Available online at www.sciencedirect.com

ScienceDirect

Journal of the Chinese Medical Association 77 (2014) 519–523

www.jcma-online.com

Original Article

Surgical outcomes of total colonic aganglionosis in children: A 26-year experience in a single institute

Yi-Ting Yeh [a], Hsin-Lin Tsai [a], Cheng-Yen Chen [b], Jen-Bin Wang [c], Tai-Wai Chin [a], Chou-Fu Wei [a,d], Chin-Su Liu [a,b,*]

[a] *Division of Pediatric Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[b] *Division of Transplant Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[c] *Department of Surgery, Taipei Veterans General Hospital Taoyuan Branch, Taoyuan, Taiwan, ROC*
[d] *Department of Surgery, Taipei Medical University Hospital, Taipei, Taiwan, ROC*

Received October 14, 2013; accepted May 26, 2014

Abstract

Background: There is a lack of consensus regarding the treatment of total colonic aganglionosis (TCA) with respect to perioperative morbidity, mortality, complications, and functional outcomes. The aim of this study was to review the results of surgical TCA treatment over a 26-year period and characterize the outcomes.
Methods: We retrospectively reviewed the clinical characteristics, surgical courses, and outcomes of TCA patients who underwent definitive pull-through operations from 1986 to 2012. Follow-up data were collected by chart reviews and telephone interviews using a standardized questionnaire.
Results: We identified nine infants with TCA (8.6%) from among 105 infants with Hirschsprung's disease treated during the 26-year period. Neither sex predominated (male/female ratio = 4:5). All infants underwent laparotomies and simultaneous enterostomies. All patients eventually underwent modified Duhamel pull-through procedures at a mean age of 179 days (range, 47–352 days). Two infants died of complications after surgery including heart failure and sepsis. The remaining infants recovered smoothly with antilaxative medications, and all but one was weaned off these medications. Although the surviving patients did not catch up on growth, they and their families were satisfied with the surgical results.
Conclusion: Infants with TCA had satisfactory outcomes after the modified Duhamel pull-through operation. Based on our experience, we suggest that the pull-through operation could be performed earlier, even when there are loose stools from the enterostomy.

Keywords: child; fecal incontinence; Hirschsprung disease; retrospective study; total colonic aganglionosis

1. Introduction

Hirschsprung's disease is an embryonic developmental disorder characterized by the absence of ganglion cells in the lower enteric complex. The disease may associate with chromosomal anomalies, monogenic syndromes, or other congenital anomalies, such as trisomy 21, congenital central hypoventilation syndrome,[1] congenital heart disease, or urinary tract anomalies. Sporadic disease is sometimes associated with *RET* gene mutations.[2] Total colonic aganglionosis (TCA) is a rare and severe phenotype of Hirschsprung's disease occurring in about 2–13% of cases.[3] This form of disease is characterized by the absence of ganglion cells in the entire colon extending into the terminal ileum, and carries higher morbidity and mortality rates than does the short-segment

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Chin-Su Liu, Divisions of Transplantation Surgery and Pediatric Surgery, Department of Surgery, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: csliu@vghtpe.gov.tw (C.-S. Liu).

http://dx.doi.org/10.1016/j.jcma.2014.05.012

form of Hirschsprung's disease.[4] Various procedures are proposed for the surgical management of TCA. However, there is no consensus as to which method is the best, with respect to perioperative morbidity, mortality, complications, and functional outcomes, as described in a recent systematic review.[5−7] The aim of our study was to review the TCA cases treated in our institution over the past 26 years, with emphasis on the experience of early pull-through and analysis of functional outcome.

2. Methods

We retrospectively analyzed the medical records of nine consecutive patients with TCA who were treated in a tertiary referral center from 1986 to 2012. There were 105 patients with surgically treated Hirschsprung's disease in our hospital during this period. Data were analyzed for sex, clinical presentation, family history of Hirschsprung's disease and associated anomalies, weight at the definitive operation, surgical management, and pre- and postoperative complications.

Informed consent was obtained from the patient or their parents. Follow-up data were collected by telephone interviews using a standardized questionnaire previously described in the literature[8] regarding growth development, stool frequency, stool consistency, fecal soiling, incontinence, and enterocolitis. A scoring system was used for the assessment of objective functional outcomes (Table 1).[8] Enterocolitis was defined as the presence of abdominal distention, diarrhea, vomiting, and fever. Additionally, the most common complication of the pull-through operation was diarrhea, with or without perineal excoriation and enterocolitis.[9,10]

3. Results

Among the nine patients with TCA, there were four males and five females (Table 2). Four patients presented with symptoms in the neonatal period (within 28 days after birth) with features of intestinal obstruction. Four of the five remaining patients presented later in infancy (<1 year) and had previous surgeries performed at other hospitals (2 ileostomies, 1 ileostomy with a Kimura patch, and 1 misplaced sigmoid colostomy). The initial presentations of the five referred patients were intestinal obstruction in four patients and toxic megacolon with perforation in the other patient.

Table 1
Telephone questionnaire regarding functional outcome of patients with TCA.[a]

Follow-up questionnaire	Score = 2	Score = 1	Score = 0
Recurrent abdominal distension	None	Mild	Severe
Frequency of defecation	1−2/d	3−5/d	>5/d
Stool consistency	Normal	Loose	Liquid
Soiling	None	Occasionally	Permanently
Urgency period[b]	Normal	Short	Absent
Diapers required[b]	None	Occasionally	Permanently
Long-term use of medication[b]	None	Antibiotics	Antidiarrheal
Diet	Normal	Restricted	TPN
Range of scores	11−16	6−10	0−5
Objective functional outcome	Good	Fair	Poor

TCA = total colonic aganglionosis; TPN = total parenteral nutrition.
[a] See Wildhaber et al.[8]
[b] If age >3 years.

Two girls had a family history (a sibling and a father) of Hirschsprung's disease, and another boy was born of consanguineous parents. Associated anomalies were hypoplastic right heart syndrome in one patient, imperforate anus in one patient, and a complex case of urogenital sinus, vaginal atresia, and Pallister−Hall syndrome in another patient.

Eight patients (i.e., all except the girl with the misplaced sigmoid colostomy) had leveling enterostomy performed with a view to future definitive pull-through operations. All patients eventually underwent the modified Duhamel pull-through operation. We delivered the ganglionated bowel through an incision in the posterior aspect of the native aganglionated rectum. The common wall between the ganglionated pull-through colon and the aganglionated native rectum was then divided using an endo-GIA linear stapler.

The mean patient age at the definitive pull-through operation was 179 days (range, 47−352 days). The mean body weight at the definite operation was 5137 g (range, 2810−7600 g). The average interval between initial ileostomy and definitive pull-through surgery was 5.1 months (range, 1−10 months).

3.1. Preoperative period

Four of the nine patients in this series experienced preoperative complications. Three of the nine patients had one or more attacks of enterocolitis before the definitive Duhamel pull-through surgery. One patient developed toxic megacolon with perforation, another (who had a previous ileostomy with Kimura patch at another hospital) developed pouchitis with intractable diarrhea, and the third patient (who had a misplaced sigmoid colostomy at another hospital) had recurrent intestinal obstruction with enterocolitis. Wound infection with sepsis complicated the preoperative course in one other patient.

3.2. Postoperative complications

The most common post−pull-through complication was enterocolitis, which occurred in five patients. Other complications included wound infections in two patients and perineal skin excoriation in three patients. One patient with coexisting hypoplastic right heart syndrome died of heart failure, and another patient with urogenital sinus died of a presumed episode of sepsis outside the hospital. Other postoperative conditions included a herniated incision ($n = 1$), intestinal adhesions requiring enterolysis ($n = 1$), toxic megacolon with bowel perforation ($n = 1$), anal stricture requiring anoplasty ($n = 1$), and chronic lower gastrointestinal bleeding with iron deficiency anemia ($n = 1$).

3.3. Long-term follow-up

At a median follow-up age of 9 years (range, 1−28 years), one patient had died of congenital heart disease, and another was unavailable for follow-up. Two patients <3 years of age were too young to be evaluated for voluntary bowel

Table 2
Demographic and perioperative data of the study population.

No.	Sex	Initial symptoms	Age at ileostomy	Interval between ileostomy and PT	Age at PT (d)	Weight at PT (g)	Preoperative complications	Postoperative complications
1	Male	Toxic megacolon	—	—	223	n/a	Toxic megacolon with perforation	Perianal skin excoriation, chronic low gastrointestinal bleeding
2	Male	Intestinal obstruction	1 mo	6 mo	209	7600	—	Enterocolitis, adhesion ileus
3	Male	Intestinal obstruction	6 d	3 mo	98	3000	—	Wound infection, incisional hernia, anal stricture
4	Male	Delayed passage of meconium	5 d	4 mo	124	2810	—	Enterocolitis, wound infection, heart failure
5	Female	Intestinal obstruction	5 d	1 mo	47	4650	—	Enterocolitis, wound infection, toxic megacolon with perforation, perianal skin excoriation
6	Female	Delayed passage of meconium	12 d	3.5 mo	135	n/a	Wound infection with sepsis	Wound infection, perianal skin excoriation
7	Female	Delayed passage of meconium	2w/o	10 mo	352	5600	Pouchitis with intractable diarrhea	—
8	Female	Intestinal obstruction	1w/o	5 mo	159	6200	Intestinal obstruction with enterocolitis	Enterocolitis
9	Female	Delayed passage of meconium	1m/o	8 mo	268	6100	—	Enterocolitis, sepsis
				Mean = 5.1	Mean = 179	Mean = 5137		

PT = pull-through.

movements. They were taking antidiarrheal agents intermittently and had from three to six loose bowel movements per day and had one or more episodes of enterocolitis requiring hospital admission during the 1st year of follow-up. Three of the five older patients who were available for follow-up reported normal bowel control, and the remaining two were soiling on occasion. They had an average of 3.4 loose bowel movements per day. A stool score was applied to patients who were older than 3 years of age. All patients had good overall functional outcomes; the mean functional outcome score was 12.8 ± 0.84 out of a total score of 16 points, in the range indicating "good" objective functional outcome (Table 3).

Of the seven patients available for long-term follow-up, five were below the 5th percentile for height and four were below the 5th percentile for weight. Only one patient had normal growth development with height and weight in the 50th percentile (Table 4).

3.4. Illustrative cases

The following two cases demonstrate the probable benefit of early and direct pull-through surgery in these patients.

3.4.1. Case 1

A female infant was diagnosed with TCA during an exploratory laparotomy at another hospital. A subtotal colectomy and an ileostomy with an ascending colon Kimura patch were performed at the age of 2 weeks. Postoperative refractory watery diarrhea with intermittent severe metabolic acidosis and failure to thrive (body weight, 5.5 kg, <1st percentile) prompted her parents to bring her to our hospital. An upper gastrointestinal series showed severe dilatation and pooling of the contrast medium near the ileostomy and much delayed gastric emptying (Fig. 1). The patient was admitted twice to our pediatric ward because of periodic massive fluid passage from the ileostomy. We performed a second laparotomy at the age of 1 year. The operative findings were: (1) severe dilatation and thickening of the ileal pouch, (2) residual upper rectum located 1 cm above the peritoneal reflection, and (3) 120 cm of small intestine proximal to the dilated ileal pouch with biopsy-proven ganglions present. Then we performed total excision of the dilated ileal pouch and ileum pull-through using the modified Duhamel method. The postoperative course was uneventful. The patient had only two episodes of postoperative enterocolitis within 7 months, with two other

Table 3
Functional results at long-term follow-up.

Results of follow-up (n = 5)	Mean ± SD (points)	
Recurrent abdominal distension	1.6 ± 0.55	60% non
Frequency of defecation	1.4 ± 0.55	All within 5 d
Stool consistency	1.0 ± 0.00	All loose
Soiling	1.4 ± 0.55	60% occasionally
Urgency period	2.0 ± 0.00	100% normal
Diapers required	1.8 ± 0.45	80% non
Long-term use of medication	2.0 ± 0.00	100% non
Diet	1.6 ± 0.55	60% normal
Overall outcome	12.8 ± 0.84	100% good

Table 4
Growth development.

Age at operation (d)	Age at follow-up	Height (cm)	Percentile	Weight (kg)	Percentile
223	28 y	163	5th	55	10th
209	21 y	160	5th	55	10th
98	Unavailable				
124	Died				
47	11 y	133	10th	23	<5th
135	9 y	135	75th	28	50th
352	7 y	123	75th	20	25th–50th
159	1 y	84	5th	11	15th
268	Died				

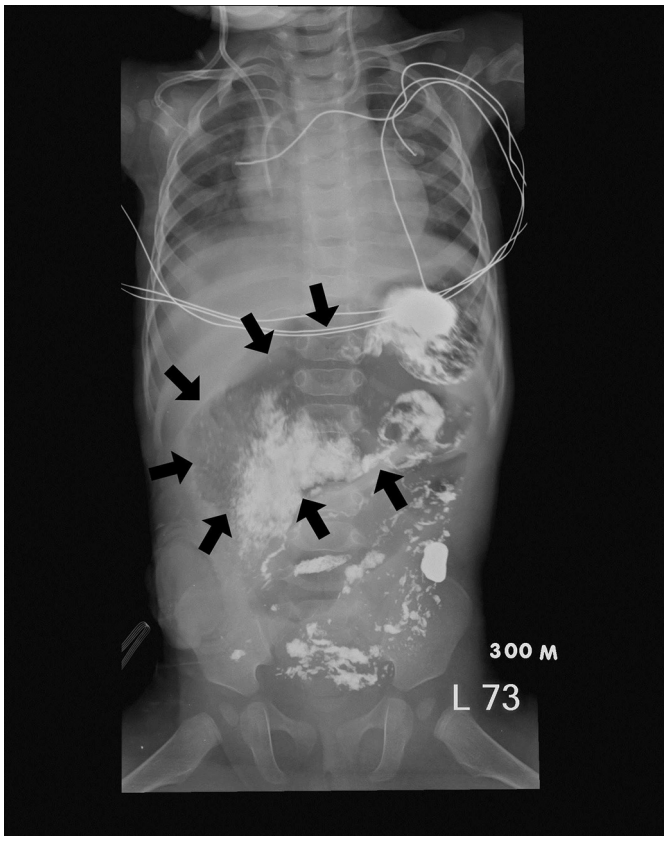

Fig. 1. Upper gastrointestinal series of patient Number 7 (illustrative Case 1) reveals severe dilation and pooling of fecal material near the ileal pouch (arrow heads) with delayed gastric emptying.

episodes in the following 8 years. She took antidiarrheal medications (dioctahedral smectite and/or loperamide) with gradual tapering for 2 years. At the latest follow-up at 9 years and 6 months of age, she measured 131 cm in height (25^{th}–50^{th} percentile) and weighed 23 kg (10^{th}–25^{th} percentile, measured upon admission for enterocolitis, which may be underestimated). She had an average of four loose bowel movements per day without regular use of antidiarrhea medications.

3.4.2. Case 2

This baby girl was diagnosed with Hirschsprung's disease at another hospital and initially presented with intestinal obstruction at the age of 1 week. The diagnosis was made by an exploratory laparotomy with open biopsy of the rectum, sigmoid colon, and appendix. The pathological diagnosis indicated aganglionosis of the rectum and sigmoid colon with the presence of ganglion cells in the appendix. A loop sigmoid colostomy was performed because the surgeon diagnosed the aganglionic segment only extending to the sigmoid colon. The patient was brought to our hospital for the definitive pull-through operation because of severe abdominal distension at 4 months of age. A lower gastrointestinal series via loop colostomy (Fig. 2) revealed severely distended bowels with small-caliber colon proximal to the loop sigmoid colostomy and segmental narrowing about 15 cm from the proximal colostomy. The contrast medium did not fill the proximal colon

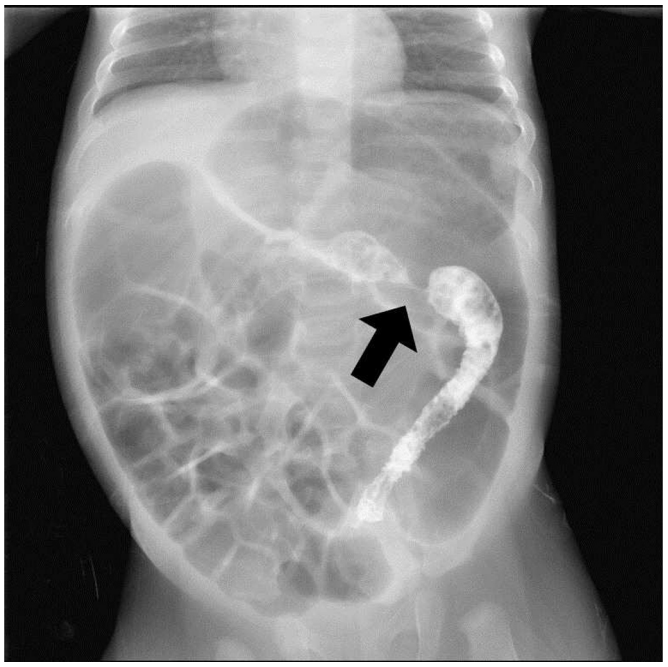

Fig. 2. Lower gastrointestinal series of patient Number 8 (illustrative Case 2) via loop colostomy reveals severe distended bowels with small-caliber colon proximal to loop sigmoid colostomy. The point of acute narrowing and stricture (arrow) is noted at about 15 cm from the sigmoid colostomy, with poor retrograde passage of contrast into the proximal colon.

owing to a segment of fibrosis, and forceful injection was not attempted. Laparotomy at 5 months of age confirmed the diagnosis of TCA, with operative findings of spasm narrowing the whole colon and dilation of the terminal ileum. Subtotal colectomy and ileum pull-through using the modified Duhamel method was performed. Frozen sections of the proximal terminal ileum showed the presence of ganglion cells, which was confirmed by permanent section. A pathological examination of the resected colon showed the absence of ganglion cells in both intramuscular and submucosal plexus, compatible with TCA. The patient's postoperative course was uneventful. She had one documented episode of enterocolitis 5 months after the pull-through surgery. She took antidiarrheal medications (dioctahedral smectite and/or loperamide) for only 3 months. At the latest follow-up at 2 years and 6 months of age, she measured 84 cm in length (5^{th} percentile) and weighed 11 kg (15^{th} percentile).

4. Discussion

TCA is a rare and severe phenotype of Hirschsprung's disease and requires more comprehensive management. The traditional "staged" operation is intended for decompression of the distended bowel and quick reestablishment of enteral feeding in these patients. A long interval between the creation of an ileostomy and the final pull-through operation is advocated out of concern for perianal skin excoriation. Additionally, there are complications with ileostomies, such as prolapse, stricture, retraction, and troublesome peristomal skin excoriation. Moreover, the colon patch graft, usually created at the time of

the ileostomy (the "Kimura patch" procedure) to slow down content transit and improve absorption, can develop pouchitis when the decompressing function of the ileostomy is in question. For managing perianal skin excoriation after the pull-through procedure, we observed that our patients had a favorable response to the combination of large dose of antidiarrheal medication (i.e., dioctahedral smectite and/or loperamide), thinned milk, and the application of topical astringent/protective cream such as zinc oxide, which helped most patients overcome this problem within a reasonable period.

With recent advances in pediatric surgery, authors of newer studies have challenged staged surgery and proposed performing the definitive pull-through operation at a younger age.[8,9,11] Some recent studies reported primary pull-through operations performed in the neonatal period with acceptable outcomes and morbidity.[7,8] Our results concur with the trend toward earlier definitive surgery, with a mean patient age at the pull-through operation of 179 days. In addition, malfunctioning enterostomies may cause additional complications, as illustrated by our two cases (1 patient who received a Kimura pouch procedure with severe postoperative pouchitis, and the other patient with misplaced colostomy) mentioned in the previous section. In these two patients, direct pull-through procedures were performed at the time of exploratory laparotomies without creating ileostomies. We believe that the pull-through operation can be safely performed, with manageable morbidity, as soon as preoperative conditions are stable (i.e., balanced fluid and electrolytes, improved nutritional status, and control of sepsis). Our experience encourages early or one-stage definite PT.

All of our patients underwent the modified Duhamel pull-through operation, which creates a rectal pouch as a reservoir, consisting of aganglionic anterior wall and ganglionic posterior wall. In fact, we tend to leave longer aganglionic segment in patients with more extensive disease. Therefore, a complete comparison between different types of pull-through procedures was not possible from the current series. A recent systematic review of various procedures for treatment of TCA revealed no superior operative method for the treatment of TCA with respect to perioperative morbidity, mortality, incidence of enterocolitis, and functional outcome.[5]

Long-term follow-up of our patients with TCA showed favorable postoperative functional outcomes. The mean objective functional outcome score reached the level of "a good outcome" in all of the patients who underwent the pull-through operation at >3 years of age, even though the trend toward better control of bowel function with age was not clearly demonstrated, possibly because of the small sample size. We propose that an earlier pull-through operation (within 4 months after decompression ileostomy, or primary pull-through within 6 months of age) would be beneficial in managing patients with TCA, especially if ileostomy-related complications occur.

The main limitation to our study is the small sample size; however, it should be noted that the disease is rare. Only through collaborative efforts between specialized centers could we accumulate enough cases for further investigation.

References

1. Lee JT, Liu C, Tsai HL, Chin T, Wei CF. Successful redo pull-through for Hirschsprung's disease in a Haddad syndrome patient. *J Chin Med Assoc* 2010;**73**:438−40.
2. Chin TW, Chiu CY, Tsai HL, Liu CS, Wei CF, Jap TS. Analysis of the RET gene in subjects with sporadic Hirschsprung's disease. *J Chin Med Assoc* 2008;**71**:406−10.
3. Moore SW. Total colon aganglionosis in Hirschsprung disease. *Semin Pediatr Surg* 2012;**21**:302−9.
4. Hoehner JC, Ein SH, Shandling B, Kim PCW. Long-term morbidity in total colon aganglionosis. *J Pediatr Surg* 1998;**33**:961−6.
5. Marquez TT, Acton RD, Hess DJ, Duval S, Saltzman DA. Comprehensive review of procedures for total colon aganglionosis. *J Pediatr Surg* 2009;**44**:257−65.
6. Bischoff A, Levitt MA, Pena A. Total colon aganglionosis: a surgical challenge−How to avoid complications? *Pediatr Surg Int* 2011;**27**:1047−52.
7. Cheung ST, Tam TH, Chong HM, Chan KW, Mou WC, Sihoe DY, et al. An 18-year experience in total colon aganglionosis: from staged operations to primary laparoscopic endorectal pull-through. *J Pediatr Surg* 2009;**44**:2352−4.
8. Wildhaber BE, Teitelbaum DH, Coran AG. Total colonic Hirschsprung's disease: a 28-year experience. *J Pediatr Surgery* 2005;**40**:203−7.
9. Anupama B, Zheng S, Xiao X. Ten-year experience in the management of total aganglionosis. *J Pediatr Surg* 2007;**42**:1671−6.
10. Menezens M, Pini Prato A, Jasonni V, Puri P. Long-term clinical outcome in patients with total colon aganglionosis: a 31-year review. *J Pediatr Surg* 2008;**43**:1696−9.
11. Escobar MA, Grosfeld JL, West KW, Scherer LR, Rouse TM, Engum SA, et al. Long-term outcomes in total colonic aganglionosis: a 32-year experience. *J Pediatr Surg* 2005;**40**:955−61.