon series should not be performed in the patients with acute severe colitis.

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Ulcerative colitis (UC) is a chronic inflammatory disease limited to the mucosal layer of the colon. It is characterized by continuous relapsing–remitting clinical scenario. The rectum is most frequently involved, however, the colon may also be involved as rectosigmoid colitis, left side colitis or total colitis.<sup>1</sup>

The incidence rate of UC is much lower in Asia compared with Northern Europe and North America. But the newly diagnosed cases were significantly increasing in the past decades in Asian countries.<sup>2</sup> It is generally believed that the environment and lifestyle could be impact factors of incidence on the disease.

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Fulminant UC, a subgroup of severe UC, is characterized by having more than 10 times of stool passage per day, persistent bleeding, abdominal pain and fullness. And patients may present with systemic inflammatory response syndrome (SIRS). Moreover, the clinical condition may develop toxic megacolon or colonic perforation if deteriorated.<sup>3</sup>

Ulcerative colitis is usually treated conservatively. Surgery is reserved for treating its complications. The medications frequently used for treatment of UC include mesalazine (5-ASA) and steroids. Immunomodulators such as azathioprine, methotrexate and cyclosporine are also suggested in severe cases. Modern development of biologic agents, like adalimumab, infliximab, vedolizumab and golimumab has changed a lot in the therapy of UC recently.

But those patients who do not respond to the conservative medications, surgery remains as an option for the management.<sup>4</sup>

The prevalence rate of ulcerative colitis in Taiwan is much lower than western countries. Therefore the experience of surgical treatment for ulcerative colitis, especially fulminant type in most surgeons is relatively limited. The aim of this study is to evaluate indications, procedures and results of surgical treatment. We also analyze patient's nutritional status and treatment for patients with fulminant UC.

## Materials and Methods

The data were obtained from the medical record of Mackay Memorial Hospital. We identified and included patients who had undergone surgical intervention for the ulcerative colitis in 33 years.

This was a retrospective study of a single-center, single-surgeon's experience. From December 1983 to October 2016, fifty patients with ulcerative colitis were operated by a single team. Twenty of them were female, and thirty were male. Age ranged from 16 to 82 years old, with an average of 47.3 years old when they were operated. Indications for operations include 29 patients for intractable disease, 12 patients for toxic colitis with or without megacolon, four patients for bowel perforation with peritonitis, two patients for

second operation following colectomies, two patients for poor result following surgery, and one patient for severe perianal fistulous abscess (Table 1).

In the sixteen patients with fulminant colitis, six of them were female, and ten were male. Age ranged from 33 to 74 years old, with an average of 46.7 years old when they were operated. Indications for operation were 12 for toxic colitis with or without megacolon, four for bowel perforation with peritonitis. Four of the patients with fulminant colitis had total colonoscopy prior to the incidence.

Nutritional parameters and assessment include preoperative albumin, body mass index (BMI), cholesterol and triglyceride. Necessity for parenteral nutrition was also analyzed. The Fisher exact test was used for categorical data, probability values < 0.05 were considered statistically significant.

## Results

Eight patients were treated with subtotal colectomies and ileorectal anastomoses, four patients had colectomy with stomy, four patients had restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) and diverting ileostomies. Among patients with IPAA with ileostomy, three ileostomies were not closed. A patient died of sepsis following colectomy with ileostomy for perforation of colon with peritonitis.

Among the sixteen patients with fulminant colitis, all patients were found to have albumin less than 3.5 mg/d and cholesterol less than 130 ml/dL prior to surgery. Fourteen patients had BMI less than 22. Fourteen patients received perioperative parenteral nutri-

**Table 1.** Surgical indication for ulcerative colitis (n = 50)

Surgical indication	Number of patients
Intractable disease	29
Toxic colitis with or without megacolon	12
Bowel perforation	4
Second operation following colectomy in other hospital	2
Poor result from previous surgery	2
Perianal fistulous abscess	1

tion. Here we also present nutritional parameters and support in patients with ulcerative colitis who received operation, in which sixteen patients of fulminant ulcerative colitis were included (Table 2). We use Fisher's exact test to compare the nutritional parameter between the patients of fulminant ulcerative colitis ( $n = 16$ ) and ulcerative colitis ( $n = 34$ ) (Table 3). There was no significant difference in terms of the BMI, preoperative triglyceride and perioperative parenteral nu-

trition between the two groups. But preoperative albumin and cholesterol were meaningfully different in our series ( $p < 0.0001$ ).

## Discussion

Ulcerative colitis is most commonly known for its chronic and refractory course. The indications for surgery include failure of medical treatment of UC and those patients presented with acute or chronic complications.

For better recognition of the severity of inflammation, UC are often classified as mild, moderate and severe based on modified Truelove and Witt's criteria (Table 4).<sup>5</sup> While patients with fulminant colitis often present with more than 10 times of bowel movement per day, accompanied by persistent bleeding, and in need of blood transfusion. Meanwhile, patients may also have abdominal fullness and tenderness. If clinical condition deteriorates, colon may start to dilate with toxic signs of sepsis, and perforation of colon may even occur.

The precise definition for fulminant colitis (FC) has not well achieved consensus yet, especially to dis-

**Table 2.** Nutritional parameters and support in patients with fulminant ulcerative colitis ( $n = 16$ ) and in patients with ulcerative colitis ( $n = 50$ )

Nutritional parameters and support	No. of patients with fulminant UC (% of total)	No. of patients with UC (% of total)
Preoperative albumin		
< 3.5 gm/dL	16 (100)	32 (64)
< 3.0 gm/dL	14 (87.5)	14 (28)
< 2.0 gm/dL	3 (18.8)	4 (8)
BMI < 22	14 (87.5)	37 (74)
Preoperative cholesterol < 130 mg/dL	16 (100)	20 (40)
Preoperative triglyceride < 35 mg/dL	2 (12.5)	3 (6)
Perioperative parenteral nutrition	14 (87.5)	37 (74)

**Table 3.** Nutritional parameters and support in patients with FC ( $n = 16$ ) and UC ( $n = 34$ )

	N=16		N=34		p-value
	n	%	n	%	
Preoperative albumin					< .0001
< 2.0 gm/dL	3	18.75	1	2.94	
2.0-3.0 gm/dL	11	68.75	3	8.82	
3.0-3.5 gm/dL	2	12.50	30	88.24	
BMI					0.179
< 22	14	87.50	23	67.65	
≥ 22	2	12.50	11	32.35	
Preoperative cholesterol					< .0001
< 130 mg/dL	16	100	4	11.76	
≥ 130 mg/dL	0	0	30	88.24	
Preoperative triglyceride					0.237
< 35 mg/dL	2	12.50	1	2.94	
≥ 35 mg/dL	14	87.50	33	97.06	
Perioperative parenteral nutrition					0.179
Yes	14	87.50	23	67.65	
No	2	12.50	11	32.35	

p-values were calculated by Fisher's exact test.

Probability values < 0.05 were considered statistically significant.

**Table 4.** Modified Truelove and Witt's criteria for classification of severity of ulcerative colitis<sup>5</sup>

	Mild	Moderate	Severe
Bloody stools per day	< 4	4-6	> 6
Temperature	< 37.5 °C	≤ 37.8 °C	> 37.8 °C
Pulse	< 90 bpm	≤ 90 bpm	> 90 bpm
Hemoglobin	> 11.5 gm/dL	≥ 10.5 gm/dL	< 10.5 gm/dL
CRP	Normal	≤ 30 mg/dL	> 30 mg/dL
ESR	< 20 mm/h	≤ 30 mm/h	> 30 mm/h

tinguish the term severe colitis from fulminant colitis. Since it is difficult to differentiate severe colitis from fulminant colitis, some authors like to use the term of acute severe colitis instead of FC.<sup>6</sup> If toxic megacolon occurs, patients will have dilatation of colon with diameter over 6 cm or dilatation of cecum with diameter over 9 cm together with systemic toxicity, and without presence of obstruction. Surgery is often indicated within 24~72 hrs.<sup>7</sup>

Inflammatory bowel disease (IBD) and infectious colitis are the most common cause of FC, especially in patients with ulcerative colitis and clostridium difficile (CD) colitis.<sup>3</sup> It is important to differentiate whether the patient's worsening clinical condition is exacerbation of IBD or infectious colitis. Because the immunosuppressant agents is helpful for the patients with IBD, however, they could worsen the infectious status of the patients with infectious colitis.

All the patients with UC or FC should have a complete history which includes previous medical history, recent travel and contact history. Laboratory examination may include complete blood counts, biochemistry, electrolyte, C-reactive protein, erythrocyte sedimentation rate, stool studies and CD toxin examination. A simple film of plain abdomen can be helpful for identification of mechanical or paralytic ileus as the cause of dilatation of bowel lumen. Computed tomography can give us more detailed information and help in detecting complications, so as to be more specifically in making differential diagnosis. Histologic and serologic findings are also important for the diagnosis of UC.<sup>8</sup> Literatures suggested that complete colonoscopy for patients with fulminant colitis was absolutely prohibited.<sup>3</sup> Flexible sigmoidoscopy with low pressure inflation together with biopsy was suggested in such circumstances. The endoscopic fea-

tures of UC are inflammatory change of the mucosa continuously, with involvement from rectum to proximal colon which could be ended anywhere. Disappearance of vascular pattern and haustral folds, mucosal erosion, edematous and ulcerative change with tendency of easily contact bleeding are often found. Pseudopolyps are usually seen in patients with long existing UC. Detailed endoscopic examination could offer clinician more information about the mucosal pattern, and so may further differentiate inflammatory bowel disease from pseudomembrane colitis, ischemic colitis or radiation proctitis.<sup>9</sup>

Oral aminosalicylate, including mesalazine and sulfasalazine are often used for mild to moderate cases of UC. Topical use of aminosalicylate is suggested for those with left side colitis and proctitis.

Corticosteroid is usually used in patients with moderate to severe colitis caused by ulcerative colitis as the initial treatment or the second line treatment after mesalazine failed.<sup>10,11</sup> But before initiating steroid therapy, infection caused by cytomegalovirus (CMV) and Crohn's disease must first be ruled out by rectal biopsy or toxin survey. Immunomodulators such as cyclosporine may be used if steroids is contraindicated or patient is not responding well to steroids. Intensive monitoring by multidisciplinary team, which includes surgeon and gastroenterologist, is necessary. If the first line steroid therapy failed, then cyclosporine, infliximab, adalimumab, vedolizumab or operation may be considered for patients with severe or fulminant colitis.<sup>12</sup> While cyclosporine is not safe for long-term use, azathioprine (AZA) and 6-mercaptopurin (6-MP) can be administered as an alternative choice. Infliximab (Anti-TNF agent) is usually recommended for those patients who failed AZA/6-MP treatment. Similar report also suggested to use various

biologic agents such as adalimumab and vedolizumab in the patients with moderate to severe colitis.

Surgical treatment of UC is usually the option for patients whose medical treatment failed or the side effect of medication is intolerable. Fulminant colitis, toxic megacolon, bowel perforation, massive bleeding, uncontrollable extraintestinal manifestations, possible malignant change, intractable bowel disease and growth retardation are the main surgical indications.<sup>13-15</sup> In our series, toxic colitis with or without megacolon and bowel perforation were the main surgical indications for the sixteen fulminant colitis patients (Table 5), and none of them were cancer in the final pathology report. Surgery could be curative in patients with ulcerative colitis because the affected colon and rectum can be removed completely.

Literature had showed that the risk of surgery 1, 5, and 10 years after diagnosis of ulcerative colitis was 4.9% (95% CI, 3.8%-6.3%), 11.6% (95% CI, 9.3%-14.4%), and 15.6% (95% CI, 12.5%-19.6%), respectively.<sup>16</sup> There was another one large cohort retrospective study in which a total of 561 patients were included, with a median follow-up of 21.4 years since disease onset. A total of 97 patients (17.3 percent) underwent surgery was reported.<sup>17</sup> There are different choices of operation for ulcerative colitis such as subtotal colectomy with ileorectal anastomosis, total proctocolectomy with ileostomy and restorative proctocolectomy with or without temporary ileostomy.<sup>18,19</sup>

Subtotal colectomy with ileorectal anastomosis has advantages of low morbidity and good quality of life. But infection of rectal segment may persist and subsequent colorectal cancer is always a threat. The patient who have total proctocolectomy with permanent ileostomy has no more threat of colorectal cancer with low morbidity post-operatively. However, life quality of the patient may be worse with presence of a permanent stomy.

Restorative proctocolectomy includes procedures of total colectomy, mucosal proctectomy, ileal pouch, pouch-anal anastomosis with or without temporary ileostomy. This operation will remove all colon and most of rectum, but leave the anal sphincter muscle intact. Creation of a pouch, either J-pouch, S-pouch, W-pouch or L-pouch, by suturing a few loops of small

intestine together is then performed and attached to the anal canal, as an artificial reservoir for stool collection. The advantages of the surgery are fair to good quality of life, and no more threat of developing cancer or having persistent inflammation of rectum. However, IPAA is regarded to be associated with high morbidity and it usually needs at least two stages operations.<sup>20,21</sup> Most medical centers recommend three-stage procedure in emergent circumstances. First procedure is sub-total colectomy and ileostomy. Second step is to create IPAA and defunctioning temporary ileostomy 3 to 6 months later. Final step is the closure of stomy and restoration of bowel continuity.

In the sixteen cases with fulminant colitis in our series, all patients had albumin < 3.5 mg/d before surgery. Fourteen patients had BMI < 22. Sixteen patients had preoperative cholesterol < 130 ml/dL. Fourteen patients received peri-operative parenteral nutrition. Parenteral nutrition is often needed perioperatively because of preexisting malnutrition and associated complications.<sup>22</sup> Our data suggested that malnutrition is common in the patients with ulcerative colitis who received operation. But among the subgroup of FC, some of the nutritional parameters were even worse.

Among the sixteen patients with fulminant colitis, there was only one case expired. This patient was known to have poor heart function in the past medical history. She initially visited our emergency department and was then admitted to medical intensive care unit. Emergent consultation was called for bowel perforation and then we performed colectomy with ileostomy. Unfortunately, the patient died of sepsis with multiple organ failure.

Four of our cases with fulminant ulcerative colitis underwent restorative proctocolectomy with pouch anal anastomoses and diverting ileostomies. Among the four patients, three ileostomies were not closed. Restorative proctocolectomy probably should not be

**Table 5.** Surgical indication for fulminant colitis (n = 16)

Surgical indication	Number of patients
Toxic colitis with or without megacolon	12
Bowel perforation	4

the first choice in the patients with fulminant colitis, but further prospective study is necessary for the optimal management of patients with fulminant colitis.

## Conclusion

Surgery should be reserved for complicated ulcerative colitis, especially fulminant type. Malnutrition is common in the patient with ulcerative colitis who received the operation, and some of the nutritional parameters were even worse among the subgroup of fulminant colitis. Parenteral nutrition is frequently needed perioperatively because of preexisting malnutrition and associated complications. Total colonoscopy or colon series should not be performed in the patients with acute severe colitis to avoid toxic colitis or colonic perforation. Restorative proctocolectomy is not a perfect operation, but can offer a reasonable good quality of life to the patient with ulcerative colitis.

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原 著

## 爆發性潰瘍性結腸炎的外科治療

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**目的** 潰瘍性結腸炎通常以保守治療為主，當產生併發症時往往必須採用外科治療。醫師在面對這樣病人的經驗常常有限。這篇回顧性研究分析，主要是針對爆發性潰瘍性結腸炎的手術適應症、手術方法以及術前營養指標來做分析。

**方法** 從 1983 年 12 月到 2016 年 10 月，這三十多年來共有 50 位潰瘍性結腸炎的病人接受了手術治療。手術都由同一位外科醫師執行，共計女性有 20 位，男性有 30 位，年紀從 16 到 82 歲，平均年齡為 47.3 歲。其中有 16 位病人為爆發性潰瘍性結腸炎病患，女性有 6 位，男性有 10 位。年紀從 33 到 74 歲，平均年齡為 46.7 歲。

**結果** 在 16 位爆發性潰瘍性結腸炎患者中，有 8 位接受了次全結腸切除及迴腸直腸吻合術。4 位接受了結腸切除及腸造口手術，而另外 4 位則是接受了復原性大腸直腸切除術（包括全大腸直腸、製作迴腸儲存袋、迴腸肛門吻合術、及迴腸造口分流手術）。這 16 位病人的術前白蛋白皆低於 3.5 gm/dL，而其中有 14 位病人使用了手術前後的靜脈營養補充。有 1 位病人在因腸穿孔及腹膜炎接受了結腸切除及腸造口手術後，因為敗血症而死亡。

**結論** 外科治療可用在爆發性潰瘍性結腸炎。潰瘍性結腸炎的病人常有營養不良的問題，而在爆發性的病人族群裡，一些營養指標則是顯著性的更差。復原性大腸直腸切除如果可以施行成功的話，對於病人的術後生活品質將有幫助。在猛爆性結腸炎發作的病患應該避免施行大腸鏡及下消化道攝影檢查。

**關鍵詞** 爆發性潰瘍性結腸炎、營養、外科治療、潰瘍性結腸炎。