**Original Article**

Prognostic factors in children with total colonic aganglionosis treated with the Soave procedure: the experience of 43 patients from a single institution

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Received October 8, 2015; Accepted March 17, 2016; Epub May 15, 2016; Published May 30, 2016

**Abstract:** Total colonic aganglionosis (TCA) is an uncommon and severe form of intestinal developmental malformation. The aim of this study is to identify the prognostic factors in children with TCA treated with the Soave procedure. Forty-three children with TCA who were treated with the Soave procedure between February 2008 and August 2013 were included in the study and followed up. Follow-up data were collected regarding growth development, stool frequency and consistency, incontinence, and enterocolitis. Parents of 31 (72.1%) of the 43 patients were followed up. Four patients underwent a primary pull-through procedure, while 27 patients underwent ileostomy and a later definitive operation. The remaining length of the small intestine was 164 ± 53 cm, and pathology revealed 22 cases with mature ganglion cells in the proximal intestine, while there were 9 cases with ecumenical mature ganglion cells in the proximal intestine. Growth development was normal in 19 patients, while mild malnutrition was observed in 8 patients, and moderate malnutrition was observed in 4 patients. Stool consistency was mushy or shaped in 25 patients and mushy or watery in 6 patients. Twenty-eight patients had a frequency of stool ranging between 1-5 bowel movements per day, and 3 patients had more than 6 bowel movements per day. Twenty-five patients suffered from less than 2 bouts of postoperative enterocolitis, and 6 patients suffered from more than 3 episodes of postoperative enterocolitis. Long-term outcomes of children with TCA who are treated with the Soave procedure are satisfactory with good anorectal function and quality of nutrition. The remaining length of the small intestine and the neurodevelopment of the proximal intestine ganglion cells are important prognostic factors.

**Keywords:** Total colonic aganglionosis, Soave procedure, prognosis

**Introduction**

Total colonic aganglionosis (TCA), with or without involvement of the small intestine, is a relatively uncommon and severe form of intestinal developmental malformation. This rare condition occurs in approximately 2% to 13% of cases of Hirschsprung disease (HD) and is characterized by the absence of ganglion cells in the entire colon extending into the terminal ileum. TCA carries higher morbidity and mortality rates than the classic types of HD [1]. Despite recent advances in surgical techniques and meticulous pre- and post-operative management, surgical treatment for TCA remains challenging. Various procedures have been proposed for the surgical management of TCA. In our previous study, we compared the Soave and Martin procedures [2]. However, long-term follow-up interviews are needed. The purpose of this study was to identify the prognostic factors in patients with total colonic aganglionosis who underwent the Soave procedure by reviewing cases of TCA at the Children’s Hospital of Fudan University that were treated with this procedure over the past 5 years and to follow up the patients involved.

**Materials and methods**

In this study, we reviewed the medical records of 43 patients with TCA who were admitted to the Children’s Hospital of Fudan University between February 2008 and August 2013 and treated with the Soave procedure. The diagnosis was confirmed by an intraoperative frozen-section biopsy of the rectum, colon, appendix, and ileum. Case patients were evaluated for...
their descriptive data (sex, age, body weight at the definitive operation, preoperative, perioperative, and postoperative management, ileal involvement in centimeters, and pathological examination at the definitive operation).

The study was approved by the Institutional Review Board of Fudan University. Informed consent was obtained from all patient guardians. Follow-up data were collected from the parents using a standardized telephone questionnaire. Families were given a detailed questionnaire about growth development, stool frequency, stool consistency, fecal soiling, incontinence, anal stricture, and enterocolitis. Enterocolitis was defined as the presence of abdominal distention, diarrhea, vomiting, and fever.

Data were analyzed using SPSS version 20.0 for Windows (SPSS Inc., Chicago, IL). Categorical variables were compared using the Fisher’s exact test. A *P*-value <0.05 was considered statistically significant.

**Results**

Over a period of 5.5 years, 43 patients were diagnosed with total colonic aganglionosis, and the parents of 31 of the 43 patients were followed up. The follow-up rate was 72.1%.

**Diagnosis**

Among these 43 patients, 31 (72.1%) were diagnosed during the neonatal period, whereas 12 (27.9%) were diagnosed later in infancy. The diagnosis was confirmed by an intraoperative frozen-section biopsy of the rectum, colon, appendix, and ileum. Five (11.6%) patients had already undergone ileostomy at other hospitals before coming to our hospital. Three of these five patients were failed diagnoses at the time of laparotomy, and ileostomy was performed in other hospitals. Forty-one patients were diagnosed by intraoperative frozen-section biopsy in our hospital.

**Definitive operation**

For the definitive operation, 4 (9.3%) patients underwent a primary pull-through procedure, while the remaining 39 (90.7%) underwent an ileostomy and later definitive surgery. Thirty-six of 39 patients who had a stage pull-through procedure had their ileostomy closed at the time of the definitive operation. Another 3 cases underwent ileostomy closing at a later time because one patient developed a severe anal infection and a redo ileostomy, and the other two patients were at high risk of developing postoperative intestinal fistulae. Blood transfusion was needed for 32 (74.4%) patients during surgery.

The weight of the patients during the definitive operation was 5.3 ± 2.1 kg (range, 3.8-9.5 kg), and the age at the definitive operation was 156 ± 68 days (range, 41-396 days). The length of ileum involvement was the same as that during ileostomy for all the patients who underwent a definitive operation. The remaining length of the small intestine was 164 ± 53 cm (range, 65-250 cm), and histopathologic examination revealed that 31 (72.1%) cases presented with mature ganglion cells in the proximal intestine, while 12 (27.9%) cases had ecumenical mature ganglion cells in the proximal intestine. In our series, there was no maturation of ganglion cells in the ileum between the time of ileostomy and the definitive operation.

**Follow-up and prognostic analysis**

Parents of 31 (72.1%) of the 43 patients were followed up with a standardized telephone questionnaire. The mean follow-up time was 3.6 ± 2.1 years (range, 1.8-6.4 years). The mean follow-up age of the 31 patients was 4.2 ± 2.4 years (range, 1.5-6.6 years), and the mean follow-up weight was 17.4 ± 3.7 kg (range, 12.1-23.5 kg). Follow-up data were collected regarding growth development, stool frequency and property, incontinence, anal stricture and enterocolitis.

The WFA (weight-for-age) median percentage was used to evaluate the nutritional status according to the classification of American Pediatric Society [3]. The WFA median percentage of the 31 patients was (91.6 ± 8.7)%.

Follow-up results showed that growth development was normal in 19 patients, mild malnutrition was observed in 8 patients, and moderate malnutrition was observed in 4 patients (Table 1).

Twenty-three patients had a frequency of stool ranging between 3-5 bowel movements per day, and 5 patients had 1 to 2 bowel movements per day. Only 3 patients experienced an
Increased frequency of stool more than 6 times per day. Stool consistency was mushy or shaped in 3 patients, mushy in 23 patients, mushy or watery in 4 patients and watery in only 1 patient. There were no cases of fecal incontinence, and 3 patients had fecal contamination.

The follow-up results showed that the longer the remaining length of the small intestine, the fewer the bowel movements and the better the stool consistency (Table 2). According to the prognostic analysis of the remaining length of the small intestine and stool situation, the group with >100 cm had a lower stool frequency per day than the group with ≤100 cm (P<0.05, Table 3). Fifteen patients suffered from 1-2 bouts of postoperative enterocolitis, and 6 patients suffered from more than 3 bouts of postoperative enterocolitis. Postoperative enterocolitis did not occur in 10 patients. The incidence of EC in patients with mature ganglion cells in the proximal intestine was lower than that in patients with ecumenical mature ganglion cells (P<0.01, Table 4). The occurrence of postoperative enterocolitis did not correlate with the remaining length of the small intestine (P>0.05).

Among the 31 patients who were followed up, 3 (9.7%) had undergone a primary pull-through procedure, while 28 (90.3%) had undergone a staged definitive operation. The follow-up results of the 3 patients who underwent a primary pull-through operation are presented in Table 5.

**Discussion**

Total colonic aganglionosis is a rare developmental malformation of the intestinal nervous system in pediatric surgery, with a pathological scope ranging from the entire colon to the terminal ileum. Forty-three patients were diagnosed with TCA and underwent a definitive pull-through operation in the Children’s Hospital of Fudan University during the 5.5-year period (2008.2-2013.8). None of the cases presented with aganglionosis confined to the cecum. All the cases were of the ultra-long form with ileal involvement.
Prognostic factors of TCA with Soave procedure

Total colonic aganglionosis is associated with more diagnostic problems. These patients often require multiple surgeries before a definitive procedure. In our study, 3 patients (7.0%) had been operated on previously at some other hospital before a definite diagnosis was reached. Intestinal obstruction and spontaneous perforation of the intestine in neonates is a common condition and caused by various diseases with 3.2% to 4.4% of bowel perforations occurring in patients with HD [4]. If bowel obstruction with perforation and peritonitis of unknown etiology occur in a neonate, careful examination to identify the transitional zone is required. If HD is suspected, frozen-section biopsy may be required to confirm the disease. There is no alternative to histopathologic confirmation. The total colon and ileum must be carefully inspected during laparotomy in children with long-segment HD [5]. In our department, the diagnosis is established intraoperatively from seromuscular biopsies of the rectum, colon, appendix, and ileum by a technique using acetylcholinesterase. The extent of aganglionosis was determined at the time of ileostomy in 39 patients and at the time of primary pull-through in 4 patients.

The definitive operation is the best treatment for total colonic aganglionosis. Non-surgical treatment and ileostomy are transitional measures for the maintenance of bowel movements and growth development because of age or technical constraints. In our study, all 43 cases underwent a definitive operation (abdominal perineal Soave procedure). This included 4 patients who had undergone a primary pull-through procedure and the remaining 39 patients who had undergone ileostomy and later a definitive operation.

A number of surgical procedures for treating TCA have been reported. The Martin modification has been the most widely used technique [6]. In recent years, the Soave pull-through procedure has been commonly used in our hospital. The definitive Martin procedure is generally planned approximately 8 to 10 months after ileostomy because the procedure is more complicated and the operating time is longer. This ensures that a sufficient period for growth and clinical observation transpires to determine whether the ileum has developed adequate function. However, the Soave pull-through procedure is easier to perform compared with the Martin modification and takes a shorter amount of time. This method can be safely used in newborns with TCA [7]. Our previous study comparing the effectiveness of the Soave and Martin procedures for the treatment of TCA found that patients with TCA who were managed with the Soave procedure had fewer operative complications compared with those who underwent the Martin procedure [2]. However, the patients managed with the Soave procedure took longer to establish normal defecation. Although each procedure has advantages and disadvantages, the Soave procedure is more promising for the treatment of TCA, especially with regard to postoperative complications. Nonetheless, a long-term follow-up study is still required.

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 [8-10]. Some recent studies have reported that primary pull-through operations performed in the neonatal period have acceptable outcomes and morbidity [8, 11]. In our study, 28 followed-up cases had undergone staged definitive surgery due to insufficient conditions, while 3 followed-up patients had undergone a primary pull-through procedure with good results. Although there may be a chance of incorrect leveling of the aganglionic segment in the primary pull-through procedure, based on our experience, the primary pull-through operation is associated with fewer problems with electrolyte imbalances and a lower likelihood of malnourishment compared with the staged pull-through procedure with ileostomy. Moreover, the primary pull-through operation avoids the burden of ileostomy and ileostomy closing, postoperative care, as well as the economic and mental stress experienced by parents. Therefore, if the patient’s condition can be evaluated during the neonatal period, a primary pull-through operation should be considered.

Our follow-up results showed that the postoperative nutritional status and long-term stool property are satisfactory. Our results are consistent with the findings of Fortuna who reported that gradual recovery of intestinal function can be expected postoperatively in patients with TCA. Furthermore, the “pulled-through” ileum eventually substitutes for the colon in
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absorbing water [12]. Analysis of the stool condition at follow-up and the remaining length of small intestine revealed that the group with >100 cm had better stool character and bowel movements than the group with ≤100 cm. Thus, the longer the remaining length of small intestine, the fewer the bowel movements and the better the stool character. This finding underscores the significance of the intraoperative frozen biopsy site and the importance of an adequate scope of the intestinal excision. Our follow-up results illustrate that a primary or staged Soave procedure is an ideal surgery for TCA that is simpler and secure, as long as the functioning of the ileum postoperatively meets the body’s physical requirements.

Enterocolitis is still the most commonly encountered complication associated with HD and carries significant morbidity and mortality. Our follow-up analysis showed that the incidence of EC in patients with ecumenical mature ganglion cells in the proximal intestine was higher than that in patients with mature ganglion cells. This may be associated with the poor intestinal motility observed in patients with ecumenical mature ganglion cells leading to retention of intestinal contents and bacterial infection. Thus, the neurodevelopment of the proximal intestine ganglion cells increases the risk of postoperative EC, and vigilance regarding the potential development of postoperative EC must be elevated in patients with ecumenical mature ganglion cells.

Long-term outcomes of children with total colonic aganglionosis treated with the Soave procedure are satisfactory with good anorectal function and quality of nutrition. The remaining length of small intestine and the neurodevelopment of the proximal intestine ganglion cells are important prognostic factors.

Disclosure of conflict of interest

None.

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References