# **Original Article**

Early Outcome of Patient with Ulcerative Colitis who Received High Dose of Steroid and Underwent Two Staged Total Proctocolectomy

## Abstract

**Background:** Ulcerative colitis (UC) is an idiopathic inflammatory disorder. Currently, the final treatment is colectomy. The aim of this study was to investigate the outcomes of proctocolectomy in patients that used a high dose of prednisolone. **Materials and Methods:** Seventy-five patients presenting for surgical management of histopathologically proven UC. All patients were offered total proctocolectomy (TPC) with ileal pouch-anal anastomosis (IPAA). Patients were divided into two groups: low dose of steroids (Group A) and high dose of steroid (Group B) consumers. Data from these patients after 2 years were reviewed and analyzed. **Results:** From total patients, 34 of them were male and 34 ones were female and seven patients underwent laparatomy. Overall incontinence rate was 8.8%; dysplasia was 22%, pouchitis was 18.9% while mortality was nil. The length of hospital stay was 6.76 days in Group A and 9.21 days in Group B (P = 0.399). Leakage was observed in nine of the patients after surgery (P = 0.589). Fecal incontinence between two groups was not statistically different (P = 0.063). **Conclusions:** Laparoscopic TPC-IPAA is feasible in patients needing surgical management of UC. Preoperative treatment with high-dose corticosteroids is associated with an increased risk of complications and reoperations.

**Keywords:** *Early outcome, ileal pouch-anal anastomosis, ileorectal anastomosis, proctocolectomy, ulcerative colitis* 

# Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease of unknown etiology with a wide spectrum of disease severity. Patients with UC are initially managed pharmacologically includes aminosalicylates, corticosteroids, purine antimetabolites, and tumor necrosis factor antagonists, used sequentially or in combination. A number of previous studies have proposed UC treatment without steroid is not possible.<sup>[1]</sup> In clinical practice, disease activity is assessed through the evaluation of symptoms and severity of colon inflammation by colonoscopy or sigmoidoscopy. Patients with chronic UC and histological evidence of acute inflammation usually showed a great risk of relapse after 12-month. In a prospective cohort study, 48.1% (33 males and 41 females), relapsed during this time and the main medication (80%) of the patients was mesalazine in Iran.<sup>[2]</sup> UC usually followed by dysplasia or cancer, and the development of Crohn's disease.<sup>[3]</sup> Young people with pancolitis have a lifetime risk

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of colorectal cancer more than 15%.[4] However, some patients with UC develop complications such as hemorrhage, perforation or near perforation, and toxic megacolon that may require emergent surgery.<sup>[1,5]</sup> Steroids have been the most important medicines of UC therapy for many years, and their efficacy for remission was established.<sup>[6,7]</sup> Steroids have many side effects in long time consumption, and it should be tapered after the acute period of disorder even it failed to remission sometimes.[8]

There are many options for surgical management of patients with UC. The gold surgical standard for UC is a total proctocolectomy (TPC) with ileal pouch-anal anastomosis (IPAA).<sup>[3,5]</sup> One of the challenges in UC therapy is the steroid dose-dependent patient, and it should be mentioned by surgeon.

Many surgeons are preferred two-stage operation (TPC with IPAA), and some surgeons recommended three-stage operation (total colectomy with ileostomy,

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then proctectomy and pouch making and in the third stage closure of ileostomy) especially for who received high dosage of steroid. Each of these approaches has some advantage and disadvantages, but the main goals of surgical treatment are to obtain good functional outcomes and improve quality of life. Our approach is two-stage operation even for a patient with high dosage of steroid that may cause higher complication in these patients.

However, there are conflicting and contradictory reports with regards to postoperative complications, hospital stay, and type of surgery for the laparoscopic approach. This manuscript focused their attention on postoperative complications including fecal incontinency, anastomotic leak, and pouchitis and compared results between who received high/low dose of prednisolone. Thus, we evaluated the preoperative risk factor of steroid consumption associated with postoperative complications in UC patients.

## **Materials and Methods**

#### **Study population**

Hospital administrative databases were retrospectively evaluated to identify adult patients ( $\geq$ 18 years) with UC undergoing surgery (laparoscopic TPC) between 2007 and 2014 at the Shahid Faghihi hospital, in Shiraz. The diagnosis of UC was established by experts using clinical, radiological, histopathological, and colonoscopy criteria. Refractory to medical management of UC, dysplasia or cancer, and acute complication forms is good reasons for colectomy. Ethics approval for the study protocol was approved by the Ethics Committee at the Shiraz University of Medical Sciences with number 8632.

Finally, a group of 75 patients with acute form of UC unresponsive to medical treatment with a frequently relapsing form of exacerbation entered this study. All the patients included in this study were given prednisolone before the operation. The patients divided into two groups based on the dose of prednisolone: Group A = low dose ( $\leq 20 \text{ mg/day}$ ) and Group B = high dose ( $\geq 20 \text{ mg/day}$ ). For treatment of UC, single dose of 40 mg daily used for moderate to severe conditions and for mild UC or tapered dose to 20 mg or lower is usual.<sup>[9]</sup> Exclusion criteria: Patients that did not receive prednisolone before surgery or whom had a history of two-stage surgery. The number of bowel movements with/without blood, fever, and other complications assessed after operations and compare between two groups.

#### Statistical analysis

The complication rates were compared with the *t*-test for the differences between the two proportions (high/low dose of prednisolone) and the differences accepted as nonsignificant at P > 0.05 using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Qualitative data were analyzed by Chi-square test.

#### **Results**

There were 75 patients who underwent surgery for UC. Finally, 68 patients entered the study after exclusion of seven patients due to laparotomy. There were 34 (50%) males and 34 (50%) females. The mean age was  $34.1 \pm 1.2$  years (range: 20–59 years). The median duration of disease before an operation was 6 years (range: 8 months to 30 years). Group A consisted of 25 patients who received prednisolone ≤20 mg/day, whereas Group B comprised 43 patients who received prednisolone >20 mg/day. There were no postoperative deaths in the surveyed group of patients. Fecal incontinence occurred in 8.8% (95% confidence interval [CI]: 2.9%-16.2%) patients and leakage reported in 13.2% (95% CI: 5.9%-22.1%) patients that these are the most frequent and severe general complication. Dysplasia was seen in 15 patients (22.1%; 95% CI: 13.2%–32.4%) and pouchitis developed in 13 patients. The differences between the investigated groups of patients were not statistically significant [Tables 1 and 2]. A bowel movement of patients was not different between two groups before surgery (P = 0.101). The duration of disease was not different between two groups (P = 0.600) and hospital stay after surgery was not different between them (P = 0.399). Data demonstrated that prednisolone with dose upper than 20 mg/day increased the risk of postoperative complications such as fecal incontinence, leakage, dysplasia, and pouchitis nonsignificantly [Table 2].

## Discussion

By increasing number of patients with acute colitis unresponsive to intense medical treatment, there is a significant group of patients operated and approximately 10% of UC patients require a colectomy within 10 years of diagnosis.<sup>[10,11]</sup>

Restorative proctocolectomy with IPAA remains the most commonly operation in the treatment of patients with acute UC refractory to medical therapy. However, IPAA carries on its own risks.<sup>[3]</sup> Steroids can impair healing of any anastomosis and decrease the ability to combat infection and keep patients in poor general condition. However, the dose of prednisolone exceeding 20 mg before the operation is an independent risk factor of anastomosis dehiscence or pouchitis.<sup>[11]</sup>

In a study, pouchitis was reported in 18.8% (95% CI: 15.7%–22.4%) of patients and in another study, pouchitis was seen with a rate of 26.8% (95% CI: 21.0%–33.5%) and even in 35.3% of patients.<sup>[3,12]</sup> In our study, it was occurred with a rate of 18.9% (95% CI: 10.8%–28.4%). Pouchitis was the most serious surgical complication in this survey and can affect functional outcomes, quality of life and might also increase risk of dysplasia in the pouch.<sup>[3]</sup> Proctocolectomy should be considered as an important treatment when dysplasia is identified by colonoscopy. On the other hand, there were some reports

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Table 1: Demographic data and early complications after operations for acute ulcerative colitis													
Groups	Gender		Age	Bowel movements per	Duration	Months of	Dose of	Hospital	Months				
	Male	Female		day before surgery	of disease	consumption	prednisolone	stay (day)	to closure				
				(95% CI)	(year)		(mg/day)						
Group A	13	12	35.76±2.43	12.24±1.86 (8.72-15.67)	6.86±1.10	44.76±8.12	9.29±0.99	6.76±0.79	2.88±0.18				
(≤20 mg prednisolone)													
Group B	21	22	33.34±1.49	16.11±1.51 (13.31-19.3)	7.58±1.06	38.79±7.22	44.03±2.30	9.21±2.38	2.93±0.19				
(>20 mg prednisolone)													
Р			0.386	0.101	0.600	0.604	< 0.001	0.399	0.867				
CI: Confidence interval	1												

Table 2: Fecal incontinence, dysplasia, leakage, and pouchitis incidence in patients												
Groups	Ge	ender	Fecal incontinence	Leakage	Dysplasia	Pouchitis						
	Male	Female										
Group A (≤20 mg prednisolone)	13	12	0	4	5	3						
Group B (>20 mg prednisolone)	21	22	6	5	10	10						
<u>P</u>	0.801		0.063	0.589	0.845	0.248						

Nil.

that showed preoperative treatment with high-dose corticosteroids was associated with an increased risk of complications such as impaired perineal wound healing and reoperations (18/26 vs. 12/28; P = 0.06).<sup>[13]</sup>

The average frequency of bowel movements per 24 h was 14.2 (range: 0-40). Fecal incontinence was reported in 8.8% of patients. We showed more sever patients before surgery, and after surgery, however, the rate of complications did not exceed the frequency of complications reported from other centers. In our study, the rate of early complications between the investigated groups of patients was not statistically significant.

TPC still remains the procedure of choice in patients with impaired anal sphincter function and high-risk of pouch failure, and it will help surgeons to provide a tailored treatment for UC patients.<sup>[10]</sup> The three-stage operation could prevent from complications that we evaluated in Group B, because of a free-drug period that patients had between procedures. Based on our results, we did not see a significant difference between two groups of patients but the rate of complication was higher in Group B, and we recommend a three staged operation for those received high dose of steroids.

# Conclusions

TPC with IPAA in the treatment of UC refractory to medical management carries its own risks including anastomotic failure and pouchitis. Our data demonstrated that prednisolone with dose upper than 20 mg/day increased the risk of postoperative complications nonsignificantly and the difference may become significant in higher population size.

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#### **Conflicts of interest**

There are no conflicts of interest.

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