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ORIGINAL ARTICLE

Optimal time for single-stage pull-through colectomy in infants with short-segment Hirschsprung disease

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Abstract

Objective Short-segment Hirschsprung disease (HSCR) is the predominant type of HSCR that affects approximately 75% of patients. Whether single-stage endorectal pull-through (ERPT) surgery is appropriate for neonatal patients with HSCR has not been definitively determined. This retrospective cohort study concerning infants with short-segment HSCR investigated the optimal age for single-stage ERPT surgery, regardless of the operative approach.

Methods The 198 patients were stratified by operative age ≤ 3 or > 3 months (groups A or B, respectively, $n = 62$ and 136, respectively). Diagnoses of short-segment HSCR were conducted by preoperative contrast enema and rectal suction biopsy with acetylcholinesterase immunohistochemical staining. The perioperative clinical course for all patients was reviewed and the accuracy rate of the preoperative diagnoses and postoperative short- and midterm outcomes were assessed.

Results The rates of diagnostic accuracy, according to the results of the preoperative contrast enema or rectal suction biopsy, were lower in group A (67.2 and 93.5%, respectively) than in group B (81.4 and 94.9%, respectively). In groups A and B, 49 (79.1%) and 108 (79.4%) infants, respectively, completed follow-up examinations. The short-term outcomes were postoperative HSCR-associated enterocolitis, adhesive bowel obstruction, anastomosis leakage, and anal stenosis during the first 12 months after surgery. The midterm outcomes were incontinence and constipation at ~24 months after surgery. Compared with group B, group A experienced more incidences of anastomotic leakage in the short-term and more soiling in the midterm. In groups A and B, the rates of constipation recurrence were nil and 1.9%, respectively.

Conclusion Infants with HSCR ≤3 months old at the time of single-stage ERPT surgery showed lower rates of accurate and conclusive diagnostic results and poorer postoperative outcomes. Waiting to perform this surgery until infants are older might be more beneficial.

Keywords Short-segment Hirschsprung disease · Infants · Colectomy · Enterocolitis

Introduction

Hirschsprung disease (HSCR) is a congenital disorder characterized by the absence of ganglion cells in the submucosal and myenteric plexus of the bowel. The short-segment type of HSCR, which affects ~ 75% of patients with HSCR, features the complete absence of neuronal ganglion cells in the rectosigmoid region of the colon [1]. Infants with HSCR frequently present with massive abdominal distension, gas and stool retention, and delayed passage of meconium during the neonatal period [2].

For neonatal patients with HSCR, it remains controversial whether primary endorectal pull-through (ERPT) surgery is appropriate [3]. Some surgeons insist that delaying surgical treatment until the infants are older might result in persistent colorectal obstruction and associated malnutrition and will increase the risk of HSCR-associated enterocolitis (HAEC) [4]. It is also presumed easier to handle the mucous membranes in ERPT surgeries of neonates, making the surgeries more convenient [5]; however, this surgery in neonatal patients can destroy the delicate structures that control defecation, and the onset of HAEC is more likely in the immature immune system of very young infants [6]. Therefore, some pediatric surgeons prefer giving short-term transient conservative treatment, including colon enema and anal distention, and

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delay performing ERPT surgery until patients are older to ensure that the surgery is safe and effective [7].

This retrospective cohort study assessed the optimal diagnostic procedure and age for treating infants with short-segment HSCR, whether through the open, laparoscopic, or transanal operative approach.

Methods

This was a retrospective case study performed by reviewing the charts of 198 patients. All patients who had received a preoperative diagnosis of short-segment HSCR and were surgically treated from October 2010 to November 2015 were considered for inclusion in the study. All study protocols were approved by the institutional review board of Tongji Medical College (number TJ-C201610025).

The criteria for inclusion in the study were as follows: (1) preoperative diagnosis of HSCR based on the results of rectal suction biopsy (RSB), (2) significant obstruction of the narrow distal bowel in the rectosigmoid colon that was diagnosed as short-segment HSCR after contrast enema (CE) examination, and (3) ≤ 12 months old at the time of primary ERPT surgery. The exclusion criteria were as follows: (1) staged enterostomy performed, (2) diagnosed as having long-segment HSCR or total colon aganglionosis, or (3) declined treatment in this hospital or had complicated additional gastrointestinal anomalies.

Patients were divided into two groups based on patient age when the surgery was performed. Group A were those patients who had undergone surgery at ≤ 3 months old; group B were those who had undergone surgery at ages from 3 to 12 months old. The preoperative examination included RSB and CE. The diagnosis accuracy was defined as the results of the radiological transitional zone (TZ) in the preoperative CE examination being comparable to the final pathological TZ results. In the meantime, the accuracy of the RSB results was produced if there was aganglionosis in the distal rectum, when preoperative RSB revealed the presence of acetylcholinesterase-positive hypertrophic nerve fibers.

Furthermore, the correlation between the radiological TZ and the range of bowel resection was analyzed in both groups. Two sections of full-thickness bowel wall 3–5 cm above and below the radiological TZ bowel were excised from each patient during the surgery. The results were considered as previously described [8] (i.e., a negative result was defined as the presence of ganglion cells in the bowel proximal to the 3–5 cm of radiological TZ; a positive result was aganglionosis in the bowel distal to the 3–5 cm of radiological TZ. The postoperative pathological reports provided the final diagnostic criteria. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated.

Relevant patient characteristics were compiled, such as demographic data, age at surgery, and the length of the aganglionosis segment. The clinical outcomes and bowel functions of patients after surgery were also assessed during the short-term and midterm follow-ups [7]. The short-term outcomes included postoperative HAEC, adhesive bowel obstruction, anastomosis leakage, and anal stenosis during the first 12 months after surgery. HAEC was diagnosed in patients who developed any symptoms of foul-smelling diarrhea, vomiting, or fever [9]. The midterm outcomes included incontinence and constipation at ~ 24 months after surgery. After discharge, all patients received anal dilation for 1–3 months in accordance with the protocols of the clinical rehabilitation program [10].

Statistical analyses

The unpaired Student's *t* test was performed to examine the differences between demographic and clinical characteristics of the two groups of patients. The significance of the differences in categorical values was analyzed using the chi-squared test. Logistical regression and odds ratio analyses were used to estimate possible correlations between analyzed factors and the incidence of complications. All statistical analyses were completed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). $P < .05$ was considered statistically significant.

Results

The study population comprised 62 and 136 infants in groups A and B, respectively, apportioned according to age at surgery— ≤ 3 months (group A) or 3–12 months (group B) (Table 1).

The radiological TZ and pathological results were compared in each patient (Table 2). The accuracy of the diagnosis was 67.7% (42/62) for the patients in Group A and 80.9%

Table 1 Basic characteristics of the study groups

	Group A	Group B	*P*
Subjects, *n*	62	136	–
Age at operation, month	1.8 ± 0.5	8.2 ± 0.3	< 0.05
Males, *n* (%)	48 (77.4%)	110 (80.9%)	> 0.05
Meconium passage > 24 h, *n* (%)	57 (91.9%)	122 (89.7%)	> 0.05
Diagnosis of trisomy 21, *n*	0	1	< 0.05
Length of resection bowel (cm)	22 ± 5.3	39 ± 4.1	< 0.05
Operative time, min	181 ± 13.2	192 ± 14.4	> 0.05
Postoperative hospital stay, (day)	14 ± 1.2	11 ± 1.2	< 0.05
Total length of hospital stay (day)	21 ± 2.3	20 ± 2.6	> 0.05

Table 2 Radiological transitional zone (TZ) and final pathological results

		Radiological TZ, n			
		Group A[a,c]		Group B[b,d]	
		Rectum	Sigmoid	Rectum	Sigmoid
Pathological TZ, n (%)	Rectum	36 (58.1%)	2 (3.2%)	75 (55.1%)	2 (1.5%)
	Sigmoid	7 (11.3%)	3 (4.8%)	13 (9.6%)	30 (22.1%)
	Descending	5 (8.1%)	5 (8.1%)	1 (0.7%)	8 (5.9%)

[a] $n = 62$

[b] $n = 136$

[c] Four infants (6.5%) in group A were diagnosed as having immature ganglia by postoperative pathology

[d] Seven infants (5.1%) in group B were diagnosed as having immature ganglia by postoperative pathology

(110/136) for those in group B. The sensitivity of the radiological TZ in judging the pathological abnormal bowel was 76.7 and 85.2% in groups A and B, respectively; the specificity was 88.2 and 92.7%, the positive predictive value was 90.3 and 93.4%, and the negative predictive value was 72.6 and 83.8%, respectively.

The diseases in four patients (6.5%) in group A were misdiagnosed and confirmed to have immature ganglia by postoperative pathology; while those in seven patients (5.1%) in group B were diagnosed as having immature ganglia. The accuracy of acetylcholinesterase immunohistochemistry results was comparable in groups A (93.5%) and B (94.9%); however, the rate of inconclusive results was higher in group A (43.5%) than in group B (25.7%).

All children underwent rectosigmoid colectomy. The exact length of the resected bowel is shown in Table 1. In groups A and B, 34 and 79 infants underwent laparoscopic colectomy, respectively, and 26 and 34 infants underwent transanal ERPT. The average operative time was 181 ± 13.2 min in group A and 192 ± 14.4 min in group B; the average postoperative hospital stay was 14.3 days in group A and 11.4 days in group B (Table 1). All patients received postoperative anal dilatation for 1~3 months as outpatients, followed by enrollment in a rehabilitation program, which was performed to prevent anal stenosis and was helpful for recovery of normal defecation [7].

In groups A and B, 49 (79.1%) and 108 (79.4%) infants, respectively, completed follow-up examinations. In groups A and B, postoperative complications during the first 12 months after surgery occurred in 22.4 and 18.5%, respectively, and midterm examinations 24 months after surgery revealed complications in 4.1 and 5.6%, respectively. None of the patients experienced anastomotic strictures; however, in groups A and B, anastomotic leakage occurred in 6.1 and 0.9%, respectively ($P < .05$) and postoperative enterocolitis was observed in 16.3 and 17.6%, respectively ($P > .05$). In terms of anastomotic leakage, all cases had to undergo a transient ileostomy and a stoma closure surgery was performed ~ 3 months later. The leakages observed in this study could self-heal; therefore, an extra repair surgery for leakage or a re-colectomy was not necessary.

Changes in anal defecation and the ability to control defecation were the focus of the midterm follow-up examinations. The stool characteristics of the two groups were similar. In groups A and B, the incidence rates of soiling were 12.2 and 3.7%, respectively ($P < .05$), but the recurrence of constipation was nil in group A and 1.9% in group B (Table 3).

Discussion

Recent advancements in anesthetic techniques, improvements in patient care in neonatal intensive care units, and the introduction of minimally invasive surgical techniques have enabled surgeons to perform operations on neonates with minimal mortality rates and good results. In addition, ERPT is more easily performed in neonates because of their shallow pelvic region [5, 11]. At the same time, early diagnosis of HSCR is believed to decrease the risk of life-threatening HAEC [12]; therefore, many pediatric centers are performing one-stage ERPT procedures on newborn patients with HSCR but without stable results [2, 13]. A survey of the European Pediatric Surgeons' Association showed that ~ 30% of pediatric surgeons prefer to perform ERPT surgery on neonates [3]; however, there were many difficulties in preoperatively diagnosing neonatal HSCR [14]. For example, in CE radiographs, the classic radiologic description of TZ includes proximal dilatation with a spastic distal segment, but this is often not apparent in patients within the first few weeks after birth. Our study also showed that in infants ≤ 3 months old, the sensitivity and specificity of the CE examination to identify TZ bowel was 76.7 and 88.2%, respectively. This was lower than those of the older patients, although the difference did not reach significance. Yet, the risk of an inconclusive result was significantly higher in the younger patients; therefore, in very young infants [12], CE examination is generally

Table 3 Short- and midterm follow-ups

	Group A	Group B	*P*
Subjects, *n*	49	108	–
Anastomotic stenosis	0	0	–
Anastomotic leakage	3 (6.1%)	1 (0.9%)	< 0.05
Postoperative Hirschsprung disease-associated enterocolitis	8 (16.3%)	19 (17.6%)	> 0.05
Constipation recurrence	0	2 (1.9%)	< 0.05
Soiling	6 (12.2%)	4 (3.7%)	< 0.05

recommended to provide evidence for screening, but not diagnosing, HSCR [8].

The appropriate age for RSB in neonates is also controversial. Some researchers have concluded that there is no variation in the diagnostic accuracy of RSB for patients of different ages [15]. Our results indicated that although the accuracy of RSB was similar in both groups, 43.5% of the results in infants ≤ 3 months old were inconclusive. This was significantly higher than that in children > 3 months old. The most common theory for these inconclusive results is that the enteric nervous system is still developing in neonates; therefore, the results of acetylcholinesterase staining were most likely be false positives in neonates before the classical pathology features develop [16]. On the other hand, an inadequate sample, such as the lack of adequate amounts of submucosa in the specimen and the need for a second biopsy, always influences the results [17, 18]. Compared with RSB, the advantage of full-thickness rectal biopsy (FTRB) is that the sample tissues contain submucous and myenteric plexuses; the disadvantages are the need for anesthesia and the risk of intestinal perforation, which is higher for neonates and young infants than for older infants [2]. In our opinion, for suspected HSCR in neonates, CE could be used as a screening tool, and histopathological findings should be used to assist in the diagnosis, including RSB or FTRB, when neonates cannot be diagnosed with HSCR, and whose general condition is stable. Conservative management, including anal dilation, colonic lavage, and dietary adjustment, could be provided, and follow-up examinations should be standard if there is no remission within 1–3 months.

In terms of the surgical approach, despite that the degree of bowel-wall thickening or dilatation ultimately determines the surgical technique, minimally invasive techniques, including transanal ERPT or laparoscopic-assisted pull-through surgery, have become the most common strategy of choice for short-segment HSCR in patients ≤ 3 months old [19]. Indeed, there were more cases that underwent open or laparoscopic surgeries in the early phases of our study; however, recently, ERPT was deemed to be the main protocol for short-segment HSCR, and the short- and long-term postoperative complications are the main considerations in patients with HSCR.

HAEC is the most serious and potentially life-threatening complication of HSCR, with significant morbidity and mortality rates [20]. In the present study, the HAEC morbidity rates were 16.3 and 17.6% in groups A and B, respectively, which is consistent with the results of other studies [21]. It is clear that the systemic and intestinal immune function in newborns or low-weight infants is immature and more likely to be susceptible to HAEC [22]. Similarly, there was a higher incidence of anastomotic leakage in the neonatal group in our study, the cause of which might also be a result of low immune function leading to a high incidence of anastomotic infection.

In our study, all patients underwent systematic rehabilitation, which included anal distention, colonic lavage, and dietary adjustment for 1–3 months after surgery. These treatments enabled them to regain defecation function and decrease the risk of HAEC recurrence [10]. At the same time, sphincter spasms and anastomotic strictures and the presence of a postoperative intestinal obstruction might also be important factors in postoperative HAEC [23]. In our patients, the routine placement of an anal draining tube through the anastomosis for 3–7 days after surgery, and anal dilation for 1–3 months on an outpatient basis, greatly reduced any occurrence of perianal ulcers and anastomosis strictures.

In long-term follow-up examinations, the sense of needing to defecate and the ability to assess the stool conditions of children treated surgically for HSCR were the focus of attention [24]. There are multiple reasons that patients experience incontinence after an ERPT procedure, including injury of the internal sphincter and pelvic nerves or sensory deficits of the anal skin during surgical dissection. These are more likely to occur in neonatal cases [24]; therefore, greater care is necessary during ERPT in neonatal patients.

Recent research has shown that neonates require more postoperative time than older infants to stabilize their stooling patterns [6]. On the other hand, in the present study, two patients in group B suffered recurrent constipation and finally had to undergo a subsequent surgery. The pathology results indicated residual TZ, which is the most common reason for constipation according to other article [25]. What is interesting is that no patients in group A of the current study suffered from recurrent constipation. We infer that this might be because of the extensive secondary degeneration of ganglion

cells in the proximal bowel resulting from passive dilation or recurrent HAEC.

Conclusion

The timing for surgery on infants with short-segment HSCR is controversial. The results of our study showed that there were higher rates of preoperative inconclusive diagnoses and poorer postoperative outcomes in infants from newborns ≤ 3 months old, compared with infants from 3 to 12 months old; therefore, it might be more beneficial to perform single-stage ERPT in infants > 3 months old. Conservative management could be provided for most short-segment HSCR before ERPT surgery, including anal dilation, colonic lavage, and dietary adjustment for bowel decompression and HAEC prevention; however, if, in patients suffering severe complications, a diverting stoma should still be considered, as in patients with severe HAEC, malnutrition, a huge fecalith, or highly dilated bowels with an unidentified lesion.

Study limitations

There were limitations to our study. First, this was single-center cohort study and there might have been selection bias. Second, there were no long-term results available at this writing. We suggest that a longer follow-up (e.g., > 3 years) should be conducted and the results and surgical procedures reassessed for these patients.

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