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ORIGINAL ARTICLE

# Residual aganglionosis after pull-through operation for Hirschsprung's disease: a systematic review and meta-analysis

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**Abstract**
*Purpose* Most patients with Hirschsprung's disease (HD) have a satisfactory outcome after pull-through (PT) operation. However, some children continue to have persistent bowel symptoms after the initial operation and may require redo PT. Redo PT operation in HD is usually indicated for anastomotic strictures or residual aganglionosis (RA). We designed this meta-analysis to determine the incidence and outcome of RA among patients with HD following PT operation.
*Methods* A meta-analysis of redo PT operations for HD reported in the literature between 1985 and 2011 was performed. Detailed information was recorded in patients with RA and transition-zone bowel (TZB), including recurrent bowel problems, histological findings on repeat rectal biopsy, type of redo PT operation and outcome.
*Results* Twenty-nine articles reported 555 patients with redo PT operations. 193 (34.8%) patients demonstrated abnormal histological findings on rectal biopsy with 144 patients showing RA and 49 patients showing TZB. These 193 patients presented with persistent constipation ($n = 135$), recurrent enterocolitis ($n = 45$) and abnormal histology of the pulled-through bowel ($n = 13$). Mean age at redo PT was 4.4 years (range 4 months–17 years). Redo procedures were Duhamel ($n = 57$), transanal endorectal PT ($n = 40$), Soave ($n = 35$), Swenson ($n = 10$), posterior sagittal approach ($n = 1$) and not reported ($n = 50$). Follow-up information after redo PT was available in 134 (69.4%) patients and not available in 59 patients. Of the 134 patients, 99 (73.9%) patients had normal bowel habits, 19 patients had persistent constipation/soiling and 16 patients had recurrent enterocolitis.
*Conclusion* This meta-analysis reveals that RA and TZB are the underlying causes of persistent bowel symptoms in one-third of all patients with HD requiring redo PT operation. Most patients have a satisfactory outcome after redo operation. Rectal biopsy should be performed in all patients with recurrent bowel problems after PT operation.

**Keywords** Residual aganglionosis · Transition-zone bowel · Redo pull-through operation · Reoperation Hirschsprung's disease · Hirschsprung's disease outcome

## Introduction

Pull-through (PT) operations for Hirschsprung's disease (HD) generally result in a satisfactory outcome [1]. However, some patients after definitive PT operation have disturbances of bowel function such as constipation, enterocolitis and recurrent obstructive symptoms [2–9]. In the majority of these patients, residual bowel problems can be managed by non-surgical treatment such as laxatives, enemas or intrasphincteric botulinum toxin injection [10–12]. In a few patients, persistent abdominal distension, constipation or enterocolitis is due to postoperative stricture or retained aganglionic segment which may require a redo PT operation [13–17]. We designed this meta-analysis to determine the incidence and outcome of residual aganglionosis (RA) in patients with HD following PT operation.

## Methods

PubMed® and MEDLINE® databases were searched for all studies that reported cases of patients with HD who had

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undergone redo PT operations for RA or transition-zone bowel (TZB) after initial operation between 1985 and 2011. The search terms were "residual aganglionosis", "transition-zone bowel", "redo and repeat pull-through", "reoperation Hirschsprung's disease" and "postoperative follow-up and outcome Hirschsprung's disease". The reference lists from retrieved articles were reviewed for additional cases. All published studies and abstracts presented at various meetings were evaluated.

Detailed information was recorded regarding type of study, gender, recurrent bowel symptoms, histological findings on repeat rectal biopsy, patient's age at initial PT and redo PT operation, type of surgical procedures performed and postoperative follow-up with recurrent symptoms. Only publications containing all the relevant details were included in the literature review. Publications not giving adequate clinical data of patients were excluded.

## Results

Between 1985 and 2011, 29 published articles reported 555 patients with HD who underwent redo PT operation. 193 (34.8%) patients demonstrated abnormal histological findings on repeat rectal biopsy. 144 (74.6%) patients revealed RA and 49 (25.4%) patients TZB (Table 1). 24 articles (82.8%) were from single centers, and 5 (17.2%) were from multicenter studies.

Information about patient's gender was reported in 135 (69.9%) patients. A male-to-female ratio of 3.5:1 was observed. In 143 (74.0%) patients, the initial procedure was documented. 82 had a Soave procedure, 24 had a Duhamel procedure, 15 had a Rehbein procedure, 14 had a Swenson procedure, 7 had a transanal endorectal PT (TERPT), and 1 had a posterior sagittal approach. In 50 patients, the initial type of procedure was not reported.

In 13 (6.7%) patients redo PT operation was performed because of histological evidence of RA in the resected proximal margin of the pulled-through bowel. Of the remaining 180 patients, 135 had persistent abdominal distension/constipation and 45 had recurrent episodes of enterocolitis.

Patient's age at redo PT operation was documented in 108 (56.0%) patients with a mean of 4.4 years (range 4 months–17 years). Time between initial PT and redo PT operation was reported in 74 (38.3%) patients with a mean of 2.8 years (range 6 months–8 years). In 143 (74.1%) patients, the redo procedure was documented. 57 had a Duhamel procedure, 40 had a TERPT, 35 had a Soave procedure, 10 had a Swenson procedure and 1 had a posterior sagittal approach. In 50 patients, the type of redo procedure was not reported.

Follow-up was reported in 134 (69.4%) patients with a mean follow-up time of 4.1 years (range 3 months–23 years). Of the 134 patients, 99 (73.9%) patients had normal bowel habits after redo PT operation. Nineteen patients had persistent or intermittent constipation with occasional soiling and 16 patients had recurrent enterocolitis with or without perianal excoriation. Except for occasional soiling most of the patients were fecally continent and had normal bowel movements. There was no significant difference in functional outcome between the various redo PT procedures.

## Discussion

Over the years, various PT operations have been used to treat patients with HD [18–23]. It has been shown in several studies that there is no statistically significant difference in the functional outcome with respect to bowel function between the various PT procedures [24–27]. For a PT operation to be successful, it is essential that all aganglionic bowel is resected and bowel with normal innervations is anastomosed to the anus. Our meta-analysis reveals that RA and TZB are the underlying causes of persistent bowel symptoms in one-third of all patients requiring redo PT operation.

A redo PT operation for RA or TZB is potentially preventable by accurate identification of the proximal margin of the aganglionic bowel and transition-zone by an experienced histopathologist [28]. During frozen section analysis at the time of the initial PT operation, the pathologist must confirm normal ganglion cells and absence of nerve trunks at the site of the planned anastomosis. One major problem with the intraoperative frozen section biopsies is that it can indicate the presence of ganglion cells without differentiating between hypo- and dysganglionosis [29]. Shayan et al. [30] reported that 3% of 304 children who had intraoperative frozen section analysis during PT operation showed a discrepancy between the frozen section diagnosis and the final pathological diagnosis. The use of rapid technique of acetylcholinesterase staining may help overcome this problem [31, 32]. Another factor which may help prevent pulling-through the transition-zone for anastomosis is resecting several centimetres above the proximal ganglionic bowel identified by the pathologist during frozen sections.

Constipation after PT operation in the vast majority of patients can be managed by non-operative methods such as laxatives and enemas [10, 11]. Postoperative enterocolitis requires rectal irrigation with or without metronidazole prophylaxis [25]. However, if a patient continues to have persistent constipation, abdominal distension or recurrent

**Table 1** Published articles reporting redo pull-through (PT) operations for residual aganglionosis (RA) and transition-zone bowel (TZB) between 1985 and 2011

| Author | Year | No. of patients with redo PT operation | No. of patients with | | Initial operation | Recurrent symptoms after initial operation | Redo operation |
|---|---|---|---|---|---|---|---|
| | | | RA | TZB | | | |
| Polley et al. [7] | 1985 | 6 | 1 | | Soave | Constipation | Soave |
| West et al. [9] | 1990 | 4 | 2 | | Duhamel, Swenson | Constipation | Swenson |
| Liem et al. [35] | 1995 | 3 | 1 | | Swenson | Constipation | Swenson |
| Langer et al. [36] | 1996 | 36 | 3 | | Soave | | |
| Wilcox and Kiely [17] | 1998 | 22 | 9 | | Soave, Duhamel, Swenson | Constipation | Duhamel |
| Weber et al. [16] | 1999 | 38 | 3 | | Soave | Constipation | Soave, Duhamel |
| Langer [13] | 1999 | 9 | 6 | | Soave, Duhamel, Swenson | Constipation, enterocolitis | Duhamel |
| Langer et al. [37] | 2000 | 4 | 1 | | Soave | Constipation | |
| van Leeuwen et al. [15] | 2000 | 19 | 5 | | Soave, Rehbein | Constipation | Soave, Duhamel, Swenson |
| Aggarwal et al. [38] | 2002 | 4 | 1 | | Soave | Constipation | Soave + posterior sagittally |
| Ghose et al. [29] | 2002 | 13 | | 7 | Soave, Duhamel | Constipation, incontinence | Duhamel |
| Langer et al. [39] | 2003 | 4 | 1 | | Soave | Constipation | Duhamel |
| Keshtgar et al. [40] | 2003 | 2 | 2 | | Duhamel | Constipation, incontinence | Duhamel |
| Teitelbaum and Coran [14] | 2003 | 26 | 8 | | | Constipation | Soave, Duhamel, Swenson |
| Farrugia et al. [41] | 2003 | 1 | | 1 | Duhamel | Enterocolitis | |
| Wildhaber et al. [42] | 2004 | 5 | 5 | | | Constipation | |
| Langer [43] | 2004 | 19 | 8 | | Soave, Duhamel, Swenson | Constipation, enterocolitis | Duhamel |
| Wester et al. [44] | 2006 | 2 | 2 | | Rehbein | Constipation | Soave |
| Gobran et al. [45] | 2007 | 7 | 4 | 2 | TERPT, Soave | Obstruction | TERPT |
| Schweizer et al. [46] | 2007 | 17 | 4 | 11 | Soave, Duhamel, Rehbein | Constipation | Duhamel |
| Hadidi et al. [47] | 2007 | 18 | 14 | 4 | Soave, Duhamel, Swenson, Rehbein | Constipation, enterocolitis | TERPT |
| Peña et al. [28] | 2007 | 45 | 8 | | TERPT, Soave, Duhamel, Swenson | Enterocolitis, incontinence | TERPT, posterior sagittally |
| Obermayr et al. [48] | 2008 | 8 | 7 | | Soave, Duhamel, Rehbein | Constipation, enterocolitis | Soave |
| Gad El-Hak et al. [49] | 2010 | 2 | 2 | | Swenson | Constipation | Swenson |
| Levitt et al. [33] | 2010 | 75 | 15 | 8 | | | TERPT, posterior sagittally |
| Vũ et al. [50] | 2010 | 2 | 2 | | TERPT | Constipation | TERPT |
| Pini-Prato et al. [34] | 2010 | 70 | 23 | 6 | Soave, Duhamel, posterior sagittally | Constipation, enterocolitis | Soave, Duhamel, Swenson |
| Stensrud et al. [27] | 2010 | 1 | 1 | | TERPT | Constipation | Soave |
| Lawal et al. [51] | 2011 | 93 | 6 | 10 | Soave, Duhamel, Swenson | Constipation, enterocolitis | TERPT, posterior sagittally |
| **Total no.** | | 555 | 144 | 49 | | | |

*TERPT* transanal endorectal PT

episodes of enterocolitis, a full thickness rectal biopsy is indicated to rule out RA or TZB [33].

The presence of RA or TZB means that resection of this section of bowel may cure the patients of their recurrent symptoms. Thus, a redo PT is generally recommended for surgical management of RA. However, the choice of which procedure to use is far from being obvious. Any surgical technique may be considered, depending on conditions of each patient's anatomy. Therefore, type of previous failed procedure, level of anastomosis, rectal blood supply and presence of fibrosis or inflammation in the perirectal pouches must be considered [34]. In the present meta-analysis, most patients with HD had normal bowel function after redo PT operation. The vast majority of patients had either Duhamel procedure, TERPT or Soave procedure for redo PT operation.

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