

ORIGINAL ARTICLE

Gastroenterology

Current practice in the care of children with functional constipation: What is the hold up?

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Abstract

Objectives: For children with intractable functional constipation (FC), there are no evidence-based guidelines for subsequent evaluation and treatment. Our objective was to assess the practice patterns of a large, international cohort of pediatric gastroenterologists.

Methods: We administered a survey to physicians who attended the 2nd World Congress of Pediatric Neurogastroenterology and Motility held in Columbus, Ohio (USA) in September 2023. The survey included 29 questions on diagnostic testing, nonpharmacological and pharmacological treatment, and surgical options for children with intractable FC.

Results: Ninety physicians from 18 countries completed the survey. For children with intractable FC, anorectal manometry was the most commonly used diagnostic test. North American responders were more likely than Europeans to use stimulant laxatives (97% vs. 77%, $p = 0.032$), prosecretory medications (69% vs. 8%, $p < 0.001$), and antegrade continence enemas (ACE; 83% vs. 46%, $p = 0.009$) for management. Europeans were more likely than North Americans to require colonic transit testing before surgery (85% vs. 30%, $p < 0.001$). We found major differences in management practices between Americans and the rest of the world, including use of prosecretory drugs (73% vs. 7%, $p < 0.001$), anal botulinum toxin injections (81% vs. 58%, $p = 0.018$), ACE (81% vs. 58% $p = 0.018$), diverting ileostomies (56% vs. 26%, $p = 0.006$), and colonic resections (42% vs. 16%, $p = 0.012$). No differences were found when respondents were compared by years of experience.

Conclusions: Practice patterns in the evaluation and treatment of children with intractable FC differ widely among pediatric gastroenterologists from around the world. A clinical guideline regarding diagnostic testing and surgical decision-making is needed.

KEYWORDS

anorectal manometry, antegrade continence enemas, colonic manometry, intractable constipation

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1 | INTRODUCTION

Functional constipation (FC) is common in children worldwide, with a global pooled prevalence of 9.5%.¹ After 6–12 months, 40% of patients with FC referred to a pediatric gastroenterologist are still symptomatic and 20% continue to struggle after 10 years of treatment.² These children are considered to have *intractable* FC and their treatment is challenging.²

In 2014, the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) jointly published an evidence-based guideline with recommendations to standardize the assessment and treatment of children with FC. However, the guideline did not clearly recommend when surgery should be considered. In 2016, Koppen et al. published the results of a survey assessing management practices of pediatric surgeons and gastroenterologists for children with intractable FC.³ They noted that the approach toward children with intractable FC differed considerably, likely because of a lack of guidelines.

To date, there are still no guidelines providing recommendations on diagnostic testing before surgical treatment. Recently, several studies on novel pharmacological options for children with FC and the utilization of manometry testing to guide surgical treatment have been published.^{4–7} The aim of this study was to evaluate whether there have been changes in the diagnostic and surgical approaches of children with intractable FC by physicians over recent years and to determine if discrepancies in approach exist based on geographic region or years of experience.

2 | METHODS

We conducted a cross-sectional study involving a survey distributed to physicians attending the 2nd World Congress of Pediatric Neurogastroenterology and Motility, held in Columbus, Ohio (USA) in September 2023. The Nationwide Children's Hospital Institutional Review Board approved the study protocol (STUDY00003585). The survey consisted of 29 multiple-choice questions covering demographics, diagnostic testing, utilization of nonpharmacological and pharmacological treatments, and surgical interventions for children with intractable FC (Supplement A). Building upon the survey by Koppen et al., we incorporated the latest treatment modalities and introduced inquiries regarding the utilization and perspective of rectal medications. The survey included the same four questions as Koppen et al.'s survey, presenting theoretical cases of children with intractable FC. Participants were asked to choose a surgical treatment based on anorectal

What is Known

- For children with intractable functional constipation (FC), there are no evidence-based guidelines for subsequent evaluation and treatment.
- The diagnostic and therapeutic approach toward children with intractable FC differs considerably, even among physicians with interest and expertise in the fields of pediatric gastroenterology and pediatric surgery.

What is New

- The persisting diversity in approaches emphasizes the complex nature of managing children with intractable FC.
- The use of anorectal and colonic manometry to guide surgical decision making is increasing.
- A clinical guideline regarding diagnostic testing and surgical decision-making for children with intractable FC is needed.

manometry (ARM) and colonic manometry (CM) results. Comparison of results was conducted using Fisher's exact test. p -values < 0.05 were considered statistically significant. Statistical analyses were conducted with SPSS for Windows, version 28.0.0.0 (SPSS, Inc).

3 | RESULTS

The survey was sent to 197 physicians working in pediatric gastroenterology or pediatric surgery and was completed by 90 physicians (46% response rate) from 18 different countries (USA [59], Australia [3], Brazil [3], Canada [3], The Netherlands [3], Thailand [3], United Kingdom [3], Italy [2], Mexico [2], Austria [1], Belgium [1], Denmark [1], France [1], Indonesia [1], Israel [1], Kuwait [1], New Zealand [1], Poland [1]). Eighty-nine worked in pediatric gastroenterology (73 faculty, 13 fellows, three residents), and one worked in pediatric surgery (faculty). The experience of these physicians was reported as follows: 0–5 years (26%), 5–10 years (16%), 10–15 years (22%), and >15 years (37%).

3.1 | Diagnostic workup

Answers to the questions related to the diagnostic approach to children with intractable FC are shown in Table 1. Respondents usually or always used the following tests in the evaluation of children with intractable FC: digital rectal examination (50%),

TABLE 1 Diagnostic tools and frequency of use: *n* (%).

	Always	Usually	Sometimes	Rarely	Never	Not available	Missing
Digital rectal examination	21 (23)	24 (27)	21 (23)	22 (24)	2 (2)	-	0 (0)
Abdominal X-ray (plain)	11 (12)	19 (21)	36 (40)	22 (24)	2 (2)	0 (0)	0 (0)
CTT (marker study)	8 (9)	15 (17)	31 (34)	21 (23)	9 (10)	4 (4)	2 (2)
CTT (scintigraphy)	3 (3)	2 (2)	8 (9)	20 (22)	37 (41)	18 (20)	2 (2)
Anorectal manometry	21 (23)	31 (34)	22 (24)	5 (6)	7 (8)	3 (3)	1 (1)
Colonic manometry	5 (6)	14 (16)	25 (28)	23 (26)	9 (10)	13 (14)	1 (1)
Contrast enema	10 (11)	20 (22)	38 (42)	16 (18)	6 (7)	0 (0)	0 (0)
Defecography	0 (0)	1 (1)	12 (13)	25 (28)	34 (38)	17 (19)	1 (1)
Transabdominal ultrasound	2 (2)	4 (4)	5 (6)	12 (13)	59 (66)	7 (8)	1 (1)
Transrectal ultrasound	0 (0)	0 (0)	3 (3)	10 (11)	63 (70)	13 (14)	1 (1)

Note: Total number of respondents: 90. Abbreviations: CTT, colonic transit testing.

abdominal X-ray (33%), contrast enema (33%), and colonic transit testing (CTT) with radiopaque markers (26%). ARM was usually or always used by 57% and CM by 22%. Ultrasonography had the lowest utilization among respondents.

Of the 79 respondents using ARM, 95% utilized it to rule out Hirschsprung disease, 84% to diagnose anal achalasia, 86% to detect pelvic floor dyssynergia, 58% to assess sphincter integrity, and 37% to guide pelvic floor surgery decision-making. Of the 67 respondents using CM, 56 answered the question for what reasons they used it: 91% to guide surgical decision-making, 70% to differentiate an underlying organic disease from a functional disorder, 69% to assess disease severity, and 65% to differentiate neuropathic from myopathic dysmotility.

3.2 | Nonpharmacological and pharmacological treatment

Table 2 summarizes the treatment approaches of the respondents toward children with FC. Most commonly used nonpharmacological interventions were a toilet program (92%), a reward system (80%), referral to psychology (74%), a bowel diary (71%), pelvic floor physical therapy (69%), and biofeedback (64%). Of the 58 respondents using biofeedback, 95% considered it when ARM shows dyssynergia, 62% when behavior modification and laxative medication fail, and 38% in children with hypertensive anal sphincter at ARM.

Osmotic laxatives (97%), stimulant laxatives (93%), and enemas (73%) were the most commonly used pharmacological treatments. Approximately 50% of the respondents used serotonergic (e.g., prucalopride) or prosecretory (e.g., linaclotide or lubiprostone) medications.

Nearly all (91%) respondents prescribed rectal medications (suppositories, enemas, or transanal

irrigation) to be used as needed and 70% prescribed daily rectal medications on a regular basis. However, only 27% of respondents estimated that >50% of their patients would be able to use rectal medications as needed and only 10% estimated that >50% would be able to use these daily. According to 66% of the respondents, rectal medications would be more widely used if patient and/or parent acceptance was not a factor.

3.3 | Surgical treatment

Among respondents, the most commonly used surgical treatments for children with intractable FC were antegrade continence enemas (ACE; 73%), anal botulinum toxin injections (73%), and diverting ileostomies (45%). Colonic resection (33%), colostomy (28%), anal dilatation (18%) and sacral nerve stimulation (16%) were also used. However, 10% of the respondents never considered surgical treatment for children with FC. Out of the 73% who have used ACE in the past 5 years, 73% considered it for children with evidence of colonic dysmotility, 65% for children who refuse rectal medications, and 50% for severe symptoms regardless of the diagnostic testing. Out of the 73% who utilized anal botulinum toxin injections, 92% considered it for anal achalasia, 77% for high resting anal pressure, 74% for evidence of outlet dysfunction, and 53% to treat pelvic floor dyssynergia.

3.4 | Differences by region and experience

Although the numbers of respondents between regions are different, when respondents from North America ($n = 64$) and Europe ($n = 13$), the two largest groups,

TABLE 2 Nonpharmacological and pharmacological treatments and frequency of use: *n* (%).

Nonpharmacological treatment	<i>n</i> (%)	Pharmacological treatment	<i>n</i> (%)
Toilet program	82 (92)	Osmotic laxatives (e.g., PEG 3350/lactulose)	87 (97)
Reward system	72 (80)	Stimulant laxatives (e.g., bisacodyl/senna)	84 (93)
Referral to psychology (e.g., behavioral therapy)	67 (74)	Enemas	66 (73)
Bowel diary	64 (71)	Prosecretory drugs (e.g., linaclotide/lubiprostone)	45 (50)
Pelvic floor physical therapy	62 (69)	Serotonergic drugs (e.g., prucalopride)	41 (46)
Biofeedback	58 (64)	Fiber	24 (27)
Physical activity advice	48 (53)	Lubricants (e.g., mineral oil)	19 (21)
Transanal irrigation	41 (46)		
Additional fiber beyond daily requirement	19 (21)		
Additional fluid beyond daily requirement	16 (18)		
Pre-/pro-/synbiotics	9 (10)		
Alternative medicine (e.g., acupuncture)	8 (9)		
Posterior tibial nerve stimulation ^a	1 (1)		

Note: Total number of respondents: 90. Abbreviation: PEG, polyethylene glycol.

^aThis answer was not provided on the survey, it was added by a responder.

were compared, several differences were found (Supplement B). Respondents from Europe used CTT more often than those from North America (62% vs. 17%, $p=0.003$). When asked about mandatory testing before surgical treatment, Europeans were more likely to require CTT (85% vs. 30%, $p<0.001$), ultrasonography (31% vs. 0%, $p<0.001$), rectal suction biopsy (69% vs. 38%, $p=0.035$), and full thickness rectal biopsy (62% vs. 20%, $p=0.005$). Respondents from North America used stimulant laxatives (97% vs. 77%, $p=0.032$) and prosecretory drugs (69% vs. 8%, $p<0.001$) more often. ACE was more frequently used by respondents from North America (83% vs. 46%, $p=0.009$), while other surgical treatments were similar between the two groups.

Given the differences between the healthcare systems in the United States and the rest of the world, these two groups were compared (Supplement C). In the diagnostic work-up of children with intractable FC, respondents from the United States were more likely to use CM (27% vs. 10%, $p=0.049$) and less likely to use CTT (19% vs. 39%, $p=0.048$), ultrasonography (2% vs. 16%, $p=0.018$), and scintigraphy (2% vs. 13%, $p=0.044$) compared to respondents from the rest of the world. Respondents from the United States were more likely to consider CM (75% vs. 42%, $p=0.002$) and a contrast enema (80% vs. 52%, $p=0.006$) mandatory tests before moving to surgery, while respondents of the rest of the world were more likely to consider CTT (81% vs. 25%, $p<0.001$), ultrasonography (26% vs. 0%, $p<0.001$), and full thickness rectal biopsy (55% vs. 22%, $p=0.002$) mandatory testing. In

the pharmacological management of FC, respondents from the United States used stimulant laxatives (98% vs. 84%, $p=0.017$), enemas (81% vs. 58%, $p=0.018$), prosecretory drugs (73% vs. 7%, $p<0.001$), and lubricants (29% vs. 7%, $p=0.014$) more often. In addition, American respondents felt that parental resistance is more of a barrier in prescribing rectal treatment (81% vs. 61%, $p=0.038$) and that this treatment should be more widely used if patient nor parent acceptance was a factor (77% vs. 49%, $p=0.008$). Anal botulinum toxin injections (81% vs. 58%, $p=0.018$), ACE (81% vs. 58% $p=0.018$), diverting ileostomies (56% vs. 26%, $p=0.006$), colonic resections (42% vs. 16%, $p=0.012$), and colostomies (36% vs. 13%, $p=0.022$) were all more frequently used by respondents from the United States.

When answers from respondents with 0–10 years of experience were compared with respondents with >10 years of experience, no differences were found in diagnostic and therapeutic approach toward children with FC (Supplement D).

3.5 | Case-based questions

Respondents who reported using both ARM and CM ($n=54$), were given the opportunity to answer the questions about four theoretical cases (Table 3). For each case, respondents were asked to choose their initial therapy for a child with intractable FC with specific manometry findings. The first case described a child with a normal ARM and normal CM. Half of the

TABLE 3 Answers to four case-based questions by 54 respondents using anorectal manometry and colonic manometry: *n* (%).

	Case 1 ARM: normal, CM: normal	Case 2 ARM: absent RAIR, ^a CM: normal	Case 3 ARM: high RP, CM: normal	Case 4 ARM: normal, CM: abnormal ^b
Anal botulinum toxin injections	19 (35)	46 (85)	48 (89)	1 (2)
Anal Sphincter myectomy	0 (0)	0 (0)	0 (0)	0 (0)
Anal dilation	0 (0)	0 (0)	0 (0)	0 (0)
Antegrade continence enemas	26 (48)	4 (7)	1 (2)	32 (59)
Sacral nerve stimulation	0 (0)	0 (0)	0 (0)	0 (0)
Diverting ileostomy	0 (0)	0 (0)	0 (0)	4 (7)
(Segmental) colonic resection	0 (0)	0 (0)	0 (0)	5 (9)
Colostomy	0 (0)	0 (0)	0 (0)	1 (2)
Ileo-anal anastomosis	0 (0)	0 (0)	0 (0)	0 (0)
Other	3 (6)	2 (4)	3 (6)	7 (13)
Not applicable/I don't know	4 (7)	1 (2)	2 (4)	4 (7)
Missing	2 (4)	1 (2)	0 (0)	0 (0)

Note: Respondents were asked to select their preferred initial treatment based on the case. Abbreviations: ARM, anorectal manometry; CM, colonic manometry; RAIR, rectoanal inhibitory reflex; RP, resting pressure.

^aNormal rectal biopsy.

^bAbsence of high-amplitude propagating contractions in the left colon.

respondents (48%) chose an ACE as initial surgical treatment, while 35% preferred anal botulinum toxin injections. The second case had an absent rectoanal inhibitory reflex on ARM with a normal rectal biopsy and had a normal CM. The third case had high anal canal resting pressure on ARM and a normal CM. In both cases, the majority of respondents chose anal botulinum toxin injections (respectively 85% and 89%). The fourth case was a child who had a normal ARM, but an abnormal CM showing absence of high amplitude propagating contractions in the left colon. For this case, ACE was selected most often (59%) followed by (segmental) colonic resection (9%).

4 | DISCUSSION

The results of our survey demonstrate significant differences in the diagnostic and therapeutic approaches among pediatric gastroenterologists worldwide when addressing children with intractable FC. Despite years of research and the accumulation of new insights since the study conducted by Koppen et al. in 2016, the persisting heterogeneity in approaches emphasizes the complex nature of managing children with intractable FC.

From a diagnostic standpoint, ARM was the most commonly used diagnostic test in the evaluation of children with intractable FC, with 57% of respondents always or usually using this test. This is a substantial

increase compared to the 20% previously described by Koppen et al. who used ARM routinely.³ The increase in utilization could suggest the more widespread adoption of ARM testing. A survey distributed by NASPGHAN in 2022 showed that there has been a substantial increase in the number of centers offering pediatric neurogastroenterology and motility services in North America in recent years.⁸ Another interesting finding is that the routine use of abdominal X-rays in the care of children with intractable FC has decreased over time. Among our respondents, 33% used abdominal X-rays either usually or always in the evaluation of children with FC. In the survey of Koppen et al., 54% used abdominal X-rays routinely.³ This can be considered a positive development, as multiple studies have concluded that there is insufficient evidence to support the use of plain radiography in diagnosing FC.^{2,9,10}

When asked about management, respondents usually used a toilet program, a reward system, and a referral to a psychologist as nonpharmacological treatments, in agreement with guidelines.^{2,11} Although there are controversial results on the benefit of biofeedback and pelvic floor physical therapy for children with FC, the majority reported to use these options.^{2,12–14} Additional fiber and fluid beyond the daily requirement was recommended by one-fifth of respondents. This is surprising, since there is evidence that neither improves constipation.^{2,15,16} It might be possible that these respondents did not notice the

addition of “beyond the daily requirement” when answering these questions. Since multiple studies have shown that most children do not meet the daily requirements for fiber and fluid intake, most children should be recommended to increase their consumption of fibers and fluid.^{17,18}

The pharmacological treatments used usually consisted of osmotic laxatives, stimulant laxatives, and enemas, in compliance with the ESPGHAN/NASPGHAN recommendations.² This is consistent with the findings of Koppen et al.³ However, a major recent development is the usage of serotonergic or prosecretory agents. Despite the fact that the serotonergic agent, prucalopride, has been tested in a phase 3, randomized, controlled trial in pediatric patients with FC demonstrating no superiority over placebo, 46% of our respondents reported usage compared to 1% in the study of Koppen et al.^{3,19} It is likely that prucalopride is being prescribed off-label to patients who have failed conventional pharmacological treatments or that a substantial amount of respondents are participating in a clinical trial, as at present, an ongoing phase 3 multicenter clinical trial is investigating the efficacy of prucalopride in children with FC.²⁰ The increase in usage of prosecretory agents to 50% from 11% can be due to the results of a recent clinical trial showing that patients of 6–17 years of age with FC who received linaclotide experienced a greater improvement in stooling per week than patients who received placebo.⁷ Based on this study, the FDA has approved linaclotide to treat FC in children 6–17 years of age. However, in other countries, linaclotide neither has been tested or approved for children yet. This most likely explains the difference in usage between the United States and the rest of the world (73% vs. 7%, $p < 0.001$) as well as difference in usage between North America and Europe (69% vs. 8%, $p < 0.001$).

When asked about the practice of prescribing rectal medications, it was striking that nearly all respondents prescribed these, many on a daily basis, while at the same time they estimated that the majority of their patients will not be able to use them on a daily or as needed basis, mostly because of patient or parental resistance. While parental resistance was more of a barrier in prescribing rectal medications in the opinion of American respondents when compared to respondents from the rest of the world, the frequency of prescribing such medications was comparable in both groups. Given that 66% of our respondents believed that rectal medications should see broader utilization if patient and/or parent acceptance were not a consideration, exploring ways to enhance acceptance becomes an intriguing objective for future research.

In our case of intractable FC with normal manometry testing, half of our respondents chose ACE while one-third chose anal botulinum toxin injections. In the study of Koppen et al. only 7% chose anal botulinum

toxin injections.³ At the time, several studies had already shown that the use of botulinum toxin injections into the internal anal sphincter can lead to improved defecation patterns in constipated patients with outlet dysfunction.^{21–23} Recently, one study demonstrated that children with normal sphincter dynamics based on ARM studies had similar responses to botulinum toxin injections into the internal anal sphincter as children with abnormal sphincter dynamics, potentially explaining the increase of choice for anal botulinum toxin injections among our respondents.²⁴

In cases 2 and 3 about a child with intractable FC with abnormal anal sphincter function or pressure on ARM, the majority of the respondents chose anal botulinum toxin injections as initial surgical treatment (85% and 89%, respectively). Already in the study of Koppen et al., the majority of respondents opted for intra-anal botulinum toxin injections (46% and 64%, respectively).³ However, since then, even more studies have demonstrated the effectiveness of botulinum toxin injections for children with FC.^{25,26} None of our respondents chose anal dilation or anal sphincter myectomy, the two common other answers for these case-based questions in the study by Koppen et al.³ This is encouraging, since these procedures, unlike botulinum toxin injections, can have permanent effects with the potential risk of fecal incontinence. Complications related to botulinum toxin injections into the anal sphincter are rare and appear to be self-limited,^{25,27} supporting even more to opt for internal anal sphincter botulinum injections as first-choice treatment.

While 91% of respondents utilized CM to guide surgical decision-making, the responses to the fourth case-based question showed significant variability. This observation aligns with Koppen et al.'s findings, emphasizing the necessity for future studies to assess the value of CM in guiding surgical decisions for the management of pediatric patients with intractable FC.³ One study that systematically evaluated the role of CM in guiding initial therapy and predicting need for surgery, demonstrated that individuals with an abnormal CM are more likely to require surgery.⁴ The study recommended performing CM when all medical therapies have proved ineffective and surgical intervention is under consideration. It is suggested that for those with a normal CM, ACE or transanal irrigation should be initiated, while in those with substantial manometric abnormalities, a diverting ostomy proximal to the region of dysfunction can be considered.⁵ Given that CM is advocated as the gold standard for assessing colonic neuromuscular function in children with intractable FC and is becoming more widely available globally, the development of clinical guidelines regarding surgical treatment options for children with intractable FC based on CM results becomes imperative.

Some limitations need to be taken into account when interpreting our results. This survey was

administered to a large group of pediatric specialists who attended the World Congress of Pediatric Neurogastroenterology and Motility, potentially introducing selection bias. We suspect that our respondents represent pediatric specialists who regularly care for children with intractable FC. One limitation relevant to our comparisons between regions is our predominance of respondents from North America. However, in the comparison between North America and Europe, the European respondents are from countries that do represent the larger tertiary care centers where children with intractable FC are usually evaluated and treated. Unfortunately, given the fewer responses from other continents, we did not feel it would be appropriate to evaluate for differences between other regions. A future study with more focus on geographical representation could be considered.

In conclusion, practice patterns differ widely among pediatric gastroenterologists worldwide in the management of children with intractable FC. Clinical guidelines regarding diagnostic testing and surgical decision-making for children with intractable FC is needed, especially since the use of ARM and CM to guide surgical-decision making is increasing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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