



Long-term Follow-up of Patients with Hirschsprung Disease: Unusual Late Complications After Pull-through

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Abstract

Background: A large number of patients who undergo pull-through surgery due to Hirschsprung disease (HD) are not surveilled properly postoperatively and suffer from various complications such as fecal soiling, constipation, etc. Although some of these complications may resolve over time, it is rational to consider an evaluative protocol to identify anatomical or pathological complications in these patients. The present study aimed to evaluate and introduce the long-term postoperative complications of patients with HD.

Methods: In this historical cohort study, 193 patients with HD who had undergone pull-through surgery between 2006 to 2013 were considered. All files and questionnaires were used to collect patients' information. The patients were also physically examined. The mean length of follow-up was 96.4±17.2 months, ranging from 60 to 144 months. Follow-up was performed for all children through outpatient clinics or by phone. All statistical information was analyzed by SPSS software version 17.

Results: At first presentation, intestinal obstruction was more frequent than constipation. The most commonly involved segment was the rectosigmoid. The predominant early postoperative complication was stricture in the anal canal, while the most common late complications were constipation and fecal soiling.

Conclusion: The present longstanding follow-up study revealed anal stricture, enterocolitis, constipation, and fecal soiling to be the predominant long-term complications of HD following pull-through surgery. Physicians should be aware of these issues and an appropriate long-term follow-up protocol should be devised. Further studies assessing the long-term psychosocial complications of patients treated for HD seem warranted.

Keywords: Constipation, Enterocolitis, Fecal soiling, Hirschsprung disease, Incontinence, Pull-through surgery

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Introduction

Hirschsprung disease (HD) refers to a lack of ganglion cells in the terminal segments of the

colon and represents a smooth muscle relaxation disorder that causes functional obstruction. Its estimated incidence is 1 in 5000 live births (1, 2). The most common neonatal symptoms are abdominal

distention, delayed meconium passage, and in some cases biliary vomiting. Neonatal meconium defecation should be in the first 48 hours; otherwise, the neonate should be evaluated for HD. Classically, diagnosis is based on a lack of ganglion cells in the specimen obtained via rectal biopsy.

To date, various surgical procedures have been introduced as definite treatments of HD; these surgical approaches share the common purpose of dissecting the distal aganglionic bowel segment (3-5). Despite the advancements in surgical procedures, inadvertent injuries to adjacent organs and their innervation may lead to long-term complications. Among these procedures, endorectal pull-through techniques under direct vision may carry less risk than other techniques (6-8). However, recent studies demonstrate that still, a large number of patients who undergo pull-through surgery due to HD suffer from complications such as fecal soiling, constipation, frequent enterocolitis, failure to thrive, and urinary problems (9).

Although some of the long-term complications may improve over time, it is rational to consider an evaluative protocol to identify anatomical or pathological complications in these patients. The present study evaluates and follows-up on the long-term complications of patients with HD treated with the pull-through operation, clarifying the gradual changes in these complications.

Materials and Methods

In this historical cohort study, we considered 193 HD patients who had been managed with the pull-through procedure between 2006 and 2013 in our center. Roughly 230 patients were operated on during the mentioned period but only 193 patients accepted to be re-visited, with the remaining rejecting our invitation or not being available to contact.

According to our inclusion criteria, the study participants were children who had undergone the pull-through operation for HD between 2006 and 2013 in our surgery center, had accessible patient files, and accepted our invitation to participate in the long-standing follow-up. Patients with missing data on the type of operation, length of postoperative hospitalization, and the incidence of early complications after surgery (incontinence/soiling, constipation, and enterocolitis) were excluded, together with those with missing or incorrect phone numbers and those who did not wish to participate for examination.

Outcome Parameters

The mean length of the follow-up was 96.4 ± 17.2 months, ranging from 60 to 144 months. Follow-up was done at three and six months, then yearly after surgery. The follow-ups were performed for all patients via outpatient clinics or by telephone.

Data collected from medical records of the children

integrated essential demographics, age at the time of surgery, pathological category, kind of surgery, duration of hospital stay, bowel function, short- and long-term complications, medical history, examination results, preparation before surgery, and operative information. Cases were followed-up for at least three months after the procedure. Informed consent was gained from the parents of the children at the long-term follow-ups. The late complications, stool quality, and control of stool during day and night were recorded during the follow-up.

Statistical Analysis

We used files and detailed questionnaires to collect information and each patient was physically examined. All collected information was analyzed by SPSS software version 17. Discrete variables were reported as numbers and percentages. All continuous variables were provided as mean and standard deviation. Patient demographics, preoperative information, operation details, and early complications after surgery were expressed as mean/standard deviation or median/range.

Results

Among our patients, 147 were male (76.2%) and 46 were female (23.3%). At the time of the pull-through procedure, the mean age of the patients was 20.65 ± 5.6 months (7 days – 54 months); 29% were less than one month of age. The mean hospital stay was 16.18 ± 11.2 days (5-42 days) after surgery.

In total, 109 patients had an acute presentation (obstruction), while 78 had a chronic presentation (constipation). The most common manifestations were abdominal distention with delayed meconium passage, while failure to thrive was least common. Only 16 patients (8%) had associated anomalies, the most common of which was trisomy 21 (9 patients). The most commonly involved segment was the rectosigmoid segment, with the predominant type of repair being the transanal repair performed through a single stage. Only 30 patients had a proximal ostomy. The mean duration of surgery was 139.84 ± 66.2 minutes. Five patients had a rectal biopsy and pull-through operation at the same time. In 166 patients (86%), the results of the frozen section and permanent biopsies were similar. The baseline patient characteristics and clinical information are summarized in Table 1.

In Table 2, the early (about one month after surgery) and late repair-induced complications are summarized. About one month after the pull-through operation, 15 patients (7%) had anal canal stricture and required anal dilation; 11 patients (5%) had enterocolitis, which responded to conservative management; 7 patients (3%) had constipation. In the evaluation of the condition at the time of discharge after the initial surgery, 190 patients were in good condition (98.4%) but 3 patients had expired (1.6%).

Table 1: Baseline patient characteristics and clinical information

Characteristic (n=193)	Value
Sex	
Male	76%
Female	24%
Mean age at the time of operation (months)	20.65±5.6 months (7 days - 54 months)
Mean duration of hospital stay (days)	16.18±11.2 days (5-42 days)
First presentation	
Acute (obstruction)	58.3%
Chronic (constipation)	41.7%
Delayed meconium passage	44%
Positive family history	1%
Associated anomalies	8%
Length of segment	
Rectosigmoid	75%
Transverse colon	10%
Ultrashort	6%
Descending colon	5%
Total colonic	5%
Type of repair	
Transanal	43%
Swenson	32%
Soave	17%
Duhamel	3%
State	3%
Myectomy	2%
Stages of repair	
Single-stage repair	48%
Two-stage repair	38%
Three-stage repair	14%
Mean duration of surgery (mins)	139.84±66.2
Frozen section accuracy	86%

Other early complications included anastomotic leaks in two patients (1%), pelvic abscess formation in 2 patients (1%), wound infection in 5 cases (2%), urinary retention in 2 cases (2%), perianal fistula formation in one patient (0.5%), and obstruction following adhesion band development in 3 cases (1.5%).

The mean duration of the follow-up was 96.4±17.2 months, ranging from 60 to 144 months after surgery. In the late postoperative complications (Table 2), 18 patients experienced enterocolitis once, 5 patients twice, and 3 patients thrice. For enterocolitis, only 3 patients required a colostomy and the others responded to conservative treatment.

For rectoanal stricture management, 17 patients underwent an anal dilation program with parental cooperation, 7 underwent v-y anoplasty surgery, 5 had a repeated pull-through operation, and 5 underwent bougie dilation under general anesthesia.

A perianal fistula was reported in 4 patients; Seton was used for 2 patients and 2 underwent colostomy operation. A massive perianal abscess was reported in 4 patients, who were managed by colostomy surgery. Neurogenic bladder was reported in 2 patients.

At the time of the final follow-up, 35 patients (18.5%) reported constipation (Table 3), nine of which were manageable by diet changes. On the other hand, 53 patients (28%) experienced transient fecal soiling (Table 3), with almost a third of these patients having social problems due to this complication. To manage fecal soiling, four patients underwent the Malone procedure, while the rest were given conservative treatment.

Table 2: Early and late postoperative complications after pull-through surgery for Hirschsprung disease

Postoperative complication	Type	Frequency	
Early (total patients=193)	Early stricture	15 (7%)	
	Enterocolitis	11 (5%)	
	Constipation	7 (3%)	
	Expired	3 (1.5%)	
	Pelvic abscess formation	2 (1%)	
	Wound infection	5 (2%)	
	Urinary retention	2 (1%)	
	Peri anal fistula	1 (0.5%)	
	Obstruction (adhesion band)	3 (1.5%)	
	Fecal peritonitis	2 (1%)	
	Late (total patients=190)	Retained anastomosis aganglionic segment	2 (1%)
		Anal stricture	34 (17%)
		Transient fecal soiling	53 (27%)
Enterocolitis		26 (13%)	
-Once		18	
-Twice		5	
-Thrice		3	
Constipation		35 (18.5%)	
Massive perianal abscess		4 (2%)	
Perianal fistula		4 (2%)	
Rectovesical fistula		1 (0.5%)	
Abscess & fistula to sacrum		2 (1%)	
Suprapubic enterocutaneous fistula		1 (0.5%)	
Neurogenic bladder		3 (1.5%)	
Expired	2 (1%)		

Table 3: Grades of constipation and fecal soiling as late complications after pull-through surgery for Hirschsprung disease

	Frequency	Percent
Constipation (35 patients)		
Grade I: manageable by diet changes	9	5%
Grade 2: required laxatives	14	7.2%
Grade 3: opposed to diet changes and laxatives	12	6.2%
Total	35	18.4%
Fecal soiling (53 patients)		
Grade 1: once or twice per week	19	10%
Grade 2: every day, no social problems	17	9%
Grade 3: constant, social problems	17	9%
Total	53	28%

Discussion

In this cross-sectional study, we considered 193 patients with HD who had undergone pull-through surgery. General complications following the pull-through operation consist of enterocolitis, anastomotic site stricture, constipation, retained aganglionic segment, and fecal incontinence. Fistula formation between the rectum and skin, urethra, or vagina are observed in some cases. In our study, we faced late fistula formation that was quite challenging in some cases. In fact, the fistulae could not be resolved in five cases:

Case 1: A 10-year-old male with huge late enterocutaneous fistula in the gluteal region. He presented with total colonic aganglionic HD and underwent the State procedure when he was 10 months old. At the age of 2.5 years, a mild anastomotic stricture was found and was resolved by anal beguinage. The boy presented with one attack of mild enterocolitis at the age of 3 years, which responded to conservative treatment. He later presented with a massive gluteal abscess, which transformed into an enterocutaneous fistula after drainage. Hence, a diverting colostomy was established. The fistula was complex and had multiple branches, making it resistant to several attempts of seton placement.

Case 2: A 15-year-old male with a delayed massive gluteal abscess that transformed into an enterocutaneous fistula. The patient had a history of the Soave pull-through operation when he was 5 years old following ultra-short HD. After surgery, he had fecal soiling and underwent the Malone procedure at the age of 11 years. He had no anastomotic stricture and complained of fecal soiling. At this time, he underwent a diverting colostomy operation.

Case 3: An 8.5-year-old male with a massive suprapubic enterocutaneous fistula following a history of the Swenson procedure during infancy. He presented with the fistula 2 years ago; the fistula was repaired but recurred following colostomy closure. Colostomy was established for him again, and a repeat pull-through was performed six months later.

Case 4: A 9-year-old male who presented with a colovesical fistula following a history of the transanal pull-through operation when he was 23 days old. Because of mild anastomotic stricture, he

was under the beguinage program. However, at the age of 19 months, he presented with a colovesical fistula and underwent vesicostomy and colostomy insertion. The fistula was successfully repaired but recurred one year later, at which time the patient underwent a reoperation via the posterior sagittal transsphincteric approach.

Case 5: This case was similar to the previous cases; the patient was diagnosed with recalcitrant sacral and perianal enterocutaneous fistulae and expired despite several operations.

Marwa Khalil (1) evaluated the health-related quality of life of 53 patients after pull-through surgery using PedsQL 4.0. Interestingly, the physical function score decreased to 87.3 by overflow incontinence, while the social function score decreased to 92.3 by failure to thrive and incontinence. The emotional function score was 92.5. The overall quality of life was good with no impairment.

Unlike gender, age at the time of operation had a significant effect on the quality of life. The study of Zimmer and Tomuschat in 2016 (3) showed that nearly 15% of patients with HD and history of the transanal pull-through operation experienced constipation as a major problem. The authors suggested that long-term studies should be performed on patients operated with this technique to evaluate their defecation and urination patterns and sexual function as well as the quality of life during adolescence.

Jarvi et al. (10) and Heikkinen separately evaluated bowel function quality among 92 adults who had been operated on for HD during infancy; rectosigmoid involvement was reported in 94% of cases (11, 12). The researchers reported that bowel function gets worse with rising age after pull-through, but is coupled with minimal change in the quality of life.

In our study, 11 patients had early enterocolitis that responded to conservative management. In the long-term follow-up of about 8.5 years, 18 patients experienced late enterocolitis once, five patients twice, and 2 patients thrice. For late enterocolitis, only 3 patients underwent colostomy; the other patients responded to conservative treatment.

Yang, L et al. (13) performed the transanal endorectal pull-through for 137 patients with HD and evaluated the long-term outcome. In all cases, the aganglionic segment was in the distal colon. The

mean age at the operation time was 165±74 days. The mean postoperative hospital stay was 7±2 days. Early complications after the procedure were perianal excoriation (27.7%), enterocolitis (1.4%), and anastomotic leaks (1.4%). Late complications included perianal excoriation (11.7%), anal stricture (1.4%), constipation (2.8%), enterocolitis (7.3%), and soiling (4.4%). The mean follow-up of the study was about 56 months. In children more than 4 years of age, 85.4% reported high-quality bowel function, 9.4% had fair bowel function, and 5.2% had terrible bowel function.

In our study, 35 patients experienced constipation in the long-term follow-up; this complication was resistant to diet changes and laxatives in 12 cases. Furthermore, 53 patients experienced fecal soiling, with almost a third of them having social problems due to this complication; 4 patients required the Malone procedure. In a similar study, Neuvonen et al. (5) followed-up on 57 patients with HD who had undergone the transanal endorectal pull-through procedure. Interestingly, 42% (24/57) experienced more than one episode of enterocolitis, and 21% (24/57) experienced more than four episodes of enterocolitis after definitive surgery. No significant association was noted between enterocolitis and bowel function impairment as 75% of the patients were socially continent. The researchers reported that 25 patients experienced staining for less than once a week and 14 experienced frequent fecal soiling that required underwear change, but no one experienced daily fecal soiling. Up to adulthood, impaired fecal control was reported but 75% had no problem with social activity. They reported that fecal soiling and rectal sensation improved over time in most of the patients.

In the study of Catto-Smith on 84 patients who had undergone the Soave operation due to HD, constipation and fecal incontinence presented in 36% and 17% of patients, respectively, exerting a significant effect on social activity and quality of life (14). Aworanti and McDowell (9), in 2016, showed that after pull-through surgery, continence improves over time but constipation may persist as an ongoing problem. The study of Rintala and Pakarinen (14) in Helsinki University showed that complications such as fecal soiling, constipation, and psychosocial

difficulties are common late sequela and may pass on to adulthood. They stated that patients may be at an increased risk of further complications (e.g., cancer), so an appropriate long-term follow-up protocol should be considered. In the long-standing outcomes of 156 patients with HD, medullary thyroid cancer was reported in two patients and rectum adenocarcinoma occurred in one patient. In this follow-up study, most patients reported gradual improvements in complications like fecal soiling and constipation, especially during adolescence (15, 16).

We suggest more studies to have a more definitive judgment about the improvement of complications over time, together with a detailed evaluation of the psychosocial problems. The current study, when combined with the related literature, may facilitate the early diagnosis and treatment of some long-term complications such as constipation and fecal soiling, though further studies are required to evaluate other long-term and irreversible complications such as sexual disorders and psychosocial problems.

Conclusion

The present longstanding follow-up study revealed anal stricture, enterocolitis, constipation, and fecal soiling to be the predominant long-term complications of HD following pull-through surgery. Physicians should be aware of these issues and an appropriate long-term follow-up protocol should be devised. Further studies assessing the long-term psychosocial complications of patients treated for HD seem warranted.

Ethical Approval: All operations were carried out in agreement with the ethical standards of the Ethics Committee of the Faculty of Medicine of Shahid Beheshti University of Medical Sciences (Approval Code: IR.SBMU.MSP.REC.1398.607).

Informed consent: Informed consent was obtained from all participants.

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Conflicts of interests: None declared.

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