Journal of Pediatric Surgery (2011) **46**, 342–347

ELSEVIER

Journal of Pediatric Surgery

www.elsevier.com/locate/jpedsurg

Redo pull-through in Hirschprung's disease for obstructive symptoms due to residual aganglionosis and transition zone bowel

Taiwo A. Lawal[a], Kaveer Chatoorgoon[a], Margaret H. Collins[b], Alex Coe[a], Alberto Peña[a], Marc A. Levitt[a,*]

[a]*Colorectal Center for Children, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229, USA*
[b]*Department of Pathology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229, USA*

Received 26 October 2010; accepted 4 November 2010

Key words:
Hirschsprung disease;
Aganglionosis;
Transition zone;
Pull-through;
Enterocolitis;
Reoperation

Abstract

Background: Reoperations in Hirschsprung disease may be required for residual aganglionosis or transition-zone bowel found at the distal pull-through. We aimed to review the management of patients who had this complication and offer suggestions on how to avoid it.

Methods: Ninety-three patients with Hirschsprung disease were referred to our institution with recurrent problems after a pull-through done elsewhere. All required reoperations with a variety of indications, and of these, 25 had residual aganglionosis/transition-zone histology. This was the only indication for redo in 16 children.

Results: Children (range, 2-17 years) presented 6 to 66 months after the initial pull-through. The predominant symptoms were enterocolitis (n = 9 [56%]), constipation (n = 7 [44%]), failure to thrive (n = 5 [31%]), and impaction (n = 4 [25%]). The rectal biopsy performed as part of their post pull-through work up showed hypertrophic nerves (n = 16), absent ganglion cells (n = 6), and normal ganglion cells (n = 10). The original frozen-section biopsy, determining the level of the pull-through, only sampled the seromuscular layer in 3 children, leading to misdiagnosis. Reoperations involved a transanal resection (n = 15) and a posterior sagittal approach (n = 1). In all cases, obstructive symptoms were resolved, and no patient has had recurrent enterocolitis.

Conclusion: Patients' post pull-through with recurrent obstructive symptoms may have residual aganglionosis or transition-zone bowel. Reoperation can result in the resolution of these symptoms. A full-thickness biopsy at the time of the initial pull-through to include the mucosa and submucosa may increase the possibility of identifying hypertrophic nerves.

Most patients who undergo treatment of Hirschsprung disease (HD) have a satisfactory outcome [1]. Patients with persistent constipation, enterocolitis, failure to thrive, and distension constitute a group that is not doing well, and they are often referred to specialized centers for further

* Corresponding author. Department of Surgery, Division of Pediatric Surgery, University of Cincinnati, Colorectal Center for Children, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229. Tel.: +1 513 636 3240; fax: +1 513 636 3248.
E-mail address: marc.levitt@cchmc.org (M.A. Levitt).

0022-3468/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.jpedsurg.2010.11.014

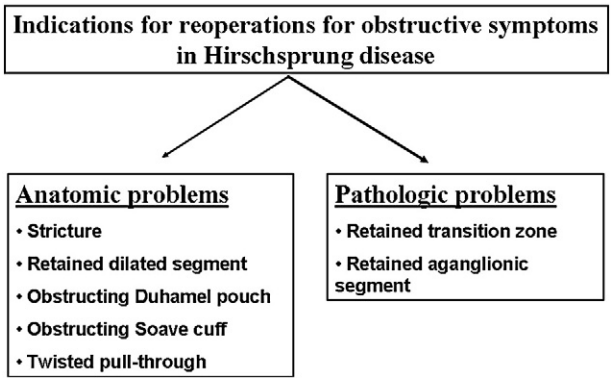

Fig. 1 Indications for reoperations for obstructive symptoms in Hirschsprung disease.

management. The reasons why a patient may have obstructive symptoms after pull-through and require reoperation may be either anatomical or histopathologic [2,3] (Fig. 1). In this review, we focus on the latter.

Residual aganglionosis and transition-zone pull-throughs, as indications for reoperations in patients with HD, have been reported (Table 1) [1,2,4-12]. We believe that this complication is preventable. The recognition of the proximal extent of aganglionosis depends on an adequate biopsy specimen as well as an accurate interpretation of the histopathology [12]. Vital to the correct diagnosis is understanding the transition zone, which is between the normal ganglionated and the aganglionic segments of the intestine. In this review, we evaluated the course and outcome in patients with HD post pull-through who had residual aganglionosis or transition-zone bowel and required reoperations for persistent obstructive symptoms.

1. Materials and methods

Ninety-three children with HD who required reoperation were referred to us between January 1996 and December 2009 for recurrent problems after a pull-through performed at another institution. All were evaluated with a history and physical examination, a contrast enema, and an examination under anesthesia with a rectal biopsy when indicated [3,13]. We have previously published our results on reoperations for gross anatomical causes such as strictures, fistulae, constricting cuffs, and megarectal pouches [2,3]. In this review, we chose to analyze those with histologic indications. Twenty-five patients had residual aganglionosis and/or histopathologic changes consistent with a transition zone at the distal pull-through. Nine of these were excluded because they had additional indications for surgery such as a constricting Soave cuff, stricture, or megarectal pouch. We reviewed the clinical presentation, operative management, and the postoperative course after the reoperation for the remaining 16 children who only had a histopathologic indication. Data are quoted as median (range).

2. Results

Children (median age, 7.5 [2-17] years) presented at 6 to 66 months after initial pull-through (performed at median, 5.5 months [5 days-2 years]). Fourteen were boys, and 2 were girls. One patient had a family history of HD—in a sibling who is doing well after pull-through. Eight of the patients had a primary pull-through at the initial surgery, whereas the rest had staged procedures. The pull-through technique was transabdominal Soave (n = 7), transanal

Table 1 Series of reoperated patients with HD reported in the literature for histopathologic indications

Author	Number undergoing reoperation	For pathology indications	Histopathology findings
Wilcox and Kiely, 1998 [8]	22	10	Aganglionosis (n = 9), abnormal acetylcholinesterase activity (n = 1)
Langer, 1999 [6]	9	6	Aganglionosis (n = 6), "intestinal neuronal dysplasia" (n = 1)
Weber et al, 1999 [7]	38	3	Aganglionosis (n = 3)
Ghose et al, 2000 [12]	13	13	Transition zone (n = 13)
van Leeuwen at al, 2000 [9]	19	5	Aganglionosis (n = 5)
Teitelbaum and Coran, 2003 [1]	26	8	Aganglionosis (n = 8)
Gobran et al, 2007 [5]	7	5	Aganglionosis (n = 4), "hypoganglionosis" (n = 1)
Hadidi et al, 2007 [11]	18	18	Aganglionosis (n = 14), "hypoganglionosis"/"dysganglionosis" (n = 4)
Peña et al, 2007 [2]	45	8	
Schweizer et al, 2007 [4]	17	16	Aganglionosis/dysganglionosis (n = 4), "hypoganglionosis"/"dysganglionosis" (n = 11), "dysganglionosis" (n = 1)
Obermayr et al, 2008 [10]	8	7	Aganglionosis (n = 7)

Soave-like (n = 7) (with laparoscopy [n = 4], robotic [n = 1], transanal alone [n = 2]), transanal Swenson-like (n = 1), and Duhamel (n = 1).

The predominant presenting symptoms were enterocolitis (n = 9 [56%]) and constipation (n = 7 [44%]). Five children (31%) had failure to thrive after the initial pull-through, and 5 (31%) had episodes of fecal impaction between the time of pull-through and presentation to us for evaluation.

The transition zone at the time of the initial pull-through was in the rectosigmoid (n = 11) and descending colon (n = 2) (location not stated, n = 3). None of the children who were studied had total colonic aganglionosis. We were able to review the slides of the intraoperative frozen-section biopsy taken at the level of the planned pull-through in 3 children. The decision as to where to perform the anastomosis was made based on this frozen section. All of these were seromuscular biopsies without submucosa. The rectal biopsy that we did later, during our evaluation of these children, showed the presence of hypertrophic nerves in the submucosa, with normal ganglion cells, consistent with a transition-zone pull-through (Fig. 2).

All of the 16 children with only histopathologic indications for a redo had hypertrophic nerves. Ten had hypertrophic nerves with normal ganglion cells. In the remaining 6, our biopsy showed both absent ganglion cells and hypertrophic nerves.

Eleven children with abdominal distension were placed on irrigations while awaiting surgery, and metronidazole was given to those with enterocolitis. Two children needed a diversion before the reoperation: 1 was severely impacted and did not tolerate irrigations, and the other had enterocolitis and failure to thrive.

The reoperation consisted of a transanal pull-through (n = 15) or a redo via a posterior sagittal approach (n = 1), preferred because of excessive pelvic scar tissue. Of the 15 who had a transanal pull-through, 10 had laparoscopy or laparotomy to complete the colonic mobilization. In 5 patients, the redo was done transanally alone. The median length of bowel resected at the reoperation was 15 (6-31) cm.

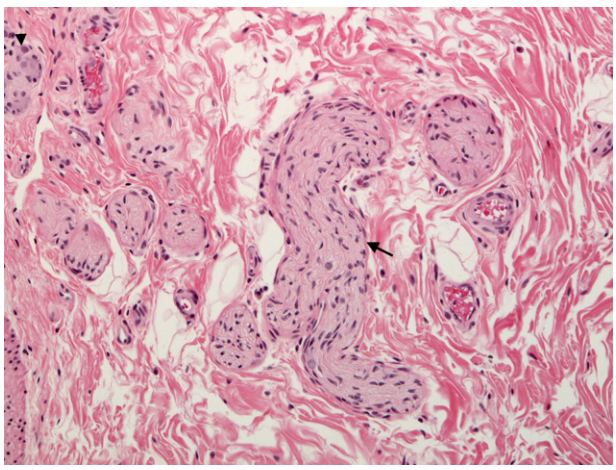

Fig. 2 Histologic section of the transition zone characterized by abundance of ganglion cells and hypertrophic nerves.

Median follow-up period was 16 months (3 months-10 years). Eleven (85%) of the 13 patients who are above the age of toilet training have voluntary bowel movements, with normal stooling while on little or no medication (laxatives). One child with Down's syndrome had the initial pull-through bowel anastomosed to the anocutaneous junction and still has a diverting stoma. We have reported previously that the loss of the dentate line is a cause for fecal incontinence [13] and the decision was made to leave him diverted. Another patient has soiling, despite having an intact anal canal and daily enemas. One patient was lost to follow-up. The remaining 2 patients are less than 3 years of age and have not been assessed for fecal continence.

No patient had recurrent enterocolitis requiring irrigations after the reoperation, and all thrived with good weight gain.

3. Discussion

Although many surgeons tell the parents of a child who has had a pull-through and is now having problems that they will "outgrow" them, we believe there is a need to have a high index of suspicion for those not doing well after a pull-through to detect those with anatomically or histopathologically correctable problems [3]. Children with persistent problems including constipation, enterocolitis, fecal impaction, and failure to thrive can present early or years after their initial pull-through [4,8]. Although some will improve over time, despite having early postoperative problems, a protocol to evaluate such patients is vital to detect those with anatomical or pathologic complications [2,3]. Nonoperative measures, such as rectal irrigations, for those with physiologic problems are beneficial before reoperation [13].

The shift toward primary pull-through has made the issue of intraoperative biopsy vital [14,15]. Surgeons are very dependent upon intraoperative frozen section [16]. In a review of 304 children who had intraoperative frozen-section analysis during surgery for HD, 9 (3%) had a discrepancy between the frozen-section diagnosis and the final pathologic diagnosis, with a significant impact on clinical results and management [17]. Sources of errors that can occur during the interpretation of the frozen section include sampling error and technical problems such as misreading and misdiagnosis [17,18]. Our study suggests that a seromuscular biopsy (without submucosa) for intraoperative frozen section is not adequate for the determination of the level of aganglionosis because it may miss submucosal nerve hypertrophy. This is similar to what others have shown, that the use of single-point extramucosal biopsies contributed to the incorrect mapping

of the level of aganglionosis in children [12,18]. In the original reports of De la Torre-Mondragón and Ortega-Salgado [14] and Langer et al [15] popularizing the single-stage transanal pull-through, which many surgeons now perform, full-thickness intraoperative biopsies were taken. In Georgeson's technique of primary laparoscopic-assisted endorectal pull-through, the intraoperative biopsy involves using a laparoscopic Metzenbaum scissors to take seromuscular biopsies and incising down to the mucosa [19], which would include the submucosa in the specimen. We are concerned that, in an attempt to avoid incising the mucosa and then needing to stitch it closed, the sample may not be taken deep enough. If the biopsy technique is not done correctly, submucosa can be missed. If the sample was thin, once the pulled-through bowel is ready for anastomosis, perhaps a confirmatory full-thickness biopsy should be sent to reduce the risk of pulling through a transition-zone segment of bowel [3,12,18]. Another option is to elevate the rectosigmoid to the umbilicus with a Hegar dilator and do an open-technique full-thickness biopsy [20].

The diameter of the nerve trunks is a vital histologic feature that is often overlooked in the determination of transition-zone bowel [12]. A nerve trunk that is larger than 40 μm is positively predictive of a transition zone or an area of aganglionosis [21]. It is vital that the pathologist reports not only on the presence or absence of ganglion cells but also on the thickness of the nerve trunks, and the surgeon should insist on this reporting of the frozen section.

Acquired aganglionosis is an entity sometimes proposed as a cause of persistent obstruction post pull-through [1,22]. Relative ischemia at the point of anastomosis, owing to devascularization, excessive retraction, or stretching, and circulating autoantibodies have been proposed as possible etiologic mechanisms [1,22,23]. West et al [22] presented 5 children who had aganglionosis after pull-through for HD and reported normal ganglion cells on review of the slides of the original pull-through. Although, there was no comment on whether the nerve trunks were examined. Considering that most reports on acquired aganglionosis date back more than 10 years [22,23], with subsequent improvement in the histopathologic diagnosis of HD [24,25] and our current knowledge of the possible pitfalls of histopathology [4,12], a more detailed histopathologic examination will be needed to confirm the acquired nature of aganglionosis in this subset of patients. Possible explanations for the discrepancies between the frozen section and postoperative pull-through histology in these reports are unevenness in the circumferential distribution of ganglion cells in the transition zone [18,26], that there was an error in the histopathology, or that submucosa was not sampled. Freeze artifacts in the intraoperative sample may also play a role [17]. In certain centers, without access to frozen-section pathology, a reasonable approach is laparoscopic biopsy only and then waiting for permanent section analysis.

Intestinal neuronal dysplasia (IND) [27] is frequently reported as responsible for the persistence of obstructive symptoms after an HD pull-through [28,29]. Yet others have found that IND is rarely associated with the problems that occur after the pull-through [1,7,30]. We suspect that many interpretations of IND are actually transition-zone pathology in HD [30] and would advocate for a reanalysis of these specimens with this concept of *transition zone* in mind.

Although some children with persistent constipation improve with conservative management [13], the presence of aganglionosis or transition-zone bowel means that resection of this section of bowel may cure them of their symptoms. A reoperation is generally recommended for the surgical management of residual aganglionosis [5,12]. Less extensive procedures such as sphincter myotomy or myectomy have been proposed but are limited by the proximal extent of the procedure, are associated with unsatisfactory and inconsistent results, and can lead to fecal incontinence [4,7,12,31]. Wildhaber et al [31], in one of the largest reports on posterior sphincter myectomy, reported a failure rate of 83% in children with persistent post pull-through constipation and residual aganglionosis who underwent the procedure. In these cases, it is unclear what the original technique used for the pull-throughs was. For example, perhaps a posterior myectomy in a post Soave case is actually incising a constricting cuff.

Only 5 (38%) of 14 children had a totally transanal approach; severe scarring of the neorectum and adhesions to the pelvic wall in the remaining 10 patients necessitated laparoscopy or laparotomy to complete the mobilization. We have shown that the dissection of the distal pull-through can be done transanally in almost all cases; only when the pelvis is frozen is the posterior sagittal incision required [2].

The comparison of results between studies is limited because of the different variables used by each author. In those that are above the age of toilet training, most (83%) have voluntary bowel movements after reoperation. Only 1 child, who had the anal canal damaged at the initial pull-through with an anocutaneous anastomosis [13], now has an ileostomy. Because of this finding in a series of patients, we and others advise commencing the transanal dissection 1 to 2 cm above the dentate line to prevent such problems [13,20]. Eighty percent of children in one series had good "stooling" outcome after the redo pull-through [4]. Similarly, 15 of 19 patients who had redo pull-through during a 24-year period were continent of stools between bowel movements but included patients with other indications for the repeated pull-through [9]. Ninety-one percent of the children who had redo pull-through in another series were considered cured by the authors—cure was characterized by absence of diversion, normal stooling pattern for age with

little or no oral medications, and requiring occasional rectal irrigations or enemas [7]. Conversely, in a review of 12 children who had reoperative surgery for a transition-zone pull-through, 4 are fully continent, 3 have permanent stomas, 2 are clean on antegrade continent enemas, and 3 remain incontinent [12]. Finally, in another review, 70% of children have normal or near normal fecal control and 25% are on some form of bowel management [8].

In conclusion, the child with recurrent symptoms after pull-through for HD may have residual aganglionosis or transition-zone bowel and could benefit from reoperative treatment. A full-thickness biopsy at the time of the initial pull-through, to include the mucosa and submucosa, may increase the possibility of identifying hypertrophic nerves and, therefore, identifying the transition zone.

References

[1] Teitelbaum DH, Coran AG. Reoperative surgery for Hirschsprung's disease. Semin Pediatr Surg 2003;12:124-31.
[2] Peña A, Elicevik M, Levitt MA. Reoperations in Hirschsprung disease. J Pediatr Surg 2007;42:1008-14.
[3] Levitt MA, Dickie B, Peña A. Evaluation and treatment of the patient with Hirschsprung disease who is not doing well after a pull-through procedure. Semin Pediatr Surg 2010;19:146-53.
[4] Schweizer P, Berger S, Schweizer M, et al. Repeated pull-through surgery for complicated Hirschsprung's disease—principles derived from clinical experience. J Pediatr Surg 2007;42:536-43.
[5] Gobran TA, Ezzat A, Hassan ME. Redo transanal endorectal pull-through: a preliminary study. Pediatr Surg Int 2007;23:189-93.
[6] Langer JC. Repeat pull-through surgery for complicated Hirschsprung's disease: indications, techniques, and results. J Pediatr Surg 1999;34:1136-41.
[7] Weber TR, Fortuna RS, Silen ML, et al. Reoperations for Hirschsprung's disease. J Pediatr Surg 1999;34:153-7.
[8] Wilcox DT, Kiely EM. Repeat pull-through for Hirschsprung's disease. J Pediatr Surg 1998;33:1507-9.
[9] van Leeuwen K, Teitelbaum DH, Elhalaby EA, et al. Long-term follow-up of redo pull-through procedures for Hirschsprung's disease: efficacy of the endorectal pull-through. J Pediatr Surg 2000;35:829-33.
[10] Obermayr F, Hacker HW, Bornemann A, et al. Redo-endorectal pull through following various pull through procedures in Hirschsprung's disease. Langenbecks Arch Surg 2008;393:493-9.
[11] Hadidi A, Bartoli F, Waag KL. Role of transanal endorectal pull-through in complicated Hirschsprung's disease: experience in 18 patients. J Pediatr Surg 2007;42:544-8.
[12] Ghose SI, Squire BR, Stringer MD, et al. Hirschsprung's disease: problems with transition-zone pull-through. J Pediatr Surg 2000;35:1805-9.
[13] Levitt MA, Martin CA, Olesevich M, et al. Hirschsprung disease and fecal incontinence: diagnostic and management strategies. J Pediatr Surg 2009;44:271-7.
[14] De la Torre-Mondragón L, Ortega-Salgado JA. Transanal endorectal pull-through for Hirschsprung's disease. J Pediatr Surg 1998;33:1283-6.
[15] Langer JC, Minkes RK, Mazziotti MV, et al. Transanal one-stage Soave procedure for infants with Hirschsprung's disease. J Pediatr Surg 1999;34:148-51.
[16] Maia DM. The reliability of frozen-section diagnosis in the pathologic evaluation of Hirschsprung's disease. Am J Surg Pathol 2000;24:1675-7.
[17] Shayan K, Smith C, Langer JC. Reliability of intraoperative frozen sections in the management of Hirschsprung's disease. J Pediatr Surg 2004;39:1345-8.
[18] Farrugia MK, Alexander N, Clarke S, et al. Does transitional zone pull-through in Hirschsprung's disease imply a poor prognosis? J Pediatr Surg 2003;38:1766-9.
[19] Georgeson KE, Robertson DJ. Laparoscopic-assisted approaches for the definitive surgery for Hirschsprung's disease. Semin Pediatr Surg 2004;13:256-62.
[20] De la Torre L, Langer JC. Transanal endorectal pull-through for Hirschsprung disease: technique, controversies, pearls, pitfalls, and an organized approach to the management of postoperative obstructive symptoms. Semin Pediatr Surg 2010;19:96-106.
[21] Monforte-Muñoz H, Gonzalez-Gomez I, Rowland JM, et al. Increased submucosal nerve trunk caliber in aganglionosis: a "positive" and objective finding in suction biopsies and segmental resections in Hirschsprung's disease. Arch Pathol Lab Med 1998;122:721-5.
[22] West KW, Grosfeld JL, Rescorla FJ, et al. Acquired aganglionosis: a rare occurrence following pull-through procedures for Hirschsprung's disease. J Pediatr Surg 1990;25:104-9.
[23] Smith VV, Gregson N, Foggensteiner L, et al. Acquired intestinal aganglionosis and circulating autoantibodies without neoplasia or other neural involvement. Gastroenterology 1997;112:1366-71.
[24] Thapar N. New frontiers in the treatment of Hirschsprung disease. J Pediatr Gastroenterol Nutr 2009;48:S92-4.
[25] Staines WA, Bettolli M, De Carli C, et al. Fast evaluation of intraoperative biopsies for ganglia in Hirschsprung disease. J Pediatr Surg 2007;42:2067-70.
[26] White FV, Langer JC. Circumferential distribution of ganglion cells in the transition zone of children with Hirschsprung disease. Pediatr Dev Pathol 2000;3:216-22.
[27] Meier-Ruge W. Über ein Erkrankungsbild des Colon mit Hirschsprung-Symptomatik. Verh Dtsch Ges Pathol 1971;55:506-9.
[28] Kobayashi H, Hirakawa H, Surana R, et al. Intestinal neuronal dysplasia is a possible cause of persistent bowel symptoms after pull-through operation for Hirschsprung's disease. J Pediatr Surg 1995;30:253-9.
[29] Moore SW, Millar AJW, Cywes S. Long-term clinical, manometric, and histological evaluation of obstructive symptoms in the postoperative Hirschsprung's patient. J Pediatr Surg 1994;29:106-11.
[30] Csury L, Peña A. Intestinal neuronal dysplasia: myth or reality? Literature review. Pediatr Surg Int 1995;10:441-6.
[31] Wildhaber BE, Pakarinen M, Rintala RJ, et al. Posterior myotomy/myectomy for persistent stooling problems in Hirschsprung's disease. J Pediatr Surg 2004;39:920-6.

Discussion

Q: Agostino Pierro, Institute of Child Health, London, UK: I was a little confused by some of the data presented – you said that you did 93 re-do pull-through operations and in 25 you had a histological problem, so what were the indications for the others?

A: Taiwo Lawal: The other ones had anatomic problems such as a twist in the original pull-through procedure; or stricture; or an obstructing cuff or sometimes there was a histologically normal but abnormally functioning bowel. Twenty five had abnormal pathology but nine were excluded from this study because they also had anatomical problems

(e.g. strictures). So therefore we only reviewed the 16 patients who had purely a histological problem.

Q: Ian Sugarman, Leeds General Infirmary, UK: Can I ask what operation they had primarily and is there a correlation between that and problems?

A: Although we looked at that, the number of patients (n = 16), was not really large enough for us to determine any real relationship. However it seemed to be irrelevant.

Q: Dr Rameep, Queen's Medical Centre, Nottingham, UK: Of the 16 patients, only six were confirmed as having a segment which was aganglionic and had hypertrophic nerves. I gather that you consider hypertrophic nerves alone as sufficient abnormality for redo surgery?

A: Yes, we considered any patient with post-operative problems that had hypertrophic nerves but were ganglionic in our rectal biopsy as abnormal.