APS
Advances in Pediatric Surgery

Case Report

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Long-Term Outcome of Patients Undergoing Total Proctocolectomy with Ileal Pouch-Anal Anastomosis in Childhood

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ABSTRACT

Purpose: Total proctocolectomy with ileal pouch-anal anastomosis (T-IPAA) in childhood is a surgical procedure mainly applied to familial adenomatous polyposis (FAP) or ulcerative colitis (UC), but it can be applied to non-FAP/non-UC disease (NFNU). Studies regarding the role of T-IPAA who underwent the operation in childhood, especially in terms of long-term gastrointestinal function, complications, and quality of life (QOL) are limited. The aim of this study was to evaluate the characteristics of patients receiving T-IPAA and to compare their bowel function outcomes and QOL.

Methods: Patients aged ≤18 years at the time of T-IPAA were included. Their medical records were retrospectively reviewed. Krickenbeck classification, Cleveland Clinic Incontinence (CCI) score, 36-item Short-form Health Survey Questionnaire, and Gastrointestinal Quality of Life Index were used for the evaluation of bowel function and QOL. The median follow-up period was 9.8 years.

Results: Of the 25 patients, 9 had FAP, 9 had UC, and 7 had NFNU. NFNU include 3 of Hirschsprung disease, 2 of intestinal neuronal dysplasia, and 2 of imperforate anus. The median age at T-IPAA was 17.8, 14.2, and 9.3 years for FAP, UC, and NFNU, respectively (p=0.001). Bowel function was satisfactory in terms of voluntary bowel movement (VBM), soiling, and constipation. VBM and constipation were not different between the groups, but soiling was most in NFNU (100%, p=0.047). However, QOL was best in the NFNU group in surveys (p=0.034 and 0.004, respectively).

Conclusion: T-IPAA could be safely applied not only for FAP and UC but also for other diseases in selective cases, with caution.

Keywords: Ileoanal pouches; Familial adenomatous polyposis; Ulcerative colitis; Pediatrics; Hirschsprung disease

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INTRODUCTION

Total proctocolectomy with ileal pouch-anal anastomosis (T-IPAA) is a known standard operation in familial adenomatous polyposis (FAP) and ulcerative colitis (UC) [1,2]. In adult patients with UC and FAP, studies on surgical outcomes and complications after T-IPAA reported generally good bowel function and gradually increasing pouch problems with longer follow-ups [3-7].

However, data regarding the role of T-IPAA in pediatric patients, especially in terms of long-term gastrointestinal function, complications, and quality of life (QOL) are limited [8-10]. T-IPAA remains a technically demanding procedure and may be associated with morbidity which may influence long-term pouch function and QOL. In addition, studies on T-IPAA due to diseases other than FAP or UC have been rarely conducted. To our knowledge, only a few studies in the English literature have reported the results of IPAA in pediatric non-FAP/non-UC disease (NFNU) [9,11-13].

The aim of this study was to evaluate the characteristics of patients receiving T-IPAA for FAP, UC, and other diseases in childhood and to compare their bowel function outcomes and QOL.

METHODS

1. Study design

This study was performed in patients who underwent T-IPAA at age 18 or below in our tertiary hospital between June 1991 and December 2014. The study group comprised 25 patients, median age of T-IPAA was 14.1 years (range, 0.7–18.9). The underlying diseases for which T-IPAA was performed were FAP, UC, NFNU, including Hirschsprung disease (HD), intestinal neuronal dysplasia (IND), and imperforate anus (IA).

We retrospectively reviewed the medical records for the patients' age, sex, body weight, preoperative medication, operative methods, operation time, postoperative hospital stay, and postoperative complications. The median follow-up duration was 9.8 years (range, 2.1–25.9).

The current bowel function and QOL were analyzed prospectively using questionnaires and a retrospective chart review. Respondents to the questionnaires were patients aged ≥18 years and the guardians of patients aged <18 years. Of the 25 patients, 21 (88%) responded. Four patients were excluded from the evaluation because of current ostoma in 1 patient and missing questionnaire response in 3.

2. Bowel function and QOL evaluation of patient status

The Krickenbeck classification for postoperative results and the Cleveland Clinic Incontinence (CCI) score were used to evaluate bowel function. The Krickenbeck classification can evaluate voluntary bowel movement (VBM), soiling, and constipation [14]. The CCI score consists of evaluations in 5 different situations where incontinence occurs. Each type of incontinence is rated on a scale from 0 (never) to 4 (always) to yield a total score that can range from 0 to 20, with higher scores indicating higher levels of incontinence [15].

The 36-item Short-Form Health Survey Questionnaire (SF-36) and Gastrointestinal Quality of Life Index (GIQLI) were used to evaluate QOL [16,17]. Complications were classified as early (within 30 days after surgery) and late (30 days after surgery) complications.

3. Statistical analysis

Data were analyzed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were reported using median (range) for continuous variables and frequency (percent) for categorical variables. The nonparametric variance analysis was performed using the Kruskal-Wallis method, and t-tests were performed for mean comparisons. Correlations between variables were evaluated using the χ^2 test. The α level was set at <0.05 for statistical significance. This study was approved by the Institutional Review Board (IRB) of our hospital (IRB No. 1707-053-867).

RESULTS

1. Demographics and clinical course

Nine patients with FAP, 9 with UC, and 7 with NFNU were treated. The median age at the time of T-IPAA was 14.1 years, and the oldest and youngest (17.8 and 9.3 years) patients were among those who underwent FAP and NFNU, respectively (p=0.001). Ileostomy was performed in all the patients except in 2 in the FAP group and 1 in the UC group. The median operation time was the longest at NFNU (301.8 minutes) and the lowest at UC (202 minutes), but not statistically significant. The median postoperative hospital stay was 19.3 days and was longest in the UC group (24 days, p=0.049; **Table 1**). The differences in early and late complications among the 3 groups were not statistically different. In particular, pouchitis occurred in 11.1% of the FAP group and 22.2% of the UC, and did not occur in the NFNU, which was more likely to occur in the UC, but not statistically significant (**Table 2**).

2. Clinical features of the patients with NFNU

Of the patients with NFNU, 3 were diagnosed as having HD; 2, IND type B; and 2, IA with visceral neuropathy or hypoganglionosis. Operation indications were thoroughly investigated for each patient.

All HD patients were complicated cases, not just simple HD patients. One patient with rectosigmoid HD had septic shock with total colonic necrosis and had to undergo T-IPAA. The other 2 patients with HD were diagnosed as having total colonic aganglionosis and

Table 1. Demographics and operation-related data

Variables	Total	FAP	UC	NFNU	p-value
No. of patients	25 (100.0)	9 (36.0)	9 (36.0)	7 (28.0)	
Male	16 (64.0)	5 (55.6)	6 (66.7)	5 (71.4)	0.871
Age (yr)					
at diagnosis	11.6 (0.2–18.7)	16.6 (13.6–18.7)	11.1 (5.1–13.7)	5.8 (0.2–15.0)	0.001
at T-IPAA	14.1 (0.7–18.9)	17.8 (15.1–18.9)	14.2 (12.6–16.0)	9.3 (0.7–15.4)	0.001
Weight (kg) at T-IPAA	42.6 (8.0–70.1)	55.4 (36.7–67.1)	41.9 (22.5–70.1)	27.2 (8.0–43.0)	0.103
Preoperative medication	10 (40.0)	1 (11.1)	9 (100.0)	0	0.001
Laparoscopic surgery	3 (12.0)	2 (22.2)	0	1 (14.3)	0.156
IPAA anastomosis method					0.959
Hand-sewing	13 (52.0)	4 (44.4)	5 (55.6)	4 (57.1%)	0.655
Using stapler	12 (48.0)	5 (55.6)	4 (44.4)	3 (42.9)	0.712
Ileostomy formation	22 (88.0)	7 (77.8)	8 (88.9)	7 (100.0)	0.411
Operation time (min)	243 (145–415)	224 (150–390)	202 (145–340)	301.8 (155–415)	0.075
Postoperative hospital stays (day)	19.3 (7–56)	11 (7–23)	24 (10–56)	15.0 (9–46)	0.049
Follow-up (yr)	9.8 (2.1–25.9)	8.1 (2.1–17)	13.8 (6.3–25.9)	6.9 (5.4–6.8)	0.615

Values are presented as number of patients (%) or median (range).
FAP, familial adenomatous polyposis; UC, ulcerative colitis; NFNU, non-familial adenomatous polyposis/non-ulcerative colitis disease; IPAA, ileal pouch-anal anastomosis.

Table 2. Complications

Variables	Total	FAP	UC	NFNU	p-value
No. of patients	25 (100.0)	9 (36.0)	9 (36.0)	7 (28.0)	
Early	6 (24.0)	2 (22.2)	4 (44.4)	0	0.128
Fluid collection	1 (4.0)	0	1 (11.1)	0	0.435
Wound complication	1 (4.0)	0	1 (11.1)	0	0.435
Ileus	4 (16.0)	2 (22.2)	2 (22.2)	0	0.384
Internal herniation	1 (4.0)	0	1 (11.1)	0	0.411
Late	16 (64.0)	8 (88.9)	4 (44.4)	4 (57.1)	0.143
Wound complication	3 (12.0)	2 (22.2)	0	1 (14.3)	0.309
Perianal fistula	3 (12.0)	0	1 (11.1)	2 (28.6)	0.260
Rectovaginal fistula	2 (8.0)	0	2 (22.2)	0	0.435
Anal stricture	2 (8.0)	0	2 (22.2)	0	0.395
Ileus	8 (32.0)	5 (55.5)	2 (22.2)	1 (14.3)	0.105
Pouchitis	3 (12.0)	1 (11.1)	2 (22.2)	0	0.175

Values are presented as number of patients (%).
FAP; familial adenomatous polyposis, UC; ulcerative colitis; NFNU, non-familial adenomatous polyposis/non-ulcerative colitis disease.

Table 3. Evaluation of bowel functions by applying scoring methods

Variables	Total	FAP	UC	NFNU	p-value
No. of patients	21 (100.0)	8 (38.1)	7 (33.3)	6 (28.6)	
Krickenbeck continence score					
Voluntary bowel movement	20 (95.2)	7 (87.5)	7 (100.0)	6 (100.0)	0.287
Soiling (no)	10 (47.6)	5 (62.5)	5 (71.4)	0	0.047
Grade 1	8 (38.1)	3 (37.5)	1 (14.3)	4 (66.7)	0.394
Grade 2	1 (4.8)	0	0	1 (16.7)	0.287
Grade 3	2 (9.5)	0	1 (14.3)	1 (16.7)	0.287
Constipation (no)	1 (4.8)	0	1 (14.3)	0	0.368
Grade 1	18 (85.7)	7 (87.5)	6 (85.7)	5 (83.3)	0.977
Grade 2	2 (9.5)	1 (12.5)	0	1 (16.7)	0.572
Grade 3	0	0	0	0	1.00
CCI score	4.2	3.9	2.3	5.2	0.409

FAP, familial adenomatous polyposis; UC, ulcerative colitis; NFNU, non-familial adenomatous polyposis/non-ulcerative colitis disease; CCI, Cleveland Clinic Incontinence.

initially underwent Duhamel operation. After performing initial anastomosis in both patients, it was observed that the small bowel mesentery had torsion and was caught in the anastomosis line; therefore, pouch formation had to be conducted. The remaining 4 patients had persistent colonic dilatation and fecal incontinence before undergoing T-IPAA. In the final review, the diagnosis was IND type B in 2 patients, IA with visceral neuropathy of the colon in 1, and IA with hypoganglionosis with immature ganglion cells in 1. Owing to the difficulties in the diagnosis of IND, visceral neuropathy, and hypoganglionosis or "variant HD" [18], these patients underwent a median of 4 operations (range, 1–9) before performing T-IPAA (**Table 3**).

3. Bowel function outcomes

The questionnaires were administered to 8, 7, and 6 patients in the FAP, UC, and NFNU groups, respectively. In the Krickenbeck classification, VBM was observed in 20 of 21 patients, and differences among the groups were not significant. Fecal soiling was observed in 11 of 21 patients and was most frequent in the NFNU group (100%, p=0.047). Eight out of 11 patients with soiling were grade 1 (which happens occasionally). Two patients with soiling grade 3 (which is consistent) were in the FAP and NFNU groups. Twenty of the 21 patients had constipation, but 18 of them were grade 1, which was manageable by diet modification. The degree of incontinence evaluated on the basis of CCI scores was not significantly different among the groups (all <7), which means "good continence" (**Table 4**).

Table 4. Clinical features of NFNU patients

Case	Sex	Diagnosis	At IPAA operation		Cause of total proctocolectomy with IPAA	No. of operations before IPAA
			Age (yr)	Weight (kg)		
1	M	Hirschsprung's disease (RSA)	13	29.8	Septic shock with total colonic necrosis	3
2	M	Intestinal neuronal dysplasia, type B	12.7	36.9	Persistent colonic dilatation and fecal incontinence	7
3	M	Hirschsprung's disease (TCA)	3.66	13.9	Duhamel anastomosis failure	3
4	M	Hirschsprung's disease (TCA)	0.72	8	Duhamel anastomosis failure	1
5	F	Intestinal neuronal dysplasia, type B	13.7	40	Persistent colonic dilatation and fecal incontinence	9
6	M	IA (RUF), Visceral neuropathy	15.4	43	Persistent colonic dilatation and fecal incontinence	4
7	F	IA (RVF), Hypoganglinosis with immature ganglion cell	6.5	18.6	Persistent colonic dilatation and fecal incontinence	4

NFNU, non-familial adenomatous polyposis/non-ulcerative colitis disease; IPAA, ileal pouch anal anastomosis; RSA, rectosigmoid aganglinosis; TCA, total colonic aganglionosis; IA, imperforate anus; RUF, recto-urethral fistula; RVF, recto-vaginal fistula.

**Table 5.** Evaluation of quality of life by applying scoring system

Variables	Total	FAP	UC	NFNU	p-value
SF-36	75 (61–92)	74 (61–92)	62 (52–82)	78 (68–87)	0.034
GIQLI	116 (73–133)	111 (91–125)	89 (73–122)	125 (113–133)	0.004

Values are presented as median (range).
FAP, familial adenomatous polyposis; UC, ulcerative colitis; NFNU, non-familial adenomatous polyposis/non-ulcerative colitis disease; SF-36, Short-Form 36 Health Survey Questionnaire; GIQLI, Gastrointestinal Quality of Life Index.

4. QOL

For analysis of QOL, the median SF-36 and GIQLI scores were 75 (range, 61–92) and 116 (range, 73–133), respectively, and showed significant differences among the groups. The best results were found in the NFNU group; and the worst results in the UC group (p=0.034 and 0.004, respectively; **Table 5**). In the subgroup analysis of the SF-36 scores, 3 items of physical and emotional role functioning and general health perceptions showed differences between the groups. For these items, the NFNU and UC groups showed the best and worst results, respectively. In the GIQLI survey, the categories of gastrointestinal symptoms, physical function, and emotional function showed significant differences, and the NFNU group showed the best results (**Fig. 1**).
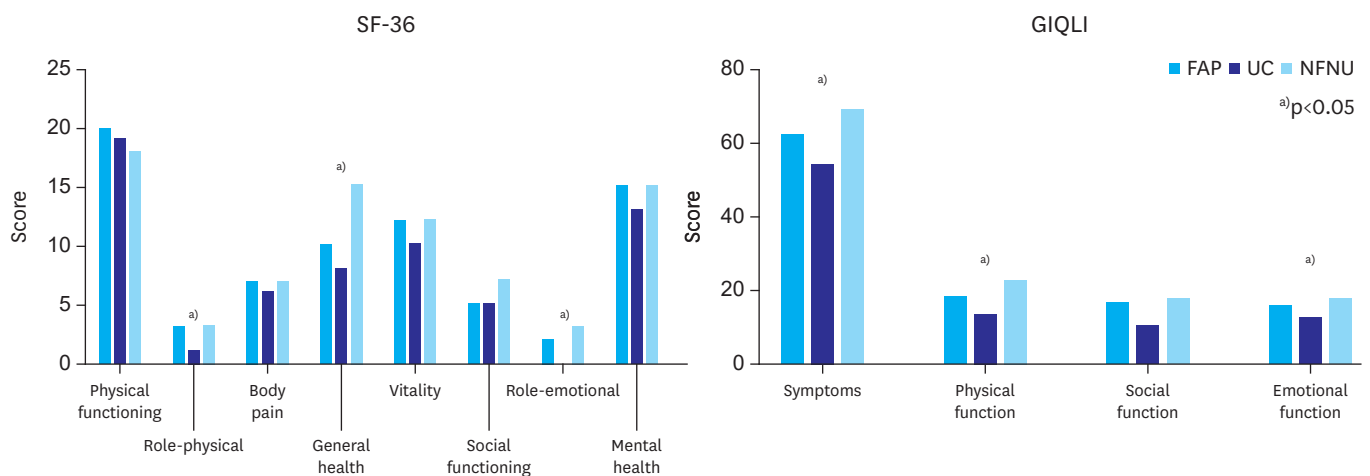
Fig. 1. Detailed results of quality of life evaluation by questionnaires.
SF-36, Short-Form 36 Health Survey Questionnaire; GIQLI, Gastrointestinal Quality of Life Index; FAP, familial adenomatous polyposis; UC, ulcerative colitis; NFNU, non-familial adenomatous polyposis/non-ulcerative colitis disease.

DISCUSSION

IPAA, first described by Parks and Nicholls in 1978 [19], has been the surgical approach of choice in medically refractory mucosal UC, indeterminate colitis, and FAP in adult patients. However, for pediatric patients, straight pull-through was considered to be superior to pouch formation in terms of reducing the risk of pouchitis, until the mid-1990s [20]. Since the publication of favorable outcomes of IPAA in pediatric patients with UC and FAP, IPAA has also been the standard method of operation in children [21,22].

In terms of surgical indications, pediatric patients with UC undergo surgical corrections for medically uncontrolled status, severe bleeding, obstruction, cancer risk, perforation, and side effects of chronic medical therapy. In children with FAP, operation is indicated to reduce the life-long risk of developing cancer. Pediatric patients who undergo T-IPAA for FAP and UC are usually in their mid to late teens [9].

The studies on pediatric patients with FAP and UC have reported postoperative outcomes, including complications. Fonkalsrud [11] evaluated 116 pediatric patients who underwent T-IPAA and found that complications occurred in 41% of the patients, of which 15.5% had pouchitis, which occurred only in the patients with UC. This study followed up the patients for a mean of 7.1 years, and 92.2% of the patients reported good progress. In another recent report, 41 patients aged 2 to 17 years who had inflammatory bowel disease and FAP underwent IPAA, of which 9 (21.9%) developed pouchitis and 3 (7.3%) had pouch failure during 22 months of follow-up [23]. In a recent systematic review article on T-IPAA in childhood, the incidence of chronic pouchitis was reported to be 13.2% [24]. In the study of adults, the incidence of pouchitis was known to range from 7% to 46% [25]. In this present study, pouchitis occurred in 12% of patients during median 9.8 years of follow-up.

T-IPAA has been performed rarely in pediatric patients with diseases other than FAP or UC. A study reported the results of restorative proctocolectomy with J-pouch ileoanal anastomosis applied in 8 newborn infants with total colonic aganglionosis. In this study, IPAA was performed at a median age of 1.1 months. For the short-term bowel function outcome evaluated at a median age of 3.2 years, the overall satisfaction with the operative results was high [12]. Rintala and Lindahl [13] reported the results of T-IPAA in 10 patients with HD who underwent T-IPAA at a median age of 1.5 years. No pouchitis-like symptoms occurred during the 3-year follow-up period, and 3 patients had episodes of postoperative enterocolitis. In addition, all the patients aged >3 years were reported to be continent.

In our study, T-IPAA was applied in 25 pediatric patients between June 1991 and December 2014, and their underlying diseases were UC, FAP, HD, IND, and IA. For UC and FAP, T-IPAA is a standard procedure for surgical treatment, and our center followed the indications such as medically intractable status or increased risk of malignancy for treating the patients. For patients with NFNU, the operation indications were investigated for each patient thoroughly, and T-IPAA was performed because bowel continuity could not be maintained with the colon for various reasons.

Bowel function after total T-IPAA was satisfactory because VBM was identified in 20 of 21 patients, of which 18 had no soiling or grade 1 soiling, and 90.5% had no constipation or showed improvement with diet modification. CCI score also showed good continence. The significantly more frequent occurrence of soiling in the NFNU group may have been due to

multiple prior operations that caused injuries in the perianal area and could be the reason for the highest rate of fecal soiling in the group.

QOL analysis revealed the best score in the NFNU group, contrary to the bowel function outcomes. This could imply that patients with NFNU with prior co-morbidities that persisted before the IPAA procedure may have enhanced the satisfaction after T-IPAA, as seen in the history of these patients with NFNU.

The UC group showed worst QOL in our study. This result could be explained by many reasons, one of which is the use of medications for treating underlying diseases. A research study that included patients with UC and FAP with IPAA for a long-term follow-up of 10 years reported that long-term steroid used before surgery in patients with UC prolonged the time to normalize bowel function [26]. In our study, the UC group used more preoperative steroids than the FAP or NFNU group. This may have also influenced the poor QOL scores of the patients in the UC group.

The limitations of our study include its retrospective nature and small study population, and the recall bias during the collection of information through the questionnaire survey.

T-IPAA was mainly applied for FAP or UC, but could also be performed when the colon could not be used for anastomosis for various reasons in children. Postoperative bowel function was satisfactory in terms of VBM, soiling, and constipation, but fecal soiling was more frequently observed in the patients with NFNU, possibly because of multiple operations before T-IPAA. When the QOL was surveyed, the NFNU group showed the best results and UC group showed the worst results, contrary to the bowel function outcomes. Therefore, T-IPAA could be safely applied not only for FAP and UC, but also for other diseases such as HD, IND, or IA in selective cases, with caution.

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