Functional defecation disorders in children
Associated comorbidity and advances in management
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SURGICAL DECISION-MAKING IN THE MANAGEMENT OF CHILDREN WITH INTRACTABLE FUNCTIONAL CONSTIPATION

What are we doing and are we doing it right?

I.J.N. Koppen, S. Kuizenga-Wessel, P.L. Lu, M.A. Benninga, C. Di Lorenzo, V.A. Lane, M.A. Levitt, R.J. Wood, D. Yacob

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ABSTRACT

Background
Children with intractable functional constipation (FC) may eventually require surgery, often guided by motility testing. However, there are no evidence-based guidelines for the surgical management of intractable FC in children.

Aim
To assess the diagnostic and surgical approach of pediatric surgeons and pediatric gastroenterologists towards children with intractable FC.

Methods
A survey was administered to physicians attending an international conference held simultaneously in Columbus (Ohio, USA) and Nijmegen (the Netherlands). The survey included 4 questions based on cases with anorectal and colonic manometry results.

Results
74 physicians completed the questionnaire. Anorectal manometry was used by 70%; 52% of them would consider anal sphincter botulinum toxin injections for anal achalasia and 21% would use this to treat dyssynergia. Colonic manometry was used by 38%; 57% of them reported to use this to guide surgical decision-making. The surgical approach varied considerably among responders answering the case questions based on motility test results; the most commonly chosen treatments were antegrade continence enemas and anal botulinum injections.

Conclusion
Surgical decision-making for children with intractable FC differs among physicians. There is a need for clinical guidelines regarding the role of anorectal and colonic manometry in surgical decision-making in children with intractable FC.
INTRODUCTION

Childhood constipation is a common problem in pediatric healthcare. It is characterized by infrequent bowel movements (b3 per week), hard and/or large stools, painful defecation and it is often accompanied by abdominal pain. Approximately 75–90% of children with chronic constipation seen by a pediatric gastroenterologist suffer from fecal incontinence, caused by the leakage of soft stools around a large and hard fecal mass accumulated in the rectum. In most cases, an organic cause for constipation is not found and affected children are diagnosed with functional constipation (FC). The reported prevalence of FC among children ranges from 0.7% to 29.6% with a mean female/male ratio of 2.1. A subset of patients with FC experience severe and long-lasting symptoms that respond poorly to conventional behavioral, dietary and pharmacological management, these children are considered to have intractable FC. In tertiary care centers, 50% of children referred to a pediatric gastroenterologist are still symptomatic after 5 years, and 20% still struggle with symptoms after 10 years. Symptoms can even persist into adulthood despite intensive laxative treatment. Persistent FC symptoms negatively affect quality of life in multiple ways (e.g., social interactions, school achievements, self-esteem) and account for significant associated healthcare costs.

Children with intractable FC may eventually require alternative therapeutic interventions including surgery. The most recent joint guidelines from the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) state that colonic manometry may be indicated in children with intractable FC because evaluation of colonic motility may help guide surgical management. This recommendation is mostly based on expert opinion and relies on the results of few retrospective studies that reported that normal colonic manometry predicts a successful response to antegrade continence enemas (ACE) and abnormal manometry was associated with successful surgical interventions. However, there are no guidelines that clearly recommend which surgical treatment should be performed based on manometry results. Without such guidelines, it is likely that the surgical approach towards children with severe FC differs among centers and among individual surgeons. Surgery is usually considered a treatment of last resort and is generally performed with a step-up approach, beginning with the least invasive treatment and progressing to more invasive interventions only if needed. The choice of what type of surgery to perform is usually determined based on a comprehensive evaluation of the colonic and anorectal anatomy.
and physiology, although this evaluation may differ among centers. Generally, medical care for children with intractable FC is a joint venture, where both pediatric gastroenterology and pediatric surgery are involved. Intraspincteric botulinum toxin injections and ACE are considered to be less invasive surgical strategies and are commonly employed in the treatment of intractable FC\textsuperscript{10}. More invasive surgical interventions include colonic resection and diversion of the colon via an ostomy, either an ileostomy or a colostomy\textsuperscript{10,11}. In their recent systematic review, Siminas et al. concluded that the evidence to support surgical interventions for intractable FC in children is mostly of low quality\textsuperscript{10}. Siminas et al. provided a comprehensive overview of the literature and showed that there is no consensus regarding the diagnostic-work up that is required for surgical decision-making\textsuperscript{10}. Therefore, the aim of this study was to assess the diagnostic and therapeutic approach of pediatric surgeons and pediatric gastroenterologists towards pediatric patients with intractable FC.

**MATERIAL & METHODS**

We developed a survey and administered it to physicians attending the 2015 Pediatric Colorectal, Motility and Pelvic Reconstruction Conference, held simultaneously in Columbus, Ohio (USA) and Nijmegen (the Netherlands) in November 2015. In total, 265 physicians from different specialties (pediatric and adult surgery, gastroenterology, urology and radiology) attended the conference at both locations; 147 in Columbus and 118 in Nijmegen. In Columbus, the attendees included 71 physicians from pediatric surgery (36 faculty members, 35 fellows/residents) and 29 from pediatric gastroenterology (21 faculty members, 8 fellows/residents). In Nijmegen, the distribution of physicians according to their specialties was unknown (89 faculty members, 29 fellows/residents). The questionnaire involved 19 multiple choice questions on work experience, routine diagnostic workup in children with FC, use of nonpharmacological and pharmacological treatment for FC and use of surgery in intractable FC (Appendix). In addition, the survey included multiple choice questions on 4 theoretical cases of children with intractable FC; anorectal and colonic manometry results were given and responders were asked which surgical treatment they would choose. For each question, responders had the option to an open answer in case the multiple choice answers were insufficient. For this study, only surveys answered by physicians from pediatric surgery and pediatric gastroenterology were included. The results are represented as percentages of the total number of responders unless otherwise specified.
RESULTS

The survey was completed by 74 physicians working in pediatric surgery or gastroenterology in 16 different countries: 55 (74%) worked in pediatric surgery (29 faculty members, 23 fellows, 3 residents) and 19 (26%) in pediatric gastroenterology (14 faculty members, 5 fellows). The experience of these physicians was reported as follows: 0–5 years (43%), 5–10 years (25%), 10–15 years (8%) and >15 years (25%). Results are presented separately for pediatric surgery (surgery) and pediatric gastroenterology (GI) in all tables.

Diagnostic work-up

Table 1 summarizes the data from the questions related to the diagnostic approach. Most responders utilized digital rectal examination in the evaluation of children with FC. Plain abdominal X-rays were obtained by the majority of physicians. In total, 62/69 of responders who used plain abdominal X-rays did not use a scoring system (e.g., Barr, Leech or Blethyn (12)) to score the radiographs. Colonic transit studies were used infrequently, whereas the use of contrast enemas was reported to be more common.

Anorectal manometry

Anorectal manometry was used routinely by 15 responders while 37 responders used it occasionally (Table 1). These responders (n=52) utilized this test to rule out Hirschsprung’s disease (65%; 83% in GI and 56% in surgery), to diagnose anal achalasia (58%; 78% in GI and 47% in surgery), to detect dyssynergia (56%; 67% in GI and 50% in surgery), to assess sphincter integrity (50%; 50% in GI and 50% in surgery) and for guidance prior to possible pelvic floor surgery (27%; 22% in GI and 29% in surgery). Out of the 52 physicians utilizing anorectal manometry, 52% (67% in GI and 44% in surgery) would consider anal sphincter botulinum toxin injections for anal achalasia and 21% (28% in GI and 18% in surgery) would use it to treat dyssynergia.

Colonic manometry

Colonic manometry was used routinely by 8 and occasionally by 20 responders (Table 1). Among these responders (n = 28), 61% (91% in GI and 41% in surgery) employed it to differentiate neuropathic from myopathic dysmotility, 57% (64% in GI and 53% in surgery) to guide surgical decision-making, 54% (55% in GI and 53% in surgery) to differentiate an underlying organic disease from a functional disorder and 36% (73% in GI and 12% in surgery) to assess disease severity.
### Table 1  Diagnostic tools and frequency of use: n (%). Total number of responders: 74

<table>
<thead>
<tr>
<th>Tool</th>
<th>Routinely</th>
<th>Occasionally</th>
<th>Never</th>
<th>Not available</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital rectal examination</td>
<td>50 (68)</td>
<td>21 (28)</td>
<td>1 (1)</td>
<td>-</td>
<td>2 (3)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>12 (63)</td>
<td>7 (37)</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Transrectal ultrasound</td>
<td>38 (69)</td>
<td>14 (26)</td>
<td>1 (2)</td>
<td>-</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Abdominal X-ray (plain)</td>
<td>40 (54)</td>
<td>29 (39)</td>
<td>5 (7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GI surgery</td>
<td>5 (26)</td>
<td>12 (63)</td>
<td>2 (11)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Transabdominal ultrasound</td>
<td>35 (64)</td>
<td>17 (31)</td>
<td>3 (6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CTT (radiopaque markers)</td>
<td>10 (14)</td>
<td>36 (49)</td>
<td>19 (26)</td>
<td>5 (7)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>1 (5)</td>
<td>16 (84)</td>
<td>2 (11)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CTT (scintigraphy)</td>
<td>2 (3)</td>
<td>7 (10)</td>
<td>37 (50)</td>
<td>20 (27)</td>
<td>8 (11)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>0</td>
<td>2 (11)</td>
<td>13 (68)</td>
<td>4 (21)</td>
<td>0</td>
</tr>
<tr>
<td>Anorectal manometry</td>
<td>15 (20)</td>
<td>37 (50)</td>
<td>11 (15)</td>
<td>10 (14)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>4 (21)</td>
<td>14 (74)</td>
<td>0</td>
<td>1 (5)</td>
<td>0</td>
</tr>
<tr>
<td>Colonic manometry</td>
<td>8 (11)</td>
<td>20 (27)</td>
<td>22 (30)</td>
<td>18 (24)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>3 (16)</td>
<td>8 (42)</td>
<td>4 (21)</td>
<td>4 (21)</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>5 (9)</td>
<td>12 (22)</td>
<td>18 (33)</td>
<td>14 (26)</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Contrast enema</td>
<td>26 (35)</td>
<td>38 (51)</td>
<td>7 (10)</td>
<td>1 (1)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>2 (11)</td>
<td>15 (79)</td>
<td>2 (11)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>24 (44)</td>
<td>23 (42)</td>
<td>5 (9)</td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Defecography</td>
<td>5 (7)</td>
<td>28 (38)</td>
<td>24 (32)</td>
<td>12 (16)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>0</td>
<td>5 (26)</td>
<td>10 (53)</td>
<td>4 (21)</td>
<td>0</td>
</tr>
<tr>
<td>Transabdominal ultrasound</td>
<td>5 (9)</td>
<td>23 (42)</td>
<td>14 (26)</td>
<td>8 (15)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>0</td>
<td>10 (14)</td>
<td>37 (50)</td>
<td>10 (14)</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Defecography</td>
<td>0</td>
<td>10 (14)</td>
<td>37 (50)</td>
<td>10 (14)</td>
<td>7 (10)</td>
</tr>
<tr>
<td>GI surgery</td>
<td>0</td>
<td>1 (5)</td>
<td>13 (68)</td>
<td>3 (16)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>surgery</td>
<td>0</td>
<td>9 (16)</td>
<td>24 (44)</td>
<td>7 (13)</td>
<td>15 (27)</td>
</tr>
</tbody>
</table>

CTT, colonic transit time; GI, gastroenterology. The boldface entries represent the total number of responders who preferred a certain treatment for the specific case.
### Table 2  Non-pharmacological and pharmacological treatments and frequency of use: n (%). Total number of responders: 74

| Non-pharmacological treatment          | n (%)
|----------------------------------------|--------
| Bowel diary                            | 52 (70)
| GI                                     | 13 (68) |
| Surgery                                | 39 (71) |
| Reward system                          | 27 (37) |
| GI                                     | 14 (74) |
| Surgery                                | 13 (24) |
| Toilet program                         | 56 (76) |
| GI                                     | 19 (100) |
| Surgery                                | 37 (67) |
| Dietary advice                         | 61 (82) |
| GI                                     | 11 (58) |
| Surgery                                | 50 (91) |
| Referral psychology                    | 31 (42) |
| GI                                     | 13 (68) |
| Surgery                                | 18 (33) |
| Biofeedback                            | 23 (32) |
| GI                                     | 4 (21)  |
| Surgery                                | 20 (36) |
| Pre-, pro-, synbiotics                 | 13 (18) |
| GI                                     | 1 (5)   |
| Surgery                                | 12 (22) |
| Transanal irrigation (e.g. Peristeen)  | 30 (41) |
| GI                                     | 4 (21)  |
| Surgery                                | 26 (47) |
| Transcutaneous electrical nerve stimulation | 1 (1) |
| GI                                     | 1 (5)   |
| Surgery                                | 0       |

| Pharmacological treatment              | n (%)
|----------------------------------------|--------
| Osmotic laxatives (e.g. PEG)           | 65 (88) |
| GI                                     | 19 (100) |
| Surgery                                | 46 (84) |
| Stimulant laxatives (e.g. bisacodyl)   | 57 (77) |
| GI                                     | 18 (95) |
| Surgery                                | 39 (71) |
| Lubricants                             | 25 (34) |
| GI                                     | 8 (42)  |
| Surgery                                | 17 (31) |
| Serotonergic drugs (e.g. prucalopride) | 1 (1)   |
| GI                                     | 1 (5)   |
| Surgery                                | 0       |
| Prosecretory drugs (e.g. lubiprostone) | 8 (11)  |
| GI                                     | 7 (37)  |
| Surgery                                | 1 (2)   |
| Enemas                                 | 53 (72) |
| GI                                     | 12 (63) |
| Surgery                                | 41 (75) |

GI: gastroenterology; PEG: polyethylene glycol. The boldface entries represent the total number of responders who preferred a certain treatment for the specific case.  
1 1 missing value for all non-pharmacological answers (surgery).  
2 4 missing values for all pharmacological answers (all surgery).  
3 This answer was not provided on the questionnaire, it was added by a responder.
Table 3  Answers to case-based questions by 28 responders using AMAN and CM (11 from GI, 17 from surgery); n (%). Responders were asked to select their preferred initial treatment based on the case.

<table>
<thead>
<tr>
<th>CASE 1</th>
<th>CASE 2</th>
<th>CASE 3</th>
<th>CASE 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal botulinum toxin injections</td>
<td>2 (7)</td>
<td>13 (46)</td>
<td>18 (64)</td>
</tr>
<tr>
<td>GI</td>
<td>1 (9)</td>
<td>7 (64)</td>
<td>9 (82)</td>
</tr>
<tr>
<td>surgery</td>
<td>1 (6)</td>
<td>6 (35)</td>
<td>9 (53)</td>
</tr>
<tr>
<td>Anal sphincter myectomy</td>
<td>0</td>
<td>1 (4)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>0</td>
<td>1 (6)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Anal dilation</td>
<td>2 (7)</td>
<td>1 (4)</td>
<td>3 (11)</td>
</tr>
<tr>
<td>GI</td>
<td>1 (9)</td>
<td>1 (9)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>surgery</td>
<td>1 (6)</td>
<td>0</td>
<td>2 (12)</td>
</tr>
<tr>
<td>Antegrade continence enemas</td>
<td>17 (61)</td>
<td>4 (14)</td>
<td>0</td>
</tr>
<tr>
<td>GI</td>
<td>9 (82)</td>
<td>2 (18)</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>8 (47)</td>
<td>2 (12)</td>
<td>0</td>
</tr>
<tr>
<td>Sacral nerve stimulation</td>
<td>1 (4)</td>
<td>2 (7)</td>
<td>0</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>1 (6)</td>
<td>2 (12)</td>
<td>0</td>
</tr>
<tr>
<td>Diverting ileostomy</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>1 (6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(Segmental) colonic resection</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Colostomy</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ileo-anal anastomosis</td>
<td>0</td>
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</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I don’t know</td>
<td>3 (11)</td>
<td>4 (14)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>surgery</td>
<td>3 (18)</td>
<td>4 (24)</td>
<td>2 (12)</td>
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<tr>
<td>Missing</td>
<td>2 (7)</td>
<td>3 (11)</td>
<td>4 (14)</td>
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<tr>
<td>GI</td>
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<td>1 (9)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>surgery</td>
<td>2 (12)</td>
<td>2 (12)</td>
<td>3 (18)</td>
</tr>
</tbody>
</table>
Surgical decision-making

Non-pharmacological and pharmacological treatment

The non-pharmacological and pharmacological approach towards children with FC among responders is shown in Table 2. Most commonly employed non-pharmacological interventions included a bowel diary (70%), a toilet program (76%) and dietary advice (82%). Osmotic laxatives (88%), stimulant laxatives (77%) and enemas (72%) were the most commonly used pharmacological treatments.

Case-based questions

The case-based questions (Attachment 1) resulted in a variety of approaches among the 28 responders (16 faculty, 11 fellows and 1 resident) who reported using both anorectal manometry and colonic manometry. For each case, responders were asked to choose their initial therapeutic option for a child with intractable FC and specific manometry findings. The first case was a child who had normal colonic and anorectal manometry. The second case had an absent rectoanal inhibitory reflex (RAIR) on anorectal manometry in the presence of normal rectal biopsy results and a normal colonic manometry. The third case had a high anal canal resting pressure on anorectal manometry and a normal colonic manometry. The fourth case described a child who had a normal anorectal manometry and an abnormal colonic manometry showing absence of high amplitude propagating contractions in the colon distal to the transverse colon. The answers to these case-based questions are shown in Table 3. There was a considerable variety in the answers to each question. In the first case, the majority (61%) chose ACE. In the second and third case, most responders preferred anal botulinum toxin injections (respectively 46% and 64%). In the fourth case, ACE was selected most often (43%), although this question was also left unanswered by a considerable amount of responders (32%).

\[\text{AMAN: anorectal manometry; CM: colonic manometry; GI: gastroenterology; RAIR: rectoanal inhibitory reflex; RP: resting pressure. The boldface entries represent the total number of responders who preferred a certain treatment for the specific case.}^1\text{Normal rectal biopsy.}^2\text{Absence of high-amplitude propagating contractions in the left colon.}\]
DISCUSSION

Our survey results show that the diagnostic and therapeutic approach towards children with intractable FC differs considerably even among physicians with interest and expertise in the fields of pediatric surgery and pediatric gastroenterology. This emphasizes the need for more studies on this topic and the development of evidence-based guidelines for children who respond poorly to optimal pharmacological management. Furthermore, it is necessary to assess why the available guidelines are poorly adhered to, a problem that has been described before\textsuperscript{13,14}, and how to improve guideline adherence.

Diagnostic work-up

It has been reported that many physicians are reluctant to perform a digital rectal examination in children\textsuperscript{15}. However, a digital rectal examination can provide valuable information on the presence of a rectal fecal mass (one of the six diagnostic Rome III criteria for FC) and be helpful in the assessment of anorectal sensation and sphincter tone\textsuperscript{16-18}. Among the responders of this survey, the vast majority of physicians performed digital rectal examination routinely or occasionally. This result may be related to the fact that the majority of responders worked in pediatric surgery, where patients are often referred for suspected anatomical problems and with severe long-lasting symptoms, which makes it essential to rule out organic causes of constipation. An interesting finding was that the vast majority of responders (93%) used abdominal X-rays either routinely or occasionally. Multiple studies have shown that there is insufficient evidence to support the use of plain abdominal X-rays as a diagnostic tool in children with functional defecation disorders\textsuperscript{1,12,19-22}. There is no clear association between clinical symptoms of constipation and fecal loading as determined by abdominal X-ray\textsuperscript{22,23}. Moreover, the sensitivity and specificity of the different scoring systems used to evaluate fecal loading based on abdominal X-rays (Barr, Leech, Blethyn) are unsatisfactory, with low inter- and intraobserver reliability\textsuperscript{22}. The finding that none of these scoring systems was used by the responders is likely a consequence of the low reliability of this diagnostic tool in clinical practice. However, if this modality is to have clinical value, a novel reliable and objective method for evaluation is needed, since the lack of a standardized method to assess these radiologic images may lead to inaccuracy and substantial differences in interpretation. In this survey, contrast enemas were commonly used in the diagnostic work-up of children with FC. Although contrast enemas are not a valid alternative to rectal biopsy or anorectal manometry to exclude or diagnose Hirschsprung’s disease\textsuperscript{1}, they can
be helpful to identify anatomical abnormalities in children with constipation (e.g., megarectum or megasigmoid). It has been postulated that development of these abnormalities may make FC particularly difficult to treat and that patients with significant dilation of the distal colon may benefit from surgery24.

Non-pharmacological and pharmacological treatment
The non-pharmacological treatments used by our responders usually consisted of a toilet program (behavioral intervention) and a bowel diary, in compliance with the ESPGHAN NASPGHAN recommendations1. Although use of a reward system has been shown to improve therapy compliance, this measure was only used by a minority of responders25. Furthermore, pre-, pro- or synbiotics were used as a non-pharmacological intervention by one-fifth of responders. This is surprising, since there is insufficient evidence to support this practice26. The pharmacological management of FC mainly consisted of osmotic laxatives, stimulant laxatives and enemas, in agreement with the ESPGHAN-NASPGHAN guidelines1. The regular use of enemas is not recommended in these guidelines, but these guidelines were developed for FC in general, and do not address intractable FC specifically. Prosecretory agents (e.g., lubiprostone and linacotide) were also reported to be used by a substantial amount of responders despite the fact that neither has been tested and approved for use in children yet. It could be that a large proportion of these children with severe symptoms participate in clinical trials, as lubiprostone is currently being investigated in a multicenter randomized controlled trial, or it could be that these medications are being prescribed off-label to patients who have failed conventional pharmacological management.

Anorectal manometry and surgery
Anorectal manometry is most commonly used to differentiate between FC and Hirschsprung’s disease, but it is also useful in detecting anal achalasia and dyssynergia27. In cases of intractable FC with abnormal anal sphincter pressure or function (after Hirschsprung’s disease had been ruled out), most responding physicians opted for intra-anal botulinum toxin injections. Several studies, both retrospective and prospective, have shown that injection of botulinum toxin into the internal anal sphincter can be an effective treatment for these patients28-31. Although less commonly described, there have also been reports of successful outcomes after injection of botulinum toxin into the external anal sphincter32,33. Botulinum toxin causes a temporary chemical paralysis of smooth and striated muscle fibers by blocking the release of acetylcholine from neurons. The effect of botulinum toxin usually lasts for 3 to 6 months and, if necessary, repeated
injections can be administered after the initial effect wears off. Other common answers to this case-based question included anal dilation and anal sphincter myectomy. Unlike botulinum toxin injections, these procedures usually have a permanent effect. The major risk of these two procedures is that the basal pressure of the anal sphincter can be weakened to the point of causing fecal incontinence. Therefore, in cases of intractable FC with high sphincter pressure or a non-relaxing sphincter, after ruling out Hirschsprung’s disease, it seems sensible to opt for internal anal sphincter botulinum injections. Subsequent symptomatic improvement would confirm that the anal sphincter dysfunction is contributing to the problem. There have been reports of symptom improvement after botulinum toxin injections lasting longer than 6 months\textsuperscript{28,31}, which suggests that the pathophysiology of the nonrelaxing anal sphincter is complex and that breaking the vicious cycle of painful defecation and withholding behavior could be an important additional benefit of this treatment.

**Colonic manometry and surgery**

The responses to our case-based questions highlight the complexity of therapeutic decision making and the broad variance in interpretation of colonic manometry results with regards to the surgical management of intractable FC. Colonic manometry is used to differentiate between myopathic and neuropathic motility disorders and to identify dysmotile colonic segments amenable for surgery\textsuperscript{27,34,35}. Dysmotility of the colon is usually defined by the absence of high amplitude propagating contractions (HAPCs) and in severe cases this abnormality can be used to justify a total or partial colonic resection and/or diversion of the dysmotile colonic segment by means of an ostomy\textsuperscript{11,36-38}. However, it has also been shown that findings of dysmotility are potentially reversible and that motility as measured by colonic manometry can improve after decompression of the colon\textsuperscript{36-38}. An improvement in colonic motility has also been demonstrated to occur in patients after using ACE\textsuperscript{39}. This suggests that colonic dysmotility may not only contribute to the severity of the constipation but may also be a consequence of long-standing constipation, possibly because of fecal stasis and colonic distension which in turn may lead to suboptimal motor function. Although total or partial colonic resection may lead to symptom improvement\textsuperscript{40}, it has never been investigated whether this is necessary or if temporary decompression through diversion alone might be equally effective. Furthermore, with the development of high-resolution colonic manometry, there is an increasing body of evidence suggesting that colonic dysmotility is more complex than just an evaluation of the presence and morphology of HAPCs and that there are other motor abnormalities that may
be of clinical importance. Future studies are needed to further evaluate the utility of high-resolution colonic manometry in surgical decision-making in the management of children with intractable FC.

Limitations
This survey was intended to acquire more information on the current diagnostic and therapeutic approach towards children with FC, especially with regard to manometry and surgical interventions, and was therefore administered to physicians from both pediatric surgery and pediatric gastroenterology. Since the questionnaire was administered during a conference, it was kept brief to increase the response rate. Although we tried to be comprehensive, it would have been interesting to obtain more detailed information (e.g., regarding the specific dietary advice given or the maximum dosage of medication used). In addition, it would have been interesting to explore why physicians chose certain answers. To assess this, an interview-based study would be necessary. Furthermore, this survey was administered to physicians attending a conference on colorectal diseases and disorders, likely representing physicians with a special interest in this topic. It is unknown whether this sample is a fair representation of pediatric surgeons and gastroenterologists in general. However, since manometry and surgery in the management of intractable FC are usually performed in specialized centers and by specialized physicians, we assume that this is a reliable representation of the population that we wanted to study and in fact may even underestimate the inconsistencies that exist in clinical practice. Additionally, our study is at risk for selection bias. We could not specify the specialty of the physicians attending the conference in Nijmegen (the Netherlands), therefore we were unable to provide an exact response rate. However, if all physicians attending the conference in Nijmegen were from pediatric surgery or gastroenterology, the response rate for this survey would have been 74/(100 + 118) = 31%. If the distribution of physicians in Nijmegen was similar to that in Columbus (68% of attending physicians from pediatric surgery/gastroenterology), the response rate would have been 74/(100 + (0.68*118)) = 41%. Finally, the group of responders consisted of staff members and fellows. It is possible that the fellows were less experienced in the field of motility studies, which may have influenced the results. However, for each question responders could indicate if they did not know the answer or if the question was not applicable to them. Therefore, we assume that responders who answered the questions indeed gave answers that reflect their true personal approach.
CONCLUSION

Surgical decision-making for children with intractable FC differs among physicians worldwide. Anorectal and colonic manometry are often used to guide surgical decision making. However, since there are no guidelines for surgical management of FC in children, the application and interpretation of manometry vary among physicians, resulting in different surgical approaches. This survey demonstrates the need for clinical guidelines regarding the role of anorectal and colonic manometry in surgical decision-making in children with intractable FC.

Acknowledgements

The authors sincerely thank all responders who participated in this survey.
REFERENCES


**Attachment 1 Questionnaire 2015**

**Pediatric Colorectal, Motility and Pelvic Reconstruction Conference**

**QUESTIONS ON WORK EXPERIENCE**

1) I work in:
- [ ] pediatric surgery
- [ ] pediatric gastroenterology
- [ ] pediatric urology
- [ ] adult surgery
- [ ] adult gastroenterology
- [ ] adult urology

2) I work as a
- [ ] faculty member
- [ ] fellow
- [ ] resident
- [ ] nurse
- [ ] other: _________

3) Years of experience:
- [ ] 0-5
- [ ] 5-10
- [ ] 10-15
- [ ] >15

4) I work in:
- [ ] the Netherlands
- [ ] other country: __________________________

5) I am involved in the treatment of pediatric patients with (please check all that apply):
- [ ] constipation
- [ ] fecal incontinence
- [ ] I don’t treat children

6) I define functional constipation in children as
- [ ] defecation freq < 3x/week
- [ ] defecation freq < 3x/week and hard/painful stools
- [ ] Rome II criteria
- [ ] Rome III criteria
- [ ] other: _______________________________

7) In the diagnostic workup of children with functional constipation I use the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Routinely</th>
<th>Occasionally</th>
<th>Never</th>
<th>Not available to me</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital rectal examination</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal X-ray (plain)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Colonic transit time (marker study)</td>
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<tr>
<td>Colonic transit time (scintigraphy)</td>
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</tr>
<tr>
<td>Anorectal manometry</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Colonic manometry</td>
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<tr>
<td>Contrast enema</td>
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<td></td>
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</tr>
<tr>
<td>Defecography</td>
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<td></td>
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<tr>
<td>Transabdominal</td>
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<td></td>
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<tr>
<td>ultrasound of rectum</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Transrectal ultrasound</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other: please specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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8) If I use plain abdominal X-rays to assess fecal load in children with constipation
   I use this scoring system (check all that apply):
   - Barr
   - Leech
   - Blethyn
   - I use plain abdominal X-rays, but I don’t use a scoring system
   - other________________________
   - not applicable/I don’t know

9) I use anorectal manometry in children with constipation for the following reason(s)
   (check all that apply):
   - to rule out Hirschsprung’s disease
   - to diagnose Hirschsprung’s disease
   - to detect dyssynergia
   - to diagnose anal achalasia
   - to assess anal sphincter integrity
   - to guide pelvic floor surgery decision-making
   - I never use anorectal manometry
   - other________________________
   - not applicable/I don’t know

10) I use colonic manometry in children with constipation for the following reason(s)
    (check all that apply):
    - to assess disease severity
    - to differentiate functional from organic forms of constipation
    - to guide surgical decision-making
    - to differentiate between neurogenic/myogenic dysmotility
    - I never use colonic manometry
    - other________________________
    - not applicable/I don’t know

11) In the non-pharmacological treatment of children with functional constipation I use the following
    (check all that apply):
    - bowel diary
    - reward system
    - toilet program
    - diet advice
    - referral to psychology (e.g. behavioral therapy)
    - biofeedback
    - pre-/pro-/synbiotics
    - transanal irrigation (e.g. Peristeen)
    - not applicable/I don’t know
    - other________________________

12) In the pharmacological treatment of children with functional constipation I routinely use the
    following (check all that apply):
    - osmotic laxatives (e.g. PEG/lactulose)
    - stimulant laxatives (e.g. bisacodyl/senna)
    - lubricants (e.g. mineral oil)
    - serotonergic drugs (e.g. prucalopride)
    - prosecretory drugs (e.g. linaclotide/lubiprostone)
    - enemas
    - other________________________
    - not applicable/I don’t know
13) I usually try the following treatments, before I consider surgery in children with functional constipation (check all that apply):

- osmotic laxatives
- stimulant laxatives
- novel laxatives (serotonergic/prosecretory agents)
- systemic intensive cleanouts (transanal irrigation/regular enemas)
- I never consider surgery for functional constipation
- other: ____________________________
- not applicable/I don't know

14) In the surgical treatment of children with functional constipation over the past 5 years I used the following (check all that apply):

- anal botox injections
- anal sphincter myectomy
- anal dilatation
- antegrade continence enemas (ACE)
- sacral neurostimulation
- diverting ileostomy
- (segmental) colonic resection
- colostomy
- ileo-anal anastomosis
- other: ____________________________
- not applicable/I don't know

15) I consider anal botox injections in children with functional constipation and (check all that apply):

- severe symptoms, regardless of diagnostic assessment
- young age (<4 years), regardless of diagnostic assessment
- signs of outlet obstruction (e.g. markers in rectum during CTT)
- dyssynergia at anorectal manometry
- high resting pressure at anorectal manometry
- anal achalasia
- other: ____________________________
- not applicable/I don't know

17) For a child with functional constipation refractory to medications who has a normal anorectal and a normal colonic manometry, my initial surgical treatment would be (check one option):

- anal botox injections
- anal sphincter myectomy
- anal dilatation
- antegrade continence enemas (ACE)
- sacral neurostimulation
- diverting ileostomy
- (segmental) colonic resection
- colostomy
- ileo-anal anastomosis
- other: ____________________________
- not applicable/I don't know
Surgical decision-making

18) For a child with functional constipation refractory to medications who has an absent recto-anal inhibitory reflex on anorectal manometry but with normal rectal biopsy and a normal colonic manometry, my initial treatment would be (check one option):

- anal botox injections
- antegrade continence enemas (ACE)
- diverting ileostomy
- colostomy
- other: ___________________________
- anal sphincter myectomy
- anal dilatation
- sacral neurostimulation
- (segmental) colonic resection
- ileo-anal anastomosis
- not applicable/I don’t know

19) For a child with functional constipation refractory to medications who has a high anal canal resting pressure on anorectal manometry and a normal colonic manometry, my initial treatment would be (check one option):

- anal botox injections
- anal dilatation
- sacral neurostimulation
- colostomy
- other: ___________________________
- anal sphincter myectomy
- antegrade continence enemas (ACE)
- diverting ileostomy (segmental) colonic resection
- ileo-anal anastomosis
- not applicable/I don’t know

20) For a child with functional constipation refractory to medications who has a normal anorectal manometry and an abnormal colonic manometry showing absence of high amplitude propagating contractions (HAPCs) of the left colon, my initial treatment would be (check one option):

- anal botox injections
- antegrade continence enemas (ACE)
- diverting ileostomy
- colostomy
- other: ___________________________
- anal sphincter myectomy
- anal dilatation
- sacral neurostimulation
- (segmental) colonic resection
- ileo-anal anastomosis
- not applicable/I don’t know

Thank you for participating!