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ORIGINAL ARTICLE

Gastroenterology

Utility of colonic manometry in children with Hirschsprung disease

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Abstract

Objectives: Abnormal motility of the residual colon has been reported in post-pull-through Hirschsprung disease (PT-HSCR) patients with persistent defecation problems. We reviewed the role of colonic manometry (CM) in the management of defecation disorders in these patients.

Methods: We retrospectively reviewed the medical record of PT-HSCR children who underwent CM for persistent symptoms of abnormal defecation. We reviewed their clinical course and its relation to CM findings.

Results: Thirty PT-HSCR patients underwent CM, of which five were diagnosed with transition zone pull-through and were excluded. Of the remaining 25 patients, 16 had colonic dysmotility, 8 had normal CM, and one had colonic hypermotility. In patients with dysmotility, five responded to ongoing medical management, three required surgical intervention (ileostomy), three remained symptomatic with medical management but not yet received surgical intervention, and five were lost to follow-up. In patients with normal CM, four responded to ongoing medical therapy, two required additional surgery (antegrade enema procedure), and two were lost to follow-up. The patient with hypermotility improved with adding loperamide.

Conclusions: Colonic dysmotility can occur in PT-HSCR patients with persistent defecation problems. CM was helpful in delineating the degree of colonic neuromuscular dysfunction. CM results were used in conjunction with other clinical data to determine optimal management. Our findings support that medical management should first be optimized before consideration of colonic manometry and surgical interventions.

KEYWORDS

colonic dysmotility, colonic hypermotility, fecal incontinence, utility

1 | INTRODUCTION

Hirschsprung disease (HSCR) is a congenital motor disorder of the intestine characterized by the absence of intrinsic ganglion cells in the submucosal and myenteric plexus of the intestinal tract.[1] The aganglionic segment includes the most distal colon and extends proximally to varying lengths. During peristalsis, the aganglionic segment fails to relax, producing a functional obstruction.[1] The mainstay of therapy is surgical resection of the aganglionic segment and a pull-through of the ganglionated segment. Despite a well-done surgical pull-through, more than 20% of patients experience persistent post-surgical defecatory problems, including constipation and fecal incontinence.[2,3] Persistent postsurgical defecatory problems may be secondary to aberrations in anatomy

(mechanical obstruction, compromised integrity of the anorectum), histopathology (residual aganglionosis, transition zone pull-through [TZPT]), or function (anorectal and/or colonic dysfunction).[2,4] Previous studies have reported abnormal motility of the residual colon despite the presence of ganglion cells.[4–6] The pathophysiology of colonic dysmotility in HSCR is not fully understood. However, abnormal ion channels,[7] altered neurotransmitter expression,[8] and a reduced number of interstitial cells of Cajal[9] have been implicated. Colonic manometry (CM) plays an essential role in evaluating the neuromuscular integrity of the colon, and in the medical and surgical management of children with defecation disorders.[10–12] However, the role of utilizing CM in postsurgical HSCR patients who have persistent defecatory problems is not well studied. In the present study, we aimed to describe the CM findings in postsurgical HSCR children with persistent defecatory concerns and to demonstrate their management and clinical outcomes in correlation with the CM results.

What is Known

- Post-pull-through Hirschsprung disease (PT-HSCR) patients with persistent defecation problems may have abnormal colonic motility.
- Colonic manometry has been used in these patients to understand the pathophysiology of their persistent symptoms.

What is New

- Colonic manometry is helpful in identifying existing colonic dysfunction in children with post-pull-through Hirschsprung disease (PT-HSCR) who present with persistent defecation problems.
- Medical management should first be optimized before consideration of colonic manometry and surgical interventions.
- Colonic manometry findings should be used in conjunction with the patient's clinical history and response to medical therapy to make surgical decisions in the appropriate clinical setting.

2 | METHODS

2.1 | Patient selection and clinical outcome

We conducted a single-center retrospective review of postsurgical HSCR patients under 21 years of age who underwent a CM study from 2012 to 2021 due to persistent postsurgical defecatory problems at Children's Hospital Los Angeles (CHLA). This study was approved by the Institutional Review Board at CHLA. We reviewed the medical records for patient demographics, clinical course, diagnostic workup, medical/surgical treatment rendered, and clinical outcomes. Elements of the diagnostic workup reviewed included barium enema, anorectal manometry (ARM), CM, and histopathology (rectal biopsy [RBx], surgical pathology). Treatments abstracted included oral and rectal therapy, biofeedback, and surgical interventions, including internal anal sphincter (IAS) botulinum toxin (BT) injection, redo pull-through, ileostomy or colostomy creation/takedown, colectomy, stricture dilation/stricturoplasty, rectal myomectomy, and/or appendicostomy/cecostomy.

2.2 | Colonic manometry assessment

All patients undergoing CM were admitted 2 days before the procedure and received a solution of polyethylene glycol 3350 with electrolytes through a nasogastric tube for bowel preparation. A rectal exam under anesthesia was performed for all patients before the colonoscopy to rule out distal mechanical obstruction. A water-perfused CM catheter with 8–16 recording sites spaced 5 or 10 cm apart was placed via colonoscopy, with the tip of the CM catheter clipped to the cecum. Before 2019, manometry studies were performed on the same day as catheter placement. Since 2019, the studies were conducted the next day following catheter placement. Colonic motility was assessed in the fasting state for 4 h and 1–1.5 h following the meal and medication provocation. The fasting period was shortened to 2 h if three or more high-amplitude propagated contractions (HAPCs) were noted throughout the colon during the first 2 h. Meal provocation included the usual tolerated meal for the patient with a minimum of 250 mL of formula provided orally or via G-tube or 400–1000 kcal regular diet as tolerated. Medication provocation was performed using a Bisacodyl enema solution (0.2–0.25 mg/kg rounded up to the nearest whole number, to a maximum of 10 mg), administered via the central lumen of the manometry catheter such that the solution was dispensed at the most proximal site of the colon corresponding to the tip of the catheter. A second dose of bisacodyl (either an equivalent or half dose compared to the first administration) was given 30 min after the first dose if suboptimal or no colonic response was noted. Colonic motility was assessed by evaluating the presence of HAPCs, defined as contractions with an amplitude of at least 60 mmHg, lasting at least 10 s, and having antegrade propagation of at least 30 cm. The study was considered normal if (a) the gastrocolic response to a meal was present and (b) meal- or bisacodyl-induced HAPCs were observed propagating from the proximal colon to the rectosigmoid junction or neorectum.[5,10,12] Colonic dysmotility was

characterized as total colonic dysmotility if no HAPCs were noted throughout all recording sites, or partial colonic dysmotility if HAPCs were limited to the proximal 50% of the recording sites only. Hypermotility of the colon was defined as the presence of three or more HAPCs traveling throughout the colon within the protocol fasting period.

3 | RESULTS

3.1 | Clinical characteristics

A total of 30 postsurgical patients with HSCR underwent CM. Five were noticed to have TZPT and were excluded from the analysis. Of the rest 25 patients, twenty-one (84%) were male. The median age when the CM study was performed was 7 years (range: 17 months– 21 years). The median interval between the primary surgery and the first CM study was 7 years (range: 2 months–19 years). Fifteen (60%) patients had their initial diagnosis, surgeries, and treatments outside our institution and were referred for motility evaluation. Fourteen (56%) patients had short-segment HSCR, four (16%) had long-segment HSCR (two left colonic, two transverse colonic), and seven (28%) were unknown. Eighteen (72%) had primary pull-through surgery before 1 year of age. Twelve (48%) patients had the Soave procedure, and one (4%) had the Swenson procedure. The type of pull-through was not documented in 12 (48%) patients. Sixteen (64%) patients had normal RBx with the presence of ganglion cells documented before the CM, and nine (36%) patients' post pull-through RBx results before the CM were not available.

Eight (32%) patients had chronic fecal retention (FR) without incontinence, 15 (60%) had chronic fecal retention with fecal incontinence (FRFI), and 2 (8%) had non-retentive fecal incontinence (NRFI). Before undergoing CM, twenty-one (84%) patients received oral laxatives, and 17 (68%) were on rectal regimens; of them, 14 (56%) were given both oral and rectal therapy. In addition, four patients (16%) received IAS BT injection. Seventeen patients had colonic manometry study performed on the same day as catheter placement, while e patients received the study on the day following catheter placement. Patient demographics and clinical characteristics are shown in Table 1.

TABLE 1 Patient demographics and clinical information.

Clinical information	Number (%)
Sex	
Male	21 (84%)
Female	4 (16%)
Age of primary pull-through surgery	
Less than 1 year of age	18 (72%)
Over 1 year of age	7 (28%)
Type of primary pull-through surgery	
Soave	12 (48%)
Swenson	1 (4%)
Unknown	12 (48%)
Type of Hirschsprung based on aganglionic segment	
Short segment	14 (56%)
Long segment	4 (16%)
Total	0 (0%)
Unknown	7 (28%)
Presenting symptoms	
Fecal retention without incontinence	8 (32%)
Fecal retention with incontinence	15 (60%)
Non-retentive fecal incontinence	2 (8%)
Intra-anal pressure on anorectal manometry (mmHg)	
<30	2 (8%)
30–60	9 (36%)
60–90	9 (36%)
>90	2 (8%)
Unknown	3 (12%)
Rectal biopsies before colonic manometry	
Normal rectal biopsies	16 (64%)
Unknown	9 (36%)
Treatments before colonic manometry	
Oral laxatives	21 (84%)
Rectal therapy	17 (68%)
Anal sphincter botulinum toxin injection	4 (16%)

3.2 | Colonic manometry characteristics and management outcomes

Of the 16 patients with normal RBx before CM, eleven (69%, FR = 5, FRFI = 6) were found to have colonic dysmotility including nine with total colonic dysmotility and two with partial colonic dysmotility. Five of the eleven patients with colonic dysmotility (45%) improved with an escalation of medical therapy by reinforcing compliance, modifying or optimizing laxative types and dosage (such as providing a higher dose of polyethylene glycol, and adding or increasing doses of senna or bisacodyl), and/or adding rectal therapy

(administrating normal saline plus minus glycerin or bisacodyl rectal irrigation); 2/11 (18%) underwent ileostomy formation with or without reversal, 3/11 (27%) were doing poorly on medical therapy and were offered surgical intervention including ostomy formation but declined or not yet performed, and 1/11 (9%) was lost to follow-up. Four of the sixteen patients (25%, FRFI = 4) had normal colonic motility; of them, one responded well to medical management, two proceeded with appendicostomy for poor tolerance of oral therapy with improved quality of life, and one was lost to follow-up. The final patient with normal RBx was diagnosed with colonic hypermotility and had improved continence after he was started on loperamide. Of the nine patients with unavailable RBx results before CM, five had colonic dysmotility (one received ileostomy creation and four were lost to follow-up) and four had normal colonic motility (three improved with ongoing medical therapy and one was lost to follow-up). Patient CM results and their treatment outcomes are shown in Figure 1.

We further divided these patients into two groups based on the timing of the manometry study. Eight patients had colonic manometry study performed the next day after catheter placement, of which 6/8 had documented normal RBx before CM. Of these patients, three were found to have total colonic dysmotility (one improved with ongoing medical management, and two responded poorly to medical therapy and were offered surgery), and the other three patients had normal CM (one improved with medical management, one received appendicostomy, and one lost to follow up) (Figure 2). Seventeen patients received a colonic manometry study on the same day of catheter placement. Their treatment courses are shown in Figure 3.

4 | DISCUSSION

In the present study, we describe the CM findings and the treatment outcomes of postsurgical HSCR patients with persistent defecation problems. In our study cohort, we observed that colonic dysmotility is common in patients with ongoing fecal retention with or without fecal incontinence. We demonstrate variable colonic manometry findings in our patient cohort. Our findings support that medical management should first be optimized before consideration of colonic manometry and surgical interventions. We identified one patient with colonic hypermotility who subsequently had improvement in fecal soiling with the addition of loperamide.

The pooled prevalence of long-term fecal incontinence and constipation in postsurgical HSCR patients is 20% and 14%, respectively.[3] Persistent

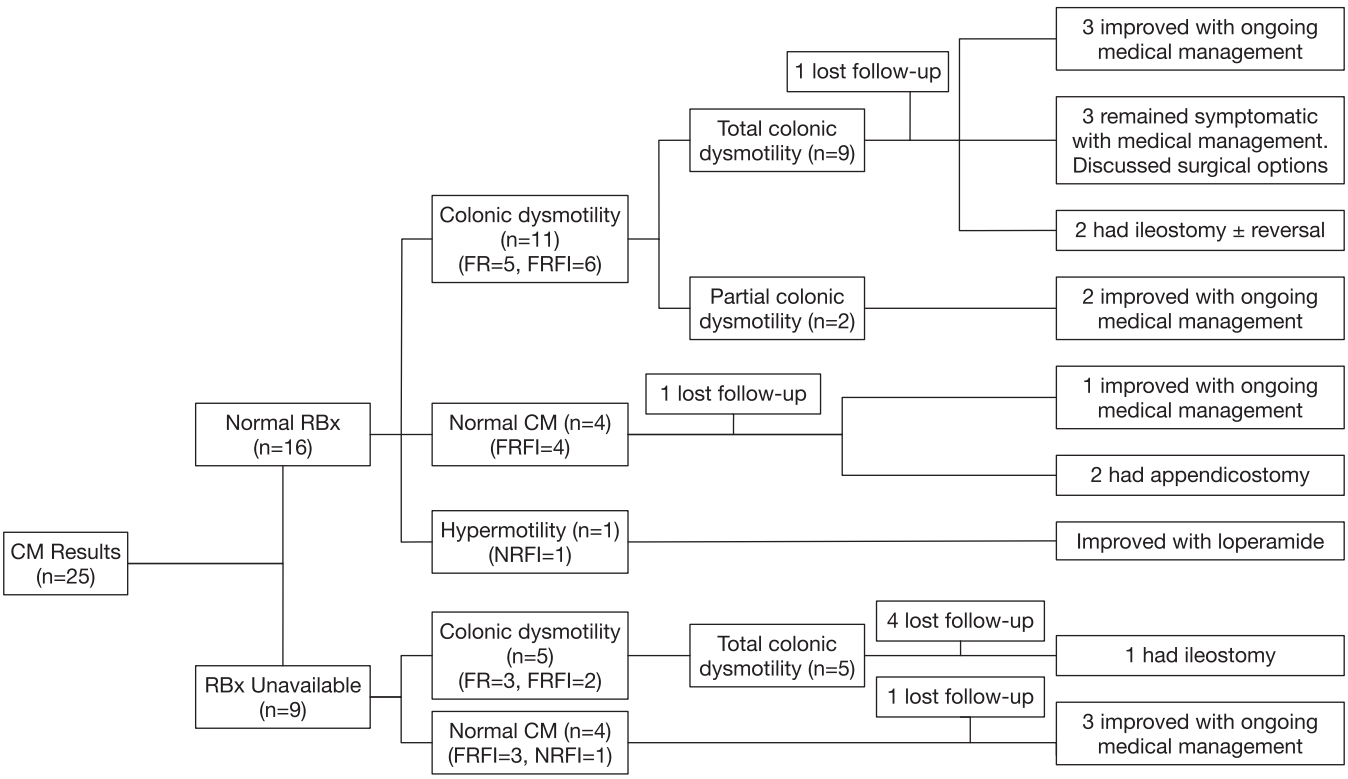

FIGURE 1 Patient colonic manometry results and treatment outcomes. CM, colonic manometry; FR, fecal retention; FRFI, fecal retention with fecal incontinence; NRFI, non-retentive fecal incontinence; RBx, rectal biopsies.

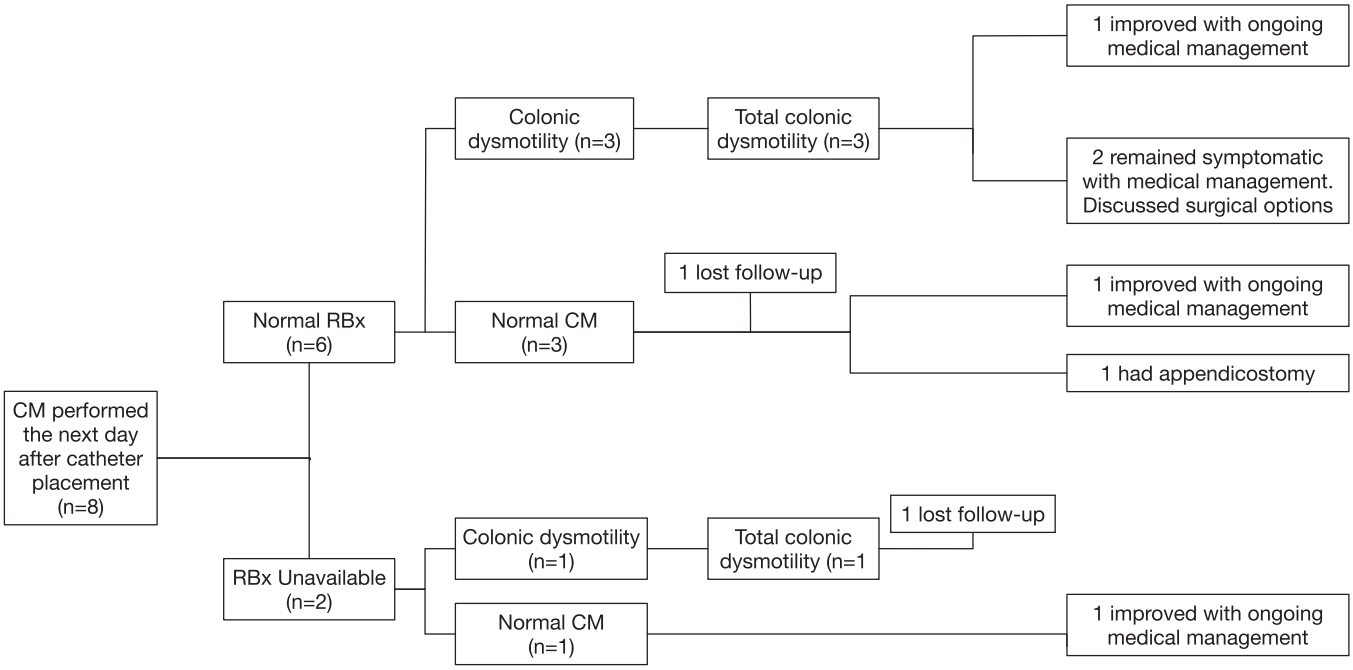

FIGURE 2 The colonic manometry results and treatment outcomes in patients who had CM performed the next day after catheter placement. CM, colonic manometry; RBx, rectal biopsies.

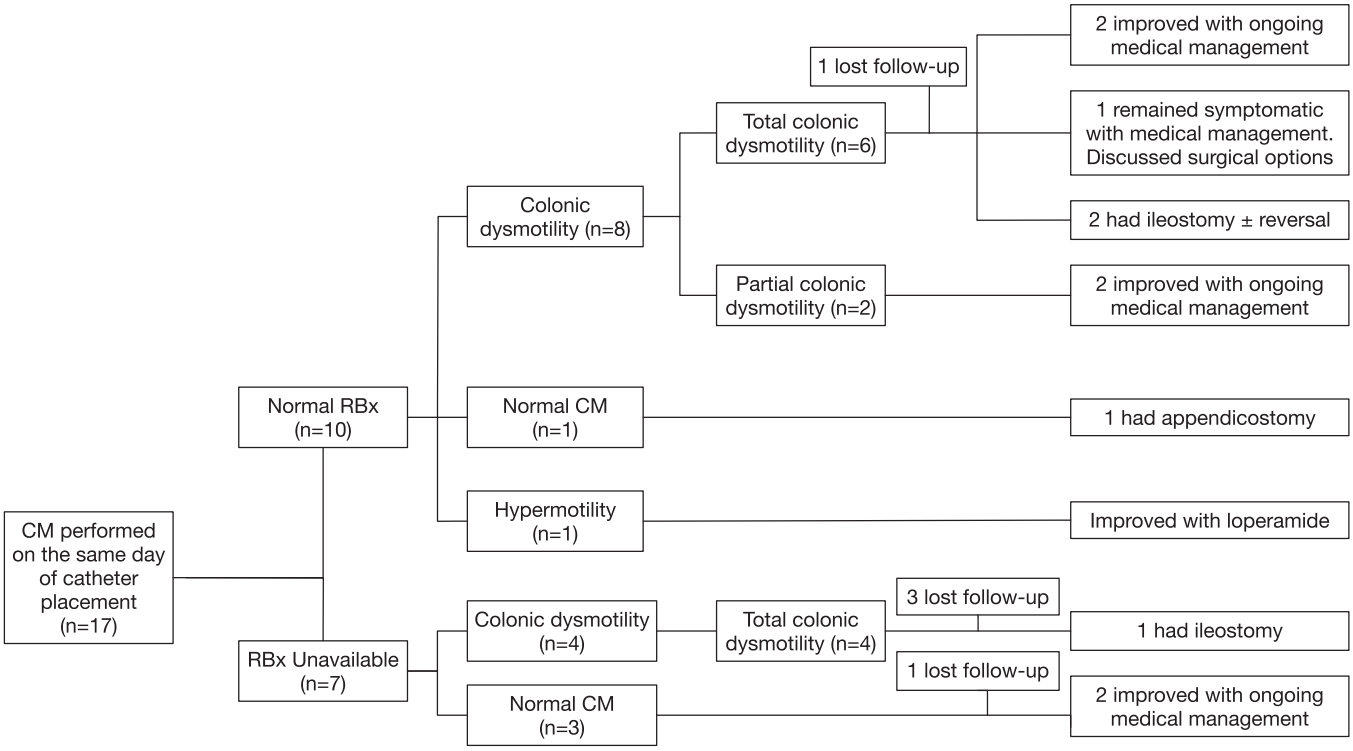

FIGURE 3 The colonic manometry results and treatment outcomes in patients who had CM performed on the same day of catheter placement. CM, colonic manometry; RBx, rectal biopsies.

obstructive symptoms can result from mechanical obstruction, residual or acquired aganglionosis and anorectal or colonic dysfunction.[13,14] And persistent soiling can be due to abnormal sensation, loss of sphincter function, fecal impaction, and hypermotility.[4,15] When evaluating postsurgical HSCR patients with obstructive symptoms, a contrast enema, a rectal examination under anesthesia, and a rectal

biopsy should be performed to assess for mechanical or histopathological etiologies. Surgical repair of the mechanical or histopathological abnormalities should be the first-line therapy for these patients.[14] For the cohort of patients with ongoing defecatory issues with no mechanical or histopathologic abnormalities or those where these issues have been addressed and defecatory issues persist, CM has been sought to aid in further management decisions. Previous studies have described several different motility patterns on CM in these patients.[16] Patterns observed include segmental or total colonic dysmotility, colonic hypermotility, uninhibited normal contractions extending to the neorectum, and normal colonic motility with preserved rectal dampening of contraction.[5,17,18] We observed similar variable patterns in our study.

Previous reports have described using the patterns observed on CM to guide management decisions for HSCR patients with persistent defecatory dysfunction after pull-through surgery. In the cohort of patients described by Di Lorenzo et al., patients with colonic dysmotility identified on CM underwent surgical resection of the abnormal colon with improved constipation in all patients.[5] Martin et al. also described the use of diverting ileostomy in two postsurgical HSCR patients with total colonic dysmotility with a return of normal CM of the diverted colon 4 to 6 months post-surgery.[19] Langer et al. recommend colonic resection for segmental dysmotility and bowel management, stoma, or antegrade colonic enema (ACE) procedure for generalized dysmotility.[14] However, it's unclear what the outcomes are in patients with identified dysmotility who were managed medically. In our cohort, nearly 70% of patients with normal RBx were found to have colonic dysmotility. Interestingly, we observed that a finding of colonic dysmotility did not implicate patient response to medical management. Among the patients with dysmotility, including those with both partial and total colonic dysmotility, 45% responded to an escalation of medical therapy by reinforcing compliance, modifying or optimizing types and dosage of laxatives, and/or adding rectal therapy and did not need surgical intervention. It is important to note that 17 out of 25 patients had same-day manometry studies. The colonic dysmotility could have normalized the following day and thus may explain why such a high percentage of patients responded to an escalation of medical therapy. We further examined the subgroup of patients with CM performed the day after catheter placement. Nearly 50% (3/6) of patients with normal RBx were found to have colonic dysmotility. Amongst the patients with dysmotility, one responded to ongoing medical management and two patients with ongoing symptoms despite medical therapy were recommended to have surgery. These results indicate CM is helpful in identifying existing colonic dysfunction that could contribute to symptoms. CM findings can be used in conjunction with the patient's clinical history and response to medical therapy to make surgical decisions in the appropriate clinical setting.

In subjects without colon resection, a normal CM is defined as an increase in motility after a meal and the occurrence of spontaneous, meal-induced or bisacodyl-induced HAPC propagating to the rectosigmoid junction.[10] These contractions do not reach the rectum in the majority of the cases.[20] Thus, it is hard to define “normal motility” in postsurgical patients when an intact rectosigmoid junction is not preserved. We report a normal CM in these patients when appropriate contractions are observed throughout the colon to the rectosigmoid junction or neorectum, whereas Di Lorenzo et al. and Jacobs et al. further grouped these patients into two categories: HAPCs migrating from the proximal colon through neorectum to the anal sphincter and normal CM where rectal dampening of contraction is noted respectively.[5,18] Eight patients in our cohort were found to have normal colonic motility on CM. Di Lorenzo et al. reported a good response to medical and behavior therapy in patients with normal CM, which is similar to our cohort.[5] In our study, we observed that while most patients with normal colonic motility improved with optimizing medical management, 25% eventually required surgical intervention (ACE procedure) due to poor tolerance of oral therapy or poor quality of life. This highlights the importance of using CM findings in conjunction with clinical and radiographic data to determine optimal management.

In our cohort, one patient was found to have colonic hypermotility on CM. There is a paucity of defined criteria for colonic hypermotility. Younger children tend to have more HAPCs during fasting and after-meal than older children.[21] In our center, we defined colonic hypermotility as the presence of three or more HAPCs traveling throughout the colon within the protocol fasting period. Kaul et al. first described the increased frequency of HAPCs in postsurgical HSCR patients compared to children with functional constipation (control group). They defined colonic hyperactivity as ≥0.11 HAPCs/min, which is two standard deviations above the control group.[17] Jacobs et al. also reported increased HAPCs per hour during fasting and postprandial period in postsurgical HSCR patients who presented with fecal incontinence compared to those with constipation.[18] In our cohort, we had one patient with NRFI who was diagnosed with colonic hypermotility that subsequently improved with the addition of

loperamide treatment. Despite different definitions, increased colonic motility should be considered in postsurgical HSCR patients with NRFI, as they might benefit from antidiarrheal therapy.

Our study has several limitations. This is a single-center retrospective study with a small patient cohort. More than half of the patients were referred to us for motility evaluation from other institutions. As such, data regarding diagnostic workup and treatment courses before CM were not always available, and 28% of patients in our cohort were lost to follow-up following the CM study. Seventeen patients in our cohort underwent CM study on the same day as catheter placement per institutional protocol at the time of the study. Abnormal studies were not repeated the following day, and thus the effect of anesthesia cannot be assessed. In addition, the management algorithms and the threshold for referral for manometry evaluation likely varied between institutions and providers, which could alter the treatment choices after CM.

In summary, abnormal colonic motility can occur in postsurgical HSCR patients with persistent defecation problems. After mechanical and histopathological abnormalities are ruled out, CM may help to understand the pathophysiology of their symptoms by assessing the motor function of the remaining colon in select patients. We observed variable colonic motility findings in our patient cohort in alignment with previous studies. Colonic manometry was helpful in identifying existing colonic dysfunction in children with PT-HSCR who presented with persistent defecation problems. Our findings support that medical management should first be optimized before consideration of colonic manometry and surgical interventions.[22] CM findings should be used in conjunction with the patient's clinical history and response to medical therapy to make surgical decisions in the appropriate clinical setting. CM may assist in patients' medical decision-making where hypermotility is identified during the study. Moving forward, a multi-center collaborative effort is necessary to delineate the role of CM in surgical decision-making in this patient population.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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