



Long-term outcomes and sex differences after restorative proctocolectomy in pediatric patients with ulcerative colitis



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ABSTRACT

Background: Restorative proctocolectomy (RPC) for ulcerative colitis (UC) could result in a higher patient quality of life, avoiding frequent disease flares; however, pouch failures and pouch-related complications (PRCs) can develop.

Purpose: No cohort studies have examined pouch failure and the differences between adult and pediatric patients or the sex differences in pediatric UC. Therefore, the pouch failure rates were compared between adults and pediatric patients, and pouch failure and PRCs in pediatric UC were evaluated.

Methods: UC patients who underwent RPC between January 1987 and June 2014 at Hyogo College of Medicine were included. Patient background characteristics, PRCs, and pouch failure were reviewed.

Results: A total of 1347 adult UC patients and 90 (51 boys, 39 girls) pediatric UC patients were included in the study. The cumulative rate of pouch failure at 10 years after RPC was significantly higher in pediatric UC (9.5%) than in adult UC (2.1%; $p < 0.01$). In pediatric UC, the independent risk factors for pouch failure were pouchitis (hazard ratio (HR) 19.3) and anal fistula (HR 5.5). Although a sex difference was not seen in pouch failure, an independent risk factor for PRCs was being a girl (HR 2.5).

Conclusions: Pouch failure was more common in pediatric than in adult UC. PRCs after RPC were more common in girls in pediatric UC.

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In pediatric ulcerative colitis (UC), some patients must be treated via colectomy because of disease severity and refractoriness to therapy. Previous studies have reported that colectomy at a young age provided a higher quality of life than having to suffer frequent disease flares, long-term care, or several hospitalizations [1,2]. Although over 90% of the patients were satisfied with a pouch operation according to the results of a questionnaire survey of 30 pediatric UC patients, 7% of the patients required pouch excision [3]. In other previous reports, pouch excision and permanent ostomy after pouch surgery were performed in 4%–18% and 9%–26% of cases, respectively, during 1.9–7.2 years of postoperative follow-up [4–6]. Moreover, although it was not confirmed as an independent risk factor for pouch failure, pouchitis, which is a major pouch-related complication (PRC) after restorative proctocolectomy

(RPC), occurred at a high incidence (19%–64%) during the same period. Although the functional outcomes after pouch surgery in pediatric UC are good, similar to adults, differences in the rates of pouch failure and pouchitis between adult and pediatric UC remain unclear [3].

Furthermore, with respect to sex differences in pediatric inflammatory bowel disease, although Crohn's disease (CD) has a male preponderance, females with CD have a more severe disease, a higher prevalence of extra-intestinal manifestations (EIMs), and an increased risk of surgery [7,8]. However, Herzog et al. [9] and Lee et al. [10] previously reported that no sex differences were found among pediatric UC patients. In Japan, it was reported that the sex ratio in pediatric UC was close to 1, with no sex difference in the patients' backgrounds [11]. Additionally, no cohort studies have examined the sex differences in outcomes after pouch surgery. In this study, first, the incidence of pouch failure was thus examined and compared between adult and pediatric UC patients. Second, long-term outcomes, including pouch failure and PRCs, and the predicting factors after RPC in pediatric UC were analyzed and compared in relation to sex.

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Table 1

Patients' demographic characteristics and preoperative details.

	Overall RPC (N = 1439)			Pediatric RPC (N = 90)		
	Adult UC (N = 1347)	Pediatric UC (N = 90)	p Value, adult vs. pediatric	Boy (N = 51)	Girl (N = 39)	p Value, boy vs. girl
Age at onset of UC (years)	33.2 ± 15.3	12.8 ± 2.7	<0.01	12.9 ± 2.8	12.5 ± 2.9	0.21
Age at initial surgery (years)	41.4 ± 15.1	15.5 ± 2.2	<0.01	15.6 ± 2.4	15.7 ± 2.0	0.59
Disease duration (months)	100.4 ± 88.0	35.0 ± 28.7	<0.01	33.5 ± 33.4	40.5 ± 33.2	0.24
Extent of colitis						
Pan colitis	1074 (79.7)	84 (93.3)	0.03	50 (98.0)	34 (87.2)	0.45
Left sided colitis	262 (19.5)	6 (6.7)		1 (1.1)	5 (12.8)	
Proctitis	8 (0.6)	0 (0)		0 (0)	0 (0)	
Segmental colitis	3 (0.2)	0 (0)		0 (0)	0 (0)	
Disease severity						
Mild	256 (19.0)	15 (16.7)	0.37	8 (15.7)	7 (17.9)	0.99
Moderate	784 (58.2)	47 (52.2)		27 (52.9)	20 (51.3)	
Severe	286 (21.2)	27 (30.0)		15 (29.4)	12 (30.8)	
Fulminant	21 (1.6)	1 (1.1)		1 (2.0)	0 (0)	
Preoperative treatments						
Corticosteroid	1095 (81.3)	83 (92.2)	0.01	50 (98.0)	34 (87.2)	0.08
Total given PSL dose (mg)	13,885.8 ± 16527.5	10,380.6 ± 10176.5	0.04	11,321.5 ± 12987.5	8987.4 ± 5967.5	0.88
Preoperative PSL dose (mg/kg/day)	0.41 ± 0.38	0.91 ± 0.63	<0.01	1.05 ± 0.71	0.98 ± 0.76	0.06
Immunomodulators	352 (26.1)	37 (41.1)	<0.01	24 (47.1)	13 (33.3)	0.19
Thiopurines	302 (22.4)	31 (34.4)	<0.01	20 (39.2)	11 (28.2)	0.28
CNIs	92 (6.8)	11 (12.2)	0.05	7 (13.7)	4 (10.3)	0.86
Biologics	91 (6.8)	7 (7.8)	0.88	4 (7.8)	3 (7.7)	0.71
Surgical indication						
Massive bleeding	120 (8.9)	11 (12.2)	<0.01	7 (13.7)	4 (10.3)	0.99
Toxic mega colon	60 (4.5)	0 (0)		0 (0)	0 (0)	
Cancer/dysplasia	148 (11.0)	0 (0)		0 (0)	0 (0)	
Perforation	50 (3.7)	2 (2.2)		2 (3.9)	0 (0)	
Refractory	873 (64.8)	71 (78.9)		38 (74.5)	33 (84.6)	
Stricture	46 (3.4)	0 (0)		0 (0)	0 (0)	
EIMs	50 (3.7)	3 (3.3)		1 (2.0)	2 (5.1)	
Growth retardation	0 (0)	3 (3.3)		3 (5.9)	0 (0)	

RPC = restorative proctocolectomy, UC = ulcerative colitis, PSL = prednisolone, CNIs = calcineurin inhibitors, EIMs = extra intestinal manifestations.

Data are numbers with percentages in parentheses unless otherwise indicated. Continuous variables are given as the mean value with the standard deviation.

1. Patients and methods

1.1. Patients and data collection

Between January 1987 and June 2014, 1,439 patients with UC underwent RPC with an ileal pouch anal anastomosis (IPAA) at Hyogo College of Medicine. UC was diagnosed preoperatively by clinical and histological features and confirmed with the histological findings of resected specimens. The demographic data and surgical details, which included age at the onset of UC, age at surgery, disease behavior, the extent of colitis, preoperative treatment, indication for surgery, and surgical procedure, were reviewed. In adult UC, the incidence of pouch failure

was identified. In pediatric UC, pouch failure and PRCs after RPC were identified using clinical charts. A total of 201 of the adult patients and 10 of the pediatric patients were lost to follow-up. Therefore, the duration between complete RPC and the last visit day confirmed via clinical records was set as the time from RPC for the Kaplan–Meier or Cox regression analyses.

Pediatric patients were defined as those younger than or equal to 18 years old, and their outcomes were identified through the database that was prospectively collected from the data of the initial surgery.

All the study protocols were approved by the institutional review board at Hyogo College of Medicine, and informed consent and agreement for the use of the patient data were obtained before surgery.

Table 2

Surgical details.

	Overall RPC (N = 1437)			Pediatric RPC (N = 90)		
	Adult UC (N = 1347)	Pediatric UC (N = 90)	p Value, adult vs. pediatric	Boy (N = 51)	Girl (N = 39)	p Value (boy vs. girl)
Surgical procedure						
1-stage	272 (20.2)	1 (1.1)	<0.01	1 (2.0)	0 (0)	0.74
2-stage	767 (56.9)	53 (58.9)		32 (62.7)	21 (53.8)	
3-stage	308 (22.9)	36 (40.0)		18 (35.3)	18 (46.2)	
Type of IPAA						
Hand-sewn	1312 (97.4)	90 (100)	0.23	51 (100)	39 (100)	Not estimable
Stapled	35 (2.6)	0 (0)		0 (0)	0 (0)	
Timing of surgery						
Elective	1,065 (79.1)	64 (71.1)	0.08	35 (68.6)	29 (74.4)	0.55
Urgent/emergent	282 (20.9)	26 (28.9)		16 (31.4)	10 (25.6)	
Rate of complete RPC	1320 (98.0%)	88 (97.8)	0.81	50 (98.0)	38 (97.4)	0.6

RPC = restorative proctocolectomy, UC = ulcerative colitis, IPAA = ileal-pouch anal anastomosis.

1-stage = restorative proctocolectomy without ileostomy, 2-stage = restorative proctocolectomy with diverting ileostomy, 3-stage = total colectomy was performed as initial surgery. Complete RPC = patients whose final ostomy closure could be performed.

Data are numbers with percentages in parentheses unless otherwise indicated.

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