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Hirschsprung disease: common and uncommon variants

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OVERVIEW OF SHORT-SEGMENT HIRSCHSPRUNG DISEASE

The most common variant of Hirschsprung disease (HSCR) is short-segment or rectosigmoid disease. The majority (70%–85%) of HSCR is limited to the rectum or sigmoid colon.[1] These patients usually present in the neonatal period with 'typical' signs and symptoms: failure to pass meconium within the first 24–48 hours, abdominal distention, vomiting, explosive passage of stool/gas, and failure to thrive.[1 2] Patients may also present with signs and symptoms of Hirschsprung-associated enterocolitis (HAEC), which include abdominal tenderness, fever, explosive diarrhea, and bloody stools.[3] Rectal irrigation is usually an effective first-line management strategy in patients with short-segment HSCR and is the mainstay of treatment for HAEC.

In short-segment HSCR, a contrast enema may show a transition zone between contracted distal aganglionic rectosigmoid and dilated proximal ganglionic colon. It is worth noting, however, that the radiographic transition zone may not correlate with the histologic transition zone.[4] A rectosigmoid ratio of <1 is also suggestive of HSCR.[5] Though imaging may be helpful in establishing the diagnosis and formulating a surgical plan, rectal biopsy remains the gold standard for diagnosing all variants of HSCR.[6]

Most short-segment HSCR can be treated with a primary endorectal pull-through without the need for diversion. Timing of the pull-through and the type of pull-through performed depends on surgeon preference and comfort level. A recent retrospective study found that delaying primary pull-through ≥31 days with interim rectal irrigations is a safe alternative to neonatal repair; most of the studied patients had short-segment disease.[7] This delayed approach may make technical aspects of the operation easier and has the added benefit of allowing parents to gain experience with rectal irrigation. Studies comparing Swenson, Yancey-Soave and Duhamel pull-through for short-segment disease have been limited by small sample sizes, heterogeneous patient selection and their retrospective nature. Many of these studies have reported conflicting results. One study looking mostly at patients with short-segment HSCR found that patients had less soiling after a Yancey-Soave pull-through compared with Duhamel.[8] A survey of European Paediatric Surgeons' Association (EUPSA) members found that most surgeons (65%) would perform a Yancey-Soave pull-through for short-segment HSCR.[9] A total transanal approach is possible for short-segment HSCR and has gained popularity due to its minimally invasive and scarless nature,[9] but it is not yet known how long-term outcomes compare to laparoscopic pull-through.[10–12] Caution with the total transanal approach is advised since, even for short-segment disease, the transition zone may be greater than 5 cm and additional mobilization may be needed.[13] Identifying the level of normally ganglionated bowel prior to starting the transanal dissection prevents the situation of unexpectantly discovering long-segment disease after having already performed the rectal dissection. This can be achieved either with laparoscopy or transumbilical biopsy with a rectal dilator. Regardless of the type of pull-through performed, the presence of normal ganglion cells at the circumferential proximal resection margin should be confirmed by frozen section at the time of pull-through.[14]

Long-term outcomes for short-segment HSCR are generally favorable, but complications are not uncommon and postoperative vigilance is paramount. One US-based study found that 17% of patients were re-admitted to the hospital within 30 days of pull-through procedure, including 9% with HAEC. Within 2 years of pull-through, 10% of patients required a reoperation.[15] Several guidelines exist for the evaluation and management of the patient with HSCR who is not doing well after pull-through surgery.[16–21] Guidelines also exist for the early diagnosis and treatment of HAEC, a major cause of disease-related

Table 1 Recommend nomenclature for common and uncommon variants of Hirschsprung disease

Nomenclature	Definition
Ultrashort-segment	No clear definition and usage of this term should be abandoned
Short-segment	Aganglionosis up to the sigmoid colon-descending colon junction
Long-segment	Aganglionosis that extends above the sigmoid colon but does not involve the entire colon
Total colonic	Aganglionosis of the entire colon and <5 cm of terminal ileum
Small intestinal	Aganglionosis involving >5 cm of small intestine
Total intestinal	<20 cm of ganglionated intestine beyond the ligament of Treitz
Skip segment	Segmental aganglionosis (skip lesions) in one or more areas of the intestine

Adapted from Kawaguchi *et al*.[25]

mortality in patients with HSCR.[3] So far studies have found no benefit to the use of prophylactic Botox[22 23] or probiotics[24] for the prevention of HAEC. Rectal irrigation, often in combination with antibiotics, is currently the only effective remedy for HAEC.[3]

LONG-SEGMENT AND TOTAL COLONIC HSCR

Though the definition of long-segment HSCR varies in the literature, the American Pediatric Surgical Association Outcomes and Evidence Based Practice Committee defines long-segment disease as aganglionosis from sigmoid colon-descending colon junction up to the cecum with ganglion cells present in the colon, or in other words, aganglionosis that extends above the sigmoid colon but does not involve the entire colon.[25] This is in contrast to total colonic HSCR, which is defined as aganglionosis of the entire colon and less than 5 cm of distal small intestine and small intestinal HSCR which is defined as aganglionosis involving greater than 5 cm of small intestine[25] (table 1).

About 15% of HSCR is long-segment.[25] In contrast to short-segment HSCR, contrast enema is less accurate in predicting the transition zone for long-segment and total colonic aganglionosis and the rectosigmoid ratio may be normal in these variants.[4] Instead, a microcolon or a comma-shaped colon may be seen.[25] Optimum timing of pull-through surgery for long-segment HSCR is complex and depends on several factors. In many cases, intestinal diversion is needed as rectal irrigations may not be effective for decompressing long-segment HSCR. Most surgeons recommend a temporary ileostomy and full-thickness colonic mapping if ganglion cells cannot be identified proximal to the splenic flexure.[26] In operations for long-segment HSCR, blood supply to the pull-through segment is an important consideration. Disease extending to the descending colon requires mobilization of the splenic flexure and may require ligation of the left colic artery. Disease extending to the transverse colon or ascending colon may require ligation of the middle colic artery or right colic artery, respectively. Furthermore, de-rotation of the colon is required to prevent obstruction of the distal duodenum and twisting of the mesentery around the ileocolic artery. In all of these scenarios, special care must be taken to preserve the marginal artery which will supply the pull-through segment.

Approximately 8% of HSCR is total colonic.[25] Unlike short-segment HSCR which has a 4:1 male predominance, total colonic HSCR is equally common in girls and is more likely to be associated with a family history of HSCR.[2] Patients with total colonic HSCR should be managed with a diverting ileostomy at the time of diagnosis with close follow-up for nutritional support and monitoring of fluid/electrolyte balances. A pull-through operation can be performed when the ileostomy output reaches an applesauce-like consistency and is <30 mL/kg/day.[26] Fiber supplements and loperamide can be used to help achieve these goals. In addition, urine sodium should be >20 mmol/L and the patient should be maintaining an adequate growth trajectory. These milestones are usually met between 9 months and 18 months of age.[26] As with short-segment HSCR, there are few studies that rigorously compare the various surgical approaches to total colonic HSCR. In a survey of EUPSA members, Duhamel pull-through was the most common technique for total colonic HSCR (52%).[9] A recent multicenter study comparing Swenson versus Duhamel pull-through for total colonic aganglionosis found equivalent short-term and medium-term outcomes.[27] Long-term outcomes after pull-through for total colonic HSCR are expectedly worse than those for short-segment HSCR with 17.5% of patients requiring some sort of reoperation and 6.5% of patients requiring conversion to a permanent ileostomy due to postoperative complications.[28]

An extremely rare variant of HSCR is skip segment (skip lesion) or segmental aganglionosis in which a normally ganglionated segment of intestine is surrounded proximally and distally by aganglionic intestine.[29] This is most commonly associated with total colonic HSCR.[30] With preoperative colonic mapping, skip segment HSCR may be recognized and segments of functional colon may be preserved during pull-through surgery.

MANAGEMENT OF TOTAL INTESTINAL AGANGLIONOSIS

Near-total or total intestinal aganglionosis is rare (<1% of all cases)[1] and is defined as ganglionated small bowel length of <20 cm past the ligament of Treitz.[25] This rare

variant can be incredibly challenging to manage and the risk of intestinal failure is high. A recent consensus statement from the European Reference Network for rare Inherited and Congenital Anomalies recommended early referral to an intestinal rehabilitation center with timely listing for small bowel transplantation. They found that children with less than 80 cm of small bowel remaining had a poorer chance of weaning off parenteral nutrition.[31]

Once total intestinal aganglionosis is confirmed pathologically, a jejunostomy should be formed at least 40 cm distal to the ligament of Treitz. This will inevitably include aganglionic intestine proximal to the stoma. There is no benefit to resecting proximal aganglionic intestine beyond 40 cm.[31] It is the authors' opinion that the distal diverted bowel should be resected as this may increase the risk of enterocolitis and bacterial overgrowth; however, some surgeons may leave most or all of the aganglionic intestine in situ at the time of proximal diversion and consider resection only if symptoms of HAEC or overgrowth develop. Preserving the aganglionic intestine has the advantage of preserving the intra-abdominal domain for future intestinal transplantation and leaves the option for future colon patch-type pull-through procedures.

Treatment options for total intestinal HSCR are similar to treatments for other forms of intestinal failure due to short gut, namely: parenteral nutrition, GLP-2 agonists, bowel lengthening procedures, and intestinal transplantation. Specific to HSCR, there are several autologous intestinal reconstructive techniques intended to functionalize aganglionic bowel.[32 33] These operations are rarely performed now in the era of intestinal transplantation. A recent meta-analysis reported a survival rate of 66% after intestinal transplantation for total intestinal aganglionosis.[34]

DELAYED DIAGNOSIS AND STRATEGIES FOR MEGARECTUM

Some patients with HSCR present later in life with long-standing symptoms of constipation. There is no clear age delineation for delayed diagnosis, but studies suggest that worse outcomes may exist for patients diagnosed at 1 year of age and older.[35 36] Patients with delayed diagnosis usually have short-segment HSCR.[37] These patients may have a very distended rectum and/or colon (megarectum/megacolon) due to chronic functional obstruction. Motility in the dilated segments of colon is often impaired as it is in chronic idiopathic constipation.[38] Preoperative decompression of dilated colorectum should be considered either with rectal irrigations or a diverting stoma. Irrigations can prove challenging in this situation as the patients are older at initiation and the stool is often very thick. The goal of such decompression is both to improve function in the ganglionic bowel as well as to reduce colonic dilation and facilitate safe coloanal anastomosis. Manometry may be helpful in determining the function of chronically dilated segments and may guide operative planning for resection and pull-through.[39] In one study of 90 patients diagnosed with HSCR as adults, long-term functional outcome was strongly correlated with the degree of preoperative megacolon present.[40]

A recent multi-institutional study from the Pediatric Colorectal and Pelvic Learning Consortium found that patients diagnosed with HSCR at later ages were more likely to require intervention for constipation or incontinence and to require a diverting ostomy after pull-through.[36] Other studies have similarly found that patients with late diagnosis of HSCR are more likely to have postoperative complications such as anastomotic dehiscence.[35 37] Thus, a protective temporary diverting ostomy may be considered prior to or at the time of pull-through for patients with delayed diagnosis of HSCR.

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